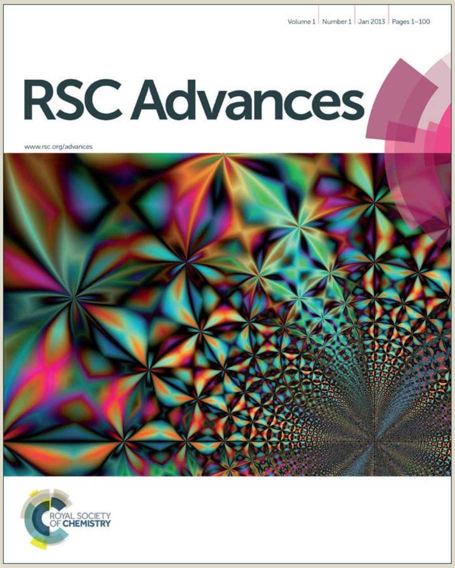
RSC Advances



ROYAL SOCIETY
OF CHEMISTRY

www.rsc.org/advances

Efficient synthesis of Xanthene derivatives using carboxyl functionalized graphene quantum dots as an acidic nano-catalyst under microwave irradiation

Ashkan Shomali, Hassan Valizadeh*, Alireza Banan, Rahim Mohammad-Rezaei

Department of Chemistry, Faculty of Sciences, Azarbaijan Shahid Madani University, Tabriz, Iran.

Abstract

Carboxyl functionalized graphene quantum dots (CGQDs) was applied as a highly efficient and green acidic catalyst for the coupling reaction of 2-naphthole and benzaldehyde derivatives for the preparation of 14*H*-dibenzo xanthene derivatives, under solvent-free microwave irradiation conditions. The structures of the 14*H*-dibenzo xanthene derivatives were confirmed by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectroscopic techniques. The structure of catalyst was also confirmed by FT-IR, XRD, TEM and PL techniques. In order to demonstrate the positive impact of CGQDs catalyst, the reaction times and yields of the products were compared with similar products which have been reported previously. 14*H*-Dibenzo xanthene derivatives were synthesized in simple procedure, good to excellent yields via the present procedure.

Keywords: Carboxyl functionalized graphene quantum dots; 14*H*-Dibenzo xanthene derivatives; Microwave irradiation; Solvent-free; Acidic nano-catalyst

---

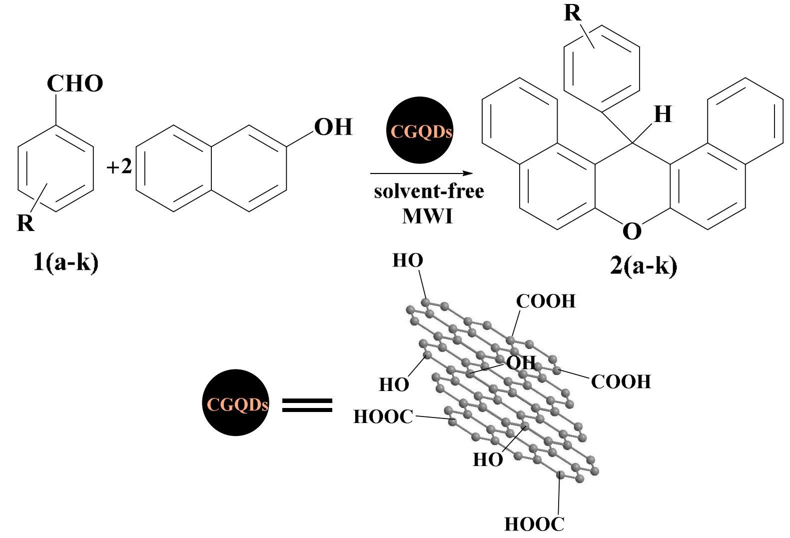
*Corresponding author: Tel: +98-411-33856447, Fax: +98-4134327541; P.O. Box 53714-161; E-mail address: hvalizadeh2@yahoo.com

1. Introduction

Benzoxanthenes are an important class of oxygen heterocyclic compounds in organic chemistry.[1] These compounds are cited for pharmacological activities such as antiviral,[2] anticancer,[3] antibacterial,[4] anti-inflammatory activities[5] and also sensitizers in photodynamic therapy (PDT) for abolishing the tumor cells.[6] Benzoxanthene derivatives have also widely applied as dyes,[7] in laser technologies[8] and fluorescent materials.[9] Recently, various procedures have been reported for the synthesis of xanthenes and benzoxanthenes such as the reaction of aryloxy magnesium halides with triethyl orthoformate,[10] trapping of benzynes with phenols,[11] cyclodehydration reaction.[12] Different acidic catalysts such as hydrochloric acid,[13] H_3PO_4 or $HClO_4$,[14] p-toluenesulfonic acid,[15] sulfamic acid,[16] silica sulfuric acid,[17] heteropoly acid[18] have been used for the facile synthesis of xanthenes and benzoxanthene products. Although many synthetic methods have been reported for the synthesis of xanthenes and benzoxanthene,[19-21] however these methods have some limitations. Due to the fact that mineral acid is harmful to the environment, the use of an acid catalyst with green feature have important role. For the removal of toxicity, decrease of the cost, efficient yields, and also decreasing of the synthesis time, research on a more efficient and safer route for the synthesis of benzoxanthene derivatives is even required.

Graphene quantum dots (GQDs) are a new class of compounds consisting of a single atomic layer of nano-sized graphene.[22] In recent years, according to some excellent characteristics of GQDs, this compound have emerged intensive research interests. These feature include high surface area, excellent solubility, low toxicity, biocompatibility, stable photoluminescence, excellent thermal and chemical stability, and easy functionalization.[23-32] These exceptional properties have wide application in different kind of fields such as ranging from high-speed and radio-frequency logic devices,[33] thermally and electrically conductive reinforced composites, sensors[34, 35] and photocatalysts,[36, 37] transparent electrodes, liquid crystal displays,[38, 39] solar cells[40] and catalyst.[41]

In the present work, we report an efficient and green procedure for the synthesis of 14*H*-dibenzo xanthene derivatives from 2-naphthol and benzaldehyde derivatives with using carboxyl functionalized graphene quantum dots as an acidic nano-catalyst in the absence of mineral acid catalyst under microwave irradiation (scheme 1).



Scheme 1. CGQDs nano-catalyst for the synthesis of 14*H*-dibenzo xanthene derivatives

2. Experimental

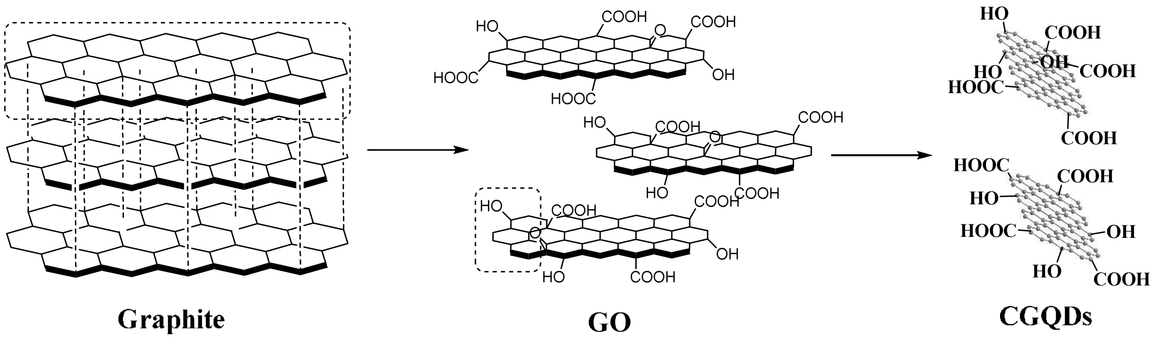
2.1. Materials and instrumentation

All reagents were bought from Merck Company and used without further purification. Infrared spectra (FT-IR) were recorded with KBr on a Perkin-Elmer FT-IR spectrometer. Melting points were determined in open glass-capillaries using a Stuart melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance AC-300MHz using $CDCl_3$ and DMSO-d_6 as the deuterated solvents and TMS as an internal standard. Catalyst structure was supported by X-ray diffractometry (XRD; Bruker AXS model D8 Advance).

Transmission-electron microscopy (TEM) images were obtained by Philips CM-10 (Eindhoven, The Netherlands). Fluorescence spectra and intensity measurements were carried out using an FP-6200 spectrofluorometer (JASCO Corporation, Tokyo, Japan). MW experiments were conducted in a Milestone MicroSynth apparatus.

2.2. Synthesis of carboxyl functionalized graphene quantum dots (CGQDs)

In this study, the hydrothermal method was used for synthesis of GQDs.[24] firstly, graphene oxide was prepared by chemical oxidization of graphite powder according to the modified Hummers method.[42] The as prepared graphene oxide was deoxidized in a tube furnace at 200-300 ˚C for 2 h and a heating rate of 5 ˚C min^{-1} in a nitrogen atmosphere. The obtained graphene sheets (0.05g) were oxidized in concentrated H_2SO_4 (10 mL) and HNO_3 (30 mL) for 15-20 h under mild ultrasonication (500 W, 40 kHz). The oxidized graphene sheets were diluted and purified with microporous membrane and dispersed in deionized water. Then the suspension was heated at 200 ˚C for 10 h in an autoclave. The resulting suspension was filtered with microporous membrane and a brown GQDs solution was obtained. To remove larger graphene nanoparticles, the colloidal solution was dialyzed in a dialysis bag (retained molecular weight: 3500 Da) overnight and GQDs were obtained having stability for more than 3 months (Scheme 2).



Scheme 2. Preparation of CGQDs

2.3. General procedure for the synthesis of 14*H*-dibenzo xanthene derivatives:

CGQDs (0.002 g) was added to a mixture of 2-naphthol (2 mmol) and benzaldehyde (1 mmol). The reaction mixture was heated at 90 °C with full power MWI (300 W) at 2 min. The progress of the reaction was monitored by thin layer chromatography (TLC). Ingredient of reaction was completely consumed after about 1 min of inception reaction. Then the reaction mixture was cooled to room temperature and ethyl acetate was added and stirred thoroughly. Then water was added to the ethyl acetate solution in order to extraction of CGQDs. This procedure was repeated 3 times until the catalyst was completely extracted into the aqueous phase. For reuse of the catalyst, the aqueous phase was removed under the heat and vacuum conditions. Then, Ethyl acetate was evaporated under the vacuum which led to the crude product. Also further purification was carried out by recrystallization from ethyl acetate /n-hexane to afford the pure products in high yields (**2a-k**).

In order to study the reusability of the catalyst, the synthesis of 14-phenyl-14*H*-dibenzo xanthene was repeated in 3 times with the same catalyst. The results was showed that the efficiency of the catalyst after the extract and reuse was appropriately close to each other (96±2.4%).

3. Results and discussion

3.1. Preparation and structural features of CGQDs

Fig. 1A shows the TEM image of CGQDs. The distribution of CGQDs is uniform and the average diameter was estimated to be 5 to 10 nm. Fig. 1B shows the XRD pattern of CGQDs representing a wide-angle peaks belong to the (002) planes of CGQDs.[32, 33] The interlayer spacing of CGQDs was 3.82 Å which is larger in comparison with bulk graphite (3.34 Å).

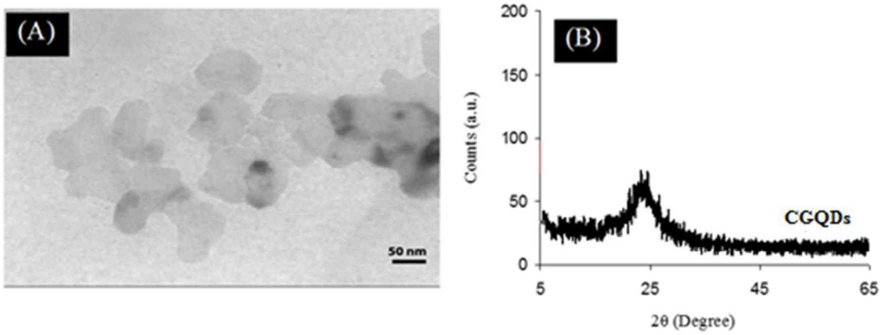


Fig. 1. TEM image (A) and XRD patterns (B) of the synthesized CGQDs

The FT-IR spectrum of CGQDs is shown in Fig. 2A. The signal at 1723 cm^{-1} is assigned to C=O stretch of carboxylic functional group and a broad signal at 3427 cm^{-1} is related to O-H band. The strong photoluminescence (Fig. 2B) at 503 nm in CGQDs is resulted from free zigzag sites with a carbene-like triplet ground state.[24] The response GQDs in photoluminescence with strong peak can be used in fluorescence sensing and imaging applications.

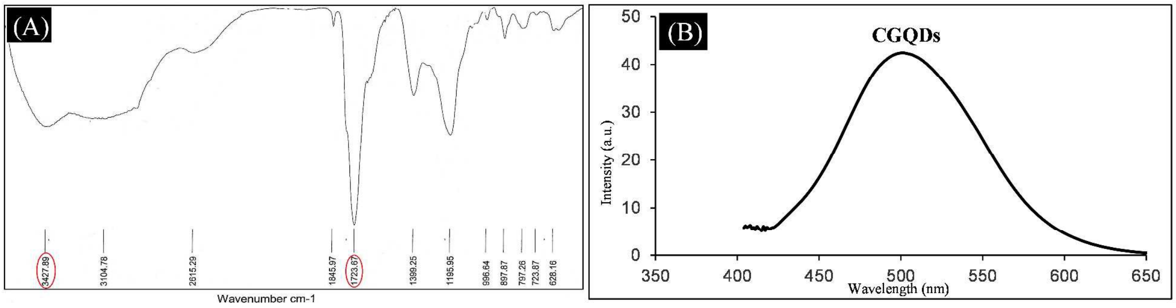


Fig. 2. FT-IR spectrum (A) and fluorescence spectrum (B) of CGQDs

3.2. Reactions

In this study, the reaction of 2-naphthol (2 mmol) with benzaldehyde (1 mmol) in the presence of CGQDs (0.0005 g) as an acidic nanocatalyst was chosen as a sample reaction at 70 ˚C under MWI. This reaction led to 14*H*-dibenzo xanthene derivative (**2a**) in 35% yield after 2 min (Table 1, entry 1). Then, the various amount of catalyst was examined for the optimization ratio catalyst/aldehyde derivatives. The results showed that the best ratio is catalyst (0.002 g)/aldehyde (1 mmol) and increasing of the amount of the catalyst has no considerable effect on the yield of the product and also on reaction time (Table 1).

<<Table 1>>

<<Table 2>>

In addition, the procedure under MWI conditions was compared with the reaction under conventional heating conditions and showed that the reaction was carried out in very shorter reaction time and in higher yield under MWI conditions. The various derivatives of aldehydes were used for the synthesis of the related 14*H*-dibenzo xanthene derivatives (Table 2). The products were characterized by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectra. Comparison of the yields of the products and reaction times in this procedure with the reported value were shown in Table 3 and also compared to the types of catalysts reported in Table 4 were used for demonstrating the positive effect of the CGQDs on reaction time and efficiency.

<<Table 3>>

<<Table 4>>

Table 1. Optimization of reaction conditions for compound (**2a**)

Entry	Temperature (°C)	Catalyst (g)	Aldehyde (mmol)	Time (min)	Yield[a] (%)
1	70	0.0005	1	2	35
2	70	0.0005	1	3	48
3	90	0.0005	1	3	48
4	70	0.001	1	3	63
5	80	0.001	1	2	70
6	90	0.001	1	2	73
7	70	0.002	1	2	86
8	70	0.002	1	3	86
9	90	0.002	1	2	95
10	90	0.002	1	3	95
11	70	0.003	1	2	87
12	70	0.003	1	3	87
13	90	0.003	1	2	96
14	90	0.003	1	3	96

[a] Isolated yield

Table 2. Synthesis of 14*H*-dibenzo xanthene derivatives using CGQDs

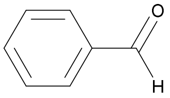
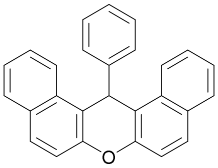
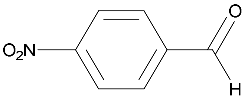
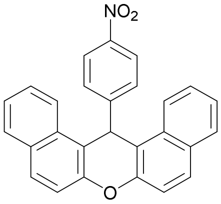
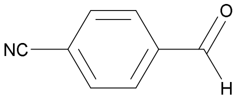
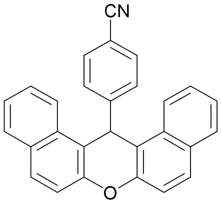
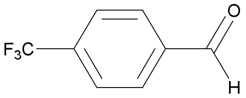
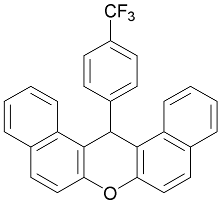
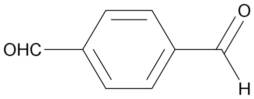
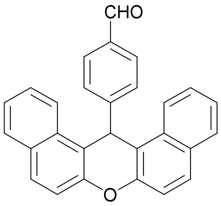
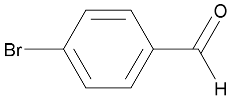
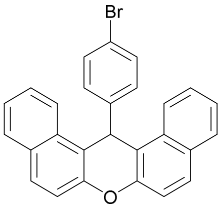
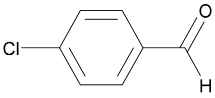
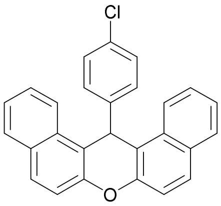
Entry	Aldehyde	Reactant number	Product	Product Number
1		**1a**		**2a**
2		**1b**		**2b**
3		**1c**		**2c**
4		**1d**		**2d**
5		**1e**		**2e**
6		**1f**		**2f**
7		**1g**		**2g**

Table 2.

Entry	Aldehyde	Reactant Number	Product	Product Number

(*Continued*)

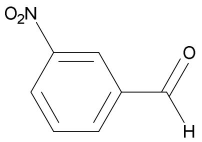
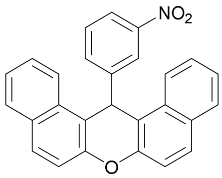
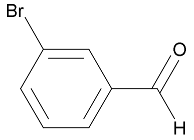
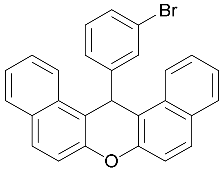
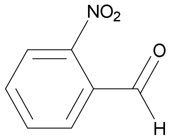
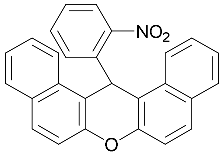
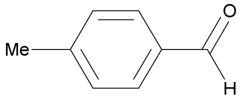
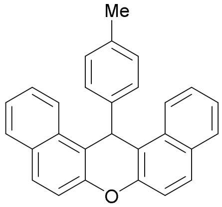
8		**1h**		**2h**
9		**1i**		**2i**
10		**1j**		**2j**
11		**1k**		**2k**

Table 3. Comparison of the yields of products with reported values

Entry	Product number	Time (min)	M.P ˚C		Yield^a (%)	
			Found	Reported [Ref.]	Found	Reported [Ref.]
1	**2a**	3	189-190	186-187 [43]	95	88 [43]
2	**2b**	2	312-313	311-313 [47]	98	95 [47]
3	**2c**	2	294-295	291-292 [43]	94	86 [43]
4	**2d**	2	260-261	258-259 [44]	98	97 [44]
5	**2e**	2	253-254	251-253 [45]	92	78 [45]
6	**2f**	3	295-296	296-297 [48]	88	87 [48]
7	**2g**	3	287-288	288-289 [47]	91	87 [47]
8	**2h**	3	213-214	210-212 [45]	80	73 [45]
9	**2i**	3	293-294	294-297 [45]	89	90 [45]
10	**2j**	2	215-217	214-215 [46]	93	93 [46]
11	**2k**	3	226-227	227-229 [48]	87	84 [48]

^{a}Isolated yield

Table 4. Comparison of CGQDs with other catalyst used in literature for product **2b**

Name of Catalyst	Amount of Catalyst	Time	Yield (%)	Solvent/ condition	Ref.
[2-(sulfooxy)ethyl]sulfamic acid	15%	20 min	76	Solvent-free /150℃	45
Functionalized mesoporous materials	20 mg	4 h	82	DCM/25℃	49
Camphor-10-sulphonic acid	2 mol%	30 min	84	Solvent-free /MWI	43
$HClO_4$	0.3 mmol	2.5 min	85	Solvent-free /MWI	50
Poly(AMPS-co-AA)	0.04 g	25 min	86	Solvent-free /110℃	51
Phosophosulforic acid	5 mol%	55 min	88	Solvent-free /110℃	44
Disulfonic acid imidazolium carboxylate	25 mol%	25 min	88	Solvent-free /100℃	52
Vanadate sulfuric acid (VO_2-OSO_3H)	10 mol%	15 min	92	Solvent-free /80℃	43
CuO NPs	7 mg	14 min	93	Solvent-free /80℃	48
CuS QDs	6 mg	6 min	95	Solvent-free /80℃	47
CGQDs (this work)	2 mg	2 min	98	Solvent-free /MWI	-

4. Conclusions

In summary, we introduced a new efficient acidic catalyst for the synthesis of 14*H*-dibenzo xanthene derivatives. Green reaction conditions under MWI conditions and simple reaction procedure are advantages of this method. Excellent yields for the products were obtained in shorter reaction times.

Acknowledgment

The partial financial assistance from the Research Vice Chancellor of Azarbaijan Shahid Madani University is gratefully acknowledged.

References

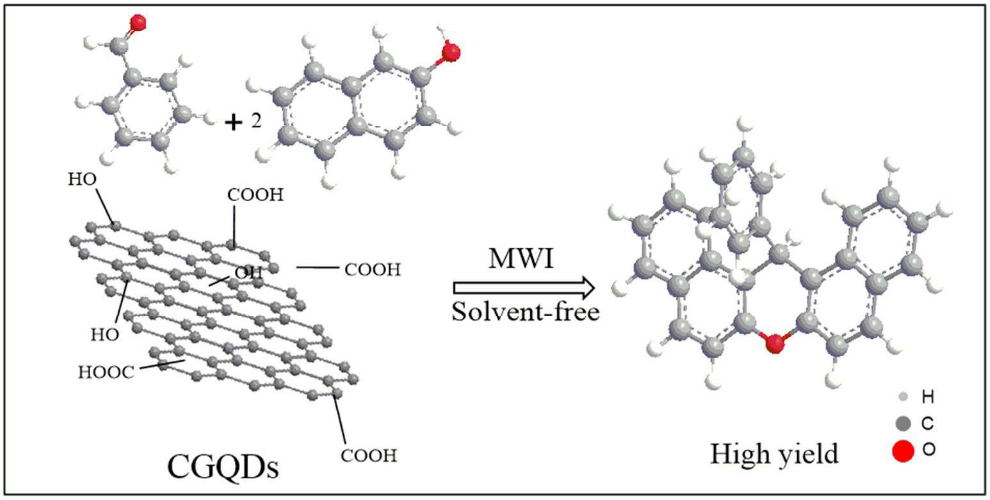
1. R. M. N. Kalla, M. Akkarapalli and H. Osman, *J. Drug Metab. Toxicol.*, 2014, **5**, 1.
2. R. W. Lambert, J. A. Martin, J. H. Merrett, K. E. B. Parkes, G.J. Thomas, PCT Int Appl WO 9706178, 1997.
3. K. V. Shashidhara, A. Kumar, R. P. Dodda and B. Kumar, *Tetrahedron*, 2012, **53**, 3281.
4. T. Hideo, JP 56005480, 1981.
5. J. M. Jamison, K. Krabill, A. Hatwalkar, E. Jamison and C. Tsai, *Cell. Biol. Int. Rep.*, 1990, **14**, 1075.

6. *(a)* R. M. Ion, *Prog. Catal.*, 1997, **2**, 55; *(b)* R. M. Ion, D. Frackowiak, A. Planner and K. Wiktorowicz, *Acta Biochim. Pol.*, 1998, **45**, 833.
7. A. Banerjee and A. K. Mukherjee, *Stain. Technol.*, 1981, **56**, 83.
8. M. Ahmad, T. A. King, D. K. Ko, B. H. Cha and J. Lee, *J. Phys. D: Appl. Phys.*, 2002, **35**, 1473.
9. C. G. Knight and T. Stephens, *Biochem. J.*, 1989, **258**, 683.
10. G. Casiraghi, G. Casnati and M. Cornia, *Tedrahedron Lett.*, 1973, **14**, 679.
11. D.W. Knight and P.B. Little, *J. Chem. Soc. Perkin. Trans. 1*, 2001, **15**, 1771.
12. C. A. Buehler, D. E. Cooper and E. O. Scrudder, *J. Org. Chem.*, 1943, **8**, 316.
13. J. A. Van Allan, D. D. Giannini and T. H. Whitesides, *J. Org. Chem.*, 1982, **47**, 820.
14. A. Khoramabadi-zad, Z. Kazemi and H. A. Rudbari, *J. Korean. Chem. Soc.*, 2002, **46**, 541.
15. A. R. Khosropour, M. M. Khodaei and H. Moghannian, *Synlett*, 2005, **6**, 955.
16. B. Rajitha, B. S. Kumar, Y. T. Reddy, P. N. Reddy and N. Sreenivasulu, *Tetrahedron Lett.*, 2005, **46**, 8691.
17. H. R. Shaterian, M. Ghashang and A. Hassankhani, *Dyes and Pigments*, 2008, **76**, 564.
18. M. M. Amini, N. Seyyedhamzeh and A. Bazgir, *Appl. Catal. A: Gen.*, 2007, **323**, 242.
19. A. Shaabani, M. Mahyari and F. Hajishaabanha, *Res. Chem. Intermed.,* 2014, **40**, 2799.
20. S. Saha and C. Schneider, *Org. Lett.*, 2015, **17**, 648.
21. Q. Zhang, H. Su, J. Luo and Y. Wei, *Green Chem.*, 2012, **14**, 201.
22. Y. H. Li, L. Zhang, J. Huang, R. P. Liang and J. D. Qiu, *Chem. Commun.*, 2013, 49, 5180.
23. X. Zhou, Y. Zhang, C. Wang, X. Wu, Y. Yang, B. Zheng, H. Wu, S. Guo and J. Zhang, *ACS Nano*, 2012, **6**, 6592.
24. D. Y. Pan, J. C. Zhang, Z. Li and M. H. Wu, *Adv. Mater.*, 2010, **22**, 734.

25. L. Tang, R. Ji, X. Cao, J. Lin, H. Jiang, X. Li, K. S. Teng, C.M. Luk, S. Zeng, J. Hao and S. P. Lau, *ACS Nano*, 2012, **6**, 5102.
26. S. Zhuo, M. Shao and S. T. Lee, *ACS Nano*, 2012, **6**, 1059.
27. S. Zhu, J. Zhang, S. Tang, C. Qiao, L. Wang, H. Wang, X. Liu, B. Li, Y. Li, W. Yu, X. Wang, H. Sun and B. Yang, *Adv. Funct. Mater.*, 2012, 22, 4732.
28. H. Razmi and R. Mohammad-Rezaei, *Biosensors and Bioelectronics*, 2013, **41**, 498.
29. H. Zhao, Y. Chang, M. Liu, S. Gao, H. Yu and X. Quan, *Chem. Commun.*, 2013, **49**, 234.
30. S. Zhu, J. Zhang, C. Qiao, S. Tang, Y. Li, W. Yuan, B. Li, L. Tian, F. Liu, R. Hu, H. Gao, H. Wei, H. Zhang, H. Sun and B. Yang, *Chem. Commun.*, 2011, **47**, 6858.
31. Y. Dong, C. Chen, X. Zheng, L. Gao, Z. Cui, H. Yang, C. Guo, Y. Chi and C. M. Li, *J. Mater. Chem.*, 2012, **22**, 8764.
32. V. Gupta, N. Chaudhary, R. Srivastava, G.D. Sharma, R. Bhardwaj and S. Chand, *J. Am. Chem. Soc.*, 2011, **133**, 9960.
33. J. S. Wu, W. Pisula and K. Müllen, *Chem. Rev.*, 2007, **107**, 718.
34. F. Schedin, A. K. Geim, S. V. Morozov, E. W. Hill, P. Blake, M. I. Katsnelson and K. S. Novoselov, *Nat. Mater.*, 2007, **6**, 652.
35. J. T. Robinson, F. K. Perkins, E. S. Snow, Z. Q. Wei and P. E. Sheehan, *Nano Lett.*, 2008, **8**, 3137.
36. J. D. Fowler, M. J. Allen, V. C. Tung, Y. Yang, R. B. Kaner and B. H. Weiller, *ACS Nano*, 2009, **3**, 301.
37. H. Zhang, X. Lv, Y. Li, Y. Wang and J. Li, *ACS Nano*, 2010, **4**, 380.
38. H. Liu, S. Ryu, Z. Chen, M. L. Steigerwald, C. Nuckolls and L. E. Brus, *J. Am. Chem. Soc.*, 2009, **131**, 17099.
39. K. S. Kim, Y. Zhao, H. Jang, S. Y. Lee, J. M. Kim, K. S. Kim, J. -H. Ahn, P. Kim, J. -Y. Choi and B. H. Hong, *Nature*, 2009, **457**, 706.

40. P. Blake, P. D. Brimicombe, R. R. Nair, T. J. Booth, D. Jiang, F. Schedin, L. A. Ponomarenko, S. V. Morozov, H. F. Gleeson, E. W. Hill, A. K. Geim and K. S. Novoselov, *Nano Lett*., 2008, **8**, 1704.
41. H. Valizadeh, A. Shomali, S. Nourshargh and R. Mohammad-Rezaei, *Dyes and Pigments*, 2015, **113**, 522.
42. Y. Xu, H. Bai, G. Lu, C. Li and G. Shi, *J. Am. Chem. Soc*., 2008, **130**, 5856.
43. K. Kundu and S. K. Nayak, *J. Serb. Chem. Soc*., 2014, **79**, 1.
44. A. R. Kiasat, A. Mouradzadegun and S. J. Saghanezhad, *J. Serb. Chem. Soc*., 2013, **78**, 1291.
45. S. Sajjadifar, M. Fadaeian, M. Bakhtiyari and S. Rezayati, *Chem. Sci. Trans*, 2014, **3**, 107.
46. M. Nasr-Esfahani and T. Abdizadeh, Rev. Roum. Chim., 2013, **58**, 27.
47. P. Bansal, G. R. Chaudhary, N. Kaur, S. K. Mehta, *RSC Adv*., 2014, **5**, 8205.
48. G. R. Chaudhary, P. Bansal, N. Kaur and S. K. Mehta, *RSC Adv*., 2014, **4**, 49462.
49. J. Mondal, M. Nandi, A. Modak and A. Bhaumik, *J. Mol. Catal. A: Chem*., 2012, **363-364**, 254.
50. N. N. G. Mohammed and M. S. Pandharpatte, *Der Pharma Chemica*, 2011, **3**, 65.
51. B. Maleki, S. Barzegar, Z. Sepehr, M. Kermanian and R. Tayebee, *J. Iran. Chem. Soc*., 2012, **9**, 757.
52. A. K. Dutta, P. Gogoi and R. Borah, *RSC Adv*., 2014, **4**, 41287.

Graphical Abstracts



Graphical Abstract
81x46mm (300 x 300 DPI)