1,3,5-Tris (2-hydroxyethyl) isocyanurate - Cu(II) functionalized magnetic graphene oxide (MGO-THEIC-CuII): a highly efficient and recoverable nanocatalyst for the one-pot synthesis of substituted 2,4,5-trisubstituted imidazoles under microwave irradiation

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Abstract

In this paper, we have synthesized a series of 2,4,5-trisubstituted imidazoles from a new, highly efficient and green method. The reaction is performed in ethanol, by using 1,3,5-Tris (2-hydroxyethyl) isocyanurate-Cu(II) functionalized magnetic graphene oxide (MGO-THEIC-CuII), which has done under microwave irradiation. All compounds have been well characterized by IR and NMR spectral data.

introduction

Catalysts are one of the main contributors to green synthesis. Homogeneous and heterogeneous catalysis made enormous contributions to the improvement of society. Both types possess several advantages, however, heterogeneous catalysis appears to be more suitable for the large scale industrial processes, which prefer continuous flow systems. Easy handling, robustness, lower sensitivity to common conditions (e.g. moisture, air etc.), longer shelf life, are the most important advantages of using heterogeneous catalysts.[1] The use of carbocatalysts is attractive owing to their low cost and high natural abundance. Carbocatalyts have been demonstrated in the oxidative aromatization and preparation of heteroaromatic compounds such as pyridine, imidazole, and pyrimidine. Recently, graphene oxide (GO) has attracted attention as a new carbocatalyst in organic synthesis. Graphene oxide (GO)) is a 2D carbon material with abundant oxygen-containing groups at the edge (e.g. carboxyl) and surface defects (e.g. hydroxyl and epoxy groups). Comparing with graphene, GO is much easier to be synthesized, functionalized and chemically assembled. GO has been widely applied in multidisciplinary fields, including energy storage, advance catalysis, sensitive detectors and environmental pollutant management.[2] The existence of various types of hydrophilic groups allows GO to be easily exfoliated, when it is in the liquid state. These active groups can be used to induce chemical reactions and provide GO with additional functional groups after the modification, thereby increasing the flexibility and diversity of GO applications. For example, GO layers can be intercalated or cross-linked with primary aliphatic amines, amino acids, diaminoalkanes, boronates, acyl chloride, and isocyanates, or they can be covalently linked to polymers through esterification.[3] In recent years, the importance of imidazoles in biological systems has attracted considerable interests because of their chemical and biochemical properties, and pharmaceutical compounds with an imidazole ring system. The heterocyclic compounds including 2,4,5-trisubstituted imidazoles possess

versatile pharmaceutical actions such as being anti-bacterial, anti-tumor agents, anti-inflammatory, p38 MAP kinase inhibitors, glucagon receptor antagonists and inhibitors of mammalian 15-LOX. These vital compounds have demonstrated considerable interests among synthetic organic and medicinal chemists in recent years. Thus, several methods for the construction of imidazoles have been developed. Among these methods, the one-pot reaction of diketones is extensively used for the synthesis of 2,4,5-trisubstituted imidazoles. Various catalysts and methods can be used in this reaction such as heteropolyacids, uranyl nitrate hexahydrate supported on acidic alumina, cellulose sulfuric acid, Y(TFA), Mo(IV), $Eu(OTf)_3$, $SbCl_3/SiO_2$, $ZrCl_4$, $NiCl_2{,}6H_2O$, $H_{14}[NaP_5W_{30}O_{110}]$, iodine, MoO_3/SiO_2, silica sulfuric acid, L-proline, PEG-400, $Cu(TFA)_2$, p-TSA/TBAI, lipase, NBS, $Zr(acac)_4$ and different fluoroboric acid derived catalysts. Nevertheless, many of these approaches suffer from a long reaction time, low yield, acidic media, tedious work-up, and excessive use of reagents and catalysts. Therefore, introducing a new efficient heterogenous catalyst having good recyclability is of prime importance.[1]

On the other hand, several efforts have been dedicated on providing regular updates on the ever-increasing growth of research field in organic synthesis, with a recent example, which focuses on the application of microwaves in catalysis. Varma introduced the application of solid catalysts to microwave-assisted organic synthesis (MAOS). Since then, a broad array of new heterogeneous catalytic applications has been reported and reviewed periodically. There are several advantages of using solid catalysts in MAOS in order to ensure the environmentally benign preparation of the desired products.[4] In continuation of our ongoing efforts to develop efficient catalysts for different MCRs, we report herein the catalytic application of a 1,3,5-Tris (2-hydroxyethyl) isocyanurate-Cu(II) functionalized magnetic graphene (MGO-THEIC-CuII), as a new, highly efficient and recoverable catalyst, for the synthesis of 2,4,5-trisubstituted imidazoles derivatives under microwave irradiation.[5,6]

Experimental

Reagents and Apparatus

All commercially available chemicals were obtained from Merck and Aldrich, and used without further purifications, except for benzaldehyde, which was used as a fresh distilled sample. Infrared (IR) spectra were acquired on a Shimadzu FT-IR-8400S spectrometer. Analytical TLC was performed using Merck 0.2 mm silica gel 60F-254Al-plates. All compounds well characterized by IR and NMR spectral data as compared with those obtained from authentic samples or reported in the literature.

General procedure for the preparation of the GO

Graphene oxide (GO) was prepared from natural graphite powders via a modified Hummers' method through oxidation of graphite flakes ($>$99.95% purity).

First, 23mL of H_2SO_4 was added into a 250mL flask, and then cooled followed by stirring. 1g of graphite powder and 0.5g of $NaNO_3$ were subsequently added under vigorous stirring. Then, 3g

of $KMnO_4$ was added gradually under sonicate and the temperature of the mixture was kept below 20°C. The mixture was stirred at room temperature. The diluted suspension was stirred at 98°C, followed by addition of 12mL of H_2O_2 32% and 2mL of HCl 32%. Finally, the mixture was filtered and washed with deionized water repeatedly to remove any impurities. The product was dried at 60 °C for 24 h in a vacuum drying oven prior to use.

General procedure for the preparation of (MGO-THEIC-CuII)

The above GO (100 mg) and of acetic anhydride (200 mg) were added into a round bottom flask charged with 10 mL deionized water. The mixture was ultrasonically mixed for 1.5 h. Then, 1,3,5- tris(2-hydroxyethyl) isocyanurate (THEIC) (300 mg) was added into a mixture and again ultrasonication for 2.5 h. Next, the obtained suspension was separated using centrifuge (12000 rpm) for 20-30 minutes and then 20 mL of HCl 9.6 M was added into the above-mentioned suspension. The resulting mixture was allowed to stand for 1 h at 80 °C. The resulting solid was isolated by using centrifuge, washed completely with deionized water to remove excess of HCl or THEIC. Finally, the black solid was dried at 50 °C for 24 h under air.[6] The two types of functionalized GO-THEIC with magnetic nanoparticles and $Cu(OAc)_2$ were designed and characterized as a new and efficient catalyst for imidazole derivatives synthesis.

General experimental procedure for the synthesis of 2,4,5-trisubstituted imidazoles derivatives catalysed by MGO-THEIC-Cu(II)

A mixture of benzil (**2**) or benzoin (**3**) (1 mmol), various aldehyde (1 mmol,**4**), ammonium acetate (2.5 mmol, **5**), and MGO-THEIC-CuII (0.02 g, **1**) had been stirred under microwave irradiation for an appropriate period of time. After completion of the reaction as indicated by TLC, the reaction mixture had been dissolved in hot ethanol and the catalyst was recovered by external magnet, washed, dried and then reused in successive reaction. The reaction mixture had been recrystallized with ethanol to afford pure desired 2,4,5-trisubstituted imidazoles.

Results and discussion

The catalytic ability of the MGO-THEIC-CuII was evaluated in catalyzing a three-component reaction between benzoin or benzil, various aldehyde, ammonium acetate for the efficient synthesis of trisubstituted imidazoles. It was found that the quantitative yield can be achieved when the reaction was carried out in the presence of 0.02 g catalyst for 10-30 min under microwave irradiation. The results have been summarized in Table 1.

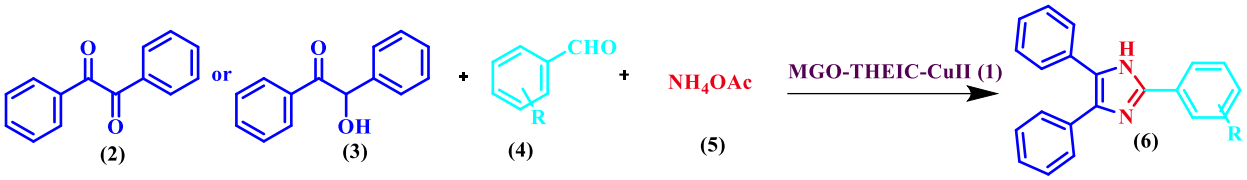
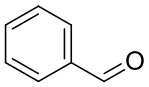
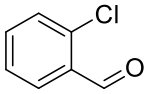
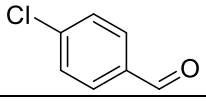
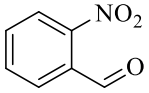
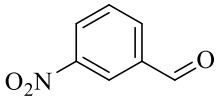
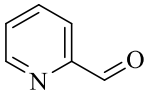
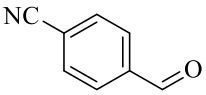


Table 1. Synthesis of imidazole derivatives in the presence of MGO-THEIC-Cu(II)

Entry	4	Time (min) (2)	Yield (%) (2)	Time (min) (3)	Yield (%) (3)
1		25-30	82.90	15	82
2		20	83.4	15	85
3		15	98	10	98
4		10	95	5	96.5
5		20	94.2	10	96
6		<10	90.81	5	92
7		<10	99.37	5	99.98

The MGO-THEIC-CuII were easily separated with an external magnet and the recovered catalyst was reused for at least six runs without significant degradation in catalytic activity and performance.

Conclusion

In this experiment, the catalytic application of functionalized superparamagnetic graphene-oxide has been demonstrated for the synthesis of a wide range of trisubstituted imidazole derivatives. The progress of reaction had been significantly affected by catalyst loading, reaction time and solvent. The catalyst illustrated high efficiency for the one-pot three-component synthesis of substituted imidazole derivatives using a variety of aldehydes and benzil or benzoin and ammonium acetate in EtOH under microwave irradiation conditions. Therefore, the attractive features of this procedure are low catalyst loading, avoiding the use of toxic reactive reagents for modification of the catalytic activity, short reaction times, high yields, elimination of toxic organic solvents, reusability and re-activity of the catalyst and simple procedure.

Refrences

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