

# Efficient Synthesis of 12-Aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones using Ionic Liquid Pyrazinium Di(hydrogen sulfate) {Py(HSO<sub>4</sub>)<sub>2</sub>} as a Novel, Green and Homogeneous Catalyst

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**Abstract.** An efficient and simple solvent-free procedure for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-one derivatives *via* the one-pot multi-component condensation of dimedone with aromatic aldehydes and β-naphthol in the presence of protic acidic ionic liquid pyrazinium di(hydrogen sulfate) {Py(HSO<sub>4</sub>)<sub>2</sub>} as a green and homogeneous catalyst is described. All reactions proceed efficiently, and the title compounds are produced in high yields and in short reaction times.

**Key words:** 12-Aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-one, pyrazinium di(hydrogen sulfate) {Py(HSO<sub>4</sub>)<sub>2</sub>}, protic acidic ionic liquid, homogeneous catalyst, one-pot multi-component reaction, solvent-free.

**Resumen.** Se describe un procedimiento simple y eficiente para la síntesis de derivados de 12-aril-8,9,10,12-tetrahidrobenzo[*a*]-xanthen-11-ona mediante la condensación de multicomponentes en un solo paso de dimedona con aldehídos aromáticos y β-naftol en presencia del líquido iónico ácido di(sulfato ácido) de pirazonio [Py(HSO<sub>4</sub>)<sub>2</sub>] como catalizador homogéneo y verde. Todas las reacciones procedieron eficientemente en tiempos cortos de reacción.

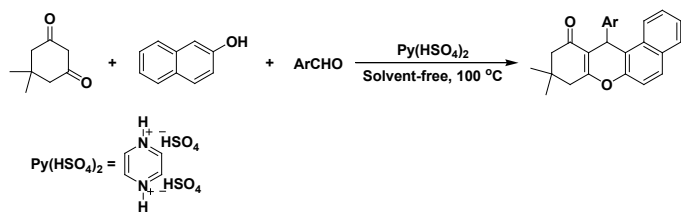
**Palabras clave:** 12-Aril-8,9,10,12-tetrahidrobenzo[*a*]-xanthen-11-ona, líquido iónico ácido [Py(HSO<sub>4</sub>)<sub>2</sub>], catalizador homogéneo y verde, condensación de multicomponentes en un solo paso.

## Introduction

Benzoxanthene derivatives such as 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones are of importance since they have various biological activities, such as anti-inflammatory [1], antiviral [2] and antibacterial [3] properties. They are also being utilized as antagonists for the paralyzing action of zoxazolamine [4], in photodynamic therapy [5], as leuco-dyes in laser technology [6], and as pH-sensitive fluorescent materials for visualization of biomolecules [7]. Generally, this type of compounds is prepared by the pot multi-component condensation of dimedone with aldehydes and β-naphthol [8-16]. Some catalysts has been used to promote this transformation, including InCl<sub>3</sub> and P<sub>2</sub>O<sub>5</sub> [8], *p*-toluenesulfonic acid (PTSA)/ ionic liquid [9], dodecatungstophosphoric acid [10], iodine [11], HClO<sub>4</sub>/SiO<sub>2</sub> [12], proline triflate [13], Sr(OTf)<sub>2</sub> [14], H<sub>14</sub>[NaP<sub>5</sub>W<sub>30</sub>O<sub>110</sub>] [15] and ceric ammonium nitrate (CAN) [16]. Nevertheless, in spite of the wide range of applications of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones, most of the reported methods for their preparation are associated with one or more of the following disadvantages: (i) the use of toxic and expensive catalysts, (ii) prolonged reaction times, (iii) moderate yields, (iv) the use of volatile organic solvents, and (v) poor compliance with the green chemistry protocols. Hence, there is highly need to develop novel, efficient and

green protocols and catalysts for the synthesis of the benzoxanthene derivatives.

Ionic liquids (ILs) are defined as pure compounds, consisting only of cations and anions which melt at or below 100 °C [17, 18]. ILs when used in place of classical organic solvents, offers a new and environmentally benign approach toward modern synthetic chemistry. They have interesting advantages such as extremely low vapor pressure, excellent thermal stability, reusability, talent to dissolve many organic and inorganic substrates, and so have been successfully applied in various classical organic chemistry [17-22]. Moreover, in the last decade, ILs, especially acidic ones, have been utilized as efficient catalysts and reagents in organic synthesis [23-30]. For example, protic acidic ionic liquids have been introduced as excellent candidate to replace solid acids and traditional mineral liquid acids like sulfuric acid and hydrochloric acid in catalytic organic reactions [23-30]. Pyrazinium di(hydrogen sulfate) {Py(HSO<sub>4</sub>)<sub>2</sub>} is certainly an interesting, green and inexpensive protic acidic ionic liquid which has been more recently synthesized by our research group, and applied as an efficient catalyst for the preparation of β-acetamido ketones [30]. In fact, Py(HSO<sub>4</sub>)<sub>2</sub> is a solid at room temperature, but it melts at 80-81 °C; thus, according to the definition of ILs [17, 18], it is an ionic liquid (in the mentioned work [30], we have introduced Py(HSO<sub>4</sub>)<sub>2</sub> as solid acid, because the reaction was



Scheme 1

carried out at room temperature, and the catalyst was solid at this temperature).

Multi-component reactions (MCRs) have drawn great interest enjoying an outstanding status in modern organic synthesis and medicinal chemistry because they are one-pot processes bringing together three or more components and show high atom economy and high selectivity. MCRs have several advantages such as synthetic efficiency, simplicity of operation, reduction of isolation and purification steps, and minimization of costs, energy, time, and waste production [31-34].

Having the above points in mind, we report here an efficient, eco-friendly and simple method for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-one derivatives by the one-pot multi-component condensation of dimedone with arylaldehydes and  $\beta$ -naphthol in the presence of ionic liquid pyrazinium di(hydrogen sulfate) {Py(HSO<sub>4</sub>)<sub>2</sub>} as an inexpensive and homogeneous protic acidic catalyst at 100 °C under solvent-free conditions (Scheme 1). Interestingly, our method has none of the above-mentioned disadvantages at all.

## Results and discussion

To establish the optimal reaction conditions, a set of experiments varying amount of the catalyst and temperature were carried out on the one-pot multi-component reaction of dimedone with 4-nitrobenzaldehyde and  $\beta$ -naphthol under solvent-free conditions. The results are summarized in Table 1. As Table 1 indicates, in the absence of Py(HSO<sub>4</sub>)<sub>2</sub>, the corresponding 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-one was obtained in trace yield after 120 min; 5 mol% of the catalyst was

not sufficient to promote the reaction effectively; 10 mol% of it efficiently catalyzed the reaction and gave the product in excellent yield (93%) within relatively short reaction time (25 min); and any excess amount of Py(HSO<sub>4</sub>)<sub>2</sub> didn't lead to increasing the yield and decreasing the reaction time. Furthermore, the product was obtained in moderate yield (58%) at 90 °C in relatively long reaction times (60 min); and higher yield and shorter reaction time were observed when the reaction was performed at 100 °C. Increment the temperature decreased the reaction yield. Then, the optimized amount of the catalyst and the reaction temperature were 10 mol% and 100 °C, respectively.

In another study, to recognize the important role of Py(HSO<sub>4</sub>)<sub>2</sub> in the reaction, the solvent-free condensation of dimedone with  $\beta$ -naphthol and 4-nitrobenzaldehyde was examined in the presence of 10 mol% of the starting materials used for the preparation of the catalyst (i.e. pyrazine and H<sub>2</sub>SO<sub>4</sub>) as well as pyrazinium dichloride, separately. The reaction was carried out at 100 °C and the catalytic results are presented in Table 2. It can be seen that pyrazine, H<sub>2</sub>SO<sub>4</sub> and pyrazinium dichloride afforded low yields of the product in long reaction times; however, Py(HSO<sub>4</sub>)<sub>2</sub> efficiently catalyzed the reaction with high yield and short reaction time.

Afterward, to assess the efficacy and the scope of the method, dimedone was treated with different aromatic aldehydes, having electron-withdrawing substituents, electron-donating substituents as well as halogens, and  $\beta$ -naphthol under the optimized reaction conditions to undergo the reaction smoothly giving the corresponding benzoxanthenes in high yields (79-93%) and in short reaction times (15-45 min) (Table 3). Thus, the method was efficient and general.

**Table 2.** The condensation of dimedone with 4-nitrobenzaldehyde and  $\beta$ -naphthol using Py(HSO<sub>4</sub>)<sub>2</sub>, pyrazine, H<sub>2</sub>SO<sub>4</sub> as well as pyrazinium dichloride under solvent-free conditions at 100 °C.

Entry	Catalyst	Time (min)	Yield <sup>a</sup> (%)
1	Py(HSO <sub>4</sub> ) <sub>2</sub>	25	93
2	Pyrazine	100	16
3	H <sub>2</sub> SO <sub>4</sub>	70	53
4	Pyrazinium dichloride	70	41

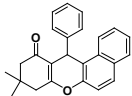
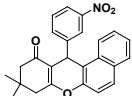
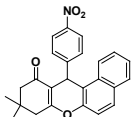
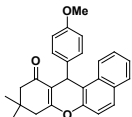
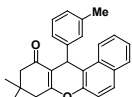
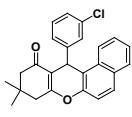
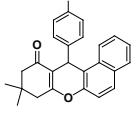
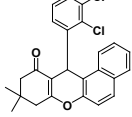
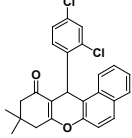
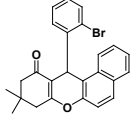
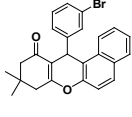
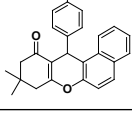
<sup>a</sup>Isolated yield.

**Table 1.** Effect of the catalyst amount and temperature on the reaction of dimedone with 4-nitrobenzaldehyde and  $\beta$ -naphthol in the absence of solvent.

Entry	Catalyst amount (mol %)	Temperature (°C)	Time (min)	Yield <sup>a</sup> (%)
1	—	100	120	Trace
2	5	100	45	79
3	10	100	25	93
4	15	100	25	93
5	10	90	60	58
6	10	110	25	90
7	10	120	20	86

<sup>a</sup>Isolated yield.

**Table 3.** The solvent-free preparation of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-one catalyzed by  $\text{Py}(\text{HSO}_4)_2$  at 100 °C.

Entry	Product	Time (min)	Yield <sup>a</sup> (%)	M.p. °C (lit.)
1		15	89	148-150 (151-153) [8]
2		20	90	169-171 (168-170) [8]
3		25	93	176-178 (178-180) [8]
4		45	79	199-201 (204-205) [8]
5		45	88	178-180 (—) [35]
6		45	85	175-178 (—) [9]
7		30	87	181-183 (180-182) [8]
8		40	89	223-225
9		45	86	183-185 (181-182) [10]
10		20	89	169-171 (—) [9]
11		15	91	159-162 (—) [9]
12		20	84	184-186 (186-187) [11]

<sup>a</sup>Isolated yield.

**Table 4.** Comparison of the results of the reaction of dimedone with benzaldehyde and  $\beta$ -naphthol using our method with those obtained by the reported methods.

Catalyst, conditions	Mol% of Catalyst	Time (min)	Yield (%)	TOF ( $\text{min}^{-1}$ )	Ref.
Py(HSO <sub>4</sub> ) <sub>2</sub> , 100 °C, Solvent-free	10	15	89	0.593	Our method
InCl <sub>3</sub> , 120 °C, Solvent-free	30	30	84	0.093	8
P <sub>2</sub> O <sub>5</sub> , 120 °C, Solvent-free	20	40	76	0.095	8
PTSA, 120 °C, Solvent-free	2	45	88	0.977	9
PTSA, 80 °C, [bmim]BF <sub>4</sub>	10	180	90	0.05	9
Dodecatungstophosphoric acid, 120 °C, Solvent-free	5	70	86	0.245	10
I <sub>2</sub> , 60 °C, Solvent-free	10	75	90	0.12	11
HClO <sub>4</sub> /SiO <sub>2</sub> , 80 °C, Solvent-free	5	72	89	0.25	12
Proline triflate, H <sub>2</sub> O, Reflux	10	300	79	0.026	13
Sr(OTf) <sub>2</sub> , 80 °C, Cl(CH <sub>2</sub> ) <sub>2</sub> Cl	10	300	85	0.028	14
CAN, 120 °C, Solvent-free	5	30	94	0.62	16

To compare the efficacy and the applicability of our method with the previously reported methods for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones, we have tabulated the reaction conditions, the reaction temperatures, times, yields and turn over frequency (TOF) values related to these methods for the condensation between dimedone, benzaldehyde and  $\beta$ -naphthol in Table 4. As Table 4 indicates, our procedure is superior to the reported procedures in most of the terms.

Recyclability of the catalyst was also studied. For this purpose, the condensation of dimedone (0.140 g, 1 mmol) with  $\beta$ -naphthol (0.144 g, 1 mmol) and 4-nitrobenzaldehyde (0.151 g, 1 mmol) using Py(HSO<sub>4</sub>)<sub>2</sub> (0.028 g, 0.1 mmol) was performed five times, and the reaction mixtures were combined and powdered. Afterward, H<sub>2</sub>O (25 mL) was added to the resulting mixture, stirred for 3 min, and filtered (the catalyst is soluble in H<sub>2</sub>O; however, the product is not soluble in this solvent). The filtrate was washed with CHCl<sub>3</sub> (2×20 mL), and the solvent of the aqueous phase was evaporated under powerful vacuum to give recycled Py(HSO<sub>4</sub>)<sub>2</sub> (0.134 g, 96% of the earlier amount). The catalyst was recycled and reused for three times without significant loss of catalytic activity.

## Conclusion

In summary, we have introduced a new protocol for the one-pot multi-component reaction between dimedone, arylaldehydes and  $\beta$ -naphthol using more recently reported ionic liquid Py(HSO<sub>4</sub>)<sub>2</sub> as catalyst. The promising point for the presented methodology are generality, efficiency, simple work-up procedure and purification, easy synthesis and recyclability of the catalyst, short reaction times, clean production of the products

in high yields, low cost and finally agreement with the green chemistry protocols which makes it as an attractive procedure for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones as biologically important compounds.

## Experimental

### General

All chemicals were purchased from Merck or Fluka Chemical Companies. All known compounds were identified by comparison of their melting points and spectral data with those reported in the literature. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The <sup>1</sup>H NMR (300 or 500 MHz) and <sup>13</sup>C NMR (75 or 125 MHz) were run on Bruker Avance DPX, FT-NMR spectrometers ( $\delta$  in ppm). Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

*Preparation of pyrazinium di(hydrogen sulfate) {Py(HSO<sub>4</sub>)<sub>2</sub>}*  
A 25 mL flask charged with sulfuric acid 98% (2.50 g, containing 25 mmol of the acid) was put into an ice-bath, and pyrazine (1.00 g, 12.5 mmol) was added to it in small portions over a period of 5 min. The resulting mixture was stirred for 20 min, and then CHCl<sub>3</sub> (30 mL) was added to it, and stirred for 3 min. The resulting solid was filtered, washed with CHCl<sub>3</sub>, and dried to give Py(HSO<sub>4</sub>)<sub>2</sub> (3.42 g, 99%) as a pale yellow solid [30].

*Pyrazinium di(hydrogen sulfate)*

M.p. 80-81 °C (lit. [30] m.p. 80-81 °C). <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.22 (s, 4H), 10.70 (s, 4H). <sup>13</sup>C NMR (75 MHz, DMSO-d<sub>6</sub>)  $\delta$  141.6.

*General procedure for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-ones*

To a mixture of compounds consisting of dimedone (0.140 g, 1 mmol),  $\beta$ -naphthol (0.144 g, 1 mmol) and arylaldehyde (1 mmol) in a test tube, was added  $\text{Py}(\text{HSO}_4)_2$  (0.028 g, 0.1 mmol). The resulting mixture was firstly stirred magnetically, and after solidification of the reaction mixture with a small rod at 100 °C. After completion of the reaction, the mixture was cooled to room temperature,  $\text{H}_2\text{O}$  (3 mL) was added to it, stirred for 3 min and filtered. The solid residue was recrystallized from aqueous ethanol (90%) to give the pure product.

*9,9-Dimethyl-12-phenyl-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 1*

$^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.84 (s, 3H), 1.02 (s, 3H), 2.09 (d,  $J = 16.2$  Hz, 1H), 2.30 (d,  $J = 16.2$  Hz, 1H), 2.60 (Distorted AB System, 2H), 5.54 (s, 1H), 7.00 (t,  $J = 7.2$  Hz, 1H), 7.14 (t,  $J = 7.8$  Hz, 2H), 7.27 (d,  $J = 7.8$  Hz, 2H), 7.36-7.48 (m, 3H), 7.89 (d,  $J = 8.5$  Hz, 2H), 8.01 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO-d}_6$ )  $\delta$  26.6, 29.2, 32.3, 34.5, 40.7, 50.5, 113.6, 117.6, 117.7, 123.7, 125.4, 126.6, 127.6, 128.5, 128.6, 129.0, 129.5, 131.0, 131.5, 145.3, 147.6, 164.3, 196.2.

*9,9-Dimethyl-12-(3-nitrophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 2:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.84 (s, 3H), 1.04 (s, 3H), 2.13 (d,  $J = 16.0$  Hz, 1H), 2.33 (d,  $J = 16.1$  Hz, 1H), 2.64 (Distorted AB System, 2H), 5.77 (s, 1H), 7.40-7.49 (m, 4H), 7.73 (d,  $J = 7.8$  Hz, 1H), 7.89-7.95 (m, 3H), 8.03 (d,  $J = 8.4$  Hz, 1H), 8.17 (t,  $J = 1.8$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ )  $\delta$  27.0, 29.5, 32.7, 34.8, 41.7, 50.8, 113.2, 116.7, 117.0, 118.0, 122.3, 123.4, 124.0, 126.0, 128.3, 129.5, 130.6, 131.2, 132.0, 135.6, 147.7, 148.1, 148.4, 165.2, 196.8.

*9,9-Dimethyl-12-(4-nitrophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 3:*

$^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.82 (s, 3H), 1.02 (s, 3H), 2.11 (d,  $J = 15.9$  Hz, 1H), 2.32 (d,  $J = 16.2$  Hz, 1H), 2.63 (Distorted AB System, 2H), 5.75 (s, 1H), 7.38-7.48 (m, 4H), 7.72 (d,  $J = 7.5$  Hz, 1H), 7.88-7.94 (m, 3H), 8.02 (d,  $J = 8.4$  Hz, 1H), 8.15 (s, 1H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO-d}_6$ )  $\delta$  26.6, 29.1, 32.4, 34.4, 40.8, 50.4, 112.8, 116.4, 117.6, 121.9, 123.0, 123.6, 125.6, 127.9, 129.1, 130.2, 130.8, 131.5, 135.3, 147.3, 147.7, 148.0, 164.8, 196.4.

*9,9-Dimethyl-12-(4-methoxyphenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 4:*

$^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.87 (s, 3H), 1.05 (s, 3H), 2.13 (d,  $J = 15.4$  Hz, 1H), 2.34 (d,  $J = 16.1$  Hz, 1H), 2.72 (Distorted AB System, 2H), 3.58 (s, 3H), 5.86 (s, 1H), 7.11-7.32 (m, 3H), 7.34-7.52 (m, 4H), 7.90 (s, 2H), 8.03 (s, 1H).

*9,9-Dimethyl-12-(*m*-tolyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 5:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.87 (s, 3H), 1.06 (s, 3H), 2.14 (d,  $J = 16.0$  Hz, 1H), 2.32 (d,  $J = 16.0$  Hz, 1H), 2.62

(Distorted AB System, 2H), 3.36 (s, 3H), 5.59 (s, 1H), 7.12 (t,  $J = 7.8$ , 1H), 7.23-7.25 (m, 2H), 7.41-7.50 (m, 4H), 7.90 (t,  $J = 7.0$  Hz, 2H), 6.96 (d,  $J = 8.4$  Hz, 1H).

*9,9-Dimethyl-12-(3-chlorophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 6:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.88 (s, 3H), 1.03 (s, 3H), 2.11 (d,  $J = 12.8$  Hz, 1H), 2.32 (d,  $J = 16.1$  Hz, 1H), 2.61 (Distorted AB System, 2H), 5.60 (s, 1H), 7.11 (s, 1H), 7.19 (d,  $J = 4.4$  Hz, 2H), 7.36 (s, 1H), 7.40-7.50 (m, 3H), 7.89-8.01 (m, 2H), 8.02 (d,  $J = 8.3$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ )  $\delta$  27.0, 29.6, 32.7, 34.7, 41.0, 50.9, 113.5, 117.3, 118.0, 124.0, 125.9, 127.2, 127.6, 128.2, 128.8, 129.4, 130.3, 130.9, 131.3, 131.9, 133.5, 148.0, 148.1, 165.0, 196.7.

*9,9-Dimethyl-12-(4-chlorophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 7:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.86 (s, 3H), 1.04 (s, 3H), 2.12 (d,  $J = 16.1$  Hz, 1H), 2.32 (d,  $J = 16.1$  Hz, 1H), 2.56 (d,  $J = 17.3$  Hz, 1H), 2.66 (d,  $J = 17.4$  Hz, 1H), 5.58 (s, 1H), 7.23 (d,  $J = 8.4$  Hz, 2H), 7.30 (d,  $J = 8.4$  Hz, 2H), 7.41-7.49 (m, 3H), 7.89-7.92 (m, 2H), 7.99 (d,  $J = 8.3$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ )  $\delta$  27.0, 29.6, 32.7, 32.4, 41.0, 50.9, 113.6, 117.5, 118.0, 124.0, 125.9, 128.1, 128.9, 129.4, 130.2, 130.8, 131.3, 131.6, 131.9, 144.6, 148.0, 164.8, 196.7.

*9,9-Dimethyl-12-(2,3-dichlorophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 8:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.88 (s, 3H), 1.06 (s, 3H), 2.10 (d,  $J = 16.0$  Hz, 1H), 2.32 (d,  $J = 16.0$  Hz, 1H), 2.57 (d,  $J = 17.3$  Hz, 1H), 2.69 (d,  $J = 17.3$  Hz, 1H), 5.86 (s, 1H), 7.16-7.22 (m, 1), 7.27 (s, 1H), 7.36 (d,  $J = 7.7$  Hz, 1H), 7.41-7.43 (m, 2H), 7.50 (t,  $J = 7.8$  Hz, 1H), 7.91 (t,  $J = 6.6$  Hz, 2H), 8.04 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ )  $\delta$  26.7, 29.2, 32.3, 33.6, 50.5, 55.3, 113.6, 113.8, 115.0, 117.6, 118.0, 123.7, 125.4, 127.5, 128.9, 129.4, 129.5, 131.0, 131.5, 137.5, 147.5, 157.8, 163.1, 164.0, 196.4. MS  $m/z$ : 424 ( $\text{M}^+ + 1$ ), 423 ( $\text{M}^+$ ).

*9,9-Dimethyl-12-(2,4-dichlorophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 9:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.89 (s, 3H), 1.05 (s, 3H), 2.09 (d,  $J = 16.0$  Hz, 1H), 2.31 (d,  $J = 16.0$  Hz, 1H), 2.65 (d,  $J = 16.8$  Hz, 1H), 2.67 (d,  $J = 17.3$  Hz, 1H), 5.77 (s, 1H), 7.22-7.28 (m, 2H), 7.37-7.42 (m, 3H), 7.47-7.50 (m, 1H), 7.88-7.91 (m, 2H), 8.03 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-d}_6$ )  $\delta$  27.0, 29.5, 32.5, 32.6, 41.1, 51.0, 118.0, 123.7, 125.9, 127.5, 128.1, 128.3, 129.6, 129.7, 130.5, 131.6, 131.8, 132.5, 133.7, 140.7, 148.2, 165.1, 196.5.

*9,9-Dimethyl-12-(2-bromophenyl)-9,10-dihydro-8H-benzo[*a*]xanthen-11(12H)-one-Table 3, entry 10:*

$^1\text{H}$  NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  0.89 (s, 3H), 1.06 (s, 3H), 2.09 (d,  $J = 16$  Hz, 1H), 2.32 (d,  $J = 16$  Hz, 3H), 2.57 (d,  $J = 17.4$  Hz, 1H), 2.70 (d,  $J = 17.3$  Hz, 1H), 5.76 (s, 1H), 6.97-7.00 (m, 1H), 7.18 (t,  $J = 7.2$  Hz, 1H), 7.22 (s, 1H), 7.41-7.43

(m, 2H), 7.47-7.51 (m, 2H), 7.89-7.92 (m, 2H), 8.20 (d,  $J = 16$  Hz, 1H).

*9,9-Dimethyl-12-(3-bromophenyl)-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one-Table 3, entry 11:*

$^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  0.88 (s, 3H), 1.05 (s, 3H), 2.13 (d,  $J = 16.1$  Hz, 1H), 2.31 (d,  $J = 16.1$  Hz, 1H), 2.62 (Distorted AB System, 2H), 5.52 (s, 1H), 6.85 (d,  $J = 6.2$  Hz, 1H), 7.03-7.07 (m, 2H), 7.11 (s, 1H), 7.40-7.50 (m, 3H), 7.89 (d,  $J = 8.7$  Hz 2H), 8.04 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz, DMSO- $d_6$ )  $\delta$  27.0, 29.6, 32.7, 34.9, 41.1, 51.3, 114.1, 118.0, 118.2, 124.1, 125.8, 126.2, 127.7, 127.9, 128.8, 129.3, 129.5, 129.8, 131.5, 131.9, 137.9, 145.7, 148.0, 164.9, 196.7.

*9,9-Dimethyl-12-(4-bromophenyl)-9,10-dihydro-8H-benzo[a]xanthen-11(12H)-one-Table 3, entry 12:*

$^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  0.86 (s, 3H), 1.04 (s, 3H), 2.12 (d,  $J = 16.0$  Hz, 1H), 2.32 (d,  $J = 16.0$  Hz, 1H), 2.61 (Distorted AB System, 2H), 5.56 (s, 1H), 7.24 (d,  $J = 8.3$  Hz, 2H), 7.36 (d,  $J = 8.3$  Hz, 2H), 7.40-7.49 (m, 3H), 7.90 (t,  $J = 5.0$  Hz 2H), 7.98 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz, DMSO- $d_6$ )  $\delta$  27.1, 29.6, 32.7, 34.5, 41.0, 50.9, 113.5, 117.4, 118.0, 120.1, 124.0, 125.9, 128.1, 129.4, 130.2, 131.2, 131.3, 131.91, 131.96, 145.0, 148.0, 164.8, 196.7.

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