Med Chem Res
DOI 10.1007/s00044-014-1124-8

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

# Synthesis, DNA-binding study, and antioxidant activity of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives

**Andivelu Ilangovan · Karnambaram Anandhan · Kaushik Mahabir Prasad · Pakkiri Vijayakumar · Rajalingam Renganathan · Devanesan Arul Ananth · Thilagar Sivasudha**

Received: 6 April 2014 / Accepted: 19 June 2014


**Abstract** A simple and efficient one-pot method for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives using $Ni(ClO_4)_2{\cdot}6H_2O$ as a catalyst is described. DNA-binding properties of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives **1a**, **1j**, **1l**, **1m**, and **1n** were investigated using calf thymus DNA by electronic absorption spectroscopy and fluorescence spectroscopy. Binding constant ($K_b$) with DNA was calculated from the absorption measurements. The spectral changes observed such as hypochromicity, red shift, and isosbestic point are consistent with the intercalation mode of binding of the chromophore into the stack DNA base pairs. Among the five, compound **1n** with strong electron donating substituents on the phenyl ring shows better intercalative binding with DNA. Investigations of antioxidant properties show that the dibenzo[*a*,*j*]xanthene **1m** with –OH group substitution has high radical scavenging properties against DPPH and $ABTS^+$.

**Keywords** Dibenzo[*a*,*j*]xanthene · $Ni(ClO_4)_2{\cdot}6H_2O$ · Multicomponent reaction · DNA binding · Antioxidant

**Electronic supplementary material** The online version of this article (doi:10.1007/s00044-014-1124-8) contains supplementary material, which is available to authorized users.

A. Ilangovan (✉) · K. Anandhan · P. Vijayakumar · R. Renganathan
School of Chemistry, Bharathidasan University, Tiruchirappalli 620024, India
e-mail: ilangovana@yahoo.co.uk; ilangovanbdu@yahoo.com

K. M. Prasad
Defence R&D Establishment, Jhansi Road, Gwalior 474002, Madhya Pradesh, India

D. A. Ananth · T. Sivasudha
Department of Environmental Biotechnology, Bharathidasan University, Tiruchirappalli 620024, India

## Introduction

Xanthenes (**1**) and its derivatives such as benzo[*k*,*l*]xanthenes (**2**), dibenzo[*a*,*k*,*l*]xanthenes (**3**), and dibenzo[*a*,*j*]xanthenes (**4**) are structurally related heterocyles, in which at least two benzene rings are directly fused to pyran ring. As result of conjugation and nearly planar structural characteristics, these compounds find large number of application as photosensitive materials (Callan *et al*., 2005) and biologically active compounds (Lambert *et al*., 1997). Xanthene dyes can be used as stable laser dyes (Ahmad *et al*., 2002), fluorescent sensor (Muñiz *et al*., 2008), CCR1 receptor antagonists (Naya *et al*., 2003), protein labeling fluorophores (Chen *et al*., 2012), and DNA-binding cellular probes (Carreon *et al*., 2005; Li *et al*., 2007). Antitumour active benzo[*k*,*l*]xanthene lignans (**3**) were found to act as peroxyl radical ($ROO^{\cdot}$) scavengers (Spatafora *et al*., 2013) and bind with DNA via intercalation and minor groove binding (Micco *et al*., 2011). Dihydrodibenzo[*a*,*k*,*l*]xanthenes (**2**) were found to be anti-cancer agents, hydroxyl radical ($OH^-$) scavengers, and interact with calf thymus-deoxyribonucleic acid (CT-DNA) by intercalation. Similarly, dibenzox[*a*,*j*]xanthenes show molecular recognition (Bhattacharya *et al*., 2009) properties and cytotoxic activity (Wang *et al*., 2012; Song *et al*., 2013) (Fig. 1).

Electronic absorption spectroscopy is an important method to examine the binding mode of xanthenes derivatives with DNA (Bhattacharya *et al*., 2009; Ghodratbeigi *et al*., 2011). A comparative study on acridine, xanthone, and xanthenes revealed that the ability of these compounds to intercalate with DNA is related to their structure. While acridine and xanthone adopt flat, highly conjugated ring structures, and bind with DNA, the xanthenes buckle about the pyran ring and loose DNA-binding properties. Thus, the structural characteristic of xanthenes and its derivatives

Published online: 15 July 2014

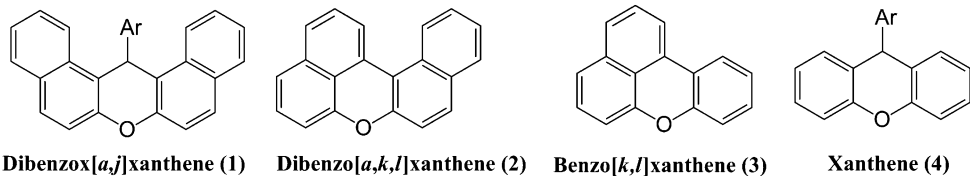



**Fig. 1** Different types of xanthene derivatives

**Dibenzox[*a*,*j*]xanthene (1)** **Dibenzo[*a*,*k*,*l*]xanthene (2)** **Benzo[*k*,*l*]xanthene (3)** **Xanthene (4)**

mainly contribute to the DNA-binding properties (Giri *et al*., 2010). Dibenzox[*a*,*j*]xanthenes (**1**), due to the presence of butterfly like planar naphthalene rings on both the sides of pyran ring, are potential candidates to show DNA-binding properties. However, such activity has not yet been examined. This prompted us to examine DNA interaction and antioxidant properties of dibenzox[*a*,*j*]xanthenes **1a**, **1j**, **1l**, **1m**, and **1n**, using UV and fluorescent spectroscopic techniques.

Dibenzox[*a*,*j*]xanthenes (**4**) are usually prepared by domino reaction between two molecules of 2-naphthol and an aldehyde in the presence of a suitable catalyst such as Dowex-50W (Shakibaei *et al*., 2007), Montmorillonite K10 (Dabiri *et al*., 2008), polytungstozincate acid (Amini *et al*., 2009), $Mg(HSO_4)_2$ (Shaterian *et al*., 2010), $SiO_2$–Cl (Wu *et al*., 2010), zirconyl triflates (Baltork *et al*., 2011), saccharin sulfonic acid (Zare *et al*., 2012), tetramethylguanidinium triflouroacetate and TFA (Rahmati, 2010), *N*,*N*′-dibromo-*N*,*N*′-1,2-ethane-diylbis(*p*-toluenesulfonamide) (Vaghei and Malaekehpoor, 2010), ceric ammonium nitrate (Kumar *et al*., 2010), succinimide-*N*-sulfonic acid (Shirini and Khaligh, 2012), 1,3,5-trichloro-2,4,6-triazinetrion (Maleki *et al*., 2011), and $Mg(BF_4)_2$ doped in [BMIm][$BF_4$] (Moghadam and Azimi, 2012). However, these methods are associated with drawbacks such as poor yield, prolonged reaction time, toxic organic solvents, use of excess reagents and catalysts, and harsh reaction conditions. Thus, there is a need to develop better method.

$Ni(ClO_4)_2{\cdot}6H_2O$ is a moderate, but soft Lewis acid finds application as catalyst in several asymmetric organic transformations (Yanagita *et al*., 2006; Sibi *et al*., 2004). The explosive character of perchlorates is largely limited to ammonium perchlorate, and majority of the metal perchlorates can be used as powerful catalysts similar to that of other metal catalysts (Dalpozzo, 2010). Thus, in continuation of our interest on development of efficient method for the construction of xanthenes derivatives (Ilangovan *et al*., 2011, 2012), synthesis of dibenzo[*a*,*j*]xanthenes was carried out using $Ni(ClO_4)_2{\cdot}6H_2O$ as a catalyst, and its DNA-binding properties were studied using UV and fluorescent spectroscopic techniques. Besides antioxidant activity of dibenzo[*a*,*j*]xanthenes was evaluated using 1,1-diphenyl-2-picryl hydrazyl (DPPH) and 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) ($ABTS^+$) radical scavengers. Herein, we present our results.

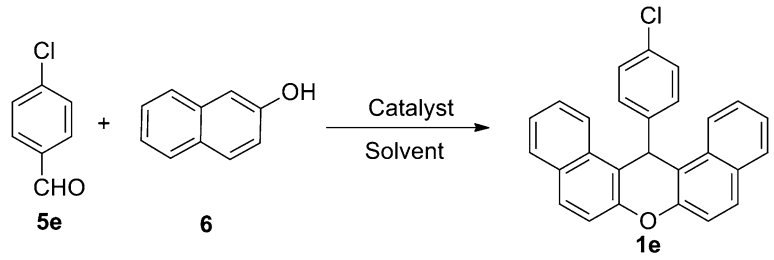
## Results and discussion

The present study began with the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes needed to study DNA-binding properties. As shown in Table 1, reaction between 4-chloro benzaldehyde **5e** (1 mmol) and 2-naphthol **6** (2 mmol) was taken as a model reaction for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes and studied in the absence and presence of different metal perchlorates in different solvents and temperature conditions.

When the reaction was carried out without a catalyst and solvent, at 100 °C, the expected product **1e** was obtained only in 58 % yield after 3 h, and the reaction was not completed. When 10 mol% of different metal perchlorates such as $Mg(ClO_4)_2{\cdot}6H_2O$, $Fe(ClO_4)_3{\cdot}6H_2O$, $Co(ClO_4)_2{\cdot}6H_2O$, $Cu(ClO_4)_2{\cdot}6H_2O$, and $Ni(ClO_4)_2{\cdot}6H_2O$ were used as catalyst, in refluxing dichloroethane (DCE), the product **1e** was obtained in 0, 65, 67, 63, and 95 %, respectively. Among all the perchlorates examined, $Ni(ClO_4)_2{\cdot}6H_2O$ acted as a effective catalyst to provide compound **1e** in short time (4.5 h), high yield (95 %), thus identified as suitable candidate catalyst for further study. When low boiling solvents such as $CHCl_3$ (entry 8) or MeOH (entry 9) were used, product **1e** was obtained in 50 % (24 h) and 71 % (7 h) yield, respectively. Increasing the quantity of $Ni(ClO_4)_2{\cdot}6H_2O$ to 20 mol% (entry 7) had no significant change in the yield of compound **1e** or reaction time. Thus, the optimized reaction condition for further study was identified as 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$ in DCE at reflux temperature.

To examine the applicability of the optimized reaction condition for the synthesis of different dibenzo[*a*,*j*]xanthenes derivatives, reaction between 2-naphthol (**6**) and different aromatic aldehydes (**5a**–**p**) was examined. A smooth one-pot conversion took place to produce a series of corresponding dibenzo[*a*,*j*]xanthenes (**1a**–**p**) in very high yield, and the results are summarized in the Table 2. The aldehydes 4-$OCH_3C_6H_4CHO$ (**5j**, entry 10), 4-$OHC_6H_4$-CHO (**5l**, entry 12), 3-$OCH_3$,4-OH $C_6H_3CHO$ (**5m**, entry 13), 3,4-$(OCH_3)_2C_6H_3CHO$ (**5n**, entry 14), 3,4,5-$(OCH_3)_3$ $C_6H_2CHO$ (**5o**, entry 15), and 4-*N*,*N*′$CH_3C_6H_4CHO$ (**5p**, entry 16) with strong electron donating substituent took long time (8–15 h) for the reaction to complete. Presence of electron donating –OMe group at mesomerically less favoured meta position in 3-$OCH_3C_6H_3CHO$ (**5k**, entry 11) had only little influence in retarding the reaction, and the

**Table 1** Optimizing the reaction conditions




| No. | Catalyst | Catalyst quantity (mol%) | Solvent | Temperature (°C) | Time (h) | Yield[a] (%) |
|---|---|---|---|---|---|---|
| 1 | No catalyst | Nil | Nil | 100 | 3.0 | 58[b] |
| 2 | $Mg(ClO_4)_2{\cdot}6H_2O$ | 10 | DCE | reflux | 24.0 | NR |
| 3 | $Fe(ClO_4)_3{\cdot}6H_2O$ | 10 | DCE | reflux | 5.0 | 65 |
| 4 | $Co(ClO_4)_2{\cdot}6H_2O$ | 10 | DCE | reflux | 5.0 | 67 |
| 5 | $Cu(ClO_4)_2{\cdot}6H_2O$ | 10 | DCE | reflux | 7.0 | 63 |
| 6 | $Ni(ClO_4)_2{\cdot}6H_2O$ | 10 | DCE | reflux | 4.5 | 95 |
| 7 | $Ni(ClO_4)_2{\cdot}6H_2O$ | 20 | DCE | reflux | 4.5 | 94 |
| 8 | $Ni(ClO_4)_2{\cdot}6H_2O$ | 10 | $CHCl_3$ | 65 | 7.0 | 71 |
| 9 | $Ni(ClO_4)_2{\cdot}6H_2O$ | 10 | MeOH | 65 | 24 | 50 |

[a] Isolated yield

[b] Reaction was not completed

reaction took place in short time (4 h) to give the product **1k** in high yield. In general, aromatic aldehydes with electron withdrawing substituent(s) underwent faster reaction compared to electron donating substituent(s). Sterically hindered *ortho* substituents (**5d**, entry 4) led to slow reaction. Formation products **1a**–**p** were confirmed by comparison of melting point, $^1$H-NMR, and $^{13}$C-NMR values with the data already known in the literature.

## DNA-binding studies

Subtle changes in the structure of the 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes are likely to influence the extend of binding to DNA. In order to have comparison of the substituent effect, substrates **1a**, **1j**, **1l**, **1m,** and **1n** with and without –OH group and –OMe substituent were selected.

## Ground state interactions

The ground state interaction of CT-DNA with 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes **1a**, **1j**, **1l**, **1m,** and **1n** was probed through UV–Vis absorption measurements.

In the UV–Vis absorption spectrum of compound **1a,** two characteristic maxima were observed at 217 and 241 nm (Fig. 2). Absorption spectrum of all other compounds **1j**, **1l**, **1m**, and **1n** is provided in supporting information. Increasing the concentration of CT-DNA led to bathochromic and hypochromic shift. This observation shows that the interaction of dibenzo[*a*,*j*]xanthenes **1a** with CT-DNA resulted in a strong decrease of the absorption intensity at both peaks, accompanied by a shift toward higher wavelengths. The isosbestic point of compound **1a** was observed at 284 nm. Hypochromism (**1a**, 36.53 %) was suggested to be due to strong interactions between the electronic states of the intercalating chromophore of the dibenzo[*a*,*j*]xanthenes and that of the DNA base pairs (Liu *et al*., 2009; Kamatchi *et al*., 2012). The spectral changes observed are consistent with the intercalation mode of the compound **1a** into the stack DNA base pairs. Similarly, all the other dibenzo[*a*,*j*]xanthenes **1j**, **1l**, **1m,** and **1n** exhibited a regular decrease in intensity of the absorption band.

Binding constant ($K_b$) for binding of the dibenzo[*a*,*j*] xanthene molecules with DNA is determined using Eq. (1), where [DNA] is the concentration of DNA in base pairs, $\varepsilon_a$ is the apparent extinction coefficient obtained by calculating $A_{obs}$/[complex], $\varepsilon_f$ corresponds to the extinction coefficient of the complex in its free form, and $\varepsilon_b$ refers to the extinction coefficient of the complex in the bound form (Fig. 3).

$$[\mathrm{DNA}]/(\varepsilon_a - \varepsilon_f) = [\mathrm{DNA}]/(\varepsilon_b - \varepsilon_f) + 1/K_b(\varepsilon_b - \varepsilon_f) \quad (1)$$

A plot of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA] gave a straight line with a slope of 1/($\varepsilon_b - \varepsilon_f$) and a *y*-intercept of 1/$K_b$ ($\varepsilon_b - \varepsilon_f$), and $K_b$ was determined from the ratio of the slope to intercept. The binding constant determined from the straight line is given in Table 3. The observed binding affinity decreases in the order **1n** > **1m** > **1l** > **1j** > **1a**.

**Table 2** $Ni(ClO_4)_2{\cdot}6H_2O$ catalyzed synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes (**1**)


| Entry | Ar | Product | Time (h) | Yield[a] (%) | Mp (°C)/1 | |
|---|---|---|---|---|---|---|
| | | | | | Found | Reported |
| 01 | $C_6H_5$ (**5a**) | **1a** | 5.0 | 85.0 | 180–182 | 182–183[b] |
| 02 | 4-$NO_2C_6H_4$ (**5b**) | **1b** | 5.0 | 95.0 | 310–312 | 310–312[b] |
| 03 | 3-$NO_2C_6H_4$ (**5c**) | **1c** | 3.0 | 90.0 | 209–211 | 215–216[b] |
| 04 | 2-$NO_2C_6H_4$ (**5d**) | **1d** | 5.0 | 97.0 | 214–215 | 214–215[b] |
| 05 | 4-$ClC_6H_4$ (**5e**) | **1e** | 4.5 | 95.0 | 289–291 | 289–291[c] |
| 06 | 2-$ClC_6H_4$ (**5f**) | **1f** | 5.0 | 90.0 | 214–216 | 215–217[b] |
| 07 | 3-$BrC_6H_4$ (**5g**) | **1g** | 4.5 | 97.0 | 194–196 | 194–195[c] |
| 08 | 4-$FC_6H_4$ (**5h**) | **1h** | 4.0 | 88.0 | 237–239 | 229–230[b] |
| 09 | 4-$CH_3C_6H_4$ (**5i**) | **1i** | 5.0 | 91.0 | 233–234 | 234–236[b] |
| 10 | 4-$OCH_3C_6H_4$ (**5j**) | **1j** | 8.0 | 97.0 | 204–206 | 203–205[c] |
| 11 | 3-$OCH_3C_6H_4$ (**5k**) | **1k** | 4.0 | 91.0 | 187–190 | 186–187[d] |
| 12 | 4-$OHC_6H_4$ (**5l**) | **1l** | 8.0 | 90.0 | 139–140 | 135–136[c] |
| 13 | 3-$OCH_3$,4-OH $C_6H_3$ (**5m**) | **1m** | 8.0 | 50.0 | 208–211 | 205–206[d] |
| 14 | 3,4-$(OCH_3)_2C_6H_3$ (**5n**) | **1n** | 8.0 | 70.0 | 189–192 | 194–195[d] |
| 15 | 3,4,5-$(OCH_3)_3C_6H_2$ (**5o**) | **1o** | 8.0 | 93.0 | 208–210 | – |
| 16 | 4-*N*,*N*′$CH_3C_6H_4$ (**5p**) | **1p** | 15.0 | 84.0 | 184–186 | – |

[a] Isolated yield

[b] Liua *et al*. (2009)

[c] Rostamizadeh *et al*. (2009)

[d] Bhattacharya *et al*. (2009)

The observed result suggests that addition of methoxy substitutents increases the binding constant. For instance, **1n** having two methoxy substituents possess higher binding constant than **1m** with one methoxy substituent. Further, the hydroxy-substituted dibenzo[*a*,*j*]xanthene **1l** was found to show lower binding constant, hence lower binding affinity than the corresponding methoxy substituted compound **1j**. The unsubstituted **1a** possess still lower binding constant. The observed results reveal that the nature of the substituents plays an important role in binding with the DNA.

## Excited state interactions

The excited state interaction of ETBr-DNA with dibenzo[*a*,*j*]xanthenes **1a**, **1j**, **1l**, **1m,** and **1n** was carried out through fluorescence measurements. Figure 4 shows the emission spectrum of ETBr-DNA in the absence and presence of **1l**. The emission intensity of ETBr-DNA decreases with increase in the concentration of **1l** ($2–10 \times 10^{-5}$ M), which indicates that the fluorescence quenching of ETBr-DNA has occurred. Similar behavior was observed for all other dibenzo[*a*,*j*]xanthenes **1a**, **1j**, **1m,** and **1n.** Emission spectrum for compounds **1a**, **1j**, **1m,** and **1n** is provided in supporting information.

The observed fluorescence quenching is due to the intercalation of the dibenzo[*a*,*j*]xanthenes **1l** with DNA by replacing ETBr. Both the ground state and excited state measurements suggest the intercalative binding phenomenon of all the dibenzo[*a*,*j*]xanthenes with DNA

## Anti-oxidant activity

DPPH is the stable free radical at room temperature, which produces a purple color in ethanol. This radical accepts an electron of hydrogen radical to form a stable molecule, and the decolourization of radical was measured at 517 nm (Balasundram *et al*., 2005). $ABTS^+$ is a protonated free radical, and the maximum absorbance was observed at

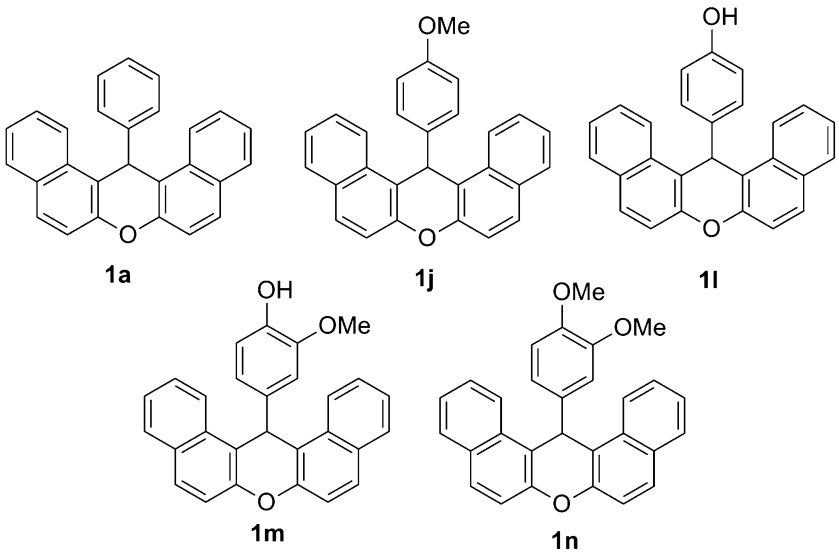



**Fig. 2** Dibenzo[*a*,*j*]xanthenes (**1**) derivatives identified for DNA-binding study

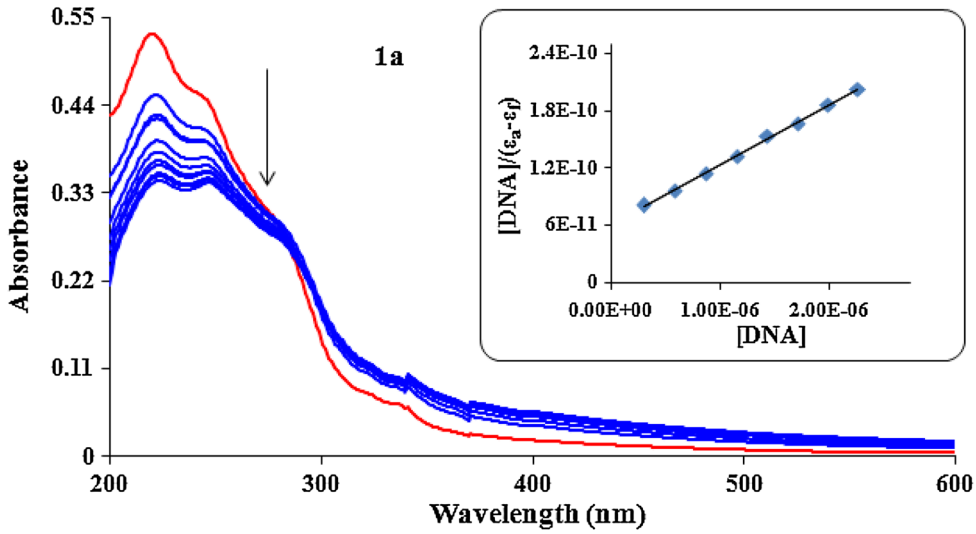



**Fig. 3** Absorption spectrum of **1a** ($1 \times 10^{-5}$ M) in the absence and presence of DNA (3, 6, 9, 12, 15, 18, 21, 24, 27, and $30 \times 10^{-7}$ M) in water. The *arrow* indicates decrease in absorbance with increasing concentration of DNA. The *inset* figure shows a plot of $[DNA]/(\varepsilon_a - \varepsilon_f)$ versus [DNA]

**Table 3** Binding constant ($K_b$) calculated from the absorption measurements of dibenzo[*a*,*j*]xanthenes and DNA

| S. no. | Dibenzo[*a*,*j*]xanthenes | $K_b/(\times 10^6\ M^{-1})$ |
|---|---|---|
| 1 | **1a** | 1.02 |
| 2 | **1j** | 1.35 |
| 3 | **1l** | 1.62 |
| 4 | **1m** | 2.30 |
| 5 | **1n** | 2.91 |

734 nm (Sasikumar *et al*., 2010). The DPPH and $ABTS^+$ free radical scavenging activity of dibenzo[*a*,*j*]xanthenes **1a**, **1j**, **1l**, **1m**, **and 1n** is shown in Figs. 5 and 6. To achieve antioxidant activity, dibenzo[*a*,*j*]xanthenes may either donate electron or hydrogen atom to neutralize both ABTS and DPPH free radicals and their butylated hydroxytoluene (BHT). The dibenzo[*a*,*j*]xanthenes significantly inhibited the free radicals of DPPH and ABTS in concentration dependant manner. DPPH radical scavenging activity of compounds **1a**, **1j**, **1l**, **1m,** and **1n**, at the concentration of 250 μg $mL^{-1}$, was found to be 31.05, 47.13, 53.08, 86.78, and 52.64 %, respectively.

Similarly, the ABTS inhibition activity of compounds **1a**, **1j**, **1l**, **1m**, and **1n** at the concentration of 250 μg $mL^{-1}$ was found to be 63.55, 67.46, 73.19, 83.13, and 70.78 %, respectively. $IC_{50}$ values observed for compounds **1a**, **1j**, **1l**, **1m**, **and 1n** against DPPH and ABTS are shown in Table 4. This shows that the dibenzo[*a*,*j*]xanthenes are effective scavengers for ABTS rather than DPPH.

Among the five compounds, **1m** substituted with 3-OMe and 4-OH in the phenyl ring was found to be more effective inhibitor against both DPPH (86.78 %) as well as $ABTS^+$

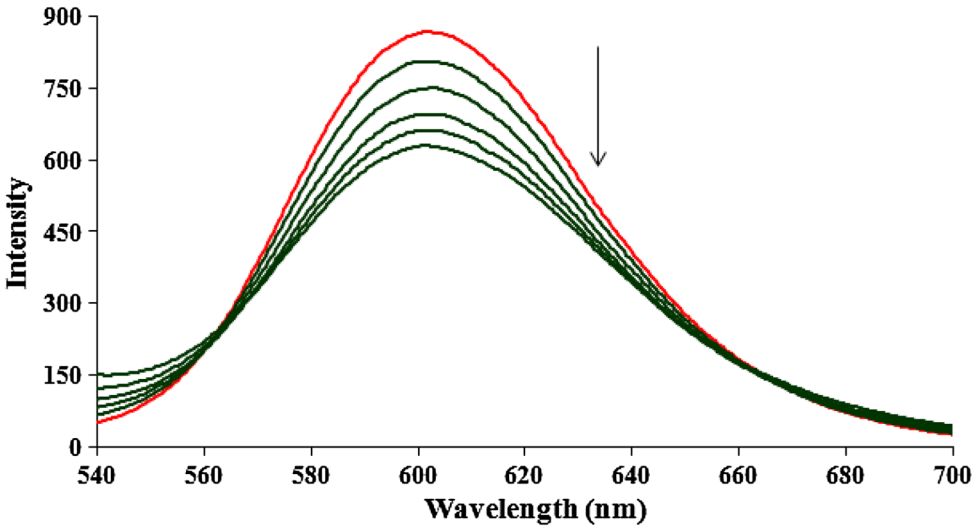



**Fig. 4** Emission spectrum of ETBr-DNA in the absence and presence of **1l** (2, 4, 6, 8, and $10 \times 10^{-5}$ M) in aqueous solution. The *arrow* indicates the decreases in intensity with increasing in concentration of **1l**

(83.32 %). This result is consistent with the trend observed in case of caffeic acid ester (Micco *et al*., 2011).

## Experimental section

### Materials

Calf thymus-deoxyribonucleic acid (CT-DNA), ethidium bromide (ETBr), DPPH, ABTS, and BHT were purchased from Sigma Aldrich. All the commercial reagents and solvents were used without further purification unless otherwise stated. Phosphate buffer was used for preparing DNA solutions. All yields reported are based on isolated compounds. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 A F254 pre-coated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and staining with $I_2$ on silica gel. Flash column chromatography was performed using Silica Gel 60–120 Å (32–63 μm).

### Instrumentation

NMR spectra were recorded on FT-NMR Bruker 400 MHz spectrometer as $CDCl_3$/DMSO-$D_6$ solutions with TMS as internal reference. Absorption spectra were recorded using JASCO V630 UV–Vis spectrophotometer. Fluorescence measurements were carried out using Perkin Elmer LS 55 spectrofluorimeter. The excitation and emission wavelengths of ETBr-DNA are 480 and 602 nm, respectively. Silt widths 10 nm and scan rate (400 nm/min) were kept constant for all measurements. Quartz cells (4 × 1 × 1 cm) with high vacuum Teflon stopcocks were used for measurements. Melting point, $^1$H and $^{13}$C NMR values are given and compared with the spectral data already known.

### General procedure for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes (**1a**–**p**)

A mixture of aldehyde **5**, (1.0 mmol), 2-naphthol **6**, (2.0 mmol), and $Ni(ClO_4)_2{\cdot}6H_2O$ (0.1 mmol) in DCE (5.0 mL) was refluxed at 83–85 °C. Progress of the reaction was monitored by TLC (EtOAc: Hexane; 3:7). After completion, the reaction mixture was quenched with water, extracted with DCM (2 × 20 mL), and washed with water (2 × 20 mL); the combined organic layer was dried ($Na_2SO_4$) and concentrated. Wherever it is necessary, the crude product was purified through column chromatography. The structure and numbering scheme of compounds **1a**–**p** is provided in Table 5.

#### *Synthesis of 14-phenyl-14H-dibenzo[a,j]xanthenes (**1a**)*

The title compound **1a** was prepared by the reaction of benzaldehyde (**5a**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a white solid; yield: 87 %; mp 180–182 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.39$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 8.39 (4H, d, $J = 8.4$ Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.59–7.47 (6H, m, ArH), 7.40 (2H, t, $J = 7.2$ Hz, ArH, C-22 H, C-27 H), 7.13 (2H, t, $J = 7.6$ Hz, ArH, C-23 H, C-26 H), 6.98 (1H, t, $J = 7.2$ Hz, ArH, C-6 H) 6.49 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.8$ (C, C-9, C-11), 145.0 (C, C-3), 131.5 (C, C-13, C-20), 131.1 (CH, C-1, C-5), 128.8 (CH, C-9, C-11), 128.7 (C, C-14, C-19), 128.5 (CH, C-15, C-18, C-24, C-25), 128.2 (CH, C-2, C-4),

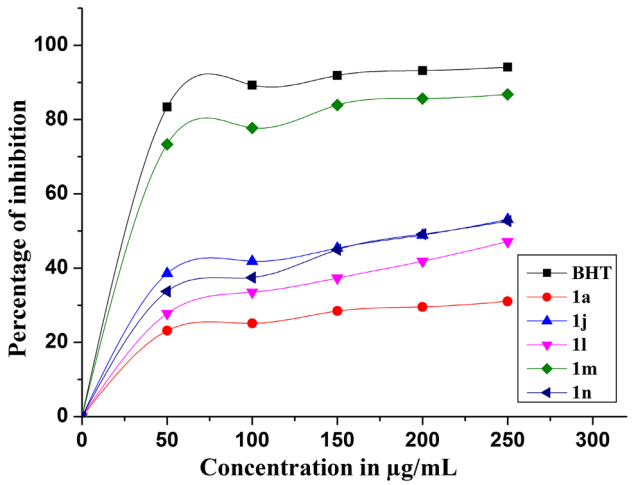



**Fig. 5** DPPH radical scavenging activity of compounds **1a**, **1j**, **1l**, **1m**, and **1n** compared with BHT. Each value is expressed as the mean ± standard deviation ($n = 3$)

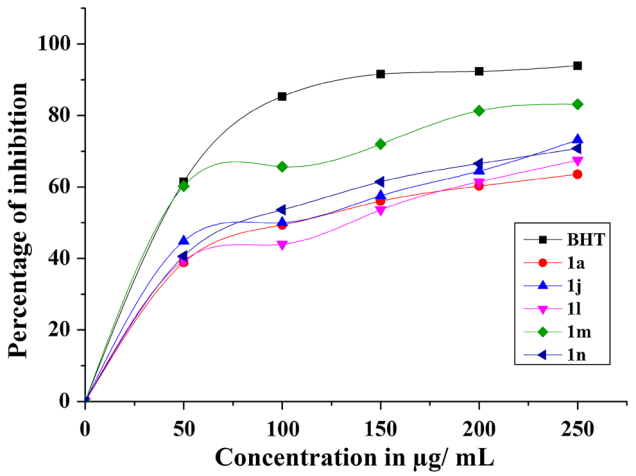



**Fig. 6** ABTS radical scavenging activity of compounds **1a**, **1j**, **1l**, **1m,** and **1n** compared with BHT. Each value is expressed as the mean ± standard deviation ($n = 3$)

126.8 (CH, C-6), 126.4 (CH, C-22, C-27), 124.2 (CH, C-21, C-28), 122.7 (CH, C-23, C-26), 118.0 (CH, C-16, C-17), 117.35 (C, C-8, C-12), 38.0 (CH, C-7).

*Synthesis of 14-(4-nitrophenyl)-14H-dibenzo[a,j]xanthenes (**1b**)*

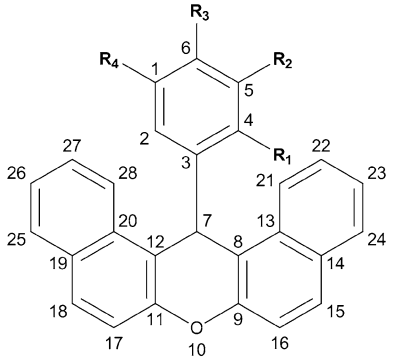
The title compound **1b** was prepared by the reaction of 4-nitrobenzaldehyde (**5b**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a yellow solid; yield: 95 %; mp 310–312 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.28$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 8.0 (2H, d, $J = 8.4$ Hz, ArH, C-24 H, C-25 H), 7.85 (4H, t, $J = 8.4$ Hz, ArH, C-22 H, C-23 H, C-26 H, C-27 H), 7.68 (2H, d, $J = 8.8$ Hz, ArH, C-15 H, C-18 H), 7.58 (2H, dd, $J = 1.2$, 8.8 Hz, ArH, C-1 H, C-5 H), 7.50 (2H, d, $J = 8.8$ Hz, ArH, C-16 H, C-17 H), 7.46 (2H, dd, $J = 1.2$, 7.6 Hz, ArH, C-2 H, C-4 H), 6.60 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 152.0$ (C, C-9, C-11), 148.8 (C, C-3), 146.3 (C, C-6), 131.1 (C, C-13), 129.6 (C, C-20), 128.9 (CH, C-1, C-5), 127.2 (C, C-14, C-19), 124.6 (CH, C-15, C-18, C-24, C-25), 123.9 (CH, C-2, C-4), 122.0 (CH, C-22, C-27, C-21, C-28), 118.0 (CH, C-16, C-17), 115.8 (CH, C-23, C-26), 115.2 (C, C-8, C-12), 37.8 (CH, C-7).

**Table 4** Antioxidant profiles of compounds **1a**, **1j**, **1l**, **1m**, and **1n**

| S. no. | Dibenzo[*a,j*]xanthene | $IC_{50}$ values (µg $mL^{-1}$) | |
|---|---|---|---|
| | | DPPH | $ABTS^+$ |
| 1 | **1a** | 225.12 | 100.14 |
| 2 | **1j** | 226.36 | 143.56 |
| 3 | **1l** | ND | 75.94 |
| 4 | **1m** | 26.82 | 38.02 |
| 5 | **1n** | ND | 76.25 |
| 6 | BHT | 24.40 | 38.96 |

*ND* not determined

**Table 5** Structure and numbering scheme of compounds **1a–p**




| Compound | **1a** | **1b** | **1c** | **1d** | **1e** | **1f** | **1g** | **1h** |
|---|---|---|---|---|---|---|---|---|
| $R_1$ | H | H | H | $NO_2$ | H | Cl | H | H |
| $R_2$ | H | H | $NO_2$ | H | H | H | Br | H |
| $R_3$ | H | $NO_2$ | H | H | Cl | H | H | F |
| $R_4$ | H | H | H | H | H | H | H | H |

| Compound | **1i** | **1j** | **1k** | **1l** | **1m** | **1n** | **1o** | **1p** |
|---|---|---|---|---|---|---|---|---|
| $R_1$ | H | H | H | H | H | H | H | H |
| $R_2$ | H | H | OMe | H | OMe | OMe | OMe | H |
| $R_3$ | Me | OMe | H | OH | OH | OMe | OMe | N,N′-$Me_2$ |
| $R_4$ | H | H | H | H | H | H | OMe | H |

*Synthesis of 14-(3-nitrophenyl)-14H-dibenzo[a,j]xanthenes (**1c**)*

The title compound **1c** was prepared by the reaction of 3-nitrobenzaldehyde (**5c**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a pale yellow solid; yield: 90 %; mp 209–211 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 7.80$ (4H, dd, $J = 6.0$, 8.8 Hz, ArH, C-21 H, C24 H, C-25 H, C-28 H), 7.60–7.55 (4H, m, ArH), 7.49 (2H, d, $J = 8.8$ Hz, ArH, C-16 H, C-17 H), 7.39 (2H, t, $J = 7.6$ Hz, ArH, C-22 H, C-27 H), 7.14 (2H, t, $J = 7.6$ Hz, ArH, C-23 H, C-26 H), 7.00 (1H, t, ArH, C-1 H), 6.49 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 154.2$ (C, C-9, C-11), 153.1 (C, C-3), 137.3 (C, C-5), 137.3 (C, C-13), 133.4 (C, C-20), 130.2 (CH, C-1, C-6), 129.8 (C-15, C-18), 128.9 (C, C-14, C-19), 127.4 (CH, C-24, C-25), 123.5 (CH, C-2, C-4), 122.5 (CH, C-22, C-27), 119.9 (CH, C-21, C-28), 118.2 (CH, C-16, C-17), 115.2 (C, C-8, C-12), 105.3 (C-23, C-26), 43.0 (CH, C-7).

*Synthesis of 14-(2-nitrophenyl)-14H-dibenzo[a,j]xanthene (**1d**)*

The title compound **1d** was prepared by the reaction of 2-nitrobenzaldehyde (**5d**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a white solid; Yield: 97 %; mp 214–215 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 7.83$–7.79 (6H, m, ArH), 7.62 (2H, m, ArH), 7.52 (1H, s, ArH, C-2 H), 7.51 (3H, m, ArH,), 7.43 (2H, t, $J = 8.8$ Hz, ArH, C-22 H, C-27 H), 7.21 (1H, t, $J = 7.2$ Hz, ArH, C-1 H), 7.08 (1H, t, $J = 7.2$ Hz, ArH, C-6 H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 149.4$ (C, C-9, C-11), 147.0 (C, C-3), 140.3 (C, C-4), 134.1 (C, C-13), 132.2 (C, C-20), 130.9 (CH, C-1, C-5), 129.5 (C, C-14, C-19), 128.7 (CH, C-15, C-18, C-24, C-25), 127.6 (CH, C-2, C-5), 127.4 (CH, C-6), 124.9 (C-21, C-28), 124.8 (CH, C-16, C-17), 122.6 (CH, C-23, C-26), 118.0 (C, C-8, C-12), 117.56 (CH, C-22, C-27), 32.5 (CH, C-7).

*Synthesis of 14-(4-chlorophenyl)-14H-dibenzo[a,j] xanthene (**1e**)*

The title compound **1e** was prepared by the reaction of 4-chlorobenzaldehyde (**5e**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a white solid; yield: 95 %; mp 289–291 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.31$ (2H, d, $J = 8.0$ Hz, ArH, C-21 H, C-28 H), 7.84–7.78 (4H, m, ArH), 7.56 (2H, d, $J = 6.8$ Hz, ArH, C-15 H, C-18 H), 7.48–7.42 (6H, m, ArH), 7.09 (2H, d, $J = 8.0$ Hz, ArH, C-16 H, C-17 H), 6.46 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.8$ (C, C-9, C-11), 143.5 (C, C-3), 132.1 (C, C-6), 131.3 (C, C-13, C-20), 131.1 (CH, C-1,C-5), 129.5 (C, C-14, C-19), 129.1 (CH, C-2, C-4), 128.9 (CH, C-24, C-25), 128.6 (CH, C-15, C-18), 126.9 (CH, C-22, C-27), 124.4 (CH, C-21, C-28), 122.4 (CH, C-23, C-26), 118.0 (CH, C-16, C-17), 116.8 (C, C-8, C-12), 37.4 (CH, C-7).

*Synthesis of 14-(2-chlorophenyl)-14H-dibenzo[a,j] xanthene (**1f**)*

The title compound **1f** was prepared by the reaction of 2-chlorobenzaldehyde (**5f**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a white solid; yield: 90 %; mp 214–216 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 9.19$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 8.26 (4H, dd, $J = 1.6$, 8.4 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 8.09 (2H, t, $J = 1.6$, 8.4 Hz, ArH, C-15 H, C-18 H), 7.94 (2H, d, $J = 8.8$ Hz, ArH, C-16 H, C-17 H), 7.90–7.83 (3H, m, ArH), 7.72–7.70 (1H, m, ArH), 7.38–7.34 (2H, m, ArH), 7.25 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 147.9$ (C, C-9, C-11), 142.5 (C, C-3), 130.7 (C, C-4), 130.7 (C, C-13, C-20), 129.8 (CH, C-1), 129.0 (C, C-5), 128.5 (C, C-14), 128.0 (C, C-19), 127. 6 (CH, C-2, C-6), 126.9 (CH, C-15, C-18), 126.8 (CH, C24, C-25), 125.8 (CH, C-22, C-27), 123.7 (CH, C-21, C-28), 122.4 (CH, C-16), 117.0 (C, C-8, C-12), 116.9 (CH, C-17), 33.6 (CH, C-7).

*Synthesis of 14-(3-bromophenyl)-14H-dibenzo[a,j] xanthene (**1g**)*

The title compound **1g** was prepared by the reaction of 3-bromobenzaldehyde (**5g**), 2-naphthol (**6**) and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a pale yellow solid; yield: 97 %; mp 194–196 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.32$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.82 (4H, dd, $J = 1.6$, 8.4 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.62–7.58 (3H, m, ArH), 7.50–7.47 (3H, m, ArH), 7.43(2H, t, $J = 8.8$ Hz, ArH, C-22 H, C-27 H), 7.13–7.11(1H, m, ArH), 7.02 (1H, t, $J = 7.2$ Hz, ArH, C-1 H), 6.45 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.8$ (C, C-9, C-11), 147.2 (C, C-3), 131.3 (C, C-5), 131.2 (C,C-13, C-20), 131.1 (CH, C-1), 129.9 (C, C-14, C-19),129.7 (CH, C-15, C-18), 129.2 (C, C-24, C-25), 128.9 (CH, C-2, C-4), 126.9 (CH, C-22, C-27), 126.8 (CH, C-6), 124.4 (CH, C-21), 122.8 (CH, C-28), 122.4 (CH, C-23, C-26), 118.1 (CH, C-16, C-17), 116.5 (C, C-8, C-12), 37.8 (CH, C-7).

*Synthesis of 14-(4-fluorophenyl)-14H-dibenzo[a,j]xanthene (**1h**)*

The title compound **1h** was prepared by the reaction of 4-fluorobenzaldehyde (**5h**), 2-naphthol (**6**) and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a dirty white solid;

yield: 88 %; mp 227–229 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.32$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.80 (4H, dd, $J = 1.6$, 8.4 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.57 (2H, t, $J = 7.2$ Hz, ArH, C-22 H, C-27 H), 7.47–7.38 (6H, m, ArH), 6.80 (2H, t, $J = 8.4$ Hz, ArH, C-23 H, C-26 H), 6.46 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 162.4$ (C, C-6), 153.9 (C, C-9, C-11), 148.7 (C, C-3), 140.8 (CH, C-13, C-20), 140.7 (C, C-1, C-5), 131.3 (CH, C-9,C-11), 129.5 (CH, C-15, C-18), 129.1 (C, C-14, C-19), 128.9 (CH, C-24, C-25), 128.6 (CH, C-2, C-4), 126.9 (CH, C-6), 124.4 (CH, C-22, C-27), 122.4 (CH, C-21, C-28), 118.0 (CH, C-23, C-26, C-16, C-17), 116.8 (C, C-8, C-12), 37.4 (CH, C-7).

*Synthesis of 14-(p-tolyl)-14H-dibenzo[a,j]xanthene (**1i**)*

The title compound **1i** was prepared by the reaction of 4-methylbenzaldehyde (**5i**), 2-naphthol (**6**) and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a dirty white solid; Yield: 91 %; 233–234 °C $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.29$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.80 (4H, dd, $J = 7.2$, 8.0 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.57 (2H, t, $J = 6.8$ Hz, ArH, C-22 H, C-27 H), 7.47 (2H, d, $J = 8.8$ Hz, ArH, C-2 H, C-4 H), 7.42–7.38 (4H, m, ArH), 6.95 (2H, d, $J = 8.0$ Hz, ArH, C-16 H, C-17 H), 6.45 (1H, s, CH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.7$ (C, C-9, C-11), 142.1 (C. C-3), 135.9 (C, C-6), 131.5 (C, C-13, C-20), 131.1 (CH, C-1, C-5), 129.2 (C, C-14, C-19), 128.8 (CH, C-2, C-4), 128.7 (CH, C-15, C-18), 128.0 (CH, C-24, C-25), 126.7 (CH, C-22, C-27), 124.2 (CH, C-21, C-28), 122.7 (CH, C-23, C-26), 118.0 (CH, C-16, C-17), 117.5 (C, C-8, C-12), 37.6 (CH, C-7), 20.9 ($CH_3$, $C_6$–C).

*Synthesis of 14-(4-methoxyphenyl)-14H-dibenzo[a,j] xanthene (**1j**)*

The title compound **1j** was prepared by the reaction of 4-methoxybenzaldehyde (**5j**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a pale yellow solid; Yield: 97 %; mp 204–206 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.37$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.80 (4H, dd, $J = 8.4$, 9.2 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.57 (2H, t, $J = 8.4$ Hz, ArH, C-22 H, C-27 H), 7.47 (2H, d, $J = 8.8$ Hz, ArH, C-2 H, C-4 H), 7.43–7.38 (4H, m, ArH), 6.67 (2H, d, $J = 6.8$ Hz, ArH, C-16 H, C-17 H), 6.44 (1H, s, CH); 3.61 (3H, s, –$OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 157.8$ (C, C-6), 148.7 (C, C-9, C-11), 137.4 (C, C-3), 131.4 (C, C-13, C-20), 131.1 (CH, C-1, C-5), 129.1 (C, C-14, C-19), 128.8 (CH, C-2, C-4), 128.7 (CH, C-15, C-18), 126.7 (CH, C-24, C-25), 124.2 (CH, C-22, C-27), 122.7 (CH, C-21, C-28), 118.0 (CH, C-23, C-26), 117.6 (C, C-8, C-12), 113.9 (CH, C-16, C-17), 55.1 ($OCH_3$, $C_6$–C), 37.1 (CH, C-7).

*Synthesis of 14-(3-methoxyphenyl)-14H-dibenzo[a,j] xanthene (**1k**)*

The title compound **1k** was prepared by the reaction of 3-methoxybenzaldehyde (**5k**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a yellow solid; Yield: 91 %; mp 187–190 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.39$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.80 (4H, dd, $J = 8.0$, 8.4 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.57 (2H, t, $J = 6.8$ Hz, ArH, C-22 H, C-27 H), 7.47 (2H, d, $J = 8.8$ Hz, ArH, C-2 H, C-4 H), 7.40 (2H, t, $J = 8.0$ Hz, ArH, C-23 H, C-26 H), 7.16 (1H, d, $J = 8.4$ Hz, ArH, C-6 H), 7.09–7.02 (2H, m, ArH), 6.51 (2H, d, $J = 8.0$ Hz, ArH, C-16 H, C-17 H), 6.46 (1H, s, CH); 3.63 (3H, s, –$OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 159.5$ (C, C-5), 148.7 (C, C-9, C-11), 146.4 (C, C-3), 131.4 (C, C-13), 131.0 (C, C-20), 129.2 (CH, C-1), 128.8 (C, C-14), 128.7 (C, C-19), 126.7 (CH, C-6), 124.2 (CH, C-2, C-4, C-15, C-18), 122.7 (CH, C-24, C-25), 120.7 (CH, C-22, C-27), 117.9 (CH, C-21, C-28), 117.1 (C, C-8, C-12), 114.9 (CH, C-23, C-26), 110.9 (CH, C-16, C-17), 54.9 (OMe, $C_5$–C) 37.9 (CH, C-7).

*Synthesis of 4-(14H-dibenzo[a,j]xanthen-14-yl)phenol (**1l**)*

The title compound **1l** was prepared by the reaction of 4-hydroxybenzaldehyde (**5l**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a pale orange solid; Yield: 90 %; mp 139–140 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.36$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.80 (4H, dd, $J = 8.0$, 8.8 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.56 (2H, t, $J = 7.2$ Hz, ArH, C-22 H, C-27 H), 7.46 (2H, d, $J = 8.8$ Hz, ArH, C-2 H, C-4 H), 7.42–7.35 (4H, m, ArH), 6.58 (2H, d, $J = 6.4$ Hz, ArH, C-16 H, C-17 H), 6.43 (1H, s, CH), 2.00 (1H, s, –OH); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 153.8$ (C, C-6), 148.6 (C, C-9, C-11), 137.5 (C, C-3), 131.4 (C, C-13, C-20), 131.1 (CH, C-1, C-5), 129.3 (C, C-14, C-19), 128.8 (CH, C-2, C-4), 128.7 (CH, C-15, C-18), 126.7 (CH, C-24, C-25), 124.2 (CH, C-22, C-27), 122.7 (CH, C-21, C-28), 117.9 (CH, C-23, C-26), 117.5 (C, C-8, C-12), 115.3 (CH, C-16, C-17), 37.1 (CH, C-7).

*Synthesis of 4-(14H-dibenzo[a,j]xanthen-14-yl)-2-methoxyphenol (**1m**)*

The title compound **1m** was prepared by the reaction of 4-hydroxy-3-methoxybenzaldehyde (**5m**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a brownish white solid; Yield: 50 %; mp 208–211 °C;

$^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.40$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.81 (4H, dd, $J = 8.0$, 8.8 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.58 (2H, t, $J = 8.4$ Hz, ArH, C-22 H, C-27 H), 7.48 (2H, d, $J = 8.8$ Hz, ArH, C-2 H, C-4 H), 7.41 (2H, t, $J = 8.4$ Hz, ArH, C-22 H, C-27 H), 7.16 (1H, d, $J = 8.0$ Hz, ArH, C-1 H), 6.84 (1H, s, ArH, C-4 H), 6.72 (1H, d, $J = 8.4$ Hz, ArH, C-2 H), 6.43 (1H, s, CH), 3.65 (1H, s, $–OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.7$ (C, C-6), 146.7 (C, C-9, C-11), 144.1 (C, C-3), 137.1 (C, C-13, C-20), 131.4 (CH, C-5), 131.1 (CH, C-1), 128.8 (C, C-14, C-19), 128.7 (CH, C-2, C-4), 126.7 (CH, C-15, C-18), 124.3 (CH, C-24, C-25), 122.7 (CH, C-22, C-27), 120.9 (CH, C-21, C-28), 117.9 (CH, C-23, C-26), 113.7 (C, C-8, C-12), 110.7 (CH, C-16, C-17), 55.7 (OCH3, $C_5$–C), 37.6 (CH, C-7).

*Synthesis of 14-(3,4-dimethoxyphenyl)-14H-dibenzo[a,j] xanthene (**1n**)*

The title compound **1n** was prepared by the reaction of 3,4-dimethoxybenzaldehyde (**5n**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a dirty white solid; Yield: 70 %; mp 189–192 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.40$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.81 (4H, dd, $J = 8.0$, 8.8 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.57 (2H, t, $J = 8.4$ Hz, ArH, C-22 H, C-27 H), 7.48 (2H, d, $J = 8.8$ Hz, ArH, C-1 H, C-2 H), 7.43–7.39 (2H, m, ArH), 7.13 (1H, d, $J = 8.0$ Hz, ArH, C-4 H), 6.92 (1H, s, ArH, C-4 H), 6.45 (1H, s, CH), 3.69 (1H, s, $–OCH_3$), 3.67 (1H, s, $–OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.7$ (C, C-9, C-11), 146.7 (C, C-6), 144.1 (C, C-5), 137.1 (C, C-3), 131.4 (C, C-13, C-20), 131.1 (C, C-1), 128.8 (CH, C-2, C-4), 128.7 (CH, C-15, C-18), 126.7 (CH, C-24, C-25), 124.3 (CH, C-22, C-27), 122.7 (CH, C-21, C-28), 120.9 (CH, C-23, C-26), 117.9 (CH, C-23), 117.5 (C, C-8, C-12), 113.0 (CH, C-26), 110.6 (CH, C-16, C-17), 55.6 ($OCH_3$, $C_5$–C, $C_6$–C) 37.5 (CH, C-7).

*Synthesis of 14-(3,4,5-trimethoxyphenyl)-14H-dibenzo[a,j]xanthene (**1o**)*

The title compound **1o** was prepared by the reaction of 3,4,5-trimethoxybenzaldehyde (**5o**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a white solid; yield: 93 %; mp 208–210 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.41$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.85 (4H, dd, $J = 8.0$, 8.8 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.59 (2H, t, $J = 8.4$ Hz, ArH, C-22 H, C-27 H), 7.48 (4H, m, ArH), 6.70 (1H, s, ArH, C-2 H, C-4 H), 6.44 (1H, s, CH), 3.71 (6H, s, $–OCH_3$), 3.65 (3H, s, $–OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.7$ (C, C-9, C-11), 143.4 (C, C-1, C-5), 132.1 (C, C-3), 131.2 (C, C-6), 131.0 (C, C-13, C-20), 129.5 (C, C-14, C-19), 129.1 (CH, C-2, C-4), 128.9 (CH, C-24, C-25), 128.6 (CH, C-22, C-27), 126.9 (CH, C-21, C-28), 124.4 (CH, C-23, C-26), 122.4 (CH, C-16, C-17), 118.0 (C, C-8, C-12), 37.4 (CH, C-7).

*Synthesis of 4-(14H-dibenzo[a,j]xanthen-14-yl)-N,N-dimethylaniline (**1p**)*

The title compound **1p** was prepared by the reaction of 4-(dimethylamino)benzaldehyde (**5p**), 2-naphthol (**6**), and 10 mol% $Ni(ClO_4)_2{\cdot}6H_2O$. It was obtained as a bluish green solid; yield: 84 %; mp 184–186 °C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta = 8.40$ (2H, d, $J = 8.4$ Hz, ArH, C-21 H, C-28 H), 7.79 (4H, dd, $J = 8.0$, 8.8 Hz, ArH, C-15 H, C-18 H, C-24 H, C-25 H), 7.54 (2H, t, $J = 8.4$ Hz, ArH, C-22 H, C-27 H), 7.46 (2H, d, $J = 8.8$ Hz, ArH, C-2 H, C-4 H), 7.41–7.37 (4H, m, ArH), 6.54 (1H, s, CH), 2.75 (6H, s, $–NCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 148.8$ (C, C-9, C-11), 148.7 (C, C-6), 133.5 (C, C-3), 131.6 (C, C-13, C-20), 131.1 (CH, C-1, C-5), 128.8 (CH, C-14, C-19), 128.7 (CH, C-15, C-18, C-24, C-25), 128.5 (CH, C-2, C-4), 126.7 (CH, C-22, C-27), 124.1 (CH, C-21, C-28), 122.9 (CH, C-23, C-26), 117.9 (C, C-8, C-12), 112.6 (CH, C-16, C-17), 40.5 ($CH_3$, $C_6$–C), 36.9 (CH, C-7).

## DNA-binding experiments

UV–Vis absorption spectroscopic studies and the DNA-binding experiments were performed at room temperature. Purity of the CT-DNA was verified by taking the ratio of the absorbance values at 260 and 280 nm in the respective buffer, which was found to be 1.8:1, indicating that the DNA was sufficiently free of protein (Liu *et al*., 2009; Kamatchi *et al*. 2012). The DNA concentration per nucleotide was determined by absorption spectroscopy using the molar extinction coefficient value of 6,600 $dm^3\ mol^{-1}\ cm^{-1}$ at 260 nm. The concentration of DNA stock solution is $3.2 \times 10^{-4}$ M (Paramaguru *et al*., 2011). The competitive binding experiments were used to find out extend of binding with DNA of some of the xanthene dyes prepared under the present study. The fluorescence spectra of EB were measured using an excitation, and the emission wavelengths are 515 nm and 613 nm, respectively.

## Antioxidant assays

The ability of dibenzo[*a*,*j*]xanthene to act as free radical scavengers was explored by conducting a series of in vitro antioxidant assays involving DPPH radical and ABTS radical, and comparing the results with BHT was taken as reference standard.

### 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity

The DPPH free radical scavenging activity was estimated after slight modified method reported (Liyana-Pathiranan and Shahidi, 2005). A solution of 0.135 mM DPPH in methanol was mixed with 1 mL of compound (**1a**, **1j**, **1l**, **1m**, and **1n**) at different concentrations, in the range of 50–250 μg $mL^{-1}$. The reaction mixture was vortexed and allowed to stand in the dark for 20 min at 25 °C. Finally, the absorbance of the mixture was measured spectrophotometrically at 517 nm. The percentage of DPPH free radical inhibition was calculated by the following equation:

$$\text{Percentage of DPPH radical scavenging activity} = [(\text{Abs con} - \text{Abs sample})]/(\text{Abs con})] \times 100,$$

where Abs con is the absorbance of control and Abs sample is the absorbance of test sample/standard.

### 2,2′-Azinobis-3-ethylbenzothiozoline-6-sulfonic (ABTS) radical scavenging activity

Re *et al.* (1999) reported a useful method to determine the ABTS radical scavenging activity of organic compounds. A stock solution was prepared by mixing 7 mM ABTS in methanol and 2.4 mM potassium persulfate in distilled water. The working solution was prepared by mixing equal volume the stock solution and incubates over night at room temperature in the dark. One mL of $ABTS^{+}$ solution was mixed with appropriate quantity of methanol to obtain an absorbance of $0.706 \pm 0.002$ at 734 nm using spectrophotometer. Compounds (**1a**, **1j**, **1l**, **1m**, **and 1n**) with various concentration ranging from 50 to 250 μg $mL^{-1}$ were allowed to react with $ABTS^{+}$ solution, and after 7 min incubation period, the absorbance was taken at 734 nm. The percentage of ABTS free radical inhibition was calculated by the following equation:

$$\text{Percentage of ABTS radical scavenging activity} = [(\text{Abs con} - \text{Abs sample})]/(\text{Abs con})] \times 100,$$

where Abs con is the absorbance of control and Abs sample is the absorbance of test sample/standard. BHT was taken as reference standard.

## Conclusion

$Ni(ClO_4)_2{\cdot}6H_2O$ has been identified as an efficient catalyst for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives for the first time. The catalyst is inexpensive and easy to handle, and the product could be isolated by simple workup procedure. Aldehydes containing electron donating substituents (4-OMe, 3,4,5-$OCH_3$) are better candidates for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes compared to aldehydes with electron withdrawing substituents (3-Br, 4-Cl, 2-Cl, 4-$NO_2$, and 3-$NO_2$). Ground state and excited state interactions of dibenzo[*a*,*j*]xanthenes **1a**, **1j**, **1l**, **1m,** and **1n** with DNA were examined using absorption and emission spectroscopy and found that these compounds bind with DNA through intercalative electrostatic interactions. Dibenzo[*a*,*j*]xanthene containing strong electron donating substituents on the phenyl ring exhibited better intercalative binding. Also these compounds exhibited excellent free radical scavenging activity against DPPH and ABTS cationic radical. Compounds substituted with free –OH group were acted as a better scavengers compared to compounds with a protected –OH group. This study demonstrates for the first time dibenzo[*a*,*j*]xanthenes can bind with DNA through intercalative mode and act as good radical scavengers. Further, this study provides further insights into the some of the biological activities already observed with dibenzo[*a*,*j*]xanthenes.

**Acknowledgments** AI, KA and KMP are thankful to the Defence Research Development Organisation (DRDO), New Delhi for financial support (ERIP/ER/0900377/M/01/1245, dt 23.05.2008). We thank DST-FISR for use of the NMR and XRD facility at the School of Chemistry, Bharathidasan University, Tiruchirappalli-620024, INDIA.

## References

Ahmad M, King AT, Ko DK, Cha BH, Lee J (2002) Performance and photostability of xanthene and pyrromethene laser dyes in sol–gel phases. J Phys D 35:1473–1476

Amini MM, Fazaeli Y, Yassaee Z, Feizi S, Bazgir A (2009) Polytungstozincate acid: a new and efficient catalyst for the synthesis of xanthenes under solvent-free conditions. Open Catal J 2:40–44

Balasundram N, Ai TY, Sambanthamurthi R, Sundaram K, Saman S (2005) Nutritional status of women and children in Malaysian rural populations. Asia Pac J Clin Nutr 4:319–324

Baltork IM, Moghadam M, Mirkhani V, Tangestaninejad S, Tavakoli HR (2011) Highly efficient and green synthesis of 14-aryl(alkyl)-14*H*-dibenzo[*a*,*j*]xanthene and 1,8-dioxooctahydroxanthene derivatives catalyzed by reusable zirconyl triflate [$ZrO(OTf)_2$] under solvent-free conditions. Chin Chem Lett 22:9–12

Bhattacharya AK, Rana K, Mujahid M, Sehar I, Saxena AK (2009) Synthesis and in vitro study of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes as cytotoxic agents. Bioorg Med Chem Lett 19:5590–5593

Callan JF, Desilva P, Magri DC (2005) Luminescent sensors and switches in the early 21st century. Tetrahedron 61:8551–8588

Carreon JR, Roberts MA, Wittenhagen LM, Kelley SO (2005) Synthesis, characterization, and cellular uptake of DNA-binding rose bengal peptidoconjugates. Org Lett 7:99–102

Chen X, Wu Q, Henschke L, Weber G, Weil T (2012) An efficient and versatile approach for the preparation of a rhodamine B ester bioprobe library. Dyes Pigm 94:296–303

Dabiri M, Azimi SC, Bazgir A (2008) One-pot synthesis of xanthene derivatives under solvent-free conditions. Chem Pap 62:522–526

Dalpozzo R et al (2010) Perchloric acid and its salts: very powerful catalysts in organic chemistry. Chem Rev 110:3501–3551

Ghodratbeigi M, Ranjbar PR, Abbasi A (2011) Design, modeling and synthesis of molecular tweezers with self-assembly properties. J Mol Struct 990:140–151

Giri R, Goodell JR, Xing C, Benoit A, Kaur H, Hiasa H, Ferguson DM (2010) Synthesis and cancer cell cytotoxicity of substituted xanthenes. Bioorg Med Chem Lett 18:1456–1463

Ilangovan A, Malayappasamy S, Muralidharan S, Maruthamuthu S (2011) A highly efficient green synthesis of 1,8-dioxo-octahydroxanthenes. Chem Cent J 5:81–86

Ilangovan A, Muralidharan S, Sakthivel P, Malayappasamy S, Karuppusamy S, Kaushik MP (2012) Simple and cost effective acid catalysts for efficient synthesis of 9-aryl-1,8-dioxooctahydroxanthene. Tetrahedron Lett 54:491–494

Kamatchi TS, Chitrapriya N, Lee H, Fronczek CF, Fronczek RF, Natarajan K (2012) Ruthenium(II)/(III) complexes of 4-hydroxypyridine-2,6-dicarboxylic acid with PPh3/AsPh3 as co-ligand: impact of oxidation state and co-ligands on anticancer activity in vitro. Dalton Trans 41:2066–2077

Kumar A, Sharma S, Maurya RA, Sarkar J (2010) Diversity oriented synthesis of benzoxanthene and benzochromene libraries via one-pot, three-component reactions and their anti-proliferative activity. J Comb Chem 12:20–24

Lambert RW, Martin JA, Merrett JH, Parkes KEB, Thomas J (1997) Pyrimidine nucleosides. Chem Abstr 126:p212377y

Li J, Wei YX, Wei YL, Dong C (2007) Study on the spectral behavior of four fluorescent dyes and their interactions with nucleic acid by the luminescence method. J Lumin 124:143–150

Liu Z, Jiang M, Li Y, Wu Z, Yang J (2009) One-dimesional copper(II) polymer with bridging μ-trans-oxamidate and thiocyanate ligands: synthesis, crystal structure and DNA binding studies. Inorg Chim Acta 362:1253

Liua YH, Taoa XY, Leia LQ, Zhang ZH (2009) Fluoroboric acid adsorbed on silica-gel-catalyzed synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives. Synth Commun 39:580–589

Liyana-Pathiranan CM, Shahidi F (2005) Antioxidant activity of commercial soft and hard wheat (*Triticum aestivum* L.) as affected by gastric pH conditions. J Agric Food Chem 53: 2433–2440

Maleki B, Gholizadeh M, Sepehr Z (2011) 1,3,5-Trichloro-2,4,6-triazinetrion: a versatile heterocycle for the one-pot synthesis of 14-aryl- or alkyl -14*H*-dibenzo[a,j]xanthene, 1,8-dioxooctahydroxanthene and 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]xanthene-11-one derivatives under solvent-free conditions. Bull Korean Chem Soc 32:1697–1702

Micco SD, Mazué F, Daquino C, Spatafora C, Delmas D, Latruffe N, Tringali C, Riccio R, Bifulco G (2011) Structural basis for the potential antitumour activity of DNA-interacting benzo[*k*,*l*]xanthene lignans. Org Biomol Chem 9:701–710

Moghadam KR, Azimi SC (2012) $Mg(BF_4)_2$ doped in $[BMIm][BF_4]$: a homogeneous ionic liquid-catalyst for efficient synthesis of 1,8-dioxo-octahydroxanthenes, decahydroacridines and 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes. J Mol Catal A 363:465–469

Muñiz FM, Simón L, Sáez S, Raposo C, Alcázar V, Morán JR (2008) A fluorescent sensor for dinitrobenzoic acid based on a cyanuric acid and xanthene skeleton. Sensors 8:1637–1644

Naya A, Ishikawa M, Matsuda K, Ohwaki K, Saeki T, Noguchi K, Ohtake N (2003) Sodium etiobilirubin-IVγ-C10-sulfonate: a highly solvated bile pigment structure containing two different non-ridge-tile conformers in the unit cell. Bioorg Med Chem Lett 11:875–884

Paramaguru G, Vijaysolomon RV, Venuvanalingam P, Renganathan R (2011) Spectroscopic studies on $TiO_2$ enhanced binding of hypocrellin B with DNA. J Fluoresc 21:1887–1895

Rahmati A (2010) A rapid and efficient method for the synthesis of 14*H*-dibenzo[α,*j*] xanthenes, aryl-5*H*-dibenzo [*b*,*i*]xanthene-5,7,12,14-(13*H*)-tetraone and 1,8-dioxo-octahydroxanthenes by acidic ionic liquid. Chin Chem Lett 21:761–764

Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Evans CR (1999) Antioxidant activity applying an improved ABTS radical cation decolorization assay. Free Radic Biol Med 26:1231–1237

Rostamizadeh S, Amani AM, Mahdavinia GH, Shadjou N (2009) Silica supported ammonium dihydrogen phosphate ($NH_4H_2PO_4$/$SiO_2$): a mild, reusable and highly efficient heterogeneous catalyst for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes. Chin Chem Lett 20:779–783

Sasikumar JM, Maheshu V, Smilin B, Aseervatham G, Darshini DTP (2010) In vitro antioxidant activity of *Hedyotis corymbosa* (L.) Lam. aerial parts. Indian J Biochem Biophys 47:49–52

Shakibaei GI, Mirzaei P, Bazgir A (2007) Dowex-50W promoted synthesis of 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene and 1,8-dioxo-octahydroxanthene derivatives under solvent-free conditions. Appl Catal A 325:188–192

Shaterian HR, Doostmohammadi R, Khorami F, Ghashang M (2010) Magnesium hydrogensulfate $[Mg(HSO_4)_2]$ as an efficient catalyst for the preparation of silyl ethers, dibenzo[*a*,*j*]xanthenes, and octahydroxanthene derivatives. Phosphorus Sulfur Silicon 185: 171–180

Shirini F, Khaligh NG (2012) Succinimide-*N*-sulfonic acid: an efficient catalyst for the synthesis of xanthene derivatives under solvent-free conditions. Dyes Pigm 95:789–794

Sibi MP, Itoh K, Jasperse CP (2004) Chiral lewis acid catalysis in nitrile oxide cycloadditions. J Am Chem Soc 126:5366–5367

Song Y, Yang Y, You J, Liu B, Wu L, Hou Y, Wang W, Zhu J (2013) Design, synthesis and anticancer activity of N3, N11-bis(2-hydroxyethyl)-14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes-3,11-dicarboxamide. Chem Pharm Bull 61:167–175

Spatafora C, Daquino C, Tringalia C, Amorati R (2013) Reaction of benzoxanthene lignans with peroxyl radicals in polar and non-polar media: cooperative behaviour of OH groups. Org Biomol Chem 11:4291–4294

Vaghei RG, Malaekehpoor SM (2010) Facile one-pot synthesis of tetrahydrobenzo[*a*]xanthene-11-one and aryl-14*H*-dibenzo[*a*,*j*] xanthene. Org Prep Proced Int 42:494–498

Wang XZ, Yang BY, Lin GJ, Xie YY, Huang HL, Liu YJ (2012) Cytotoxicity, cell cycle arrest, antioxidant activity and interaction of dibenzoxanthenes derivatives with DNA. DNA Cell Biol 31:1468–1474

Wu L, Yang C, Yang L, Yang L (2010) Synthesis of 14-substituted-14*H*-dibenzo[*a*,*j*] xanthenes and 1,8-dioxo-octahydroxanthenes using silica chloride ($SiO_2$–Cl) under solvent-free conditions. Phosphorus Sulfur Silicon 185:903–909

Yanagita H, Kodama K, Kanemasa S (2006) Double catalytic enantioselective Michael addition reactions of tertiary nucleophile precursors—tertiary/quaternary and quaternary/quaternary carbon–carbon bond formations. Tetrahedron Lett 47:9353–9357

Zare A, Mokhlesi M, Hasaninejad A, Hekmat-Zadehk T (2012) Solvent-free synthesis of 1,8-dioxo-octahydroxanthenes and 14-aryl-14*H*-dibenzo[*a*,*j*]xanthenes using saccharin sulfonic acid as an efficient and green catalyst. J Chem 9:1854–1863