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Graphene Oxide as Highly Effective and Readily Recyclable Catalyst Using for the One-Pot Synthesis of 1,8-Dioxoacridine Derivatives

Burak Aday[1, †], Handan Pamuk[2, †], Muharrem Kaya[2, *], and Fatih Sen[2, *]

[1] *Chemistry Department, Faculty of Arts and Science, Dumlupınar University, Evliya Çelebi Campus 43100 Kütahya, Turkey*
[2] *Biochemistry Department, Faculty of Arts and Science, Dumlupınar University, Evliya Çelebi Campus 43100 Kütahya, Turkey*

Graphene oxide as a highly stable, reusable, isolable, and efficient catalyst has been used for the first time for the synthesis of acridinedione derivatives from dimedone, aromatic aldehydes and various amines with great catalytic performance. One pot synthesis of acridinedione compounds were performed using highly efficient graphene oxide.

Keywords: Graphene Oxide, 1,8-Dioxoacridine, Multi-Component Reaction, One-Pot Synthesis, Cyclization.

1. INTRODUCTION

In recent years, within the fields of medicinal and organic synthetic chemistry, there has been an increasing interest in synthetic techniques based on multicomponent reactions (MCR). Especially 1,8-dioxoacridine derivatives have been synthesized using the MCR system components and those types of compounds are quite important for synthetic and drug chemistry due to their intensive fluorescence feature.[1, 2] Furthermore these compounds have been also used for anti-tumor,[3] cytotoxic,[4] anti-microbial,[5] fungicides,[6] as anti-multidrug-resistant,[7] β-channel opener in cardiovascular disease,[8] carbonic anhydrase inhibitor for glaucoma treatment.[9–13]

In literature different types of catalysts, for instance Amberlyst-15,[14, 15] Amberlite IR-120H,[16] CBSA,[17] CTAB,[18] DBSA,[9, 19] FSG-Hf$(Npf_2)_4$,[20] Glucose sulfonic acid,[21] H_2SO_4,[11] Melamine-formaldehyde resin supported H^+,[22] Proline[23] have been reported for the one-step synthesis of 1,8-dioxoacridine. Since these types of catalysts have lots of limitations such as difficulty of separating the catalyst, the cost of the catalysts, and the formation of side reactions, low efficiency and high reaction temperatures, there is a scope for discovery of a new catalyst with mild reaction condition, short reaction time, high yield and recovery.[24, 25]

Graphene oxide (GO) is two-dimensional material of graphene obtained by the addition of covalently bonded C–O bond.[26] It is worth mentioning that graphene oxide is often used as a catalyst in batteries, the hydrogen storage, sensors, super-capacitors, solar cells etc.[27–32] but its use as a catalyst for synthesizing acridinedione derivatives from different aromatic aldehydes and various amines has not been reported before. Addressed herein, we report for the first time graphene oxide as a catalyst for the synthesis of 1,8-dioxoacridine derivatives.

2. EXPERIMENTAL DETAILS

2.1. Materials and Instrumentation

De-ionized water was filtered by Millipore water purification system (18 MΩ) analytical grade. All glassware and Teflon-coated magnetic stir bars were cleaned with aqua regia, followed by washing with distilled water before drying in an oven.

The chemicals used in the synthesis of 1,8-dioxoacridine derivatives were obtained from Merck and Aldrich Chemical Company. All chemicals and solvents used for the synthesis were of spectroscopic reagent grade.

Melting points were measured on a Bibby Scientific Stuart Digital, Advanced, SMP30. Ultraviolet-Visible

*Authors to whom correspondence should be addressed.
†These two authors contributed equally to this work.

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(UV-Vis) spectra of the samples were collected on a Perkin-Elmer LAMBDA 750 spectrophotometer. Fourier Transform Infrared (FT-IR) spectra were recorded on Bruker Optics, ALPHA FT-IR spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were obtained in DMSO-d_6 with Bruker DPX-300 as solvents with tetramethylsilane as the internal reference. The mass analyses were performed on a Agilent Technologies 6530 Accurate-Mass Q-TOF LC/HRMS.

2.2. Preparation of Graphene Oxide

Graphene oxide (GO) was synthesized from graphite powder using modified Hummer's method. In brief, 1 g of graphite and 0.5 g of sodium nitrate were mixed together followed by the addition of 23 ml of conc. sulphuric acid under constant stirring. After 1 h, 3 g of $KMnO_4$ was added gradually to the above solution while keeping the temperature less than 20 °C to prevent overheating and explosion. The mixture was stirred at 35 °C for 12 h and the resulting solution was diluted by adding 500 ml of water under vigorous stirring. To ensure the completion of reaction with $KMnO_4$, the suspension was further treated with 30% H_2O_2 solution (5 ml). The resulting mixture was washed with HCl and H_2O respectively, followed by filtration and drying, graphene oxide sheets were thus obtained.

2.3. General Procedure for Preparation of 1,8-Dioxoacridine Derivatives (4a–j) Using Graphene Oxide as the Catalyst

A mixture of 2 mmol dimedone **1**, 1 mmol benzaldehyde **2a**, 1 mmol 4-bromoaniline **3b** and Graphene oxide (10 mg) in 3 ml DMF was heated to 100 °C continuously for 90 min. The reaction progress was monitored by TLC. The solid product was filtered, washed with 500 ml water, and recrystallized from ethanol (91–94%).

2.4. Characterization of 1,8-Dioxoacridine Derivatives

2.4.1. 10-(4-chlorophenyl)-3,3,6,6-Tetramethyl-9-Phenyl-3,4,6,7,9,10-Hexahydroacridine-1,8(2H,5H)-Dione (4a)

As yellow crystals, (0.422 g, 92%), mp. (300–302 °C)[22] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.78 (*d*, 2H, J = 17.43 Hz, –CH_2), 2.00 (*d*, 2H, J = 16.00 Hz, –CH_2), 2.16 (*d*, 2H, J = 4.00 Hz, –CH_2), 2.22 (*d*, 2H, J = 5.44 Hz, –CH_2), 5.05 (*s*, 1H, –CH), 7.07–7.12 (*m*, 1H, Ar–H), 7.21–7.32 (*m*, 4H, Ar–H), 7.48 (*d*, 2H, J = 5.44 Hz, 10.58, Ar–H), 7.68 (*d*, 2H, J = 8.84 Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.50, 29.72, 32.33, 32.44, 41.35, 50.03, 113.55, 126.26, 127.97, 128.38, 130.56, 134.37, 137.79, 146.57, 150.58, 195.54; IR (cm^{-1}): 3026 w (Ar–H), 2954 s (–CH), 1634 s (C═O), 1590 s (C═C); HRMS (QTOF-ESI): m/z $[M+H]^+$ calcd. For $C_{29}H_{31}ClNO_2$: 460.2043; found $[M+H]^+$: 460.2061.

2.4.2. 10-(4-chlorophenyl)-3,3,6,6-Tetramethyl-9-(4-nitrophenyl)-3,4,6,7,9,10 Hexahydroacridine-1,8(2H,5H)-Dione (4b)

As yellow crystals, (0.478 g, 91%), mp. (315–317 °C)[33] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.80 (*d*, 2H, J = 17.35 Hz, –CH_2), 2.01 (*d*, 2H, J = 16.13 Hz, –CH_2), 2.18–2.24 (*m*, 4H, –CH_2), 5.10 (*s*, 1H, –CH), 7.54–7.60 (*m*, 4H, Ar–H), 7.70 (*d*, 2H, J = 8.51 Hz, Ar–H), 8.14 (*d*, 2H, J = 8.68 Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.57, 29.61, 32.47, 33.35, 41.39, 49.86, 112.51, 119.43, 123.76, 129.43, 134.55, 137.55, 146.16, 151.32, 154.01, 195.53; IR (cm^{-1}): 3054 w (Ar–H), 2958 w (–CH), 1632 s (C═O), 1592 w (C═C); HRMS (QTOF-ESI)-: m/z $[M+H]^+$ calcd. For $C_{29}H_{29}ClN_2NaO_4$: 527.1714; found $[M+Na]^+$: 527.1729.

2.4.3. 10-(4-chlorophenyl)-3,3,6,6-Tetramethyl-9-(3-nitrophenyl)-3,4,6,7,9,10 Hexahydroacridine-1,8(2H,5H)-dione (4c)

As yellow crystals, (0.464 g, 92%), mp. (285–287 °C)[34] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.82 (*d*, 2H, J = 17.44 Hz, –CH_2), 2.02 (*d*, 2H, J = 16.04 Hz, –CH_2), 2.20 (*d*, 2H, J = 3.30 Hz, –CH_2), 2.25 (*d*, 2H, J = 4.95 Hz, –CH_2), 5.15 (*s*, 1H, –CH), 7.51–7.61 (*m*, 3H, Ar–H), 7.72 (*d*, 2H, J = 8.79 Hz, Ar–H), 7.78 (*d*, 1H, J = 7.87 Hz, Ar–H), 7.99–8.03 (*m*, 1H, Ar–H), 8.12–8.13 (*m*, 1H, Ar–H)); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.47, 29.62, 32.52, 32.92, 41.34, 49.84, 112.72, 121.50, 122.56, 130.21, 130.65, 134.58, 134.75, 137.52, 147.88, 148.60, 151.39, 195.63; IR (cm^{-1}): 3049 w (Ar–H), 2956 w (–CH), 1636 s (C═O), 1576 s (C═C); HRMS (QTOF-ESI): m/z $[M+H]^+$ calcd. For $C_{29}H_{29}ClN_2NaO_4$: 527.1714; found $[M+Na]^+$: 527.1655.

2.4.4. 9-(4-bromophenyl)-10-(4-chlorophenyl)-3,3,6,6-Tetramethyl-3,4,6,7,9,10 Hexahydroacridine-1,8(2H,5H)-Dione (4d)

As yellow crystals, (0.504 g, 94%), mp. (304–305 °C)[33] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.78 (*d*, 2H, J = 17.47 Hz, –CH_2), 2.01 (*d*, 2H, J = 16.05 Hz, –CH_2), 2.19 (*d*, 4H, J = 16.09 Hz, –CH_2), 5.00 (*s*, 1H, –CH), 7.26 (*d*, 2H, J = 8.42 Hz, Ar–H), 7.42–7.50 (*m*, 4H, Ar–H), 7.68 (*d*, 2H, J = 8.77 Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.56, 29.66, 32.27, 32.45, 41.35, 49.96, 113.08, 119.25, 130.33, 130.54, 131.26, 134.44, 137.67, 145.96, 150.81, 195.54; IR (cm^{-1}): 3062 w (Ar–H), 2956 w (–CH), 1635 s (C═O), 1576 s (C═C); HRMS (QTOF-ESI): m/z $[M+H]^+$ calcd. For $C_{29}H_{30}BrClNO_2$: 538.1148; found $[M+H]^+$: 538.1123.

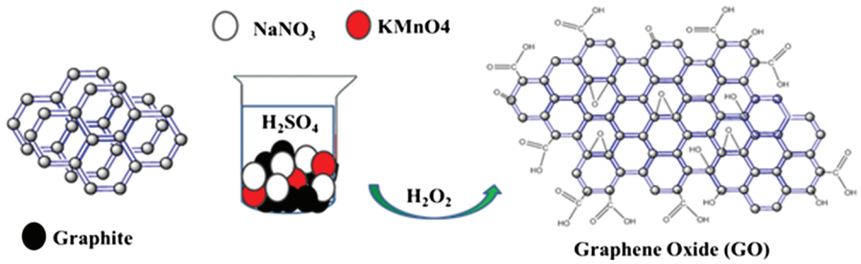


Figure 1. Synthesis of graphene oxide from graphite.

2.4.5. 10-(4-chlorophenyl)-9-(4-fluorophenyl)-3,3,6,6-Tetramethyl-3,4,6,7,9,10-Hexahydroacridine-1,8(2H,5H)-Dione (4e)

As yellow crystals, (0.434 g, 91%), mp. (280–282 °C)[35] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.78 (*d*, 2H, J = 17.43 Hz, –CH_2), 2.01 (*d*, 2H, J = 16.08 Hz, –CH_2), 2.16–2.22 (*m*, 4H, –CH_2), 5.05 (*s*, 1H, –CH), 7.05 (*t*, 2H, J = 8.84 Hz, Ar–H), 7.29–7.34 (*m*, 2H, Ar–H), 7.48 (*d*, 2H, J = 7.15 Hz, Ar–H), 7.68 (*d*, 2H, J = 8.70 Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.52, 29.68, 31.84, 32.45, 41.35, 49.98, 113.42, 114.86, 129.79, 130.53, 134.42, 137.72, 142.80, 150.64, 159.29, 195.55; IR (cm^{-1}): 3054 w (Ar–H), 2957 s (–CH), 1637 s (C═O), 1576 s (C═C); HRMS (QTOF-ESI): m/z [M+H]$^+$ calcd. For $C_{29}H_{30}ClFNO_2$: 478.1949; found [M+H]$^+$: 478.1956.

2.4.6. 10-(4-chlorophenyl)-3,3,6,6-Tetramethyl-9-(p-tolyl)-3,4,6,7,9,10-Hexahydroacridine-1,8(2H,5H)-Dione (4f)

As yellow crystals, (0.435 g, 91%), mp. (262–265 °C)[34] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.75 (*s*, 6H, 2x-CH_3), 0.80 (*s*, 6H, 2x-CH_3), 1.76 (*d*, 2H, J = 17.29 Hz, –CH_2), 1.97–2.22 (*m*, 9H, –CH_2 and –CH_3), 5.00 (*s*, 1H, –CH), 7.04 (*d*, 2H, J = 8.05 Hz, Ar–H), 7.18 (*d*, 2H, J = 8.00 Hz, Ar–H), 7.35–7.55 (*m*, 2H, Ar–H), 7.68 (*d*, 2H, J = 8.82 Hz, Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 26.53, 29.15, 31.83, 32.32, 32.43, 41.33, 50.05, 113.69, 127.87, 128.40, 128.96, 134.34, 135.10, 137.83, 143.69, 150.43, 195.54; IR (cm^{-1}): 3050 w (Ar–H), 2952 w (–CH), 1636 s (C═O), 1577 s (C═C); HRMS (QTOF-ESI): m/z [M+H]$^+$ calcd. For $C_{30}H_{33}ClNO_2$: 474.2200; found [M+H]$^+$: 474.2215.

2.4.7. 10-(4-chlorophenyl)-9-(4-methoxyphenyl)-3,3,6,6-Tetramethyl-3,4,6,7,9,10-Hexahydro Acridine-1,8(2H,5H)-dione (4g)

As yellow crystals, (0.440 g, 91%), mp. (255–257 °C)[36] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.75 (*s*, 6H, 2x-CH_3), 0.85 (*s*, 6H, 2x-CH_3), 1.76 (*d*, 2H, J = 17.40 Hz, –CH_2), 1.97–2.22 (*m*, 6H, –CH_2), 3.70 (*s*, 1H, –OCH_3), 4.95 (*s*, 1H, –CH), 6.80 (*d*, 2H, J = 8.62 Hz, Ar–H), 7.20 (*d*, 2H, J = 8.61 Hz, Ar–H), 7.40–7.55 (*m*, 2H, Ar–H), 7.68 (*d*, 2H, J = 8.78 Hz, Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 26.56, 29.73, 31.39, 32.44, 50.07, 55.31, 113.71, 113.83, 128.93, 130.56, 134.34, 137.85, 138.92, 150.28, 157.76, 195.55; IR (cm^{-1}): 3006 w (Ar–H), 2951 w (–CH), 1638 s (C═O), 1577 s (C═C); HRMS (QTOF-ESI): m/z [M+H]$^+$ calcd. For $C_{30}H_{33}ClNO_3$: 490.2149; found [M+H]$^+$: 490.2160.

2.4.8. 10-(4-bromophenyl)-3,3,6,6-Tetramethyl-9-Phenyl-3,4,6,7,9,10-Hexahydroacridine-1,8(2H,5H)-Dione (4h)

As yellow crystals, (0.472 g, 94%), mp. (303–305 °C)[37] (ethanol). ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.78 (*d*, 2H, J = 17.39 Hz, –CH_2), 2.00 (*d*, 2H, J = 16.90 Hz, –CH_2), 2.16–2.23 (*m*, 4H, –CH_2), 5.05 (*s*, 1H, –CH), 7.07–7.40 (*m*, 7H, Ar–H), 7.81 (*d*, 2H, J = 8.74 Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.50, 29.71, 32.32, 32.45, 41.35, 50.03, 113.54, 123.01, 126.27, 127.97, 128.37, 133.54, 138.22, 146.57, 150.51, 195.54; IR (cm^{-1}): 3028 s (Ar–H), 2954 s (–CH), 1634 s (C═O), 1575 s (C═C); HRMS (QTOF-ESI): m/z [M+H]$^+$ calcd. For $C_{29}H_{31}BrNO_2$: 504.1538; found [M+H]$^+$: 504.1529.

2.4.9. 10-(4-bromophenyl)-3,3,6,6-Tetramethyl-9-(4-nitrophenyl)-3,4,6,7,9,10-Hexahydroacridine-1,8(2H,5H)-Dione (4i)

As yellow crystals, (0.510 g, 93%), mp. (310–312 °C) (ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH_3), 0.90 (*s*, 6H, 2x-CH_3), 1.80 (*d*, 2H, J = 17.46 Hz, –CH_2), 2.00 (*d*, 2H, J = 15.93 Hz, –CH_2), 2.20 (d, 4H, J = 15.70 Hz, 2x-CH_2), 5.10 (*s*, 1H, –CH) 7.48 (*d*, 2H, J = 8.46 Hz, Ar–H), 7.58 (*d*, 2H, J = 8.70 Hz,

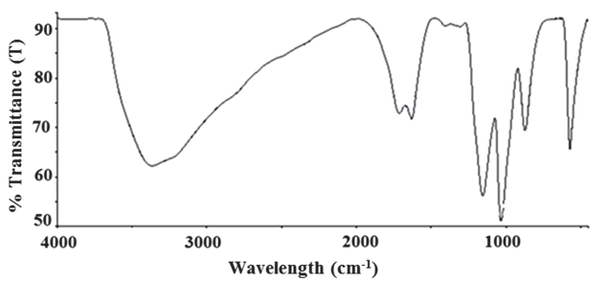


Figure 2. FT-IR of graphene oxide.

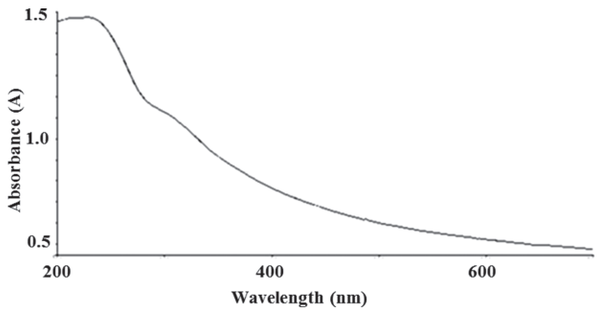


Figure 3. UV-Vis of graphene oxide.

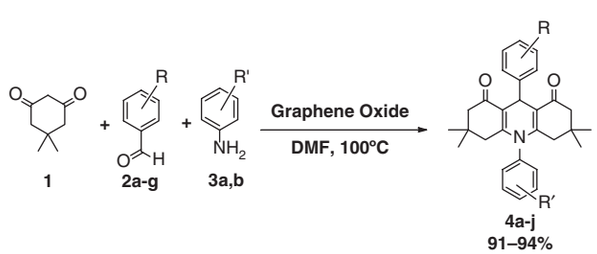
Ar–H), 7.83 (*d*, 2H, $J = 8.40$ Hz, Ar–H), 8.14 (*d*, 2H, $J = 8.61$ Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.57, 29.60, 32.47, 33.35, 41.38, 49.86, 112.50, 123.21, 123.75, 129.42, 132.46, 133.50, 137.98, 146.16, 151.25, 154.00, 195.51; IR (cm^{-1}): 3047 w (Ar–H), 2956 w (C–H), 1631 s (C═O), 1575 m (C═C); HRMS (QTOF-ESI): m/z $[M + Na]^+$ calcd. for $C_{29}H_{29}BrN_2NaO_4$: 571.1208; found $[M + Na]^+$: 571.1209.

2.4.10. 10-(4-bromophenyl)-9-(4-chlorophenyl)-3,3,6,6-Tetramethyl-3,4,6,7,9,10Hexahydroacridine-1,8(2H,5H)-Dione (4j)

As yellow crystals, (0.496 g, 93%), mp. (308–310 °C) (ethanol). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 0.70 (*s*, 6H, 2x-CH$_3$), 0.90 (*s*, 6H, 2x-CH$_3$), 1.80 (*d*, 2H, $J =$ 17.30 Hz, –CH$_2$), 2.01 (*d*, 2H, $J = 16.07$ Hz, –CH$_2$), 2.18–2.24 (*m*, 4H, –CH$_2$), 5.10 (*s*, 1H, –CH), 7.48 (*d*, 2H, $J = 8.54$ Hz, Ar–H), 7.58 (*d*, 2H, $J = 8.74$ Hz, Ar–H), 7.66 (*d*, 2H, $J = 8.50$ Hz, Ar–H), 8.14 (*d*, 2H, $J =$ 8.71 Hz, Ar–H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ (ppm): 26.56, 29.60, 32.48, 33.35, 41.38, 49.85, 112.50, 123.21, 123.75, 129.43, 133.52, 137.97, 146.16, 151.25, 154.00, 195.52; IR (cm^{-1}): 2955 s (–CH), 1632 s (C═O), 1594 s (C═C); HRMS (QTOF-ESI): m/z $[M + H]^+$ calcd. For $C_{29}H_{30}BrClNO_2$: 538.1160; found $[M + H]^+$: 538.1148.

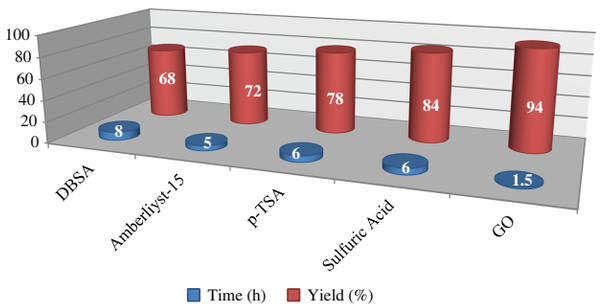
3. RESULTS AND DISCUSSION

GO was synthesized by the modified hummer's method (Fig. 1). Briefly, a mixture of sulfuric acid, sodium nitrate, and potassium permanganate is still widely used with some modifications.[38]



Scheme 1. Synthesis of 1,8-dioxoacridines in the presence of GO.

Table I. The model study for the one-pot synthesis of 1,8-dioxoacridines in the presence of various catalysts.



The prepared GO was characterized by Fourier Transform Infrared (FT–IR) and UV-Vis Spectrophotometer.

FT-IR spectra of graphene oxide (Fig. 2) indicate that a broad absorption band between 3200–3600 cm^{-1} correspond to the –OH stretching mode.[39] Furthermore, carbonyl groups at around 1632 cm^{-1} and the stretching vibration of C–O of carboxylic acid and C–OH of alcohol at around 1155–1032 cm^{-1} indicate the formation of GO.[40]

Moreover, UV-Vis spectrum of graphene oxide also indicates the formation of GO as shown in Figure 3. The peak at ~235 nm and shoulder peak at ~300 nm may be due to π–π^* transition of the atomic C–C bonds and n–π^* transitions of aromatic C–C bonds, respectively.[41]

It is worth mentioning that graphene oxide is often used as a catalyst in lots of reactions but its use as a catalyst for synthesizing 1,8-dioxoacridine derivatives from aromatic aldehydes and various amines has not been reported before. The synthesis of 1,8-dioxoacridine derivatives were carried out in a single step containing dimedone (**1**), aromatic aldehydes (**2a–g**) and various amines (**3a, b**) by using GO as a catalyst in DMF solution (Scheme 1).

Besides, the other catalysts such as sulfuric acid, Amberliyst-15, DBSA, *p*-TSA have also been tested for model reaction and compared with GO as shown Table I. To the best of our knowledge, GO as a catalyst showed

Table II. A comparison of various solvents employed in the synthesis of the 1,8-dioxoacridine derivatives.

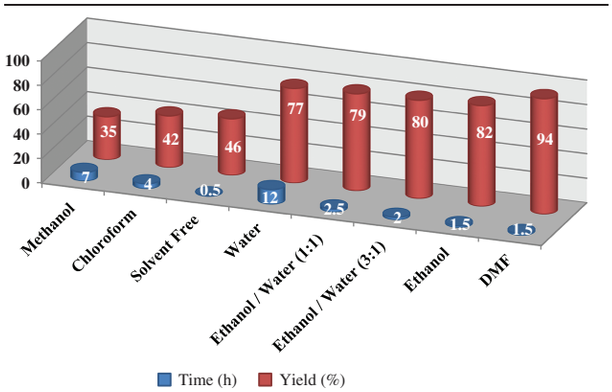
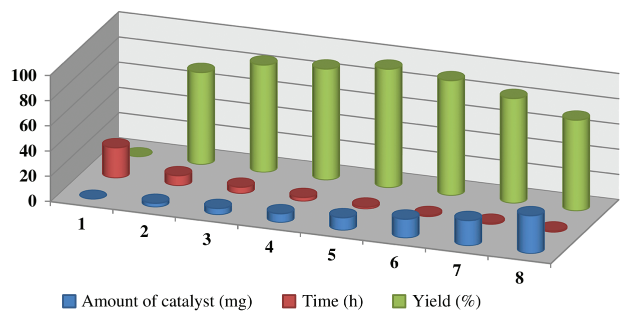


Table III. The optimization of catalyst concentration for the preparation of acridinedione derivatives using graphene oxide as catalyst in DMF.



	1	2	3	4	5	6	7	8
Amount of catalyst (mg)	0	3	5	7	10	15	20	30

Table V. Synthesis of 1,8-dioxoacridines 4a–j in the presence of 10 mg GO.[a]

Entry	R	R′	Time (min)	Yield[b] (%)	Mp. (°C) Found	Mp. (°C) Reported (ref.)
4a	–H	4-Cl	60	92	300–302	309–311 [22]
4b	4-NO_2	4-Cl	90	91	315–317	>300 [33]
4c	3-NO_2	4-Cl	120	92	285–287	285–286 [34]
4d	4-Br	4-Cl	75	93	304–305	>300 [33]
4e	4-F	4-Cl	75	91	280–282	>300 [35]
4f	4-CH_3	4-Cl	75	91	262–265	268–269 [34]
4g	4-OCH_3	4-Cl	75	91	255–257	269–270 [36]
4h	–H	4-Br	60	94	303–305	269–272 [37]
4i	4-NO_2	4-Br	75	93	310–312	–
4j	4-Cl	4-Br	120	93	308–310	–

Notes: [a]Reactions were carried out with dimedone, aromatic benzaldehyde and various amine, in 2:1:1 molar ratio. [b]Yields refer to isolated pure products.

the highest yield and lowest reaction time for the synthesis of 1,8-dioxoacridine derivatives compared to the other catalysts in the literature.

The model reaction was carried out in presence of various solvents such as methanol, chloroform, water, ethanol/water, ethanol, DMF and solvent-free media (Table II). Since the reaction proceeded with the highest yield in the presence of DMF compared to other solvents, we have chosen DMF as the solvent for our reaction.

Since the amount of catalyst is another important parameter in terms of the reaction efficiency, eight sets of model reactions have been performed to determine the optimum catalyst concentration for the best possible yield. The first set where no catalyst was used led to no formation of product but while the product yield has been increased increasing amount of catalyst increase gradually from 3 to 10 mg it has been decreased from 10 to 30 mg possibly due to the protonation of amine groups in the aromatic ring by the help of carboxylic acid groups of the graphene oxide (Table III).

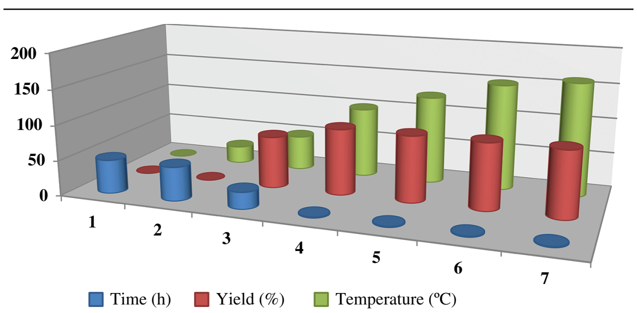
After optimization of the solvent and catalyst amount for the model reaction, we have tried to find optimum temperature and it was observed that no desired product was obtained even after 48 h of stirring at room and/or lower temperatures. The yield of desired product gradually increased with increasing temperature from room temperature to 100 °C as shown in Table IV.

As a summary, the highest efficiency on the model reaction was observed at 100 °C by using 10 mg of GO in DMF. All reactions have been performed under these optimum conditions as shown in Table V.

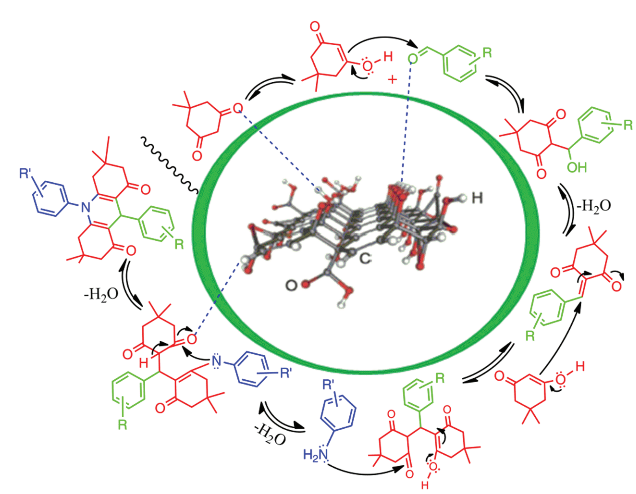
A plausible mechanism for the synthesis 1,8-dioxoacridine derivatives in the presence of graphene oxide is shown in Scheme 2. Firstly, the GO bind with oxygen of carbonyl group, hence it increases the carbonyl activity which in turn makes alpha hydrogen very acidic thereby facilitating the enolization and nucleophilic attack to the aromatic aldehydes leading to the formation of knoevenagel product. Then the knoevenagel product reacted in Michael fashion with another molecule of C–H active molecule and furnished intermediate. Then aniline derivatives induced cyclization offered the desired produced.

All the products have been characterized by FT-IR, NMR, and HRMS analyzes. The infrared (FT-IR) spectra

Table IV. The optimization of temperature for preparation of 1,8-dioxoacridine derivatives using graphene oxide as catalyst in DMF.

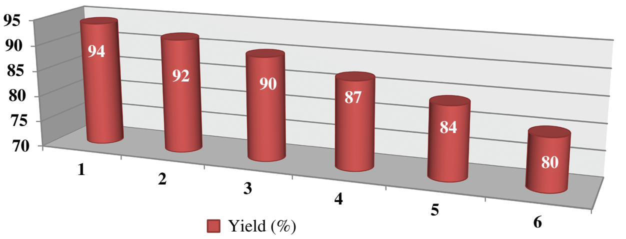


	1	2	3	4	5	6	7
Time (h)	48	48	24	1.5	1.5	1.5	1.5



Scheme 2. Recommended mechanism pathway for the graphene oxide catalyzed synthesis of 1,8-dioxoacridine derivatives.

Table VI. Recyclable performance of GO in the model reaction.



of all the 1,8-dioxoacridine (**4a-j**) indicated that aromatic C–H and the aliphatic C–H stretching bands were observed between 3061–3006 cm^{-1} and 2959–2952 cm^{-1}, respectively.[42] Besides, in the IR spectra of all **4a-j** compounds, the carbonyl groups showed sharp peaks between 1653 and 1632 cm^{-1}.

The ^{1}H-NMR spectra of the compounds **4a-j** belonging to protons of the methyl groups showed singlet peaks in position 3 and 6 approximate between 0.70–0.90 ppm.[43] The methoxy protons of compound **4g** were observed 3.70 ppm. The signals for the –CH protons were observed at 4.95–5.15 ppm and the signals for the aromatic protons were observed in the range between 6.61–8.14 ppm.

The ^{13}C-NMR (APT) spectra of all the compounds **4a-j** showed carbonyl carbon peaks between 195.52–195.63 ppm. The signals observed in ^{13}C-NMR (APT) spectrums of all the acridinedione **4a-j** molecules are determined to be in line with the recommended molecule structures.

Also, when their high resolution mass spectra (HRMS) are examined, the observed molecule ion peaks are in good agreement with the recommended structures.

After completion of the model reaction GO was separated, washed with acetone, dried and reused for six times and product was obtained in high yields (Table VI). It should be pointed out that no extra care should be taken in order to store and handle the catalyst due to air or moisture insensitivity of GO.

As a summary, GO was used, for the first time, for the synthesis of 1,8-dioxoacridine as a catalyst in literature and it is expected that GO will be highly used as a supporting materials and a catalyst for the synthesis of 1,8-dioxoacridines and also other types of reactions.[44,47]

4. CONCLUSIONS

Easy, effective and practical synthetic method has been developed for the synthesis of 1,8-dioxoacridine condensation reactions of the various amine, aromatic aldehyde compounds and dimedone in the presence of highly efficient graphene oxide as the catalyst. This reusable catalyst offers advantages like simple work-up and high yields. Furthermore, the given methodology is efficient and environmentally benign. This method, which enabled 1,8-dioxoacridine to be prepared in excellent yields and short reaction times, would be a rather attractive synthetic method in the future.

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