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La(OTf)$_2$-amine Grafted-GO as the First Multifunctional Catalyst for the One-pot Three-component Synthesis of α-Aminophosphonates

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In this paper, the applicability of immobilized lanthanum(III) triflate on amine grafted graphene oxide [La(OTf)$_2$-amine grafted-GO] as the first multifunctional catalyst is described for the efficient synthesis of α-aminophosphonates by the one-pot three-component reaction of carbonyl compounds, substituted anilines and trialkyl phosphites. Various α-aminophosphonates were synthesized in good to high yields under solvent-free conditions at room temperature. The catalyst was reused five times without significant loss of its activity.

Keywords: Multifunctional catalyst, One-pot reaction, α-Aminophosphonates, Kabachnik-Fields reaction

INTRODUCTION

Nature has developed enzymatic catalysts for the multistep synthesis of complex chemical building blocks needed for the cells' metabolism from nutrients in a perfect chemical factory which is called living cells [1,2]. The multistep synthesis of metabolites occurs *via* a series of sequential reactions in which the product of one reaction serves as a substrate for the subsequent reaction. The efficient catalytic ability of enzymes in these multistep reactions is due to cooperative interactions between accurately positioned functional groups such as metal centers, acids, bases, hydrogen bond donors and hydrogen bond acceptors in the active sites. These groups perform many important roles including activation and stabilization of transition states and substrate recognition through hydrogen bonding, electrostatic or covalent interactions [3-6]. Mimicking of the bio-system in artificial heterogeneous catalysis would be a great interest for chemists not only in industry but also in academe [7,8]. In this regard, most chemists have focused their attention on the development of heterogeneous multifunctional catalysts for performing multistep organic synthesis of a desired compound *via* one-pot cascade reactions [9-11]. Using multifunctional catalysts in cascade reactions combining two or more catalytic transformations in one-pot process eliminates the time and yield losses associated with the isolation and purification of intermediates in multistep sequences.

Synthesis of α-aminophosphonates, an important class of organophosphorus compounds, has attracted considerable attention because of their potential application in biochemical and pharmaceutical chemistry [12,13]. The uses of α-aminophosphonates as enzyme inhibitors [14], anti-cancer [15], antibiotics [16], peptide mimics [17], nervous system activator [18], pharmacological agents [19] and many other applications have also been well documented [20,21]. Nucleophilic addition of phosphite esters to imines, formed upon the reaction of carbonyl compounds and amines, are an important general method for the formation of the N-C-P bonds. This reaction is usually promoted by

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Brønsted/Lewis acids and bases following the pioneering work of Pudovik [22-24]. Kabachnik-Fields reaction is an alternative method leading to the formation of α-aminophosphonates *via* one-pot three-component condensation of aldehydes, amines, and phosphite esters. The most important advantage of this method is its versatility and avoiding to isolate an imine as an intermediate [25,26]. In recent years, several catalysts have been designed and employed for this reaction [27-31]. However, in spite of their potential utility, these procedures typically suffer from one or more disadvantages such as the use of moisture-sensitive, poisonous, unrecoverable or stoichiometric amounts of the catalyst, tedious work-up procedures and using hazardous solvents. Therefore, the introduction of a reusable heterogeneous catalyst for the efficient and environmentally benign synthesis of α-aminophosphonates *via* a one-pot three-component method is still in demand.

In contunation of our recent works on the development of new heterogeneous catalysts [32-38], herein, we wish to report the one-pot synthesis of α-aminophosphonates *via* Kabachnik-Fields reaction catalyzed by immobilized lanthanum(III) triflate on amine grafted graphene oxide [$La(OTf)_2$-amine grafted-GO].

EXPERIMENTAL

General

Chemicals were purchased from Merck Chemical Company and used without any further purification. NMR spectra were recorded on a Bruker Advance DPX-250 in $CDCl_3$ as solvent and TMS as internal standard. The purity of the products and the progress of the reactions were accomplished by TLC on silica-gel polygram SILG/UV254 plates. FT-IR spectra were recorded on a Shimadzu Fourier Transform Infrared Spectrophotometer (FT-IR-8300). Transmission electron microscopy (TEM) analysis was performed using TEM microscope (Philips CM30). Scanning electron microscopy (SEM) and energy dispersive spectroscopy (EDS) were determined using a field emmission scanning electron microscopy (FESEM), model Mira 3-XMU. $La(OTf)_2$-amine grafted-GO was synthesized and characterized according to the procedure previously reported by us [36].

General Procedure for the One-pot Three-component Synthesis of α-Aminophosphonates

A mixture of carbonyl compound (1 mmol), amine (1 mmol), trialkyl phosphite (1 mmol) and $La(OTf)_2$-amine grafted-GO (0.1 mol%) was stirred at room temperature for the appropriate time (Table 2). The reaction mixture was diluted with EtOAc. The catalyst was separated by centrifugation. Evaporation of the solvent of the filtrate under reduced pressure gave the crude products. The pure products were obtained by flash chromatography on silica gel eluted with *n*-hexane-EtOAc (1:1).

Diethyl (phenyl)-N-(phenyl)aminomethyl-phosphonate. M. P.: 89-90 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.11 (t, 3H, $^2J_{H,H}$ = 7.1 Hz), 1.28 (t, 3H, $^2J_{H,H}$ = 7.1 Hz), 3.59-3.69 (m, 1H), 3.88-3.95 (m, 1H), 4.07-4.16 (m, 2H), 4.75 (d, 1H, $^2J_{H,H}$ = 26.4 Hz), 4.79 (bs, 1H), 6.59 (d, 2H, $^2J_{H,H}$ = 7.9 Hz), 6.68 (t, 1H, $^2J_{H,H}$ = 7.3 Hz), 7.10 (t, 2H, $^2J_{H,H}$ = 8.0 Hz), 7.25-7.35 (m, 3H), 7.47 (d, 2H, $^2J_{H,H}$ = 7.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.8 Hz), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz), 56.4 (d, $^1J_{C,P}$ = 150.4 Hz), 63.7 (d, $^2J_{C,P}$ = 7.0 Hz), 114.2, 118.8, 128.2 (d, $J_{C,P}$ = 5.5 Hz), 128.3 (d, $J_{C,P}$ = 3.5 Hz), 129.0 (d, $J_{C,P}$ = 2.7 Hz), 129.6, 136.3, 146.7 (d, $J_{C,P}$ = 14.6 Hz) ppm.

Dimethyl (phenyl)-N-(phenyl)aminomethyl-phosphonate. M. P.: 85-87 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 3.40 (d, 3H, $^2J_{P,H}$ = 10.0 Hz), 3.69 (d, 3H, $^2J_{P,H}$ = 10.0 Hz), 4.66-4.79 (m, 2H), 6.51-6.63 (m, 3H), 7.00-7.07 (m, 2H), 7.19-7.31 (m, 3H), 7.39-7.42 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 52.8 (d, $^2J_{C,P}$= 7.1 Hz), 54.6 (d, $^1J_{C,P}$ = 151.5 Hz), 112.8, 117.5, 126.8 (d, $J_{C,P}$ = 5.3 Hz), 127.0, 127.7, 128.2, 134.5, 145.0 (d, $J_{C,P}$ = 13.6 Hz) ppm.

Di-iso-propyl (phenyl)-N-(phenyl)aminomethyl-phosphonate. Semi solid, ^{1}H NMR ($CDCl_3$, TMS): δ 0.83-1.09 (m, 3H), 1.16-1.26 (m, 9H), 4.37-4.40 (m, 2H), 4.55-4.67 (m, 2H), 6.50-6.63 (m, 5H), 7.02 (t, 2H, $^2J_{H,H}$ = 7.5 Hz), 7.19-7.27 (m, 1H), 7.39 (d, 2H, $^2J_{H,H}$ = 7.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 23.2 (d, $^2J_{C,P}$ = 5.8 Hz), 23.8 (d, $^2J_{C,P}$ = 5.8 Hz), 56.5 (d, $^1J_{C,P}$ = 151.8 Hz), 71.9 (d, $^2J_{C,P}$ = 7.6 Hz), 72.0 (d, $^2J_{C,P}$ = 8.4 Hz), 113.8, 118.2, 127.7, 128.0 (d, $J_{C,P}$ = 5.4 Hz), 128.4, 129.1, 136.2, 146.5 (d, $J_{C,P}$ = 14.6 Hz) ppm.

Diethyl (4-methoxyphenyl)-N-(phenyl)aminomethyl-phosphonate. M. P.: 58-60 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.02-1.08 (m, 3H), 1.18-1.22 (m, 3H), 3.70 (s, 3H), 3.63-3.65, 3.84-3.89, 4.01-4.06 (m, 4H), 4.58-4.67 (m, 2H), 6.50-6.63 (m, 3H), 6.77-6.81 (m, 2H), 7.00-7.03 (m, 2H), 7.29-7.31 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.7 (d, $^3J_{C,P}$ = 5.8), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz), 55.7 (d, $^1J_{C,P}$ = 152.1 Hz), 55.6, 63.5, 114.3, 114.4, 114.5, 118.7, 129.3, 129.4, 129.5 ppm.

Diethyl (4-cholorophenyl)-N-(phenyl)aminomethyl-phosphonate. M. P.: 147-149 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.09 (t, 3H, $^2J_{H,H}$ = 7.1 Hz), 1.21 (t, 3H, $^2J_{H,H}$ = 7.1 Hz), 3.69-4.09 (m, 4H), 4.60-4.70 (m, 2H), 6.48 (d, 2H, $^2J_{H,H}$ = 7.8 Hz), 6.63 (t, 1H, $^2J_{H,H}$ = 7.3 Hz), 7.03 (t, 2H, $^2J_{H,H}$ = 7.8 Hz), 7.23 (d, 2H, $^2J_{H,H}$ = 8.4 Hz), 7.32-7.36 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.8 Hz), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz), 55.9 (d, $^1J_{C,P}$ = 150.5 Hz), 63.7 (d, $^2J_{C,P}$ = 6.1 Hz), 63.8 (d, $^2J_{C,P}$ = 6.3 Hz), 114.2, 119.1, 129.2 (d, $J_{C,P}$ = 2.7 Hz), 129.5 (d, $J_{C,P}$ = 5.4 Hz), 129.7, 134.1, 134.9, 146.4 (d, $J_{C,P}$ = 14.6 Hz) ppm.

Diethyl (2-nitrophenyl)-N-(phenyl)aminomethyl-phosphonate. M. P.: 157-159 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.01 (t, 3H, $^3J_{H,H}$ = 8.0 Hz), 1.21 (t, 3H, $^3J_{H,H}$ = 2.6 Hz), 3.74-3.88 (m, 2H), 4.06-4.12 (m, 2H), 5.05 (bs, 1H), 6.05-6.15 (d, 1H, $^1J_{H,H}$ = 26.2 Hz), 6.59-6.67 (m, 2H), 7.01-7.08 (m, 2H), 7.31-7.45 (m, 2H), 7.66-7.69 (m, 2H), 7.89-7.92 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 15.9 (d, $^3J_{C,P}$ = 5.6 Hz), 16.3 (d, $^3J_{C,P}$ = 5.6 Hz), 49.9 (d, $^1J_{C,P}$= 151.4 Hz), 63.3 (d, $^2J_{C,P}$ = 7.2 Hz), 63.8 (d, $^2J_{C,P}$ = 6.9 Hz), 113.5, 118.8, 125.2 (d, $J_{C,P}$ = 2.3 Hz), 128.5-128.8, 129.4, 131.9 (d, $J_{C,P}$ = 1.8 Hz), 133.5 (d, $J_{C,P}$ = 3.1 Hz) , 145.5 (d, $J_{C,P}$ = 14.0 Hz), 149.5 ppm.

Diethyl (2,6-dichlorophenyl)-N-(phenyl)amino-methylphosphonate. Viscouse colourless oil, ^{1}H NMR ($CDCl_3$, TMS): δ 1.02-1.07 (m, 3H), 1.24-1.29 (m, 3H), 3.81-4.01 (m, 2H), 4.10-4.19 (m, 2H), 5.40 (t, 1H), 5.77 (dd, 1H, $^3J_{H,H}$ = 9.95 Hz, $^2J_{P,H}$ = 28.6 Hz), 6.56-6.66 (m, 3H), 7.01-7.27 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.1 (d, $^3J_{C,P}$ = 5.8 Hz), 16.5 (d, $^3J_{C,P}$ = 5.8 Hz), 53.1 (d, $^1J_{C,P}$ = 157.9 Hz), 63.1 (d, $^2J_{C,P}$ = 6.8 Hz), 63.4 (d, $^2J_{C,P}$ = 6.8 Hz), 113.5, 118.7, 128.3 (d, $J_{C,P}$ = 1.7 Hz), 129.3 (d, $J_{C,P}$ = 2.4 Hz), 130.5 (d, $J_{C,P}$ = 2.7 Hz), 131.5, 136.8, 145.7 (d, $J_{C,P}$ = 15.3 Hz) ppm.

Diethyl (phenyl)-N-(4-methylphenyl)aminomethyl-phosphonate. ^{1}H NMR ($CDCl_3$, TMS): M. P.: 117-119 °C, δ 1.15 (t, 3H, $^2J_{H,H}$ = 7.0 Hz), 1.31 (t, 3H, $^2J_{H,H}$ = 7.0 Hz), 2.21 (s, 3H), 3.70-3.76 (m, 1H), 3.92-4.02 (m, 1H), 4.11-4.20 (m, 2H), 4.72-4.82 (m, 2H), 6.55 (d, 2H, $^2J_{H,H}$ = 8.2 Hz), 6.93 (d, 2H, $^2J_{H,H}$ = 8.1 Hz), 7.29-7.38 (m, 3H), 7.48-7.51 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.8 Hz), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz), 20.7, 56.7 (d, $^1J_{C,P}$ = 150.4 Hz), 63.6 (d, $^2J_{C,P}$ = 3.0 Hz), 63.7 (d, $^2J_{C,P}$= 3.2 Hz), 114.4, 127.9, 128.2, 128.3, 128.9 (d, $J_{C,P}$ = 2.5 Hz), 130.0 ,136.4, 144.3 (d, $J_{C,P}$ = 15.1 Hz) ppm.

Diethyl (phenyl)-N-(4-chlorophenyl)aminomethyl-phosphonate. M. P.: 104-106 °C, δ 0.99-1.03 (m, 3H), 1.18-1.24 (m, 3H), 3.45-3.70 (m, 1H), 3.80-4.00 (m, 1H), 4.02-4.04 (m, 3H), 4.62 (d, 1H, $^2J_{P,H}$ = 24.1 Hz), 6.41-6.45 (m, 2H), 6.93-6.98 (m, 2H), 7.21-7.25 (m, 2H), 7.34-7.38 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 15.1 (d, $^3J_{C,P}$ = 5.8 Hz), 15.4 (d, $^3J_{C,P}$ = 5.8 Hz), 55.1 (d, $^1J_{C,P}$ = 15.09 Hz), 62.2 (d, $^2J_{C,P}$ = 8.8 Hz), 62.3 (d, $^2J_{C,P}$ = 7.1 Hz), 114.0, 122.0, 126.8 (d, $J_{C,P}$ = 5.4 Hz), 127.0 (d, $J_{C,P}$ = 3.2 Hz), 127.6 (d, $J_{C,P}$ = 2.6 Hz), 127.9, 134.4, 143.8 (d, $J_{C,P}$ = 14.5 Hz) ppm.

Diethyl (phenyl)-N-(2-chlorophenyl)aminomethyl-phosphonate. M. P.: 110-112 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.16 (t, 3H, $^3J_{H,H}$ = 7.5 Hz), 1.26 (t, 3H, $^3J_{H,H}$ = 7.5 Hz), 3.97-4.13 (m, 4H), 4.78 (dd, 2H, $^3J_{H,H}$ = 7.4 Hz, $^1J_{P,H}$ = 24.2 Hz), 5.42 (t, 1H), 6.45 (d, 1H, $J_{H,H}$ = 8.1 Hz), 6.61 (t, 1H, $J_{H,H}$ = 7.5 Hz), 6.92-6.96 (m, 1H), 7.22-7.46 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.2 (d, $^3J_{C,P}$ = 5.6 Hz), 16.4 (d, $^3J_{C,P}$ = 5.6 Hz), 56.0 (d, $^1J_{C,P}$ = 150.8 Hz), 63.3 (d, $^2J_{C,P}$ = 7.0 Hz), 63.5 (d, $^2J_{C,P}$ = 7.0 Hz), 112.6, 118.4, 120.0, 127.7 (d, $J_{C,P}$ = 6.6 Hz), 128.0 (d, $J_{C,P}$ = 3.1 Hz), 128.6 (d, $J_{C,P}$ = 2.5 Hz), 129.2, 135.3 (d, $J_{C,P}$ = 3.1 Hz), 142.3 (d, $J_{C,P}$ = 14.3 Hz) ppm.

Diethyl (4-methoxyphenyl)-N-(4-chlorophenyl) aminomethylphosphonate. M. P.: 160-162 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.06 (t, 3H, $^3J_{H,H}$ = 7.0 Hz), 1.22 (t, 3H, $^3J_{H,H}$ = 7.1 Hz, 3H), 3.42-3.70 (m, 1H), 3.71 (s, 3H), 3.81-3.88 (m, 1H), 3.99-4.07 (m, 2H), 4.50-4.62 (m, 2H), 6.45 (dd, 2H, $J_{H,H}$ = 6.7 Hz, $J_{H,H}$ = 2.0 Hz), 6.79 (d, 2H, $J_{H,H}$ = 8.5 Hz), 6.97 (dd, 2H, $J_{H,H}$ = 6.7 Hz, $J_{H,H}$ = 2.0 Hz), 7.25-7.29 (m, 2H); ^{13}C NMR ($CDCl_3$, TMS): δ 16.2 (d, $^3J_{C,P}$ = 5.8), 16.4 (d, $^3J_{C,P}$ = 5.7 Hz), 55.2, 55.4 (d, $^1J_{C,P}$ = 152.6 Hz), 63.1 (d, $^2J_{C,P}$ = 7.0 Hz), 63.3 (d, $^2J_{C,P}$ = 7.0 Hz), 114.1 (d, $J_{C,P}$ = 2.5 Hz), 115.0, 122.1, 127.1 (d, $J_{C,P}$ = 3.1

Hz), 128.8, 128.9 (d, $J_{C,P}$ = 2.3 Hz), 144.9 (d, $J_{C,P}$ = 15.2 Hz), 159.4 ppm.

Diethyl 3-phenyl-1-(phenylamino)allylphosphonate. M. P.: 101-103 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.26-1.33 (m, 6H), 4.10-4.23 (m, 5H), 4.47 (dd, 1H, $^2J_{H,H}$ = 6.0 Hz, $^2J_{P,H}$ = 27.5 Hz), 6.24-6.30 (m, 1H), 6.68-6.77 (m, 4H), 7.14-7.37 (m, 7H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 23.0 (d, $^3J_{C,P}$ = 5.8 Hz), 23.2 (d, $^3J_{C,P}$ = 3.5 Hz), 60.5 (d, $^1J_{C,P}$ = 153.3 Hz), 69.5 (d, $^2J_{C,P}$ = 7.6 Hz), 70.0 (d, $^2J_{C,P}$ = 7.6 Hz), 120.3, 124.9, 125.0, 130.0 (d, $J_{C,P}$ = 4.7 Hz), 133.1 (d, $J_{C,P}$ = 1.7 Hz), 134.3, 135.1, 135.7, 135.8, 139.4 (d, $J_{C,P}$ = 12.6 Hz) ppm.

Diethyl (2-thienyl)-N-(Phenyl) aminomethylphosphonate. Semi solid, ^{1}H NMR ($CDCl_3$, TMS): δ 0.78-0.85 (m, 3H), 1.10-1.24 (m, 3H), 3.82-4.11 (m, 4H), 4.50 (bs, 1H), 4.97 (d, 1H, $^2J_{P,H}$ = 23.65 Hz), 6.58-6.70 (m, 3H), 6.89-6.91 (m, 1H), 7.04-7.15 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.2 (d, $^3J_{C,P}$ = 5.8 Hz), 16.4 (d, $^3J_{C,P}$ = 5.8 Hz), 52.1 (d, $^1J_{C,P}$ = 158.2 Hz), 63.4 (d, $^2J_{C,P}$ = 7.0 Hz), 63.6 (d, $^2J_{C,P}$ = 7.0 Hz), 114.0, 119.0, 125.2 (d, $J_{C,P}$ = 3.6 Hz), 126.1 (d, $J_{C,P}$ = 7.2 Hz), 127.0 (d, $J_{C,P}$ = 2.9 Hz), 129.2, 139.9, 146.1 (d, $J_{C,P}$ = 13.0 Hz) ppm.

Diethyl (2-furyl)-N-(phenyl)aminomethylphosphonate. Semi solid, ^{1}H NMR ($CDCl_3$, TMS): δ 1.18-1.36 (m, 6H), 3.85-4.21 (m, 4H), 4.52 (bs, 1H), 4.67 (dd, 1H, $^3J_{H,H}$ = 7.0 Hz, $^2J_{P,H}$ = 75.5 Hz), 6.32-6.38 (m, 2H), 6.65-6.77 (m, 3H), 7.12-7.38 (m, 2H), 8.20 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.30 (d, $^3J_{c,p}$ = 5.7 Hz), 16.4 (d, $^3J_{c,p}$ = 5.7 Hz), 50.3 (d, $^1J_{C,P}$ = 159.5 Hz), 63.3 (d, $^2J_{C,P}$ = 6.9 Hz), 63.5 (d, $^2J_{C,P}$ = 7.1 Hz), 108.8 (d, $J_{C,P}$ = 7.0 Hz), 110.8 (d, $J_{C,P}$ = 2.4 Hz), 114.0, 118.9, 129.2, 142.5 (d, $J_{C,P}$ = 3.1 Hz), 146.1 (d, $J_{C,P}$ = 13.0 Hz), 149.4 ppm.

Diethyl (2-naphthyl)-N-(phenyl) aminomethylphosphonate. Semi solid, ^{1}H NMR ($CDCl_3$, TMS): δ 1.13 (t, 3H, $^3J_{H,H}$ = 6.8 Hz), 1.33 (t, 3H, $^3J_{H,H}$ = 6.8 Hz), 3.63-3.75 (m, 1H), 3.90-4.06 (m, 1H), 4.14-4.21 (m, 2H), 4.92-5.04 (m, 2H), 6.66-6.75 (m, 3H), 7.10-7.16 (t, 2H, $^3J_{H,H}$ = 6.8 Hz), 7.48 (d, 2H, $^3J_{H,H}$ = 3.3 Hz), 7.65 (d, 1H, $^3J_{H,H}$ = 7.1 Hz), 7.85 (s, 3H), 7.98 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, $^3J_{C,P}$ = 5.7 Hz), 16.8 (d, $^3J_{C,P}$ = 5.8 Hz), 56.7 (d, $^1J_{C,P}$ = 150.1 Hz), 63.7 (d, $^3J_{C,P}$ = 6.9 Hz), 114.3, 118.9, 126.0 (d, $J_{C,P}$ = 4.1 Hz), 126.4, 126.6, 127.3 (d, $J_{C,P}$ = 7.0 Hz), 128.1, 128.4, 128.8 (d, $J_{C,P}$ = 2.1 Hz), 129.6, 133.5, 133.7, 133.9 (d, $J_{C,P}$ = 3.3 Hz), 146.7 (d, $J_{C,P}$ = 14.8 Hz) ppm.

Diethyl (n-propyl)-N-(phenyl)aminomethylphosphonate. Yellow oil, ^{1}H NMR ($CDCl_3$, TMS): δ 0.84 (t, 3H, $^2J_{H,H}$ = 7.2 Hz), 1.09-1.24 (m, 6H), 1.50-1.82 (m, 4H), 3.60-3.65 (m, 2H), 3.94-4.09 (m, 4H), 6.58 (d, 2H, $^2J_{H,H}$ = 8.2 Hz), 6.65 (d, 1H, $^2J_{H,H}$ = 7.4 Hz), 7.09 (t, 2H, $^2J_{H,H}$ = 7.6 Hz) ppm.

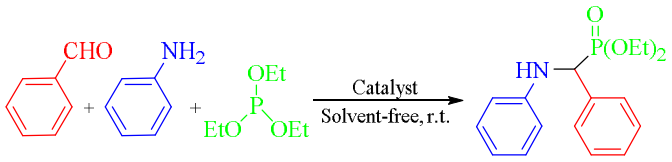
Diethyl aminocyclopentylphosphonate. Semi solid, ^{1}H NMR ($CDCl_3$, TMS): δ 1.29 (t, 6H, $^2J_{HH}$ = 7.2 Hz, OCH_2CH_3), 1.54–1.69 (m, 4H, C_5H_8), 1.87-2.04 (m, 6H, C_5H_8, NH_2), 4.08-4.20 (m, 4H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, TMS): δ 16.6 (d, 3 J_{CP} = 5.7 Hz, OCH_2CH_3), 24.6 (d, $^2J_{CP}$ = 11.3 Hz, C_5H_8), 36.3 (d, $^3J_{CP}$ = 6.9 Hz, C_5H_8), 58.7 (d, 1 J_{CP} = 154.7 Hz, C_5H_8), 62.2 (d, $^2J_{CP}$ = 6.9 Hz, OCH_2CH_3) ppm.

Diethyl aminocyclohexylphosphonate. M. P.: 102-104 °C, ^{1}H NMR ($CDCl_3$, TMS): δ 1.29 (t, 6H, $^2J_{HH}$ = 7.2 Hz, OCH_2CH_3), 1.52-1.72 (m, 12H, C_6H_{10}, NH_2), 4.04-4.15 (m, 4H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, TMS): δ 16.5 (d, $^3J_{CP}$ = 5.7 Hz, OCH_2CH_3), 19.8 (d, 115 $^3J_{CP}$ = 11.3 Hz, C_6H_{10}), 25.5, 31.3 (C_6H_{10}), 51.6 (d, $^1J_{CP}$ = 151 Hz, C_6H_{10}), 62.1 (d, $^2J_{CP}$ = 8.2 Hz, OCH_2CH_3) ppm.

RESULTS AND DISCUSSION

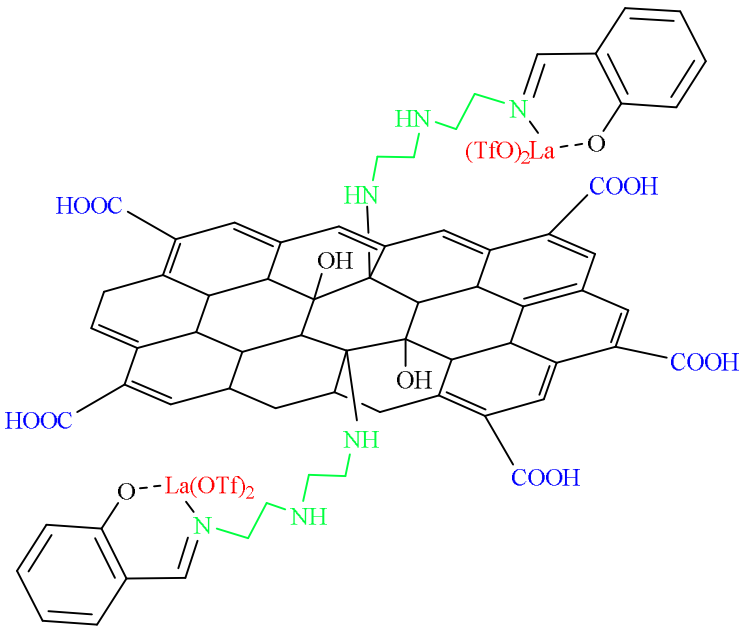
At first, a one-pot three-component reaction of benzaldehyde, aniline and triethyl phosphite at room temperature was chosen as a model reaction to optimize the reaction conditions (Table 1). The model reaction was performed at room temperature under solvent-free conditions using 0.05 and 0.1 mol% of La(OTf)$_2$-amine grafted-GO (Table 1, entries 1 and 2). The yield of the product was higher in the presence of 0.1 mol% of the catalyst. Increasing the molar ratio of the catalyst to 0.5 mol% did not have any significant effect on the progress of the reaction (entry 3). To see the influence of acidic and basic functional groups of the catalyst on the progress of the reaction, similar reactions in the absence of the catalyst and in the presence of GO, La(OTf)$_3$ and Schiff-base supported on amine grafted GO were examined (Table 1, entries 4-7). As seen in Table 1, the product was obtained in 49% yield after 30 min in the absence of any catalyst (entry 4). When the reaction was carried out in the presence of GO, which contains only Brønsted acidic groups (CO_2H), or in the

Table 1. One-pot Three-component Reaction of Benzaldehyde, Aniline and Triethyl Phosphite under Different Conditions

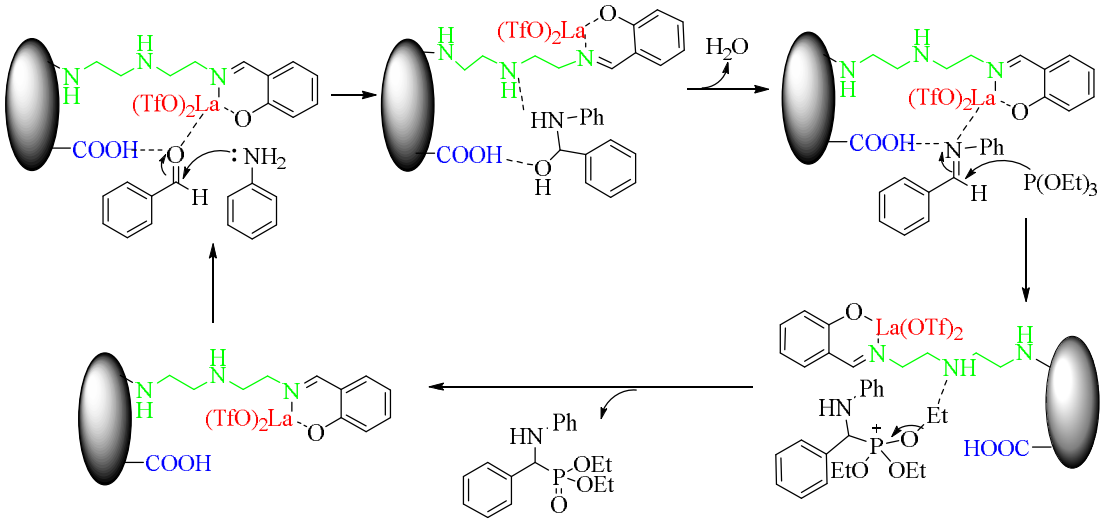


Entry	Catalyst (mol%)	Time (min)	Yield (%)[a]
1	La(OTf)$_2$-amine grafted-GO (0.05 mol%)	15	90
2	La(OTf)$_2$-amine grafted-GO (0.1 mol%)	5	98
3	La(OTf)$_2$-amine grafted-GO (0.5 mol%)	5	98
4	-	30	49
5	GO (0.1 g)	5	58
6	La(OTf)$_3$ (0.1 mol%)	5	52
7	Schiff-base supported on amine grafted GO (0.1 mol%)	5	75

[a]Isolated yield. Reaction conditions: benzaldehyde (1 mmol), aniline (1 mmol), triethyl phosphite (1 mmol), solvent-free, room temperature.



Scheme 1. Immobilized lanthanum(III) triflate on amine grafted graphene oxide [La(OTf)$_2$-amine grafted-GO].



Scheme 2. A plausible mechanism for the synthesis of α-aminophosphonates catalyzed by La(OTf)$_2$-amine grafted-GO.

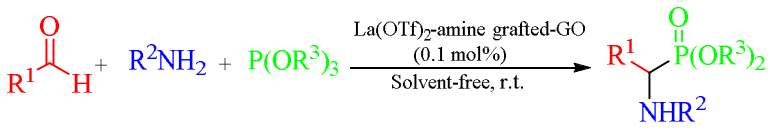
presence of La(OTf)$_3$ (Lewis acid), the desired products were obtained in 5 min with 58 and 52% yields, respectively (entries 5 and 6). A positive effect of basic linker on increasing the yield of the product was observed in the case of Schiff-base supported on amine grafted GO (entry 7). These results showed the cooperative interactions between the acidic and basic groups on the GO in La(OTf)$_2$-amine grafted-GO on the rate enhancement.

Based on these observations, a plausible mechanism for the one-pot reaction of benzaldehyde, aniline and triethyl phosphite in the presence of La(OTf)$_2$-amine grafted-GO is outlined in Scheme 1. In the first step, the carbonyl group of benzaldehyde was activated by La(OTf)$_2$-amine grafted-GO and underwent nucleophilic reaction with aniline to produce an imine. In the second step, the addition of phosphite to the imine was facilitated by the activation of imine by the catalyst and the desired α-amino phosphonate was obtained (Scheme 2).

To establish the generality of this method, synthesis of various α-aminophosphonates was studied using various aldehydes, amines, and trialkyl phosphites in the presence of La(OTf)$_2$-amine grafted-GO (0.1 mol%) under optimized reaction conditions. The results are summarized in Table 2. As indicated in Table 2, the reaction of benzaldehyde with aniline proceeded in good to high yields using different trialkyl phosphites (Table 2, entries 1-3). The reaction of different substituted benzaldehydes containing electron-donating and electron-withdrawing groups with aniline and triethyl phosphite proceeded well to give the corresponding α-aminophosphonates in good to high yields (Table 2, entries 4-7). This catalytic system was also successfully applied for the reaction of various amines with benzaldehyde and triethyl phosphite and produced the desired products in high yields (Table 2, entries 8-11). Cinnamaldehyde and heteroarylaldehydes, such as thiophene-2-carbaldehyde and furan-2-carbaldehyde generated the corresponding products without any polymerization or decomposition under the optimized reaction conditions (Table 2, entries 12-14). Naphthalene-2-carbaldehyde underwent the reaction with aniline and triethyl posphite to afford the desired product in 81% yield (entry 15). Encouraged by these satisfying results, the reaction was examined for some aliphatic carbonyl compounds. The results showed successful application of the present method for the synthesis of α-aminophosphonates from *n*-butyraldehyde, cyclopentanone and cyclohexanone (entries 16-18).

Lifetime and recyclability of a catalyst are very important for industrial applications. To evaluate the reusability of La(OTf)$_2$-amine grafted-GO, after completion

Table 2. One-pot Three-component Synthesis of α-Aminophosphonates Catalyzed by La(OTf)$_2$-amine Grafted-GO



Entry	Aldehyde	Amine	Phosphite	Time (min)	Yield (%)[a]
1	C_6H_5CHO	$C_6H_5NH_2$	$P(OEt)_3$	5	98
2	C_6H_5CHO	$C_6H_5NH_2$	$P(OMe)_3$	5	85
3	C_6H_5CHO	$C_6H_5NH_2$	P(O-*iso*-Pr)$_3$	5	95
4	4-MeO-C_6H_4CHO	$C_6H_5NH_2$	$P(OEt)_3$	15	95
5	4-Cl-C_6H_4CHO	$C_6H_5NH_2$	$P(OEt)_3$	15	91
6	2-NO_2-C_6H_4CHO	$C_6H_5NH_2$	$P(OEt)_3$	5	73
7	2,6-Cl_2-C_6H_3CHO	$C_6H_5NH_2$	$P(OEt)_3$	30	95
8	C_6H_5CHO	4-Me-$C_6H_4NH_2$	$P(OEt)_3$	5	96
9	C_6H_5CHO	4-Cl-$C_6H_4NH_2$	$P(OEt)_3$	10	91
10	C_6H_5CHO	2-Cl-$C_6H_4NH_2$	$P(OEt)_3$	30	93
11	4-MeO-C_6H_4CHO	4-Cl-$C_6H_4NH_2$	$P(OEt)_3$	15	95
12	PhCH=CHCHO	$C_6H_5NH_2$	$P(OEt)_3$	10	95
13	Thiophene-2-carbaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	15	92
14	Furan-2-carbaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	5	98
15	Naphthalene-2-carbaldehyde	$C_6H_5NH_2$	$P(OEt)_3$	60	81
16	$CH_3(CH_2)_2CHO$	$C_6H_5NH_2$	$P(OEt)_3$	10	96
17	Cyclopentanone	$C_6H_5NH_2$	$P(OEt)_3$	120	82
18	Cyclohexanone	$C_6H_5NH_2$	$P(OEt)_3$	180	75

[a]Isolated yield. Reaction conditions: aldehyde (1 mmol), amine (1 mmol), trialkyl phosphite (1 mmol), catalyst (0.1 mol%), solvent-free, room temperature.

of the reaction, EtOAc was added to the reaction mixture and the catalyst was separated by centrifugation and washed with EtOAc, dried and used for another reaction. No significant decrease in the catalyst activity was observed after being used repetitively for five times (Table 3).

As shown in the FT-IR spectra of the catalyst after five times reused (Fig. 1), the absorption peak at 1664 cm^{-1}, due to C=N stretching vibrations, justifies that the imine group remained intact during the reaction.

The FESEM of the catalyst after five times reused (Fig.

Table 3. Reusability of $La(OTf)_2$-amine Grafted-GO for the One-pot Three-component Synthesis of α-Aminophosphonates

Run	1	2	3	4	5
Yield (%)[a]	98	98	95	95	93

[a]Isolated yield. Reaction conditions: benzaldehyde (1 mmol), aniline (1 mmol), triethyl phosphite (1 mmol), catalyst (0.1 mol%), solvent-free, room temperature.

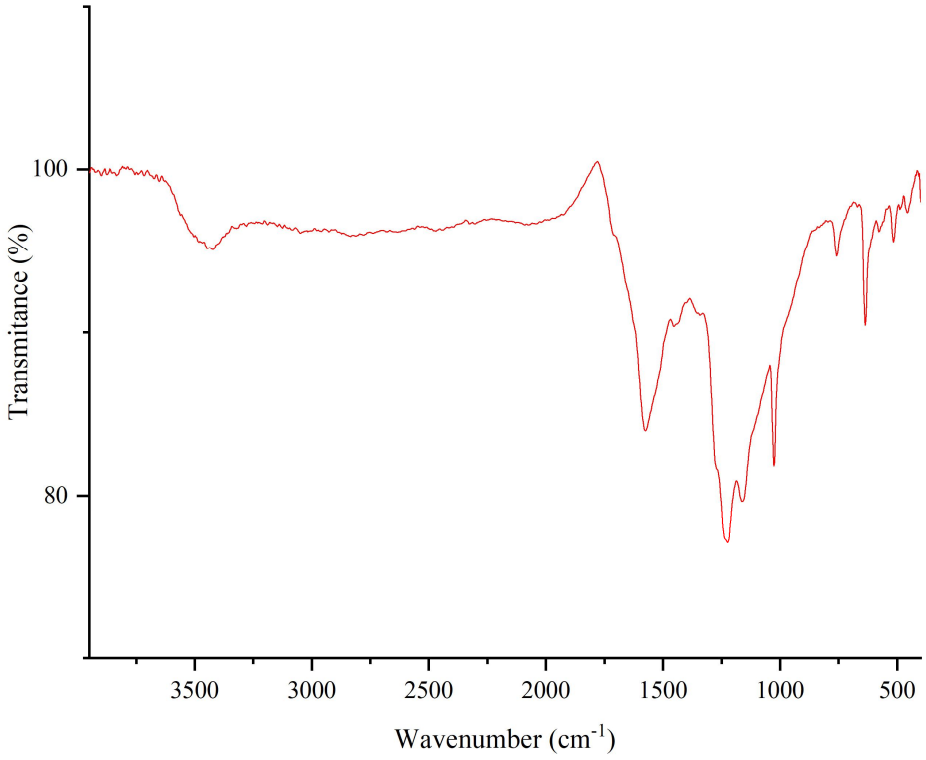


Fig. 1. FT-IR spectrum of the catalyst after five times reused.

2) reveals that $La(OTf)_2$-grafted-GO has a crumpling structure consistent with TEM observations (Fig. 3).

Finally, the reactivity of $La(OTf)_2$-amine grafted-GO was compared with the previously reported catalysts for the one-pot reaction of benzaldehyde, aniline and triethyl phosphite (Table 4). As is obvious in Table 4, much higher values of turnover number (TON) and turnover frequency (TOF) were obtained for $La(OTf)_2$-amine grafted-GO compared with the other catalytic methods. These findings may be attributed to the cooperative behavior of the acidic and basic groups incorporated on the GO in $La(OTf)_2$-amine grafted-GO. It is worth mentioning that this is the first report on the synthesis of α-aminophosphonates catalyzed by a multifunctional catalyst.

CONCLUSIONS

In summary, various α-aminophosphonates were

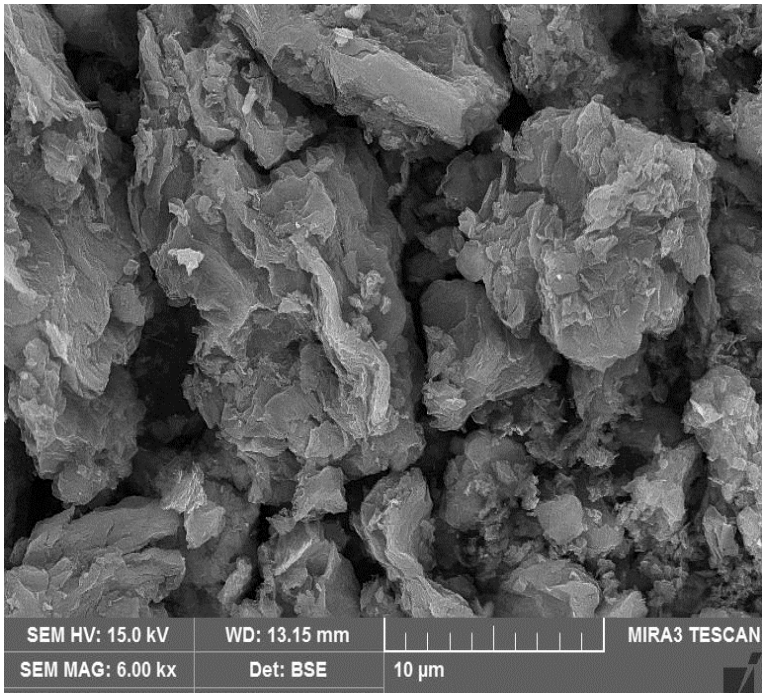


Fig. 2. FESEM image of the catalyst after five times reused.

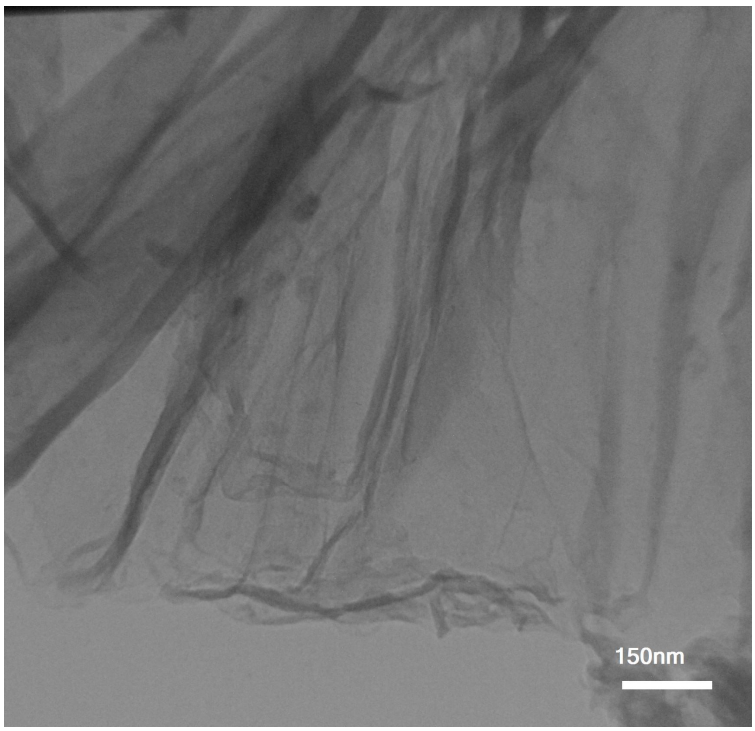


Fig. 3. TEM image of the catalyst after five times reused.

Table 4. Comparison of the Catalytic Efficiency of $La(OTf)_2$-amine Grafted-GO as a Multifunctional Catalyst with Various Catalysts Used for the Reaction of Benzaldehyde, Aniline and Triethyl Phosphate

Entry	Catalyst (mol%)	Reaction conditions	Yield (%) [Ref.]	TON/TOF[a]
1	20% DTP/SiO_2 (0.35)[b]	CH_3CN, r.t., 60 min	98 [27]	280/280
2	$HClO_4$-SiO_2 (3)	Solvent-free, 80 °C, 100 min	93 [31]	31/18.6
3	$HfCl_4$ (2)	EtOH, 60 °C, 30 min	98 [39]	49/98
4	KH_2PO_4 (5)	Solvent-free, r.t., 40 min	93 [40]	18.6/28
5	γ-Fe_2O_3@SiO_2-PA (1)[c]	water, 80 °C, 1 h	95 [25]	95/95
6	SiO_2-OSO_3H (10)	CH_3CN, r.t., 5 h	87 [29]	8.7/1.7
7	PPh_3 (10)	Solvent-free, 60 °C, 1 h	87 [28]	8.7/8.7
8	$La(OTf)_2$-amine grafted-GO (0.1)[d]	Solvent-free, r.t., 5 min	98	980/11807

[a]TON = mol of the product/mol of the catalyst, TOF (h^-) = TON/reaction time (h). [b]Silica supported dodeca-tungstophosphoric acid. [c]Phosphoric acid supported on magnetic core-shell nanoparticles. [d]This work.

synthesized in good to high yields by the reaction of different types of carbonyl compounds, substituted anilines and trialkyl phosphites catalyzed by $La(OTf)_2$-amine grafted-GO as a multifunctional catalyst. Solvent-free conditions, reusability of the catalyst and high TON and TOF made this method an environmentally benign protocol for the synthesis of α-aminophosphonates. It is worth mentioning that this is the first report of using a multifunctional catalyst for the synthesis of α-aminophosphonates.

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