Est. 1984

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

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2013, Vol. 29, No. (2):
Pg. 783-785

Synthesis of 1, 4-Dihydropyridine Derivatives using $FeCl_3$ as Catalyst under Solvent-free Condition

ABDORRAHMAN KEYHANI* and FARHAD HATAMJAFARI

Department of Chemistry, Faculty of Science,
Islamic Azad University-Tonekabon Branch, Tonekabon, Iran.
*Corresponding author E-mail: keyhaniabdorrahman@yahoo.com

DOI: http://dx.doi.org/10.13005/ojc/290260

(Received: February 29, 2013; Accepted: April 12, 2013)

ABSTRACT

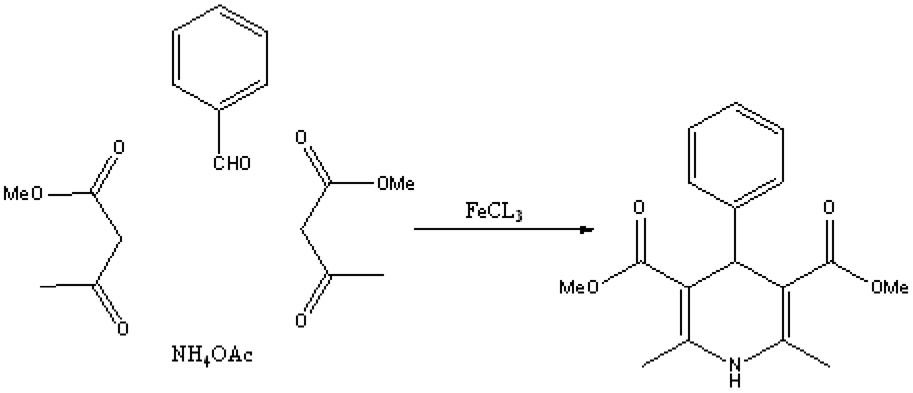
A mixture of ethyl acetoacetate, benzaldehyde and ammonium acetate and in the presence of $FeCl_3$ under solvent-free condition were converted to 1, 4-dihydropyridines with good yields.

Key words: 1, 4-dihydropyridines, ammonium acetate, ethyl acetoacetate, $FeCl_3$.

INTRODUCTION

Chemistry of dihydropyridines in 1882 with Arthur Hansh reports the β-keto ester, aldehydes and ammonia can be combined to form 1, 4-dihydropyridine was developed. Because of the many benefits of 1, 4-dihydropridine is presented and now as vital medicines to treat angina, high blood pressure and allergies have been introduced. The combination of amlodipine and infedipines as brand name drugs[1-5]. Another successful treatment of 4-aryl -1, 4-dihydropridine is that they use as calcium channels blockers in the treatment of cardiovascular disease and hypertension. Calcium channel blockers are a class of drugs that control entrance of calcium into cells and exit of calcium from cellular stores. These compounds lower blood pressure by relaxing smooth muscle wall of heart and arteries and reduce their external resistance. According to the various applications of these compounds , different method for synthesis of derivatives of 1, 4-dihydroprydines in different conditions and different catalysts are presented ,considering that some of these methods are time consuming, less economical and are harmful for the environment, provide appropriate methods, with short time, high efficiency, environmental friendly is valuable[5-11].

Previously, we have synthesized a number of heterocyclic compounds[12-20]. Although numerous methods are capable of affecting these synthesis has been previously reported. $FeCl_3$ has been used previously as a catalyst for synthesis of organic compound[21], herein we report $FeCl_3$ a new catalyst for the synthesis of 1, 4-DHPs at one pot reaction with high yields and easy separation under solvent-free condition (Scheme 1).



Scheme 1:

EXPERIMENTAL

General Procedure for the Preparation of 1, 4-dihydropyridine derivatives

A mixture of ethyl acetoacetate (2 mol), aromaticaldehyde (1 mol) and ammonium acetate (1 mol) and $FeCl_3$ (0.004 $_g$) was refluxed in 110^{o}C for 1h. The obtained solid was filtered; the solid was washed with water and recrystallized using absolute ethanol (5a-f).

Compound 5a: Diethyl 1,4-dihydro-2,6-dimethyl-4-phenylpyridine-3,5-dicarboxylate

$Yellow\,solid, yield:(89\%),\ mp\ 154-158\ ^0C$
$FT-IR\,(KBr\ disc):3365\,(N-H_{str});\ 3005\,(CH_{arom\ str});$
$1693\,(C=O_{\ str});1486,1648\ (C=C_{\ str});\ 1210\,(C-O_{str});\ cm^{-1}.$
$^1H\ \ NMR\,(CDCl_3,\delta,\ ppm);\delta=1.14\,(6H,s,2CH_3);$
$2.22\,(6H\ ,s,2CH_3);\ 3.97\,(4H,s,2\,CH_2);\ 4.92\,(1H\ ,s,CH);$
$7.13\,(5H,s,H_{arom});\ 5.81\,(1H,s,NH).$

Compound 5b: Diethyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate

$Yellow\,solid, yield:(90\%),\ mp\ 163-166\ ^0C$
$FT-IR\,(KBr\ disc):3355\,(N-H_{str});\ 3010\,(CH_{arom\ str});$
$1705\,(C=O_{\ str});\ 1488,1644\,(C=C_{\ str});\ 1347,1530\,(NO_{2\ \ str});$
$1214\,(C-O_{\ str})\,cm^{-1}.$
$^1H\ \ NMR\,(CDCl_3,\delta,\ ppm)\ ;\ \delta=1.13\,(6H,t,2CH_3,\ j=7.2_{Hz});$
$2.27\,(6H,s,2CH_3);$
$3.88-4.14\,(4H\ ,q,2CH_2,\ j=7.2_{Hz});5.02\,(1H,s,CH);$
$7.27-8/04\ (4H,m,H_{arom});\ 5.9\,(1H\ ,s,NH).$

Compound 5C: Diethyl 4-(2,4-dichlorophenyl)-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate

$Yellow\ solid, yield:(85\%),\ \ mp\ 146-149\ ^0C$
$FT-IR\,(KBr\ disc):3379\,(N-H_{str});\ 3006\,(CH_{arom\ str});$
$1681\,(C=O_{\ str});1497,1617\,(C=C_{\ str});\ 1202\ (C-O_{\ str})\,cm^{-1}.$
$^1H\ \ NMR\,(CDCl_3,\delta,\ ppm)\ ;\ \delta=1.15\,(6H,t,2CH_3,\ j=7.2_{Hz});$
$2.20\,(6H,s,2CH_3);$
$3.9-4.13\,(4H\ ,q,2CH_2,\ j=7.2_{Hz});5.27\,(1H,s,CH);\ 6.93-7.18$
$(3H,m,H_{arom});\ 5.74\,(1H\ ,s,NH).$

Compound 5d: Diethyl 1,4-dihydro-2,6-dimethyl-4-m-tolylpyridine-3,5-dicarboxylate

$Yellow\ solid, yield:(87\%),\ mp\ 127-134\ ^0C$
$FT-IR\,(KBr\ disc):3367\,(N-H_{str});\ 3004\,(CH_{arom\ str});$
$1696(C=O_{\ str});1483,1651(C=C_{\ str});\ 1208\ (C-O_{\ str})\,cm^{-1}.$
$^1H\ \ NMR\,(CDCl_3,\delta,\ ppm)\ ;\ \delta=1.14\,(6H,t,2CH_3,\ j=7.2_{Hz});$
$2.20\,(3H,s,CH_3);\ 2.24\,(6H\ ,s,2CH_3);$
$3.8-4.1(4H,q,2\,CH_2,\ j=7.2_{Hz});4.89\,(1H,s,CH);\ \ 6.98-7.01$
$(4H,m,H_{arom});\ 5.61\,(1H\ ,s,NH).$

Compound 5e: Diethyl 4-(4-(dimethylamino) phenyl)-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate

$Yellow\ solid, yield:(88\%),\ mp\ 128-133\ \ ^0C$
$FT-IR\,(KBr\ disc):3165\,(N-H_{str});\ 3012\,(CH_{arom\ str});$
$1693(C=O_{\ str});1486,1651(C=C_{\ str});\ 1213\ (C-O_{\ str})\,cm^{-1}.$
$^1H\ \ NMR\,(CDCl_3,\delta,\ ppm)\ ;\ \delta=1/04-1/24\,(6H,t,2CH_3,\ j=7.2_{Hz});$
$2/20\,(6H,s,2CH_3);\ 2.97\,(6H\ ,s,N(CH_3)_2);$
$3.87-4.14\,(4H,q,2\,CH_2,\ j=7.2_{Hz});4.82\,(1H,s,CH);$
$6.47-6.58\,(2H,d,J=8.82\ _{Hz},H_{arom});7.01-7.12$
$(2H,d,J=8.75_{Hz},H_{arom});\ 5.9\,(1H\ ,s,NH).$

Compound 5f: Diethyl 1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3,5-dicarboxylate

$Yellow\ solid, yield :(95\%),\ mp\ 118-124\,^{0}C$

$FT-IR\,(KBr\ disc):3341\,(N-H_{str});\ 3006\,(CH_{arom\ str});$

$1702\,(C=O_{str});\ 1486,1648\,(C=C_{str});1342-1519\,(NO_{2\ str});$

$1213\ (C-O_{str})\,cm^{-1}.$

$^{1}H\ \ NMR\,(CDCl_3, \delta, ppm)\ ;\ \delta=1/13\,(6H, t, 2CH_3,\ j=7.2_{Hz});$

$2.27\,(6H, s, 2CH_3);$

$3.97-4.06\,(4H, q, 2CH_2,\ j=7.2_{Hz});5.02\,(1H, s, CH);\ \ 7.41-7.94$

$(4H, dd, H_{arom});\ 5.55\,(1H, s, NH).$

RESULTS AND DISCUSSION

Herein, we report $FeCl_3$ as catalyst which could provide an efficient, cheap, easy separation, high yield and simple route under solvent-free condition for the synthesis of 1,4-DHPs.

ACKNOWLEDGEMENTS

We gratefully acknowledge the financial support from the Research Council of Tonekabon Branch Islamic Azad University.

REFERENCES

1. David J. T., *Biochemical Pharmacology.*, **74**: 1-9 (2007).
2. Love B., Goodman M., Snader K., Tedeschi R and Macko E., *J. Med. Chem.*, **17**: 956 (1974).
3. Bossert F., Meyer H and Wehinger E., *Angew. Chem. Int. Ed. Engl.*, **20**: 762 (1981).
4. Breitenbucher J.G and Figliozz G., *Tetrahedron Lett.*, **41**: 4311 (2000).
5. Boer R and Gekeler V., *Drugs Fut.*, **20**: 499 (1995).
6. Wang L.M., Sheng J. Zhang L., Han J.W., Fan Z.Y., Tian H and Qian C.Y., *Tetrahedron.*, **61**: 1539 (2005).
7. Ji S.J., Jiang Z.Q., Lu J and Loh T.P., *Synlett.,* 831 (2004).
8. Ko S., Sastry M.N.V., Lin, C and Yao, C.F., *Tetrahedron Lett.*, **46**: 5771 (2005).
9. Dzvinchuk I.B and Tolmacheva, N.A., *Chem. Heterocycl. Comp.*, **37**: 506 (2001).
10. Chebanov V.A., Saraev V.E., Kobzar K.M., Desenko S.M., Orlov, V.D and Gura, E.A., *Chem. Heterocycl. Comp.*, **40**: 475 (2004).
11. Bidram A., Hatamjafari F and Doryeh A., *Orient. J. Chem.*, **29**: (2013 in press).
12. Azizian J., Hatamjafari F., Karimi A. R. and Shaabanzadeh M., *Synthesis*. **5**: 765 (2006).
13. Azizian J., Shaabanzadeh M., Hatamjafari F. and Mohammadizadeh M.R., *Arkivoc.*, (xi): **47** (2006).
14. Hatamjafari F., *Synthetic Communications.*, ý **36**: 3563 (2006).
15. Azizian J., Hatamjafari F. and Karimi A. R., *Journal of Heterocyclic Chemistry.*ý, **43**: 1349 (2006).
16. Hatamjafari F and Montazeri N., *Turkish Journal of Chemistry.*ý, **33**: 797 (2009).
17. Hatamjafari F., *Orient. J. Chem.*, **28**: 141 (2012).
18. Hatamjafari F., *Orient. J. Chem.*, **29**: (2013 in press).
19. Hatamjafari F and Alijanichakoli F., *Orient. J. Chem.*, **29**: (2013 in press).
20. Hatamjafari F and Hosseinian A., *Orient. J. Chem.*, **29**: (2013 in press).
21. Lu J and Bai Y., *Synthesis.*, 466 (2002).