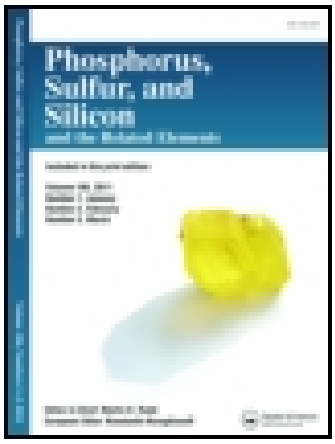

Phosphorus, Sulfur, and Silicon and the Related Elements

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Benzimidazolium Dicationic Ionic Liquid as an Efficient and Reusable Catalyst for the Synthesis of α-aminophosphonates and Bis (α-aminophosphonates) under Solvent-free Condition

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Benzimidazolium dicationic ionic liquid as an efficient and reusable catalyst for the synthesis of α-aminophosphonates and bis (α-aminophosphonates) under solvent-free condition

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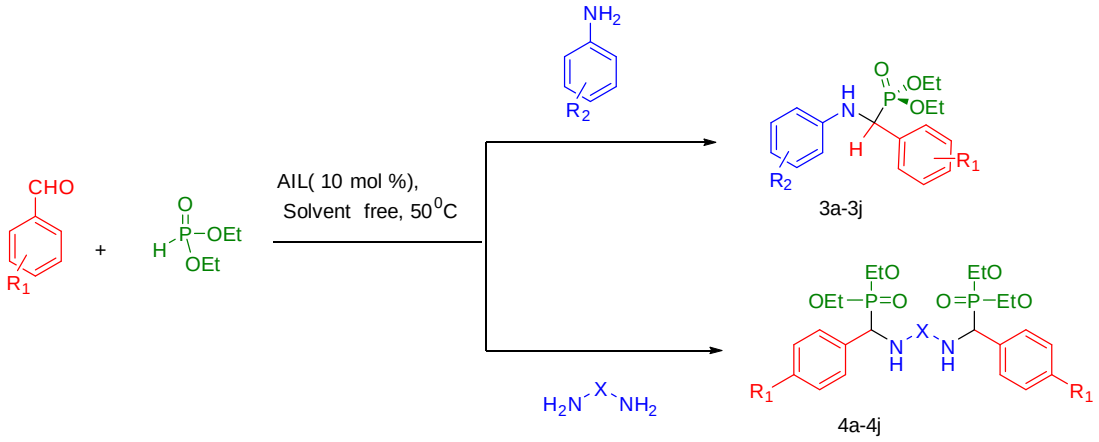
Abstract Benzimidazolium based on dicationic acidic ionic liquid (AIL)is designed, synthesized, and successfully used as a catalyst for the one-pot synthesis of α-aminophosphonates derivatives. The application of this acidic ionic liquid is studied in a new one-pot method for the synthesis of α-aminophosphonates derivatives under solvent-free conditions. The advantages of this method are the reusability of the catalyst, high conversion, short reaction time, and simple experimental procedure.



Keywords Acidic ionic liquid, Benzimidazolium cation, Reusable catalyst, α-Aminophosphonates

INTRODUCTION

In recent year ionic lidiuds(ILs) have received great attention due to their high thermal stability, broad liquid range, biological activities such as antiviral, antifungal and anticancer activities, catalyst in organic synthesis, analytical chemistry.[1]Dicationic ILs have also been used widely in various fields of Science. Dicationic ionic liquids based organic cation contain moeties imidazol,[2] pyridine,[3] 6alkyl/aryl[4] and chains contain alkyl, aryl, and alkoxy with different anion were used as catalysis in organic synthesis.[1a,1b,5]

Benzimidazoles have received significant attention because of their biological activities such as antihistaminic, antiphrastic, antiulcer, antihypertensive, antiviral, antifungal and anticancer activities. [6] Many reports are available that benzimidazole has been used as organic cations ionic lidiuds (ILs) in synthesis organic compound. [7]

As a part of our green technology program we would also like to disclose here a more practical green alternative for a new method to synthesize α-aminophosphonate by a three-component condensation reaction. The application of ionic liquids in the synthesis of α-aminophosphonates were reported.[8]

α-aminophosphonates are considered to be structural analogs of the corresponding esters of α-aminoacids have been reported to exert several pharmacological activities such as their potential usage as anticancer agents,[9] antiviral activities,[10] HIV protease,[11] anti-thrombotic agents,[12] inhibitors of protein tyrosine phosphatases,[13] peptide mimics [14] and enzyme inhibitors.[15]

Recently, nucleophilic addition of phosphite to imines, catalyzed by an acid or a base, has emerged as an important alternative for the synthesis of α-aminophosphonates. Typically, Lewis acids such as$SnCl_2$,[16] $Al(OTf)_3$,[17] $InCl_3$,[18] $Mg(ClO_4)_2$,[19] $Mg(OTf)_3$,[20] $CeCl_3.7H_2O$,[21] $FeCl_3$,[22]

TiO_2,[23] $NaHSO_4$-SiO_2,[24] nano Fe_3O_4[25] and ethyl ammonium nitrate [26] have been used as catalysts for this process. However, these reactions could not be carried out efficiently in a single step with carbonyl, amine and phosphite functionalities because amines and the water formed during imine formation can decompose or deactivate these Lewis acids.

Herein, we report the synthesis of dicationic acidic ionic liquid (AIL) which contains benzimidazolium cations, ethyleneoxy bridge and also a sulfonic acid group (That participates in dissolving organic compounds in AIL with its ethyleneoxy bridge) and SO_3H functional groups act as a Brønsted AIL catalyst. we describe an efficient method for the synthesis of α-aminophosphonates and bis-(α-aminophosphonates) through three-component reactions of aldehydes, amines, and diethyl phosphite using catalytic amounts of AIL under solvent-free conditions. (Scheme 1)

Scheme 1

RESULTS AND DISCUSSION

Preparation and characterization of dicationic acidic ionic liquid

We designed and synthesized AIL based on benzimidazolium cations with a triethylenoxy spacer. In this protocol, we first synthesized 1,2-bis(2-(1H-benzimidazol-1-yl)ethoxy)ethane through the reaction between benzimidazole and 1,2-bis(2- chloroethoxy)ethane in the presence of potassium hydroxide in DMSO.[27] Then, for acidic functionalization, we used chlorosulfonic acid in dry dichloromethane and AIL **(2)** was obtained in 96 % yield as a viscous oil (Scheme 2).

Scheme 2 Here

The IR spectrum of AIL showed a broad peak at 2700–3484 cm^{-1} related to the OH of the SO_3H groups. Moreover, two peaks observed in 1088 cm^{-1} and 1282 cm^{-1} correspond to the vibrational modes of N-SO_2 bond.

One of the key properties of Brønsted ILs is their Brønsted acidity which has a strong correlation to the catalytic activity of this compound in the many organic synthesis reactions[28]. SO_3H-functionalized AIL have been employed as Brønsted IL catalysts for the synthesis of several acid-catalyzed organic reactions. In recent years, there have been reports about Brønsted AIL based on the sulfonic acid group which have good activity.[7a,29] The purpose of the preparation of this AIL is to increase the solubility[7a] of the organic compounds in the AIL through triethyleneoxy spacer that increase its flexibility and hydrophobicity. Solubility of synthesized AIL was determined in several selected solvents at ambient temperature. In general dicationic ionic liquid showed good solubility in polar solvents, while insoluble in ethyl acetate, diethyl ether, cyclohexane, and toluene, that may be attributed to the bridged oxygen atoms in cations generating hydrogen bonding with polar solvent. In addition, longer oligo (ethylene glycol) chains may improve the hydrophobicity of the overall AIL.[30] In the synthesis of this AIL, the sulfonic acid group is covalently tethered to the AIL benzimidazolium cation and this part of the AIL can increase its hydrophilicity. So, features of both hydrophilicity and hydrophobicity are responsible for increasing the dissolution of organic compounds in this AIL.

The pH value for the mentioned AIL was determined using a 0.1 mol L^{-1} solution of IL and was titrated with 0.114 mol L^{-1} of NaOH (a solution of potassium hydrogen phetalate (KHP) was prepared at concentration 0.100 M. 25.00 ml of KHP solution was further used to standardized a

NaOH solution). The pH of the solution was measured using a calibrated glass electrode pH meter. The pH value of the AIL is 2.2. This AIL can be used as a catalyst in many different organic transformations.

The measurement of the acidic scale of this AIL was conducted on an UV-vis spectrophotometer with a basic indicator according to the literature reported previously.[7d,31,32] With the increase of acidic scale of the AIL, the absorbance of the unprotonated form of the basic indicator decreased. Whereas the protonated form of the indicator could not be observed because of its small molar absorptivity and its location, so the $[I]/[IH^+]$ (I represents indicator) ratio could be determined from themeasured absorbance differences after addition of AIL, and then the Hammett function H_0, was calculated by using Eq (1). This value could be regarded as the relative acidity of the IL

$$H_0=pK(I)_{aq} + \log [I]/[IH^+] \qquad \text{Eq (1)}$$

Under the same concentration of 4-nitroaniline (10 mg/L, pK_a=0.99) and AIL (5 mmol/L) in dichloromethane, we determined the H_0value of the AIL. The maximum absorbance of the unprotonated form of the indicator was observed at 350 nm in CH_2Cl_2. When AIL was added, the absorbance of the unprotonated form of the indicator decreased (Figure S 1, Supplemental Materials). The results obtained show the acidity strength of AIL (Table 1).

Table1 Here

Thermal gravimetric (TG) and derivative thermal gravimetric (DTA) analysis of AIL were studied in a range of temperature between 25 and 600 ºC with a temperature increase rate of 10°C.min^{-1} in a Argon atmosphere (Figure S2) .The TG and DTA of the catalyst showed three weight losses. The first observed in 80 ºC that related to loss H_2O, the second weight loss

observed after 320 ºC, and the three weight loss appears after 380 ºC. Therefore, AIL could be applied as catalysts below 320 ºC, and decomposed after 320 ºC.

The reaction of diethyl phosphite, 4-cholorobenzaldehyde and 4-methoxy aniline was optimized in different temperature and mol % of the catalyst. In the best conditions, the corresponding α-aminophosphonate was obtained in high yield at 50 ºC in the presence of 10mol % of the sulfonic acid functionalized dicationic ionic liquid (Table 2).

Table 2

In order to examine the scope of this process, several aromatic aldehydes and amines were reacted under the optimized conditions and the results are shown in (Table 3). Both either electron-donating or electron-withdrawing aldehydes and anilines reacted to form efficiently giving excellent yields of the expected α-aminophosphonates.

The synthesized compounds (**3a-3j**) gave satisfactory elemental analyses, and their molecular structure was confirmed by IR and ^{1}H, ^{13}C and ^{31}P NMR spectroscopy that was reported previously in literatures. The IR spectra showed the expected absorption bands at 2985–3305 and 1225–1236 cm^{-1}, which are attributed to NH and P=O stretching vibrations, respectively.[33] The ^{1}H NMR spectra of compounds, recorded in $CDCl_3$ solution, exhibit the signal of CHP proton as a doublet of doublet at 4.64and 4.70 ppm (**1a**).[34] The NH proton signal of (**3a**) appears as a triplet. There is a correlation between NH,CHP and P that decouplage P indicate correlation between NH, CHP and on addition of D_2O the NH signal disappeared and the signal of CHP that appeared as doublet, and the doublet at 55.4 ppm with $^{1}J_{PC}$ =155 Hz, observed in its ^{13}C NMR spectrum (Figure S3). The values are typical for the proton and carbon atom from a CHP fragment.[34] The methyl protons from the ethoxy groups give two triplets, owing to the

nonequivalence of these groups. The $POCH_2$ proton signals appear as three multiplets at about 3.60-4.20 ppm.

Bis(α-aminophosphonates) are interesting compounds, as they are multidentate ligands which may be used for the extraction of metals from solutions and they can be employed as the monomers for the preparation of macrocyclic or polymeric compounds carrying phosphonate and amine moieties. In addition, and more importantly, investigation of their biological activity would be of great interest.[35] Through this study, it was also investigated the applicability of the catalyst for the preparation of bis(α-aminophosphonates) via a one-pot three-component reaction of structurally diverse diamines (1,4-phenylenediamine and 4,4'-diaminobiphenyl) (1.0 mmol), electron-rich and electron-deficient aromatic aldehydes (2.0 mmol) and diethylphosphite(2.0 mmol) in the presence of AIL (10 mol%).

The reactions progressed well at 50 ºC and the desired bis(α-aminophosphonates) were produced in excellent isolated yields (85–96%) (Scheme 1, Table 4). However, 1,2-phenylenediamine and 1,3-phenylenediamine failed to react under similar reaction conditions.

Table 3, Table 4

One of the advantages of this AIL is its ability to be recycled from the reaction medium. We were able to readily separate the catalyst from the residue by washing with CH_2Cl_2. The catalyst was recovered by evaporation of the water of the aqueous layer at 50 ºC in a vacuum oven which gave 95 % yields and could be reused for the same experiment for four more times (Table 5). The ^1H NMR spectrum of the recycled AIL catalyst compared with the freshly prepared catalyst and at significant purity was observed.

Table 5 Here

This study compared with reported synthetic methods for the synthesis of α-aminophosphonate (Table 6). As is shown in Table 6, AIL afforded the products in higher yields and in extremely milder reaction conditions.

Table 6 Here

EXERIMENTAL

Materials and instrumentation

All reagents were purchased from Merck and used without further purification. The melting points of the products were determined with an Electrothermal Type 9100 melting point apparatus. The FT-IR spectra were recorded on an Avatar 370 FT-IR Thermal Nicolet spectrometer. The mass spectra were recorded on a 5973 Network Mass Selective Detector. The ^{1}H,^{13}C and ^{31}PNMR spectra were recorded on a Bruker AC 100 and Bruker DRX-400 Avance spectrometers at 400 ,161.99 and 100.65 MHz, respectively, using DMSO-d_6 or $CDCl_3$ as the deuterated solvents. Chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hz.

Synthesis of 1,2-bis(2-(1H-benzimidazol-1-yl)ethoxy)ethane (1):

A mixture of benzimidazole (20 mmol, 2.36 g) and potassium hydroxide (20 mmol, 1.792 g) in DMSO (25 ml) was stirred at 70 ºC for 0.5 h. After this time, 1,2-bis(2- chloroethoxy)ethane (10 mmol, 1.55 mL) was added to the reaction mixture and stirred for 24 h. The resulting mixture was poured into of water (100 mL) and extracted with methylene chloride (3 × 20 mL). The combined organic layer was washed with water (3 × 20 mL), dried with anhydrous $MgSO_4$, and concentrated to give 1,2-bis(2-(1H-benzimidazolimidazol-1-yl)ethoxy)ethane **(1)**.

^{1}H NMR ($CDCl_3$, 100 MHz) δ: 3.45 (s, 4H, $\underline{CH_2}O$), 3.76 (t, 4H, *J* = 4.6 Hz, $\underline{CH_2}O$), 4.64 (t, 4H, *J* = 4.6 Hz, $\underline{CH_2}O$), 7.50-8.00 (m, 8H, Ar), 9.55 (s, 2H, N$\underline{C}$HN).

Synthesis of 1,10-((ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(3-sulfo-1H-benzimidazol-3-ium) chloride (2):

A 100 mL round-bottomed flask was charged with 1,2-bis(2-(1H-benzimidazol-1-yl)ethoxy)ethane **(1)** (10 mmol, 3.50 g) in dry CH_2Cl_2(50 mL), and then chlorosulfonic acid (20 mmol, 1.32 mL was added dropwise over a period of 30 min at room temperature. Afterward, the reaction mixture was stirred for 1 h, and the CH_2Cl_2 was decanted. The residue was washed with dry CH_2Cl_2 (3×20 mL) and dried under vacuum to give 1,10-((ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(3-sulfo-1H-benzimidazol-3-ium) chloride **(2)** as a viscous colorless oil.

^{1}H NMR (DMSO, 400 MHz) δ: 3.40 (s, 4H, $\underline{CH_2}O$), 3.73 (t, 4H, J = 4.4 Hz. $\underline{CH_2}O$), 4.60 (t, 4H, J = 4.4 Hz, $\underline{CH_2}O$), 7.48-7.90 (m, 8H, Ar), 9.47 (s, 2H, N$\underline{CH}$N), 13.1 (b, 2H, $SO_3\underline{H}$). ^{13}C NMR ($CDCl_3$, 100 MHz) 46.8(O$\underline{C}H_2$), 68.0 (-O-$\underline{C}H_2\underline{C}H_2$-O-), 69.9 (-N-$CH_2\underline{C}H_2O$), 113.8(C7& C6), 114.8 (C5), 126.5 (C8), 130.6 (C4), 134.3(C9), 140.7(C2); m/z, calcd. for $C_{20}H_{24}Cl_2N_4O_8S_2$ $[M]^+$: 582.04, found: 582.0

General procedure for preparation of α-aminophosphonate (3a-3j).

To a mixture of aldehydes (1.0 mmol), anilines (1.0 mmol), and diethyl phosphite (1.0 mmol), AIL **(2)** (10 mol %) was added and stirred at 50ºC for appropriate time. After completion of the reaction as monitored by TLC, the mixture was washed with CH_2Cl_2 (3 × 3 mL). The combined extracts were filtered and the solvent was removed under reduced pressure to afford the crude product, which was purified by recrystallization from ethylacetate/n-Hexane. The catalyst, which

does not dissolve in CH_2Cl_2, remained in the residue. Selected ^1H, ^{13}C and ^{31}P NMR spectra for compound 3d are presented in the Supplemental Materials (Figures S 4 – S 6)

Selected spectroscopic data:

Diethyl (((4-chlorophenyl) amino) (4-methoxyphenyl) methyl) phosphonate (**3a**)[36]

Solid, Yield: 94%, m.p: 101-102 ºC.IR (ν_{max},cm^{-1}): 3293 (NH), 1234 (P=O), 1055(P-OEt); ^1H NMR ($CDCl_3$, TMS, 400 MHz): 1.15 (t, 3H, *J*=7.2 Hz, -P-OCH_2-$\underline{CH_3}$), 1.30 (t, 3H, *J*=7.2 Hz, -P-OCH_2-$\underline{CH_3}$), 3.60-3.75 (m, 1 H, -P-O$\underline{CH_2}$-CH_3), 3.74 (s, 3 H, Ar-O$\underline{CH_3}$), 3.90-4.05 (m, 1 H, -P-O$\underline{CH_2}$-CH_3), 4.0-4.20 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 4.67 (dd, 1H, $^1J_{PH}$=23.2,^2J=7.6 Hz, -$\underline{CH}$P), 4.92 (m, 1H, NH), 6.53 (d, 2H, *J*=8.8 Hz, Ar), 6.88 (d, 2H, *J*=8.4 Hz, Ar), 7.05 (d, 2H, *J*=8.8 Hz, Ar), 7.38 (d, 2H, *J*=8.4 Hz, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.2 (d, $^3J_{cp}$=6 Hz,-$OCH_2\underline{C}H_3$), 16.4 (d, $^3J_{cp}$= 6 Hz,- $OCH_2\underline{C}H_3$), 55.2(Ar-O$\underline{C}H_3$), 55.4 (d, $^1J_{pc}$= 152 Hz, $\underline{C}$HP), 63.1 (d, $^2J_{pc}$=6 Hz, -O$\underline{C}H_2CH_3$), 63.3 (d, $^2J_{pc}$=6 Hz, - O$\underline{C}H_2CH_3$), 114.1(Ar, C3), 115.0 (Ar, C5), 122.9(Ar, C11), 127.2 (Ar, C10, C12), 128.9 (d, $^3J_{pc}$=4.5, Ar, C9, C13), 144.9 (Ar, C4,C6), 145.0 (d, $^2J_{pc}$=13, Ar, C8), 159.0 (Ar, C2); ^{31}P (162.5 MHz, $CDCl_3$, TMS): 22.5 ppm. MS (EI) *m/z*: 383.11(M^+), 245; Elemental analysis for $C_{18}H_{23}ClNO_4P$ requires C, 56.32; H, 6.04; N, 3.65. Found: C, 56.10; H, 5.90; N, 3.30%.

Diethyl (((4-chlorophenyl) amino) (p-tolyl) methyl) phosphonate(**3b**)[37]

Solid, Yield: 92%, m.p: 98-99ºC.IR (ν_{max}, cm^{-1}): 3305 (NH), 1225 (P=O), 1048(P-OEt); ^1H NMR ($CDCl_3$, TMS, 100 MHz): 1.13 (t, 3H, *J*=7.0 Hz, -P-OCH_2-$\underline{CH_3}$), 1.20 (t, 3H, *J*=7.0 Hz, -P-OCH_2-$\underline{CH_3}$) , 2.30 (s, 3H, Ar-$\underline{CH_3}$), 3.50-3.65 (m, 1H, -P-O$\underline{CH_2}$-CH_3), 3.80-3.95 (m, 1H, -P-O$\underline{CH_2}$-CH_3) 4.05-4.15 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 4.67(d, 1H, *J*=22.5 Hz, -$\underline{CH}$P), 4.70 (br, 1H,

NH), 6.50 (d, 2H, *J*=8.4 Hz, Ar), 7.00-7.4 (m, 6H, Ar); ^{31}P (162.5 MHz, $CDCl_3$, TMS):23.2 ppm. MS (EI) *m/z*: 367.81(M^+), 229; Elemental analysis for $C_{18}H_{23}ClNO_3P$ requires C, 58.78; H, 6.30; N, 3.81. Found: C, 58.45; H, 6.20; N, 3.61%.

Diethyl (((4-chlorophenyl)amino)(4-nitrophenyl)methyl)phosphonate (3d)[38]

Solid, Yield: 90%, m.p: 105-106ºC. IR (ν_{max}, cm^{-1}): 3300 (NH), 1230 (P=O), 1044 (P-OEt); ^{1}H NMR ($CDCl_3$, TMS, 100 MHz): 1.03-1.40 (m, 6H, -P-OCH_2-$\underline{CH_3}$), 3.80-4.20 (m, 4H, -P-O$\underline{CH_2}$-CH_3), 4.65 (d, 1H, *J* = 22.0 Hz, -$\underline{CH}$P), 4.75 (br, 1H, NH), 6.60 (d, 2H, *J* = 8.0 Hz, Ar), 6.80-7.50 (m, 6H, Ar); ^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.3 (d, $^3J_{cp}$= 6 Hz,-$OCH_2\underline{C}H_3$), 16.7 (d, $^3J_{cp}$= 7 Hz,- $OCH_2\underline{C}H_3$), 55.7 (d, $^1J_{pc}$= 150 Hz, $\underline{C}$HP), 63.2 (d, $^2J_{pc}$= 7 Hz, -O$\underline{C}H_2CH_3$), 63.9 (d, $^2J_{pc}$= 7 Hz, - O$\underline{C}H_2CH_3$), 117.0 (Ar, C3), 118.2 (Ar, C5), 120.0 (Ar, C11), 122.1 (Ar, C10, C12), 129.4 (Ar, C9, C13), 131.6 (Ar, C4,C6), 141.1 (, Ar, C8), 147.8 (Ar, C2); ^{31}P (162.5 MHz, $CDCl_3$, TMS):20.8 ppm. MS (EI) *m/z*: 398.10 (M^+), 262; Elemental analysis for $C_{17}H_{20}ClN_2O_5P$ requires C, 51.20; H, 5.06; N, 7.02. Found: C, 51.10; H, 5.01; N, 6.98%.

Diethyl ((4-nitrophenyl) (phenylamino) methyl) phosphonate(3g)[37]

Solid, Yield: 90%, m.p: 126-127ºC. IR (ν_{max}, cm^{-1}): 3287 (NH), 1232 (P=O), 1054(P-OEt);^{1}H NMR ($CDCl_3$, TMS, 100 MHz): 1.1-1.4 (m, 6H, -P-OCH_2-$\underline{CH_3}$), 3.50-4.14 (m, 4 H, -P-O$\underline{CH_2}$-CH_3), 4.50(br, 1H, NH), 4.60 (d, 1H, *J*=22.5 Hz, -$\underline{CH}$P), 6.50-8.40 (m, 8H, Ar);^{31}P (162.5 MHz, $CDCl_3$, TMS): 21.4 ppm MS (EI) *m/z*: 364.12 (M^+), 226; Elemental analysis for $C_{17}H_{21}N_2O_5P$ requires C, 56.04; H, 5.81; N, 7.69. found: C, 55.80; H, 5.71; N, 7.34%.

Diethyl ((4-methoxyphenyl) (phenylamino) methyl) phosphonate (3j)[36]

Solid, Yield: 85%, m.p: 101-102ºC.IR (ν_{max}, cm^{-1}): 3293 (NH), 1232 (P=O), 1048(P-OEt);^{1}H NMR ($CDCl_3$, TMS, 100 MHz): 1.20 (t, 3H, J=7.2 Hz, -P-OCH_2-$\underline{CH_3}$), 1.25(t, 3H, J=7.2 Hz, -P-

OCH_2-$\underline{CH_3}$), 3.78(s, 3H, O$\underline{CH_3}$), 3.50-4.50 (m, 4 H, -P-O$\underline{CH_2}$-CH_3), 4.50(d, 1H, *J*=23 Hz, $\underline{CH}$P), 4.55(br, 1H, NH), 6.50-7.5(m, 8H, Ar);^{31}P (162.5 MHz, $CDCl_3$, TMS): 22.4 ppm; MS (EI) *m/z*: 349.14 (M^+), 211; Elemental analysis for $C_{18}H_{24}NO_4P$ requires C, 61.88; H, 6.92; N, 4.016. Found: C, 61.65; H, 6.87; N, 3.85%.

General procedure for preparation of bis α-aminophosphonate (4a-4j).

To a mixture of aldehydes (2.0 mmol), p-Phenylenediamine or benzidin (1 mmol), and diethyl phosphite (2.0 mmol), AIL (10 mol %) was added and stirred at 50 ˚C for appropriate time. After completion of the reaction as monitored by TLC, the mixture was washed with CH_2Cl_2 (3 × 30 mL). The combined extracts were filtered and the solvent was removed under reduced pressure to afford the crude product, which was purified by recrystallization from ethylacetate/n-Hexane. The catalyst, which does not dissolve in CH_2Cl_2, remained in the residue. Selected ^{1}H, ^{13}C and ^{31}P NMR spectra for compound 4e are presented in the Supplemental Materials (Figures S 7 – S 9)

Spectroscopic data:

Tetraethyl- 1, 1'-biphenyl-4, 4' bis [(4-(dimethylamino) phenyl) methylene]) diphosphonate (4a)

Solid, Yield: 92%, m.p: 161-162ºC.IR (ν_{max}, cm^{-1}): 3292 (NH), 1230 (P=O), 1044(P-OEt); ^{1}H NMR ($CDCl_3$, TMS, 400 MHz): 1.16 (t, 6H, *J*=7.2 Hz,-P-OCH_2-$\underline{CH_3}$), 1.30 (t, 6H, *J*=7.2 Hz, -P-OCH_2-$\underline{CH_3}$), 3.67-3.73 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 2.93 (s, 12 H, -N($\underline{CH_3}$)$_2$), 3.93-3.99 (m, 2 H, -P-O$\underline{CH_2}$-CH_3), 4.07-4.18 (m, 4 H, -P-O$\underline{CH_2}$-CH_3), 4.69 (dd, 2H, $^1J_{PH}$=23.6,^2J=7.2 Hz, -$\underline{CH}$P), 4.75 (br, 1H, NH), 6.63 (d, 4H, *J*=8.4 Hz, Ar), 6.70 (d, 4H, *J*=8.8 Hz, Ar), 7.24 (d, 4H, *J*=8.8 Hz, Ar), 7.33 (dd, 4H, ^1J=8.4,^2J=2.2 Hz, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.3 (d, $^3J_{cp}$=5.7 Hz,-P-$OCH_2\underline{C}H_3$),

16.4 (d, $^{3}J_{cp}$= 5.7 Hz,-P-OCH$_2$<u>C</u>H$_3$), 40.5(-N<u>C</u>H$_3$), 55.4 (d, $^{1}J_{pc}$= 152 Hz,<u>C</u>HP), 63.1(d, $^{2}J_{pc}$=9.9 Hz,-P-O<u>C</u>H$_2$CH$_3$), 63.1 (d, $^{2}J_{pc}$=9.9 Hz,-P-O<u>C</u>H$_2$CH$_3$), 112.5 (C3´), 114.1 (C2), 123.0 (C2´), 127.0 (C3), 128.0(d, $^{2}J_{pc}$=5.5, C1´), 131.3 (C3), 145.1 (d, $^{3}J_{pc}$=14.8, C1), 150.2 (C4);^{31}P (162.5 MHz, CDCl$_3$, TMS): 23.3 ppm. MS (EI) *m/z*: 722.79 (M^+), 584, 446; Elemental analysis for $C_{38}H_{52}N_4O_6P_2$ requires C, 63.50; H, 7.25; N, 7.75. Found: C, 63.40; H, 7.15; N, 7.70%.

Tetraethyl- 1, 1'-biphenyl-4, 4' bis [(4-(diethylamino) phenyl) methylene]) diphosphonate(**4b**)

Solid, Yield: 94%, m.p: 101-102ºC. IR (ν_{max}, cm^{-1}): 3299(NH), 1234 (P=O), 1054 (P-OEt);^{1}H NMR (CDCl$_3$, TMS, 400 MHz): 1.12-1.26 (m, 6H, -P-OCH$_2$-<u>CH$_3$</u>, 12H, -P-NCH$_2$-<u>CH$_3$</u>), 1.28 (t, 6H, *J*=7.2Hz, -P-OCH$_2$-<u>CH$_3$</u>), 3.29 (q, 8 H, *J*=7.2Hz, -P-N<u>CH$_2$</u>-CH$_3$), 3.68-3.72 (m, 2 H, -P-O<u>CH$_2$</u>-CH$_3$), 3.93-3.97 (m, 2 H, -P-O<u>CH$_2$</u>-CH$_3$), 4.08-4.14 (m, 4 H, -P-O<u>CH$_2$</u>-CH$_3$), 4.66 (d, 2H, *J*=23.2 Hz, -<u>CH</u>P), 4.70 (br, 2H,NH), 6.60-6.80 (m, 8H, Ar), 7.20-7.28(m, 8H, Ar);^{13}C NMR (CDCl$_3$, TMS, 100 MHz):12.5 (-NCH$_2$<u>C</u>H$_3$), 16.2 (d, $^{3}J_{cp}$= 5 H, -P-OCH$_2$<u>C</u>H$_3$), 16.4 (d, $^{3}J_{cp}$= 5 Hz, -P-OCH$_2$<u>C</u>H$_3$), 44.3 (-N<u>C</u>H$_2$CH$_3$) , 55.4 (d, $^{1}J_{pc}$= 145 Hz, <u>C</u>HP), 63.0 (d, $^{2}J_{pc}$=8 Hz, -P-O<u>C</u>H$_2$CH$_3$), 63.1(d, $^{2}J_{pc}$=8 Hz, -P-O<u>C</u>H$_2$CH$_3$), 111.9 (C3´), 114.1 (C2), 121.8 (C1´), 127.0 (C2´), 128.8 (C3), 131.2 (C4), 145.2 (d, $^{3}J_{cp}$= 15 Hz, C1), 147.5 (C4´);^{31}P (162.5 MHz, CDCl$_3$, TMS): 23.7 ppm. MS (EI) *m/z*: 778.90 (M^+), 640, 502; Elemental analysis for $C_{42}H_{60}N_4O_6P_2$ requires C, 64.76; H, 7.76; N, 7.19. Found: C, 64.60; H, 7.70; N, 7.04%.

Tetraethyl (1, 4-phenylene bis(azanediyl)) bis(p-methoxy methylene) diphosphonate(**4c**)

Solid, Yield: 96%, m.p: 156-157ºC. IR (ν_{max}, cm^{-1}): 3280 (NH), 1231 (P=O), 1051 (P-OEt); ^{1}H NMR (CDCl$_3$, TMS, 400 MHz): 1.10-1.30 (m, 12H, -P-OCH$_2$-<u>CH$_3$</u>), 3.69 (s, 6H, ArO<u>CH$_3$</u>), 3.65-3.80 (m, 2H, -P-O<u>CH$_2$</u>-CH$_3$), 3.93-3.97 (m, 2 H, -P-O<u>CH$_2$</u>-CH$_3$), 4.08-4.14 (m, 4H, -P-O<u>CH$_2$</u>-CH$_3$),4.36 (br, 2H, NH), 4.57 (2H, dd, $^{1}J_{PH}$ = 23 Hz,$^{2}J_{PH}$ = 7.2 Hz, CHP), 6.57-6.70 (m,

12H, Ar-H), 7.24-7.26 (m, 4H, Ar-H);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.29 (d, $^{3}J_{cp}$= 6 Hz, -$OCH_2\underline{C}H_3$), 16.4 (d, $^{3}J_{cp}$= 6Hz, -$OCH_2\underline{C}H_3$), 44.3 (Ar-$O\underline{C}H_3$), 56.2 (d, J_{pc}= 152 Hz, $\underline{C}$HP), 63.0 (-P-$O\underline{C}H_2CH_3$), 63.0 (-P-$O\underline{C}H_2CH_3$), 111.8 (C2), 114.6 (C3´), 115.2 (C2´), 121.8 (C3), 128.8 (d, $^{2}J_{pc}$= 5Hz, C1´), 140.7 (d, $^{3}J_{cp}$= 1.5 Hz, C1), 147.5 (C4), 152.4 (C4´); ^{31}P (162.5 MHz, $CDCl_3$, TMS): 23.9 ppm. MS (EI) *m/z*: 696.71 (M^+), 453, 415; Elemental analysis for $C_{36}H_{46}N_2O_8P_2$ requires C, 62.06; H, 6.66; N, 4.02. Found: C, 61.90; H, 6.48; N, 3.90%.

Tetraethyl- 1, 1'-biphenyl-4, 4' bis [(4-(isopropyl) phenyl) methylene])diphosphonate (4d)

Solid, Yield: 90%, m.p: 160-161ºC.IR (ν_{max}, cm^{-1}): 3296 (NH cm^{-1}), 1236(P=O), 1065 (P-OEt);^{1}H NMR ($CDCl_3$, TMS, 400 MHz): 1.07 (t, 6H, J=6.8 Hz, -P-OCH_2-$\underline{C}H_3$), 1.17 (d, 12H, J=7 Hz, -$CH(\underline{C}H_3)_2$), 1.27 (t, 6H, J=6.8 Hz, -P-OCH_2-$\underline{C}H_3$), 2.85-2.95 (m, 2H, -$\underline{C}H(CH_3)_2$) 3.63-3.71 (m, 2 H, -P-$O\underline{C}H_2$-CH_3), 3.90-3.97 (m, 2 H, -P-$O\underline{C}H_2$-CH_3), 4.08-4.16 (m, 4 H, -P-$O\underline{C}H_2$-CH_3), 4.60 (d, 2H, *J*=24 Hz, -$\underline{C}$HP), 4.68 (br, 2H, NH), 6.21 (d, 4H, *J*=8.4, Ar), 7.19 (d, 4H, *J*=7.6, Ar), 7.18 (d, 4H, *J*=8.4, Ar), 7.38 (d, 4H, *J*=7.6, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.1 (d, $^{3}J_{cp}$= 6 Hz, -P-$O\underline{C}H_2CH_3$), 16.4 (d, $^{3}J_{cp}$= 6 Hz, -P-$O\underline{C}H_2CH_3$), 23.5 ($CH(\underline{C}H_3)_2$), 33.7 ($\underline{C}H(CH_3)_2$), 55.8 (d, $^{1}J_{pc}$= 150 Hz, $\underline{C}$HP), 63.2 (d, $^{2}J_{pc}$=10 Hz), 63.3 (d, $^{2}J_{pc}$=10 Hz), 114.3 (C2), 126.5 (C3´), 127.0 (C2´), 127.7(d, $^{2}J_{pc}$=6Hz, C1´), 131.3 (C4), 133.0 (C3), 145.0 (d, $^{3}J_{pc}$=14Hz, C1), 148.6 (C4´); ^{31}P(162.5 MHz,$CDCl_3$,TMS): 23.3 ppm. MS (EI) *m/z*: 720.35 (M^+), 506, 368; found: 720.30, Elemental analysis for $C_{40}H_{54}N_2O_6P_2$ requires C, 66.65; H, 7.55; N, 3.89. Found: C, 66.50; H, 7.50; N, 3.85%.

Tetraethyl- 1, 1'-biphenyl-4, 4' bis [(p-tolylmethylene]) diphosphonate (4e)

Solid, Yield: 90%, m.p: 148-149ºC. IR (ν_{max}, cm^{-1}): 3296 (NH), 1232 (P=O), 1060 (P-OEt);^{1}H NMR ($CDCl_3$, TMS, 400 MHz): 1.19 (t, 6H, *J*=7.2 Hz, -P-OCH_2-$\underline{C}H_3$), 1.34 (t, 6H, *J*=7.2Hz, -P-

OCH_2-$\underline{CH_3}$), 2.36 (s, 6 H, Ar-$\underline{CH_3}$), 3.70-3.80 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 3.96-4.05 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 4.13-4.23 (m, 4 H, -P-O$\underline{CH_2}$-CH_3), 4.81(d, 2H, *J*=23.6 Hz,-$\underline{CH}$P), 4.90 (br, 2H,NH), 6.67 (d, 4H, *J*=8.4, Ar), 7.20 (d, 4H, *J*=6.4, Ar), 7.33 (d, 4H, *J*=8.4, Ar), 7.43 (d, 4H, *J*=6.4, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.2 (d, $^3J_{cp}$= 6 Hz, -P-OCH_2-$\underline{C}H_3$), 16.5 (d, $^3J_{cp}$= 6 Hz, -P-OCH_2-$\underline{C}H_3$), 21.1 (Ar-$\underline{C}H_3$), 55.9 (d, $^1J_{pc}$= 150 Hz, $\underline{C}$HP), 63.2 (d, $^2J_{pc}$=10 Hz, -P-O$\underline{CH_2}$-CH_3), 63.3 (d, $^2J_{pc}$=10 Hz, -P-O$\underline{CH_2}$-CH_3), 114.1(C2), 129.1(C2´), 131.4 (C3), 132.8 (C3´), 137.6 (C4), 145.9 (C1´), 146.4 (4´), 148.0 (C1);^{31}P (162.5 MHz, $CDCl_3$, TMS): 22.9 ppm. MS (EI) *m/z*: 664.28 (M^+), 506, 368; Elemental analysis for $C_{36}H_{46}N_2O_6P_2$ requires C, 65.03; H, 6.98; N, 4.21. Found: C, 64.80; H, 6.88; N, 4.03%.

Tetraethyl (1, 4-phenylene bis(azanediyl)) bis(4-(dimethylamino)phenyl)methylene])) diphosphonate (4f)

Solid, Yield: 94%, m.p: 155-156ºC. IR (ν_{max}, cm^{-1}): 3297 (NH),1233 (P=O), 1057 (P-OEt);^{1}H NMR ($CDCl_3$, TMS, 400 MHz): 1.13 (t, 6 H, *J*=8.2, -P-OCH_2-$\underline{CH_3}$), 1.27 (t, 6 H, *J*=7.2Hz, -P-OCH_2-$\underline{CH_3}$), 2.98(s, 12 H, -N($\underline{CH_3}$)$_2$), 3.65-3.71 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 3.89-3.95 (m, 2H, -P-O$\underline{CH_2}$-CH_3), 4.04-4.11 (m, 4 H, -P-O$\underline{CH_2}$-CH_3), 4.53 (d, 2H, *J*=23.2 Hz, -$\underline{CH}$P), 4.66 (br, 2H, NH), 6.43(s, 4H, Ar), 6.69 (d, 4H, *J*=8.4 Hz, Ar), 7.27 (d, 4H, *J*=8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.2(d, $^3J_{cp}$=6.1 Hz, -P-OCH_2-$\underline{C}H_3$), 16.3(d, $^3J_{cp}$= 6.1Hz, -P-OCH_2-$\underline{C}H_3$),41.3(N$\underline{C}H_3$), 55.5 (d, $^1J_{pc}$= 151 Hz, $\underline{C}$HP), 63.3 (d, $^2J_{pc}$=8.7 Hz, -P-O$\underline{CH_2}$-CH_3), 63.4 (d, $^2J_{pc}$=8.7 Hz, -P-O$\underline{CH_2}$-CH_3), 112.5 (C3´), 123.0 (C2), 128.3 (d, $^2J_{pc}$=7, C1´), 132.4 (C2´), 146.2 (d, $^3J_{cp}$= 13 Hz, C1), 148.0 (C4´);^{31}P (162.5 MHz, $CDCl_3$, TMS): 23.0 ppm. MS (EI) *m/z*: 646.30 (M^+), 508, 370; Elemental analysis for $C_{32}H_{48}N_4O_6P_2$ requires C, 59.43; H, 7.48; N, 8.66. Found: C, 59.35; H, 7.41; N, 8.42%.

Tetraethyl (1, 4-phenylene bis (azanediyl)) bis (4-(diethylamino) phenyl) methylene])) diphosphonate (4g)

Solid, Yield: 92%, m.p: 150-151°C.IR (ν_{max}, cm^{-1}): 3301 (NH), 1236 (P=O), 1064 (P-OEt);^{1}H NMR ($CDCl_3$, TMS, 400 MHz): 1.13 (t, 12H, *J*=7.2Hz, -P-NCH_2-CH_3),1.31 (t, 6H, *J*= 7.0 Hz, -P-OCH_2-$\underline{CH}_3$), 1.16 (t, 6H, *J*= 8 Hz, -P-OCH_2-$\underline{CH}_3$), 3.33 (q, 8H, *J* = 7.0 Hz, -P-$N\underline{CH}_2$-CH_3), 3.66-4.73 (m, 2H, -P-$O\underline{CH}_2$-CH_3), 3.91-3.98 (m, 2H, -P-$O\underline{CH}_2$-CH_3), 4.07-4.17 (m, 4H, -P-$O\underline{CH}_2$-CH_3), 4.60 (2H, dd, $^{1}J_{PH}$ = 23 Hz, $^{2}J_{PH}$ = 7.2 Hz, CHP), 4.78 (br, 2H, NH), 6.52 (s, 4H, Ar), 6.63 (d, 4H, *J*=8.2 Hz, Ar), 7.21 (d, 4H, *J*=8.2 Hz, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz):12.5(-$NCH_2\underline{C}H_3$), 16.3 (d, $^{3}J_{cp}$= 5.6 Hz, -P-OCH_2-$\underline{C}H_3$), 16.5 (d, $^{3}J_{cp}$= 5.6 Hz, -P-OCH_2-$\underline{C}H_3$), 44.3(-$N\underline{C}H_2CH_3$), 55.3 (d, $^{1}J_{pc}$= 152.15 Hz, $\underline{C}$HP), 63.0 (d, $^{2}J_{pc}$=7 Hz, -P-$O\underline{C}H_2$-CH_3), 63.3(d, $^{2}J_{pc}$=7 Hz, -P-$O\underline{C}H_2$-CH_3), 109.0 (C3´), 111.8 (C2), 115.5 (C1´), 120.9 (C2´), 131.8 (C1), 147.5 (C4´);^{31}P (162.5 MHz, $CDCl_3$, TMS): 23.1 ppm. MS (EI) *m/z*: 702.80 (M^+), 564, 426; Elemental analysis for $C_{36}H_{56}N_4O_6P_2$ requires C, 61.52; H, 8.03; N, 7.97. Found: C, 61.20; H, 7.95; N, 7.86%.

Tetraethyl (1,4-phenylene bis(azanediyl)) bis(p-methoxy methylene) diphosphonate (**4h**)

Solid, Yield: 96%, m.p: 158-159ºC. IR (ν_{max}, cm^{-1}): 3303 (NH), 1232(P=O), 1051 (P-OEt);^{1}H NMR ($CDCl_3$, TMS, 400 MHz): 1.13 (t, 6H, *J*=7.20, -P-OCH_2-$C\underline{H}_3$), 1.27 (t, 6H, *J*=7.20, -P-OCH_2-$\underline{CH}_3$), 3.68-3.74 (m, 2H, -P-$O\underline{CH}_2$-CH_3), 3.78 (s, 6 H, $Ar(CH_3)_2$), 3.89-3.93 (m, 2 H, -P-$O\underline{CH}_2$-CH_3), 3.94-3.97 (m, 4H, -P-$O\underline{CH}_2$-CH_3), 4.36 (br, 2H, NH), 4.59 (d, 2H, *J*=23.6, -$\underline{CH}$P), 6.43 (s, 4H, Ar), 6.85 (d, 4H, *J*=8.4, Ar), 7.34 (dd, 4H, $^{1}J_{PH}$=8.4 Hz, $^{2}J_{PH}$=2.4 Hz, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.2 (d, $^{3}J_{cp}$= 6 Hz, -P-OCH_2-$\underline{C}H_3$), 16.4 (d, $^{3}J_{cp}$= 6Hz, -P-OCH_2-$\underline{C}H_3$), 55.2 (Ar-$O\underline{C}H_3$), 56.4 (d, $^{1}J_{pc}$= 151 Hz, $\underline{C}$HP), 63.0 (d, $^{2}J_{pc}$=7 Hz, -P-$O\underline{C}H_2$-CH_3), 63.1 (d,

$^{2}J_{pc}$=7 Hz, -P-O<u>C</u>H$_2$-CH$_3$), 113.9 (C3´), 115.5 (C2), 128.0 (C2´), 128.9 (C1´), 139.0 (d, $^{3}J_{pc}$= 3 Hz, C1), 159.2(C4´); ^{31}P (162.5 MHz, CDCl$_3$, TMS): 24.0 ppm. MS (EI) *m/z*: 620.24 (M^+), 482, 368; Elemental analysis for $C_{30}H_{42}N_2O_8P_2$ requires C, 58.06; H, 6.82; N, 4.51. Found: C, 57.96; H, 6.78; N, 4.44%.

Tetraethyl (1,4-phenylene bis(azaneiyl)) bis(4-(isopropyl)phenyl)methylene])) diphosphonate (4i)

Solid, Yield: 85%, m.p: 156-157ºC. IR (ν_{max}, cm^{-1})3300 (NH), 1232 (P=O), 1033 (P-OEt); ^{1}H NMR (CDCl$_3$, TMS, 400 MHz): 1.09-1.29 (m, 12H, POCH$_2$<u>C</u>H$_3$, 12H, CH(<u>C</u>H$_3$)$_2$), 2.86-2.88 (m, 2H, <u>C</u>H(CH$_3$)$_2$) 3.68-4.14 (m, 8 H, PO<u>C</u>H$_2$CH$_3$), 4.78 (d, 2H, *J*=24 Hz, <u>C</u>HP), 4.55 (br, 2H, NH), 6.63 (s, 4H, Ar), 7.19-7.85 (m, 8H, Ar);^{13}C NMR (CDCl$_3$, TMS, 100 MHz): 16.0 (d, $^{3}J_{cp}$= 5.5 Hz, -P-OCH$_2$<u>C</u>H$_3$), 16.3 (d, $^{3}J_{cp}$= 5.5 Hz, -P-OCH$_2$<u>C</u>H$_3$), 22.3 (-CH(<u>C</u>H$_3$)$_2$), 31.6 (-<u>C</u>H(CH$_3$)$_2$), 55.3 (d, $^{1}J_{pc}$= 151 Hz, <u>C</u>HP), 63.2 (d, $^{2}J_{pc}$=8 Hz, -P-O<u>C</u>H$_2$CH$_3$), 63.3 (d, $^{2}J_{pc}$=8 Hz, -P-O<u>C</u>H$_2$CH$_3$), 115.9 (C2), 117.4 (C3´), 126.19 (C2´), 129.2 (C1´), 142.0 (d, $^{3}J_{pc}$= 4 Hz, C1), 158.1 (C4´);^{31}P (162.5 MHz, CDCl$_3$, TMS): 23.3 ppm. MS (EI) *m/z*: 644.72 (M^+), 506, 368; Elemental analysis for $C_{34}H_{50}N_2O_6P_2$ requires C, 63.34; H, 7.82; N, 4.35. Found: C, 63.20; H, 7.70; N, 4.10%.

Tetraethyl (1,4-phenylene bis(azanediyl)) bis(4-(p-tolylmethylene)methylene])) diphosphonate (4j)

Solid, Yield: 86%, m.p: 162-163ºC. IR (ν_{max}, cm^{-1}): 3290 (NH), 1236 (P=O), 1068 (P-OEt); ^{1}H NMR (CDCl$_3$, TMS, 400 MHz): 1.15(t, 6H, *J*=7.2 Hz, POCH$_2$<u>CH$_3$</u>), 1.31(t, 6H, *J*=7.2Hz, POCH$_2$<u>CH$_3$</u>), 2.14 (s, 6 H, Ar-CH$_3$), 3.65-3.71 (m, 2 H, PO<u>CH$_2$</u>CH$_3$), 3.92-3.98(m, 2 H, PO<u>CH$_2$</u>CH$_3$), 4.01-4.18 (m, 4 H, PO<u>CH$_2$</u>CH$_3$), 4.62(d, 2H, *J*=24.2 Hz, <u>C</u>HP), 4.80 (br, 2H, NH),

6.50(s, 4H, Ar), 6.70 (d, 4H, J=7.6 Hz, Ar), 7.25 (d, 4H, *J*=7.6 Hz, Ar);^{13}C NMR ($CDCl_3$, TMS, 100 MHz): 16.2(d, $^{3}J_{cp}$= 6 Hz, -P-$OCH_2\underline{C}H_3$), 16.5 (d, $^{3}J_{cp}$= 6 Hz, -P-$OCH_2\underline{C}H_3$), 30.5 (Ar-$\underline{C}H_3$), 55.3(d, $^{1}J_{pc}$= 152 Hz, $\underline{C}$HP), 63.0(d, $^{2}J_{pc}$=10 Hz, -P-$O\underline{C}H_2CH_3$), 63.3(d, $^{2}J_{pc}$=10 Hz, -P-$O\underline{C}H_2CH_3$), 109.8 (C2), 112.5 (C2´), 115.56 (C3´), 128.0 (d, $^{2}J_{PC}$ = 5 Hz, C1´), 131.8 (d, $^{3}J_{PC}$ = 15 Hz, C1), 145 (C4´);^{31}P (162.5 MHz, $CDCl_3$, TMS): 23.0 ppm. MS (EI) *m/z*: 588.12 (M^+), 450, 312; Elemental analysis for $C_{30}H_{42}N_2O_6P_2$ requires C, 61.22; H, 7.19; N, 4.76. Found: C, 61.05; H, 7.10; N, 4.60%.

Conclusion

In conclusion, we have designed and synthesized an AIL based on benzimidazolium cations and have successfully used it as a catalyst for the one-pot synthesis of α-aminophosphonate and bis(α- aminophosphonate). The remarkable feature of this new catalyst is its ethyleneoxy bridge which participates in dissolving organic compounds. The application of this AIL is studied in a new one-pot method for the synthesis of α-aminophosphonate and bis(α- aminophosphonate) derivatives under solvent-free conditions. The advantages offered by this protocol include reusability of the catalyst, high conversion, short reaction time, and simple experimental procedure

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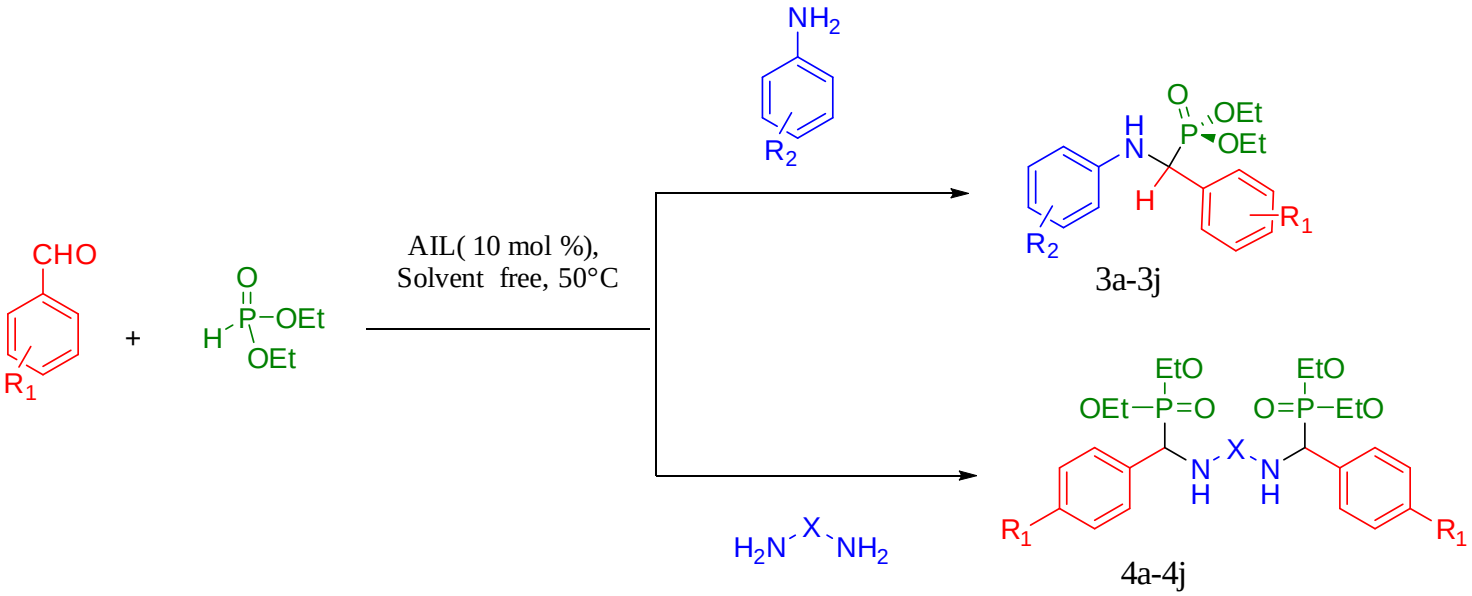
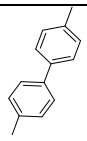
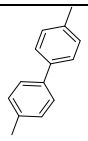
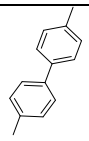
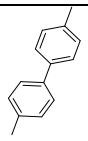
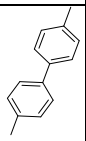
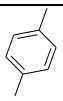
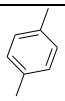
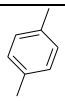
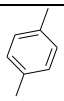
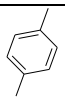
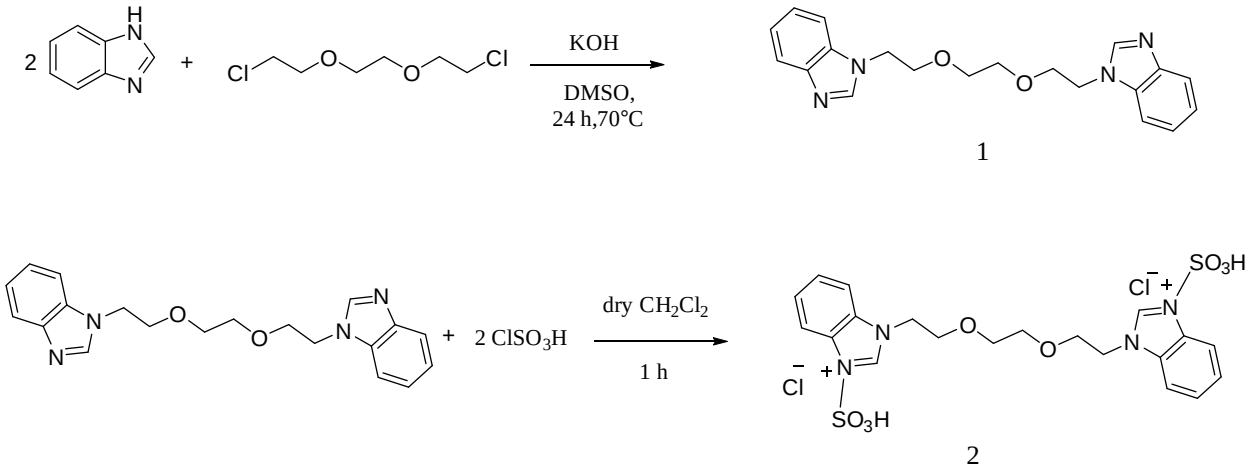


compound	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**
R_1	4-OCH_3	4-CH_3	4-NO_2	H	4-Cl	3-Cl	4-NO_2	3-NO_2	H	4-OCH_3
R_2	4-Cl	4-Cl	4-Cl	4-Cl	H	H	H	H	H	H
compound	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**	**4h**	**4i**	**4j**
X										
R_1	4-$N(CH_3)_2$	4-$N(Et_2)_2$	4-OCH_3	4-$CH(CH_3)_2$	4-CH_3	4-$N(CH_3)_2$	4-$N(Et_2)_2$	4-OCH_3	4-$CH(CH_3)_2$	4-CH_3

Scheme 1 Three-component reaction of aromatic aldehydes with amines and diethylphosphite in AIL.



Scheme 2 Synthesis of acidic ionic liquid

Table 1 Calculation of the Hammett acidity function (H_0) for AIL

Entry	catalyst	A_{max}	[I]%	$[HI^+]$%	H_0
1	--------	2.80	100	0	-----
2	AIL	1.84	65	35	1.25

Table 2. Optimization of reaction conditions for preparation of α-aminophosphonate (**3a**)

Entry	Catalyst (mol %)	Temperature(ºC)	Time(h)	Isolated Yield (%)
1	-	rt	24	20
2	-	50ºC	24	30
3	5	rt	1	55
4	10	rt	1	60
5	20	rt	1	50
6	5	50ºC	1	75
7	10	50ºC	1	96
8	20	50ºC	1	80

Reaction conditions: 4-methoxy benzaldhyde (1.0 mmol), 4- chloroaniline (1.0 mmol), diethyl phosphite (1.0 mmol), and AIL as a catalyst.

Table 3 Results of α-aminophosphonate derivatives synthesis using AIL (2)

Entry	R_1	R_2	time	Yield %	Mp(ºC)
3a	4-OCH_3	4-Cl	1	94	101-102[36]
3b	4-CH_3	4-Cl	1.5	92	98-99[38]
3c	4-NO_2	4-Cl	2	96	94-95
3d	H	4-Cl	1.5	90	105-106[39]
3e	4-Cl	H	2	95	77-80[36]
3f	3-Cl	H	1	88	88-90[23]
3g	4-NO_2	H	1.5	90	126-127[36]
3h	3-NO_2	H	2	92	98-99[36]
3j	4-OCH_3	H	2.5	85	100-102[36]

Table 4 Results of bis α-aminophosphonate derivatives synthesis using AIL (**2**)

Entry	R_1	Time(h)	Yiled %	Mp(°C)
4a	4-$N(CH_3)_2$	1.5	92	161-162
4b	4-$N(Et)_2$	2	88	158-159
4c	4-OCH_3	1	96	156-157
4d	4-$CH(CH_3)_2$	2	90	160-161
4e	4-CH_3	3	90	148-149
4f	4-$N(CH_3)_2$	2.5	94	155-156
4g	4-$N(Et)_2$	1.5	92	150-151
4h	4-OCH_3	0.45	96	158-159[40]
4i	4-$CH(CH_3)_2$	3.5	85	156-157
4j	4-CH_3	1.5	86	162-163[40]

Table 5 Reported synthetic methods for the synthesis of α-aminophosphonate (**3a**)

entry	catalyst	Solvent	Temperature(ºC)	Time(h)	Yield (%)	Ref.
1	organocatalyst	ethanol	rt	24	78	[41]
2	Fe/SWCNTs	Solvent free	50ºC	2.5	93	[36]
3	Sodium Dodecyl Sulfate (SDS)	H_2O	50ºC	15 min	95	[42]
4	[psmim][HSO_4]	H_2O	rt	1	81	[43]
5	AIL	Solvent free	50ºC	1	94	This work

Table 6 Recyclability of AIL

Reusability[a]	AIL	Run 1	Run 2	Run 3	Run 4
Yield (%)[b]	94	92	90	90	86

[a]Reusability of the recovered catalyst

[1-4]Reusability of the recovered catalyst in new runs from run 1 to run 4

[b] Isolated yields