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Graphene oxide: an efficient and reusable carbocatalyst for aza-Michael addition of amines to activated alkenes^{†‡}Sanny Verma, Harshal P. Mungse, Neeraj Kumar, Shivani Choudhary, Suman L. Jain,*
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Graphene oxide was found to be a highly efficient, reusable and cost-effective organocatalyst for the aza-Michael addition of amines to activated alkenes to furnish corresponding β -amino compounds in excellent yields.

Development of innovative synthetic approaches involving the use of chemicals that reduce the risks to humans and the environment have gained prime interest in recent decades.¹ In this regard, utilization of catalysts that combine the toxicological benefits of a metal-free synthesis with the facile recovery and recycling of a heterogeneous system is of tremendous importance.² The formation of new carbon–heteroatom bonds *via* aza-Michael addition is an important transformation in organic chemistry, as these compounds are extensively used in the synthesis of a variety of biologically active natural products, chiral auxiliaries, antibiotics and other nitrogen-containing molecules.³ In recent years, various methodologies involving ionic liquids,⁴ quaternary ammonium salts,⁵ β -cyclodextrin,⁶ PEG,⁷ H₂O⁸ and organocatalysts^{9,10} have been reported for this reaction. However, inefficient recovery, recycling of the catalyst, longer reaction times and moderate yield of the products are the common drawbacks with most of the reported methods. Supported organocatalysts, due to their cost effectiveness, easy workup procedures and minimization of waste generation due to reuse and recycling of the catalysts, have attracted wide attention in chemical synthesis.¹¹ In this regard, supported phenolates have been used as efficient reusable catalysts for this transformation.¹² Nevertheless, the tedious preparation of supports and high costs of the precursors, limits the utility of these catalysts.

Recently, graphene and graphene oxide have attracted enormous interest in the development of composite materials and catalysts,^{13–15} due to their remarkable physical, chemical and electrical characteristics, including a very high specific surface area.¹⁶ The synthesis of graphene nanosheets on a

large scale from graphite is a well-established route, where graphene oxide is an intermediate product.¹⁷ The presence of oxygen-carrying functionalities in graphene oxide facilitates their dispersion in water and polar solvents,¹⁸ as well as interrupts the regular π electron distribution. These unique characteristics makes graphene oxide a potent material for the immobilization of various nanoparticles,^{14a,19} polymeric composites^{13a,b,20} and catalytic activities.^{13a,14,15} Herein, we report the use of graphene oxide, a readily available, inexpensive and efficient organocatalyst, for the synthesis of various β -amino compounds in excellent and efficient yields.

Here, graphene oxide was prepared by the oxidation of graphite powder under harsh oxidizing conditions. The presence of various chemical functionalities on graphene oxide nanosheets and their dispersion in water were examined by XRD, FTIR, UV-Vis and zeta potential. Fig. 1a shows the XRD patterns obtained for both graphite and graphene oxide powder. A sharp peak (002) at 26.5° for graphite powder reveals an interlayer spacing of 0.345 nm with very good crystalline order of graphitic layers. Graphene oxide shows a little broad peak (002) centered at 11.6°, corresponding to an interlayer spacing of 0.76 nm. The oxidation of graphite powder leads to the introduction of various functional groups. These functional groups are bonded on both basal planes and edges of graphitic layers, as well as the presence of trapped water molecules between these layers, expanding the interlayer spacing in graphene oxide.

Further, the nature of the chemical functionalities was characterized by FTIR (a full spectra is given in the supporting information[†]). An intense and broad peak appeared at 3404 cm⁻¹,

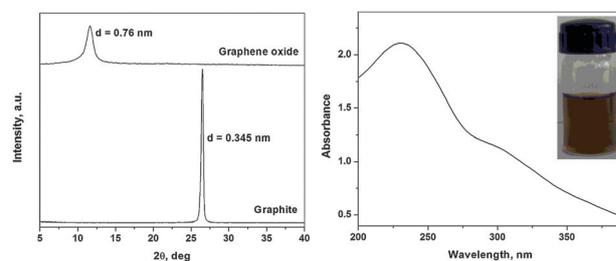


Fig. 1 (a) X-ray diffraction patterns of the pristine graphite and graphene oxide powder, (b) UV-Vis absorption spectra of graphene oxide (0.04 mg ml⁻¹) using water as a dispersing solvent. A photograph of an aqueous dispersion of graphene oxide is shown in the inset image.

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attributed to the stretching mode of a O–H bond, reveals the abundance of hydroxyl groups in graphene oxide. The strong band at 1726 cm^{-1} ($\nu_{\text{C=O}}$) represents carboxylic acid and carbonyl groups. Furthermore, the bands at 1227 cm^{-1} and 1058 cm^{-1} are attributed to the presence of C–OH and C–O(epoxy) groups, respectively, in graphene oxide. The UV-Vis spectrum of graphene oxide (Fig. 1b) exhibits a strong absorption peak at 230 nm, which is attributable to the $\pi \rightarrow \pi^*$ transition of graphitic C–C bonds and a shoulder at $\sim 300\text{ nm}$ is assigned to the $n \rightarrow \pi^*$ transitions of C=O bonds. Thus, similar to the XRD and FTIR, UV-vis spectra provided evidence of the presence of an ample number of oxygen functionalities, such as hydroxyl, epoxide, carboxylate and carbonyl on graphene oxide, which is demonstrated in Fig. 2.

For efficient catalytic performance, graphene oxide nanosheets need to be highly dispersed in the reaction media to provide the maximum number of catalytic sites. Here, the hydrophilic graphene oxide was readily exfoliated as individual and/or very few sheets of graphene oxide in water and shows a zeta potential of -41 mV , which falls in the stable dispersion range.²¹ The electrostatic repulsion due to negatively charged carboxylate groups on the edges of the graphene oxide nanosheets provides dispersion stability and keeps the graphene oxide nanosheets away from each other, resulting in a high zeta potential. Furthermore, the presence of very fine morphological features on the HR-TEM image of the graphene oxide nanosheets reveals that graphene oxide is composed of a few number of layers, resulting in a high surface area (see supporting information†) for an efficient catalytic reaction.

The catalytic potential of graphene oxide nanosheets was examined for the aza-Michael addition reaction, as shown in Scheme 1.

In a typical experimental procedure, a mixture containing diethylamine (1 mmol), acrylonitrile (1.2 mmol) and graphene oxide dispersion in water (0.5 ml) was stirred for 5 min at room temperature. After reaction completion, the catalyst was recovered by extracting the reaction mixture with dichloromethane; the remaining aqueous layer containing catalyst was reused for subsequent runs. Importantly, the reaction between diethylamine and acrylonitrile in aqueous media without using graphene oxide as the catalyst was found to be slow and required 35 min in completion (Table 1, entry 1). Whereas, in the absence of water and graphene oxide, the reaction between diethylamine and acrylonitrile occurred very slowly and required 150 min to complete (entry 1). In contrast, the reaction was markedly influenced by the presence of catalytic amount of graphene oxide and could be completed within 5 min. We assumed that the oxygen functionalities located on the graphene oxide were principally responsible for this activation. To establish this, we carried out the reaction between diethylamine and

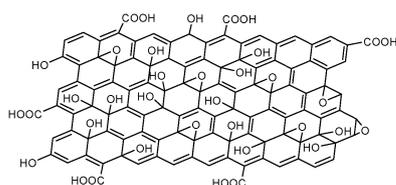
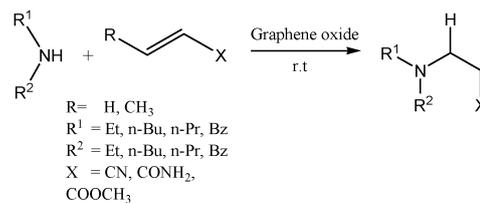


Fig. 2 A schematic model of a single sheet of graphene oxide showing oxygen-carrying functional groups.



Scheme 1 The graphene oxide-catalyzed aza-Michael addition reaction.

acrylonitrile in the presence of reduced graphene under the described reaction conditions. As expected, the reaction took place slowly and required a prolonged reaction time (30 min) to go to completion (entry 1).

Next, we extended the scope of the reaction by using a variety of primary and secondary amines with various α , β -unsaturated compounds, such as acrylamide, methyl acrylate, acrylonitrile, crotonic acid methyl ester *etc.* under the described reaction conditions to afford the corresponding β -amino compounds. These results are presented in Table 1. All of the reactants were efficiently converted to the corresponding β -amino compounds in excellent yields within 5–10 min without any evidence for the formation of by-products. Among the various amines studied, in general, aromatic amines were found to be less reactive compared to aliphatic amines. In case of primary amines, mono-addition products were selectively obtained without any evidence for the formation of bis products, as mentioned in several existing procedures.²² Aromatic amines, such as aniline and *p*-anisidine were found to be less reactive and afforded moderate product yield in longer reaction times (Table 1, entries 20 and 21). All of the products were analyzed by GCMS and characterized by comparing their physical and spectral data (IR & ^1H NMR) with authentic compounds.

Furthermore, we checked the recycling of the graphene oxide catalyst by choosing the reaction of benzylamine and acrylonitrile as a model reaction. After completion of the reaction, the catalyst could easily be recovered by simple extraction of the reaction mixture with dichloromethane, the as-obtained aqueous layer containing catalyst used for the subsequent experiments (9 runs). The results of these experiments are shown in the Table 2. As shown, the yield of the product and reaction time was found to be similar during these experiments, establishing the efficient recycling of the catalyst, as well as the heterogeneous nature of the developed methodology. The exact mechanism of the reaction is not clear at this stage, however, we assume that probably the presence of oxygen-carrying functionalities on the surface of graphene oxide plays a role in the activation for the aza-Michael addition reaction.

In summary, graphene oxide was found to be a simple and efficient catalyst for the synthesis of various amino-substituted compounds *via* aza-Michael addition of amines and electron-deficient olefins. These reactions were found to proceed under relatively mild conditions and afforded excellent product yields within shorter reaction times. Moreover, the catalyst was found to be easily recoverable and recyclable with the consistent catalytic activity. To the best of our knowledge, this is the first report of using graphene oxide for coupling-type reactions.

Table 1 Aza-Michael addition of amines to α,β -unsaturated compounds using graphene oxide as the catalyst^a

| Entry | Amine | Michael acceptor | Reaction time (min) | Yields (%) ^b |
|-------|---|---|-----------------------------------|-------------------------|
| 1 |  |  | 35, ^c 150 ^d | 96, 94 |
| | |  | 30.0, ^e 5.0 | 95, 97 |
| | |  | 5.0 | 97 |
| | |  | 7.0 | 96 |
| | |  | 5.0 | 95 |
| 2 |  |  | 5.0 | 95 |
| | |  | 7.0 | 92 |
| | |  | 5.0 | 92 |
| | |  | 5.0 | 94 |
| 3 |  |  | 7.0 | 90 |
| | |  | 10.0 | 89 |
| | |  | 10.0 | 92 |
| | |  | 10.0 | 92 |
| 4 |  |  | 5.0 | 96 |
| | |  | 10.0 | 85 |
| | |  | 7.0 | 94 |
| 5 | <i>n</i> -BuNH ₂ |  | 5.0 | 95 |
| | |  | 5.0 | 94 |
| 6 |  |  | 5.0 | 95 |
| | |  | 5.0 | 96 |
| 7 |  |  | 5.0 | 94 |
| | |  | 5.0 | 95 |
| 8 |  |  | 5.0 | 95 |
| | |  | 5.0 | 94 |
| 9 |  |  | 45 | 65 |
| 10 |  |  | 30 | 70 |

^a Conditions: Amine (1 mmol), α,β -unsaturated compounds (1.2 mmol), catalyst (0.5 ml) at room temperature; ^b Isolated yield; ^c Blank experiment in aqueous media without graphene oxide catalyst; ^d Blank experiment in the absence of water and graphene oxide catalyst; ^e Experiment carried out using reduced graphene as catalyst.

Table 2 Results of the recycling experiments^a

| Run | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|------------------------|----|----|----|----|----|----|----|----|----|
| Time (min) | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| Yield (%) ^b | 90 | 89 | 89 | 89 | 90 | 90 | 90 | 89 | 89 |

^a Conditions as mentioned in the text. ^b Isolated yield.

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