Article

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

A Green Synthesis of Substituted Coumarins Using Nano Graphene Oxide as Recyclable Catalyst

Saeed Khodabakhshi,[a] Farzaneh Marahel,[b]* Alimorad Rashidi[c] and Masoud Khaleghi Abbasabadi[a]

[a]*Department of Chemistry, College of Basic Science, Yadegar-e-Imam Khomeini (RAH) Shahre-rey Branch, Islamic Azad University, Tehran, Iran*

[b]*Department of Chemistry, Omidiyeh Branch, Islamic Azad University, Omidiyeh, Iran*

[c]*Nanotechnology Research Center, Research Institute of Petroleum Industry, Tehran, Iran*

(Received: Aug. 18, 2014; Accepted: Feb. 26, 2015; Published Online: ??; DOI: 10.1002/jccs.201400349)

One-pot synthesis of some pyranocoumarins and biscoumarins using graphene oxide nanosheets as efficient catalyst has been investigated. The green methods offer appealing attributes such as excellent yields, short reactions times, use of a safe and recyclable catalyst, and a simple workup procedure.

Keywords: Pyranocoumarins; Biscoumarins; Catalyst; Graphene oxide; Green.

INTRODUCTION

Heterocyclic compounds have gained remarkable attention due to their therapeutic properties in natural product and medicinal chemistry. Coumarins as oxygen-containing heterocycles have a wide range of biologically activities such as anticoagulant,[1] antidepressant,[2] anti-HIV,[3] antioxidant, and anti-inflammatory.[4] Besides, some coumarins are used as additive in food and cosmetics, optical brighteners, dispersed fluorescent, and laser dyes.[5] Recently, the methods for the synthesis of some substituted coumarins such as pyrano[3,2-*c*]coumarins and bis-4-hydroxycoumarin have been reviewed by Ziarani and Hajiabbasi.[6]

Organic catalytic reactions have emerged as useful tools for the synthesis of a wide spectrum of functionalized compounds. Recently, carbocatalysts have been considered for organic reactions due to their advantages over metal catalysts, such as high efficiency, environmental compatibility, low energy consumption, and corrosion resistance.[7] For example, graphene oxide (GO) is an inexpensive metal-free material which has been recently used as an oxidative catalyst in chemical transformations.[8] Simplified structure of a single layer of graphene oxide (GO) was proposed (Fig. 1).[9]

The presence of functional groups on the aromatic scaffold of GO allows these sheets to mediate ionic and nonionic interactions with a wide range of molecules.[10] On the other hand, it has been recognized that GO possess interesting and potentially useful reactivity and can act as oxidants and/or acids.[11]

The Knoevenagel and Michael addition reactions have various applications in the elegant synthesis of desired chemicals.[12] In continuation of our studies on the synthesis of substituted coumarins via multicomponent reactions (MCRs),[13-15] herein, we present new and green methods to synthesize some biscoumarins and pyranocumarins.

RESULTS AND DISCUSSION

A modified Hummers method was employed for the preparation of graphene oxide (GO). The morphology of the prepared GO nanoplatelets was observed by scanning electron microscopy (SEM). Fig. 2(A) presents the SEM image of GO nanoplatelets showing crumpled thin layers with wrinkles and folds on the surface of GO. Fig. 2(B) shows the XRD pattern of the bulk GO in its dry state. In the XRD pattern, the clear diffraction bands are centered at 2θ ~ 101 corresponding to the (002) plane of the GO with an interlayer spacing about 0.87 nm.

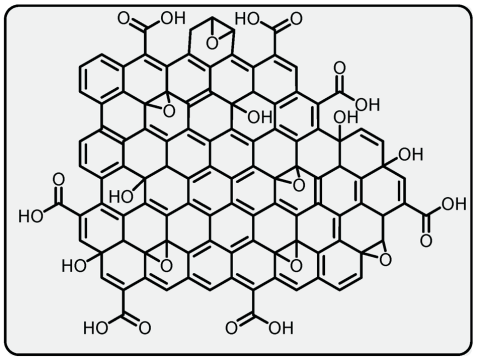


Fig. 1. Structural model of graphene oxide (GO).

* Corresponding author. Email: saeidkhm@yahoo.com

Supporting information for this article is available on the www under http://dx.doi.org/10.1002/jccs.201400349

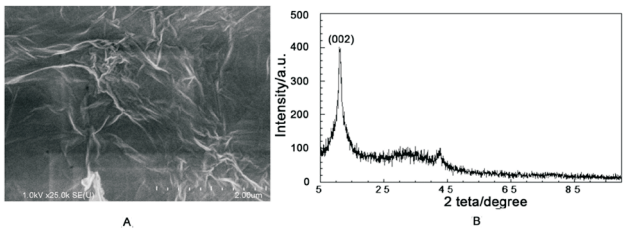
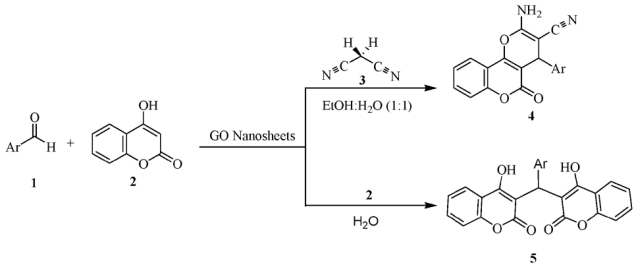


Fig. 2. (A) SEM image of GO; (B) XRD pattern of GO.

As part of an ongoing research program aiming to find green methods within organic chemistry, we have previously utilized some environmentally-friendly catalysts.[16,17] Here, we describe a three-component condensation of arylaldehydes **1** and 4-hydroxycoumarin (**2**) with malononitrile (**3**) in the presence of GO as a nanocatalyst to produce pyranocoumarins **4** (Scheme 1). Also, the GO-catalyzed reaction of **1** with **2** has been separately studied to yield corresponding bis-4-hydroxycoumarins **5**.

Scheme 1 Synthesis of pyranocoumarins and bis-4-hydroxycoumarins using GO



The nature of the solvent and catalyst plays a significant role in chemical transformations. Thus, development of a safe, mild, and reusable catalytic system for the MCRs remains of interest to the organic chemists. To optimize reaction conditions, several fundamental experiments were carried out based on the synthesis of compound **4a** and **5a** as a model. The results are summarized in Table 1.

As can be seen from Table 1, the best conditions were determined as GO (0.005 g) in H_2O/EtOH (1:1) for **4a** and GO (0.005 g) in H_2O for **5a**. After optimization of the reaction conditions, the reaction scope was extended by using different arylaldehydes **1**. The products **4** and **5** were obtained in good yields and short reaction times. It should be noted that arylaldehydes bearing both electron-withdrawing or -donating groups could participate in the reactions (Table 2).

The main disadvantage of some reported methods for the synthesis of **4** and **5** is that the catalysts are destroyed during the work-up procedure and cannot be recovered or reused. In this study, the recycled catalyst was used for four cycles and no appreciable loss for the catalytic activity observed after the last run (**4a**: 87%; **5a**: 91%).

To demonstrate the merit of this method in comparison with previously reported results in literature, we provided the results in Table 3 and 4. These reactions can be efficiently carried out under our suggested conditions with respect to reaction times and product yield.

EXPERIMENTAL

General: Chemicals were purchased from Aldrich. GO was prepared using modified Hummers method from flake graphite (Merck Company).[18] The reactions were monitored by thin layer chromatography (TLC; silica-gel 60 F_{254}, n-hexane: ethyl acetate). IR spectra were recorded on a FT-IR JASCO-680 and the ^{1}H NMR spectra were obtained on a Bruker-Instrument DPX-400 MHz Avance 2 model. SEM studies of the nanostructures were carried out with a JEOL JEM 3010 instrument operating at an ac-

Table 1. The effect of solvent and catalyst amounts on the synthesis of **4a** under reflux

Entry	Catalyst (g)	Solvent	Time (min)		Yield (%)	
			4	5	4	5
1	5	-	180	180	25	33
2	5	EtOH	10	17	87	80
3	5	MeOH	16	25	80	72
4	5	H_2O	180	10	50	93
5	5	H_2O/EtOH (1:1)	14	10	95	93
6	-	H_2O/EtOH (1:1)	180	Not tested	30	-
7	2	H_2O/EtOH (1:1)	180	Not tested	90	-
8	10	H_2O/EtOH (1:1)	10	Not tested	92	-
9	-	H_2O	Not tested	180	-	45
10	2	H_2O	Not tested	180	-	77
11	10	H_2O	Not tested	12		90

Table 2. Synthesis of **4** and **5** using GO (0.005 g) under optimized conditions

Entry	Product	Ar	Time (min)	Yield (%)[c]	Mp. (°C)
1	**4a**	Ph	14	95	261-263
2	**4b**	1-Naphthyl	20	88	262-264
3	**4c**	2-Cl-Ph	12	92	264-266
4	**4d**	4-NO_2-Ph	17	90	260-262
5	**4e**	4-Cl-Ph	20	93	262-264
6	**4f**	4-Br-Ph	12	90	256-258
7	**4g**	4-MeO-Ph	15	90	240-242
8	**5a**	H	10	93	229-231
9	**5b**	4-Cl	12	95	253-255
10	**5c**	4-Br	20	95	263-265
11	**5d**	4-NO2	17	93	232-234
12	**5e**	4-OMe	18	90	241-243
13	**5f**	2-Cl	22	94	226-228
14	**5g**	4-Me	25	90	264-266

Table 3. Comparison of the present work with other methods reported in the literature for synthesis of **4a**

Entry	Conditions	Time/Yield (%)[Ref.]
1	GO (5 g), H_2O:EtOH (1:1), Reflux	14/95[a]
2	SDS (20 mol%), H_2O, 60 °C	120/85[19]
3	$H_6P_2W_{18}O_{62}{\cdot}18H_2O$ (1 mol%), H_2O:EtOH (1:1)	30/89[20]
4	MgO (0.2 g), EtOH, Reflux	32/89[21]
5	DAHP (10 mol%), H_2O:EtOH (1:1), rt	180/81[22]
6	(*S*)-Proline (10 mol%), H_2O:EtOH (1:1), Reflux	240/72[22]
7	KF-Al_2O_3 (0.125 g), EtOH, Reflux	240/90[23]
8	TEBA (0.07 g), H_2O, 90 °C	420/96[24]

[a] This work.

celerating voltage of 300 kV. X-Ray diffraction (XRD, D8, Advance, Bruker, AXS) patterns were obtained for characterization of the heterogeneous catalyst. Melting points were measured on an electrothermal KSB1N apparatus. All products were characterized by comparison of their spectra and physical data with those reported in the literature.[19-29]

Preparation of GO catalyst: A flask containing graphite (1 g) and $NaNO_3$ (0.75 g) was placed in an ice-water bath. H_2SO_4 (75 mL) was added with stirring and then $KMnO_4$ (4.5 g) was slowly added over about 1 h. After vigorously stirring for 5 days at room temperature, 5% H_2SO_4 (140 mL) aqueous solution was added over about 1 h with stirring, and the temperature was kept at 98 ºC. The temperature was reduced to 60 ºC, 3 mL of H_2O_2 (30 wt% aqueous solution) was added, and the mixture was stirred for 2 h at room temperature. As-prepared GO was suspended in ultra-pure water to give a brown dispersion, which was subjected to dialysis to completely remove residual salts and acids. The resulting purified GO powders were collected by centrifugation and air-dried. GO powders were dispersed in water to create a 0.05 wt% dispersion. The dispersion was then exfoliated through ultrasonication for 1 h, which the bulk GO powders were transformed into GO nanoplatelets.

Table 4. Comparison of our method with other methods for the synthesis of **5a**

Entry	Conditions	Time/Yield (%)[Ref.]
1	GO/H_2O/reflux	15 min/95[a]
2	$NaHSO_4{\cdot}SiO_2$/toluene/100 ºC	30 min/89[25]
3	Indion 190 resin/toluene/100 ºC	30 min/92[25]
4	Silica-supported Preyssler nanoparticles/EtOH/r.t.	30 min/92[26]
5	SO_3H-functionalized ILs/70 ºC	2 h/95[27]
6	$H_6[PMo_9V_3O_{40}]$/EtOH:H_2O	15 h/30[28]
7	Catslyst-free/microwave/H_2O/150 W, 150 ºC	9 min/ 85[29]

[a] This work.

General procedure for the synthesis of pyrano[2,3-c]-coumarin: 4-Hydroxycoumarin (1 mmol), aromatic aldehyde (1 mmol), malononitrile (1.1 mmol) and GO (0.005 g) were added to a mixture of 10 mL EtOH/H_2O (50/50) in a 25 mL Pyrex flask and refluxed for an appropriate time (Table 2). The reaction progress was controlled by thin layer chromatography (TLC) using hexane/EtOAc (1:1). After completion of the reaction, the solvent was removed under vacuum and the residue was dissolved in hot EtOH to separate catalyst. The crude **4** was obtained after recrystallization from EtOH.

Preparation of bis-4-hydroxycoumarins: A mixture of aromatic aldehydes **1** (1 mmol), 4-hydroxycoumarin (2 mmol), and GO (0.005 g) in water (10 mL) was stirred and refluxed for an appropriate time mentioned in Tables 2. The progress of the reaction was monitored by TLC (hexane/EtOAc, 1:1). After completion of the reaction, the precipitate was filtered off and dissolved in hot EtOH to separate catalyst. The crude **5** was afforded after recrystallization from EtOH.

Characterization data for selected compounds

Compound 4b: IR (KBr): 3340, 3312, 2188, 1697, 1669, 1598, 1379, 1066 cm^{-1}. ^1H NMR (DMSO, 400 MHz): δ 8.44 (d, 1H, J = 6.4 Hz), 7.96 (d, 2H, J = 8.0 Hz), 7.83 (d, 1H, J = 8.0 Hz), 7.76-7.33 (m, 8H), 5.48 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 159.55, 157.83, 153.80, 152.07, 133.26, 132.93, 130.93, 128.47, 127.43, 126.10, 126.00, 125.85, 125.75, 124.74, 123.43, 122.43, 119.15, 116.61, 112.96, 104.65, 58.49. **Compound 4f:** IR

(KBr): 3396, 3321, 3195, 2202, 1706, 1671, 1607, 1381, 1053 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz): δ 7.90 (dd, 1H, J = 7.8, 1.2 Hz), 7.75-7.70 (m, 1H), 7.52-7.43 (m, 6H), 7.30-7.28 (m, 2H), 4.50 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 159.55, 157.94, 153.70, 152.18, 146.02, 132.99, 130.69, 130.39, 130.05, 126.94, 124.65, 122.54, 121.68, 119.05, 116.57, 112.98, 103.15, 57.31, 36.59. **Compound 5b:** ^1H NMR (DMSO-d_6, 400 MHz): δ 10.70 (b, 1H), 9.99 (s, 1H), 7.89 (d, 2H, 8 Hz), 7.58 (t, 2H, J = 8 Hz), 7.40-729 (m, 6H), 7.12 (d, 2H, J = 8.4 Hz), 6.28 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 165.89, 164.55, 152.26, 140.22, 132.69, 132.28, 131.72, 131.22, 130.74, 129.08, 123.93, 123.53, 123.16, 118.31, 116.35, 115.84, 103.60, 90.95, 35.72. **Compound 5d.** ^1H NMR ($CDCl_3$, 400 MHz): δ 11.57 (s, 1H), 11.35 (s, 1H), 8.08 (d, 1H, J = 8 Hz), 8.03 (d, 1H, J = 8 Hz), 7.68-7.64 (m, 2H), 7.44 (d, 4H, J = 8 Hz), 7.21 (dd, 2H, J = 8 Hz, 5.2 Hz), 7.03 (t, 2H, J = 8 Hz), 6.07 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.23, 166.86, 165.93, 164.63, 162.94, 160.50, 152.54, 152.29, 133.01, 130.87, 130.84, 128.22, 128.14, 124.98, 128.14, 124.98, 124.41, 116.87, 116.68, 116.39, 115.63, 115,41, 105.49, 103.95, 35.68.

CONCLUSIONS

In summary, the GO was used as a recyclable and water-tolerant nanocatalyst for the green synthesis of substituted coumarins via the one-pot reactions. The present methods may have some advantages over the previously reported ones, such as the use of a safe catalyst, avoidance of toxic solvents, high product yields, short reaction times, and an easy work-up procedure.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge partial support of this work by the Islamic Azad University, Omidiyeh Branch (Iran).

REFERENCES

1. Karami, B.; Kiani, M. *J. Chin. Chem. Soc.* **2014**, *61*, 213.
2. Capraa, J. C.; Cunhaa, M. P.; Machadoa, D. G.; Zomkowskia, A. D. E.; Mendesc, B. G.; Santos, A. R. S.; Pizzolattic, M. G.; Rodrigues, S. A. L. *Eur. J. Pharmacol.* **2010**, *643*, 232.
3. Karami, B.; Khodabakhshi, S.; Eskandari, K. *Chem. Pap.* **2013**, *67*, 1474.
4. Witaicenis, A.; Seito, L. N.; da Silveira Chagas, A.; Domingues de Almeida Junior, L.; Luchini, A. C.; Rodrigues-Orsi, P.; Cestari, S. H.; Stasi, L. C. D. *Phytomedicine* **2014**, *21*, 240.
5. Ni, X.; Guo, Y.; Bu, H.; An, J.; En, D. *J. Chin. Chem. Soc.* **2012**, *59*, 1439.
6. Ziarani, G. M.; Hajiabbasi, P. *Heterocycles* **2013**, *87*, 1415.
7. (a) Haag, D.; Kung, H. H. *Top. Catal.* **2014**, *57*, 762; (b) Sun, X.; Wang, R.; Su, D. *Chin. J. Catal.* **2013**, *34*, 508.
8. Dreyer, D. R.; Jia, H.-P.; Bielawski, C. W. *Angew. Chem. Int. Ed.* **2010**, *49*, 6813.
9. Pyun, J. *Angew. Chem. Int. Ed*. **2011**, *50*, 46.
10. Dreyer, D. R.; Jia, H.-P.; Bielawski, C. W. *Angew. Chem. Int. Ed.* **2010**, *49*, 6813.
11. (a) Dreyer, D. R.; Jia, H.-P.; Bielawski, C. W. *Angew. Chem. Int. Ed*. **2010**, *49*, 6813-6816; (b) Dreyer, D. R.; Park, S.; Bielawski, C. W.; Ruoff, R. S.; The chemistry of graphene oxide. *Chem. Soc. Rev.* **2010**, *39*, 228.
12. Khurana, J. M.; Vij, K. *Tetrahedron Lett.* **2011**, *52*, 3666.
13. Karami, B.; Eskandari, K.; Khodabakhshi, S. *Arkivoc* **2012**, *ix*, 76.
14. Karami, B.; Khodabakhshi, S.; Hashemi, F. *Tetrahedron Lett.* **2013**, *54*, 3583.
15. Karami, B.; Eskandari, K.; Khodabakhshi, S. *J. Iran. Chem. Soc.* **2014**, *11*, 631.
16. (a) Karami, B.; Taei, M.; Khodabakhshi, S.; Jamshidi, M. *J. Sulfur Chem*. **2012**, *33*, 65; (b) Karami, B.; Khodabakhshi, S.; Nikrooz, M. *Polycyclic Aromat. Compds*. **2011**, *31*, 97.
17. Karami, B.; Khodabakhshi, S.; Jamshidi, M. *J. Chin. Chem. Soc.* **2013**, *60*, 1103.
18. Hummers, W. S.; Offeman, R. E. J. *J. Am. Chem. Soc.* **1958**, *80*, 1339; (b) Yang, H.; Li, F.; Shan, C.; Han, D.; Zhang, Q.; Niu, L.; Ivaska, A. *J. Mater. Chem.* **2009**, *19*, 4632; (c) Becerril, H. A.; Mao, J.; Liu, Z.; Stoltenberg, R. M.; Bao, Z.; Chen, Y. *ACS Nano* **2008**, *2*, 463.
19. Mehrabi, H.; Abusaidi, H. *J. Iran. Chem. Soc.* **2010**, *78*, 90-894.
20. Heravi, M. M.; Jani, B. A.; Derikvand, F.; Bamoharram, F. F.; Oskooie, H. A. *Catal. Commun.* **2008**, *10*, 272-275.
21. Seifi, M.; Sheibani, H. *Catal. Lett.* **2008**, *126*, 275-279.
22. Abdolmohammadi, S.; Balalaie, S. *Tetrahedron Lett.* **2007**, *48*, 3299-3303.
23. Xiang-Shan, W.; Zhao-Sen, Z.; Da-Qing, S.; Xian-Yong, W.; Zhi-Min, Z. *Chin. J. Org. Chem.* **2005**, *25*, 1138-1141.
24. Da-Qing, S.; Jing, W.; Qi-Ya, Z.; Xiang-Shan, W. *Chin. J. Org. Chem.* **2006**, *26*, 643-647.
25. Padalkar, V.; Phatangare, K.; Takale, S.; Pisal, R.; Chaskar, A. *J. Saudi Chem. Soc.* **2015**, *19*, 42.
26. Heravi, M. M.; Nahavandi, F.; Sadjadi, S.; Oskooie, H. A.; Bamoharram, F. F. *Synth. Commun.* **2010**, *40*, 498.
27. Li, W.; Wang, Y.; Wang, Z.; Dai, L.; Wang, Y. *Catal. Lett.* **2011**, *141*, 1651.
28. Heravi, M. M.; Sadjadi, S.; Mokhtari Haj, N.; Oskooie, H. A.; Bamoharram, F. F. *Catal. Commun*. **2009**, *10*, 1643.
29. Gong, G.-X.; Zhou, J.-F.; An, L.-T.; Duan, X.-L.; Ji, S.-J. *Synth. Commun.* **2009**, *39*, 497.

