Res Chem Intermed (2013) 39:1323–1333
DOI 10.1007/s11164-012-0688-5

Efficient one-pot three-component synthesis of 3,4-dihydro-12-phenyl-2*H*-benzo[*b*] xanthene-1,6,11 (12*H*)-trione derivatives in ionic liquid

Baixiang Du · Gan Cai · Bo Zhao · Xiangxue Meng · Xiangshan Wang · Yuling Li

Received: 5 March 2012 / Accepted: 8 June 2012 / Published online: 29 June 2012
© Springer Science+Business Media B.V. 2012

Abstract A series of 3,4-dihydro-12-phenyl-2*H*-benzo[*b*]xanthene-1,6,11(12*H*)-trione derivatives have been synthesized in high yields in the presence of ionic liquid [bmim$^+$]Br$^-$. The reaction work-up is simple and the ionic liquid can be easily separated from the product and reused.

Keywords MCRs · Benzo[*b*]xanthene · Synthesis · Ionic liquid

Introduction

In current day research, multicomponent reactions (MCRs) have proven to be one of the most efficient tools to construct highly complex molecules and introduce molecular diversity from simple building blocks via one-pot reaction [1, 2]. This synthetic strategy has been widely used in organic, combinatorial, and medicinal chemistry.

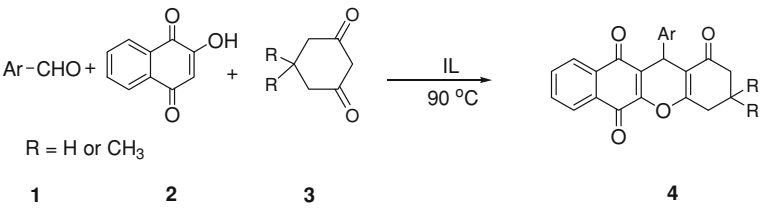
Xanthenes and benzoxanthenes are an important structural motif in biologically relevant compounds and pharmaceuticals, which possess antiviral, anti-inflammatory, anticancer, and antibacterial activities [3–6]. These are being utilized as antagonists for drug-resistant leukemia lines [7] and in photodynamic therapy [8]. In addition, these heterocyclic molecules have been widely used as dyes [9], pH-sensitive fluorescent materials for visualization of biomolecules [10]. The 1,4-naphthoquinone structure is also common in natural products associated with anti-inflammatory, antifungal, antiviral, and antitumor activities [11–14]. Therefore, the synthesis of benzoxanthenes with a 1,4-naphthoquinone structure is of great importance to organic chemists.

B. Du · G. Cai · B. Zhao · X. Meng · X. Wang · Y. Li (✉)
Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, School of Chemistry and Chemical Engineering, Jiangsu Normal University, Xuzhou 221116, China
e-mail: ylli19722@163.com

Some methods are available for the synthesis of benzoxanthenes with a 1,4-naphthoquinone structure. Chen et al. developed a rapid and efficient method to synthesize a series of benzoxanthenes with a 1,4-naphthoquinone structure by the reaction of aldehydes and 2-hydroxynaphthalene-1,4-dione in mixed solvent of acetic acid and ethylene glycol under microwave irradiation [15]. Bazgir reported similar results catalyzed by *p*-toluenesulfonic acid (*p*-TSA) [16]. Bazgir et al. synthesized dibenzo[*a*,*i*]xanthene-diones with a 1,4-naphthoquinone structure via cyclo-condensation reaction of 2-hydroxynaphthalene-1,4-dione, aromatic aldehydes, and dimedone in aqueous media in the presence of *p*-TSA [17]. Wu developed a simple and facile synthesis of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione derivatives by the one-pot condensation of 2-naphthol, aldehydes, and 2-hydroxy-1,4-naphthoquinone under solvent-free conditions in the presence of the heterogeneous catalyst silica chloride [18]. Wu prepared 12-aryl-12*H*-benzo[*i*][1,3]-dioxolo[4,5-*b*]xanthene-6,11-diones by condensing a variety of aldehydes with 3,4-methylenedioxyphenol and 2-hydroxy-1,4-naphthoquinone in the presence of a catalytic amount of $HClO_4$–SiO_2 or silica sulfuric acid under solvent-free conditions [19, 20]. However, these methods suffer from disadvantages such as the use of organic solvents, long reaction times, requirement of complicated catalysts, and harsh reaction conditions. The development of a synthetic protocol that is devoid of the above-mentioned problems and yet environmentally benign, simple, and efficient for the synthesis of benzoxanthenes with a 1,4-naphthoquinone structure is in great demand.

Ionic liquids (IL) have attracted extensive interest as benign reaction media in organic synthesis in recent years because of their unique properties of non-volatility, nonflammability, recyclability, and ability to dissolve a wide range of materials. As a result of their green credentials and potential to enhance reaction rates and selectivity, ionic liquids have found increasing applications to organic synthesis [21, 22].

In continuation of our studies in developing environmentally benign methodologies for synthesis of heterocyclic compounds, [23–25] here we report on the synthesis of a series of 3,4-dihydro-12-phenyl-2*H*-benzo[*b*]xanthene-1,6,11(12*H*)-trione derivatives by the reactions of aromatic aldehyde, 2-hydroxy-1,4-naphthoquinone, and cyclic 1,3-dicarbonyl compounds in ionic liquid [$bmim^+$][Br^-] at 90 °C (Scheme 1), and [$bmim^+$][Br^-] is used here as an efficient catalyst as well as solvent, which can be recycled and reused. To the best of our knowledge, this



Scheme 1 The synthesis of compound 4

Table 1 Optimization of the reaction conditions for synthesis of **4a**

Entry	*T*/ °C	Medium	Time/h	Yield[a]/%
1	60	Acetone	24	20
2	80	EtOH	24	35
3	100	DMF	24	36
4	70	CH_3CN	24	24
5	rt	[bmim]Br	24	0
6	70	[bmim]Br	7	65
7	90	[bmim]Br	7	80
8	110	[bmim]Br	7	80
9	90	[bmim]Br	9	86
10	90	[bmim]Br	11	85
11	90	[emim]Br	9	65
12	90	[pmim]Br	9	62
13	90	[emim]BF_4	9	60
14	90	[bmim]BF_4	9	80
15	90	[pmim]BF_4	9	66
16	90	[bmim]PF_6	9	73

Reaction condition: 5 mL of ionic liquid, 1 mmol of 4-chlorobenzaldehyde, 1 mmol of 2-hydroxy-1,4-naphthoquinone, 1 mmol of 5,5-dimethyl-1,3-cyclohexanedione

[a] Isolated yields

methodology has not been reported in the literature. The ionic liquid not only makes the synthetic process clean, and safe but also affords the products in high yield.

Results and discussion

In the initial studies, we investigated the condensation reaction of 4-chlorobenzaldehyde, 2-hydroxy-1,4-naphthoquinone, and 5,5-dimethyl-1,3-cyclohexanedione in traditional solvents (acetone, EtOH, DMF, and CH_3CN). The results are listed in Table 1. In these cases, Product **4a** was formed in low yields (Table 1, entries 1–4) even after 24 h whereas the same reaction in the presence of ionic liquid [bmim$^+$][Br$^-$] as an environmentally friendly medium provided 65 % of **4a** in only 7 h at 70 °C (Table 1, entry 6).

To further optimize the reaction conditions, we investigated the effect of temperature and reaction time on reaction rate as well as on yields of products. It showed that no product could be detected at room temperature (Table 1, entry 5) even after 24 h. The yield of product **4a** was improved and the reaction time was shortened as the temperature was increased from 70 to 110 °C. The yield plateaued when the temperature was further increased to 110 °C (Table 1, entries 6–8). So, the most suitable reaction temperature is 90 °C. The effect of reaction time on yields of product **4a** was also investigated. The reactions were performed in ionic liquid [bmim$^+$][Br$^-$] for 7, 9, or 11 h at 90 °C (Table 1, entries 7, 9, 10), leading to **4a** in 80, 86, and 85 % yield, respectively. Thus, the optimal reaction time is 9 h. Moreover, different ionic liquids were further studied as shown in Table 1 (entries 11–16). It was found that the ionic liquids with anion Br$^-$ afforded **4a** in higher yields than those with anion BF_4^- or PF_6^- (Table 1, entries 9, 14, 16). Additionally,

for ionic liquids with anion Br^-, the effect of the cation was also investigated, and the ionic liquid with cation $bmim^+$ afforded **4a** in the highest yields (Table 1, entries 9, 11, 12) among all the cations, which implied that both cation and anion in ionic liquids have effects on the reaction. On the basis of the above results, we can conclude that [bmim]Br was the best ionic liquid for this reaction. The amount of ionic liquid and ratio of reactants had no obvious effect on the reaction, and the results are provided in Table 2.

After optimizing the reaction conditions, a variety of aromatic aldehydes were employed under similar circumstances to evaluate the substrate scope of this reaction. The results are summarized in Table 3. Data from Table 3 demonstrate that aromatic aldehydes carrying both electron-withdrawing and electron-releasing substituents were converted to their corresponding benzo[*b*]xanthene-1,6,11(12*H*)-trione derivatives in good yields under the optimal conditions described above. All the products were characterized by their melting points, ^{1}H NMR, IR, and HRMS. The IR spectra of compounds **4a–q** showed intense bands in the region 1,616–1,698 cm^{-1} due to carbonyl stretching. The ^{1}H NMR spectra which were recorded in DMSO-d_6 support the proposed structure of the compounds. The CH proton (C_{12}) appeared as a single at δ 4.83–5.32 ppm in ^{1}H NMR spectral data of compounds **4a–q**. The CH_3 (C_3) protons appeared as a single at δ 0.94–1.10 ppm and CH_2 (C_2 and C_4) protons showed double at δ 2.10–2.79 ppm in ^{1}H NMR spectral data of compounds **4a–l**. The CH_2 (C_2, C_3, and C_4) protons appeared multiplet at δ 1.78–2.84 ppm in ^{1}H NMR spectral data of compounds **4m–q.**

We have not established an exact mechanism for the formation of **4**, however, a reasonable possibility is shown in Scheme 2. Firstly, Knoevenagel condensation between aromatic aldehyde **1** and cyclic 1,3-dicarbonyl compounds **3** would give intermediate **5**. Then, Michael addition of **5** to 2-hydroxy-1,4-naphthoquinone **2** would furnish intermediate **6.** By keto-enol tautomerization, **6** is in rapid equilibrium with **7**. Finally, the product **4** would be produced by an intramolecular cyclization and dehydration.

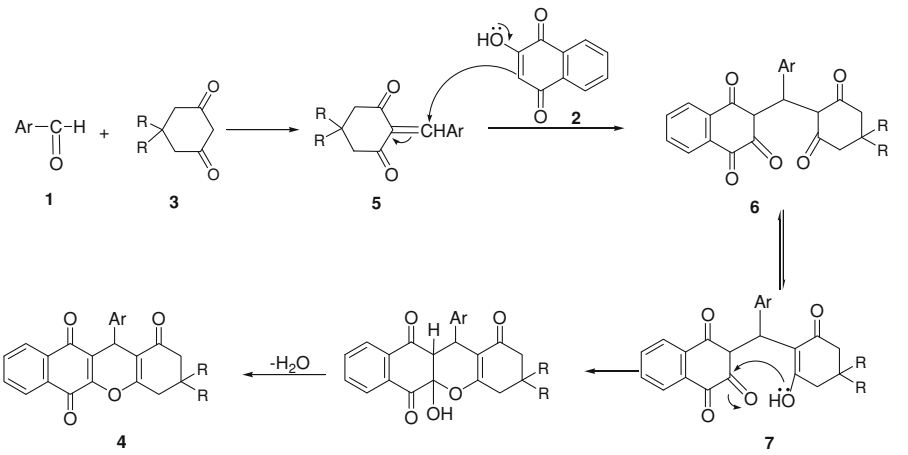
Under the reaction conditions described above, various aromatic aldehydes were reacted with 2-hydroxy-1,4-naphthoquinone and cyclic 1,3-dicarbonyl compounds smoothly in ionic liquid media to give **4** in high yields (Table 3). The work-up of the reaction involves only a filtration and simple washing step with water, then recrystallizing with DMF.

Table 2 Synthesis of **4a** in ionic liquid [bmim]Br with different conditions

Entry	Ionic liquids	Reactant ratio[a]	Volume of [bmim]Br (mL)	Yield[b] (%)
1	[bmim]Br	1/1.1/1.1	5	86
2	[bmim]Br	1.1/1/1.1	5	86
3	[bmim]Br	1.1/1.1/1	5	86
4	[bmim]Br	1/1/1	2.5	85
5	[bmim]Br	1/1/1	10	86

[a] Mol ratio of 4-chlorobenzaldehyde to 2-hydroxy-1,4-naphthoquinone and 5,5-dimethyl-1,3-cyclohexanedione at 90 °C

[b] Isolated yields



Scheme 2 Mechanism of the reaction

Table 3 Synthesis of **4** in ionic liquid [bmim^{+}][Br^{-}]

Entry	Ar	R	Product	Time/h	Yields[a]/%
1	4-ClC_6H_4	CH_3	**4a**	9	86
2	3-FC_6H_4	CH_3	**4b**	8	85
3	3-ClC_6H_4	CH_3	**4c**	9	86
4	3,4-$OCH_2OC_6H_3$	CH_3	**4d**	8	88
5	3,4-$(CH_3)_2C_6H_3$	CH_3	**4e**	9	83
6	2-BrC_6H_4	CH_3	**4f**	8	84
7	2-ClC_6H_4	CH_3	**4g**	10	85
8	4-FC_6H_4	CH_3	**4h**	9	82
9	3-OHC_6H_4	CH_3	**4i**	9	86
10	2,3-$Cl_2C_6H_3$	CH_3	**4j**	9	87
11	3-$NO_2C_6H_4$	CH_3	**4k**	8	80
12	4-$NO_2C_6H_4$	CH_3	**4l**	9	80
13	3,4-$OCH_2OC_6H_3$	H	**4m**	8	85
14	4-FC_6H_4	H	**4n**	9	86
15	3-OHC_6H_4	H	**4o**	8	88
16	4-ClC_6H_4	H	**4p**	9	89
17	2-$CH_3OC_6H_4$	H	**4q**	10	83

Reaction condition: 5 mL of ionic liquid, 1 mmol of aromatic aldehyde, 1 mmol of 2-hydroxy-1,4-naphthoquinone, 1 mmol of 5,5-dimethyl-1,3-cyclohexanedione(entries 1–12) or 1,3-cyclohexanedione(entries 13–17), 90 °C

[a] Isolated yields

Finally, the recovery and reuse of the ionic liquid [bmim^{+}][Br^{-}] were studied by using the preparation of **4a** as a model. Because of the poor solubility of the products in ionic liquids, they were easily separated by simple filtration, and the

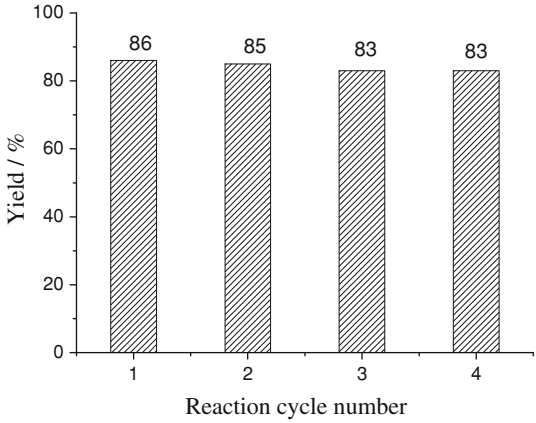


Fig. 1 Reusability of ionic liquid [bmim$^+$][Br$^-$]

filtrate could be recovered easily by drying at 80 °C in vacuum for several hours. As shown in Fig. 1, the reaction medium can be recycled at least four times without significant decrease of the yields, ranging from 86 to 83 %.

Experimental

General

Melting points were determined in open capillaries without further correction. IR spectra were recorded on a Tensor 27 spectrometer in KBr. ^{1}H NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as an internal standard using a Bruker-400 spectrometer. HRMS data were obtained using a MicroTOF-QII instrument.

General procedure for preparation of 4

A dry 50-mL flask was charged with aromatic aldehyde **1** (1 mmol), 2-hydroxy-1,4-naphthoquinone **2** (1 mmol), cyclic 1,3-dicarbonyl compounds **3** (1 mmol), and ionic liquid [bmim$^+$][Br$^-$] (5 mL). The mixture was stirred at 90 °C for 8–10 h to complete the reaction (monitored by TLC), then cooled to room temperature. The solid residue was filtered off, and the ionic liquid in filtrate was then recovered by evaporation for several hours at 90 °C in vacuum. The crude products were further purified by recrystallization from DMF and water to give **4**.

Characterization data

3,4-dihydro-3,3-dimethyl-12-(4-chlorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4a

Yellow solid; mp: 286–287 °C (lit [17]. 282–284 °C); IR (KBr): ν 2,963, 2,938, 1,681, 1,664, 1,617 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.95 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.10 (d, 1H, $J = 16.0$ Hz, CH_2), 2.32 (d, 1H, $J = 16.0$ Hz, CH_2),

2.65 (d, 1H, $J = 17.6$ Hz, CH_2), 2.70 (d, 1H, $J = 17.6$ Hz, CH_2), 5.31 (s, 1H, CH), 7.20–7.43 (m, 4H, ArH), 7.82–8.06 (m, 4H, ArH); HRMS calcd for $C_{25}H_{19}ClO_4$ $(M + Na)^+$: requires 441.0864, found: 441.0896.

3,4-dihydro-3,3-dimethyl-12-(3-fluorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4b

Brown solid; mp: 201–202 °C; IR (KBr): ν 2,954, 2,935, 1,663, 1,619 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 0.96 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 2.16 (d, 1H, $J = 16.0$ Hz, CH_2), 2.31 (d, 1H, $J = 16.0$ Hz, CH_2), 2.65 (d, 1H, $J = 17.6$ Hz, CH_2), 2.75 (d, 1H, $J = 17.6$ Hz, CH_2), 4.93 (s, 1H, CH), 6.97–7.01 (m, 1H, ArH), 7.13–7.20 (m, 2H, ArH), 7.30 (d, 1H, $J = 7.6$ Hz, ArH), 7.84–7.92 (m, 3H, ArH), 8.05–8.07 (m, 1H, ArH); HRMS calcd for $C_{25}H_{19}FO_4$ $(M + H)^+$: requires 403.1340, found: 403.1349.

3,4-dihydro-3,3-dimethyl-12-(3-chlorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4c

Brown solid; mp: 206–208 °C; IR (KBr): ν 2,959, 2,927, 1,681, 1,616, 1,619 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 0.94 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.16 (d, 1H, $J = 16.0$ Hz, CH_2), 2.31 (d, 1H, $J = 16.0$ Hz, CH_2), 2.63 (d, 1H, $J = 17.6$ Hz, CH_2), 2.73 (d, 1H, $J = 17.6$ Hz, CH_2), 4.87 (s, 1H, CH), 7.20–7.28 (m, 3H, ArH), 7.36 (s, 1H, ArH), 7.81–8.04 (m, 4H, ArH); HRMS calcd for $C_{25}H_{19}ClO_4$ $(M + H)^+$: requires 419.1045, found: 419.1069.

3,4-dihydro-3,3-dimethyl-12-(3,4-methylenedioxyphenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4d

Yellow solid; mp: 241–243 °C; IR (KBr): ν 2,959, 2,935, 1,664, 1,618 cm^{-1}; ^{1}HNMR(DMSO-d_6, 400 MHz): δ 0.97 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.19 (d, 1H, $J = 16.0$ Hz, CH_2), 2.31 (d, 1H, $J = 16.0$ Hz, CH_2), 2.63 (d, 1H, $J = 16.8$ Hz, CH_2), 2.71 (d, 1H, $J = 16.8$ Hz, CH_2), 4.83 (s, 1H, CH), 5.94 (d, 2H, $J = 7.2$ Hz. CH_2), 6.77–6.86 (m, 3H, ArH), 7.84–7.86 (m, 2H, ArH), 7.91–7.94 (m, 1H, ArH), 8.04–8.06 (m, 1H, ArH); HRMS calcd for $C_{26}H_{20}O_6(M + Na)^+$: requires 451.1152, found: 451.1159.

3,4-dihydro-3,3-dimethyl-12-(3,4-dimethylphenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4e

Yellow solid; mp: 232–233 °C; IR (KBr): ν 2,959, 1,681, 1,666, 1,618 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 0.96 (s, 3H, CH_3),1.07 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.14–2.17 (m, 4H, $CH_3 + CH_2$), 2.30 (d, 1H, $J = 16.0$ Hz, CH_2), 2.65 (d, 1H, $J = 16.8$ Hz, CH_2), 2.67 (d, 1H, $J = 16.8$ Hz, CH_2), 4.83 (s, 1H, CH), 6.99–7.08 (m, 3H, ArH), 7.83–7.92 (m, 3H, ArH), 8.04–8.06 (m, 1H, ArH); HRMS calcd for $C_{27}H_{24}O_4$ $(M + H)^+$: requires 413.1753, found: 413.1733.

3,4-dihydro-3,3-dimethyl-12-(2-bromophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4f

Pale yellow solid; mp: 275–277 °C; IR (KBr): *v* 2,958, 2,931, 1,698, 1,661 cm^{-1}; ^{1}HNMR(DMSO-d_6, 400 MHz): δ 0.99 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.12 (d, 1H, $J = 16.0$ Hz, CH_2), 2.33 (d, 1H, $J = 16.0$ Hz, CH_2), 2.74 (d, 1H, $J = 17.6$ Hz, CH_2), 2.79 (d, 1H, $J = 17.6$ Hz, CH_2), 5.07 (s, 1H, CH), 7.04–7.09 (m, 1H, ArH), 7.24–7.32(m, 2H, ArH), 7.90 (d, 1H, $J = 8.0$ Hz, ArH), 7.68–7.22 (m, 1H, ArH), 7.86–7.90 (m, 1H, ArH), 7.98–8.03 (m, 2H, ArH); HRMS calcd for $C_{25}H_{19}BrO_4$ $(M + H)^+$: requires 463.0540, found: 463.0536.

3,4-dihydro-3,3-dimethyl-12-(2-chlorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4g

Yellow solid; mp: 276–277 °C; IR (KBr): *v* 2,989, 2,943, 1,698, 1,660 cm^{-1};^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.99 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.13 (d, 1H, $J = 16.4$ Hz, CH_2), 2.33 (d, 1H, $J = 16.4$ Hz, CH_2), 2.73 (d, 1H, $J = 16.8$ Hz, CH_2), 2.75 (d, 1H, $J = 16.8$ Hz, CH_2), 5.07 (s, 1H, CH), 7.13–7.18 (m, 1H, ArH), 7.20–7.24 (m, 1H, ArH), 7.29–7.36 (m, 2H, ArH), 7.68–7.72 (m, 1H, ArH), 7.86–7.90(m, 1H, ArH), 7.97–8.03 (m, 2H, ArH); HRMS calcd for $C_{25}H_{19}ClO_4$ $(M + H)^+$: requires 419.1045, found: 419.1023.

3,4-dihydro-3,3-dimethyl-12-(4-fluorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4h

Yellow solid; mp: 227–229 °C; IR (KBr): *v* 2,956, 1,682, 1,662, 1,618 cm^{-1}; ^{1}HNMR (DMSO-d_6, 400 MHz): δ 0.95 (s, 3H, CH_3), 1.07(s, 3H, CH_3), 2.17 (d, 1H, $J = 16.4$ Hz, CH_2), 2.31 (d, 1H, $J = 16.4$ Hz, CH_2), 2.65 (d, 1H, $J = 18.0$ Hz, CH_2), 2.71 (d, 1H, $J = 18.0$ Hz, CH_2), 4.91(s, 1H, CH), 7.85–7.92 (m, 3H, ArH); 7.07 (t, 2H, $J = 8.8$ Hz, ArH), 7.35–7.81 (m, 2H, ArH), 8.04–8.06 (m, 1H, ArH); HRMS calcd for $C_{25}H_{19}FO_4$ $(M + Na)^+$: requires 425.1165, found: 425.1188.

3,4-dihydro-3,3-dimethyl-12-(3-hydroxyphenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4i

Yellow solid; mp: 200–202 °C; IR (KBr): *v* 2,955, 2,936, 1,661, 1,616 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.98 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 2.18 (d, 1H, $J = 16.4$ Hz, CH_2), 2.32 (d, 1H, $J = 16.4$ Hz, CH_2), 2.66 (d, 1H, $J = 17.6$ Hz, CH_2), 2.71 (d, 1H, $J = 18.0$ Hz, CH_2), 4.83 (s, 1H, CH), 6.52–6.54 (m, 1H, ArH), 6.71 (d, 1H, $J = 7.6$ Hz, ArH), 6.75 (s, 1H, ArH), 7.02 (t, 1H, $J = 8.0$ Hz, ArH), 7.84–7.94 (m, 3H, ArH), 8.04–8.07 (m, 1H, ArH), 9.32 (s, 1H, OH); HRMS calcd for $C_{25}H_{20}O_5$ $(M + H)^+$: requires 401.1389, found: 401.1387.

3,4-dihydro-3,3-dimethyl-12-(2,3-dichlorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4j

Yellow solid; mp: 224–226 °C; IR (KBr): ν 2,956, 1,668, 1,620 cm^{-1}; ^{1}HNMR (DMSO-d_6, 400 MHz): δ 0.94 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 2.12 (d, 1H, $J = 16.0$ Hz, CH_2), 2.31 (d, 1H, $J = 16.0$ Hz, CH_2), 2.65 (d, 1H, $J = 17.6$ Hz, CH_2), 2.71 (d, 1H, $J = 17.6$ Hz, CH_2), 5.32 (s, 1H, CH), 7.23 (t, 1H, $J = 8.0$ Hz, ArH); 7.32 (dd, 1H, $J_1 = 8.0$ Hz, $J_2 = 1.6$ Hz, ArH), 7.43 (dd, 1H, $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz, ArH), 7.83–7.91 (m, 3H, ArH), 8.05 (d, 1H, $J = 8.8$ Hz, ArH); HRMS calcd for $C_{25}H_{18}O_4Cl_2$ $(M + H)^+$: requires 453.0655, found: 453.0659.

3,4-dihydro-3,3-dimethyl-12-(3-nitrophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4k

Brown solid; mp: 194–196 °C; IR (KBr): ν 2,958, 2,923, 1,668, 1,620 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.96 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 2.25 (d, 1H, $J = 16.0$ Hz, CH_2), 2.34 (d, 1H, $J = 16.0$ Hz, CH_2), 2.70 (d, 1H, $J = 17.6$ Hz, CH_2), 2.75 (d, 1H, $J = 18.0$ Hz, CH_2), 5.04 (s, 1H, CH), 7.55–7.59 (m, 1H, ArH), 7.83–7.85(m, 3H, ArH), 8.03–8.07 (m, 3H, ArH), 8.14–8.18 (m, 1H, ArH); HRMS calcd for $C_{25}H_{19}O_6N(M + Na)^+$: requires 452.1105, found: 452.1111.

3,4-dihydro-3,3-dimethyl-12-(4-nitrophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4l

Yellow solid; mp: 234–236 °C; IR (KBr): ν 2,961, 2,870, 1,661, 1,617 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 0.95 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 2.17 (d, 1H, $J = 16.0$ Hz, CH_2), 2.33 (d, 1H, $J = 16.0$ Hz, CH_2), 2.71 (t, 2H, $J = 18.4$ Hz, CH_2), 5.03 (s, 1H, CH), 7.66 (d, 2H, $J = 8.4$ Hz, ArH), 7.85–7.89 (m, 3H, ArH), 8.06–8.13 (m, 3H, ArH); HRMS calcd for $C_{25}H_{19}O_6N(M + H)^+$: requires 430.1285, found:430.1258.

3,4-dihydro-12-(3,4-methylenedioxyphenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4m

Yellow solid; mp: 206-208 °C; IR (KBr): ν 2,951, 2,885, 1,656, 1,616 cm^{-1};^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.92–2.00 (m, 2H, CH_2), 2.33–2.37(m, 2H, CH_2), 2.73–2.81 (m, 2H, CH_2), 4.85 (s, 1H, CH), 5.94 (s, 2H, CH_2), 6.77–6.87 (m, 3H, ArH), 7.86–7.93 (m, 3H, ArH), 8.04–8.06 (m, 1H, ArH); HRMS calcd for $C_{24}H_{16}O_6$ $(M + H)^+$: requires 423.0839, found: 423.0823.

3,4-dihydro-12-(4-fluorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4n

Brown solid; mp: 242-244 °C; IR(KBr): ν 2,920, 2,850, 1,667, 1,618 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.91–2.01 (m, 2H, CH_2), 2.29–2.37 (m, 2H, CH_2), 2.73–2.81 (m, 2H, CH_2), 4.92 (s, 1H, CH), 7.06 (d, 2H, $J = 8.8$ Hz, ArH), 7.36 (dd, 2H, $J_1 = 5.6$ Hz, $J_2 = 2.8$ Hz, ArH), 7.83–7.91

(m, 3H, ArH), 8.03–8.05 (m, 1H, ArH); HRMS calcd for $C_{23}H_{15}FO_4$ $(M + Na)^+$: requires 397.0847, found:397.0830.

3,4-dihydro-12-(3-hydroxyphenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4o

Brown solid; mp: 262-264 °C; IR (KBr): *v* 3,211, 2,933, 1,669, 1,610, 1,619 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 1.89–2.05 (m, 2H, CH_2), 2.31–2.36(m, 2H, CH_2), 2.69–2.84 (m, 2H, CH_2), 4.83 (s, 1H, CH), 6.51–6.54 (m, 1H, ArH), 6.69–6.73 (m, 2H, ArH), 7.02 (t, 1H, $J = 8.0$ Hz, ArH), 7.82–7.85 (m, 2H, ArH), 7.90–7.92 (m, 1H, ArH), 8.02–8.04 (m, 1H, ArH), 9.38 (s, 1H, OH); HRMS calcd for $C_{23}H_{16}O_4$ $(M + Na)^+$: requires 395.0895, found: 395.0897.

3,4-dihydro-12-(4-chlorophenyl)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4p

Brown solid; mp: 210–212 °C; IR (KBr): *v* 2,939, 1,668, 1,621, 1,591, 1,488, 1,355, 1,198, 992, 932, 720 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 1.86–1.93 (m, 1H, CH_2), 1.97–2.03 (m, 1H, CH_2), 2.28–2.36 (m, 2H, CH_2), 2.67–2.74 (m, 1H, CH_2), 2.77–2.82 (m, 1H, CH_2), 4.87 (s, 1H, CH), 7.28 (d, 2H, $J = 8.4$ Hz, ArH), 7.34 (d, 2H, $J = 8.4$ Hz, ArH), 7.81–7.83 (m, 2H, ArH), 7.86–7.89 (m, 1H, ArH), 8.01–8.03 (m, 1H, ArH); HRMS calcd for $C_{23}H_{15}O_4Cl(M + Na)^+$: requires 413.0557, found: 413.0554.

3,4-dihydro-12-(2-methoxypheny)-2H-benzo[b]xanthene-1,6,11(12H)-trione 4q

Yellow solid; mp: 246-248 °C; IR (KBr): *v* 2,951, 2,833, 1,666, 1,619 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 1.78–1.88 (m, 1H, CH_2), 1.96–2.00 (m, 1H, CH_2), 2.25–2.32 (m, 2H, CH_2), 2.69–2.75 (m, 2H, CH_2), 3.69 (s, 3H, OCH_3), 5.00 (s, 1H, CH), 6.84–6.90 (m, 2H, ArH), 7.11–7.16 (m, 1H, ArH), 7.32 (dd, 1H, $J_1 = 7.6$ Hz, $J_2 = 2.0$ Hz, ArH), 7.81–7.85 (m, 3H, ArH), 7.86–7.88 (m, 1H, ArH); HRMS calcd for $C_{24}H_{18}O_5$ $(M + Na)^+$: requires 409.1052, found: 409.1054.

Conclusion

In conclusion, an efficient, environmentally benign, atom-economical, and simple methodology for the preparation of 3,4-dihydro-12-phenyl-2*H*-benzo[*b*]xanthene-1,6,11(12*H*)-trione derivatives in a three-component reaction in ionic liquid is reported. Prominent among the advantages of this method are operational simplicity, mild reaction conditions, higher yields (80–89 %), and environmental friendliness. Meanwhile, ionic liquid [$bmim^+$][Br^-] could be reused for several rounds without apparent loss of activity.

Acknowledgments We are grateful to the National Natural Science Foundation of China (No. 21104064, 21172188), Natural Science Foundation of XuZhou Normal University (10XLR03) and Priority Academic Program Development of Jiangsu Higher Education Institutions for financial support.

References

1. A. Domling, Chem. Rev. **106**, 17 (2006)
2. C.C.A. Cariou, G.J. Clarkson, M. Shipman, J. Org. Chem. **73**, 9762 (2008)
3. A.A. Carr, J.F. Grunwell, A.D. Sill, D.R. Meyer, F.W. Sweet, B.J. Scheve, J.M. Grisar, R.W. Fleming, G.D. Mayer, J. Med. Chem. **19**, 1142 (1976)
4. H.N. Hafez, M.I. Hegaba, I.S. Ahmed-Faragb, A.B.A. El-Gazzar, Bioorg. Med. Chem. Lett. **18**, 4538 (2008)
5. R. Giri, J.R. Goodell, C. Xing, A. Benoit, H. Kaur, H. Hiasa, D.M. Ferguson, Bioorg. Med. Chem. **18**, 1456 (2008)
6. S. Limsuwan, E.N. Trip, T.R.H.M. Kouwen, S. Piersma, A. Hiranrat, W. Mahabusarakam, S.P. Voravuthikunchai, J.M. van Dijl, O. Kayser, Phytomedicine **16**, 645 (2009)
7. H.T. Nguyen, M.C. Lallemand, S. Boutefnouchet, S. Michel, F. Tillequin, J. Nat. Prod. **72**, 527 (2009)
8. R.M. Ion, A. Planner, K. Wiktorowicz, D. Frackowiak, Acta Biochim. Pol. **45**, 833 (1998)
9. H.R. Shaterian, M. Ghashang, A. Hassankhani, Dyes Pigm. **76**, 564 (2008)
10. J.X. Liu, Z.J. Diwu, W.Y. Leung, Bioorg. Med. Chem. Lett. **11**, 2903 (2001)
11. C.H. Tseng, C.S. Lin, P.K. Shih, L.T. Tsao, J.P. Wang, C.M. Cheng, C.C. Tzeng, Y.L. Chen, Bioorg. Med. Chem. **17**, 6773 (2009)
12. H. Eilenberg, S. Pnini-Cohen, Y. Rahamim, E. Sionov, E. Segal, S. Carmeli, A. Zilberstein, J. Exp. Bot. **61**, 911 (2009)
13. E. Pérez-Sacau, A. Estévez-Braun, A.G. Ravelo, E.A. Ferro, H. Tokuda, T. Mukainaka, H. Nishino, Bioorg. Med. Chem. **11**, 483 (2003)
14. Y.M. Kanaan, J.R. Das, P. Bakare, N.M. Enwerem, S. Berhe, D. Beyene, V. Williams, Y.F. Zhou, R.L. Copeland, Anticancer Res. **29**, 191 (2009)
15. Y. Chen, S.S. Wu, S.J. Tu, C.M. Li, F. Shi, J. Heterocycl. Chem. **45**, 931 (2008)
16. A. Bazgir, Z.N. Tisseh, P. Mirzaei, Tetrahedron Lett. **49**, 5165 (2008)
17. M. Dabiri, Z.N. Tisseh, A. Bazgir, J. Heterocycl. Chem. **47**, 1062 (2010)
18. L.Q. Wu, J.L. Zhang, L.Z. Fang, C.G. Yang, F.L. Yan, Dyes Pigm. **86**, 93 (2010)
19. L.Q. Wu, Y.F. Wu, F.L. Yan, L.Z. Fang, Monatsh. Chem. **141**, 871 (2010)
20. L.Q. Wu, S.J. Chao, F.L. Yan, J. Heterocycl. Chem. **48**, 83 (2011)
21. K. Bica, P. Gaertner, Eur. J. Org. Chem. **19**, 3235 (2008)
22. H. Livier-Bourbigou, L. Magna, D. Morvan, Appl. Catal. A-Gen. **373**, 1 (2010)
23. Y.L. Li, B.X. Du, S.X. Wang, D.Q. Shi, S.J. Tu, J. Heterocycl. Chem. **43**, 685 (2006)
24. Y.L. Li, X.P. Xu, D.Q. Shi, S.J. Ji, Chin. J. Chem. **27**, 1510 (2009)
25. Y.L. Li, B.X. Du, X.P. Xu, D.Q. Shi, S.J. Ji, Chin. J. Chem. **27**, 1563 (2009)