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LI_2CO_3: An Catalyst for One Pot Synthesis of A-Hydroxy Phosphonates and Study of Their Antimicrobial Activities

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KEYWORDS
Green methodology, Facile, Cheap, Reliable and Practical.

ABSTRACT:
The α-hydroxy phosphonates exhibit crucial antiviral, antibacterial, antifungal anti-HIV, anticancer, anti-inflammatory, anti-oxidant activities, so highly efficient and convenient protocol has been accomplished for one pot synthesis of α-hydroxy phosphonates using aromatic aldehyde, diethyl phosphite in presence of eco-friendly catalyst Li2CO3 at ambient temperature by grinding method. The grinding method is green methodology which is largely used from last decade in synthesis of various biological active compounds. The method is very facile, use of cheap, radially available and easy to handle catalyst Li2CO3 makes method more simple, reliable and practical.

Introduction:

Improvement in greener synthetic methodologies along with sudden access towards the target compounds is very important fundamental objectives to accelerate current organic synthesis. [1]. With respect to these cases, use of microwave [2], ultrasound waves [3], alternate reaction media [4]. etc. are very well accepted tool for synthesis with fast reaction rate, high chemical efficiency with choice of expedient catalyst and absence of reaction medium. The examples reported demonstrate that solvent-free reactions are generally more expeditious, giving higher reactivity and involve more facile work-up procedures.

Phosphonates and their derivatives are key part in large group of chemical compounds with many various applications. Phosphonate moieties are found not only in therapeutic drugs and industrial chemicals [5] [6] but also as significant intermediates in synthetic chemistry (ylide and mitsonobu reaction). Phosphonate derivatives including both synthetic and natural product represent numerous applications in medicine (drugs), agricultural (fertilizers and herbicides), synthetic chemistry (catalysts) [7]. α-Functionalized phosphonates are important intermediates for the synthesis of many medicinal and synthetic compounds [8]. The α-hydroxy phosphonates are important class of organophosphorus compound which exhibit antiviral [9], antibacterial [10], anti-HIV [11], anticancer [12], anti-inflammatory [13], anti-oxidant [14], enzyme inhibitor [15] anti-tumor [16] activities. Phosphonate esters are a common prodrug strategy employed, with many examples having been prepared and evaluated for biological activity [17] (figure- 1).

Pudovik reaction is base catalyzed hydroxy phosphorylation of aldehydes in which C-P bond formed. [18]. The available methods for the synthesis of α-hydroxy phosphonates involving the nucleophilic addition of di or trialkylphosphite to different substituted aldehydes in the presence of various catalysts such as ethyl magnesium bromide [19], KF-alumina [20], magnesium oxide (MgO) [21], quinine [22], LDA [23], NH_4VO_3 [24]. Besides this there is bronsted acid catalyst like alumina [25], $Ti(OPri)_2$ [26], HCl [27], Amberlyst [28] have been additionally explored in recent years for the synthesis of α-hydroxy phosphonates. There are few more research work describing the reaction of trialkyl phosphite with aldehydes or ketones in the presence of acid catalysts such as $LiClO_4$: Et_2O [29] and guanidine hydrochloride [30]. However, all the subsisted methods exhibited their drawbacks, such as the environmental pollution caused by utilization of organic solvents, long reaction time, extreme reaction conditions, unsatisfactory yields, perplexed operations. Consequently, there is an immediate demand for the further development of an

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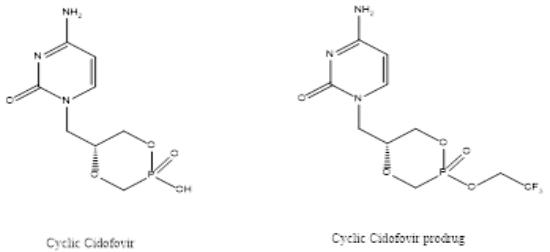
efficient and convenient method to construct such significant scaffold.



Cyclic Cidofovir | Cyclic Cidofovir prodrug

Figure 1

The use of grinding approach is a green tool for synthesis of organic compounds. [31]. An innovative work by Toda et al. [32] has shown that many reactions in organic synthesis can be achieved in high yield by just grinding solids together using a mortar and pestle a technique known as “grindstone chemistry”, which is one of the green chemistry techniques. Reactions are triggered by grinding, with the transfer of minutely minuscular quantities of energy through friction [33]. In addition to this, grinding approach increases reactivity of starting material and minimize the waste product formation. Such reaction is easy to handle, lower the pollution and relatively inexpensive to operate so it is cheaper method in chemistry [34]. In this work, mild, easily available, less harmful, inexpensive catalyst i.e. Li_2CO_3 under grinding tool was reported for synthesis of α -hydroxy phosphonates at ambient temperature.

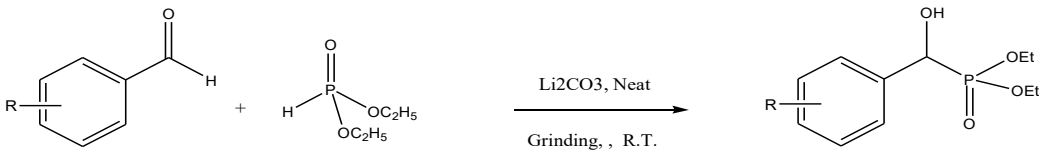
Experimental:

Material and Methods:

All the reagents, chemicals and solvents were purchased from Sigma-Aldrich, Merk, Spectrochem, Loba, and Aura were used without further purification. The melting point were recorded on digital melting/boiling point apparatus of Labtronics make and found uncorrected. The progress of reaction was monitored by Thin layer chromatography was executed on precoated plates of TLC silica gel 60 F_{254}. in 30% ethyl acetate in hexane solvent. Visualization was made with UV light (254 or 365nm). IR spectra were obtained on Shimatzu Infra-Red Spectrophotometer at Jijamata College of Arts and Science, Bhende, Ahmednagar and and absorptions (ν_{max}) were reported in wave numbers (cm^{-1}). The mass spectra were recorded on Shimadzu, Japan (Model: LCMS/MS 8040) spectrometer at Department of Chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur. The ^1H NMR spectra were recorded on BRUKER- 400 MHz (Model: AV 400) spectrometer (Sophisticated Instrument Facility, NMR Research Centre, Indian Institute of Science Bangalore) in $CDCl_3$ solvent using TMS as an internal standard and chemical shifts were measured in δ parts per million (ppm) and coupling constants (J) were measured in hertz (Hz).

General method for synthesis of α -hydroxy phosphonates derivatives:

A mixture of aromatic aldehyde (1mol eq.), diethyl phosphite (1 mol eq.) and Li_2CO_3 (1.5 mol eq.) were grinded in mortar and pestle for 8 to 10 min. at room temperature. After completion of reaction as indicated by thin layer chromatography, small amount of water was added to reaction mixture and product were extracted with ethyl acetate (3x 10 ml) which then dried over an. Na_2SO_4, filtered and concentrated under vacuum. The crude compound was purified by washing with hexane solvent followed by recrystallization using ethanol. (scheme-1). The synthesized derivatives of α -hydroxy phosphonates were summarized in table 1.



1a 2a 3a

figure 2

Scheme-1 Synthesis of hydroxy phosphonates

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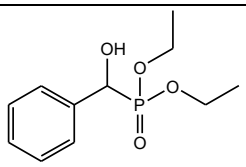
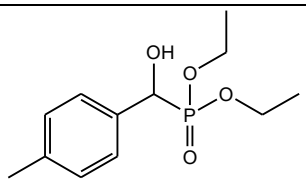
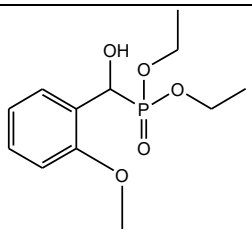
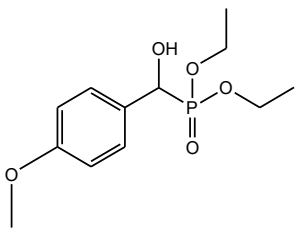
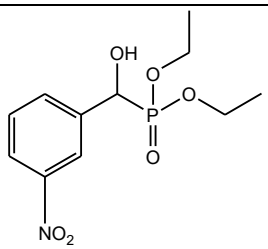
Table 1: Synthesis of α -hydroxy phosphonates derivatives.

Entry	**Aldehyde**	**Compound**	**M.P.^{o}C found**	**M.P. ^{o}C reported^{ref}**	**Yield (%)**
1	benzaldehyde	 PHO 1	74-75	75-76	93
2	4-methyl benzaldehyde	 PHO 2	95-96	94-95	90
3	2-methoxy benzaldehyde	 PHO 3	130-132	-	92
4	4-methoxy benzaldehyde	 PHO 4	120-122	120-121	88
5	3-nitro benzaldehyde	 PHO 5	80-82	81-82	96

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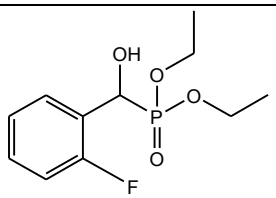
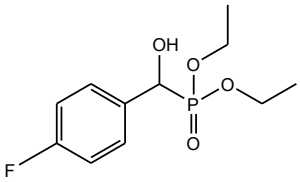
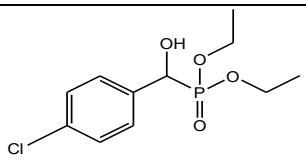
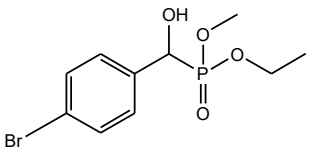
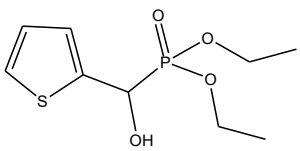
6	2-fluro benzaldehyde	 PHO 6	88-89	-	90
7	4- fluro benzaldehyde	 PHO 7	78-79	-	92
8	4-chloro benzaldehyde	 PHO 8	68-70	67-68	90
9	4-bromo benzaldehyde	 PHO 9	75-77	74-75	92
10	Thiophene 2-aldehyde	 PHO 10	Semi-solid nature	-	90

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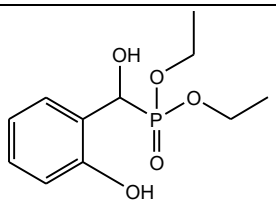
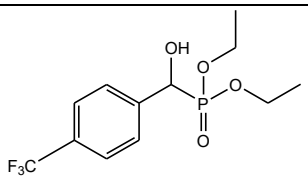
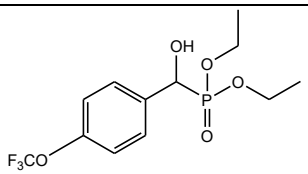
11	Salicyldehyde	 PHO 11	Semi-solid nature	-	88
12	4-trifluromethyl benzaldehyde	 PHO 12	103-104		90
13	4-trifluromethoxy benzaldehyde	 PHO 13	111-112		92

Spectral data:

Compound PHO 1: Diethyl hydroxyl (phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.26-7.49 (m, 5H, Ar-H), 5.00-5.03 (d, 1H, J= 10.8 Hz, CH-PO-), 3.94-4.10 (m, 4H, OCH_2), 1.19-1.28 (m, 6H, OCH_2CH_3), (Mass: m+1): 245

Compound PHO 2: Diethyl hydroxyl (4-methyl phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.16-7.37 (m, 4H, Ar-H), 4.95-4.98 (d, 1H, J=10.4 Hz, CH-PO-), 3.93-4.09 (m, 4H, OCH_2), 2.34 (s, 3H, Ar-CH_3), 1.20-1.29 (m, 6H, OCH_2CH_3), (Mass: m+1): 259

Compound PHO 4: Diethyl hydroxyl (4-methoxy phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 6.89-7.41 (m, 4H, Ar-H), 4.93-4.96 (d, 1H, J=10Hz, CH-PO-), 3.91-4.10 (m, 4H, OCH_2), 3.81 (s, 3H, OCH_3), 1.20-1.30 (m, 6H, OCH_2CH_3)

Compound PHO 5: Diethyl hydroxyl (3-nitro phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$,) δ ppm: 7.53-8.37 (m, 4H, Ar-H), 5.13-5.16 (d, 1H, J=11.2 Hz, CH-PO-), 4.08-4.14 (m, 4H, OCH_2), 3.59 (s, 1H, OH), 1.25-1.57 (m, 6H, OCH_2CH_3)

Compound PHO 6: Diethyl hydroxyl (2-fluoro phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$,) δ ppm: 7.02-7.68 (m, 4H, Ar-H), 5.36-5.39 (d, 1H, J=11.2 Hz, CH-PO-), 3.99-4.22 (m, 4H, OCH_2), 1.21-1.31 (m, 6H, OCH_2CH_3)

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Compound PHO 7: Diethyl hydroxyl (4-fluoro phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$,) δ ppm: 7.44-7.48 (m, 2H, Ar-H), 7.02-7.07 (m, 2H, Ar-H), 4.98-5.01 (d, 1H, J=10.4 Hz, CH-PO-), 3.97-4.10 (m, 4H, OCH_2), 1.21-1.29 (m, 6H, OCH_2CH_3)

Compound PHO 8: Diethyl hydroxyl (4-chloro phenyl) methyl phosphonates:

^{1}H NMR (400 MHz, $CDCl_3$,) δ ppm: 7.23-7.46 (m, 4H, Ar-H), 4.81-4.79 (d, 1H, J=10.8 Hz, CH-PO-), 3.99-4.26 (m, 4H, OCH_2), 1.24-1.35 (m, 6H, OCH_2CH_3)

Result and Discussions:

An efficient and environmentally benign neat one pot synthesis of α -hydroxy phosphonates by reaction of aromatic aldehyde and diethyl phosphite were grinded in presence of Li_2CO_3 as a catalyst. In order to optimize experimental condition, we carried out reaction of 3-nitro benzaldehyde and diethyl phosphite in presence of different amount of catalyst Li_2CO_3 (Table 2). Excellent result was obtained when reaction was performed with 1.5 mol eq. of Li_2CO_3 which indicated in Table 2, entry 2. With further increase in amount of catalyst 2.0 mol eq. we observed that there is no increase in yield of product which shown in Table 2, entry 3. from above observations we synthesized all other derivatives with 1.5 mol eq. amount of catalyst Li_2CO_3. From the above observation, it was clear that amount of catalyst affects the yield of product.

Table 2 effect of catalyst on synthesis of α -hydroxy phosphonates.[a]

Entry	Catalyst (mole eq.)	Time (min.)	[b]Yield (%)
1	1.0	15	80
2	1.5	10	96
3	2.0	10	96
4	2.5	10	94
5	-	overnight	0

[a]Reaction of 3-nitro benzaldehyde (1.0 mol eq.) and diethyl phosphite (1.0 mol eq.) under neat condition at R.T. [b]isolated yield.

In the absence of Li_2CO_3, the mixture was ground for 10 min and kept for overnight, the yield of the corresponding α-hydroxy phosphonates was 0 %. While in the presence of Li_2CO_3, the yield of the α -hydroxy phosphonates was 96 %. It indicated that Li_2CO_3 was important to the reaction. On the basis of these results, we performed series of experiments for synthesis of different α-hydroxy phosphonates in presence of 1.5 mol eq. amount of catalyst Li_2CO_3.

Antimicrobial activities:

All the above compounds were screened for Antimicrobial activities [35]. The Antibacterial activity of compound (PHO 1-13) was tested against the growth of *Staphylococcus aureus* (ATCC 6538) (gram +ve) and *Escherichia coli* (ATCC 25922) (gram –ve) by Agar well diffusion method at concentration 100mg/ml and results were summarized in table 3. *Streptomycin* was used as the standard compound. The compounds (PHO 1-13) showed moderate activity against *Staphylococcus aureus* and *Escherichia coli*. The highlight is that the six compounds (PHO 8-13) were more effective.

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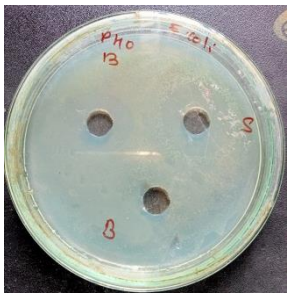
Table 3 Antibacterial activity of compound α-hydroxy phosphonates.

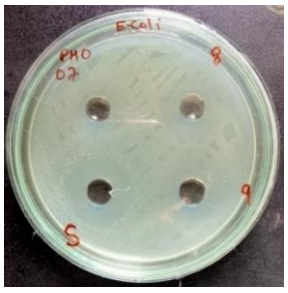
Sr. No.	Compound	Test pathogen (zone of inhibition in mm)	
		E. coli	S. aureus
1	PHO 1	14±0.40	12
2	PHO 2	12	**18±0.44**
3	PHO 3	11	12
4	PHO 4	11	NA
5	PHO 5	12	**15±0.44**
6	PHO 6	NA	**15±0.44**
7	PHO 7	12	NA
8	PHO 8	**20±0.48**	**24±0.50**
9	PHO 9	**20±0.48**	**20±0.48**
10	PHO 10	**18±0.44**	**15±0.40**
11	PHO 11	**18±0.44**	**15±0.40**
12	PHO 12	**18±0.44**	**15±0.40**
13	PHO 13	**24±0.50**	NA
14	Streptomycin*	**28±0.51**	**28±0.51**

(Zone of inhibition <15 is non-significant; NA: No activity. The values are average of triplicates;

The significant values are highlighted.) Standard*, Conc. of compound 100 mg/ml, Conc. of Standard 10 mg/ml

E. coli





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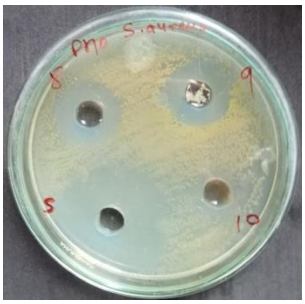
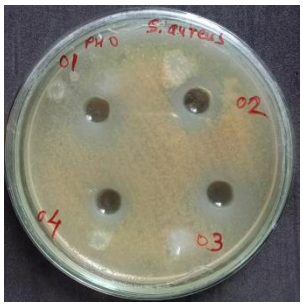
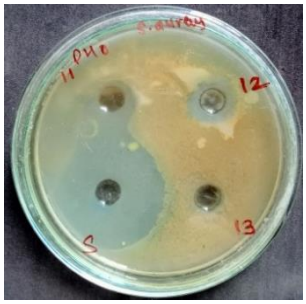
S. aureus







The compounds (PHO 1-13) were also screened for antifungal activity [35] against *Candida albicans* (ATCC 10231) and *Aspergillus niger* (ATCC 96422) along with the standard fungicide *Flucanazole* and *Griseofulvin* by Agar well diffusion method at concentration 100mg/ml and results were summarized in table 4. It is observed that the four compounds (PHO 1, PHO 8, PHO 9, PHO 11) shows moderate activity but all other compounds do not show activity against both the fungi.

Table 4 Antifungal activity of compound α-hydroxy phosphonates.

Sr. No.	**Compound**	**Test pathogen (zone of inhibition in mm)**	
		C. albicans	A. niger
1	PHO 1	NA	**15±0.40**
2	PHO 2	NA	NA
3	PHO 3	NA	NA
4	PHO 4	NA	NA
5	PHO 5	NA	NA
6	PHO 6	NA	NA
7	PHO 7	NA	NA
8	PHO 8	**18±0.51**	**22±0.49**
9	PHO 9	**16±0.44**	14
10	PHO 10	NA	12
11	PHO 11	NA	**15±0.40**
12	PHO 12	NA	NA
13	PHO 13	NA	NA
14	Standard	**32±0.62**[a]	**30±0.61**[b]

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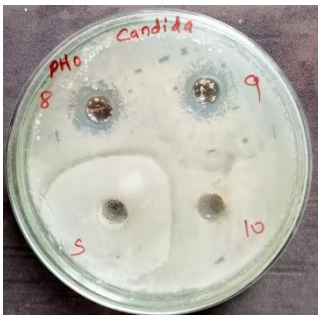
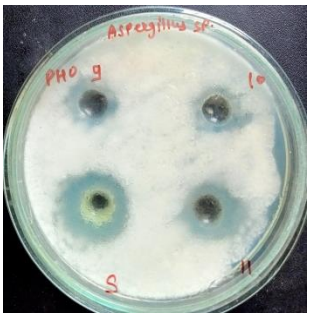
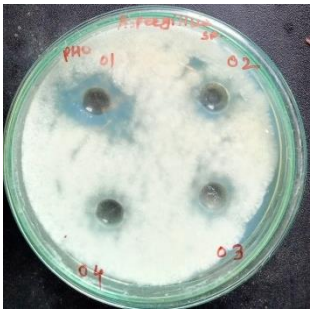
(Zone of inhibition <15 is non significant; NA: No activity. The values are average of triplicates; The significant values are highlighted.) Standard: Flucanazole[a] and Griseofulvin[b] ,Conc. of compound 100 mg/ml, Conc. of Standard 10 mg/ml

C. albicans



A. niger





Conclusions:

We have described a convenient method for the preparation of α-hydroxy phosphonates by modified Pudovik reaction using green synthetic methodology by grinding method in presence of catalyst Li_2CO_3. The catalyst is easily available, inexpensive and efficient for synthesis of α-hydroxy phosphonates and its derivatives. The incredible advantages of this method are operationally simple, mild reaction conditions, good yield, easy work-up and making it eco-friendlier alternative route to currently existing protocols.

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References:

1) Albert, P.; William, H. P. Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry toward Heterocycles and Natural Products. Organic Process Research & Development, 2004, 8, pp. 293-300. DOI: 10.1021/op034095b
2) Kappe, C. O.; Doris D.; Murphree, S. S. Practical Microwave Synthesis for Organic Chemists:

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 2830-2840 | ISSN:2251-6727

Strategies, Instruments, and Protocols. 2008, p. 299. DOI:10.1002/9783527623907

3) Saurabh, P.; Balbir, K.; Anupama, P.; Harish, K. Applications of Ultrasound in Organic Synthesis - A Green Approach. Current Organic Chemistry, 2013, 17, pp. 1790-1828. DOI: 10.2174/13852728113179990018

4) Dave, J. A.; Paul, J. D.; Stewart, J. T. Chemistry in Alternative Reaction Media. Angew. Chem. Int. Ed. 2004, 43, pp. 2195 – 2197. https://doi.org/10.1002/anie.200385107

5) Philippe, C.; Frank, H. E.; Pierrick, G.J. F.; Bisphosphonates and Cancer-Induced Bone Disease:Beyond Their Antiresorptive Activity. Cancer Res 2005; 65: (12), pp. 4971-4974. DOI:10.1158/0008-5472.CAN-05-0264

6) Nancollas, G.H.; Tang, R.; Phipps, R.J.; Henneman, Z.; Gulde, S.; Wu, W.; Mangood, A.; Russell, R.G.G.; Ebetino, F.H. Novel insights into actions of bisphosphonates on bone: Differences in interactions with hydroxyapatite. Bone 38 (2006), pp. 617–627. DOI: 10.1016/j.bone.2005.05.003

7) Kou-San, J.; James, R. D.; William, .M. Genomics-enabled discovery of phosphonate natural products

and their biosynthetic pathways. J. Ind. Microbiol Biotechnol , 2014, 41, pp. 345–356. DOI: 10.1007/s10295-013-1375-2

8) N. Z. Kiss, Z. R_adai, and G. Keglevich. Green synthesis of potentially bioactive hydroxyphosphonates and related derivatives. Phosphorus, Sulfur, and Silicon and the Related Elements, 2019, 194, 10, pp. 1003-1006. https://doi.org/10.1080/10426507.2019.1630407

9) Johan, N.; Erik De, C. Antiviral Drug Susceptibility of Human Herpesvirus 8. Antimicrobial Agents and Chemotherapy, 41, 12, 1997, pp. 2754–2756. DOI:10.1128/AAC.41.12.2754

10) Pawel, K.; Barbara, L. Application of bacteria and fungi as biocatalysts for the preparation of optically active hydroxyphosphonates. Journal of Molecular Catalysis B: Enzymatic, 2004, 29, pp. 99–104. DOI:10.1016/j.molcatb.2003.12.013

11) Edgar, A.; Eduardo, A.; Ana S.; Carlos, del P. Synthesis of N-Alkyl-(a-Aminoalkyl)Phosphine Oxides and Phosphonic Esters as Potential HIV-Protease Inhibitors, Starting from α-Aminoacids. Synlett, 2000, 5, pp. 698–700. DOI: 10.1055/s-2000-6615

12) Reddi Mohan, N. K.; Hye, R. L.; Jiafu, C.; Jin-Wookm, Y.; Il, K. Phospho sulfonic acid: an efficient and recyclable solid acid catalyst for the solvent-free synthesis of α-hydroxyphosphonates and their anticancer Properties. New J. Chem, 2015, **39**, 3916-3922. DOI: 10.1039/c5nj00312a

13) Sujatha, B.; Mohan, S.; Subramanyam, Ch.; Prasada Rao, K. Microwave-assisted synthesis and anti-inflammatory activity evaluation of some novel α-aminophosphonates. Phosphorus, Sulfur, and Silicon, 2017, 10, 192, pp. 1110-1113. DOI:10.1080/10426507.2017.1331233

14) Kalla Reddi, M. N.; Krishnammagari, S.K.; Palanisamy, A.; Chinnappareddy, B. R.; Ola, L. Synthesis of a-Hydroxyphosphonates and Their Antioxidant Properties. Arch. Pharm. Chem. Life Sci. 2012, 000, pp. 1–7. DOI: 10.1002/ardp.201200192

15) Dinesh, V. P.; Katherine, R. G.; Dcnis, E. R. Peptidic α-Hydroxy Phosphmyls C-Terminal Modification Methodology. Tetrahedron Letters, 1990, 31, 39, Pp. 5591-5594. DOI: 10.1016/s0040-4039(00)97904-8

16) Linhong, J.; Baoan, S.; Guoping, Z.; Ruiqing, X.; Sumei, Z.; Xingwen, G.; Deyu, H.; Song, Y. Synthesis, X-ray crystallographic analysis, and antitumor activity of N-(benzothiazole-2-yl)-1-(fluorophenyl)-O,O-dialkyl-*a*-aminophosphonates. Bioorganic & Medicinal Chemistry Letters, 2006, 16, pp. 1537–1543. DOI:10.1016/j.bmcl.2005.12.041

17) Kenneth, M. H.; Cynthia, S. D. Phosphonate prodrugs: an overview and recent advances. Future Med. Chem. 2019, 11, 13, pp. 1625–1643. DOI: 10.4155/fmc-2018-0591

18) Pudovik, A. N.; Konovalova, I. V. Addition reaction of esters of phosphorus (III) acids with unsaturated systems. Synthesis, 1979, 2, pp. 81-96. DOI: 10.1055/s-1979-28566

19) Oskar, G.; Chester, G.; William, R.; James, S. Bromomagnesium salts of dialkyl phosphites as intermediates in the synthesis of substituted hydroxymethyl phosphonic acid esters J. Am.

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JCHR (2024) 14(6), 2830-2840 | ISSN:2251-6727

Chem. Soc., 1953, 75, 14, pp. 3591-3592. https://doi.org/10.1021/ja01110a508

20) Petra, R.V.; Gerhard, H.; György, K. Synthesis of 3-diethylphosphonoyl-2-hydroxy-prop-2-ylphosphonate and -phosphine oxide derivatives *via* the Pudovik reaction of diethyl 2-oxopropylphosphonate on the surface of Al_2O_3/KF. Tetrahedron letters, 2021, 68, pp. https://doi.org/10.1016/j.tetlet.2021.152902

21) Sardarian, A.R..; Kaboudin, B. Surface mediated solid phase reactions: preparation of diethyl hydroxyarylmethylphosphonates on the surface of magnesia; Synthetic Comm. 1997, 27, pp. 543. http://dx.doi.org/10.1080/00397919708003324

22) Smaardijk, A. A.; Noorda, S.; Bolhuis, F.; Wynberg, H.; The absolute configuration of α-hydroxyphosphonates; Tetrahedron lett. 26, pp. 493. https://doi.org/10.1016/S0040-4039(00)61920-2

23) Vincent, J.B.; Kevin, J.K.; Christopher, D.S. Reactions of chiral phosphorus acid diamides: The asymmetric synthesis of chiral α-hydroxy phosphonamides, phosphonates and phosphonic acids. J. Org. Chem. 1995, 60, pp. 931-940. https://doi.org/10.1021/jo00109a025

24) Swapnil, S. S.; Amol, H. K.; Madhav, N. W.; Charansingh, H. G.; Bapurao, B. S.; Murlidhar, S. S. Ammonium metavanadate: an effective catalyst for synthesis of α-hydroxyphosphonates. Arkivoc, 2009, (ii) pp. 138-148. DOI:10.3998/ARK.5550190.0010.215

25) Francoise T.B.; Andre F.; Synthesis of 1-hydroxyalkanephosphonic esters on alumina. Synthesis, 1982, 11, pp. 916. DOI: 10.1055/s-1982-29993

26) Tsutomu, Y.; Takehiro, Y.; Shiroshi, S.. Enantioselective synthesis of α-hydroxyphosphonates throughasymmetric Pudovik reactions with chiral lanthanoid and titanium alkoxides. J. Chem. Soc., Perkin Trans. 1997, 1, pp. 1527-1533. https://doi.org/10.1039/A608161D

27) Waldemar, G.; Mirosław, S. The Preparation of Dialkyl 1-Hydroxyalkylphosphonates in the Reaction of Trialkyl Phosphites with Oxonium Salts derived from Aldehydes or Ketones. Synthesis, 2006, 18, pp. 3019–3024. DOI: 10.1055/s-2006-950200

28) Mahmood, T.; Akbar, H.; Mohammad, A. K.; Moslem, M. L.; Behi, Z.; Samad, K. Amberlyst-15 as a Heterogeneous Reusable Catalyst for the Synthesis of -Hydroxy Phosphonates in Water. Synlett 2007, No. 15, pp. 2347–2350. DOI: 10.1055/s-2007-985595

29) Najmedin, A.; Mohammad, R. S. Lithium Perchlorate Diethyl Ether Solution: A Highly Efficient Media for the Abramov Reaction. Phosphorus, Sulfur, and Silicon, 2003, 178, pp. 1255–1259. DOI: 10.1080/10426500390200530

30) Akbar, H.; Afsaneh, A.; Samad, K.; Mahmoud, T. Hydrophosphonylation of aldehydes catalyzed by guanidine hydrochloride in water. Catalysis Communications, 2006, 7, pp. 982–984. DOI:10.1016/j.catcom.2006.04.014

31) Zhongjiao, R.;,Weigud, C.; Weiqi, T. The Knoevenagel Condensation Reaction of Aromatic Aldehydes with Malononitrile by Grinding in the absence of solvents and catalysts. Synthetic Communications, 2002, 32, 22, pp. 3475–3479. DOI: 10.1081/SCC-120014780

32) Fumio, T.; Koichi, T.; Ayako, S. Host-Guest Complex Formation by a Solid-Solid Reaction. J. Chem. Soc., Chem. Commun., 1987, pp. 279-280. https://doi.org/10.1039/C39870000279

33) Ajay, K. B.; Suhas, P.; Subhendu, N. G.; Goutam, C.; Maghar, S. M. A simplified green chemistry approach to the Biginelli reaction using 'Grindstone Chemistry'. Tetrahedron Letters, 2004, 45, pp. 8351–8353. DOI:10.1002/chin.200507144

34) Gopalpur, N. Organic synthesis under solvent free condition: An environmentally benign procedure-I. Resonance, 2002, 7, pp. 59-68. https://doi.org/10.1007/BF02835544

35) Patil, M.P.; Patil, R.H., Maheshwari, V. L. Biological Activities and Identification of Bioactive Metabolite from Endophytic Aspergillus flavus L7 Isolated from Aegle Marmelos. Curr Microbiol (2015) 71:39–48. DOI 10.1007/s00284-015-0805-y