Sodium borohydride mediated one-pot synthesis of secondary amides from primary amides via reductive acetylation

G. Gurunadham, R. Madhusudhan Raju*, Y. Venkateswarlu

Abstract— A one-pot reduction followed by N-acetylation of primary amides to yield secondary amides using NaBH4/Acetic acid has been developed and the corresponding N-acetyl amides are obtained respectable yields.

Key words — Primary amides, NaBH4, 1, 4-Dioxane, Acetic acid, and Secondary amide.

1 INTRODUCTION

The amide function is one of the most fundamental chemical building blocks found in nature. It is essential to sustain life, making up the peptide bonds in proteins such as enzymes, and it is also one of the most prolific moieties in Natural products, functional materials, pharmaceuticals, agrochemicals, and polymers, but also serves as attractive precursors in a variety of organic transformations (Fig-1). Therefore, efficient synthesis of amides is an important topic of modern synthetic chemistry not only in academic research but also in industrial application [1-4].

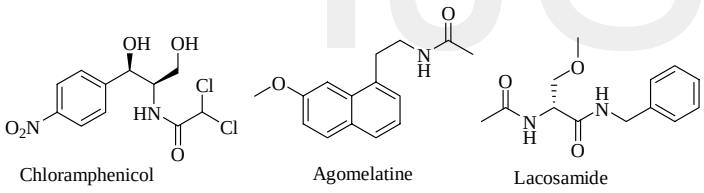


Fig-1: Biologically active amide molecules

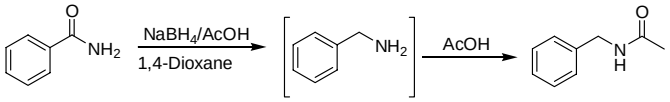
The most popular and common methods for the generation of amides involve the reaction of activated carboxylic acid derivatives, such as chlorides, anhydrides or esters, with amines [5-8]. Alternative methods for the synthesis of amides are the Schmidt reaction [9], Beckmann rearrangement [10,11], aminocarbonylation of haloarenes [12], oxidative amidation of aldehydes with amines [13-17], aminocarbonylation of aryl halides

and alkynes [18-21], direct amide synthesis from alcohols and amines [22-27], direct amidation of alcohols with nitroarenes [28], Umpolung reaction of amines with a halo nitro alkanes [29], cross coupling of formamides with alkyl/aryl halides [30], and amidation of thio acids with azides [31]. All of these methods have their own advantages, nonetheless they suffer from certain demerits, such as stoichiometric amount of amidation reagents, harsh reaction conditions, long reaction times, low selectivity's, limited substrate scopes etc. moreover, some of the catalysts have the difficulties in separation from the reaction mass and recycling, making their environmental profile unfavorable. Therefore, there is a clear need for the synthesis of amides with more efficient, under neutral conditions and without the generation of waste, which is a challenging goal [32]. In the search of more atom economical and cost effective protocols for amide synthesis, metal catalyzed organic transformations have been emerged in the last years as attractive alternatives, offering the possibility to develop previously unavailable routes starting from substrates other than carboxylic acids and their derivatives [33].

Herein we report, the synthesis of secondary amides using sodium borohydride in acetic acid as a reagent. $NaBH_4$ is known in the literature for various organic trans formations such as acyloxyborohydride species reduce indoles, quinolines, isoquinolines, related hetero cycles, imines, enamines, oximes, enamides, and similar functional groups. They reduce amides and nitriles, aryl alcohols and ketones, aldehydes in the presence of ketones, and β-hydroxyketones to 1,3-diols stereo selectively. This reagent is also useful for the *N*-alkylation of primary and secondary amines with aldehydes and ketones in a novel reductive amination process [34].

2. RESULTS AND DISCUSSION

In a typical experiment, primary carboxamides reacted with sodium borohydride ($NaBH_4$) in presence of acetic acid in 1,4-dioxane at reflux to afford the corresponding product *N*-benzylacetamide (2a) in good yield. The reaction was completed within 16 hours (Scheme-1).



Scheme-1

Initially, we have examined the effect of temperatures on reaction rate and the amount of $NaBH_4$ and reagents used in the reaction and the results were summarized in the Table-1. There was no product (Benzyl amine) formation in THF, DMSO at room temperature and at reflux conditions even after 8 and 24 hours. The product formation was observed in presence of reagent at room temperature after 24 hours. It was found that the ideal reaction conditions were at 1, 4-dioxane reflux and using the $NaBH_4$ in 4.0 eq.

G.Gurunadham, R. Madhusudhan Raju and Y. Venkateswarlu*
Departmentof Chemistry, Osmania University, Hyderabad, Telangana State-500007, India.
- Email: garlapati.gb7@gmail.com ,

Table-1: Optimization of Reduction of carbomates to primary amines with $NaBH_4$ and different reagents.

S. No	Condition. (equiv)		Solvent. (vol)	Temp (°C)	Time (h)	Yield (%)
1	$NaBH_4$ (2.3)	Iodine (2.3)	THF 20)	25	8	No conversion
2	$NaBH_4$ (5.0)	$MeSO_3H$ (1.5)	DMSO (10)	105	24	No conversion
3	$NaBH_4$ (4.5)	BF_3-Et_2O (5.0)	THF (10)	40	16	27.0
4	$NaBH_4$ (3.0)	$TiCl_4$ (1.0)	DME (10)	75	16	33.5
5	Vitride (2.5)	CH_3COOH (5.0)	THF (10)	80	24	No conversion
6	$NaBH_4$ (5.0)	CH_3COOH (5.0)	THF (10)	80	24	No conversion
7	$NaBH_4$ (5.0)	CH_3COOH (5.0)	Monoglyme (10)	30	16	40.0
8	$NaBH_4$ (5.0)	CH_3COOH (5.0)	Monoglyme (10)	85	16	60.0
9	$NaBH_4$ (4.0)	CH_3COOH (1.2)	1,4-Dioxane (20)	30	16	45.0
10	$NaBH_4$ (4.0)	CH_3COOH (1.2)	1,4-Dioxane (20)	95	16	82.0

In a similar manner, a comparative study on the role and requirement for reducing reagent has been carried out, and the obtained results are clearly shown in Table-2. The union of sodium borohydride and carboxylic acids is versatile and efficient set of reducing reagents. The reactant for this reaction are also benzamide and $NaBH_4$, AcOH in 1,4-dioxane. From our observation, $NaBH_4$ (6.0eq), AcOH (6.0eq) is adequate for the complete the conversion of benzamide into the required reductiveacetylation product.

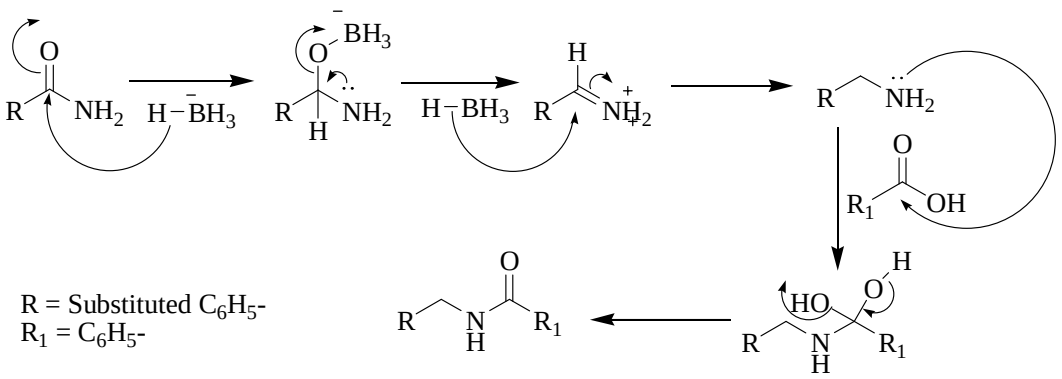
Table-2: Reductive Acetylation of carboximides with $NaBH_4$ in CH_3COOH.

S. No	Reagent (equiv)		Solvent	Temp (°C)	Time (h)	Result/Yields
1	$NaBH_4$ (6.0)	AcOH (6.0)	Toluene	120	16	No conversion
2	$NaBH_4$ (6.0)	AcOH (6.0)	2-Me THF	83	16	No conversion
3	$NaBH_4$ (6.0)	AcOH (6.0)	Ethanol	85	16	No conversion
4	$NaBH_4$ (6.0)	AcOH (6.0)	THF	60	16	No conversion
5	$NaBH_4$ (6.0)	AcOH (6.0)	Acetonitrile	80	16	No conversion
6	$NaBH_4$ (6.0)	AcOH (6.0)	1,4-Dioxane	100	16	75%

Finally, it was decided that the suitable conditions for reductive acetylation is in a solvent and in the presence of an activator or promoter. As shown in Table-3. Aromatic, hetero aromatic and aliphatic amides were reacted very well to afford the corresponding products of amide derivatives in very good yields. In general, the aromatic amides bearing electron donating groups and heteroaromatic compounds are reacting little faster when compared with other amides. In a similar manner, the aliphatic and aromatic amides containing electron withdrawing groups are reacting comparatively little slower in terms of conversion. In general, all the reactions were completed within 21 to 30 hours of reaction period and the obtained yields also 68 to 73%.

3. MECHANISM

The mechanism of the reaction of sodium borohydride with primary amide processed in the first step, H (-) detaches from the BH_4 (-) and adds to the carbonyl carbon. This forms the C-H bond, and breaks the C-O bond, Rapid reduction by the H from the hydride reagent as it adds to the electrophilic C in the iminium system. π electrons from the C=N move to the cationic N neutralizing the charge creating the amine product, this amine react acid to obtained secondary amide.



Scheme-2
Proposed mechanism for secondary amide formation from primary amide, acetic acid using $NaBH_4$

4. EXPERMENTAL SECTIONS

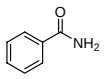
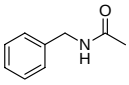
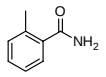
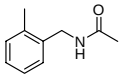
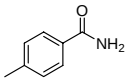
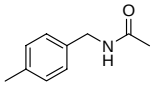
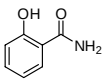
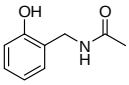
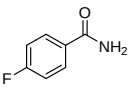
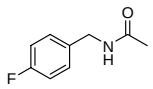
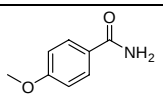
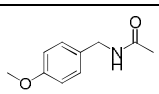
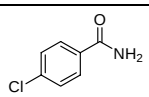
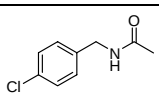
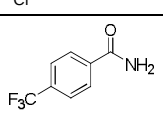
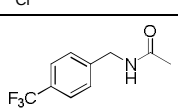
General Methods:

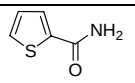
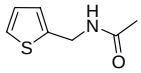
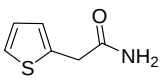
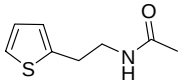
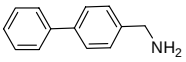
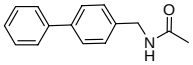
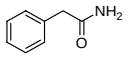
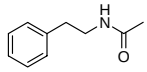
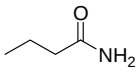
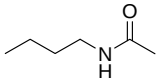
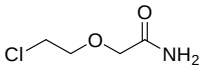
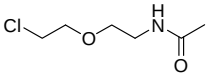
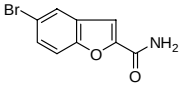
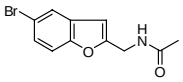
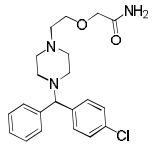
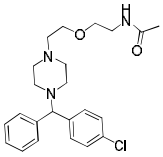
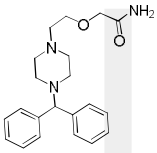
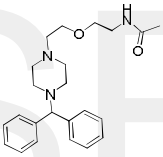
Melting points were recorded on Buchi R-535 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR spectrophotometer using KBr discs. The reactions were monitored by TLC plates Merck Silica Gel 60, F254 and visualization with UV light (254 and 365nm) ^{1}H NMR spectra were recorded on Bruker-400 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded at ionization energy 70 eV on API Q Star pulsar spectrometer using elctrospary ionization.

General procedure:

To a solution of benzamide (1.0 g, 4.6 mmol) in 1,4-dioxane (20 mL, 20 vol) cooled to 5-10 °C, and then added drop wise acetic acid lot-1 (1.67 g, 27.8 mmol), sodium borohydride (1.05 g, 27.8 mmol) with in the period of 30 min, reaction mass allowed 25-30 °C, and warm to 95-100 °C, maintained for 5-6 h. The reaction mixture was cooled 25-30 °C, progress of the reaction was monitored by TLC identified by (benzyl amine) and after added lot-II of acetic acid (2.0 mL, 2 vol) drop wise again warm to 95-100 °C maintained for overnight. Then starting material was disappearing by TLC. After completion of the reaction as indicated by TLC, the solvent was removed from reaction mass under reduced pressure. The residue was extracted with ethyl acetate (10 mL, 10 vol) followed by brine. The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to afford the products, which were purified by column chromatography using silica gel (100-200 mesh) eluted with hexane and ethyl acetate (7:3) to afford the product (Table-3). All the products were identified by their ^{1}H NMR, IR and Mass spectroscopy data.

Table-3: $NaBH_4$ and CH_3COOH catalyzed by synthesis of secondary amides

S.No	Reactant	Product (2a-2q)	Time (h)	Yield (%)
a			21	76
b			23	72
c			21	71
d			23	69
e			24	73
f			25	68
g			24	70
h			22	72

i			23	70
j			24	71
k			25	69
l			24	71
m			27	73
n			26	72
o			29	64
p			30	68
q			30	70

5. SPECTRAL DATA FOR ALL THE COMPOUNDS

N-Benzylacetamide (2a): Solid, mp: 61-63 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34-7.26 (m, 5H), 5.95 (brs, 1H), 4.56 (d, *J* = 4.4 Hz), 2.06 (s, 3H). IR (KBr) (cm^{-1}): 3290, 3082, 2988, 1640, 1551, 1369, 1291, 1078, 741, 695, 616. Mass: m/z = 150 $[(M+H)]^+$, 132 (22), 92 (100), 91 (90).

2-Methyl *N*-benzylacetamide (2b): Solid, mp: 141-143 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24 (m, 4H), 5.51 (brs, 1H), 4.49 (d, *J* = 4.8 Hz, 2H), 2.35 (s, 3H), 2.08 (s, 3H). IR (KBr) (cm^{-1}): 3294, 3063, 2924, 2876, 2815, 1637, 1546, 1457, 1280, 1046, 1000, 747, 715, 600. Mass: m/z =164.06 $[(M+H)]^+$, 100), 143 (15), 105 (25), 102 (90).

4-Methyl *N*-benzylacetamide (2c): Solid, mp: 71-73 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.18-7.13 (q, J_1 = 6.8Hz, J_2 = 6.8 Hz, 4H) 5.25 (brs, 1H), 4.38 (d, *J* = 4.8 Hz, 2H), 2.35 (s, 3H), 1.05 (s, 3H). IR (KBr) (cm^{-1}): 3287, 3077, 2923, 2357, 1639, 1551, 1444, 1370, 1286, 1017, 804, 736, 601, 544. Mass: m/z =163.9 $[(M+H)]^+$, 100), 104 (50), 72 (25).

N-(2-Hydroxybenzyl)acetamide (2d): Solid, mp: 107-108 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.05-7.01 (m, 4H), 4.64 (d, *J* = 4.4Hz, 2H), 2.02 (s, 3H). IR (KBr) (cm^{-1}): 3394, 3187, 2735, 2360, 1676, 1631, 1590, 1426, 1359, 1247, 1138, 846, 748, 644, 600. Mass: m/z =165.9 $[(M+H)]^+$, 35), 137.9 (100), 120.9 (18), 106.9 (40), 91 (10).

N-(4-Fluorobenzyl)acetamide (2e): Solid, mp: 94-96 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.28-7.24 (m, 2H), 7.15 (t, *J* = 19.2Hz, 2H), 5.75 (brs, 1H), 4.82 (d, *J* = 6.4Hz, 2H), 2.05 (s, 3H). IR (KBr) (cm^{-1}): 3288, 3069, 2935, 1642, 1553, 1508, 1371, 1213, 1157, 1091, 1010, 831, 727, 600, 544. Mass: m/z =167.9 $[(M+1)]^+$, 100), 108 (25), 72 (26).

N-(4-Methoxybenzyl)acetamide (2f): Solid, mp: 95-96 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.74 (d, *J* = 4.8 Hz, 2H), 6.72-6.71 (d, *J* = 5.6 Hz, 2H), 6.08 (brs, 1H), 3.88 (s, 3H),
3.58 (d, *J* = 4.8 Hz, 2H), 1.25 (s, 3H). IR (KBr) (cm^{-1}): 3320, 2973, 2935, 2841, 1617, 1547, 1505, 1451, 1306, 1253, 1181, 1148, 1112, 1032, 843, 757. Mass: m/z =179.9 $[(M+H)]^+$100), 120.9 (40), 100 (25).

N-(4-Chlorobenzyl) acetamide (2g): Solid, mp: 105-107 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.72 (d, *J* = 12.4 Hz, 2H), 7.41 (dd, J_1 = 4.4 Hz, J_2 = 4.4Hz, 2H), 6.17 (brs, 1H), 3.50 (t, *J* = 8.4Hz, 2H), 1.25 (s, 3H). IR (KBr) (cm^{-1}):3303, 3065, 2978, 2871, 1635, 1539, 1475, 1300, 1150, 1087, 849, 673. Mass: m/z =184$[(M+H)]^+$100), 139 (15).

N-(4-(Trifluoromethyl) benzyl) acetamide (2h): Solid, mp: 103-105 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.53-7.42 (m, 4H), 5.92 (brs, 1H), 5.18 (d, *J* = 4.2 Hz, 2H), 2.15 (s, 3H). IR (KBr) (cm^{-1}): 3291, 3071, 2929, 1651, 1555, 1440, 1326, 1167, 1125, 1076,

1029, 910, 797. Mass: m/z =184[(M+H)]+100), 195.9 (10), 175.9 (12).

N-((Thiophen-2-yl)methyl)acetamide (2i): Liquid, bp: 145-146 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34 (dd, J_2 = 4.4 Hz, J_2 = 4.4 Hz, 1H), 6.98-6.93 (m, 2H), 5.78 (brs, 1H), 4.52 (d, *J* = 4.8 Hz, 2H), 2.03 (s, 3H). IR (KBr) (cm^{-1}): 3305, 3078, 2931, 1716, 1635, 1545, 1424, 1370, 1283, 1159, 1037, 843, 704. Mass: m/z =156 [(M+H)]+45), 103 (25), 102 (100), 97 (48).

N-(2-(Thiophen-2-yl)ethyl)acetamide (2j): Solid, mp: 50-51 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.174 (d, *J* = 5.6Hz, 1H), 6.95 (t, 3.36, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 5.65 (brs, 1H), 3.53 (q, J_1 = 12.8 Hz, J_2 = 12.8 Hz, 2H), 3.03 (t, *J* = 6.8 Hz, 2H), 1.96 (s, 3H). IR (KBr) (cm^{-1}): 3303, 3053, 2933, 1635, 1540, 1323, 1271, 1083, 760, 701, 590, 471. Mass: m/z =170.2 [(M+ H)]+ 100).

3-Phenyl 2-acetamide (2k):Solid, mp: 183-184 °C, ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 7.6Hz, 2H), 7.52 (d, 8.8Hz, 2H), 7.46-7.28 (m, 5H), 5.75 (brs, 1H), 4.51 (d, *J* = 5.6Hz, 2H), 2.04 (s, 3H). IR (KBr) (cm^{-1}): 3279, 3079, 2934, 2865, 1642, 1553, 1435, 1365, 1297, 845, 703. Mass: m/z = 225 [(M+)], 100).

N-Phenethylacetamide (2l): Solid, mp: 49-50 °C, ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.15-7.37 (m, 5H), 5.57 (brs, 1H), 3.51 (m, 2H), 2.81 (t, *J* = 7.1 Hz, 2H), 1.93 (s, 3H). IR (KBr) (cm^{-1}): 3289, 1645, 1548. Mass: m/z = 186 [(M+Na)], 100).

N-Butylacetamide (2m): Liquid, bp: 117-118 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.29 (brs, 1H), 3.27 (q, *J* = 4.8 Hz, 2H), 1.48 (q, *J* = 4.8 Hz, 2H), 1.36 (q, *J* = 4.8 Hz), 0.84 (t, *J* = 4.2 Hz). IR (KBr) (cm^{-1}): 3295, 3095, 2958, 2870, 1716, 1647, 1559, 1372, 1293, 441. Mass: m/z =116 [(M+H)]+ 60), 102 (100).

N-(2-(2-Chloroethoxy)ethyl)acetamide (2n): Liquid, bp: 115-117 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.08 (brs, 1H), 3.57-3.56 (m, 2H), 3.56-3.55 (m, 2H), 3.54-3.53 (m, 2H), 3.50-3.47 (m, 2H). 2.03 (s,3H). IR (KBr) (cm^{-1}): 3312, 3097, 2875, 2599, 1718, 1647, 1557, 1436, 1373, 1290,1125, 1012, 882. Mass: m/z =165.9 [(M+H)]+ 46), 157.9 (10), 143.8 (8), 143.8 (7), 113.9 (18), 86 (100).

N-((5-Bromobenzofuran-2-yl)methyl)acetamide (2o): Solid, ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.18 (brs, 1H), 8.10 (d, *J* = 1.6Hz, 1H), 7.65-7.52 (m, 3H), 4.45 (d, *J* = 4.8 Hz, 2H), 1.97 (s, 3H). IR (KBr) (cm^{-1}): υ 3398, 3279, 2923, 2855, 1738, 1653, 1550, 1441, 1280, 1172, 1112, 10036, 941, 801, 706, 585. Mass: m/z =267.9 [(M+H)]+ 100), 241.9 (22), 208.8 (38), 186.8 (6).

N-(2-(2-(4-((4-Chlorophenyl)(phenyl)methyl)piperazin-1-yl)ethoxy) ethyl) acetamide (2p): Solid, ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.54 (brs, 1H), 7.35-7.20 (m, 9H), 4.35 (s, 1H), 3.86 (t, *J* = 4.2 Hz, 2H), 3.55 (t, 4.8 Hz, 2H), 3.42 (q, *J* = 5.2Hz, 3.10 (brs, 6H), 2.58 (brs, 4H), 2.08 (s, 2H), 2.03 (s, 3H). IR (KBr) (cm^{-1}): 3015, 2971, 1652, 1486, 1217, 1122, 1007, 758. Mass: m/z =416 [(M+H)]+ 100), 382.2 (10).

N-(2-(2-(4-Benzhydrylpiperazin-1-yl)ethoxy)ethyl)acetamide (2q): Solid, ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, *J* = 7.6Hz, 4H), 7.29-7.17 (m, 6H), 4.35 (brs, 1H), 3.82 (t, *J* = 4.2Hz, 3.53 (t, 4.8 Hz, 2H), 3.42 (t, J = 5.2 Hz, 2H), 3.05 (brs, 5H), 2.79 (brs, 4H), 2.03 (s, 1H), 2.01 (s, 3H), IR (KBr) (cm^{-1}): 3273, 2962, 2827, 1715, 1650, 1549, 1446, 1369, 1287, 1222, 1125, 757. Mass: m/z =382.2 [(M+H)]+ 100).

6. Conclusion

In conclusion, the sodium borohydride has been employed as a novel and efficient catalyst for the synthesis of secondary amides in good yields. The reaction conditions were very mild and the isolation of products also very easy.

7. Acknowledgment

The authors thanks to Osmania University

8. References

[1] (a) Humphrey, J. M.; Chamberlin, A. R. Chem. Rev.1997, 97, 2243; (b) Sewald, N.; Jakubke, H. D. Peptides: Chemistry and Biology, Wiley, New York. 2009.
[2] Cupido, T.; Puche, J. T.; Spengler, J.; Alberico, F. Curr. Opin. Drug Discovery Dev. 2007, 10, 768.
[3] (a) Ronn, R.; Lampa, A.; Peterson, S. D.; Gossas, T.; Aakerblom, E.; Danielson, U. H.; Karlen, A.; Sandstroem, A. Bioorg. Med. Chem. 2008, 16, 2955.
[4] Stolze, S. C.; Kasier, M. Synthesis. 2012, 44, 1755.
[5] Valeur, E.; Bradley, M. Chem. Soc. Rev. 2009, 38, 606.
[6] Allen, C. L.; Chhatwal, A. R.; Williams, J. M. J. Chem. Commun. 2012, 666.
[7] Lundberg, H.; Tinnis, F.; Adolfsson, H. Chem. Eur. J. 2012, 18, 3822.
[8] Prakasam, B. G.; Milstein, D. J. Am. Chem. Soc. 2011, 133, 1682.
[9] Ribelin, T.; Katz, C. E.; Enlish, D. G.; Manukyan, A. K.; Day, V. W.; Neuen swander, B.; Poutsma, J. L.; Aub, J. Angew. Chem. Int. Ed. 2008, 120, 6329.
[10] Kim, J.; Park, W.; Ryoo, R. ACS Catal. 2011, 1, 337.
[11] Owston, N. A.; Parker, A. J.; Williams, J. M. J. Org. Lett. 2007, 9, 3599.
[12] Martinelli, J. R.; Clark, T. P.; Watson, D. A.; Munday, R. H.; Buchwald, S. L. Angew. Chem. 2007, 119, 8612.
[13] Yoo, W.J.; Li, C. J. J. Am. Chem. Soc. 2006, 128, 13064.
[14] Seo, S. Y.; Marks, T. J. Org. Lett. 2008, 10, 317.
[15] Suto, Y.; Yamagiwa, N.; Torisawa, Y. Tetrahedron Lett. 2008, 49, 5732.
[16] Tillack, A.; Rudloff, I.; Beller, M. Eur. J. Org. Chem. 2001, 523.
[17] Cadoni, R.; Porcheddu, A.; Giacomelli, G.; De Luca, L. Org. Lett. 2012, 14, 5014.
[18] Namayakkara, P.; Alper, H. Chem. Commun. 2003, 2384.
[19] Wu, X. F.; Neumann, H.; Beller, M. Chem. Eur. J. 2012, 18, 419.
[20] Wu, X. F.; Schranck, J.; Neumann, H.; Beller, M. Chem Cat, Chem. 2012, 4, 69.
[21] Uenoyama, Y.; Fukuyama, T.; Nobuta, O.; Matsubara,

H.; Ryu, I. Angew. Chem. Int. Ed. 2005, 44, 1075.
[22] Gunanathan, C.; Ben-David, Y.; Milstein, D. Science. 2007, 317, 790.
[23] Zweifel, T.; Naubron, J. V.; Grutzmacher, H. Angew. Chem, Int. Ed. 2009, 48, 559.
[24] Zhang, Y.; Chen, C.; Ghosh, S. C.; Li, Y.; Hong, S. H. Defined, W. Org. Meta. 2010, 29, 1374.
[25] Cheng, C.; Hong, S. H. Org. Biomol. Chem. 2011, 9, 20.
[26] Kegnaes, S.; Mielby, J.; Mentzel, U. V.; Jensen, T.; Fristrup, P.; Riisager, A. Chem. Commun. 2008, 2427.
[27] Ghosh, S. C.; Muthaiah, S.; Zhang, Y.; Xu, X.; Homg, S. H. Adv. Synth. Catal. 2009, 351, 2643.
[28] Xiao, F.; Liu, Y.; Tang, C.; Deng, G. J. Org. Lett. 2012, 14, 984.
[29] Shen, B.; Makley, D. M.; Johnston, J. N. Nature. 2010, 465, 1027.
[30] Sawant, D. N.; Wagh, Y. S.; Bhatte, K. D.; Bhanage, B. M. J. Org. Chem. 2011, 76, 5489.
[31] (a) Kolakowski, R, V.; Shangguan, N.; Sauers, R. R.; Willams, L. J. J. Am. Chem. Soc. 2006, 128, 5695; (b) Zhang, X.; Li, F.; Liu, C. F.; Bioconjugate Chem. 2009, 20, 197.
[32] (a) Anastas, P.; Eghbali, N. Chem. Soc. Rev. 2010, 39, 301. (b) Constabe, D. J. C.; Dunn, P. J.; Hayler, J. D.; Humphrey, G. R.; Leazer, J. J. L.; Linderman, R. J.; Lorenz, K.; Manley, J.; Pearlman, B. A.; Wells, A.; Zaks, A.; Zhang, T. Y. Green Chem. 2007, 9, 411.
[33] (a) Allen, C. L.; Williams, J. M. S. Chem. Soc. Rev. 2011, 40, 3405; (b) Pattabiraman, V. R.; Bode, J. W. Nature. 2011, 480, 471; (c) Roy, S.; Gribble, G. W. Tetrahedron. 2012, 68, 9867; (d) Xie, P.; Xie, C.; Huang, H. Org. Lett. 2013, 15, 3370.; (e) Alvarez, R. G.; Crochet, P.; Cadierno, V. Green Chem. 2013, 15, 46; (f) Bode, J. W, L. Organomet. Chem. 2013, 44, 13; (g) Crochet, P.; Candiemo, V. Organomet. Chem. 2014, 48, 81.
[34] Gordon W. Gribble. Chem. Soc. Review. 1998, 27, 395.