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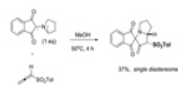
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A green and novel method for the preparation of α -aminophosphonates using eggshell as catalyst. X-ray study

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ABSTRACT

An efficient and eco-friendly green methodology is developed for the synthesis of series of α -aminophosphonate derivatives from diverse aldehydes, anilines and triethyl phosphite by using environmentally benign and cost-effective Eggshells as solid heterogeneous base catalyst. The reaction is conducted by the stepwise one pot condensation through Kabachnik–Fields addition reaction in ethanol at room temperature during 25–30 min. High yield, short reaction time, solvent-free condition, waste to wealth, and optimization with the design of experiment are the major advantages of this method. In addition, this study examines the influence of different solvents, temperature and the amount of catalyst on the yield of the reaction. A single crystal of (2S)- diethyl (phenyl) ((4-fluorophenyl)-aminophosphonate (**3g**) has been obtained after recrystallization from ethanol/dichloromethane (9/1) and selected for X-ray diffraction study. Compound **3g** crystallizes in the monoclinic space group P2₁/c. The structure of the obtained compounds was confirmed by ¹H, ¹³C, and ³¹P NMR spectroscopy, IR spectroscopy, as well as elemental analysis.

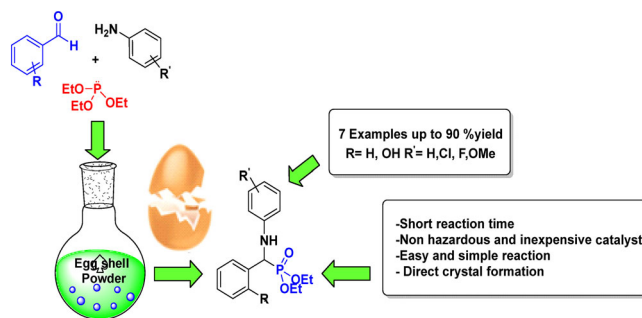
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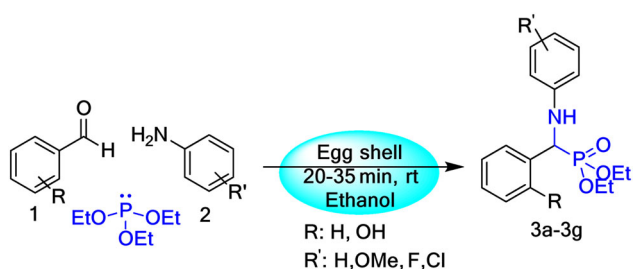
GRAPHICAL ABSTRACT



Introduction

α -Aminophosphonates have been used in a wide range of applications such as in the areas of agricultural and medicinal chemistry. They are also employed as antiviral agents, enzyme inhibitors, antibiotics, anticancer and antifungal agents and are extensively used as insecticides and herbicides.^[1–5] Some significant studies for synthesis of α -aminophosphonate derivatives have been reported.^[5–8] Among the versatile procedures, the Kabachnik–Fields reaction is one of

the basic methods for preparation of α -aminophosphonates, which was discovered in 1952 independently by Kabachnik and Fields.^[9] On the other hand, multicomponent reactions are economically viable, high convergence with high bond-forming-index (BFI).^[10] Some new investigations have been reported with reaction conditions for promotion of one-pot Kabachnik–Fields reaction such as ultrasound irradiation,^[11,12] microwave conditions,^[13] heating and acidic or basic catalysts.^[14] Recently, H. Zandieh et al. synthesized

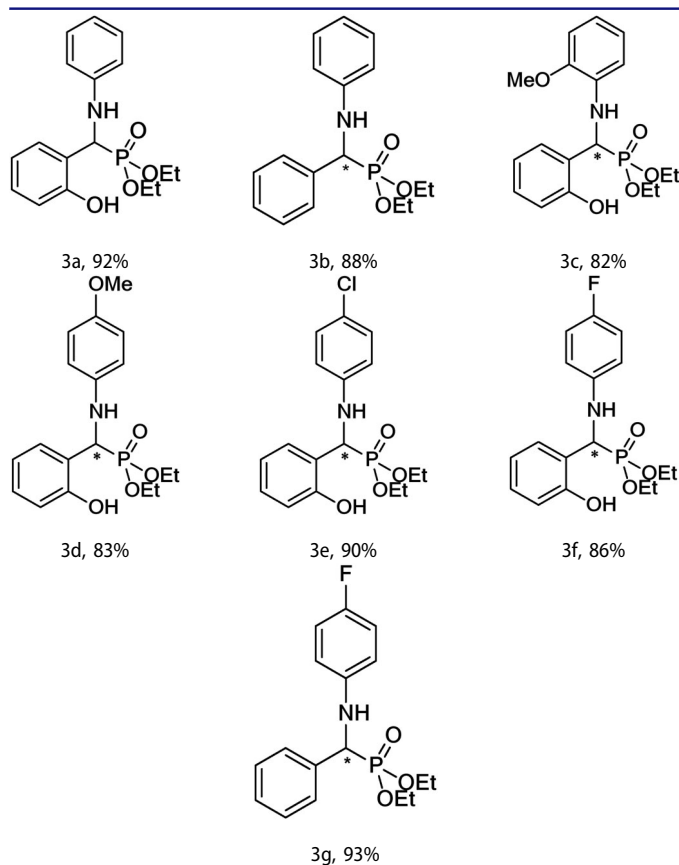


Scheme 1. Synthesis of α -aminophosphonates **3a–3g**.

α -aminophosphonates using $\text{Cu}_2(\text{BDC})_2\text{DABCO}$ (Cu-MOF) as a recyclable heterogeneous catalyst.^[15] Introduction of clean procedures by utilizing eco-friendly green catalysts have attracted great attention of researchers. It was proved that eggshell was an interesting unconventional heterogeneous biocatalyst for organic synthesis.^[16] The eggshell as a hazardous waste by European Union regulations was converted to a valuable catalyst, namely nano- $\text{Fe}_3\text{O}_4@(\text{HSO}_4)_2$. It can catalyze the organic transformation and reduce environmental problems and it is the first use of this waste material as the nano-sized catalyst in organic synthesis.^[17] Akbarpoor et al. used nano- $\text{Fe}_3\text{O}_4@1542\text{T.13}(\text{HSO}_4)_2$ in the synthesis of hexahydroquinolines and 2-amino-3-cyanopyridines derivatives.^[18] Madhukar B. Morbale et al. describe the synthesis of 1,4-dihydropyridine and polyhydroquinoline; the preparation was carried out by the condensation of dimedone, aldehydes, ethylacetoacetate and ammonium acetate using modified eggshells (MES) as base catalyst.^[19] In this particular context and in our continued research to develop novel, rapid and green approaches in the design of efficient synthetic methods using recyclable catalysts, we describe here the use of eggshell as an efficient biodegradable and recyclable heterogeneous catalyst for the preparation of aminophosphonates by a three-component condensation reaction in one pot. The reaction is carried out with excellent catalytic activity and good yields within a short reaction time.

Results and discussion

In continuation of our previous research on the synthesis of compounds containing phosphonate moiety,^[20–24] we report the synthesis of α -aminophosphonate derivatives (**3a–3g**) by three component reaction *via* Kabachnik–Field reaction catalyzed by eggshell as an efficacious recrystallizable and biodegradable heterogeneous catalyst. The reaction progressed in short time with high yields (Scheme 1). Easy availability, biodegradability and environmental acceptability of catalysts obtained from natural resources have an addition value in synthetic organic chemistry.



To develop optimum conditions, first, the effect of solvent on the rate of the reaction was studied for the preparation of diethyl ((2-hydroxyphenyl) phenyl) aminophosphonate **3a**. The highest yield was obtained with ethanol as solvent (Table 1). We have optimized the reaction conditions of compound **3a** with different solvents at room temperature.

The optimum amount of catalyst was in the range of 0.5–3%. The highest yield was obtained with 3% of the eggshell powder (Table 2). By implementing, the optimized conditions (3% of catalyst, ethanol, and room temperature), various active substitute anilines were allowed to react with different substituents on the aryl aldehydes for the synthesis of seven α -aminophosphonate derivatives (**3a–3g**).

Encouraged by all these remarkable results and after the selection of optimum reaction conditions, we next examined the extent and feasibility of the eggshell catalyzed condensation for the synthesis of various α -aminophosphonates (Scheme 1).

Mechanism

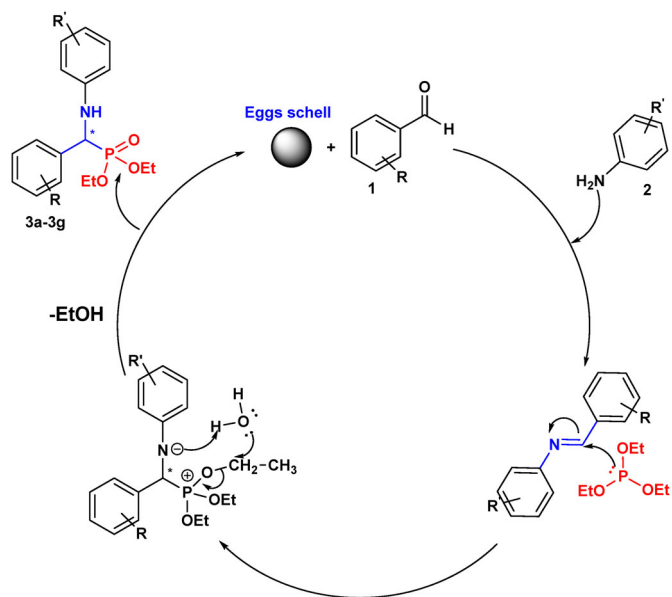
Almost 90% of the eggshell is composed of calcium carbonate, it is the main active component of the catalyst. Moreover, the eggshell contains a small number of different

Table 1. Optimization of reaction conditions of compound (3a) with different solvents at room temperature.

Entry	Solvent	Time (min)	V (mL)	Yield %
1	CH ₂ Cl ₂	25	5	70
2	THF	25	5	68
3	Toluene	25	5	65
4	Solvent-Free	30	–	66
5	EtOH	15	5	92

Table 2. Optimization of reaction conditions of compound 3a under solvent-free conditions at room temperature.

Catalyst (mol %)	Solvent	Temperature	Time (min)	Yield (%)
No catalyst	–	rt	30	66
No catalyst	–	50	15	70
No catalyst	EtOH	79	15	78
microwave	–	–	2	78
ultrasound	–	–	5	80
0.5 %	–	rt	15	70
2 %	–	rt	15	82
2 %	EtOH	rt	15	92
3 %	EtOH	rt	15	92

**Scheme 2.** A plausible mechanism for the formation of α -aminophosphonates 3a–3g.

components (Ca, Mg, Si, Sr, K, Na, Ni, Fe, Zn, Cl and phosphate) which can catalyze the reaction. A possible mechanism is depicted in Scheme 2.

Experimental

Materials and methods

The chemicals products were used without purification. All reactions were monitored by thin layer chromatography (TLC) on silica Merck 60 F254 percolated aluminum plates and were developed by spraying with ninhydrin solution. The reactions were carried at room temperature. ¹H and ¹³C NMR spectra were recorded with a Bruker NMR spectrometer at 400 and 100 MHz, respectively, using TMS as internal standard and CDCl₃ as solvent. Chemical shifts are reported in δ units (ppm) with TMS as reference ($\delta = 0.00$). All coupling constants (*J*) are reported in Hertz. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), dd (doublets), t (triplet), m (multiplet). Infrared spectra were recorded with a PerkinElmer 600 spectrophotometer. Melting points were determined in open capillary tubes on an electro-thermal apparatus and uncorrected. Microanalyses were performed by Elemental Analyzer (Euro E.A. 3000-V3.0-single-2007), and the determined values were within the acceptable limits of the calculated values.

Crystallography

Single crystal X-ray diffraction experiment of the studied compound 3g was carried out at 150 K on a APEX II, Bruker-AXS diffractometer, CCD area detector, using Mo-K α radiation ($\lambda = 0.71073$ Å). Crystal data, data collection and structure refinement details are summarized in (Table 3). The crystal structure was solved by direct methods with SIR2002^[25] and refined on the basis of *F*² using SHELXL97.^[26] The WinGX^[27] suite of software is used to prepare material for publication.

All non-hydrogen atoms were found from Fourier syntheses of electron density and were refined anisotropically. The hydrogen atoms were located in difference Fourier maps and were placed in geometrically calculated positions and refined isotropically with riding models and fixed

Table 3. Crystallographic data and refinement parameters for 3g.

	3g		3g
Formula	C ₁₇ H ₂₁ FN ₃ P	Absorption coefficient (mm ⁻¹)	0.187
Formula weight	337.32	F(000)	712
Crystal habit, color	Prism, colorless	Crystal size (mm)	0.48 × 0.33 × 0.15
Crystal system	Monoclinic	θ range for data collection (°)	2.747–27.483
Space group	<i>P</i> ₂ / <i>c</i>	Reflections collected	10810
<i>a</i> (Å)	9.1777(7)	Independent reflections	3825
<i>b</i> (Å)	23.426(2)	<i>R</i> _{int}	0.0443
<i>c</i> (Å)	7.8655	Reflections with $I \geq 2\sigma(I)$	3160
α (°)	90	Number of parameters	213
β (°)	96.298(3)	Goodness-of-fit on <i>F</i> ²	1.014
γ (°)	90	Final <i>R</i> indices [$I \geq 2\sigma(I)$]	<i>R</i> ₁ = 0.0394 <i>wR</i> ₂ = 0.1004
Volume (Å ³)	1680.9(2)	<i>R</i> indices [all data]	<i>R</i> ₁ = 0.510 <i>wR</i> ₂ = 0.1091
<i>Z</i> , <i>Z'</i>	4, 4	Largest difference peak and hole (Å ⁻³)	0.352, –0.431
Density (calculated, g cm ⁻³)	1.333	CCDC deposition no.	CCDC 2077902

isotropic displacement parameters with $U_{iso}(H) = 1.2$ or $1.5U_{eq}(C)$ for C-H groups (Figure 1).

Crystal characterization

Displacement ellipsoids are drawn at the 50% probability level. Single-crystal X-ray diffraction analysis reveals that compound **3g** crystallizes in the monoclinic space group $P2_1/c$ (Table 1) with one molecule of (2S)-diethyl phenyl ((4-fluorophenyl)aminophosphonate in the asymmetric unit. The mean planes of the two phenyl rings form a dihedral angle of $81.01(1)^\circ$. Alternating double layers parallel to (010) plane at $b = 1/4$ and $b = 3/4$ along c axis are observed in the crystal packing of **3g** structure. These layers are connected

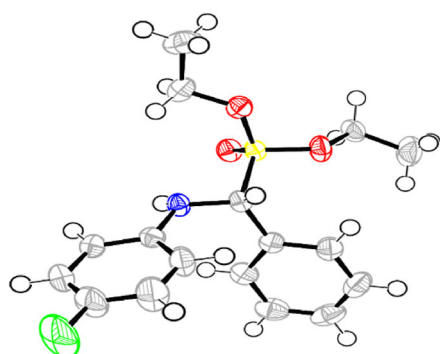


Figure 1. ORTEP view of the molecular structure of compound **3g** in the crystal; thermal ellipsoids are drawn at 50% probability level.

together *via* intermolecular C-H...O and N-H...O hydrogen bonds along the a axis (Figure 2, Table 4), to generate a three-dimensional network in which one size of hydrogen-bonded rings,^[28] i.e., $R^2_2(10)$ is formed. The crystal structure is also supported by weak intermolecular interactions of C-H... π . All these interactions link the layers to gather and reinforce the cohesion of the structure.

Catalyst preparation

Empty chicken eggshells were collected from the household and washed with tap warm water. The adhering membrane is separated manually. Then, the eggshells are washed with distilled water and dried at room temperature. The Supplemental Materials contains sample ¹H-, ¹³C-, ³¹P NMR and IR spectra of the products **3** (Figures S1–S25).

General procedure for the synthesis of α -aminophosphonate derivatives (**3a–3g**)

An equimolar mixture of the aldehyde (1 equiv.), the amine (1 equiv.) and triethyl phosphite (1.1 equiv.) was added to ethanol (10 mL) followed by addition of eggshell powder (0.1 mg). The reaction was carried out at room temperature during a time between 20 and 35 min, and checked by thin-layer chromatography. Afterward completion of the reaction the catalyst material was recuperate by filtration. The residue was purified by column chromatography on silica gel,

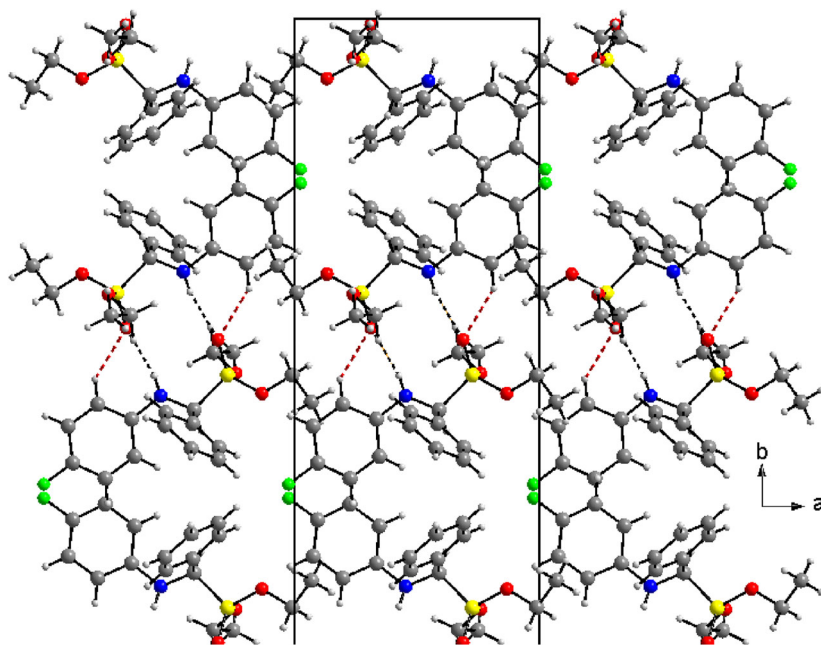


Figure 2. Packing of **3g** in the crystal viewed along the c axis showing layers parallel to (a,c), which are connected together with N-H...O (black dashed line) and C-H...O (red dashed line) hydrogen bonds.

Table 4. Distances (Å) and angles ($^\circ$) of hydrogen bonds for **3g**.

D-H...A	$d(D-H)$	$d(H...A)$	$d(D-A)$	D-H-A	Symmetry
N1-H1N...O1	0.832(18)	2.161(19)	2.9794(17)	167.7(17)	1-x,1-y,1-z
C9-H9...O1	0.95	2.66	3.3490(19)	130.00	1-x,1-y,1-z
C17-H17a...Cg1 (C2-C8)	0.95	2.87	3.6452(3)	137.00	x,y,-1+z

eluting with (AcOEt 50%/petroleum ether 50%) to yield a pure product.

(2S)-diethyl-((2-hydroxyphenyl) phenyl) aminophosphonate (3a)

Oil; 92% yield; R_f (DCM-MeOH: 99/1) = 0.34; ^1H NMR (400 MHz, CDCl_3): δ = 1.01 (t, $J_{\text{HH}} = 8.0$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 1.21 (t, $J_{\text{HH}} = 7.5$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.62-3.9 (m, 1H, $\text{CH}_2\text{-O}$), 3.82-3.88 (m, 1H, $\text{CH}_2\text{-O}$), 4.03-4.11 (m, 2H, $\text{CH}_2\text{-O}$), 5.21-5.25 (m, 1H, *CH), 6.1-6.20 (m, 1H, H_{Ar}), 6.53 (t, $J_{\text{HH}} = 8.0$ Hz, 1H, H_{Ar}), 6.71-6.83 (m, 4H, H_{Ar}), 6.99-7.08 (m, 3H, H_{Ar}), 7.43-7.45 (m, 1H, H_{Ar}), 9.9 (s, 1H, OH); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 16.0 (d, $J_{\text{PC}} = 16$ Hz, CH_3), 16.3 (d, $J_{\text{PC}} = 24.0$ Hz, CH_3), 45.9 (CH_2), 47.7 (CH_2), 62.2 (dd, $^1J_{\text{PC}} = 20.0$ Hz, $^2J_{\text{PC}} = 24.0$ Hz, *CH), 113.0 (CH), 114.8 (d, $J_{\text{PC}} = 8.0$ Hz, CH), 116.8 (CH), 119.0 (d, $J_{\text{PC}} = 4.0$ Hz, CH), 123.1 (CH), 128.4 (d, $J_{\text{PC}} = 12.0$ Hz, CH), 128.7 (d, $J_{\text{PC}} = 16.0$ Hz, CH), 147.3 (d, $J_{\text{PC}} = 56.0$ Hz, C), 155.1 (d, $J_{\text{PC}} = 28.0$ Hz, C); IR (KBr): 3181 (OH), 2909 (CH_2), 1208 (P=O), 1026 (P-O) cm^{-1} ; $^{31}\text{P}\{^1\text{H}\}$ NMR (160 MHz, CDCl_3): δ = 23.5; Anal. Calcd. for $\text{C}_{17}\text{H}_{21}\text{NO}_4\text{P}$: C, 61.89; H, 6.61; N, 4.18; Found: C, 61.81; H, 6.65; N, 4.14%.

(2S)-diethyl-(diphenyl) aminophosphonate (3b)

Oil; 88% yield; R_f (DCM-MeOH: 99/1) = 0.35; ^1H NMR (400 MHz, CDCl_3): δ = 1.12 (t, $J_{\text{HH}} = 7.2$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 1.29 (t, $J_{\text{HH}} = 7.2$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.52-3.69 (m, 1H, $\text{CH}_2\text{-O}$), 3.72-3.91 (m, 2H, $\text{CH}_2\text{-O}$), 4.08-4.19 (m, 2H, $\text{CH}_2\text{-O}$), 4.72-4.81 (m, 2H, *CH+NH), 6.58-6.71 (m, 3H, H_{Ar}), 7.10 (t, $J_{\text{HH}} = 7.1$ Hz, 2H, H_{Ar}), 7.27-7.30 (m, 3H, H_{Ar}), 7.46-7.48 (m, 2H, H_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 16.3 (d, $J_{\text{PC}} = 23.2$ Hz, CH_3), 16.6 (d, $J_{\text{PC}} = 22.8$ Hz, CH_3), 55.5 (CH_2), 57.0 (CH_2), 63.4 (dd, $^1J_{\text{PC}} = 10.8$ Hz, $^2J_{\text{PC}} = 27.6$ Hz, *CH), 114.0 (CH), 118.5 (CH), 128.0 (t, $J_{\text{PC}} = 17.2$ Hz, CH), 128.7 (d, $J_{\text{PC}} = 11.2$ Hz, CH), 129.3 (CH), 136.1 (d, $J_{\text{PC}} = 11.2$ Hz, C), 146.5 (d, $J_{\text{PC}} = 57.6$ Hz, C); IR (KBr): 3294 (NH), 2995 (CH_2), 1234 (P=O), 1021 (P-O) cm^{-1} ; $^{31}\text{P}\{^1\text{H}\}$ NMR (160 MHz, CDCl_3): δ = 22.7; Anal. Calcd. for $\text{C}_{17}\text{H}_{20}\text{NO}_3\text{P}$: C, 63.94; H, 6.94; N, 4.39; Found: C, 63.96; H, 6.97; N, 4.41%.

(2S)-diethyl-((2-hydroxyphenyl)((2-methoxyphenyl)amino)phosphonate (3c)

Green powder; m.p. = (124-126 °C); 82% yield; R_f (DCM-MeOH: 99/1) = 0.32; ^1H NMR (400 MHz, CDCl_3): δ = 1.24-1.30 (m, 6H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.91 (s, 3H, CH_3), 4.01-4.18 (m, 4H, O- CH_2), 4.97 (d, $J_{\text{HH}} = 2.3$ Hz, 1H, *CH), 6.56 (dd, $J_{\text{HH}} = 4.8$ Hz, $J_{\text{HH}} = 3.2$ Hz, 1H, H_{Ar}), 6.75-6.98 (m, 5H, H_{Ar}), 6.90 (t, $J_{\text{HH}} = 1.2$ Hz, 1H, H_{Ar}), 6.98 (d, $J_{\text{HH}} = 1.2$ Hz, 1H, H_{Ar}), 7.19 (d, $J_{\text{HH}} = 7.6$ Hz, 1H, H_{Ar}), 7.27 (dd, $J_{\text{HH}} = 2.0$ Hz, $J_{\text{HH}} = 2.4$ Hz, 1H, H_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 16.4 (d, $J_{\text{PC}} = 23.2$ Hz, CH_3), 16.5 (d, $J_{\text{PC}} = 21.6$ Hz, CH_3), 53.6 (CH_3), 55.1 (CH_2), 55.7 (CH_2), 63.9 (dd, $J_{\text{PC}} = 27.6$ Hz, $J_{\text{PC}} = 262.4$ Hz, *CH), 109.9 (CH), 112.3 (CH), 118.9 (d, $J_{\text{PC}} = 211.2$ Hz, CH), 119.0-121.8 (m,

$\text{CH}+\text{C}_q$), 128.8 (d, $J_{\text{PC}} = 24.4$ Hz, CH), 129.5 (d, $J_{\text{PC}} = 12.4$ Hz, CH), 136.3 (d, $J_{\text{PC}} = 52.4$ Hz, C), 147.9 (C), 156.0 (d, $J_{\text{PC}} = 18.0$ Hz, C); IR (KBr): 3383 (OH), 3164 (NH), 2982 (CH_2), 1225 (P=O), 1026 (P-O) cm^{-1} ; $^{31}\text{P}\{^1\text{H}\}$ NMR (160 MHz, CDCl_3): δ = 24.4; Anal. Calcd. for $\text{C}_{17}\text{H}_{21}\text{NO}_4\text{P}$: C, 56.17; H, 6.62; N, 3.83; Found: C, 56.20; H, 6.65; N, 3.40%.

(2S)-diethyl-((2-hydroxyphenyl)((4-methoxyphenyl)amino)phosphonate (3d)

Oil; 83% yield; R_f (DCM-MeOH: 99/1) = 0.32; ^1H NMR (400 MHz, CDCl_3): δ = 1.22-1.28 (m, 6H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.70 (s, 3H, CH_3), 3.97-4.20 (m, 4H, O- CH_2), 4.76 (d, $J_{\text{HH}} = 22.4$ Hz, 1H, *CH), 6.65-6.73 (dd, $J_{\text{HH}} = 13.6$ Hz, $J_{\text{HH}} = 4.8$ Hz, 4H, H_{Ar}), 6.85-6.93 (m, 2H, H_{Ar}), 7.17-7.21 (m, 2H, H_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 16.7 (d, $J_{\text{PC}} = 22.8$ Hz, CH_3), 16.8 (d, $J_{\text{PC}} = 22.8$ Hz, CH_3), 56.1 (CH_3), 56.8 (CH_2), 58.3 (CH_2), 64.2 (dd, $J_{\text{PC}} = 28.0$ Hz, $J_{\text{PC}} = 206.0$ Hz, *CH), 115.2 (CH), 117.3 (CH), 119.2 (CH), 119.3 (CH), 121.1 (d, $J_{\text{PC}} = 5.2$ Hz, CH), 121.3 (d, $J_{\text{PC}} = 16.4$ Hz, CH), 129.7 (d, $J_{\text{PC}} = 26.4$ Hz, CH), 130.0 (d, $J_{\text{PC}} = 132.4$ Hz, CH), 140.5 (d, $J_{\text{PC}} = 58.4$ Hz, C), 154.4 (C), 156.7 (d, $J_{\text{PC}} = 17.6$ Hz, C); IR (KBr): 3177 (OH), 2964 (CH_2), 1219 (P=O), 1051 (P-O) cm^{-1} ; $^{31}\text{P}\{^1\text{H}\}$ NMR (160 MHz, CDCl_3): δ = 24.0; Anal. Calcd. for $\text{C}_{17}\text{H}_{21}\text{NO}_4\text{P}$: C, 56.17; H, 6.62; N, 3.83; Found: C, 56.20; H, 6.65; N, 3.40%.

(2S)-diethyl-((2-hydroxyphenyl)((4-chlorophenyl)amino)phosphonate (3e)

Oil; 90% yield; R_f (DCM-MeOH: 99/1) = 0.30; ^1H NMR (400 MHz, CDCl_3): δ = 1.21 (t, $J_{\text{HH}} = 6.0$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 1.26 (t, $J_{\text{HH}} = 8.0$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.91-4.16 (m, 4H, O- CH_2), 4.73 (t, $J_{\text{HH}} = 8.0$ Hz, 1H, NH), 4.90 (dd, $J_{\text{HH}} = 12.0$ Hz, $J_{\text{HH}} = 8.0$ Hz, 1H, *CH), 6.57-6.60 (m, 2H, H_{Ar}), 6.87 (t, $J_{\text{HH}} = 6.0$ Hz, 1H, H_{Ar}), 6.95 (d, $J_{\text{HH}} = 8.0$ Hz, 1H, H_{Ar}), 7.06-7.08 (m, 2H, H_{Ar}), 7.15-7.20 (m, 2H, H_{Ar}), 8.70 (s, 1H, OH); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 16.4 (d, $J_{\text{PC}} = 8.0$ Hz, CH_3), 16.5 (d, $J_{\text{PC}} = 20.0$ Hz, CH_3), 56.7 (CH_2), 55.2 (CH_2), 64.0 (dd, $J_{\text{PC}} = 28.0$ Hz, $J_{\text{PC}} = 220.0$ Hz, *CH), 115.7 (CH), 119.1 (CH), 119.2 (CH), 121.1 (d, $J_{\text{PC}} = 8.0$ Hz, CH), 121.7 (d, $J_{\text{PC}} = 12.0$ Hz, CH), 124.2 (CH), 129.1 (d, $J_{\text{PC}} = 28.0$ Hz, CH), 129.6 (d, $J_{\text{PC}} = 212.0$ Hz, CH), 129.9 (C), 145.0 (d, $J_{\text{PC}} = 52.0$ Hz, C), 155.7 (d, $J_{\text{PC}} = 20.0$ Hz, C); IR (KBr): 3171 (OH), 2964 (CH_2), 1220 (P=O), 1051 (P-O) cm^{-1} ; $^{31}\text{P}\{^1\text{H}\}$ NMR (160 MHz, CDCl_3): δ = 23.0; Anal. Calcd. for $\text{C}_{17}\text{H}_{21}\text{ClNO}_4\text{P}$: C, 55.22; H, 5.72; N, 3.79; Found: C, 55.25; H, 5.77; N, 3.81%.

(2S)-diethyl-((2-hydroxyphenyl)((4-fluorophenyl)amino)phosphonate (3f)

Oil; 86% yield; R_f (DCM-MeOH: 99/1) = 0.29; ^1H NMR (400 MHz, CDCl_3): δ = 1.22 (t, $J_{\text{HH}} = 7.2$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 1.27 (t, $J_{\text{HH}} = 7.0$ Hz, 3H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.94-4.30 (m, 4H, O- CH_2), 4.85 (d, $J_{\text{HH}} = 22.8$ Hz, 1H, *CH), 6.60-6.63 (m, 2H, H_{Ar}), 6.81-6.95 (m, 4H, H_{Ar}), 7.15-7.24 (m, 2H, H_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ = 16.4 (d, $J_{\text{PC}} =$

22.8 Hz, CH₃), 16.6 (d, J_{PC} = 22.4 Hz, CH₃), 54.8 (CH₂), 56.3 (CH₂), 63.8 (dd, J_{PC} = 27.6 Hz, J_{PC} = 198.4 Hz, *CH), 116.0 (CH), 116.1 (CH), 118.9 (CH), 120.9 (d, J_{PC} = 216.0 Hz, CH), 121.3 (d, J_{PC} = 12.0 Hz, CH), 129.2 (d, J_{PC} = 24.8 Hz, CH), 129.7 (d, J_{PC} = 18.4 Hz, CH), 129.6 (CH), 142.6 (t, J_{PC} = 18.0 Hz, C), 155.9 (d, J_{PC} = 18.0 Hz, C), 156.1 (d, J_{PC} = 128.0 Hz, C), 158.2 (C); IR (KBr): 3177 (NH), 2984 (CH₂), 1222 (P=O), 1062 (P-O) cm⁻¹; ³¹P{¹H} NMR (160 MHz, CDCl₃): δ = 25.0; Anal. Calcd. for C₁₇H₂₁FNO₄P: C, 57.79; H, 5.99; N, 3.96; Found: C, 57.83; H, 6.01; N, 4.01%.

(2S)-diethyl (phenyl) ((4-fluorophenyl)aminophosphonate (3 g)

White powder; m.p. = 127–129 °C; 93% yield; R_f (DCM-MeOH: 99/1) = 0.31; ¹H NMR (400 MHz, CDCl₃): δ = 1.11 (t, J_{HH} = 7.1 Hz, 3H, CH₃-CH₂-), 1.29 (t, J_{HH} = 7.2 Hz, 3H, CH₃-CH₂-), 3.65–3.69 (m, 1H, CH₂-O), 3.71–3.96 (m, 1H, CH₂-O), 4.08–4.15 (m, 2H, CH₂-O), 4.68 (d, J_{HH} = 24.4 Hz, 2H, *CH+NH), 6.50–6.53 (m, 2H, H_{Ar}), 6.80–6.82 (m, 2H, H_{Ar}), 7.25–7.29 (m, 2H, H_{Ar}), 7.31–7.35 (m, 3H, H_{Ar}), 7.43–7.46 (m, 2H, H_{Ar}); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 16.3 (d, J_{PC} = 23.2 Hz, CH₃), 16.5 (d, J_{PC} = 22.8 Hz, CH₃), 56.2 (CH₂), 57.7 (CH₂), 63.4 (t, J_{PC} = 28.8 Hz, *CH), 115.0 (d, J_{PC} = 29.6 Hz, CH), 115.8 (d, J_{PC} = 89.6 Hz, CH), 128.0 (d, J_{PC} = 22.0 Hz, CH), 128.1 (d, J_{PC} = 12.8 Hz, CH), 128.8 (d, J_{PC} = 10.4 Hz, CH), 135.8 (d, J_{PC} = 12.0 Hz, CH), 142.7 (d, J_{PC} = 7.6 Hz, CH), 142.8 (d, J_{PC} = 8.0 Hz, CH), 155.2 (C), 157.6 (C); IR (KBr): 3296 (NH), 3065 (CH), 1237 (P=O), 1029 (P-O) cm⁻¹; ³¹P{¹H} NMR (160 MHz, CDCl₃): δ = 22.8; Anal. Calcd. for C₁₇H₂₀FNO₃P: C, 60.53; H, 6.28; N, 4.15; Found: C, 60.64; H, 6.31; N, 4.20%.

Conclusion

In summary, a convenient three-component one-pot protocol for the synthesis of α -aminophosphonates using aldehyde, triethyl phosphite and substituted aniline as raw materials was developed and improved using eggshell waste as a heterogeneous nano-catalyst with high catalytic activity and reusability with ethanol as solvent. This protocol allowed us to obtain high yields (82–93%) of the desired products in a reaction time of 20 to 35 min. We have used ethanol as an ecologically benign and economic organic solvent, readily available, inexpensive and environmentally friendly. Excellent yields, shorter reaction time, column-free, easy processing, recyclability, biodegradable material and environmental friendliness are the attractive advantages of the protocol.

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Disclosure statement

There are no conflicts to declare.

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