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Seaweed-derived κ-carrageenan: Modified κ-carrageenan as a recyclable green catalyst in the multicomponent synthesis of aminophosphonates and polyhydroquinolines

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ABSTRACT: A seaweed-derived biopolymer, κ-carrageenan (KCAR), with a slight modification was assumed as an organosulfonic-type Bronsted acid in the catalysis of polyhydroquinoline and α-aminophosphonate syntheses through one-pot multicomponent reaction procedures under aqueous conditions. In this investigation, KCAR was found to be an efficient, heterogeneous and homogeneous, recyclable, economical, and green catalyst. Moreover, biocompatibility, ease of separation, high chemoselectivity, and lower reaction time were other aspects of this catalyst. © 2015 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2016**, *133*, 43190.

KEYWORDS: applications; biodegradable; catalysts

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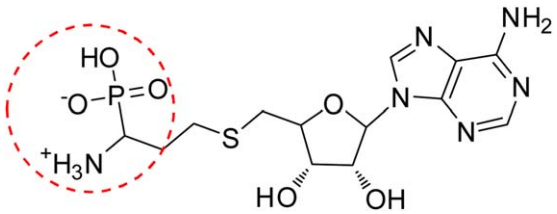
INTRODUCTION

Recently, organocatalytic reactions with green protocols have gain more attention among the other metal-based catalysts.[1–4] Also among them, the use of biodegradable and natural organocatalytic species is more interesting and rational.[5–8]

κ-Carrageenan (KCAR) is a sulfate-based polysaccharide, which is insoluble in cool water, and its cation is usually is K^+ or Na^+. Conformation of KCAR crucially depends on the type of cation.[9] This biopolymer is extracted from *Chondrus crispus* (Irish Moss).[10] There are also other types of carrageenan, including α-, β-, γ-, μ-, δ-, θ-, λ-, ι-, and ν-carrageenan. Among them, α-, β-, γ-, κ, ι-, and θ-carrageenan are more stable than the others under alkali conditions.[11] Moreover, There are many applications for carrageenans; these include their use in the food industry[12] and hydrogel and aerogel manufacturing.[13,14] KCAR can also make a complex with other types of polymers to improve mechanochemical properties.[15–18] The other applications of KCAR include biological studies and drug-delivery cases.[12,19,20] In drug-delivery cases, because of its biodegradability and nontoxicity, KCAR is used as a support for loading the drug and its controlled release from a support. KCAR has also been used as a source for K_2SO_4 and in 5-hydroxymethyl furfural furfural production.[9] However, KCAR has not merely been applied as a catalyst in organic syntheses without postmodification or pretreatment. To best of our knowledge, this was the first study in which KCAR was merely applied as a catalyst with no need for postmodification, grafting, or copolymerization.

Hence, we found a new use for KCAR through its organocatalytic capability in the syntheses of α-aminophosphonates and polyhydroquinolines (PHQs) through a multicomponent reaction approach. It encouraged us toward further study of the catalytic activity of KCAR. We found it a heterogeneous, recyclable, nontoxic, and green catalyst in the three-component synthesis of α-aminophosphonate through condensation of amine, aromatic aldehyde, and dimethyl phosphite (Scheme 1).

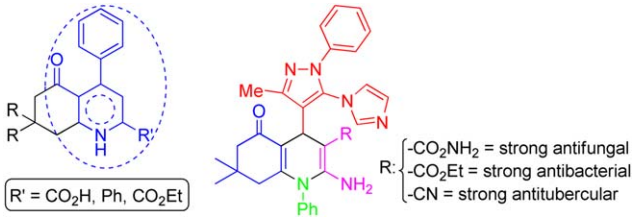
α-Aminophosphonate derivatives correspond to α-aminocarboxylic acid derivatives, which have many diverse bioactivities.[21,22] α-Amino phosphonate esters are excellent candidates as inhibitors of a wide range of proteolytic enzymes.[7–9,23–25] They are also interesting because of their antibacterial[26] and antifungal activities.[27] Benzyl aminophosphonic acids are known as potent inhibitors of human prostatic acid phosphatase.[28] Honek *et al.*[29] synthesized an α-aminophosphonate nucleoside as an analogue of *S*-adenosyl-*l*-homocysteine by a new method, and they found that it could inactivate *S*-adenosyl-*l*-homocysteine hydrolase in a time-dependent manner (Scheme 1).



Scheme 1. Example of bioactive α-aminophosphonate. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The synthesis of α-aminophosphonate derivatives has been performed with various types of homogeneous catalysts; $LiClO_4$,[22] glycerin,[30] $CoCl_2{\cdot}6H_2O$,[31] and $Cd(ClO_4)_2{\cdot}xH_2O$[32] have been used for the synthesis of α-aminophosphonates. However, these catalysts are impractical to recover and reuse, and in some cases, in particular with transition metal salts, they are toxic and costly. Also, in the case of heterogeneous catalysts, some obstacles still exist; these include a higher cost of preparation and, in some cases, an overwhelming number of steps of catalyst preparation with heavy metals, which are toxic. However, the use of KCAR as a catalyst can prevent the use heavy metals and overcome the possibility of the recovery and reuse of catalyst; this also makes for easy separation and workup. Additionally, the availability and low cost of KCAR are other advantages. Also, PHQs are a class of bioactive heterocycles that are extensively used in biological studies.[33,34] Recently, some PHQ derivatives have been found to be prospective antihyperglycemic and lipid-modulating agents (Scheme 2).[35] Moreover, some novel PHQs were synthesized via a one-pot, four-component cyclocondensation method in which the compound 5-imidazopyrazole was embedded in the structure. This led to the production of some strong bioactivities (Scheme 2).

The synthesis of PHQs have been reported with many types of heterogeneous catalysts; these include manganese-supported periodic mesoporous organosilicas (PMO),[36] Co_3O_4 supported on carbon nanotube (CNT),[37] glucosulfonic acid supported on Fe_3O_4 nanoparticles,[38] TiO_2-coated magnetite nanoparticle-supported sulfonic acid,[39] piperidine-4-carboxylic acid functionalized Fe_3O_4 nanoparticles,[40] and MgO nanoparticles.[41] However, in comparison to our suggested catalyst, these have usually been synthesized from transition metals in multistep synthetic procedures, whereas the modified KCAR is a nonmetal catalyst, which has a natural source. Also, its use as a catalyst is economically more effective than the example catalysts. Therefore, its synthesis through a green and nontoxic method with a high yield and shorter reaction time is still a concern.



Scheme 2. Some typical examples of bioactive PHQs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

EXPERIMENTAL

KCAR and cellulose powder were purchased from Sigma-Aldrich and were used without purification. All other reagents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. For all reactions in this study, fresh distilled water was used. IR spectra were recorded on a Shimadzu IR-460 spectrometer. The melting points were measured on an Electrothermal 9100 apparatus. The progress of the reactions was monitored by thin-layer chromatography (mesh = 60). All of the obtained yields were based on the isolated amount of the products. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker 300 FT-NMR instrument at 300 and 75 MHz, respectively.

Activation of KCAR

For the modification of commercial KCAR, 1 g of KCAR was mechanically mixed 1 mL of a 2*M* HCl solution for 1–2 min. After filtration and washing with distilled water and methanol (MeOH) several times to remove untreated HCl and produced salt, the acidity of KCAR was measured by standard titration. The modified KCAR was dispersed in brine solution, and the amount of H^+ was measured by titration over a standard solution of NaOH. The obtained amount of H^+ for each gram of KCAR was 2.5 mmol. This was near the amount of sulfonate motifs for each gram of KCAR. Figure 1 shows the Fourier transform infrared (FTIR) spectra and energy-dispersive spectrometry (EDS) analysis results; these proved the presence of maintenance of every function within the activated KCAR. In this regard, the broadband absorbance at 3400 cm^{-1} was related to sulfonic acid and hydroxyl groups. Also, the two peaks at 2945 and 2915 cm^{-1} were attributed to the presence of aliphatic carbons. In addition, EDS analysis indicated all of the related atoms within the structure of KCAR (Figure 1).

General Synthesis of α-Aminophosphonate

In a general method, benzaldehyde (1 mmol) and aniline (1 mmol) were mixed together in the presence of 0.02 g of κ-carrageenan and 2 mL of H_2O and stirred at room temperature (RT) for 2 min. Then, 1.1 mmol of phosphites was added to the reaction mixture; the temperature was increased to 80°C, and the solution was allowed to react for 30 min. After 30 min, the reaction was stopped and cooled to RT (25°C), and the

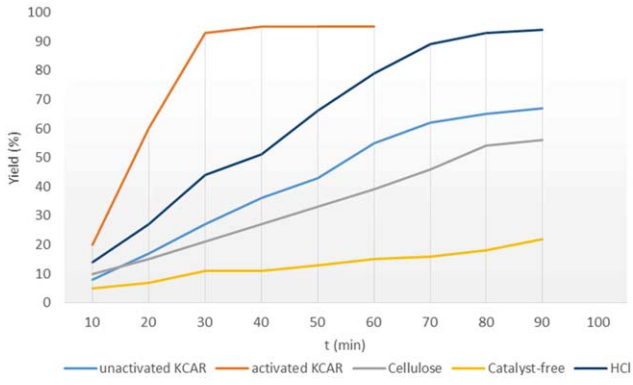


Figure 1. (a) FTIR spectra and (b) EDS analysis of modified KCAR. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

catalyst was separated by filtration and washed with cold dichloromethane (DCM) for further use in further cycles. In the reaction crude, the organic phase (DCM) was evaporated and purified by column chromatography (*n*-hexane/ethyl acetate ratio for chromatography = 3:1). All of the isolated products gave satisfactory spectral and physical data. All of the products were reported previously and were characterized by comparison with the IR and physical data. The spectral data for the selected products follow.

Dimethyl Phenyl(phenyl amino)methyl Phosphonate (4a; green oil). FTIR spectroscopy (KBr, cm^{-1}): 1025, 1595, 2981, 3292. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 3.47 (d, $^3J_{HP} = 10.5$, 3 H), 3.78 (d, $^3J_{HP} = 10.5$, 3 H), 4.84 (d, $^2J_{HP} = 24.3$, 1 H), 5.02 (br, 1 NH), 6.51–7.51 (m, 10 H).

Dimethyl (3-nitrophenyl)(phenylamino)methyl Phosphonate (4b; Yellowish Oil). FTIR spectroscopy (KBr, cm^{-1}): 1032, 1447, 1601, 1952, 2932, 3302. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 3.64 (d, $^3J_{HP} = 10.8$ Hz, 3 H), 3.83 (d, $^3J_{HP} = 10.4$, 3H), 5.00 (d, $^2J_{HP} = 25.1$, 1 H), 5.25 (br, 1 NH), 6.62–8.41 (m, 9 H).

Dimethyl (4-chlorophenyl)(phenylamino)methyl Phosphonate (4c; Yellowish Oil). ^{1}H-NMR (300.13 MHz, $CDCl_3$): 3.55 (3H, d, $^3J_{HP} = 10.8$ Hz), 3.77 (3H, d, $^3J_{HP} = 10.8$ Hz), 4.52 (1H, broad, NH), 4.79 (1H, d, $^2J_{HP} = 24.3$), 6.59–7.44 (9H, m).

General Synthesis for PHQ

In a general method, benzaldehyde (1 mmol) and dimedone (1 mmol) were mixed together in the presence of 0.02 g of KCAR and 2 mL of H_2O and stirred at RT for 5 min. Then, *β*-enaminoester (1.2 mmol) was added to the reaction mixture and allowed to react for 60 min at RT. After 60 min, the reaction was stopped, and the catalyst was separated by filtration and washed with cold DCM for use in further cycles. The organic phase reaction crude was extracted by DCM, evaporated, and purified by column chromatography (*n*-hexane/ethyl acetate ratio for chromatography = 4:1). All of the isolated products gave satisfactory spectral and physical data. All of the products were reported previously and were characterized by comparison with IR and physical data.[42]

Methyl 4-(2-methyl phenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7b; White Solid). IR spectroscopy (KBr ν_{max}; cm^{-1}): 3282, 3189, 3071, 2956, 1693, 1644, 1484. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 0.95 (s, 3 H), 1.09 (s, 3 H), 2.11–2.44 (m, 8 H), 3.62 (s, 3 H), 5.03 (s, 1 H), 5.90 (s, 1 H), 7.00–7.19 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 27.21, 29.37, 35.79, 41.23, 51.03, 127.66, 128.73.

Ethyl 4-(2-methyl phenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7c; White Solid). IR spectroscopy (KBr ν_{max}; cm^{-1}): 3245, 3078, 2958, 1701, 1600. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 0.95 (s, 3 H), 1.07 (s, 3 H), 1.22 (t, $J = 6.9$ Hz, 3 H), 2.13–2.34 (m, 10 H), 4.06 (q, $J = 6.9$ Hz, 2 H), 5.02 (s, 1 H), 6.30 (s, 1 H), 7.00–7.27 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.20, 19.31, 21.04, 27.21, 29.34, 32.74, 36.11, 41.05, 50.27, 59.85, 106.84, 112.01, 127.87, 128.63, 135.46, 143.08, 143.94, 167.38, 195.38.

Methyl 4-(2-chlorophenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7d; White Solid). ^{1}H-NMR (300.13 MHz, $CDCl_3$): 0.91 (s, 3 H), 1.07 (s, 3 H), 2.04–2.36 (m, 7 H), 3.57 (s, 3 H), 5.38 (s, 1 H), 6.81 (s, 1 H), 7.00–7.34 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.19, 27.15, 29.37, 32.54, 35.61, 40.96, 50.62, 50.83, 105.17, 111.37, 126.42, 127.26, 129.61, 131.64, 131.64, 133.10, 143.87, 144.33, 148.92, 167.91, 195.51.

Ethyl 4-(2-chlorophenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7e; White Solid). IR spectroscopy (KBr ν_{max}; cm^{-1}): 3292, 3072, 2957, 1700, 1650, 1621, 1486, 758. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 0.89 (s, 3 H), 1.07 (s, 3 H), 1.17 (t, $J = 6.9$ Hz, 3 H), 1.65–2.35 (m, 7 H), 4.04 (q, $J = 6.9$ Hz, 2 H), 5.38 (s, 1 H), 6.11 (s, 1 H), 7.00–7.41 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.19, 19.35, 27.22, 29.32, 32.53, 35.97, 41.13, 50.57, 59.83, 105.33, 111.18, 126.24, 127.27, 129.67, 132.09, 133.20, 143.56, 148.68, 167.43, 195.35.

Methyl 4-(4-methoxyphenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7f; White Solid). IR spectroscopy (KBr ν_{max}; cm^{-1}): 3274, 2960, 1705, 1648, 1608, 1494. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 0.94 (s, 3 H), 1.08 (s, 3 H), 2.10–2.38 (m, 7 H), 3.62 (s, 3 H), 3.74 (s, 3 H), 5.01 (s, 1 H), 5.95 (s, 1 H), 6.74 (d, $J = 8.7$ Hz, 2 H), 7.21 (d, $J = 8.7$ Hz, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.52, 27.16, 29.41, 35.40, 41.22, 50.68, 51.02, 55.10, 113.36, 128.75.

Methyl 4-(4-chlorophenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7g; White Solid). IR spectroscopy (KBr ν_{max}; cm^{-1}): 3288, 2958, 1645, 1610, 1391, 1218, 1074, 1012, 840, 775, 538. ^{1}H-NMR (300.13 MHz, CDCl3): 0.92 (s, 3 H), 1.08 (s, 3 H), 2.10–2.32 (m, 4 H), 2.39 (s, 3 H), 3.61 (s, 3 H, OCH_3), 5.04 (s, 1 H), 6.2 (s, 1 H), 7.15–7.27 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.45, 27.06, 28.09, 28.24, 29.42, 32.71, 35.95, 41.05, 50.63, 51.08, 105.40, 111.90, 128.10, 129.24, 131.64, 143.98, 145.36, 148.23, 167.67, 195.57.

Ethyl 4-(4-chlorophenyl)−2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-3-quinoline Carboxylate (7h; White Solid). IR spectroscopy (KBr ν_{max}; cm^{-1}): 3243, 3076, 2958, 1706, 1647, 1604, 1488, 844. ^{1}H-NMR (300.13 MHz, $CDCl_3$): 0.92 (s, 3 H), 1.08 (s, 3 H), 1.17 (t, $J = 6.9$ Hz, 3 H), 2.10–2.38 (m, 7 H), 4.06 (q, $J = 6.9$ Hz, 2 H), 5.02 (s, 1 H), 6.25 (s, 1 H), 7.15–7.27 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.19, 19.38, 27.08, 27.76, 29.41, 32.69, 36.22, 41.00, 50.64, 59.90, 105.70, 111.77, 128.00, 129.44, 131.57, 143.79, 145.60, 148.51, 167.26, 195.60.

RESULTS AND DISCUSSION

With the increasing tendency to develop green protocols for synthesis and catalysis, natural biopolymers play a significant role in the areas of organocatalysis and supporting nanoparticles.[5,6,43,44] We used KCAR, a seaweed-derived polysaccharide, as an organosulfonic-based Bronsted acid (Scheme 3). Therefore, we planned to study its catalytic activity KCAR in two kinds of organic reactions: the syntheses of α-aminophosphonates and PHQs. However, before the operation, we exchanged the K^+ ions of $-SO_3K$ moieties in KCAR with H^+ to produce a Bronsted acid with heterogeneous feature at RT under the aqueous conditions. The synthesis of α-aminophosphonates was achieved by a

Scheme 3. KCAR as a catalyst in a tricomponent synthesis. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

three-component reaction through the condensation of benzaldehyde and amine to give imine, and then, the nucleophilic addition of dimethyl phosphite to produce the final product. This biopolymer was soluble in hot water and, therefore, acted as a homogeneous catalyst, whereas at lower temperatures, it acted as a heterogeneous catalyst.

To discover the optimized conditions for the synthesis of α-aminophosphonates, various parameters, such as the temperature, amount of catalyst, and several solvents, were taken into consideration. First, the effect of the KCAR amount as the catalyst was examined on reaction under other similar conditions, including the same temperature (reflux conditions) and identical times (30 min). Several amounts of catalyst was added to the reaction mixtures, and among them, 0.02 g of KCAR was found to be more efficient from the point view of yield in each reaction (Figure 2).

Second, the effect of the temperature was monitored on the product yields under similar conditions. In this regard, three different temperatures including RT, 50, and 80°C, and the reflux conditions of water were selected. One considerable point in this comparison was that the reaction below 80°C had a lower reaction yield completion in that time (30 min; Table I). This was attributed to the different behavior of modified KCAR above 80°C. The modified KCAR gave a clear solution above 80°C because it was converted to a homogeneous-type catalyst, and hence, suitable interactions arose between KCAR and the reactants after this conversion, in which the product could be efficiently generated under reflux conditions.

Also, the effects of various solvents on the yield and chemoselectivity toward the product were investigated through the model reaction (benzaldehyde, aniline, and dimethyl phosphite). In this case, polar and nonpolar solvents were compared under similar conditions. Among them, DMF, dimethyl sulfoxide (DMSO), MeOH, ethanol (EtOH), and H_2O showed better results. However, because of the fact that water is a nontoxic, available, cheaper, and therefore, a greener solvent and also produced a bit higher product yield, it was selected as an optimized solvent in the synthesis of aminophosphonate (Table I). These solvents were used as protic solvents and could produce hydrogen bonding with the catalyst and reactants; this led to the efficient production of favorable products.

Because KCAR was a polysaccharide, we compared its catalytic activity with that of another type of polysaccharide, cellulose; they were similar to each other except for sulfonic groups on each monomer of KCAR and some small differences. Under similar conditions, we studied the effect the presence and absence of sulfonic acids on the polymer. As a result, we observed that the sulfonic acid had a critical effect on the product yield; this indicated the active catalytic centers. On the other hand, the weaker catalytic activity of cellulose was attributed to the capability of hydroxyl groups, which could establish hydrogen bonding with the reactants and activate them. This could also lead to the advent of partial catalytic activity; cellulose, in comparison with unactivated KCAR, had comparable results and showed that they had partially similar catalytic mechanisms. However, the unactivated KCAR in comparison with its activated version was differentiable and showed that activation had a crucial effect on the product yield. The activated KCAR was also compared to an equimolar amount of HCl (2 mL of 2*M* HCl aqueous solution) in viewpoint of H^+ (millimoles). This observation showed that HCl itself had a lower catalytic activity than the activated KCAR. Also, when there was no catalyst, a remarkable decrease happened in the product yield (Figure 2).

After sufficient investigations to determine the optimized reaction conditions, we aimed to explore the synthesis of α-aminophosphonate derivatives by changing the aldehyde, amine, and phosphite to evaluate the catalytic activity of KCAR in the other types of reactants (Table II). Among the reactants, the electron-donating groups on the aromatic rings of amines raised the product yields (**4f**), whereas the electron-withdrawing groups on the aromatic rings of benzaldehyde caused a decrease in the reactivity (**4d**, **4g**). These substituents directly affected the reactivity of imine with phosphite and, consequently, the product yields.

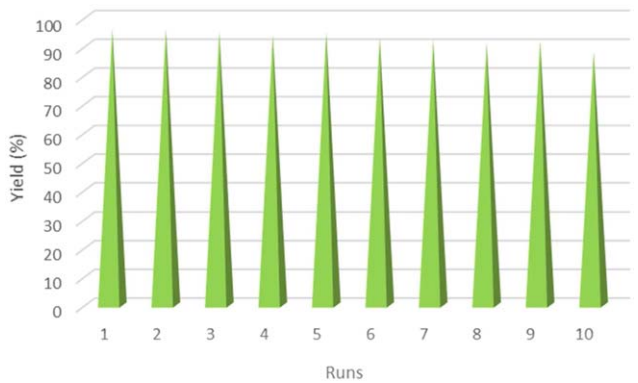


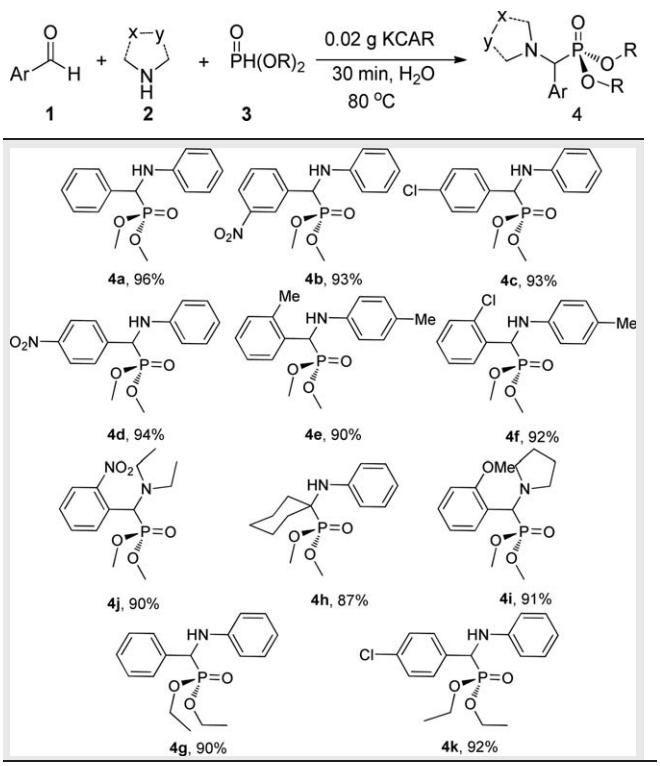
Figure 2. Comparison of the reaction progress in the presence of HCl, cellulose, unactivated KCAR, and activated KCAR and in the absence of any catalyst. Reaction conditions: 1 mmol of benzaldehyde, 1 mmol of aniline, and 1.1 mmol of dimethyl phosphite in the presence of 0.02 g of polymer under reflux conditions. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table I. Study of the Catalytic Activity of KCAR under Various Conditions[a]

Entry	Amount of catalyst (mg)	*T* (°C)	Solvent	*t* (min)	Yield (%)[b]
1	1	Reflux	H_2O	180	95
2	10	Reflux	H_2O	120	96
3	20	Reflux	H_2O	30	95
4	30	Reflux	H_2O	30	96
5	20	RT	H_2O	30	75
6	20	50	H_2O	30	88
7	20	80	H_2O	30	95
8	20	80	DMSO	30	94
9	20	80	DMF	30	90
10	20	80	CH3CN	30	84
11	20	80	EtOH	30	88
12	20	80	MeOH	30	66
13	20	80	Tetrahydrofuran	30	51
14	20	80	Dioxane	30	56
15	20	80	Toluene	30	44

T, temperature; *t*, time.
[a] Reaction conditions: 1 mmol of benzaldehyde, 1 mmol of aniline, and 1.1 mmol of phosphite in the presence of specific amount of KCAR.
[b] Isolated yields.

Table II. Synthesis of α-Aminophosphonate[a]

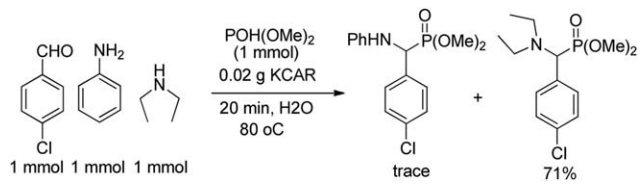


[a] Reaction conditions: 1 mmol of benzaldehyde, 1 mmol of aniline, and 1.1 mmol of dialkyl phosphite in the presence of 0.02 g of KCAR under aqueous conditions at 80°C for 30 min.

To determine the chemoselectivity of the method, we also reacted *p*-chlorobenzaldehyde with a mixture of aniline and diethyl amine under the optimized conditions. This reaction can also produce corresponding phosphonate. However, under these reaction conditions, no aniline-coupled phosphonate derivative was found; this demonstrated the chemoselectivity of this method (Scheme 4).

Thereafter, we studied the recyclability of KCAR in the model reaction. Fortunately, the results showed good recyclability in each run. This investigation led us to discover KCAR as a recyclable catalyst, at least for 10 runs with no significant decrease in the yield of the product (Figure 3).

After to our previous experiences with the synthesis of PHQs through the Bronsted acid based catalyst,[42] we benchmarked the catalytic activity of KCAR by testing in this reaction. In this regard, we allowed benzaldehyde to react with dimedone and β-enaminoester under one-pot tandem conditions. Fortunately, the reaction was completed at RT in 1 h under aqueous conditions. Therefore, PHQ was obtained according to the green chemical roles of synthesis in high yield. Hence, the other



Scheme 4. Plausible mechanisms for the syntheses of 7 and 4 under the catalysis of KCAR.

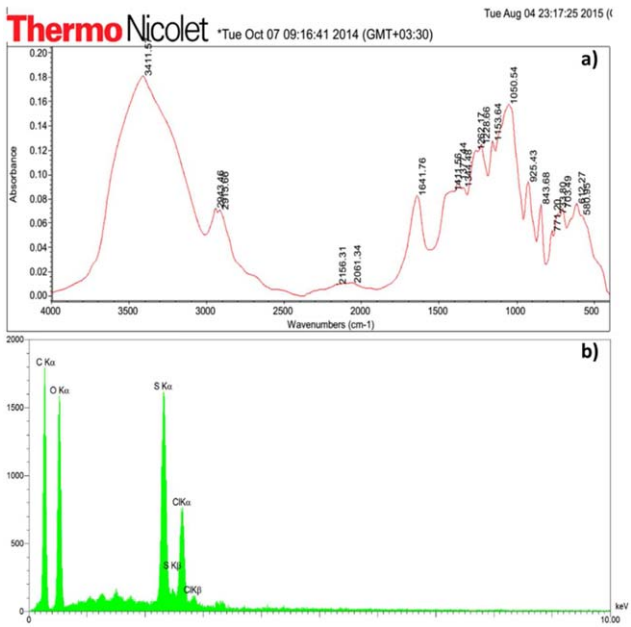
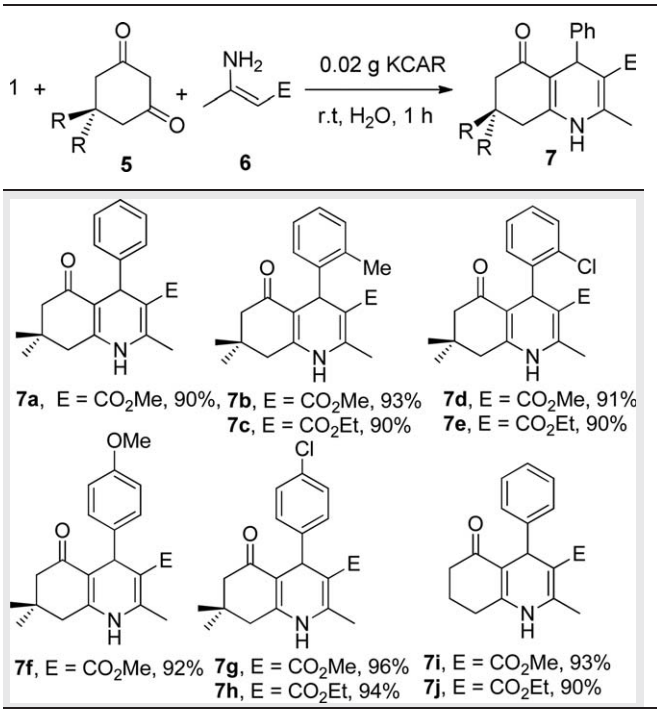


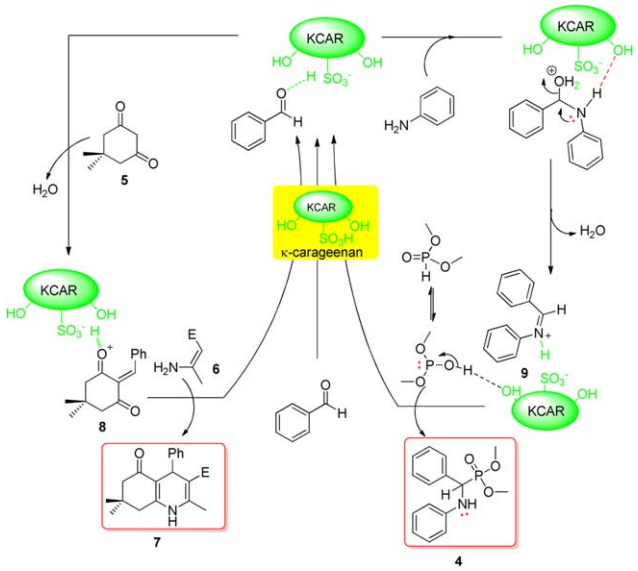
Figure 3. Recycling study of KCAR in phosphonate synthesis (scale = 10 mmol). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

derivatives of PHQ were synthesized under these conditions. All derivatives were generated in high yields with no remarkable side products (Table III).

Table III. Synthesis of the PHQ Derivatives under the Catalysis of KCAR[a,b]



[a] Isolated yields.
[b] Reaction conditions: benzaldehyde (1 mmol), dimedone (1 mmol), and β-enaminoester (1.2 mmol) in the presence of 0.02 g of KCAR under aqueous conditions.



Scheme 5. Plausible mechanisms for the syntheses of 7 and 4 under the catalysis of KCAR. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Although there is no proven mechanism for the studied reactions during the catalysis of KCAR, a probable mechanism could be predicted by the primary protonation of aldehyde and the subsequent addition of a nucleophile (aniline or dimedone).[45,46] Then, the protonated intermediates (**8** and **9**) underwent a further nucleophilic attack by dimethyl phosphite or β-enaminoester (in the case of PHQ, a Michael cyclization process occurred, and in the α-aminophosphonate mechanism, dimethyl phosphite attacked at the carbon of the imine bond). Thus, each of the related products was generated (Scheme 5).

CONCLUSIONS

The first report of modified KCAR as a catalyst was given here for the syntheses of α-aminophosphonate and PHQ derivatives. Commercially available KCAR in the catalysis role was played well with a slight activation step; it was found to be an efficient, renewable, biodegradable, and recyclable (at least for 10 consecutive runs) biopolymeric catalyst in multicomponent reactions. Its dual nature and heterogeneous and homogeneous features were other advantages of this catalyst. For these syntheses, completely green and ecofriendly protocols were developed.

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