International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 013 Published Mar. 2018
Volume No. 04, Issue No.02, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: **SYNTHESIS OF α-AMINOPHOSPHONATES AT ROOM …**

SYNTHESIS OF α-AMINOPHOSPHONATES AT ROOM TEMPERATURE BY ECO-FRIENDLY WATER MEDIATED GREEN PROTOCOL

Ayesha Durrani, S. A. Pathare, B. L. Angarkhe, Archana D. Jadhav*
Arts, Science and Commerce College Rahuri,
Po/Tal-Rahuri, Dist-Ahmednagar
Pin-413705 (Maharashtra), India
e-mail: archu1990jadhav@gmail.com
(M.S)

ABSTRACT:-
Single step synthesis of α-aminophosphonate concerns with the study of green chemistry is helpful to reduce environment pollution. The increasing environmental awareness have led to consideration of highly efficient one-pot , three component, green approaches for important organic synthons. We describe here a simple, elegant, high yielding protocol for the synthesis of α-aminophosphonate in totally solvent free, catalyst-free conditions by reacting aldehydes, amine &trimethyl phosphate at ambient conditions.This method provides mild reaction condition and less toxicity as compared to the conventional methods. The structural assignment of the final products has been done by spectral techniques.
KEYWORDS:-Aldehydes; α-Aminophosphonate; amines; trimethylphosphite; solvent free.

INTRODUCTION:-

The synthesis of α-aminophosphonates exhibiting high bio-activity has recently attracted a lot of attention. Design and development of products and processes that minimize the usage as well as generation of toxic substances have been the aim of green chemistry. To avoiding addition of supplementary chemicals like solvents, catalysts &promoters,etc. In the reaction sequence or work-up processes constitutes a significant steps for environmentally friendly reaction protocol. For designing synthetic methods at room temperature goes a long way in making the reaction totally clean and hazard –free efficient process.

Organophosphorous compounds are important substrates in the study of biochemical and pharmacological spectrum have become the interested subject in recent years.In our interest in developing environmentally benign efficient solvent-free protocols for the synthesis of important products, we describe here a simple, high yielding protocol for the synthesis of *α*-aminophosphonates in totally solvent-free & catalyst-free conditions.Nowadays, microwave irradiation is used to accomplish certain unsuccessful or low-yielding reactions, reducing the reaction time from days to minutes, and improving yields.

A number of reported methods was determined by nucleophilic addition of dimethyl phosphite or trimethylphosphite to imines (generated in situ from different aldehydes and amines) catalysed by an acid, lanthanide triflate& many methods using different catalytic systems such as,

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 013 Published Mar. 2018
Volume No. 04, Issue No.02, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: **SYNTHESIS OF α-AMINOPHOSPHONATES AT ROOM …**

$AlCl_3$, TiO_2, Oxalic acid, $FeCl_3$, H_3BO_3, $Bi(OTf)_3$ and microwave, β-cyclodextrin, etc. have been reported. Phosphorous analogues of the amino acids in which the carboxylic acid group is replaced by a phosphonate group have attracted particular interest in the preparation of numerous natural products.Their utility as antagonists in the metabolism of amino acids as enzyme inhibitors and as pharmacological agents such as antibiotics, antiviral, antifungal, etc. and many other applications are reported for that.

In many reported methods some limitations that include the use of organic solvents, expensive catalyst, harsh reaction conditions and low yields. In order to overcome such limitations, there is a need for an efficient and convenient method for construction of such significant backbone. To the best of our knowledge, this is the report where in the water mediated synthesis of α-aminophosphonates in solvent-free and catalyst free environment at ambient conditions.

2] EXPERIMENTAL:-

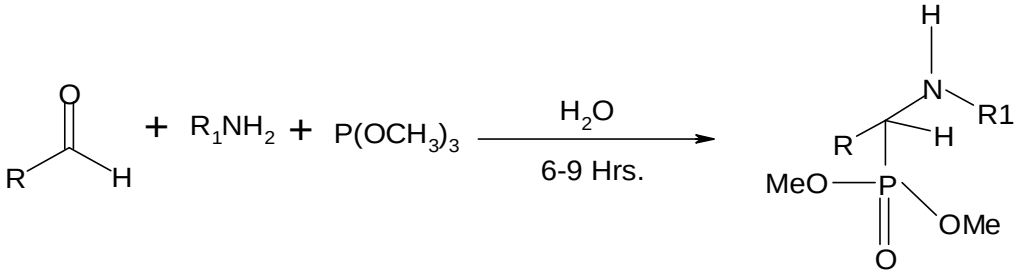
MATERIALS AND METHODS:-

Melting points were determined in open capillariesin liquid paraffin bath and are uncorrected. Purity of the compound was routinely checked on silica gel TLC glass plates using $CHCl_3$ as airrigant. ^1H NMR spectra were recorded on Bruker AV, 200 MHz spectrometers in appropriate solvents using TMS as internal standard or the solvent signals as secondary standards and the chemical chemical shifts are shown in δ scale. Multiplicities of ^1H NMR signals are designated as s(singlet), d(doublet), dd(doublet of doublet), dt(doublet of triplet), t(triplet), quin(quintet), m(multiplet)…etc. IR data were recorded an Alpha-T ATR-FTIR.

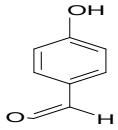
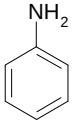
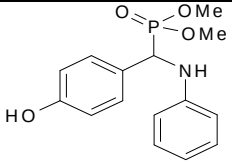
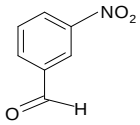
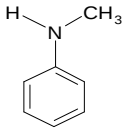
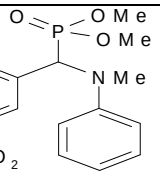
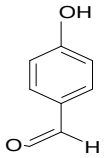
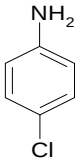
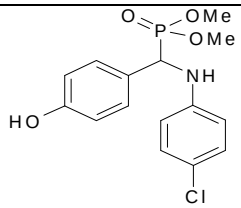
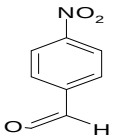
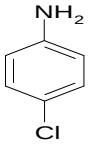
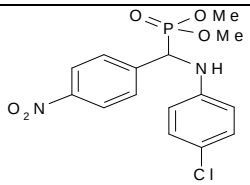
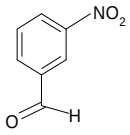
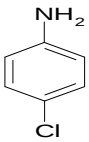
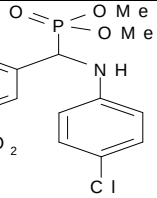
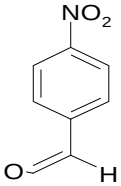
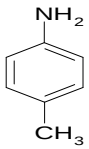
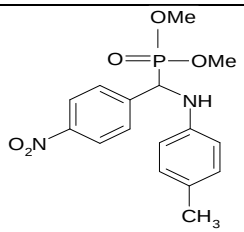
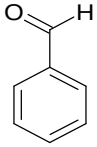
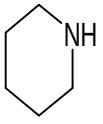
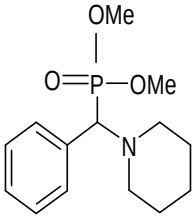
GENERAL PROCEDURE FOR PREPARATION OF A-AMINOPHOSPHONATES:-

A mixture of aldehyde(1mmol) & amine(1mmol) was stirred at room temp. for 2 min & then trimethylphosphite(1mmol) was added. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water (in case of solid products) & the product were separated by filtration & dried. The products obtained were pure enough for all practical purposes.

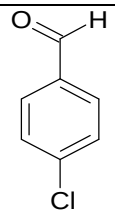
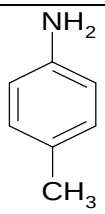
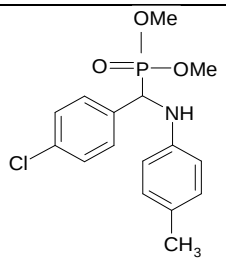
GENERAL REACTION:-



International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 013 Published Mar. 2018
Volume No. 04, Issue No.02, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: **SYNTHESIS OF α-AMINOPHOSPHONATES AT ROOM …**

Sr. No.	R	R1	Product	Time (hr)	Yield (%)	Melting Point (^{0}C)
1				8	83.54	160-162
2				7	54	58-60
3				9	77	150-154
4				8	52	96-98
5				8	51	138-142
6				6	88	210-212
7				8	72	70-71

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 013 Published Mar. 2018
Volume No. 04, Issue No.02, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: **SYNTHESIS OF α-AMINOPHOSPHONATES AT ROOM …**

8				9	80	134-136

RESULT TABLE:-

SPECTRAL DATA:-

1. dimethyl [(4-hydroxyphenyl)(phenylamino)methyl]phosphonate

(yellowish solid) m. p. 160-162^{0}C ; IR :- 2853, 3406, 1527, 733, 1347, 1194cm^{-1} ; 1H NMR (200 MHz, $CHCl_3$) δ 5.35 (bs, Ar-OH); 4.0 (bs, Ar-NH); 6.63(d, Ar-H); 6.83(dd,Ar-H); 7.06 (d, Ar-H); 3.66(s, O-CH_3); 7.23(dd, Ar-H); 6.77(dd, Ar-H)

2. dimethyl {[(4-methylphenyl)amino](4-nitrophenyl)methyl}phosphonate
(whitish solid) m.p. 210-212^{0}C ; IR: 3406, 1620,1529, 1350, 1190, cm^{-1} ; 1H NMR (200 MHz, $CHCl_3$) δ 3.66(s, O-CH_3); 2.34(s, Ar-CH_3); 7.01(d, Ar-H); 6.48(d, Ar-H); 8.14 (d, Ar-H); 7.49(d, Ar-H); 3.9(s, CH); 4.0(s, Ar-NH)

3. dimethyl {(4-chlorophenyl)[(4-methylphenyl)amino]methyl}phosphonate
(pale yellow solid) m.p. 134-136 ^{0}C ; IR: 1164, 1225, 758.44, 1449, 2951, 1591cm^{-1} ; 1H NMR (200 MHz, $CHCl_3$) δ 7.17(d, Ar-H); 7.37(d, Ar-H); 3.9(s, CH); 4.0(s, Ar-NH) 2.34(s, Ar-CH_3); 7.01(d, Ar-H); 6.48(d, Ar-H); 3.66(s, O-CH_3)

CONCLUSION:-

In our current search, we have reported the synthesis of α-aminophosphonates in one-potsynthesis from aldehyde, amines and trimethylphosphite using catalyst free and solvent free codition at room temperature. The single stage free of any chemical auxiliaries, energy efficient process and this approach for biologically significant compounds is an attractive and useful method for the green synthetic procedures.

ACKNOWLEDGEMENTS:-

It's my great pleasure to express a deep sense of gratitude to my respected guide Prof. Dr. Ayesha N. Durrani for her excellent guidance, stimulating discussion, keen interest, continuous encouragement and perceptive criticism while completing the research work.

I must express my deep sense of gratitude to Prin. Dr. S. A. Pathare, Arts, Science and Commerce College, Rahuri, for providing the necessary facilities and constant encouragement. I am also thankful to Prof. E. H. Gade, Prof. B.L. Angarkhe and all teaching and non-teaching staff of Department of Chemistry, for their kind co-operation.

REFERENCES:-

1. Atherton, F. R.; Hassall, C. H.; Lambert, R. W. *J. Med. Chem.* **1986**, *29*, 29.
2. Abdulqader Alhaider A, Atef Abdelkader M and Eric Lein J, *J Med Chem.*, 1985, **28(10)**, 1394-
1398
3. Ahmad Z, Klinkenberg LG, Pinn, M L, Fraig M M, Peloquin C A, Bishai W R, Nuermberger E

L, Grosset J H and Karakousis P C, *J Infect Dis.*, 2009, **200(7)**, 1136-1143
4. (a) Baylis E K, Campbell C D and Dingwall J G 1984 *J. Chem. Soc. Perkin. Trans*. **1** 2845; (b)
Atherton F R, Hassal C H and Lambert R W 1986 *J. Med.Chem.* **29** 29; (c) Noyori R 1994 *Asymmetric catalysis in organic synthesis*, John Wiley and Sons:New York
5. Akiyama T, SanadaMand Fuchibe K 2003 *Synlett* 1463
6. (a) Allen M C, Fuhrer W, Yuck B, Wade R and Wood JM1989 *J.Med. Chem*. **32** 1652; (b) Peman A, StahlW, Wagner K, Ruppert D and Budt K H 1994 *Bioorg. Med.Chem. Lett*. **4** 2601;
(c) Natchev I A 1988 *Liebigs. Ann. Chem*. **1988** 861; (d) Huang J and Chen R 2000 *Heteroatom Chem*. **11** 480
7. Bhattacharya A K and Kaur T 2007 *Synlett* 745
8. (a) Bhagat S and Chakraborti A K 2007 *J. Org. Chem*. **72** 1263; (b) Wu J, Sun W, Xia H and Sun X 2006 *Org. Biomol. Chem*. **4** 1663
9. Bhagat S and Chakraborti A K 2008 *J. Org. Chem*. **73** 6029
10. Chandrasekhar S, Prakash S J, Jagadeshwar V and Narsihmulu C 2001 *Tetrahedron Lett*. **42** 5561
11. Eswaran S, Adhikari A V, Pal N K and Chowdhury I H, *Bioorg Med Chem Lett.*, 2010, **20(3)**, 1040-1044
12. Firouzabadi H and JafarpourM 2008 *J. Iran Chem. Soc*.**5** 159
13. Ha H-J and Nam G-S 1992 *Synth. Commun.* **22** 1143
14. Hosseini-Sarvari M 2008 *Tetrahedron* **64** 5459
15. Hewson, A. T., Macpherson, D. T. *Tetrahedron Lett.* **1983**, *24*, 647.
16. Heydari, A.; Zarei, M.; Alijaninzadeh, R.; Tavakol, H. *Tetrahedron Lett.* **2001**, *42*, 3629.
17. Kaboudin B and Sorbiun M 2007 *Tetrahedron Lett.* **48**

18. (a) Kabachinic, M. J.; Medved, T. *Izv. Akad. Nauk. SSSR* **1953**, 1126. (b) Kabachinic, M. J.; Medved, T. *Izv. Akad. Nauk. SSSR* **1954**, 1024.
19. Kleszczynska, H.; Sarapuk, J. *Cell. Mol. Biol. Lett.*, **2001**, *6*, 83. 9015
20. Mulwad V V and Lohar M V, *Indian J Chem.*, 2003, **42B**, 1937.
21. Matveeva E D, Podrugina T A, Tishkovskaya E V, Tomilova L G, Zefirov N S *Synlett*, 2003, 2321-2324
22. Maghsoodlou M T, Khorassani S M H, Hazeri N, Rostamizadeh M, Sajadikhah S S, Shahkarami Z and Maleki N 2009 *Heteroatom Chem*. **20** 316
23. Manabe K and Kobayashi S 2000 *Chem. Commun*. 669
24. Manjula A, Rao B V and Neelakantan P 2003 *Synth. Commun*. **33** 2963

25. Vahdat S M, Baharfar R, Tajbakhsh M, Heydari A, Baghbanian S M and Khaksar S 2008 *Tetrahedron Lett*. **49** 6501
26. Vincent, J. C.; Vincent, H. W. *Proc. Soc. Expt. Biol. Med.* **1944,** *55*, 162.