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ORIGINAL PAPER

Microwave-assisted and scandium triflate catalyzed synthesis of tetrahydrobenzo[*a*]xanthen-11-ones

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Abstract Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-ones was achieved by one-pot condensation of *β*-naphthol, substituted benzaldehydes, and 1,3-dicarbonyl compounds catalyzed by $Sc(OTf)_3$ under microwave irradiation in excellent isolated yields. The catalyst was recycled up to four cycles with no appreciable loss in catalytic activity. The compounds were evaluated for Src kinase activity and anticancer activity.

Keywords Lewis acids · Multi-component reaction · Microwave-assisted synthesis · Solvent-free · Anticancer · Src kinase activity

Introduction

Xanthenes are important oxygen-containing heterocyclic molecules. Xanthenes and their derivatives exhibit a diverse array of biological and pharmacological properties, such as antiviral, antifungal, antibacterial, anti-inflammatory, and anticancer activities [1–3]. They have also been used as dyes, fluorescent materials to monitor changes in intracellular pH and visibility of bimolecular assemblies [4, 5], and in laser technology [6]. As a result of their wide spectrum of applications, development of novel synthetic methods for these heterocyclic compounds has received considerable interest in organic chemistry. Several methods have been reported for the synthesis of xanthenes [7–9]; however, there are only few methods available for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-ones using tetrabutylammonium fluoride (TBAF) and tetradecyltrimethylammonium bromide (TTAB) [10, 11], $NaHSO_4{\cdot}SiO_2$ [12], strontium triflate [13], $H_3PW_{12}O_{40}$ [14], *p*-toluenesulfonic acid (*p*-TSA) under solvent-free conditions and in [bmim][BF_4] [15, 16], I_2 [17], NH_2SO_3H [18], cyanuric chloride [19], HBF_4/SiO_2 [20], and proline triflate [21] as catalysts. Many of the reported methods for the synthesis of these heterocyclic compounds involve the use of toxic chemicals, require stoichiometric amounts of catalysts or longer reaction times, and afford products in low yields. Thus, it is still desirable to develop an efficient and convenient method in terms of operational simplicity and economical viability for the synthesis of tetrahydrobenzo[*a*]xanthen-11-one derivatives.

Microwave-assisted organic synthesis offers many advantages including faster and cleaner reactions, high product yields, and operational simplicity [22–29]. Several methods have been developed for performing reactions with microwave irradiation in solution and under solvent-free conditions [30–33]. The use of multi-component reactions (MCRs) has been shown to be remarkably successful in generating molecular complexity in a single pot with high selectivity and atom economy. Recently rare earth metal triflates have emerged as Lewis acid catalysts, and have been used in various organic transformations because of their low toxicity, high stability, and resistance to water [34–36].

MCRs consist of two or more synthetic steps, which are performed without isolation of intermediates. MCR

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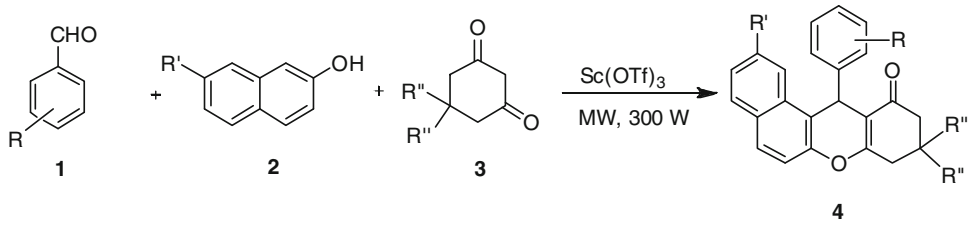
Scheme 1



strategies offer significant advantages over conventional linear-type syntheses such as reduction in overall reaction time and cost by saving energy and raw materials [37–41]. Thus, the development of new MCRs is very important in organic synthesis. In this regard the *ortho*-quinone methides (*o*-QMs) are useful intermediates in many tandem processes [42]; *o*-QMs can be generated by reaction of naphthols or phenols with different aldehydes under basic or acidic conditions [43, 44].

In continuation of our work on metal triflate catalyzed generation of *o*-QMs and their application in organic transformations [45] and our interest in the MCR synthesis of xanthenes, we herein report the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one derivatives by condensation of 2-naphthol, aldehydes, and 1,3-dicarbonyl compounds catalyzed by $Sc(OTf)_3$ under microwave irradiation (Scheme 1).

Results and discussion

Initially we examined the model reaction of 4-chlorobenzaldehyde (**1a**), 2-naphthol (**2**), and dimedone (**3**) using $Sc(OTf)_3$ as catalyst under different reaction conditions (Table 1). The reaction was very slow and gave only 30–60% yield of the desired 12-(4-chlorophenyl)-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one (**4a**) in different solvents such as acetonitrile, toluene, chloroform, dimethylformamide (DMF), or polyethylene glycol (PEG) under reflux conditions, whereas in water the formation of product was not observed. Encouraged by reported efficient rate enhancements by microwave irradiation [27–29], we next investigated this reaction under microwave irradiation (MW). After several attempts, it was observed that microwave irradiation for 5 min at 300 W with internal temperature of 120 °C is optimal in terms of efficient condensation to afford the desired product **4a** in a higher yield. Subsequently, the condensation was attempted with different metal triflate catalysts but $Sc(OTf)_3$ (20 mol%) was found to give the highest yield of the product thereby making it the most suitable catalyst for the reaction. After establishing $Sc(OTf)_3$ as an optimal catalyst in the one-pot reaction, we next studied the effect of catalyst loading. Thus the model reaction was carried out with varying amounts of catalysts. As shown in Table 1, decreasing the amount of $Sc(OTf)_3$ from 20 to 10 mol% decreased the yield of **4a** to 60%, whereas increasing the catalyst to 30 mol% did not significantly increase yield of **4a**. Thus, 20 mol% of $Sc(OTf)_3$ was selected as the optimum amount for further studies.

Table 1 Synthesis of 12-(4-chlorophenyl)-8,9,10,12-tetrahydro-9,9-dimethyl-11*H*-benzo[*a*]xanthen-11-one (**4a**) under different conditions

Entry	Catalyst	Catalyst/mol%	Solvent/method	Time/min	Yield/%[a]
1	$Sc(OTf)_3$	20	CH_3CN	600	43[b]
2	$Sc(OTf)_3$	20	Toluene	600	35[b]
3	$Sc(OTf)_3$	20	DMF	600	30[b]
4	$Sc(OTf)_3$	20	$CHCl_3$	600	55[b]
5	$Sc(OTf)_3$	20	PEG-400	600	60[b]
6	$Sc(OTf)_3$	20	H_2O	600	–[b,c]
7	$Sc(OTf)_3$	20	Neat/MW	5	83
8	$Sc(OTf)_3$	30	Neat/MW	5	85
9	$Sc(OTf)_3$	10	Neat/MW	5	60
10	$Zn(OTf)_3$	20	Neat/MW	5	56
11	$Yb(OTf)_3$	20	Neat/MW	5	50
12	$Y(OTf)_3$	20	Neat/MW	10	40
13	$Ce(OTf)_3$	20	Neat/MW	8	60
14	$La(OTf)_3$	20	Neat/MW	10	10
15	$Nd(OTf)_3$	20	Neat/MW	12	10
16	$Eu(OTf)_3$	20	Neat/MW	12	–[c]

Conditions: **1**, **2**, **3** (1 mmol each)

[a] Isolated yield

[b] Reaction carried out under reflux

[c] No reaction

To generalize the suitability of this protocol, the reaction was extended to different substituted naphthols, aromatic aldehydes, and 1,3-diones (Table 2). Three substrates (**1**–**3**) as solids were first dissolved in 1 cm^3 ethyl acetate and mixed well before microwave irradiation. The reactions proceeded smoothly with excellent yields (65–97%) for substituted aldehydes with both electron-withdrawing and electron-donating groups. All products were characterized by ^1H, ^{13}C NMR, and high-resolution time-of-flight electrospray mass spectrometry (ESI-TOF) (see Electronic supplementary information). In the case of aldehydes with electron-donating groups a minor amount (5–15%) of

Table 2 Synthesis of 12-aryl-8,9,10,12-tetrahydro-11*H*-benzo[*a*]-xanthen-11-ones catalyzed by $Sc(OTf)_3$ under microwave irradiation

Comp.	R	R′	R″	Yield/%[a]	M.p. (Lit. m.p.)/°C
4a	4-Cl	H	CH_3	83	180–182 (182–183 [6])
4b	H	H	CH_3	76	154–155 (152–153 [6])
4c	4-CH_3	H	CH_3	79	177–179 (175–176 [9])
4d	4-OCH_3	H	CH_3	71	207–209 (211–212 [6])
4e	3-Cl	H	CH_3	90	181–182 (180–181 [15])
4f	3-OCH_3	H	CH_3	65	199–201 (177–178 [21])
4g	4-NO_2	H	CH_3	96	179–180 (183–185 [6])
4h	3-NO_2	H	CH_3	97	170–171 (169–170 [14])
4i	4-Cl	OCH_3	CH_3	95	218–220
4j	H	OCH_3	CH_3	90	152–153
4k	4–CH_3	OCH_3	CH_3	87	181–182
4l	4-OCH_3	OCH_3	CH_3	72	166–167
4m	3-Cl	OCH_3	CH_3	73	137–139
4n	3-OCH_3	OCH_3	CH_3	88	213–214
4o	4-Cl	H	H	93	207–209 (205–206 [9])
4p	4-NO_2	OCH_3	CH_3	83	229–231
4q	3-NO_2	OCH_3	CH_3	85	195–196
4r	4-NO_2	H	H	88	241–243 (246–247 [6])
4s	3-OCH_3	H	H	78	221–223 (205–206 [21])

Conditions: **1**, **2**, **3** (1 mmol each), $Sc(OTf)_3$ (10 mol%), MW irradiation at 300 W

[a] Isolated yield

uncyclized dihydroxy compound was obtained. The yields of tetrahydrobenzo[*a*]xanthen-11-ones **4** were higher from aldehydes with electron-withdrawing groups as compared to the corresponding aldehydes with electron-donating groups.

A probable mechanistic rationalization of the $Sc(OTf)_3$ catalyzed reaction is shown in Scheme 2. It is expected that the reaction proceeds via an *o*-QM intermediate which is generated by the nucleophilic attack of 2-naphthol on the aldehyde followed by dehydration. In the next step, the enolic form of dimedone attacks undergoes conjugate addition to the *o*-QM to generate a dihydroxy intermediate. Finally, the dihydroxy compound gives the tetrahydrobenzo[*a*]xanthen-11-one by elimination of a water molecule. Formation of dihydroxy compounds as a minor product in the case of 4-methoxybenzaldehyde further supports the mechanism.

Table 3 Recycling and reuse of $Sc(OTf)_3$for synthesis of **4a**

Run	1	2	3	4
Yield/%[a]	83	82	80	81

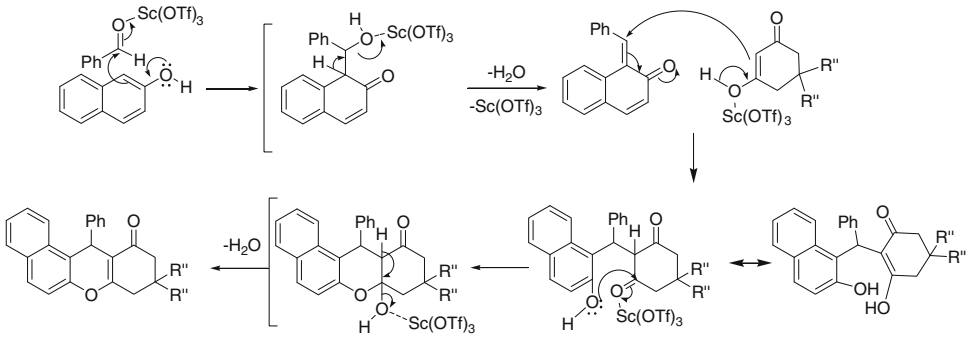
[a] Isolated yield

We studied the recyclability of catalysts for the synthesis of **4a**. After completion of the reaction and extraction of product with ethyl acetate; the aqueous layer was concentrated and the recovered catalyst was directly used for the next cycle. It is noteworthy that $Sc(OTf)_3$ was recovered and recycled conveniently up to four times without much loss in its catalytic activity (Table 3).

Although the main objective was to synthesize novel xanthene derivatives using one-pot microwave-assisted synthesis, we investigated the biological activities of the compounds. Xanthenes have been reported to demonstrate anticancer activity. The effect of compounds **4a**–**4s** (at a concentration of 50 μM) on the cell proliferation of cancer cells was evaluated against the colon adenocarcinoma (HT-29) cell line. Compounds **4c**, **4h**, **4j**, and **4s** inhibited the proliferation HT-29 cells only by 23–26%. Other compounds showed minimal inhibitory activities. Furthermore, among all the compounds **4s** minimally inhibited the Src kinase activity by 11%. It is postulated that these compounds could not fit into ATP binding site of Src kinase appropriately, because of their bulky nature and/or suboptimal bonding interactions. The data suggest that further optimization of these compounds is required to generate compounds with higher anticancer and Src kinase inhibitory activities, and/or these compounds should be screened for other previously reported biological activities for xanthenes [2, 3].

In conclusion, we have developed an efficient and greener method for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-ones catalyzed by $Sc(OTf)_3$ under microwave irradiation and evaluated their Src kinase

Scheme 2



inhibition and anticancer activities. A simple reaction procedure, shorter reaction time, high isolated yields of the pure products, tolerance of a wide range of functional groups, use of an environmentally safer catalyst, and recycling of the catalyst are the advantages of this protocol.

Experimental

Melting points were determined in open capillary tubes on an MPA120 automated melting point apparatus. IR spectra were recorded with a JASCO IR-Report-100. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Heaven 11400 (400 MHz) spectrometer using TMS as internal standard and $CDCl_3$ as solvent and the chemical shifts are expressed in ppm. All reactions were carried out in a CEM microwave digester MARS 5^{TM} as a multi-mode microwave oven at 120 °C and 300 W using microwave reaction vessel HP 500. All metal triflates, aldehydes, and 1,3-dicarbonyl compounds were purchased from Sigma–Aldrich. The products were purified by column chromatography using silica gel (60–120 mesh, S.D. Fine, India).

General procedure for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones ***4a–4s***

2-Naphthol (144 mg, 1.0 mmol), aldehyde (1.0 mmol), 140 mg dimedone (1.0 mmol), and $Sc(OTf)_3$ (10 mol%) were taken in a Teflon reaction vessel, mixed well, and irradiated in the microwave at 300-W power, programmed at 120 °C for 5 min; the irradiation continued at this temperature for 5–10 min and the mixture cooled for 20 min. Afterwards the reaction mixture was cooled to room temperature, 5 cm^3 of water was added, and extracted with ethyl acetate (2 × 20 cm^3). The organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was recrystallized with hot ethanol or purified by column chromatography on silica gel (100–200 mesh) using ethyl acetate and hexane as eluent. All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and ESI-TOF.

12-(4-Chlorophenyl)-8,9,10,12-tetrahydro-2-methoxy-9,9-dimethyl-11H-benzo[a]xanthen-11-one (**4i**, $C_{26}H_{23}ClO_3$)
$R_f = 0.52$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, $J = 6.3$ Hz, 2H), 7.31 (d, $J = 6.8$ Hz, 2H), 7.16 (d, $J = 5.6$ Hz, 3H), 7.04 (d, $J = 6.4$ Hz, 1H), 5.57 (s, 1H), 3.83 (s, 3H), 2.59 (s, 2H), 2.42–2.18 (m, 2H), 1.14 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.15$, 163.58, 142.76, 131.02, 129.31, 128.61, 128.00, 127.91, 126.64, 124.54, 122.97, 116.56, 50.37, 40.90, 33.69, 31.78, 28.82, 26.65 ppm; MS (ESI): calcd for $C_{26}H_{23}ClO_3$ 418.1336, found $m/z = 419.0346$ $[M + H]^+$.

8,9,10,12-Tetrahydro-2-methoxy-9,9-dimethyl-12-phenyl-11H-benzo[a]xanthen-11-one (**4j**, $C_{26}H_{24}O_3$)
$R_f = 0.51$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.61 (m, 2H), 7.36 (d, $J = 7.5$ Hz, 2H), 7.26–7.21 (m, 1H), 7.17 (t, $J = 8.2$ Hz, 3H), 7.05 (t, $J = 7.3$ Hz, 1H), 7.00 (dd, $J = 8.9$, 2.2 Hz, 1H), 5.57 (s, 1H), 3.80 (s, 3H), 2.56 (s, 2H), 2.28 (d, $J = 16.3$ Hz, 1H), 2.24 (d, $J = 16.3$ Hz, 1H), 1.11 (s, 3H), 0.96 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.55$, 163.37, 157.93, 147.67, 144.23, 129.33, 128.09, 127.99, 127.72, 125.78, 116.91, 116.26, 113.94, 113.65, 102.11, 54.73, 50.40, 40.92, 34.73, 31.78, 28.81, 26.70 ppm; MS (ESI): calcd for $C_{26}H_{24}O_3$ 384.1725, found $m/z = 385.1720$ $[M + H]^+$.

8,9,10,12-Tetrahydro-2-methoxy-12-(4-methylphenyl)-9,9-dimethyl-11H-benzo[a]xanthen-11-one (**4k**, $C_{27}H_{26}O_3$)
$R_f = 0.52$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57–7.54 (m, 2H), 7.17–7.10 (m, 3H), 7.08–7.06 (m, 1H), 6.91–6.81 (m, 3H), 5.45 (s, 1H), 3.74 (s, 3H), 2.47 (s, 2H), 2.21 (d, $J = 16.3$ Hz, 1H), 2.14 (d, $J = 16.3$ Hz, 1H), 2.11 (s, 3H), 1.03 (s, 3H), 0.89 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 196.98$, 163.70, 158.38, 148.08, 141.79, 135.67, 132.83, 128.88, 128.32, 126.69, 117.33, 116.92, 114.40, 114.25, 102.62, 55.20, 50.91, 41.41, 34.80, 32.26, 29.26, 27.27, 20.97 ppm; MS (ESI): calcd for $C_{26}H_{24}O_3$ 398.1882, found $m/z = 399.0477$ $[M + H]^+$, 797.0876 $[2M + H]^+$.

8,9,10,12-Tetrahydro-2-methoxy-12-(4-methoxyphenyl)-9,9-dimethyl-11H-benzo[a]xanthen-11-one
(**4l**, $C_{27}H_{26}O_4$)
$R_f = 0.52$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, $J = 3.2$ Hz, 1H), 7.64 (d, $J = 3.3$ Hz, 1H), 7.30–7.24 (m, 2H), 7.23 (d, $J = 2.0$ Hz, 1H), 7.15 (d, $J = 8.8$ Hz, 1H), 7.00 (dd, $J = 8.9$, 2.3 Hz, 1H), 6.71 (d, $J = 8.6$ Hz, 2H), 5.52 (s, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 2.56 (s, 2H), 2.29 (d, $J = 16.3$ Hz, 1H), 2.25 (d, $J = 16.3$ Hz, 1H), 1.12 (s, 3H), 0.98 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.67$, 163.18, 157.89, 147.62, 136.62, 129.32, 128.99, 127.87, 126.21, 116.84, 113.94, 113.06, 102.15, 54.73, 54.60, 50.43, 40.91, 33.81, 31.79, 28.80, 26.74 ppm; MS (ESI): calcd for $C_{27}H_{26}O_4$ 414.1831, found $m/z = 415.1843$ $[M + H]^+$.

12-(3-Chlorophenyl)-8,9,10,12-tetrahydro-2-methoxy-9,9-dimethyl-11H-benzo[a]xanthen-11-one
(**4m**, $C_{26}H_{23}ClO_3$)
$R_f = 0.53$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (t, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 7.11 (t,

$J = 7.7$ Hz, 1H), 7.07–6.95 (m, 2H), 5.55 (s, 1H), 3.82 (s, 3H), 2.57 (s, 2H), 2.30 (d, $J = 16.3$ Hz, 1H), 2.26 (d, $J = 16.3$ Hz, 1H), 1.12 (s, 3H), 0.98 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.70$, 163.95, 158.33, 147.95, 146.47, 129.73, 129.19, 128.47, 126.67, 126.39, 117.30, 115.67, 114.26, 113.31, 102.17, 55.01, 50.62, 41.17, 34.83, 32.08, 29.03, 27.03 ppm; MS (ESI): calcd for $C_{26}H_{23}ClO_3$ 418.1336, found $m/z = 419.0320$ $[M + H]^+$.

8,9,10,12-Tetrahydro-2-methoxy-12-(3-methoxyphenyl)-9,9-dimethyl-11H-benzo[a]xanthen-11-one
(**4n**, $C_{27}H_{26}O_4$)
$R_f = 0.51$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, $J = 4.3$ Hz, 1H), 7.64 (d, $J = 4.4$ Hz, 1H), 7.26 (s, 1H), 7.16 (d, $J = 8.8$ Hz, 1H), 7.10 (t, $J = 7.9$ Hz, 1H), 7.00 (dd, $J = 14.0$, 5.0 Hz, 2H), 6.89 (s, 1H), 5.56 (s, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 2.57 (s, 2H), 2.35–2.19 (m, 2H), 1.12 (s, 3H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.83$, 163.73, 159.28, 158.20, 147.94, 146.09, 132.65, 129.59, 128.27, 126.48, 121.00, 117.17, 114.54, 114.24, 111.04, 102.39, 55.02, 54.85, 50.69, 41.21, 34.93, 32.06, 29.04, 27.07 ppm; MS (ESI): calcd for $C_{27}H_{26}O_4$ 414.1831, found $m/z = 415.1843$ $[M + H]^+$.

8,9,10,12-Tetrahydro-2-methoxy-9,9-dimethyl-12-(4-nitrophenyl)-11H-benzo[a]xanthen-11-one
(**4p**, $C_{26}H_{23}NO_5$)
$R_f = 0.52$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, $J = 8.7$ Hz, 2H), 7.72 (d, $J = 8.9$ Hz, 1H), 7.69 (d, $J = 8.7$ Hz, 1H), 7.53 (d, $J = 8.6$ Hz, 2H), 7.20 (d, $J = 8.8$ Hz, 1H), 7.08–7.01 (m, 2H), 5.69 (s, 1H), 3.80 (s, 3H), 2.60 (s, 2H), 2.29 (d, $J = 16.4$ Hz, 1H), 2.25 (d, $J = 16.4$ Hz, 1H), 1.14 (s, 3H), 0.95 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.39$, 164.17, 158.24, 151.41, 147.78, 131.98, 129.65, 128.92, 128.78, 126.28, 123.12, 117.00, 114.56, 113.98, 112.41, 101.74, 54.74, 50.28, 40.92, 34.75, 31.79, 28.81, 26.61 ppm; MS (ESI): calcd for $C_{26}H_{23}NO_5$ 429.1576, found $m/z = 430.1463$ $[M + H]^+$.

8,9,10,12-Tetrahydro-2-methoxy-9,9-dimethyl-12-(3-nitrophenyl)-11H-benzo[a]xanthen-11-one
(**4q**, $C_{26}H_{23}NO_5$)
$R_f = 0.51$ (TLC, ethyl acetate/hexane 2:8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.94 (d, $J = 8.1$ Hz, 1H), 7.77 (d, $J = 7.6$ Hz, 1H), 7.70 (dd, $J = 13.9$, 8.9 Hz, 2H), 7.36 (t, $J = 7.9$ Hz, 1H), 7.20 (d, $J = 8.8$ Hz, 1H), 7.11 (s, 1H), 7.03 (d, $J = 8.8$ Hz, 1H), 5.69 (s, 1H), 3.81 (s, 3H), 2.61 (s, 2H), 2.31 (d, $J = 16.3$ Hz, 1H), 2.27 (d, $J = 16.3$ Hz, 1H), 1.14 (s, 3H), 0.97 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196.45$, 164.13, 158.22, 147.84, 147.74, 146.30, 134.27, 129.68, 128.78, 128.57, 126.28, 122.86, 121.13, 117.08, 114.10, 112.55, 101.59, 54.76, 50.25, 40.88, 34.69, 31.84, 28.78, 26.69 ppm; MS (ESI): calcd for $C_{26}H_{23}NO_5$ 429.1576, found $m/z = 430.1542$ $[M + H]^+$.

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