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EFFICIENT SYNTHESIS OF 12-ARYL-8,9,10,12-TETRAHYDROBENZO[a]XANTHEN-11-ONE DERIVATIVES CATALYZED BY *p*-DODECYLBENZENESULFONIC ACID IN AQUEOUS MEDIA UNDER ULTRASOUND IRRADIATION

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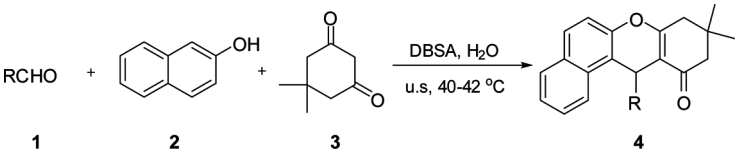
GRAPHICAL ABSTRACT



Abstract *An efficient synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives via the three-component condensation of aromatic aldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione was carried out in 76–93% yields at 40–42 °C using p-dodecylbenzenesulfonic acid as catalyst in aqueous media under ultrasound irradiation.*

Keywords Aqueous media; three-component condensation; ultrasound irradiation; xanthene

INTRODUCTION

Xanthenes and benzoxanthenes are important biologically active heterocyclic compounds that possess antiviral,[1] antibacterial[2] and anti-inflammatory activities.[3] These compounds can be used as dyes,[4,5] as pH-sensitive fluorescent materials,[6] and in laser technology.[7] Synthesis of these compounds via three-component condensation of aldehyde, 2-naphthol, and cyclic 1,3-dicarbonyl compounds was carried out under different conditions, such as solvent-free reaction catalyzed by HBF_4/SiO_2,[8] I_2,[9] para-toluenesulfonic acid (*p*-TSA),[10,11] $InCl_3$, P_2O_5,[12] $Zr(HSO_4)_4$,[13]

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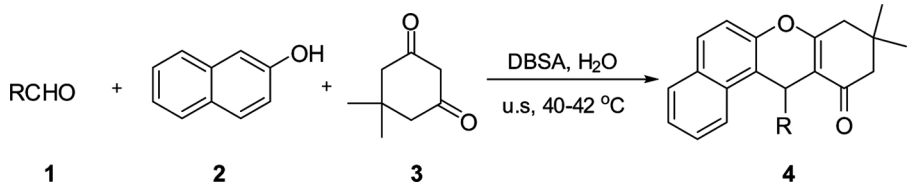

Scheme 1. Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives.

$H_3PW_{12}O_{40}$,[14] cyanuric chloride,[15] $HClO_4$-SiO_2,[16] ceric ammonium nitrate (CAN),[17] and refluxing in 1,2-dichloroethane catalyzed by $Sr(OTf)_2$[18] or $NaHSO_4 \cdot SiO_2$.[19] However, in spite of their potential utility, some of the reported methods suffer from some drawbacks, such as longer reaction time, expensive transition-metal catalyst, or organic solvent.

Organic reactions in aqueous media have attracted increasing interest because of environmental issues and the understanding of biochemical processes. Water, being the cheapest and most nontoxic solvent, is known as a "green" solvent.[20] Many organic reactions can be carried out in water.[21] The condensations of aldehyde, naphthol, and cyclic 1,3-dicarbonyl compounds catalyzed by tetrabutyl ammonium fluoride[22] or praline triflate[23] in refluxing aqueous solution have been reported, but some reactions needed a long reaction time.

p-Dodecylbenzenesulfonic acid (DBSA), as a Brønsted acid–surfactant combined catalyst, acts both as an acid catalyst to activate a substrate and as a surfactant to form stable colloidal dispersion with water-insoluble substrates.[24] This catalyst has been successfully used in many organic reactions.[25]

Ultrasound has been considered a useful protocol in organic synthesis in the past three decades.[26–28] Compared with traditional methods, this procedure is more convenient. A large number of organic reactions can be carried out in greater yield, shorter reaction time, or mild conditions under ultrasound.[29,30] The condensation of arylaldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione catalyzed by *p*-TSA has been reported to give a good results at 70 °C with sonication.[11] Herein, we report a practical and efficient synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a] xanthen-11-one derivatives using DBSA as catalyst in aqueous media under ultrasound irradiation (Scheme 1).

RESULTS AND DISCUSSION

To optimize the reaction conditions, the condensation of benzaldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione was selected as the model under ultrasound irradiation (Table 1).

The effects of the amount of DBSA on the reaction was observed. When the amounts of DBSA were 0.05 mmol, 0.075 mmol and 0.1 mmol, the yields of **4a** were 82% (entry 4), 88% (entry 3) and 93% (entry 2), respectively. Increasing the amount of DBSA to 0.2 mmol, did not improve either the yield or the reaction time compared with 0.1 mmol (entry 1). In the absence of DBSA, three-component condensation was carried out with 11% yield at 40–42 °C in 80 min under ultrasound (entry 5). In the presence of DBSA (0.1 mmol) with the same reaction time and

Table 1. Effect of reaction conditions on the synthesis of **4a** under ultrasound irradiation[a]

Entry	Amount of DBSA (mmol)	Frequency (kHz)	Temp. (°C)	Time (min)	Isolated yield (%)
1	0.2	40	40–42	80	93
2	0.1	40	40–42	80	93
3	0.075	40	40–42	80	88
4	0.05	40	40–42	90	82
5	0	40	40–42	80	11
6	0.1	40	30–33	200	91
7	0.1	25	40–42	80	89
8	0.1	—	40–42	130	85[b]
9	0.1	40	40–42	60	71[c]
10	0.1	40	40–42	120	90[d]
11	0.1	40	40–42	120	91[e]

[a]Substrate: benzaldehyde, 1 mmol; 2-naphthol, 1 mmol; 5,5-dimethyl-1,3-cyclohexanedione, 1.2 mmol; water 2 mL.
[b]Stirring alone without ultrasound.
[c]Solvent-free.
[d]Ethanol as solvent. The product is 3-ethoxy-5,5-dimethylcyclohex-2-enone.
[e]Methanol as solvent. The product is 3-methoxy-5,5-dimethylcyclohex-2-enone.

temperature, **4a** was obtained in 93% yield (entry 2). It is shown that DBSA has a significant effect on the reaction.

As shown in Table 1, the temperature had a significant effect on the reaction time, but the effect on the yield was not obvious. When the reaction was carried out at 30–33 °C, it took 200 min and gave 91% yield (entry 6), but when the temperature was 40–42 °C, the reaction time was shortened to 80 min and the yield was 93% (entry 2).

The effect of frequency of ultrasound irradiation on the reaction was also observed. The yield of **4a** with 40 kHz irradiation for 80 min (entry 2) is better than that with 25 kHz irradiation for 80 min (entry 7). We also did the experiment in the absence of ultrasound; the condensation of benzaldehyde, 2-naphthol and 5,5-dimethyl-1,3-cyclohexanedione was carried out with 85% yield (entry 8) using stirring alone in 130 min. In the presence of ultrasound, the desired product (**4a**) was obtained in 93% yield within 80 min. It is apparent that the reaction can be finished in a shorter reaction time to give better yield under ultrasound irradiation.

We also examined the effect of solvent or solvent-free conditions on the condensation under ultrasound. When the reaction was carried out in ethanol or methanol, the condensation of 5,5-dimethyl-1,3-cyclohexanedione with ethanol or methanol was performed, and no formation of the corresponding title compound was observed. Under solvent-free conditions, **4a** was obtained in 71% yield (Table 1, entry 9).

From these results the optimum reaction conditions were chosen: aldehyde (**1,** 1 mmol), 2-naphthol (**2,** 1 mmol), 5,5-dimethyl-1,3-cyclohexanedione (**3,** 1.2 mmol), DBSA (0.1 mmol), water (2 mL), ultrasound frequency 40 kHz, and reaction temperature 40–42 °C. Using this reaction system, a series of experiments for the syntheses of **4a–o** were carried out under ultrasound at 40–42 °C. The results are summarized in Table 2.

As shown in Table 2, the condensation of aromatic aldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione was carried out with good yields catalyzed by

DBSA in aqueous media under ultrasound irradiation. From these results, we can deduce that the yields are in general similar or greater than those described in the literature.[8–19,22,23] For example, in the previous report,[22] the condensation of 4-chlorobenzaldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione catalyzed by TBAF at refluxing temperature in water for 3.5 h, the yield of **4 h** was 92%, whereas present procedure needed only 100 min to give **4 h** in 92% yield (Table 2, entry h). In the reaction catalyzed by $NaHSO_4 \cdot SiO_2$,[19] the condensation of benzaldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione was carried out with 87% yield under refluxing 1,2-dichloroethane for 4 h, whereas the present procedure offered the target product in 93% yield under ultrasound for 80 min (Table 2, entry a).

To verify the effect of ultrasound irradiation, several reactions were performed by stirring alone under conditions with no ultrasound at 40–42 °C. As shown in Table 2, **4d, 4 h, 4i, 4 l**, and **4n** were obtained in 76%, 82%, 64%, 78%, and 77%, yields within 220 min, 210 min, 120 min, 180 min, and 240 min respectively, whereas under ultrasound irradiation **4d, 4 h, 4i, 4 l**, and **4n** were obtained in 87%, 92%, 79%, 84% and 82% yields within 140 min, 100 min, 60 min, 100 min, and 120 min respectively (Table 2, entries d, h, i, l, and n). It is clear that ultrasound can reduce reaction time and increase the reaction yield.

It is noted that when heterocyclic aldehydes, such as 2-furaldehyde, 2-pyridylaldehyde, 4-pyridylaldehyde or 3-indolealdehyde, were used as substrate, no reactions were observed by thin-layer chrometography (TLC). While cinnamaldehyde was used as substrate, the condensation of cinnamaldehyde and 5,5-dimethyl-1,3-cyclohexanedione took place to obtain 3,3,6,6-tetramethyl-9-(2-phenyl-ethylene)-1,8-dioxo-octahydroxanthene in 83% yield. It is shown that the present method has some limitations for some aliphatic aldehydes and heterocyclic aldehydes. When Meldrum's acid

Table 2. Synthesis of **4a–o** catalyzed by DBSA in aqueous media at 40–42 °C under ultrasound irradiation[a]

Entry	R	Time (min) (stir[b])	Product	Isolated yield (%) (stir[b])	Mp (°C)
a	C_6H_5	80 (130)	**4a**	93 (85)	151–152 (151–153)[12]
b	4-$CH_3C_6H_4$	120	**4b**	93	174–175 (175–176)[9]
c	2-$CH_3OC_6H_4$	120	**4c**	90	165–167 (163–165)[12]
d	4-$CH_3OC_6H_4$	140 (220)	**4d**	87 (76)	212–213 (211–212)[18]
e	4-OH C_6H_4	90	**4e**	81	150–151 (150–151)[19]
f	2-ClC_6H_4	120	**4f**	87	178–179 (179–180)[12]
g	3-ClC_6H_4	130	**4g**	80	178–180 (180–181)[11]
h	4-ClC_6H_4	100 (210)	**4h**	92 (82)	179–181 (180–182)[12]
i	2-HO-3-$CH_3OC_6H_3$	60 (120)	**4i**	79 (64)	212–213 (213–215)[12]
j	4-HO-3-$CH_3OC_6H_3$	110	**4j**	76	166–167 (164–166)[11]
k	3-$NO_2C_6H_4$	100	**4k**	80	169–170 (168–170)[12]
l	4-$NO_2C_6H_4$	100 (180)	**4l**	84 (78)	170–171 (175–176)[9]
m	2,4-$Cl_2C_6H_3$	120	**4m**	82	183–184 (178–180)[12]
n	3,4-$Cl_2C_6H_3$	120 (240)	**4n**	82 (77)	177–178
o	CH_3	240	**4o**	63	110–111

[a]Substrate: aryl aldehyde, 1 mmol; 2-naphthol, 1 mmol; 5,5-dimethyl-1,3-cyclohexanedione, 1.2 mmol; DBSA, 0.1 mmol; H_2O, 2 mL.

[b]Stirring alone without ultrasound.

Table 3. Comparison with the methods in aqueous media reported in literatures[a]

Entry	Catalyst	Time (min)	Temperature (°C)	Yield (%)
1	*p*-DBSA	80	40–42 (ultrasound)	93
2	Tetrabutylammonium fluoride	540	100	99[22]
3	Proline triflate	300	reflux	79[b][23]
4	*p*-TSA	180	70 (ultrasound)	30[11]
5	$Sr(OTf)_2$	300	80	Nr[18]

[a]Condensation of benzaldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione.
[b]Condensation of benzaldehyde, 1-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione.

was used instead of 5,5-dimethyl-1,3-cyclohexanedione, the condensation did not occur at all.

The comparison with other methods in aqueous media reported in literature is shown in Table 3. From these results, we can deduce that the yield is in general similar or better than those described in the literature. Compared with the reported methods, the main advantage of the procedure are greater yield, milder conditions, and shorter reaction time.

CONCLUSION

In conclusion, we have found an efficient procedure for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives via the condensation of aromatic aldehyde, 2-naphthol, and 5,5-dimethyl-1,3-cyclohexanedione catalyzed by DBSA in aqueous media under ultrasound irradiation. The procedure described here is simple, mild, efficient, and environmentally friendly.

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 600 (600-MHz) spectrometer using tetramethylsilane (TMS) as internal standard and $CDCl_3$ as solvent. Mass spectra (MS) were determined on a Bruker Apex Ultra 7.0 T spectrometer. Sonication was performed in a Shanghai Branson-BUG40-06 ultrasonic cleaner (with a frequency of 40 kHz and a nominal power of 250 W). The reaction flask was located in the ultrasonic bath, where the surface of reactants is slightly lower than the level of the water. The reaction temperature was controlled by addition or removal of water from ultrasonic bath.

General Procedure for the Synthesis of 4a–o

A 25-mL Erlenmeyer flask was charged with aldehydes (**1**, 1 mmol), 2-naphthol (**2**, 1 mmol), 5,5-dimethyl-1,3-cyclohexanedione (**3**, 1.2 mmol), DBSA (0.1 mmol), and water (2 mL). The reaction flask was irradiated in the water bath of the ultrasonic cleaner at 40–42 °C (bath temperature; the temperature inside the reactor was also 40–42 °C) for the period of time as indicated in Table 2. The reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with water (10 mL), and the solid was filtered, washed with water, and dried to give the crude

product, which was further purified by column chromatography on silica gel (200–300 mesh) eluted with petroleum ether or a mixture of petroleum ether and ethyl acetate to offer pure product **4a–o**. The authenticity of the product **4n–o** was established by ^{1}H NMR, ^{13}C NMR, and MS; the rest of the known compounds (**4a–m**) were established by ^{1}H NMR and their melting points compared with those reported in the literature.

9,9-Dimethyl-12-phenyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (4a)

White solid. ^{1}H NMR: δ_H 0.95 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.24 (d, $J=$ 16.3 Hz, 1H, CH_2), 2.30 (d, $J=16.3$ Hz, 1H, CH_2), 2.56 (s, 2H, CH_2), 5.70 (s, 1H, CH), 7.03–7.06 (m, 1H, Ph-H), 7.15–7.17 (m, 2H, Ph-H), 7.31–7.34 (m, 4H, Ph-H), 7.40–7.43 (m, 1H, Ph-H), 7.76 (t, $J=9.2$ Hz, 2H, Ph-H), 7.98 (d, $J=8.4$ Hz, 1 H, Ph-H).

9,9-Dimethyl-12-(4-methylphenyl)-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4b)

White solid. ^{1}H NMR: δ_H 0.97 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.24 (d, $J=16.2$ Hz, 1H, CH_2), 2.30 (d, $J=16.2$ Hz, 1H, CH_2), 2.56 (s, 2H, CH_2), 5.66 (s, 1H, CH), 6.96 (d, $J=7.9$ Hz, 2H, Ph-H), 7.21–7.22 (m, 2H, Ph-H), 7.31 (d, $J=8.9$ Hz, 1H, Ph-H), 7.34–7.37 (m, 1H, Ph-H), 7.41–7.44 (m, 1H, Ph-H), 7.74 (d, $J=8.9$ Hz, 1H, Ph-H), 7.76 (d, $J=7.9$ Hz, 1H, Ph-H), 8.0 (d, $J=$ 8.5 Hz, 1H, Ph-H)

12-(2-Methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4c)

White solid. ^{1}H NMR: δ_H 1.00 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.20 (dd, $J=16.2$ Hz, $J=1.0$ Hz, 1H, CH_2), 2.29 (d, $J=16.2$ Hz, 1H, CH_2), 2.55-2.62 (m, 2H, CH_2), 3.94 (s, 3H, CH_3), 5.96 (s, 1H, CH), 6.76–6.81 (m, 2H, Ph-H), 7.02–7.05 (m, 1H, Ph-H), 7.25–7.27 (m, 2H, Ph-H), 7.33–7.35 (m, 1H, Ph-H), 7.41–7.44 (m, 1H, Ph-H), 7.69 (d, $J=8.9$ Hz, 1H, Ph-H), 7.73 (d, $J=7.9$ Hz, 1H, Ph-H), 8.28 (d, $J=8.5$ Hz, 1H, Ph-H).

12-(4-Methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4d)

White solid. ^{1}H NMR: δ_H 0.97 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.24 (d, $J=16.3$ Hz, 1H, CH_2), 2.30 (d, $J=16.3$ Hz, 1H, CH_2), 2.55 (s, 2H, CH_2), 3.68 (s, 3H, CH_3), 5.65 (s, 1H, CH), 6.69–6.71 (m, 2H, Ph-H), 7.23–7.25 (m, 2H, Ph-H), 7.30 (d, $J=8.9$ Hz, 1H, Ph-H), 7.35-7.37 (m, 1H, Ph-H), 7.41-7.44 (m, 1H, Ph-H), 7.74 (d, $J=8.9$ Hz, 1H, Ph-H), 7.76 (d, $J=7.9$ Hz, 1H, Ph-H), 7.98 (d, $J=8.5$ Hz, 1H, Ph-H).

12-(4-Hydroxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4e)

White solid. ^{1}H NMR: δ_H 0.96 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.26 (d, $J = 16.3$ Hz, 1H, CH_2), 2.31 (d, $J = 16.3$ Hz, 1H, CH_2), 2.56 (s, 2H, CH_2), 5.63 (s, 1H, CH), 6.14 (s, 1H, OH), 6.59 (d, $J = 8.6$ Hz, 2H, Ph-H), 7.15–7.43 (m, 5H, Ph-H), 7.74 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.77 (d, $J = 7.9$ Hz, 1H, Ph-H), 7.97 (d, $J = 8.4$ Hz, 1H, Ph-H).

12-(2-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4f)

White solid. ^{1}H NMR: δ_H 1.00 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 2.26 (d, $J = 16.3$ Hz, 1H, CH_2), 2.31 (d, $J = 16.3$ Hz, 1H, CH_2), 2.60 (q, $J = 17.4$ Hz, $J = 3.9$ Hz, 2H, CH_2), 5.99 (s, 1H, CH), 6.97–7.00 (m, 1H, Ph-H), 7.05 (t, $J = 7.1$ Hz, Hz, 1H, Ph-H), 7.26–7.30 (m, 3H, Ph-H), 7.38 (t, $J = 7.2$ Hz, 1H, Ph-H), 7.48 (t, $J = 7.1$ Hz, 1H, Ph-H), 7.75 (t, $J = 9.1$ Hz, 2H, Ph-H), 8.22 (d, $J = 8.5$ Hz, 1H, Ph-H).

12-(3-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4g)

White solid. ^{1}H NMR: δ_H 0.98 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.26 (d, $J = 16.3$ Hz, 1H, CH_2), 2.31 (d, $J = 16.3$ Hz, 1H, CH_2), 2.58 (q, $J = 17.4$ Hz, 2H, CH_2), 5.69 (s, 1H, CH), 7.02–7.04 (m, 1H, Ph-H), 7.11 (t, $J = 7.9$ Hz, 1H, Ph-H), 7.25–7.29 (m, 2H, Ph-H), 7.33 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.38–7.40 (m, 1H, Ph-H), 7.44–7.46 (m, 1H, Ph-H), 7.79 (t, $J = 7.7$ Hz, 2H, Ph-H), 7.92 (d, $J = 8.5$ Hz, Hz, 1H, Ph-H).

12-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4h)

White solid. ^{1}H NMR: δ_H 0.96 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.24 (d, $J = 16.3$ Hz, 1H, CH_2), 2.30 (d, $J = 16.3$ Hz, 1H, CH_2), 2.56 (s, 2H, CH_2), 5.68 (s, 1H, CH), 7.12–7.14 (m, 2H, Ph-H), 7.26–7.28 (m, 2H, Ph-H), 7.31 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.37–7.39 (m, 1H, Ph-H), 7.42–7.44 (m, 1H, Ph-H), 7.77 (t, $J = 8.6$ Hz, 2H, Ph-H), 7.90 (d, $J = 8.5$ Hz, 1H, Ph-H).

12-(2-Hydroxy-3-methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (4i)

White solid. ^{1}H NMR: δ_H 0.99 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.32 (d, $J = 16.5$ Hz, 1H, CH_2), 2.39 (d, $J = 16.3$ Hz, 1H, CH_2), 2.59 (s, 2H, CH_2), 3.85 (s, 3H, CH_3), 5.82 (s, 1H, CH), 6.32 (dd, $J = 7.5$ Hz, $J = 1.3$ Hz, 1H, Ph-H), 6.56–6.61 (m, 2H, Ph-H), 7.26–7.42 (m, 3H, Ph-H), 7.75 (d, $J = 9.2$ Hz, 2H, Ph-H), 7.83 (d, $J = 8.4$ Hz, 1H, Ph-H), 8.67 (s, 1H, OH).

12-(4-Hydroxy-3-methoxyphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (4j)

White solid. ^{1}H NMR: δ_H 0.98 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.26 (d, $J = 16.3$ Hz, 1H, CH_2), 2.30 (d, $J = 16.3$ Hz, 1H, CH_2), 2.55 (s, 2H, CH_2), 3.82 (s, 3H, CH_3), 5.44 (s, 1H, OH), 5.64 (s, 1H, CH), 6.63–6.68 (m, 2H, Ph-H), 7.00 (d, $J = 1.9$ Hz, 1H, Ph-H), 7.31 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.36-7.39 (m, 1H, Ph-H), 7.42–7.44 (m, 1H, Ph-H), 7.75 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.78 (d, $J = 7.6$ Hz, 1H, Ph-H), 7.98 (d, $J = 8.3$ Hz, 1H, Ph-H).

9,9-Dimethyl-12-(3-nitrophenyl)-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4k)

White solid. ^{1}H NMR: δ_H 0.95 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.24 (d, $J = 16.3$ Hz, 1H, CH_2), 2.33 (d, $J = 16.3$ Hz, 1H, CH_2), 2.61 (s, 2H, CH_2), 5.82 (s, 1H, CH), 7.35–7.46 (m, 4H, Ph-H), 7.79–7.82 (m, 3H, Ph-H), 7.86 (d, $J = 8.2$ Hz, 1H, Ph-H), 7.92–7.94 (m, 1H, Ph-H), 8.11 (s, 1H, Ph-H).

9,9-Dimethyl-12-(4-nitrophenyl)-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4l)

White solid. ^{1}H NMR: δ_H 0.94 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.24 (d, $J = 16.3$ Hz, 1H, CH_2), 2.32 (d, $J = 16.3$ Hz, 1H, CH_2), 2.59 (q, $J = 17.6$ Hz, $J = 3.8$ Hz, 2H, CH_2), 5.81 (s, 1H, CH), 7.35 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.38–7.41 (m, 1H, Ph-H), 7.42–7.45 (m, 1H, Ph-H), 7.50–7.52 (m, 2H, Ph-H), 7.79–7.83 (m, 3H, Ph-H), 8.02–8.04 (m, 2H, Ph-H)

12-(2,4-Dichlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4m)

White solid. ^{1}H NMR δ_H 1.00 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.22 (d, $J = 16.3$ Hz, 1H, CH_2), 2.31 (d, $J = 16.3$ Hz, 1H, CH_2), 2.60 (q, $J = 17.4$ Hz, $J = 7.26$ Hz, 2H, CH_2), 5.93 (s, 1H, CH), 7.03 (dd, $J = 8.4$ Hz, $J = 1.8$ Hz, 1H, Ph-H), 7.21–7.28 (m, 3H, Ph-H), 7.39 (t, $J = 7.3$ Hz, 1H, Ph-H), 7.48 (t, $J = 7.2$ Hz, Hz, 1H, Ph-H), 7.75 (t, $J = 8.9$ Hz, 2H, Ph-H), 8.12 (d, $J = 8.5$ Hz, 1H, Ph-H)

12-(3,4-Dichlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one (4n)

White solid. ^{1}H NMR: δ_H: 0.98 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.26 (d, $J = 16.3$ Hz, 1H, CH_2), 2.31 (d, $J = 16.3$ Hz, 1H, CH_2), 2.58 (s, 2H, CH_2), 5.67 (s, 1H, CH), 7.21–7.25 (m, 2H, Ph-H), 7.33 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.37 (s, 1H, Ph-H), 7.39–7.42 (m, 1H, Ph-H), 7.44–7.47 (m, 1H, Ph-H), 7.80 (t, $J = 6.5$ Hz, 2H, Ph-H), 7.86 (d, $J = 8.5$ Hz, 1H, Ph-H); ^{13}C NMR: δ_c 196.74, 164.30, 147.81, 144.94, 132.29, 131.57, 131.10, 130.31, 130.15, 129.41, 128.60, 128.01, 127.31, 125.16, 123.29, 117.10, 116.34, 113.36, 50.84, 41.41, 34.11, 32.29, 29.22, 27.25 ppm; m/z (ESI): 423 $[M]^+$.

12-Methyl-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one (4o)

White solid. ^{1}H NMR δ_H: 1.14 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.37 (d, $J = 6.6$ Hz, 3H, CH_3), 2.36 (d, $J = 3.0$ Hz, 2H, CH_2), 2.51 (s, 2H, CH_2), 4.58 (q, $J = 6.6$ Hz, $J = 6.6$ Hz, 1H, CH), 7.19 (d, $J = 8.8$ Hz, 1H, Ph-H), 7.43 (t, $J = 7.5$ Hz, 1H, Ph-H), 7.54 (t, $J = 7.6$ Hz, 1H, Ph-H), 7.69 (d, $J = 8.8$ Hz,1H, Ph-H), 7.80 (d, $J = 8.1$ Hz 1H, Ph-H), 8.08 (d, $J = 8.5$ Hz 1H, Ph-H); ^{13}C NMR: δ_c 197.49, 164.94, 147.32, 131.43, 131.17, 128.59, 128.03, 126.84, 124.81, 123.05, 110.99, 117.07, 114.65, 51.04, 41.36, 32.23, 29.47, 27.19, 23.37, 23.00 ppm; m/z (ESI): 315 $[M+Na]^+$

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REFERENCES

1. Lambert, R. W.; Martin, J. A.; Merrett, J. H.; Parkes, E. B. K.; Thomas, G. J. Preparation of pyrimidine nucleosides as thymidine kinase inhibitors and virucides. PCT Int. Appl. WO9706178, 1997.
2. Hideo, T.; Teruomi, J. [1]Benzopyrano[2,3-b]xanthene derivatives. Jpn. Patent 56005480, 1981.
3. Poupelin, J. P.; Saint-Ruf, G.; Foussard-Blanpin, O.; Marcisse, G.; Uchida-Ernouf, G.; Lacroix, R. Synthesis and anti-inflammatory properties of bis(2-hydroxy-1-naphthyl) methane derivatives. *Eur. J. Med. Chem.* **1978**, *13*, 67–71.
4. Banerjee, A.; Mukherjee, A. K. Chemical aspects of santalin as a histological stain. *Stain Technol.* **1981**, *56*, 83–85.
5. Menchen, S. M.; Benson, S. C.; Lam, J. Y. L.; Zhen, W.; Sun, D.; Rosenblum, B. B.; Khan, S. H.; Taing, M. Sulfonated diarylrhodamine dyes for labeling polynucleotides. U.S. Patent 6583168, 2003.
6. Knight, C. G.; Stephens, T. Xanthene-dye-labelled phosphatidylethanolamines as probes of interfacial pH: Studies in phospholipid vesicles. *Biochem. J.* **1989**, *258*, 683–687.
7. Ahmad, M.; King, T. A.; Ko, D.-K.; Cha, B. H.; Lee, J. Performance and photostability of xanthene and pyrromethene laser dyes in sol-gel phases. *J. Phys. D: Appl. Phys.* **2002**, *35*, 1473–1476.
8. Zhang, Z. H.; Wang, H. J.; Ren, X. Q.; Zhang, Y. Y. A facile and efficient method for synthesis of xanthone derivatives catalyzed by HBF_4/SiO_2 under solvent-free conditions. *Monatsh. Chem.* **2009**, *140*, 1481–1483.
9. Wang, R. Z.; Zhang, L. F.; Cui, Z. S. Iodine-catalyzed synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives via multicomponent reaction. *Synth. Commun.* **2009**, *39*, 2101–2107.
10. Khurana, J. M.; Magoo, D. *p*-TSA-catalyzed one-pot synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones in ionic liquid and neat conditions. *Tetrahedron Lett.* **2009**, *50*, 4777–4780.
11. Li, J. J.; Li, J.; Fang, J.; Su, W. K. Efficient one-pot condensation of β-naphthol, aldehydes and cyclic 1,3-dicarbonyl compounds catalyzed by *p*-TSA under solvent-free and sonication conditions. *Synth. Commun.* **2010**, *40*, 1029–1039.

12. Nandi, G. C.; Samai, S.; Kumar, R.; Singh, M. S. An efficient one-pot synthesis of tetrahydrobenzo[a]xanthene-11-one and diazabenzo[a]anthracene-9,11-dione derivatives under solvent-free condition. *Tetrahedron* **2009**, *65*, 7129–7134.
13. Foroughifar, N.; Mobinikhaledi, A.; Moghanian, H. A catalytic and green procedure for synthesis of 12-aryl- or 12-alkyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one derivatives under solvent-free conditions. *Int. J. Green Nanotechnol: Phys. Chem.* **2009**, *1*, 57–63.
14. Wang, H. J.; Ren, X. Q.; Zhang, Y. Y.; Zhang, Z. H. Synthesis of 12-aryl or 12-alkyl-8,9, 10,12-tetrahydrobenzo[*a*]xanthen-11-one derivatives catalyzed by dodecatungstophosphoric acid. *J. Braz. Chem. Soc.* **2009**, *20*, 1939–1943.
15. Zhang, Z. H.; Zhang, P.; Yang, S. H.; Wang, H. J.; Deng, J. Multicomponent, solvent-free synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]-xanthen-11-one derivatives catalysed by cyanuric chloride. *J. Chem. Sci.* **2010**, *122*, 427–432.
16. Mo, L. P.; Chen, H. L. One-pot, three-component condensation of aldehydes, 2-naphthol, and 1,3-dicarbonyl compounds. *J. Chin. Chem. Soc.* **2010**, *57*, 157–161.
17. Atul, K.; Siddharth, S.; Ram, A. M.; Jayant, S. Diversity-oriented synthesis of benzoxanthene and benzochromene libraries via one-pot, three-component reactions and their anti-proliferative activity. *J. Comb. Chem.* **2010**, *12*, 20–24.
18. Li, J. J.; Tang, W. Y.; Lu, L. M.; Su, W. K. Strontium triflate catalyzed one-pot condensation of β-naphthol, aldehydes and cyclic 1,3-dicarbonyl compounds. *Tetrahedron Lett.* **2008**, *49*, 7117–7120.
19. Das, B.; Laxminarayana, K.; Krishnaiah, M.; Srinivas, Y. An efficient and convenient protocol for the synthesis of novel 12-aryl- or 12-alkyl-8,9,10,12-tetrahydrobenzo[*a*]-xanthen-11-one derivatives. *Synlett* **2007**, 3107–3112.
20. Odinets, I. L.; Matveeva, E. V. Ionic liquids and water as "green" solvents in organophosphorus synthesis. *Curr. Org. Chem.* **2010**, *14*, 1171–1184.
21. Li, C. J. Organic reactions in aqueous media with a focus on carbon–carbon bond formations: A decade update. *Chem. Rev.* **2005**, *105*, 3095–3165.
22. Gao, S. J.; Tsai, C. H.; Yao, C. F. A simple and green approach for the synthesis of tetrahydrobenzo[a]-xanthen-11-one derivatives using tetrabutyl ammonium fluoride in water. *Synlett* **2009**, 949–954.
23. Li, J. J.; Lu, L. M.; Su, W. K. A new strategy for the synthesis of benzoxanthenes catalyzed by praline triflate in water. *Tetrahedron Lett.* **2010**, *51*, 2434–2437.
24. Manabe, K.; Kobayashi, S. Mannich-type reactions of aldehydes, amines, and ketones in a colloidal dispersion system created by a Brønsted acid–surfactant-combined catalyst in water. *Org. Lett.* **1999**, *1*, 1965–1967.
25. Manabe, K.; Mori, Y.; Kobayashi, S. Three-component carbon–carbon bond-forming reactions catalyzed by a Brønsted acid–surfactant-combined catalyst in water. *Tetrahedron* **2001**, *57*, 2537–2544.
26. Luche, J. L. *Synthetic Organic Sonochemistry*; Plenum Press: New York, 1998.
27. Li, J. T.; Han, J. F.; Yang, J. H.; Li, T. S. An efficient synthesis of 3,4-dihydropyrimidin-2-ones catalyzed by NH_2SO_3H under ultrasound irradiation. *Ultrason. Sonochem.* **2003**, *10*, 119–122.
28. Mcnulty, J.; Steere, J. A.; Wolf, S. The ultrasound promoted Knoevenagel condensation of aromatic aldehydes. *Tetrahedron Lett.* **1998**, *39*, 8013–8016.
29. Li, J. T.; Wang, S. X.; Chen, G. F.; Li, T. S. Some applications of ultrasound irradiation in organic synthesis. *Curr. Org. Synth.* **2005**, *2*, 415–436.
30. Ratoarinoro, N.; Wilhelm, A. M.; Berlan, J.; Delmas, H. Effects of ultrasound emitter type and power on a heterogeneous reaction. *Chem. Eng. J.* **1992**, *50*, 27–31.