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ARTICLE TYPE

Ultrasound mediated synthesis of α-aminophosphonates and 3,4-dihydropyrimidin-2-ones using graphene oxide as a recyclable catalyst under solvent-free conditions

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Graphene oxide is utilized as an environmentally friendly and efficient catalyst for an ultrasonic mediated multi-component coupling reaction involving aldehyde, amine/ethylacetoacetate and diethyl phosphite/urea in a solvent-free condition leading to the bioactive α-aminophosphonates and 3,4-dihydropyrimidin-2-ones with excellent yield.

With the advent of materials in the nanometer dimensions, there has been a tremendous focus towards the development of eco-friendly, more efficient and atom economic nanomaterial based heterogeneous catalytic systems for organic reactions. Carboneous materials including mesoporous carbon and carbon nanotubes have been used as both supports and metal free catalysts for facilitating synthetic transformations[1]. Since the report by Geim and co-workers[2], graphene and related two-dimensional sp^2-hybridized materials have invoked incredible research interest owing to their inherent optical, electrochemical and mechanical properties[3]. The development of the wet chemical methods for chemically modified graphene in substantial quantities have sparked great excitement enabling facile fabrication of carbon based functional materials[4]. Graphene oxide (GO), the oxygenated graphene sheets covered with hydroxyl, epoxy and carboxyl groups (Figure 1) offers tremendous opportunities for functionalization that can be processed into wide variety of novel materials. In the field of catalysis, GOs have been focussed primarily as supports for catalytically active metals. Taking advantage of the large nucleation or stabilization sites present on the GO surface, catalytically active nanoparticle-GO composite materials have been synthesized and demonstrated as versatile and recyclable heterogeneous catalyst in several important organic transformations[5]. On the other hand, with the aromatic scaffold decorated with oxygenated functional groups, the inherent chemical properties of GO has been exploited recently as effective carbocatalyst that might present a green alternative to metal catalysis. GO has been used as an oxidant for the oxidation of sulphides[6], olefins and other hydrocarbons[7]. On the other hand, the acidic nature of GO has been exploited to be used as solid acid for hydration of various alkynes, Friedel-Crafts addition of indoles to α,β-unsaturated ketones, Aza-Michael addition of amines to activated alkenes, condensation and ring opening of epoxides under mild conditions[8].

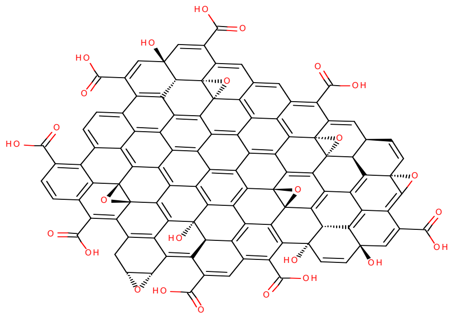

Figure 1. Schematic structure of a single layer graphene oxide (GO).

Herein, we report the exploitation of the acidic oxygenated groups on the GO sheets towards the applicability of GO as a potent catalyst for the three-component one-pot synthesis of α-aminophosphonates and 3,4-dihydropyrimidin-2-ones (DHPM), important classes of biologically active compounds. It is well known that multi-component reactions are more competent than multistep syntheses, as they require minimal workup and desired products can be obtained in one pot often in quantitative yield[9]. Hence there has been an intensified focus towards new heterogeneous catalysts for multicomponent reactions that would reinforce for environmental benefits. The synthesis of α-aminophosphonates have gained considerable interest because of their structural analogy to α-amino acids and their action as peptide mimics, enzyme inhibitors, herbicides and pharmacological agents[10]. A number of methods have been developed using various Bronsted acids, Lewis acids, heteropolyacids and nanocatalysts to accomplish the synthesis of these class of compounds[11]. Similarly, intense synthetic investigations have been carried out on DHPM scaffold due to their broad pharmacological profile such as calcium channel modulator, antiviral, anti-inflammatory, antifungal and antitumor agent[12]. The synthetic approach to DHPMs is based on ternary condensation of ethyl acetoacetate, aromatic aldehyde and urea under strong acidic conditions, first reported by Biginelli[13]. Subsequently, variety of procedures using homogeneous Lewis acid as well as protic acid or heterogeneous catalysts have been developed to accomplish this transformation[14]. However, in spite of their potential utility, many of these reported protocols suffer from various drawbacks such as use of expensive and highly corrosive catalysts, tedious separation procedures and require prolonged reaction times. Most of the existing methods use

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metal-based homogeneous catalysts, which are destroyed during the work-up procedure and their recovery and reusability is often impossible, limiting their use from the aspect of environmentally benign processes. Consequently, the design of a simple, efficient, metal-free and green catalyst would extend the scope of the synthesis of these important class of biologically active molecules. The presence of Bronsted acid sites over a large surface area of GO motivated us to test the activity of this non-toxic material as an acid catalyst for the three-component one-pot coupling reactions leading to the formation of α-aminophosphonates and 3,4-dihydropyrimidin-2-ones (Figure 2). The use of metal free catalyst such as GO follows the precepts of green chemistry in that the reactions were carried out under solvent free conditions and could be used in several cycles.

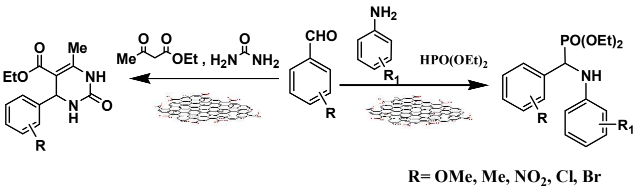


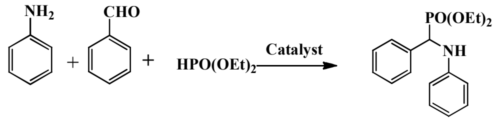
Figure 2. Syntheses of α-aminophosphonates and 3,4-dihydropyrimidin-2-ones using GO as heterogeneous catalyst.

Results and discussion

Graphene oxide was synthesized from the natural graphite powder by using a modified Hummers method[15] followed by exfoliation in aqueous solution. The solid GO catalyst was recovered by collecting the non-sedimented supernatant solution after centrifugation at 15000 rpm followed by freeze-drying. The physico-chemical properties of GO were evaluated using various spectroscopic and microscopic techniques.

In order to test the efficacy of GO as a catalyst for the one pot multi-component reactions, we choose the model Kobachnik-Fields reaction between benzaldehyde (1.0 mmol), aniline (1.0 mmol) and diethylphosphite (2.0 mmol). Effect of various reaction parameters such as influence of solvents, catalytic concentration, temperature and reaction conditions was evaluated to optimize the reaction conditions. It was noteworthy that, in the absence of GO no significant product formation was observed under similar reaction conditions. In non-polar solvents such as 1,4-dioxane, n-hexane and toluene, the reaction did not take place in presence of GO as a catalyst even after prolonged reaction time (Entry 4-6, Table 1). Whereas in the case of polar aprotic solvents such as acetonitrile, THF and DMF, the yield of the reaction was found to be very low (Entry 7-9, Table 1). Even in the case of polar protic solvents such as methanol and ethanol, the yield of the desired product was very low (Entry 10-11, Table 1). When we used water as the solvent for the reaction in presence of GO, the reaction did not progress well, we were able to isolate the coupling product with a moderate yield (18-30%) at various temperature (Entry 11-13, Table 1). Interestingly, there was a substantial enhancement in the yield when the coupling reaction was carried out under solvent free conditions with constant stirring. The desired coupling product (phenyl-phenylamino-methyl)-phosphonic acid diethyl ester was obtained in a 79% yield after reacting at room temperature for 4 hours (Entry 14, Table 1). The yield of the product increased to 92% when the reaction was carried out at elevated temperature (80 °C) (Entry 16, Table 1), however a small amount of green coloured by-product was formed that could be attributed to the emeraldine form of polyaniline and was formed by the aerial oxidation under acidic condition. It is worth mentioning that the order of mixing the substrates did not influence the product yield. GO showed equivalent or superior catalytic behaviour as an acid catalyst under solvent free conditions compared to other commonly used catalysts such as *p*-toluene sulfonic acid (*p*TSA), anhydrous $AlCl_3$ or camphor sulfonic acid (CSA) under similar reaction conditions (Entry 19-21, Table 1). For comparison, we performed the synthesis in presence of other carbon catalysts such as activated carbon, graphite and reduced graphene oxide (RGO) (reducing GO with hydrazine) (Entry 23-25, Table 1). The results suggested that the presence of acidic groups on the surface of GO played an essential role in the multi-component coupling

Table 1 Optimization of multicomponent reaction for the synthesis of α-aminophosphonates[a].



Entry	Catalyst (mg or mol%)	Reaction condition	Yield[b] (%)
1	None	[c]Water, 25°C, 3 h.	0
2	None	[c]No solvent, 25°C, 3 h.	0
3	GO (10)	[c]Water, 25°C, 4 h.	18
4	GO (10)	[c]1,4-dioxane, 25°C, 4 h.	0
5	GO (10)	[c]hexane, 25°C, 4 h.	1
6	GO (10)	[c]toluene, 25°C, 4 h.	1
7	GO (10)	[c]CH_3CN, 25°C, 4 h.	8
8	GO (10)	[c]THF, 25°C, 4 h.	12
9	GO (10)	[c]DMF, 25°C, 4 h.	8
10	GO (10)	[c]ethanol, 25°C, 4 h.	10
11	GO (10)	[c]methanol, 25°C, 4 h.	12
12	GO (10)	[c]water, 60°C, 4 h.	25
13	GO (10)	[c]water, 80°C, 4 h.	30
14	GO (10)	[c]No solvent, 25°C, 1 h.	79
15	GO (10)	[c]No solvent, 60°C, 1 h.	85
16	GO (10)	[c]No solvent, 80°C, 1 h.	92[e]
17	GO (2)	[c]No solvent, 25°C, 1 h.	41
18	GO (5)	[c]No solvent, 25°C, 1 h.	56
19	*p*TSA (10)	[c]No solvent, 25°C, 1 h.	58
20	$AlCl_3$ (10)	[c]No solvent, 25°C, 1 h.	29
21	CSA (10)	[c]No solvent, 25°C, 1 h.	77
22	GO (10)	[c]0.1 mL pyridine, 25°C, 1 h.	9
23	Amorphous carbon (10)	[c]No solvent, 25°C, 4 h.	13
24	Graphite (10)	[c]No solvent, 25°C, 1 h.	10
25	RGO (10)	[c]No solvent, 25°C, 1 h.	16
26	GO (2)	[d] No solvent, 25°C, 45 min.	82
27	GO (5)	[d] No solvent, 25°C, 15 min.	88
28	GO (10)	[d] No solvent, 25°C, 5 min.	96

[a]Unless otherwise specified, all the reactions were carried out with benzaldehyde (1.0 mmol), aniline (1.0 mmol) and diethylphosphite (2.0 mmol), [b]isolated yields, [c]under magnetic stirring, [d]under ultrasonic irradiation (50 Hz), [e]polyaniline formed as byproducts.

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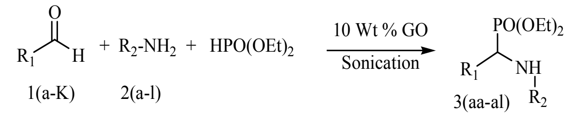
reaction. To verify this, the coupling reaction was performed in the presence of 0.1 mL of pyridine. The yield was only 9%, indicating the poisoning of the acid sites in GO (Entry 22, Table 1).

Sonochemistry has been recognized to be an efficient technique in organic synthesis as ultrasound irradiation can accelerate chemical reactions to provide improved reaction yields, shortened reaction time and increased selectivity[16]. When we performed the model coupling reaction between benzaldehyde, aniline and diethylphosphite in a ultrasonicator bath (50 Hz) under solvent-free conditions using GO as a catalyst, the reaction yield improved to 99% in a significantly shortened reaction time (5 minutes) (Table 1, entry 28). Hence it was imperative for us to use ultrasonic irradiation for developing the synthetic methodology for the synthesis of α-aminophosphonates. It is worth mentioning here that the substrate to catalyst ratio played an important role in the rate of the coupling reaction. When the catalyst-substrate ratio was low (2 wt%), the reaction yield was 82% after 45 minutes under ultrasonic irradiation, whereas there was drastic enhancement in the rate of the reaction when 10 mg (10 wt%) of the catalyst was used under similar reaction conditions (96% yield in 5 minutes) (Entry 26-28, Table 1). From the various reaction conditions as shown in Table 1, it is obvious that the superior result was obtained at condition mentioned in entry 28 (96% yield).

Having the optimal conditions in hand, we examined the scope and generality of this multi-component coupling reaction using graphene oxide as a catalyst under standard reaction conditions and the results are compiled in table 2. It was observed that there was no remarkable electronic and position effect on the three-component coupling from aromatic amines, since anilines with *p*-, *m*- or *o*-substituents resulted in the corresponding α-aminophosphonates in excellent yield. The aromatic aldehydes having either electron donating groups or even electron withdrawing groups gave excellent yield of product (Table 2, entry 1-21). However, presence of electron withdrawing groups as a substituent in the aryl moiety had considerable effect on the kinetics of the reaction, as we observed lesser yield with these substrates even after prolonged ultrasound irradiation. Similar effects were observed when electron withdrawing groups were present in aniline moiety. The reaction was found to be compatible with various functional groups such as Br, Cl, OMe, NO_2, OH and CN that do not interfere in the reaction by competitive complex formation with the catalyst or by nucleophilic substitution. Both aromatic and aliphatic amines (primary and secondary) were effective for this transformation. Moreover, fused ring, heteroaromatic and aliphatic aldehydes were effective substrates for the solvent-free Mannich-type reactions catalyzed by graphene oxide and all of them gave excellent yield within a short time (Table 2, entry 6, 7, 9, 16, 20, 22, 23). The isolated products were fully characterized from their spectral data and by direct comparison with the reported data. As GO based materials could be synthesized in large quantities, it is important to determine whether the catalytic reaction process could be scaled up. For this the gram scale preparation of α-aminophosphonates under our condition was assessed. When the reaction was carried out in solvent free conditions in presence of benzaldehyde (20 mmol), aniline (20 mmol), diethyl phosphite (40 mmol) and GO catalyst (80 mg) under ultrasonic irradiation for 40 minutes, the coupling product was isolated with a 74% yield. This exciting result reveals the possibility of using GO as a catalyst under the present reaction condition for milligram to gram scale synthesis of α-aminophosphonates.

Table 2 Synthesis of α-aminophosphonates (3aa-al):



Entry	R_1	R_2	Time (Min)	Product	Yield^{a,b} (%)
1	Ph	Ph	5	3aa	96
2	Ph	4-IC_6H_4	5	3ab	98
3	Ph	2-$NO_2C_6H_4$	30	3ac	76
4	Ph	3-$NO_2C_6H_4$	15	3ad	86
5	Ph	4-$NO_2C_6H_4$	30	3ae	80
6	Ph	3-Pyridyl	7	3af	90
7	Ph	4-Pyridyl	7	3ag	93
8	Ph	4-$COCH_3C_6H_4$	7	3ah	90
9	Ph	2-Pyridyl	5	3ai	88
10	Ph	4-CNC_6H_4	10	3aj	86
11	2-OHC_6H_4	Ph	10	3ba	94
12	4-ClC_6H_4	Ph	30	3ca	89
13	4-$MeOC_6H_4$	Ph	7	3da	95
14	4-MeC_6H_4	2-IC_6H_4	5	3ek	93
15	2,5-di$OMeC_6H_4$	4-$COCH_3C_6H_4$	7	3fh	90
16	2,5-di$OMeC_6H_4$	4-Pyridyl	7	3fg	94
17	4-ClC_6H_4	4-IC_6H_4	20	3cb	84
18	4-BrC_6H_4	4-IC_6H_4	15	3gb	90
19	2-ClC_6H_4	4-IC_6H_4	10	3hb	78
20	2-Pyridyl	2-Pyridyl	7	3ii	90
21	2-Naphthyl	4-IC_6H_4	15	3jb	97
22	Propyl	4-Pyridyl	30	3kg	78
23	Ph	3-ethyl pentyl	50	3al	80

[a] Reaction conditions: aldehyde (1.0 mmol), amine (1.0 mmol), diethyl phosphite (2.0 mmol), graphene oxide catalyst (10 mg), under solvent free conditions using ultrasound at room temperature. [b] Isolated yield by column chromatography.

Mechanistically, the formation of α-aminophosphonate preceded through the imine intermediate similar to the earlier reports[17] (Figure 3A). The formation of imine was observed when benzaldehyde was reacted with aniline at room temperature under solvent-free condition in the presence of GO as a catalyst even without ultrasonication. The product showed an absorption at 334 nm in methanol (Figure S1, †ESI), confirming imine as the key intermediate in the product-forming pathway. Lewis acid-base interaction between the GO catalyst and the imine facilitates the reaction by shifting the equilibrium towards the product formation. The presence of carboxylic acid groups on GO were primarily responsible for the activation. It was clearly evident from the observation that when the reaction was carried out in presence of reduced GO (GO reduced with hydrazine), the reaction proceeded very slowly and required a prolonged reaction time (Table 1, entry 25).

More impressively, GO catalyst shows good recyclability and could be reused by rinsing with dilute HCl (0.5 M HCl) to remove any adsorbed substrate and subsequent filtration. For the

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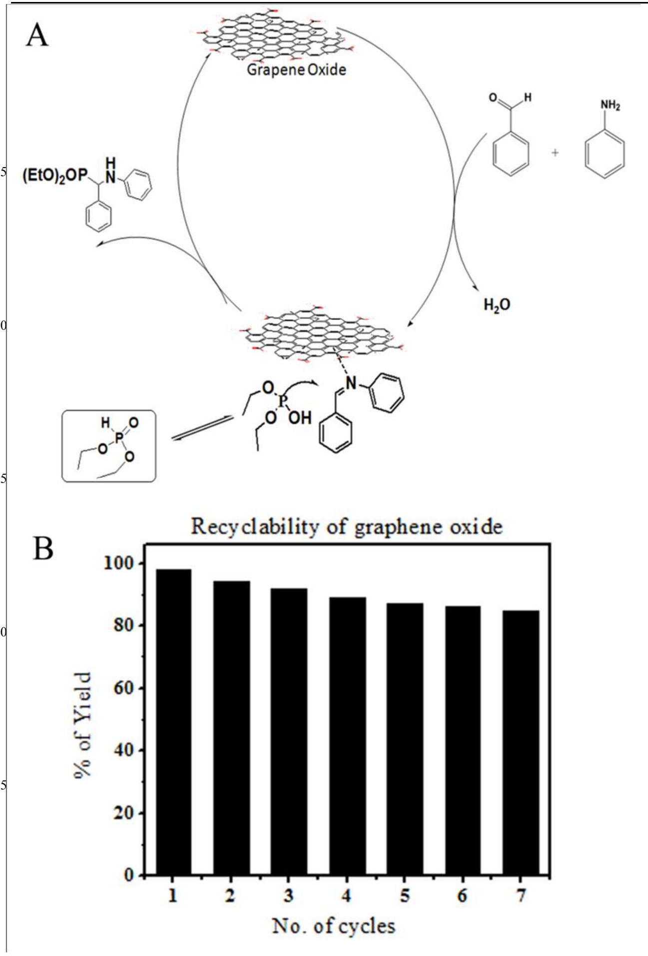

Figure 3. (A) Schematic presentation of the plausible mechanistic pathway towards the synthesis of α-amino phosphonates (B) Reusability studies of graphene oxide on the synthesis of α-amino phosphonates.

model reaction between benzaldehyde (1.0 mmol), aniline (1.0 mmol) and diethylphosphite (2.0 mmol), the GO catalyst showed very good recyclable activity up to the seventh cycle tested (Figure 3B). Notably, we have used low catalyst loading for this coupling reaction compared to the previous catalysis reactions using GO[6,7,8]. Therefore, with low catalyst loading, GO can be used as a model catalyst in a solvent-free and metal-free environment for practical application.

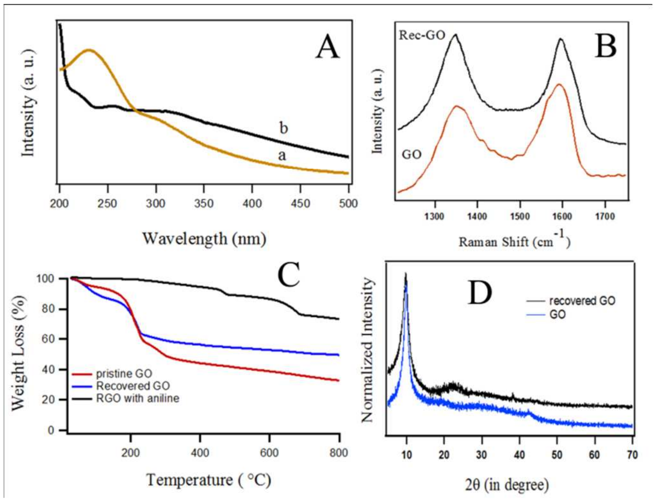

Figure 4. (A) UV-visible spectra of GO (a) and recovered GO after 5th catalytic cycles (B) Raman spectra of GO (red) and recovered GO (black) (C) TGA plots of GO (red), recovered GO (blue) and RGO synthesized by reducing GO with aniline (black). (D) powder XRD spectra of GO (blue) and recovered GO (black).

It is well known that primary amines such as aniline can function as a reducing agent[18] and it was imperative that the chemical nature of GO sheets is influenced during their participation as a catalyst. It was further evidenced by the fact that the catalytic activity of GO was reduced to some extent during the subsequent cycle of coupling reaction. To study this, we compared the physico-chemical properties of pristine GO and GO recovered after 5th cycle of reaction. From the UV-visible studies, as shown in Figure 4A, pristine GO exhibited two absorption peaks, a maximum at 230 nm corresponding to π→π* transitions of aromatic C-C bonds and a shoulder at 305 nm attributed to n→π* transitions of C=O bonds. In case of GO recovered after 5th cycle of reaction, we observed shoulders at 222 nm, 256 nm and 309 nm indicating that the electronic conjugation was somewhat restored in the graphene sheet[19]. Further we performed Raman spectroscopy (Figure 4B) in order to evaluate the crystal structure of carbon for pristine GO (red) and recovered GO (black). The D bands at ~ 1350 cm^{-1} in both samples in the Raman spectra confirmed the lattice distortions in the hexagonal graphitic layer. On the other hand, we did not observe any significant shift in the G peak (1592 cm^{-1}), in case of the recovered GO with respect to pristine GO. The G peak corresponds to the E_{2g} mode of graphite and is a signature to the sp^2 bonded carbon atoms in a two dimensional hexagonal lattice[20]. However the I_D/I_G ratio of the recovered GO exhibited a significant increase as compared to pristine GO, demonstrating a partial reduction of GO after their participation as a catalyst in the multi-component reaction. Further the quality of the pristine GO and recovered GO after 5th cycle of catalysis was examined by thermal gravimetric analysis (TGA). As shown in Figure 4C, pristine GO (red curve) showed major weight loss between 100 and 200 °C, indicating the release of oxygenated groups from the most labile functional groups during pyrolysis. At temperature below 800 °C, the weight loss was about 69%. In case of the GO recovered after the 5th cycle (blue curve), we observed a similar pattern of weight loss, however the weight loss was found to be 53% at temperature below 800 °C. For comparison, we performed the TGA analysis of reduced GO (black curve), formed by reaction of GO with aniline in an ultrasonicator bath. The curve showed a completely different pattern and the weight loss was found to be about 24% at temperature below 800 °C, that could be attributed to the presence of polyaniline on the GO surface. From the results, it was concluded that although GO was partially reduced during their action as a catalyst, and oxygen functional groups were not completely removed, ascertaining their efficiency after repeated cycles. We further measured the surface charge of GO and recovered GO after 5th cycle of reaction by zeta (ζ) potential measurements. Whereas in case of pristine GO dispersed in de-ionized water, the value of ζ was found to be -50.5 mV, the recovered GO after 5th cycle dispersed in water showed a ζ value of -44.3 mV. The results indicated that the pristine GO was partially reduced during their participation in

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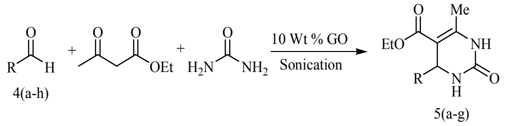
the catalytic reaction consistent with the other physico-chemical observations. Further confirmation was carried out by elemental analysis (Table S1, †ESI) of GO and recovered GO. The carbon content was found to increase from 31.4% (GO) to 33.7% (Recovered GO), while the oxygen content decreased from 43.2% (GO) to 41.2% (Recovered GO). The C/O ratio in case of recovered GO after catalytic cycles was 1.09 compared to 0.97 in case of pristine GO signifying partial reduction of GO after their participation in catalytic cycles. The detection of 1.8% nitrogen in the recovered GO suggested the adsorption of aniline on GO surface during reactions. Further powder X-ray diffraction studies on pristine GO and recovered GO was carried out in order to evaluate the structural modifications after their participation as catalysts. As shown in Figure 4D, pristine GO showed a 2θ peak at 9.84° with an interlayer distance of 8.97 Å (blue curve). In case of the GO recovered after 5th cycle of catalysis, along with the 2θ peak at 9.84° there was an additional broad peak with 2θ maxima at 22.8° with an interlayer separation of 3.89 Å (black curve). The results suggest the partial reduction of GO oxygenated groups during the catalytic reactions consistent with the other studies[21]. From the FTIR studies of GO and recovered GO, we did not observe any considerable shift in peaks corresponding to major functional groups (Figure S2, †ESI). Similar results were obtained from the morphological studies by transmission electron microscopy (TEM), where both GO and recovered GO showed rippled paper-like structure. Selected area electron diffraction (SAED) pattern of both GO and recovered GO showed their high crystallinity (Figure S3, †ESI).

Encouraged by the effectiveness of graphene oxide as a catalyst for multicomponent one-pot transformations such as the synthesis of α-aminophosphonates, we intended to study the versatility of the catalyst towards the rapid, automated and high throughput synthesis of biologically active 3,4-dihydropyrimidin-2-ones through a multicomponent reaction pathway. The one-pot cyclocondensation reaction of aromatic aldehydes, ethylacetoacetate and urea in presence of GO in a solvent free environment under ultrasonication afforded the corresponding products. However, for better conversion the reaction had to be carried out for prolonged time compared to that for synthesizing α-aminophosphonates. A wide range of aromatic aldehydes were investigated for their reaction with ethyl acetoacetate and urea in the presence of graphene oxide as catalyst under the optimized reaction conditions and the results are summarized in Table 3. Aromatic aldehydes containing electron-releasing groups (Table 3, entries 2, 3) in the *para* position afforded high yields of the products. Another important characteristic feature of this method is the tolerance and compatibility of various functional groups such as Cl, Br etc. to the reaction conditions as we did not observe formation of any side products (Table 3, entry 4,5,7). The GO catalyst used in this reaction could be recycled through simple filtration and washing and showed appreciable activity even after 3rd cycle (FIgure S4, †ESI).

Table 3 Synthesis of aryl substituted 3,4-dihydropyrimidinones



Entry	R	Product	Time (hr)	Yield (%)[a,b]
1	Ph	5a	2	90
2	4-OMeC$_6$H$_4$	5b	2	92
3	4-MeC$_6$H$_4$	5c	2	90
4	4-ClC$_6$H$_4$	5d	4	87
5	2-ClC$_6$H$_4$	5e	4	88
6	2-NO$_2$C$_6$H$_4$	5f	4	76
7	4-BrC$_6$H$_4$	5g	3	89

[a] Reaction conditions: aldehyde (5.0 mmol), urea (10.0 mmol), ethylacetoacetate (5.0 mmol), graphene oxide catalyst (50 mg), under solvent free conditions using ultrasound at room temperature. [b] Isolated yield by column chromatography

Recently Su *et. al*. reported the catalytic activity of porous graphene oxide, which were synthesized by a sequential base and acid treatment (ba-GO), for the oxidative coupling of amines to imines[22]. They reported that the oxidative coupling of various amines catalyzed by ba-GO involved molecular oxygen and the reaction followed a free radical pathway with the generation of H_2O_2. In order to have further insight into the reaction mechanism for the multicomponent coupling reactions catalyzed by GO, we studied the generation of H_2O_2 spectrophotometrically using the FOX method (details in †ESI). We did not observe any formation of H_2O_2 during the reaction, thus eliminating the involvement of molecular oxygen during the reaction. Further confirmation could be obtained from the fact that α-aminophosphonates and 3,4-dihydropyrimidin-2-ones were obtained as the sole products during the coupling reactions and no formation of polyaniline as byproducts were observed under the present reaction conditions. If H_2O_2 would have been produced during the reaction, then significant amount of polyaniline should have been formed as byproduct, as H_2O_2 is known to be a good oxidizing agent for the oxidation of aniline to form polyaniline. Moreover, when we carried out the coupling reaction of benzaldehyde, aniline and diethylphosphite under argon environment instead of air, we obtained high yield of the coupling product (Table S2, †ESI). From these observations it was clearly evident that molecular oxygen did not play any significant role in the reaction mechanism and the reaction preceded by the action of graphene oxide nanosheets only as a facilitator for the stabilization of imine intermediate via acid-base interaction.

In conclusion, we have demonstrated for the first time that graphene oxide can be used as a mild, non-toxic and sustainable catalyst for the multicomponent coupling reactions leading to biologically relevant α-aminophosphonates and 3,4-dihydropyrimidin-2-ones under solvent free conditions with low catalytic loading. Due to the acidic nature of GO, the method could be extended to other acid catalyzed one-pot multicomponent reactions. Carbocatalyst such as GO with minimal environmental footprints, low cost and possibility of scaling up in large quantities, with a multiplier effect of the surface area and presence of oxygen functionalities in the

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nanostructured carbon could be used as an effective alternative to dwindling metal catalysts. Taking advantage of oxygenated functional groups and possibility of incorporating functionality when necessitated, graphene oxide could be used as an ideal catalytic platform towards products of industrial interest through the multicomponent reaction pathway.

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Notes and references

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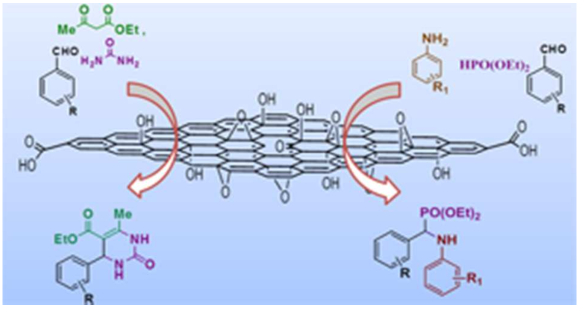
Graphical Abstract:



Graphene Oxide has been demonstrated as an effective and reusable carbocatalyst for the synthesis of α-amino phosphonates and 3,4-dihydropyrimidin-2-ones through one-pot multicomponent reaction pathway under solvent-free conditions using ultrasonic irradiation.