Phosphorus, Sulfur, and Silicon and the Related Elements

ISSN: 1042-6507 (Print) 1563-5325 (Online) Journal homepage: https://www.tandfonline.com/loi/gpss20

Polyethylene glycol (PEG-400): An efficient one-pot green synthesis and anti-viral activity of novel α-diaminophosphonates

Harika Patnala, Hanna S. Abbo, Krishna Murthy Potla, Salam J. J. Titinchi & Sampath Chinnam

To cite this article: Harika Patnala, Hanna S. Abbo, Krishna Murthy Potla, Salam J. J. Titinchi & Sampath Chinnam (2019) Polyethylene glycol (PEG-400): An efficient one-pot green synthesis and anti-viral activity of novel α-diaminophosphonates, Phosphorus, Sulfur, and Silicon and the Related Elements, 194:11, 1035-1039, DOI: 10.1080/10426507.2019.1597365

To link to this article: https://doi.org/10.1080/10426507.2019.1597365

PHOSPHORUS, SULFUR, AND SILICON AND THE RELATED ELEMENTS
2019, VOL. 194, NO. 11, 1035–1039
https://doi.org/10.1080/10426507.2019.1597365

Polyethylene glycol (PEG-400): An efficient one-pot green synthesis and anti-viral activity of novel α-diaminophosphonates

Harika Patnala[a], Hanna S. Abbo[b,c], Krishna Murthy Potla[d], Salam J. J. Titinchi[c,b], and Sampath Chinnam[e]

[a]Department of Chemistry, Andhra Loyola Institute of Engineering and Technology, Vijayawada, Andhra Pradesh, India; [b]Department of Chemistry, University of Basrah, Basrah, Iraq; [c]Department of Chemistry, University of the Western Cape, Bellville, Cape Town, South Africa; [d]Department of Chemistry, Bapatla Engineering College, Acharya Nagarjuna University Post Graduate Research Centre, Bapatla, Andhra Pradesh, India; [e]Department of Chemistry, B.M.S. College of Engineering, Bengaluru, Karnataka, India

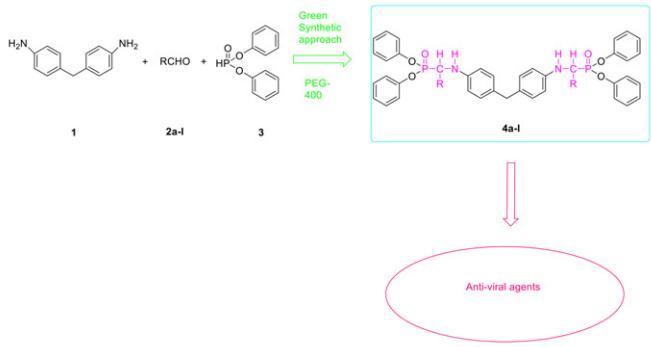
ABSTRACT

An efficient and eco-friendly protocol has been accomplished for a series of novel α-diaminophosphonates by a one-pot, three-component system *via* Kabachnik-Fields reaction of 4,4′-methylenedianiline, a variety of aryl/heteroaryl aldehydes and diphenylphosphite employing polyethylene glycol (PEG-400) as a green solvent at 80 °C. All products were obtained in good to excellent yields (80–95%). The identity of the new synthesized compounds was confirmed by IR, ^{1}H, 13C, and 31P NMR, LC-MS and elemental analysis. *In vivo* anti-viral activity was evaluated against tobacco mosaic virus (TMV). Compounds **4b**, **4c**, **4j** and **4k** exhibited the highest anti-viral activities against tobacco mosaic virus (TMV) when compared with the standard drug ningnanmycin.

ARTICLE HISTORY
Received 24 January 2019
Accepted 10 March 2019

KEYWORDS
Green synthesis; α-diaminophosphonates; anti-viral activity; Kabachnik-Fields reaction

GRAPHICAL ABSTRACT



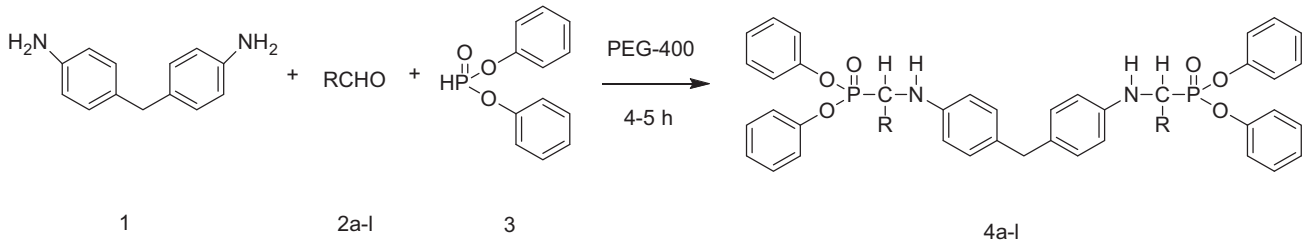
Introduction

Viral plant diseases can be found worldwide and are a serious hazard to modern agriculture. Although plant viruses are genetically rather simple, they are difficult to prevent or control and have devastating impact on crop growth. Thus plant virus is a type of plant disease, known as 'plant cancer'. During recent years, the influence of climate anomalies and the areas of crops affected by plant virus disease are increasing, resulting in tremendous economic losses in the world. The tobacco mosaic virus (TMV), one of the most important classes of common viral diseases occurring in plants, is a rod-shaped virus composed of single-stranded RNA encapsulated in a coat protein capsid. This virus seriously affects the quality, quantity, yield of tobacco and causes large economic losses. A few anti-viral agents are currently available in reality, and almost no treatment can control TMV effectively. As a consequence, development of novel, highly efficient, environmental benign new anti-viral agents through chemical synthesis has become the vital area of research for elimination and/or prevention of attack by TMV. Ningnanmycin can inhibit virus replication effectively and suppress virus symptoms.

Organophosphorus compounds are biologically active molecules and are widely applied in the areas of industrial, agricultural, organic, bioorganic and medicinal chemistry as well as in nanotechnology, owing to their unique physicochemical and biological properties.[1] Their utility as reagents and potential synthons in organic synthesis is also gaining increased attention.[2] The α-aminophosphonate moiety is a versatile and novel pharmacophore due to the broad spectrum of biological activities exhibited by

CONTACT Salam J. J. Titinchi stitinchi@uwc.ac.za Department of Chemistry, University of Basrah, Basrah, Iraq; Department of Chemistry, University of the Western Cape, Bellville, Cape Town, South Africa; C. Sampath sampathchinnam@gmail.com Department of Chemistry, B.M.S. College of Engineering, Bengaluru, Karnataka, India.

Supplemental data for this article can be accessed on the publisher's website at https://dx.doi.org/10.1080/10426507.2019.1597365.



Scheme 1. Synthesis of α-Diaminophosphonates (**4a**-**l**).

compounds bearing this structural unit. α-Aminophosphonates are an important class of compounds, which have a reduced level of toxicity and great ability to substitute naturally occurring α-amino acids (mimetics). Therefore they show great potential applications in living organisms. As a result, they are effective aminopeptidase inhibitors[3] or anti-viral agents. α-Aminophosphonates and their derivatives are interesting synthetic targets because of their significant applications in agriculture as plant growth regulators,[4] herbicides,[5] pesticides,[6] fungicides,[4] in medicine as anti-cancer agents,[7] enzyme inhibitors,[8] peptide mimics,[9] peptidases and proteinases,[10] and antibiotics.[11] They can also suppress the growth of various tumors and viruses.[12]

An large number of synthetic methods for the synthesis of α-aminophosphonates have been reported *via* Pudovik reaction, Mannich type and Kabachnik-Fields reaction. A one-pot, three-component reaction of amines, aldehydes or ketones, and dialkyl, or diaryl phosphonates *via* Kabachnik-Fields (phospha-Mannich) reaction[13] is a straight forward and widely applied methods for the construction of carbon-phosphorus bonds. In a few previous reports, this reaction was accomplished in straight-forward, one-pot procedures without any catalysts.[14] Kabachnik-Fields reaction can be performed by acidic or basic catalysts, microwave irradiation, or by heating.[15] A variety of Lewis acid catalysts, such as $FeCl_3$,[16] $LaCl_3$,[17] $CeCl_3{\cdot}7H_2O$,[18] $BiCl_3$,[19] $InCl_3$,[20] $LiClO_4$,[21] $In(OTf)_3$,[22] $Al(H_2PO_4)_3$,[23] $TaCl_5$–SiO_2[24] and solid acids (montmorillonite KSF, silica sulfuric acid, Amberlyst-15, and Amberlite-IR 120)[25] have been used. Base catalysts were also used such as potassium fluoride on alumina,[26] lithium diisoppropylamide (LDA)[27] and 1,8-diazabicycloundec-7-ene (DBU).[28] However, these methodologies endure from certain disadvantages such as use of prolonged reaction times, unsatisfactory product yields, lack of generality, toxic organic solvents, stoichiometric amounts of catalysts, harsh reaction conditions, expensive and moisture sensitive catalysts. Consequently, the development of a more efficient, eco-friendly synthetic protocol which is simple and cost-effective remains an ever-challenging objective both in academia and industrial research. The most significant principles of green chemistry are atom economy, less usage or no wastage of solvents, and usage of green solvents. The usage of a noticeably benign and inexpensive solvent like polyethylene glycol (PEG) could consequently yield noteworthy "green" chemistry benefits. PEG has been explored as a novel, powerful, eco-friendly reaction medium for several organic transformations due to its interesting properties such as nontoxicity, inexpensive, readily recyclable, safe, natural, non-flammable, biocompatibility, and biodegradable. This background encouraged us to employ PEG as reaction medium and surprisingly, it worked successfully without use of any organic solvent and catalyst.

Entry	R
4a	3-pyridinyl
4b	3-thiophenyl
4c	2-furanyl
4d	4-NO_2-C_6H_4
4e	3-pyrrolyl
4f	4-F-C_6H_4
4g	4-pyridinyl
4h	3-furanyl
4i	4-Cl-C_6H_4
4j	2-thiophenyl
4k	3-indolyl
4l	3-Br-C_6H_4

In this involvement and in continuation of our ongoing research efforts for environmentally benign protocol for various organic transformations,[29] we herein report the use of 4,4′-methylenedianiline and PEG in an efficient one-pot, three-component green synthesis and *in vivo* anti-viral activity of α-diaminophosphonates (Scheme 1). To the best of our knowledge, this is the first report on *in vivo* anti-viral activity and on the synthesis of α-diaminophosphonates employing 4,4′-methylenedianiline and PEG-400.

Results and discussion

In the current investigation, α-diaminophosphonates (**4a**-**l**) were synthesized by a one-pot, three-component protocol *via* Kabachnik-Fields reaction of 4,4′-dimethyleneaniline (**1**), a variety of substituted aryl/heteroaryl aldehydes (**2a**-**l**) and diphenylphosphite (**3**) using PEG-400 as a solvent at 80 °C during 4–5 h (Scheme 1) in good to excellent yields (80–95%).

To optimize the reaction conditions, the reaction of 4,4′-dimethyleneaniline (**1a**), 3-pyridine aldehyde (**2a**) and diphenylphosphite (**3**) were considered. The effect of various solvents on the reaction was examined and the results are outlined in Table S1. Among all the solvents screened, the best results were found when the reaction was carried out using PEG-400, which gave excellent yield (93%) of **4a** (Table S2, entry 5; Supplementary Material). In case of the reactions with other solvents such as ethanol, tetrahydrofuran (THF), toluene, and acetonitrile (MeCN), the times of reaction increased and comparatively poor yields were obtained (Table S2, entries 1–4; Supplementary Materials).

Inspired by the above accomplishments, we further explored the reaction with several aldehydes and diphenylphosphite in PEG-400 to afford α-diaminophosphonates. The results are summarized in Table S1 (Supplementary Materials).

All the chemical structures of the newly synthesized compounds (**4a**-**l**) were confirmed by spectral and elemental analysis data. The characteristic IR spectra showed typical stretching absorptions in the region 3472–3239 cm^{-1} for NH, 1289–1210 cm^{-1} for P = O, and 765–740 cm^{-1} for P–$C_{(aliphatic)}$, which confirms the functional groups for the title compounds.[30] ^{1}H NMR spectra displayed for the aromatic protons a complex pattern in the chemical shift range δ 6.30–8.56. The ^{1}H NMR signal of the methine proton (PCH) was observed as a doublet in the range δ 5.76–5.85 (J = 11.0–16.2 Hz) owing to its coupling with phosphorus. The NHCH proton exhibited a doublet[31] in the range δ 4.30–5.45 (J = 4.2–9.0 Hz) due to its coupling with the neighboring proton. The 31P NMR chemical shifts appeared in the region δ 20.4–27.3 confirming the presence of a phosphonate group[32] in the synthesized compounds. Furthermore, the 13C NMR spectra of the title compounds show signals in the predicted regions.[33] The mass spectral data confirm the identity of the new compounds in accordance with their respective molecular formulae.

Anti-viral activity

In vivo anti-viral activity of all the compounds (**4a**-**l**) were screened against TMV, and ningnanmycin was used as a standard. Table S3 (Supplementary Materials) represents the result of *in vivo* inactivation rate, protective effect, and curative effects of α-diaminophosphonates (**4a**-**l**) against TMV. Compounds **4b**, **4c**, **4j** and **4k** showed the highest inactivation of infection (inhibition rate) at 84.2 ± 0.9, 83.6 ± 0.7, 82.8 ± 0.5, and 84.5 ± 1.4, respectively. The infection protective effects of **4b**, **4c**, **4j** and **4k** were determined at 58.2 ± 0.7, 58.4 ± 0.4, 58.1 ± 0.4, and 58.6 ± 0.7, and the infection curative effects of **4b**, **4c**, **4j** and **4k** were observed at 57.7 ± 0.7, 56.1 ± 0.5, 56.5 ± 1.4 and 56.8 ± 0.7, respectively (Table S3). Chlorophyll is the photosynthetic component of plants which is responsible for photosynthesis, which is the most basic life process of green plants. The extent of viral infection in plants leads to proliferation, expansion and destruction of the chloroplast, and these factors are retarding the production of chlorophyll, which consequently leads to leaf chlorosis and mosaic. It reduces the photosynthetic pigment in TMV infected leaves. The host's resistance of TMV infected leaves is enhanced when these leaves are treated with anti-viral agents. Moreover, the efficacy of the potent title compounds **4b**, **4c**, **4j** and **4k** on the chlorophyll content in tobacco mosaic leaves was examined and the results are given in Table S4 (Supplementary Material). The results obtained show that, after treating the TMV inoculated leaves with compounds **4**b, **4c**, **4j** and **4k**, the chlorophyll content in virus gradually increased during 1–5 days and reached the highest value on the 5th day. Among them, compounds **4b** and **4k** exhibited better effectiveness, when compared with compounds **4c** and **4j**. It is evident that **4b**, **4c**, **4j** and **4k** destroy the virus of the tobacco, increasing hosts resistance toward diseases and significantly enhance the chlorophyll content.

Experimental

All chemicals and solvents were purchased from Sigma-Aldrich and used without further purification. Melting points were determined in open capillaries with Guna digital melting point apparatus expressed in °C and are uncorrected. All products were purified by column chromatography on silica gel of 60–120 mesh. The infrared (IR) spectra were recorded as KBr pellets on a Perkin-Elmer FT-IR 1000 spectrophotometer. ^{1}H, 13C and 31P NMR spectra were recorded as solutions in $CDCl_3$ with a Varian 400 MHz spectrometer operating at 400 MHz for ^{1}H, 100 MHz for 13C, and 300 MHz for 31P. The ^{1}H and 13C chemical shifts are given in ppm using tetramethylsilane (TMS) as an internal standard and 31P NMR chemical shifts are referred to 85% H_3PO_4. Chemical shifts (δ) are given in parts per million (ppm) and coupling constants (J) in Hertz (Hz). ESI mass spectra were recorded with an LCMS-2010A Shimadzu spectrometer and elemental analysis was performed with a Thermo Finnigan instrument. Abbreviations used for ^{1}H NMR signals are: s = singlet, d = doublet, t = triplet and m = multiplet. The Supplementary Materials contains sample ^{1}H, 13C 31P NMR and mass spectra for products **4d** and **4i** (Figures S1–S8).

General procedure for the synthesis of α-diaminophosphonates (4a-l)

A mixture of 4,4′-methylenedianiline **1** (0.001 mol), the aryl/heteroaryl aldehyde **2a-l** (0.002 mol), diphenylphosphite **3** (0.002 mol) and PEG-400 (10 mL) was allowed to react in a 50 mL round-bottomed flask for 4–5 h at 80 °C (Scheme 1). The progress of the reaction was monitored by TLC (hexane:ethyl acetate, 7:3). After completion of the reaction, the crude mixture was worked up in ice-cold water. The product, that separated out, was filtered and the filtrate was evaporated to remove water, leaving PEG behind. This crude product was further purified by column chromatography on silica gel (60–120 mesh) using hexane: ethyl acetate (7:3) as a mobile phase to afford the analytically pure α-diaminophosphonates (**4a**-**l**) in good to excellent yields.

Conclusion

In conclusion, a green, mild, and efficient one-pot protocol for the synthesis of novel α-diaminophosphonates in good to excellent yields (80–95%) has been established. The compounds **4b**, **4c**, **4j** and **4k** showed most potent *in vivo* anti-viral activity against tobacco mosaic virus (TMV) as compared with the standard drug ningnanmycin. The notable advantages of this current method are shorter reaction times, excellent yields of the products, mild experimental conditions, inexpensive solvent, simple work-up procedure, biodegradable nontoxic solvent, reusable green solvent and

potentially valuable new anti-viral organophosphorus compounds.

Acknowledgements

The authors are grateful to CKS Pharma Labs (P) Ltd., Vedadri, Krishna District, Jaggayyapeta, Andhra Pradesh, India for the assistance.

Disclosure statement

There are no potential conflict of interest disclosed by the authors.

ORCID

Salam J. J. Titinchi http://orcid.org/0000-0002-5785-5021
Sampath Chinnam http://orcid.org/0000-0002-5334-9076

References

[1] Moonen, K.; Laureyn, I.; Stevens, C. V. Synthetic Methods of Azaheterocyclic Phosphonates and Their Biological Activity. *Chem. Rev.* **2004**, *104*, 6177–6215. DOI: 10.1021/cr030451c.

[2] Bartlett, P. A.; Hanson, J. E.; Giannousis, P. P. Potent Inhibition of Pepsin and Penicillopepsin by Phosphorus-Containing Peptide Analogues. *J. Org. Chem.* **1990**, *55*, 6268–6274. DOI: 10.1021/jo00313a012.

[3] Lejczak, B.; Kafarski, P.; Zygmunt, J. Inhibition of Aminopetidases by Aminophosphonates. *Biochemistry* **1989**, *28*, 3549–3555. DOI: 10.1021/bi00434a060.

[4] Maier, L.; Spörri, H. Organic Phosphorus Compounds 96. Resolution of 1-Amino-2-(4- Fluorophenyl)Ethylphosphonic Acid as Well as Some di- and Tripeptides. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *61*, 69–75. DOI: 10.1080/10426509108027339.

[5] Natchev, I. A. Synthesis, Enzyme-Substrate Interaction, and Herbicidal Activity of Phosphoryl Analogues of Glycine. *Liebigs Ann. Chem.* **1988**, *9*, 861–867. DOI: 10.1002/jlac.198819880908.

[6] Fest, C.; Schmidt, K. J. *The Chemistry of Organophosphorus Pesticides*; Springer-Verlag: Berlin. **1982**, vol. 12.

[7] Kafarski, P.; Lejczak, B. Aminophosphonic Acids of Potential Medicinal Importance. *Curr. Med. Cmcaca.* **2001**, *1*, 301–302. DOI: 10.2174/1568011013354543.

[8] Allen, M. C.; Fuhrer, W.; Tuck, B.; Wade, R.; Wood, J. M. Renin Inhibitors: Synthesis of Transition-State Analogue Inhibitors Containing Phosphorus Acid Derivatives at the Scissile Bond. *J. Med. Chem.* **1989**, *32*, 1652–1661. DOI: 10.1021/jm00127a041.

[9] Kafarski, P.; Lejczak, B. Biological Activity of Aminophosphonic Acids. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *63*, 193–215. DOI: 10.1080/10426509108029443.

[10] Miller, D. J.; Hammond, S. M.; Anderluzzi, D.; Bugg, T. D. H. Aminoalkylphosphinate Inhibitors of D-Ala-D-Ala Adding Enzyme. *J. Chem. Soc., Perkin Trans. 1* **1998**, *1*, 131–142. DOI: 10.1039/a704097k.

[11] Bhatia, M. S.; Pawanjit, P. Phosphorus-Containing Heterocycles as Fungicides: Synthesis of 2,2′-Diphenylene Chlorophosphonate and 2, 2′-Diphenylenechlorothiophosphonate. *Experientia* **1976**, *32*, 1111. DOI: 10.1007/BF01927572.

[12] (a) Oleksyszyn, J.; Powers, J. C. Irreversible Inhibition of Serine Proteases by Peptide Derivatives of (α-aminoalkyl)Phosphonate Diphenyl Esters. *Biochemistry* **1991**, *30*, 485–493. DOI: 10.1021/bi00216a026. (b) Green, D.; Patel, G.; Elgendy, S.; Baban, J. A.; Claeson, G.; Kakkar, V. V.; Deadman, J. The Facile Synthesis of O, O-Dialkyl 1-Aminoalkanephosphonates. *Tetrahedron Lett.* **1993**, *34*, 6197–6920. DOI: 10.1016/S0040-4039(00)91830-6.

[13] (a) Hou, J. T.; Gao, J. W.; Zhang, Z. H. $NbCl_5$: An Efficient Catalyst for One-Pot Synthesis of α-Aminophosphonates under Solvent-Free Conditions. *Appl. Organomet. Chem.* **2010**, *25*, 47–53. DOI: 10.1002/aoc.1687. (b) Sun, G. Y.; Hou, J. T.; Dou, J. J.; Lu, J.; Xue, T.; Zhang, Z. H. Xanthan Sulfuric Acid as an Efficient Biodegradable and Recyclable Catalyst for the One-Pot Synthesis of α-Aminophosphonates. *J. Chin. Chem. Soc.* **2010**, *57*, 1315–1320. DOI: 10.1002/jccs.201000194. (c) Mohammadiyan, E.; Ghafuri, H.; Kakanejadifard, A. A New Procedure for Synthesis of α-Aminophosphonates by Aqueous Formic Acid as an Effective and Environment-Friendly Organocatalyst. *J. Chem. Sci.* **2017**, *129*, 1883–1891. DOI: 10.1007/s12039-017-1394-z. (d) Yu, Y. Q.; Xu, D. Z. A Simple and Green Procedure for the One-Pot Synthesis of α-aminophosphonates. *Synthesis.* **2015**, *47*, 1869–1876. DOI: 10.1055/s-0034-1380523.

[14] Chandrasekhar, S.; Narsihmulu, C. H.; Shameen, S. S.; Saritha, B.; Jayaprakash, S. Solvent and Catalyst Free, Three-Component Coupling of Carbonyl Compounds, Amines and Triethylphosphite: A New Synthesis of α-Aminophosphonates. *Synlett* **2003**, *4*, 505–506. DOI: 10.1055/s-2003-.37508.

[15] Ranu, B. C.; Hajra, A. A Simple and Green Procedure for the Synthesis of α-Aminophosphonate by a One-Pot Three Component Condensation of Carbonyl Compounds, Amine and Diethyl Phosphate without Solvent and Catalyst. *Green Chem.* **2002**, *4*, 551–554. DOI: 10.1039/B205747F.

[16] Rezai, Z.; Firouzabadi, H.; Iranpoor, N.; Ghaderi, A.; Jafari, A. A.; Zare, H. R. Design and One-Pot Synthesis of α-Aminophosphonates and Bis(α-Aminophosphonates) by Iron (III) Chloride and Cytotoxicity. *Eur. J. Med. Chem.* **2009**, *44*, 4266–4275. DOI: 10.1016/j.ejmech.2009.07.009.

[17] Xu, F.; Luo, Y.; Wu, J.; Shen, Q.; Chen, H. Facile One-Pot Synthesis of α-Aminophosphonates Using Lanthanide Chloride as Catalyst. *Heteroatom Chem.* **2006**, *17*, 389–392. DOI: 10.1002/hc.20219.

[18] Abbas, A. J.; Mahshid, N.; Mohammad, A. D. $CeCl_3 \cdot 7H_2O$ Catalyzed One-Pot Kabachnik- Fields Reaction: A Green Protocol for Three-Component Synthesis of α-Aminophosphonates. *Heteroat. Chem.* **2010**, *21*, 397–403. DOI: 10.1002/hc.20635.

[19] Zhan, Z. P.; Li, J. P. Bismuth (III) Chloride-Catalyzed Three, Component Coupling: Synthesis of α-Aminophosphonates. *Synth. Commun.* **2005**, *35*, 2501–2504. DOI: 10.1080/00397910500212692.

[20] Ranu, B. C.; Hajra, A.; Jana, U. General Procedure for the Synthesis of α-Amino Phosphonates from Aldehydes and Ketones Using Indium (III) Chloride as a Catalyst. *Org. Lett.* **1999**, *1*, 1141–1143. DOI: 10.1021/ol990079g.

[21] Azizi, N.; Saidi, M. R. Lithium Perchlorate-Catalyzed Three Component Coupling: A Facile and General Method for the Synthesis of α-Aminophosphonates under Solvent-Free Conditions. *Eur. J. Org. Chem.* **2003**, *23*, 4630–4633. DOI: 10.1002/ejoc.200300479.

[22] Ghosh, R.; Maiti, S.; Chakraborty, A.; Maiti, D. K. $In(OTf)_3$ Catalyzed Simple One-Pot Synthesis of α-Aminophosphonates. *J. Mol. Catal. A* **2004**, *210*, 53–57. DOI: 10.1016/j.molcata.2003.09.020.

[23] Maghsoodlou, M. T.; Habibi-Khorassani, S. M.; Heydari, R.; Hazeri, N.; Sajadikhah, S. S.; Rostamizadeh, M. M. $Al(H_2PO_4)_3$ as an Efficient and Reusable Catalyst for One-Pot Three-Component Synthesis of α-Aminophosphonates under Solvent-Free Conditions. *Chin. J. Chem.* **2010**, *28*, 285–288. DOI: 10.1002/cjoc.201090067.

[24] Chandrasekhar, S.; Prakash, S. J.; Jagadeshwar, V.; Narsihmulu, C. Three Component Coupling Catalyzed by $TaCl_5$-SiO_2: Synthesis of α-Amino Phosphonates. *Tetrahedron Lett.* **2001**, *42*, 5561–5563. DOI: 10.1016/S0040-4039(01)01053-X.

[25] Bhattacharya, A. K.; Rana, K. C. Amberlite-IR 120 Catalyzed Three-Component Synthesis of α-Amino Phosphonates in One Pot. *Tetrahedron Lett.* **2008**, *49*, 2598–2601. DOI: 10.1016/j.tetlet.2008.02.102.

[26] Texier-Boullet, F.; Lequitte, M. An Unexpected Reactivity of Simple Heterogeneous Mixture of γ-Alumina and Potassium Fluoride: 1-Hydroxyalkane Phosphonic Esters Synthesis from Non- Activated Ketones in Dry Media. *Tetrahedron Lett.* **1986**, *27*, 3515–3516. 4039(00)84837-6. DOI: 10.1016/S0040-.

[27] Blazis, V. J.; Koeller, K. J.; Spilling, C. D. Reactions of Phosphorus Acid Diamides: The Asymmetric Synthesis of α-Hydroxy Phosphonamides, Phosphonates and Phosphonic Acids. *J. Org. Chem.* **1995**, *60*, 931–940. DOI: 10.1021/jo00109a025.

[28] Pamies, O.; Backvall, J. E. An Efficient Route to Chiral α- and β-Hydroxyalkanephosphonates. *J. Org. Chem.* **2003**, *68*, 4815–4818. DOI: 10.1021/jo026888m.

[29] (a) Shrikhande, J. J.; Gawande, M. B.; Jayaram, R. V. A Catalyst-Free N-Benzyloxy-Carbonylation of Amines in Aqueous Micellar Media at Room Temperature. *Tetrahedron Lett.* **2008**, *49*, 4799–4803. DOI: 10.1016/j.tetlet.2008.05.010. (b) Singh, S. J.; Jayaram, R. V. Chemoselective *O-tert*-Butoxycarbonylation of Hydroxyl Compounds using $NaLaTiO_4$ as a Heterogeneous and Reusable Catalyst. *Tetrahedron Lett.* **2008**, *49*, 4249–4251. DOI: 10.1016/j.tetlet.2008.04.149.

[30] Sampath, C.; Naga Raju, C.; Venkata Rao, C. Synthesis, Spectral Characterization, Anti- Microbial and Anti-Oxidant Activities of Novel Phosphorylated Derivatives of Amlodipine. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2015**, *190*, 11–19. DOI: 10.1080/10426507.2014.909429.

[31] Uma Maheswara Rao, K.; Jayaprakash, S. H.; Nayak, S. K.; Suresh Reddy, C. Polyethylene Glycol in Water: A Simple and Environment Friendly Medium for C-P Bond Formation. *Cat. Sci. Technol.* **2011**, *1*, 665–1670. DOI: 10.1039/C1CY00295C.

[32] Pettersen, D.; Marcolini, M.; Bernardi, L.; Fini, F.; Herrera, P. R.; Sgarzani, V.; Ricci, A. Direct Access to Enantiomerically Enriched α-Aminophosphonic Acid Derivatives by Organocatalytic Asymmetric Hydroxyphosphonylation of Imines. *J. Org. Chem.* **2006**, *71*, 6269–6272. DOI: 10.1021/jo060708h.

[33] Lockhart, J. C.; Mc Donnell, M. B.; Tyson, P. D. Ligands for the alkali metals. Part 7. Synthesis and characterisation of crown ether macrocylces containing the di-1-naphthylmethyl unit as a novel steric barrier. *J. Chem. Soc., Perkin Trans.* **1983**, *1*, 2153-2159. DOI: 10.1039/p19830002153.