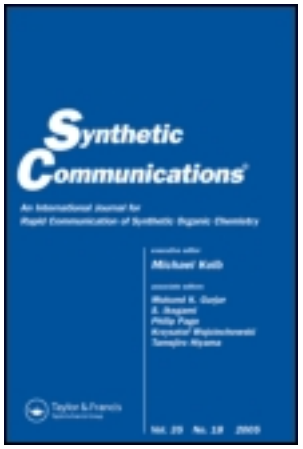

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FACILE APPROACH FOR THE SYNTHESIS OF 2,3,4,9-TETRAHYDRO-1*H*-XANTHEN-1-ONES AND 8,9,10,12-TETRAHYDRO-11*H*-BENZO[*a*]XANTHEN-11-ONES VIA TRAPPING OF *o*-QUINONE METHIDES

Vitaly A. Osyanin, Elena A. Ivleva, and Yuri N. Klimochkin
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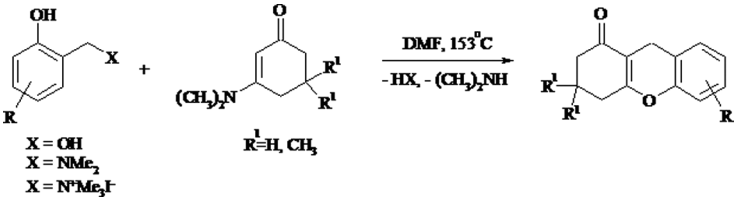
GRAPHICAL ABSTRACT



Abstract *An efficient, simple synthesis of 2,3,4,9-tetrahydro-1*H*-xanthene-1-ones and 8,9,10,12-tetrahydro-11*H*-benzo[*a*]xanthen-11-ones is reported by one-pot condensation of 3-dimethylamino-2-cyclohexen-1-ones with hydroxybenzyl alcohols, phenol, and 2-naphthol Mannich bases or their quaternized derivatives. The mechanism of the reaction is believed to involve the formation of the* o*-quinone methide intermediate.*

Keywords Enamines; hydroxybenzyl alcohols; Mannich bases; *o*-quinone methides; 8,9,10,12-tetrahydro-11*H*-benzo[*a*]xanthen-11-ones; 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones

INTRODUCTION

Compounds containing a xanthene skeleton are important biologically active heterocyclic compounds, which may possess antiviral,[1] antimicrobial,[2] anti-inflammatory,[3] anticonvulsant,[4] and antimalarial[5,6] activities. These compounds are also employed as dyes[7] (fluorescein, eosin, rhodamines), pH-sensitive fluorescent materials for visualization of biomolecules,[8] and linkers.[9] A great number of highly functionalized xanthenes occurs in nature. Some examples are the antibiotic rhodomyrtone[10] and α-glucosidase inhibitor myrtucommulones[11] (Scheme 1). Thus, the synthesis of a variety of xanthene derivatives is desirable.

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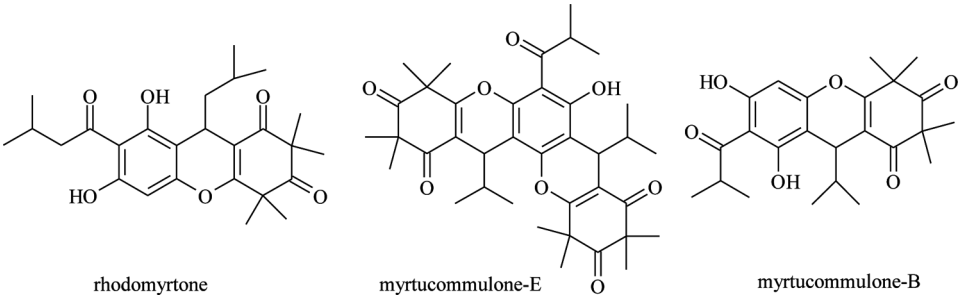


Scheme 1. Some tetrahydro-1*H*-xanthen-1-ones embodied in natural products.

o-Quinone methides (*o*-QMs) are important intermediates in many chemical and biological processes. These reactive species are efficient DNA alkylating and cross-linking agents and play a key role in the biological action of several antibiotics such as mitomycin and anthracyclines. *o*-QMs act as heterodienes in inter- and intramolecular cycloadditions with olefins to give various substituted chromanes. Like vinyl ketones, *o*-QMs also act as acceptors in Michael additions to afford *ortho*-substituted phenols.[12] Most of the methods for generating *o*-QMs involve high-temperature thermolysis and/or use of highly derivatized or structurally complex precursors. Much attention has been devoted to the development of methods to generate *o*-QMs photochemically, because this provides temporal and spatial control over their formation and subsequent reaction to give chroman products.[13,14]

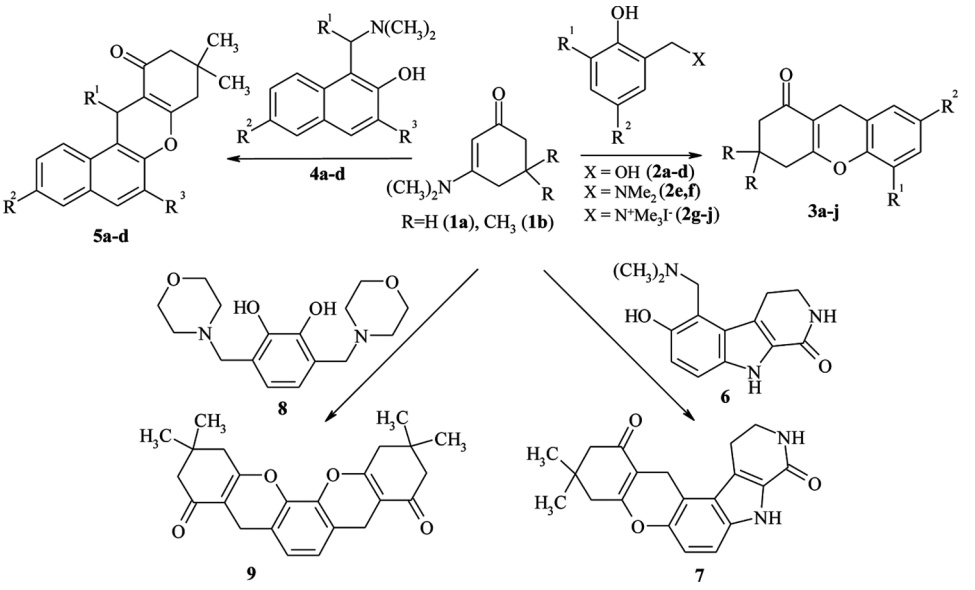
Only some examples of the reactions of *o*-QMs with enamines leading to the xanthenes derivatives are described.[15–20] Herein, we report a new procedure for the synthesis of 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones and 8,9,10,12-tetrahydro-1*H*-benzo[*a*]xanthen-11-ones from enamines (**1a,b**) and *o*-QMs generated from corresponding salicylic alcohols, Mannich bases, or quarternary ammonium salts.

It should be noted that the synthetic potential of the *o*-hydroxybenzyl alcohols and Mannich bases for a *o*-QM formation has remained largely underestimated in relation to the high temperature needed for the thermal elimination of the amine or water. The formation of quaternary ammonium salts by alkylation of the Mannich adducts is a way to induce easier removal of the amino residue and, therefore, trapping of the transient electrophilic species at lower temperature. Furthermore, elimination of the tertiary amines as an ammonium salt makes the process irreversible.[21]

RESULTS AND DISCUSSION

Initially, we investigated the condensation reaction of salicylic alcohol and dimedone enamine **1b** in dioxane, ethanol, and acetonitrile at reflux. However, no products were detected. Then, it was decided to carry out the reaction in refluxing dimethylformamide (DMF), and it was found that the reaction proceeded smoothly, giving 2,3,4,9-tetrahydro-1*H*-xanthene-1-one **3c** in 75% isolated yield.

To explore the scope and limitation of this reaction and to generalize the procedure, a variety of electronically divergent *o*-benzo- and naphthoquinone methide precursors **2a–j**, and **4a–d** were examined (Scheme 2), and the results are



Scheme 2. Synthesis of xanthene derivatives. R = R^1 = R^2 = H (**3a**); R = R^1 = H, R^2 = Br (**3b**); R = CH_3, R^1 = R^2 = H (**3c**); R = CH_3, R^1 = H, R^2 = $COCH_3$ (**3d**); R = CH_3, R^1 = NO_2, R^2 = 1-Ad (**3e**); R = CH_3, R^1 = Br, R^2 = 1-Ad (**3f**); R = CH_3, R^1 = H, R^2 = 1-Ad (**3g**); R = CH_3, R^1 = H, R^2 = NO_2 (**3h**); R = CH_3, R^1 = H, R^2 = $C(CH_3)_3$ (**3i**); R = R^2 = CH_3, R = R^2 = CH_3, R^1 = 1-Ad (**3j**); R^1 = R^1 = R^2 = H (**5a**); R^1 = R^3 = H, R^2 = 1-Ad (**5b**); R^1 = H, R^2 = R^3 = 1-Ad (**5c**); R^1 = Ph, R^2 = R^3 = H (**5d**)

summarized in Table 1. In all cases, quaternized derivatives of phenolic Mannich bases, *o*-hydroxybenzyl alcohols, and 2-naphthol Mannich bases carrying either an electron-withdrawing group or an electron-donating group reacted successfully and gave the products **3a–j** and **5a–d** in good yields. Compounds **3a–d** were prepared from *o*-hydroxybenzyl alcohols **2a–d** (X=OH), **3e,f** from Mannich bases **2e,f**, ([X=$N(CH_3)_2$]) and **3g–j** from Mannich base methiodides **2g–j** (X=$N(CH_3)_3I$). The reactions were performed in refluxing DMF at sufficiently high temperature to ensure the thermal decomposition of the *o*-QM precursors. Products can be easily purified by single recrystallization. The reaction was repeated on several different scales (up to 50 mmol), all with comparable yields.

In the reaction of enamine **1b** with 2,4-dihydroxy-3-morpholin-4-yl-methylacetophenone, only 7-acetyl-8-hydroxy-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one **3k** was isolated (Scheme 3). The structure of the product and the regioselectivity of this cycloaddition reaction were determined on the basis of a sharp, downfield chemical shift (12.82 ppm) of the unreacted phenolic proton.

In the reactions with 2-naphthol Mannich bases, the better results probably reflect the ease of formation of a *o*-QM adjacent to an aromatic ring as compared with phenol Mannich bases in which formation of the *o*-QM implies the disappearance of the only aromatic ring. It should be noted that none of the dimeric nor trimeric products that are obtained in the usual pyrolytic methods were detected.

Attempts to extend this reaction to the 2-dimethylaminomethyl-4-nitrophenol, however, failed, perhaps because of the relatively greater thermal stability of this

Table 1. 2,3,4,9-Tetrahydro-1*H*-xanthen-1-ones **3a–k** and 8,9,10,12-tetrahydro-11*H*-benzo[*a*]xanthen-11-ones **5a–d**

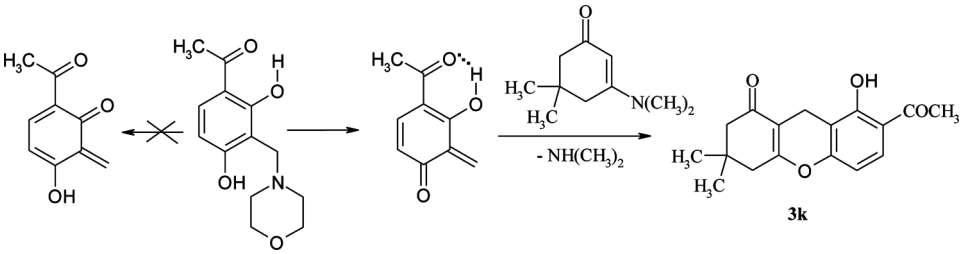
Compound	Yield (%)[a]	Mp (lit. mp) °C	Solvent for recrystallization
3a	75	89–90 (90–91[22])	Acetic acid–water
3b	55	131–132	Ethanol
3c	53	94–95 (80[23])	DMF
3d	56	144–145	Methanol
3e	81	196–198	DMF–water
3f	82	220–222	DMF
3g	60	226–227	DMF
3h	68	127–129 (116[23])	DMF–water
3i	59	150–152	DMF–water
3j	60	238–240	Toluene
3k	61	147–149	Ethanol
5a	89	157–158	Ethanol
5b	91	281–282	DMF
5c	86	>330	DMF
5d	90	151–153 (149–150[24])	Ethanol

[a]Isolated yield.

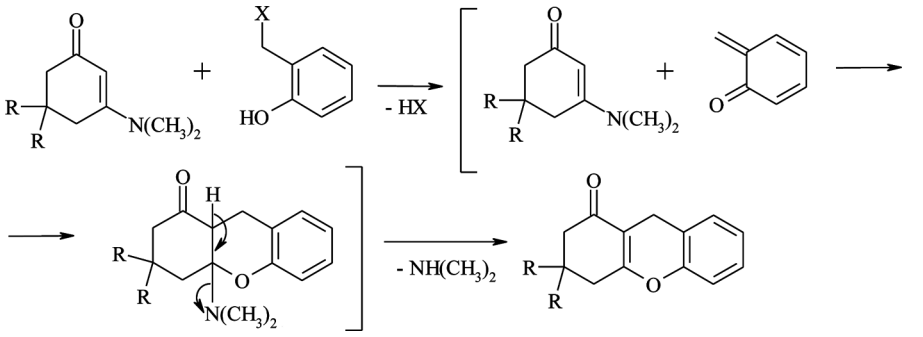
phenolic Mannich base and consequent difficulty in generating the *o*-QM under the conditions mentioned in this article. Nevertheless, in the reaction with quaternized 2-dimethylaminomethyl-4-nitrophenol **2h**, which is more reactivity precursor of *o*-QM, corresponding xanthene derivative **3h** was prepared in 68% yield.

On the basis of these results, this process was then extended to a heterocyclic precursor of *o*-QM. From 5-dimethylaminomethyl-6-hydroxy-2,3,4,9-tetrahydro-1*H*-β-carbolin-1-one **6** and enamine **1b** a novel heterocyclic system, 1,5,6,7,8,9,10,11,12,13-decahydrochromeno[3,2-*g*]β-carboline **7** was prepared in 73% yield. In a similar manner, 3,6-bis(morpholinomethyl)catechol **8** reacts with 2 equivalents of enamine **1b** in refluxing DMF to yield a novel fused heterocyclic system 1,2,3,4,5,8,9,10,11,12-decahydrochromeno[3,2-c]xanthene **9**.

Structural assignment was based on elemental analyses and absence of an OH-band in the infrared (IR) and of the phenolic proton signal in the ^{1}H NMR spectrum of the xanthenes derivatives **3a–j, 5a–d, 7**, and **9**, respectively. The IR spectra show the presence of a conjugated carbonyl group (υ_{max} 1637–1654 cm^{-1}). In the aliphatic region of the ^{1}H NMR spectra of compounds **3c–j** and **5a–c**, two characteristic 2-H singlets are present at δ 2.30–2.42 and 2.41–2.58 ppm corresponding to



Scheme 3. Synthesis of 7-acetyl-8-hydroxy-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one **(3k)**.



Scheme 4. Plausible mechanism for the synthesis of xanthene-based compounds.

the methylene protons of the carbocyclic fragment and 6-H singlet at 1.10–1.21 ppm corresponding methyl groups. The benzylic protons appear as 2-H singlets at 3.46–3.81 ppm. In the ^{1}H NMR spectrum of compound **5d**, two 3-H singlets at δ 0.94 and 1.10 ppm were assigned to the diastereotopic protons of the methyl groups. In the majority of cases, the most intensive peak in the mass spectrum corresponds to the molecular ion peak.

A mechanistic rationale portraying the probable sequence of events is given in Scheme 4. We suppose that the reaction proceeds via the *o*-quinone methide intermediate, which is formed by the thermal desamination of the Mannich bases or their methiodides, or dehydratation of the hydroxybenzyl alcohols. Subsequent cycloaddition of the *o*-QMs with 3-dimethylamino-2-cyclohexen-1-ones affords the hemiaminal, which is desaminated to give the xanthene derivative. The driving force of the reaction is the resulting rearomatization of the molecule.

In these reactions, the *o*-QM reacts as electron-deficient heterodiene. Its reaction with electron-rich enamines proceeds regioselectively 50 that the carbon connected with dimethylamino group reacts with the quinone methide oxygen and the neighboring vinylic carbon reacts with the methylene carbon of the QM. The regioselectivity can be readily explained by ionic resonance forms of the coreactants or alternatively in terms of the frontier orbital interaction of the lowest unoccupied molecular orbital (LUMO) of a QM and the highest occupied molecular orbital (HOMO) of an enamine. At the same time, the possibility of a Michael-type addition of the enamine to the QM to give zwitterionic intermediate, which is cyclized and then desaminated, must not be ruled out.[25]

CONCLUSION

We have developed a facile protocol for the synthesis of 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones and 8,9,10,12-tetrahydro-11*H*-benzo[*a*]xanthen-11-ones. Their synthesis by the suggested procedure does not require an excess of any reagents or the use of any catalysts, and it can be performed under neutral reaction conditions. Besides, the advantages of this method include the use of available reagents, simple workup procedure, easy isolation, absence of oligomeric products, and high purity

and good yields of the xanthene derivatives. The method is general for *o*-QM precursors containing both electron-withdrawing and electron-donating substituents and is compatible with considerable structural variation on both the phenol and enamine units.

EXPERIMENTAL

FTIR spectra were taken on a Shimadzu FTIR-8400S spectrophotometer in KBr pellets. NMR spectra were recorded on a Brucker AM 400-MHz spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal reference. Chemical shifts and coupling constants were recorded in units of parts per million (ppm) and hertz (Hz), respectively. Melting points were determined on an Electrothermal melting-point apparatus and are uncorrected. Elemental analyses were performed on a EuroVector EA-3000 instrument. Electron impact–mass spectrometry (EI-MS) spectra were obtained on a Finnigan Trace DSQ spectrometer (70 eV). Thin-layer chromatography (TLC) was carried out on aluminium-backed silica-gel plates (Merck 60 F_{254}) with visualization of components by ultraviolet light (254 nm) or exposure to I_2. Noncommercial *o*-hydroxybenzyl alcohols, Mannich bases, and their methiodides were prepared according to well-known methods.[26–28]

4-(1-Adamantyl)-2-nitrophenol (10)

A solution of 7 ml 94% HNO_3 in 60 ml of glacial acetic acid was added to a suspension of 40 g (0.18 mol) of 4-(1-adamantyl)phenol in 600 ml of glacial acetic acid dropwise under vigorous stirring at room temperature. The reaction mixture was stirred for 30 min and poured into crushed ice, and the precipitate was separated by filtration and washed with water until the washings were neutral. The crude product was purified by recrystallization from acetic acid to give 44 g (67%) of yellow crystals, mp 108–109 °C. ^{1}H NMR ($CDCl_3$), δ, ppm: 1.71–1.81 (m, 6H, $3CH_{2\ Ad}$), 1.85–1.87 (m, 6H, $3CH_{2\ Ad}$), 2.10 (br. s, 3H, $3CH_{Ad}$), 7.08 (d, $J = 8.7$ Hz, 1H, H-6), 7.61 (dd, $J = 8.7$ Hz, $J = 2.3$ Hz, 1H, H-5), 8.01 (d, $J = 2.3$ Hz, 1H, H-3), 10.45 (s, 1H, OH); ^{13}C NMR ($CDCl_3$), δ, ppm: 28.81 (CH), 35.87 (C), 36.56 (CH_2), 43.02 (CH_2), 119.55 (CH), 120.93 (CH), 133.33 (C), 135.09 (CH), 144.09 (C), 153.18 (C); IR, ν, cm^{-1}: 3178, 3089 (OH), 2904, 2846 (CH_{Ad}), 1623, 1585 (C=C), 1531 (NO_2), 1488, 1361, 1326 (NO_2), 1265, 1141, 1103, 837; EI-MS (70 eV) m/z (% int.): 273 (M^+, 65), 230 (26), 216 (84), 170 (100), 152 (54), 141 (46), 128 (60), 115 (93). Anal. calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.28; H, 6.97; N, 5.16.

4-(1-Adamantyl)-2-[(dimethylamino)methyl]-6-nitrophenol (2e)

Dimethylamine (8 ml of 33% aqueous solution, 0.053 mol) and formaldehyde (4 ml of 37% aqueous solution, 0.053 mol) were added to a solution of 12 g (0.044 mol) of **10** in 100 ml ethanol. The reaction mixture was refluxed for 48 h and then cooled to room temperature. The precipitate that formed was filtered, washed in ice-cold ethanol, and purified by recrystallization from ethanol to give 8 g (57%) of orange crystals, mp 86–87 °C. ^{1}H NMR ($CDCl_3$), δ, ppm: 1.67 (br. s,

6H, $3CH_{2\ Ad}$), 1.78 (br. s, 6H, $3CH_{2Ad}$), 2.00 (br. s, 3H, $3CH_{Ad}$), 2.39 [s, 6H, $(CH_3)_2N$], 3.86 (s, 2H, CH_2), 4.79 (s, 1H, OH), 7.35 (d, $J = 2.2$ Hz, 1H, H-3), 7.61 (d, $J = 2.2$ Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$), δ, ppm: 28.83 (CH_3), 35.72 (CH_2), 36.60 (C), 43.09 (CH_2), 44.59 (CH), 61.18 (CH_2), 121.00 (CH), 125.40 (C), 132.04 (CH), 135.92 (C), 141.91 (C), 152.12 (C); IR, ν, cm^{-1}: 3421, 3097 (OH), 2904, 2846 (CH_{Ad}), 1623 (C=C), 1539 (NO_2), 1469, 1377, 1342 (NO_2), 1261, 1176, 1130, 840; EI-MS (70 eV) m/z (% int.): 330 (M^+, 82), 312 (M^+–H_2O, 100), 286 [M^+–$(CH_3)_2N$, 10], 269 (83), 135 (Ad^+, 27), 58 (92). Anal. calcd for $C_{19}H_{26}N_2O_3$: C, 69.07; H, 7.93; N, 8.48. Found: C, 69.02; H, 7.97; N, 8.52.

4-(1-Adamantyl)-2-bromo-6-[(dimethylamino)methyl]phenol (2f)

Dimethylamine (3 ml of 33% aqueous solution, 0.02 mol) and formaldehyde (1.5 ml of 37% aqueous solution, 0.02 mol) were added to a solution of 5.53 g (0.018 mol) of 4-(1-adamantyl)-2-bromophenol in 50 ml ethanol. The reaction mixture was stirred at room temperature for 48 h. The precipitate that formed was then filtered, washed in ice-cold ethanol, and purified by recrystallization from ethanol to give 4.39 g (67%) of colorless crystals, mp 180–182 °C (dec). ^{1}H NMR ($CDCl_3$), δ, ppm: 1.69–1.77 (m, 6H, $3CH_{2\ Ad}$), 1.83 (br. s, 6H, $3CH_{2\ Ad}$), 2.06 (br. s, 3H, $3CH_{Ad}$), 2.32 [s, 6H, $(CH_3)_2N$], 3.62 (s, 2H, CH_2), 6.86 (s, 1H, H-5), 7.36 (s, 1H, H-3), 8.62 (br. s, 1H, OH); ^{13}C NMR ($CDCl_3$), δ, ppm: 29.02 (CH_3), 35.63 (C), 36.79 (CH_2), 43.40 (CH_2), 44.45 (CH), 63.20 (CH_2), 109.88 (C), 122.32 (C), 123.92 (CH), 128.59 (CH), 143.35 (C), 152.50 (C); IR, ν, cm^{-1}: 3244 (OH), 2958, 2904, 2846 (CH_{Ad}), 1608, 1577 (C=C), 1427, 1353, 1257, 1122, 1103, 837; EI-MS (70 eV) m/z (% int.): 365 ($M^+ + 2$, 92), 363 (M^+, 100), 284 (M^+–Br, 12), 239 (13), 170 (16), 135 (Ad^+, 30). Anal. calcd. for $C_{19}H_{26}BrNO$: C, 62.64; H, 7.19; N, 3.84. Found: C, 62.59; H, 7.22; N, 3.87.

5-(1-Adamantyl)-2-hydroxybenzyl(trimethyl)ammonium Iodide (2g)

Dimethylamine (3 ml of 33% aqueous solution, 0.02 mol) and formaldehyde (1.5 ml of 37% aqueous solution, 0.02 mol) were added to a solution of 4.1 g (0.018 mol) of 4-(1-adamantyl)phenol in 30 ml ethanol. The reaction mixture was stored at room temperature for 48 h and at −20 °C for 2 h. The precipitate formed was filtered, washed in ice-cold methanol, and dissolved in 20 ml of CH_3I. The resulting solution was refluxed for 12 h. After cooling to 0 °C, the precipitate that formed was filtered, and washed in ice-cold diethyl ester to give 5 g (65%) of colorless crystals, mp 201–203 °C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.65–1.73 (m, 6H, $3CH_{2Ad}$), 1.78–1.82 (m, 6H, $3CH_{2Ad}$), 2.02 (br. s, 3H, $3CH_{Ad}$), 2.99 [s, 9H, $(CH_3)_3N$], 4.40 (s, 2H, CH_2), 6.88 (d, $J = 8.4$ Hz, 1H, H-3), 7.30 (dd, $J = 8.4$ Hz, $J = 2.5$ Hz, 1H, H-4), 7.32 (d, $J = 2.5$ Hz, 1H, H-6), 10.01 (br. s, 1H, OH); ^{13}C NMR (DMSO-d_6), δ, ppm: 28.84 (CH_3), 35.54 (C), 36.69 (CH_2), 43.28 (CH_2), 52.58 (CH), 64.04 (CH_2), 114.53 (C), 116.22 (CH), 128.82 (CH), 131.74 (CH), 142.34 (C), 155.50 (C); IR, ν, cm^{-1}: 3182 (OH), 2901 (CH_{Ad}), 2847 (CH_{Ad}), 1612 (C=C), 1512, 1477, 1420, 1261, 1130, 1107, 879. Anal. calcd. for $C_{20}H_{30}INO$: C, 56.16; H, 7.02; N, 3.28. Found: C, 56.21; H, 6.97, N, 3.32.

2-Hydroxy-5-nitrobenzyl(trimethyl)ammonium Iodide (2h)

A solution of 5 g (0.0255 mol) of 2-dimethylaminomethyl-4-nitrophenol and 7.24 g (0.051 mol) of CH_3I in 100 ml ethanol was refluxed for 2 h. After cooling to −20 °C, the precipitate formed was filtered and washed in ice-cold ethanol to give 7.33 g (85%) of yellow crystals, mp 232–234 °C (dec). ^{1}H NMR (DMSO-d_6), δ, ppm: 3.05 [s, 9H, $N(CH_3)_3$], 4.52 (s, 2H, CH_2), 7.10 (d, $J = 8.8$ Hz, 1H, H-3), 8.23 (dd, $J = 8.8$ Hz, $J = 1.4$ Hz, 1H, H-4), 8.36 (d, $J = 1.4$ Hz, 1H, H-6), 11.92 (br. s, 1H, OH); ^{13}C NMR (DMSO-d_6), δ, ppm: 52.82 (CH_3), 62.47 (CH_2), 116.22 (C), 117.24 (CH), 128.47 (CH), 131.50 (CH), 139.97 (C), 164.22 (C); IR, ν, cm^{-1}: 3200–2800 (OH), 1616, 1593 (C=C), 1520 (NO_2), 1493, 1342 (NO_2), 1296, 1277, 1088, 891. Anal. calcd. for $C_{10}H_{15}IN_2O_3$: C, 35.50; H, 4.44; N, 8.28. Found: C, 35.55; H, 4.39, N, 8.31.

3-(1-Adamantyl)-2-hydroxy-5-methylbenzyl(trimethyl)ammonium Iodide (2j)

Dimethylamine (3 ml of 33% aqueous solution, 0.02 mol) and formaldehyde (1.5 ml of 37% aqueous solution, 0.02 mol) were added to a solution of 4 g (0.017 mol) of 2-(1-adamantyl)-4-methylphenol in 30 ml ethanol. The reaction mixture was stored at room temperature for 48 h and at −20 °C for 2 h. The precipitate that formed was filtered, washed in ice-cold methanol and dissolved in 20 ml of CH_3I. The resulting solution was refluxed for 12 h. After cooling to 0 °C, the precipitate that formed was filtered and washed in ice-cold diethyl ester to give 5.5 g (60%) of colorless crystals, mp 217–219 °C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.70 (br. s, 6H, $3CH_{2Ad}$), 2.01 (br. s, 3H, $3CH_{Ad}$), 2.05 (br. s, 6H, $3CH_{2Ad}$), 2.22 (s, 3H, CH_3), 2.95 [s, 9H, $(CH_3)_3N$], 4.49 (s, 2H, CH_2), 7.00 (s, 1H, $H_{arom.}$), 7.08 (s, 1H, $H_{arom.}$), 8.59 (s, 1H, OH); ^{13}C NMR ($CDCl_3$), δ, ppm: 20.80 (CH_3), 29.01 (CH_3), 36.96 (CH_2), 37.00 (C), 40.93 (CH_2), 48.29 (CH), 64.28 (CH_2), 115.82 (C), 130.33 (C), 131.04 (CH), 132.32 (CH), 139.60 (C), 153.61 (C); IR, ν, cm^{-1}: 3387, 3190 (OH), 2901, 2847 (CH_{Ad}), 1609 (C=C), 1462, 1269, 1211, 1180, 1011, 872, 756. Anal. calcd. for $C_{21}H_{32}INO$: C, 57.08; H, 7.25; N, 3.17. Found: C, 56.98; H, 7.29; N, 3.21.

6-(1-Adamantyl)-1-[(dimethylamino)methyl)-2-naphthol (4b)

Dimethylamine (3 ml of 33% aqueous solution, 0.02 mol) and formaldehyde (1.5 ml of 37% aqueous solution, 0.02 mol) were added to a solution of 5 g (0.018 mol) of 6-(1-adamantyl)-2-naphthol[29] in 50 ml ethanol. The reaction mixture was refluxed for 5 min, cooled to room temperature, and stored at 25 °C overnight and at −15 °C for 48 h. The precipitate formed was then filtered, washed in ice-cold methanol, and purified by recrystallization from ethanol–DMF to give 6.1 g (83%) of colorless crystals, mp 177–178 °C. ^{1}H NMR ($CDCl_3$), δ, ppm: 1.77–1.85 (m, 6H, $3CH_{2Ad}$), 1.96–2.04 (m, 6H, $3CH_{2Ad}$), 2.14 (br. s, 3H, $3CH_{Ad}$), 2.41 [s, 6H, $(CH_3)_2N$], 4.09 (s, 2H, CH_2), 7.08 (d, $J = 8.7$ Hz, 1H, $H_{arom.}$), 7.53 (dd, $J = 8.7$ Hz, $J = 1.8$ Hz, 1H, H-7), 7.65 (d, $J = 1.8$ Hz, 1H, H-5), 7.67 (d, $J = 8.7$ Hz, 1H, $H_{arom.}$), 7.78 (d, $J = 8.7$ Hz, 1H, $H_{arom.}$), 9.91 (br. s, 1H, OH); ^{13}C NMR ($CDCl_3$), δ, ppm: 29.07 (CH_3), 36.00 (C), 36.96 (CH_2), 43.24 (CH_2), 44.79 (CH), 57.98 (CH_2),

111.30 (C), 119.12 (CH), 120.84 (CH), 123.97 (CH), 124.45 (CH), 128.54 (C), 129.27 (CH), 130.80 (C), 145.28 (C), 156.33 (C); IR, ν, cm^{-1}: 3051 (OH), 2908, 2885, 2850 (CH_{Ad}), 1604 (C=C), 1512, 1423, 1338, 1276, 1149, 844; EI-MS (70 eV) m/z (% int.): 335 (M^+, 100), 290 [M^+–$NH(CH_3)_2$, 60], 233 (23), 215 (16), 165 (10), 152 (5), 44 (47). Anal. calcd. for $C_{23}H_{29}NO$: C, 82.34; H, 8.71; N, 4.18. Found: C, 82.39; H, 8.67; N, 4.21.

5-Dimethylaminomethyl-6-hydroxy-2,3,4,9-tetrahydro-1*H*-β-carbolin-1-one (6)

Dimethylamine (4.5 ml of 33% aqueous solution, 0.03 mol) and formaldehyde (2.3 ml of 37% aqueous solution, 0.03 mol) were added to a suspension of 5 g (0.025 mol) of 6-hydroxy-2,3,4,9-tetrahydro-1H-β-carboline-1-one in 20 ml ethanol. The reaction mixture was stirred at room temperature overnight. The precipitate formed was then filtered and washed ice-cold ethanol to give 4.7 g (73%) of colorless crystals, mp 160–162 °C (dec). ^{1}H NMR (DMSO-d_6), δ, ppm: 2.77 [s, 6H, $(CH_3)_2N$], 3.07 (t, $J = 6.9$ Hz, 2H, CH_2), 3.45–3.49 (m, 2H, CH_2N), 4.43 [s, 2H, $C\underline{H}_2N(CH_3)_2$], 6.93 (d, $J = 8.7$ Hz, 1H, $H_{arom.}$), 7.33 (d, $J = 8.7$ Hz, $H_{arom.}$), 7.61 (s, 1H, NH_{amide}), 9.38 (br. s, 1H, OH), 11.61 (s, 1H, NH_{indole}); ^{13}C NMR (DMSO-d_6), δ, ppm: 22.84 (CH_2), 41.52 (CH_2), 43.15 (CH_3), 53.41 (CH_2), 106.95 (C), 114.86 (CH), 115.86 (CH), 116.50 (C), 123.31 (C), 129.24 (C), 132.44 (C), 151.30 (C), 162.06 (C); IR, ν, cm^{-1}: 3410, 3279, 3248 (NH/OH), 2974, 2719, 1639 (C=O), 1585, 1547, 1516, 1462, 1431, 1369, 1346, 1304, 1242, 1211, 1165, 1138, 1076, 941, 806, 775, 660; EI-MS (70 eV) m/z (% int.): 259 (M^+, 16), 214 [$M^+ - NH(CH_3)_2$, 70], 185 (28), 157 (15), 129 (12), 102 (5), 44 (100). Anal. calcd for $C_{14}H_{17}N_3O_2$: C, 64.85; H, 6.61; N, 16.20. Found: C, 64.72; H, 6.68; N, 16.29.

General Experimental Procedure for the Synthesis of the 2,3,4,9-Tetrahydro-1*H*-xanthen-1-ones and 8,9,10,12-Tetrahydro-1*H*-benzo[*a*]xanthen-11-ones

A mixture of 0.84 g (6 mmol) of 3-dimethylamino-2-cyclohexen-1-one **1a** or 1 g (6 mmol) of 3-dimethylamino-5,5-dimethyl-2-cyclohexen-1-one **1b**[30] and 6 mmol of the appropriate *o*-quinone methide precursor (hydroxybenzyl alcohol, phenol or 2-naphthol Mannich base, Mannich base methiodide) in DMF (10 ml) was refluxed for 4 h and then stored at −10 °C overnight. The precipitate that formed was then filtered, washed ice-cold ethanol, and purified by recrystallization. If the precipitate was not formed, the reaction mixture was poured into 50 ml of cold water to yield a solid product, which was filtered, washed with water, dried, and recrystallized.

Characterization Data of the 2,3,4,9-Tetrahydro-1*H*-xanthen-1-ones and 8,9,10,12-Tetrahydro-1*H*-benzo[*a*]xanthen-11-ones

2,3,4,9-Tetrahydro-1*H*-xanthen-1-one (3a). Slightly brown crystals; ^{1}H NMR, δ, ppm: 2.06 (qui, $J = 6.5$ Hz, 2H, CH_2-3), 2.46 (t, $J = 6.7$ Hz, 2H, CH_2),

2.56 (t, $J = 6.2$ Hz, 2H, CH_2), 3.51 (s, 2H, CH_2-Ar), 6.96 (d, $J = 8.0$ Hz, 1H, H-5), 7.05 (dd, $J = 7.8$ Hz, $J = 6.7$ Hz, 1H, H-7), 7.14–7.17 (m, 2H, H-6,8); ^{13}C NMR, δ, ppm: 20.70 (CH_2), 21.22 (CH_2), 27.79 (CH_2), 36.73 (CH_2), 110.10 (C), 116.49 (CH), 120.91 (C), 124.71 (CH), 127.68 (CH), 129.79 (CH), 149.86 (C), 167.18 (C), 198.48 (C); IR, ν, cm^{-1}: 3036 ($CH_{arom.}$), 2943, 2874 ($CH_{aliph.}$), 1639 (C=O), 1581 (C=C), 1493, 1454, 1393, 1250, 1234, 1184, 1134, 995, 995, 852, 760; EI-MS (70 eV) m/z (% int.): 200 (M^+, 100), 199 (M^+–H, 84), 183 (M^+–OH, 12), 172 (M^+–CO, 14), 171 (M^+–H–CO, 15), 157 (9), 144 (70), 137 (7), 128 (7), 115 (41). Anal. calcd. for $C_{13}H_{12}O_2$, %: C, 77.98; H, 6.04. Found, %: C, 78.05; H, 5.98.

7-Bromo-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3b). Colorless crystals; ^{1}H NMR, δ, ppm: 2.07 (dd, $J = 12.5$ Hz, $J = 5.9$ Hz, 2H, CH_2), 2.46 (t, $J = 6.7$ Hz, 2H, CH_2), 2.53–2.58 (m, 2H, CH_2), 3.48 (s, 2H, CH_2-Ar), 6.84 (d, $J = 8.1$ Hz, 1H, H-5), 7.26 (d, $J = 8.1$ Hz, 1H, H-6), 7.27 (s, 1H, H-8); ^{13}C NMR, δ, ppm: 20.62 (CH_2), 21.18 (CH_2), 27.68 (CH_2), 36.70 (CH_2), 109.70 (C), 117.01 (C), 118.26 (CH), 123.19 (C), 130.69 (CH), 132.36 (CH), 148.98 (C), 166.63 (C), 197.94 (C); IR, ν, cm^{-1}: 3059 ($CH_{arom.}$), 2947, 2885 ($CH_{aliph.}$), 1639 (C=O), 1574 (C=C), 1481, 1423, 1381, 1234, 1184, 1138, 1111, 1065, 999, 864, 825; EI-MS (70 eV) m/z (% int.): 280 ($M^+ + 2$, 64), 278 (M^+, 68), 277 (M^+–H, 32), 261 (M^+–OH, 8), 250 (M^+–CO, 10), 249 (M^+–H–CO, 6), 222 (52), 199 (M^+–Br, 10), 171 (12), 142 (18), 115 (100). Anal. calcd. for $C_{13}H_{11}BrO_2$, %: C, 55.94; H, 3.97. Found, %: C, 55.85; H, 4.05.

3,3-Dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3c). Yellow crystals; ^{1}H NMR, δ, ppm: 1.12 [s, 6H, $C(CH_3)_2$], 2.32 (s, 2H, CH_2), 2.42 (s, 2H, CH_2), 3.51 (s, 2H, CH_2-Ar), 6.95 (d, $J = 8.1$ Hz, 1H, H-5), 7.05 (t, $J = 8.1$ Hz, 1H, H-7), 7.15 (d, $J = 8.1$ Hz, 1H, H-8), 7.16 (t, $J = 8.1$ Hz, 1H, H-6); ^{13}C NMR, δ, ppm: 21.10 (CH_2), 28.51 (CH_3), 32.23 (C), 41.55 (CH_2), 50.68 (CH_2), 108.82 (C), 116.56 (CH_2), 120.88 (C), 124.70 (CH_2), 127.70 (CH_2), 129.83 (CH_2), 149.96 (C), 165.32 (C), 198.19 (C); IR, ν, cm^{-1}: 3047 ($CH_{arom.}$), 2959, 2932, 2889, 2870 ($CH_{aliph.}$), 1639 (C=O), 1582 (C=C), 1493, 1458, 1393, 1246, 1231, 1180, 768; EI-MS (70 eV) m/z (% int.): 228 (M^+, 100), 227 (M^+–H, 28), 213 (M^+–CH_3, 33), 200 (M^+–CO, 8), 195 (M^+–CH_3– H_2O, 21), 185 (M^+–CH_3– CO, 30), 171 (25), 158 (21), 144 (47), 115 (42). Anal. calcd. for $C_{15}H_{16}O_2$, %: C, 78.87; H, 7.02. Found, %: C, 78.92; H, 7.10.

7-Acetyl-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3d). Brown crystals; ^{1}H NMR, δ, ppm: 1.10 [s, 6H, $C(CH_3)_2$], 2.30 (s, 2H, CH_2), 2.41 (s, 2H, CH_2), 2.53 (s, 3H, CH_3CO), 3.51 (s, 2H, CH_2-Ar), 6.98 (d, $J = 8.9$ Hz, 1H, H-5), 7.73 (s, 1H, H-8), 7.75 (d, $J = 8.9$ Hz, 1H, H-6); ^{13}C NMR, δ, ppm: 21.03 (CH_2), 26.56 (CH_3), 28.45 (CH_3), 32.20 (C), 41.28 (CH_2), 50.60 (CH_2), 108.89 (C), 116.79 (CH), 121.04 (C), 128.35 (CH), 130.54 (CH), 133.65 (C), 153.44 (C), 164.61 (C), 196.70 (C), 197.78 (C); IR, ν, cm^{-1}: 3061 ($CH_{arom.}$), 2962, 2934, 2899, 2874 ($CH_{aliph.}$), 1680 (C=O), 1637 (C=O), 1582 (C=C), 1499, 1421, 1383, 1366, 1273, 1232, 1177, 1150, 1119, 1103, 1026, 1016, 959, 833; EI-MS (70 eV) m/z (% int.): 270 (M^+, 100), 255 (M^+–CH_3, 39), 237 (M^+–CH_3– H_2O, 18), 227 (M^+–CH_3– CO, 33), 213 (19), 200 (14), 199 (22), 186 (29), 171 (22), 143 (12), 115 (19). Anal. calcd. for $C_{17}H_{18}O_3$, %: C, 75.55; H, 6.66. Found, %: C, 75.51; H, 6.71.

7-(1-Adamantyl)-3,3-dimethyl-5-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3e). Yellow crystals; ^{1}H NMR, δ, ppm: 1.11 [s, 6H, C(CH$_3$)$_2$], 1.71–1.80 (m, 6H, 3CH$_{2Ad}$), 1.86 (s, 6H, 3CH$_{2Ad}$), 2.10 (br. s, 3H, 3CH$_{Ad}$), 2.32 (s, 2H, CH$_2$), 2.48 (s, 2H, CH$_2$), 3.54 (s, 2H, CH$_2$-Ar), 7.34 (d, 2H, J = 2.2 Hz, H-8), 7.66 (d, 1H, J = 2.2 Hz, H-6); ^{13}C NMR, δ, ppm: 21.32 (CH$_2$), 28.43 (CH$_3$), 28.73 (CH), 32.31 (C), 36.18 (C), 36.48 (CH$_2$), 41.10 (CH$_2$), 42.97 (CH$_2$), 50.69 (CH$_2$), 109.06 (C), 120.46 (CH), 123.16 (C), 131.09 (CH), 138.63 (C), 140.82 (C), 147.92 (C), 164.42 (C), 197.66 (C); IR, ν, cm^{-1}: 2912, 2847 (CH$_{aliph.}$), 1650 (C=O), 1574 (C=C), 1535 (NO$_2$), 1381, 1346 (NO$_2$), 1281, 1219, 1188, 1169, 1142, 1034; EI-MS (70 eV) m/z (% int.): 407 (M$^+$, 100), 392 (M$^+$–CH$_3$, 12), 374 (M$^+$–CH$_3$– H$_2$O, 2), 364 (M$^+$–CH$_3$– CO, 11), 323 (6), 165 (13), 135 (Ad$^+$, 10). Anal. calcd. for C$_{25}$H$_{29}$NO$_4$, %: C, 73.71; H, 7.13; N, 3.43. Found, %: C, 73.69; H, 7.19; N, 3.38.

7-(1-Adamantyl)-5-bromo-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3f). Yellow crystals; ^{1}H NMR, δ, ppm: 1.10 [s, 6H, C(CH$_3$)$_2$], 1.69–1.78 (m, 6H, 3CH$_{2Ad}$), 1.82 (s, 6H, 3CH$_{2Ad}$), 2.07 (br. s, 3H, 3CH$_{Ad}$), 2.30 (s, 2H, CH$_2$), 2.48 (s, 2H, CH$_2$), 3.50 (s, 2H, CH$_2$-Ar), 7.03 (d, J = 2.2 Hz, 2H, H-8), 7.34 (d, J = 2.2 Hz, 1H, H-6); ^{13}C NMR, δ, ppm: 21.89 (CH$_2$), 28.46 (CH$_3$), 28.87 (CH), 32.28 (C), 36.00 (C), 36.64 (CH$_2$), 41.30 (CH$_2$), 43.15 (CH$_2$), 50.74 (CH$_2$), 109.12 (C), 110.50 (C), 121.98 (C), 125.39 (CH), 128.37 (CH), 144.71 (C), 149.04 (C), 165.08 (C), 197.91 (C); IR, ν, cm^{-1}: 2954, 2897, 2847 (CH$_{aliph.}$), 1654 (C=O), 1566 (C=C), 1470, 1381, 1219, 1169, 1146, 1018, 853; EI-MS (70 eV) m/z (% int.): 442 (M$^+$ + 2, 98), 440 (M$^+$, 100), 425 (M$^+$–CH$_3$, 6), 399 (M$^+$–CH$_3$– H$_2$O, 4), 397 (M$^+$–CH$_3$– CO, 4), 356 (7), 220 (7), 165 (5), 135 (Ad$^+$, 8). Anal. calcd. for C$_{25}$H$_{29}$BrO$_2$, %: C, 68.02; H, 6.58. Found, %: C, 67.97; H, 6.63.

7-(1-Adamantyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3g). Yellow crystals; ^{1}H NMR, δ, ppm: 1.11 [s, 6H, C(CH$_3$)$_2$], 1.72–1.87 (m, 6H, 3CH$_{2Ad}$), 1.87 (s, 6H, 3CH$_{2Ad}$), 2.09 (br. s, 3H, 3CH$_{Ad}$), 2.32 (s, 2H, CH$_2$), 2.41 (s, 2H, CH$_2$), 3.51 (s, 2H, CH$_2$-Ar), 6.90 (d, J = 8.3 Hz, 1H, H-5), 7.12 (d, J = 2.2 Hz, 1H, H-8), 7.16 (dd, J = 8.3 Hz, J = 2.2 Hz, 1H, H-6); ^{13}C NMR, δ, ppm: 21.40 (CH$_2$), 28.49 (CH$_3$), 28.97 (CH), 32.24 (C), 35.91 (C), 36.79 (CH$_2$), 41.60 (CH$_2$), 43.31 (CH$_2$), 50.74 (CH$_2$), 108.80 (C), 116.05 (CH), 120.13 (C), 124.25 (CH), 126.15 (CH), 147.83 (C), 148.05 (C), 165.35 (C), 198.10 (C); IR, ν, cm^{-1}: 2901, 2847 (CH$_{aliph.}$), 1647 (C=O), 1589 (C=C), 1497, 1381, 1261, 1231, 1219, 1169, 1146, 1122, 1107, 1018, 806; EI-MS (70 eV) m/z (% int.): 362 (M$^+$, 100), 347 (M$^+$–CH$_3$, 20), 329 (M$^+$–CH$_3$– H$_2$O, 5), 319 (M$^+$–CH$_3$– CO, 11), 305 (9), 292 (14), 278 (16), 221 (16), 135 (Ad$^+$, 5). Anal. calcd. for C$_{25}$H$_{30}$O$_2$, %: C, 82.87; H, 8.30. Found, %: C, 82.81; H, 8.34.

3,3-Dimethyl-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3h). Yellow crystals; ^{1}H NMR, δ, ppm: 1.12 [s, 6H, C(CH$_3$)$_2$], 2.33 (s, 2H, CH$_2$), 2.45 (s, 2H, CH$_2$), 3.58 (s, 2H, CH$_2$-Ar), 7.05 (d, J = 8.8 Hz, 1H, H-5), 8.04 (d, J = 8.8 Hz, 1H, H-6), 8.06 (s, 1H, H-8); ^{13}C NMR, δ, ppm: 21.23 (CH$_2$), 28.47 (CH$_3$), 32.29 (C), 41.19 (CH$_2$), 50.60 (CH$_2$), 108.62 (C), 117.49 (CH), 122.25 (C), 123.74 (CH), 125.71 (CH), 144.24 (C), 154.51 (C), 164.26 (C), 197.53 (C); IR, ν, cm^{-1}: 3040 (CH$_{arom.}$), 2955, 2932 (CH$_{aliph.}$), 1651 (C=O), 1582 (C=C), 1524 (NO$_2$), 1385, 1342 (NO$_2$), 1234, 1188, 1026, 748; EI-MS (70 eV) m/z (% int.): 273 (M$^+$, 100),

258 (M^+–CH_3, 19), 240 (M^+–CH_3– H_2O, 10), 230 (M^+–CH_3– CO, 28), 217 (16), 216 (12), 189 (34), 184 (21), 170 (15), 143 (16), 115 (31). Anal. calcd. for $C_{15}H_{15}NO_4$, %: C, 65.94; H, 5.50; N, 5.12. Found, %: C, 65.87; H, 5.55; N, 5.07.

3,3-Dimethyl-7-*tert*-butyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3i). Yellow crystals; ^{1}H NMR, δ, ppm: 1.10 [s, 6H, $C(CH_3)_2$], 1.28 [s, 9H, $C(CH_3)_3$], 2.30 (s, 2H, CH_2), 2.40 (s, 2H, CH_2), 3.49 (s, 2H, CH_2-Ar), 6.87 (d, $J = 8.6$ Hz, 1H, H-5), 7.13 (s, 1H, H-8), 7.16 (d, $J = 8.6$ Hz, 1H, H-6); ^{13}C NMR, δ, ppm: 21.38 (CH_2), 28.49 (CH_3), 31.49 (CH_3), 32.24 (C), 34.41 (C), 41.59 (CH_2), 50.73 (CH_2), 108.79 (C), 116.02 (CH), 120.09 (C), 124.69 (CH), 126.51 (CH), 147.73 (C), 147.82 (C), 165.35 (C), 198.07 (C); IR, ν, cm^{-1}: 3063 ($CH_{arom.}$), 2959, 2893, 2870 ($CH_{aliph.}$), 1654 (C=O), 1589 (C=C), 1504, 1462, 1273, 1184, 1150, 1126, 1026, 822; EI-MS (70 eV) m/z (% int.): 284 (M^+, 99), 283 (M^+–H, 25), 269 (M^+–CH_3, 100), 256 (M^+–CO, 4), 251 (M^+–CH_3– H_2O, 6), 241 (M^+–CH_3– CO, 12), 227 (12), 200 (17), 185 (19), 141 (7), 115 (15). Anal. calcd. for $C_{19}H_{24}O_2$, %: C, 80.28; H, 8.47. Found, %: C, 80.24; H, 8.51.

5-(1-Adamantyl)-3,3,7-trimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3j). Yellow crystals; ^{1}H NMR, δ, ppm: 1.13 [s, 6H, $C(CH_3)_2$], 1.77 (br. s, 6H, $3CH_{2Ad}$), 2.08 (br. s, 9H, $3CH_{Ad}$, $3CH_{2Ad}$), 2.25 (s, 3H, CH_3-Ar), 2.31 (s, 2H, CH_2), 2.47 (s, 2H, CH_2), 3.46 (s, 2H, CH_2-Ar), 6.79 (s, 1H, $H_{arom.}$), 6.88 (s, 1H, $H_{arom.}$); ^{13}C NMR, δ, ppm: 21.12 (CH_3), 21.49 (CH_2), 28.60 (CH_3), 29.12 (CH), 32.28 (C), 36.94 (C), 37.13 (CH_2), 41.11 (CH_2), 41.51 (CH_2), 50.78 (CH_2), 108.56 (C), 120.91 (C), 125.93 (CH), 127.93 (CH), 133.57 (C), 137.36 (C), 146.86 (C), 164.68 (C), 197.95 (C); IR, ν, cm^{-1}: 2955, 2905, 2851 ($CH_{aliph.}$), 1655 (C=O), 1593 (C=C), 1458, 1389, 1215, 1169, 1146, 1119, 1034, 852; EI-MS (70 eV) m/z (% int.): 376 (M^+, 100), 375 (M^+–H, 22), 361 (M^+–CH_3, 11), 343 (M^+–CH_3– H_2O, 3), 333 (M^+–CH_3– CO, 3), 306 (10), 292 (10). Anal. calcd. for $C_{26}H_{32}O_2$, %: C, 82.97; H, 8.52. Found, %: C, 82.91; H, 8.57.

7-Acetyl-8-hydroxy-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3k). Colorless crystals; ^{1}H NMR, δ, ppm: 1.11 [s, 6H, $C(CH_3)_2$], 2.31 (s, 2H, CH_2), 2.39 (s, 2H, CH_2), 2.55 (s, 3H, CH_3CO), 3.34 (s, 2H, CH_2-Ar), 6.48 (d, $J = 8.1$ Hz, 1H, H-5), 7.55 (d, $J = 8.1$ Hz, 1H, H-6), 12.82 (s, 1H, OH); ^{13}C NMR, δ, ppm: 16.23 (CH_2), 26.52 (CH_3), 28.50 (CH_3), 32.21 (C), 41.21 (CH_2), 50.71 (CH_2), 107.56 (CH), 109.34 (C), 110.06 (C), 115.98 (C), 129.97 (CH), 155.12 (C), 162.20 (C), 163.86 (C), 197.81 (C), 203.16 (C); IR, ν, cm^{-1}: 2959, 2928, 1651 (C=O), 1628, 1593 (C=C), 1427, 1389, 1369, 1323, 1254, 1211, 1122, 1053, 1026, 818; EI-MS (70 eV) m/z (% int.): 286 (M^+, 100), 285 (M^+–H, 50), 271 (M^+–CH_3, 25). Anal. calcd. for $C_{17}H_{18}O_4$, %: C, 71.31; H, 6.34. Found, %: C, 71.27; H, 6.37.

9,9-Dimethyl-8,9,10,12-tetrahydro-1*H*-benzo[*a*]xanthen-11-one (5a). Pink crystals; ^{1}H NMR, δ, ppm: 1.15 [s, 6H, $C(CH_3)_2$], 2.37 (s, 2H, CH_2), 2.48 (s, 2H, CH_2), 3.78 (s, 2H, CH_2-Ar), 7.15 (d, $J = 8.8$ Hz, 1H, H-6), 7.46 (ddd, $J = 8.1$ Hz, $J = 6.9$ Hz, $J = 1.2$ Hz, 1H, H-3), 7.57 (ddd, $J = 8.3$ Hz, $J = 6.9$ Hz, $J = 1.5$ Hz, 1H, H-2), 7.70 (d, $J = 8.8$ Hz, 1H, H-5), 7.80 (d, $J = 8.1$ Hz, 1H, H-4), 7.90 (dd, $J = 8.6$ Hz, $J = 1.0$ Hz, 1H, H-1); ^{13}C NMR, δ, ppm: 19.02 (CH_2), 28.58 (CH_3), 32.30 (C), 41.44 (CH_2), 50.79 (CH_2), 108.82 (C), 113.64 (C), 117.17 (CH), 123.24

(CH), 125.08 (CH), 127.09 (CH), 128.35 (CH), 130.87 (C), 132.14 (C), 147.01 (C), 164.80 (C), 198.34 (C); IR, ν, cm^{-1}: 3070 ($CH_{arom.}$), 2959, 2935, 2889 ($CH_{aliph.}$), 1647 (C=O), 1596 (C=C), 1620, 1597 (C=C), 1512, 146, 1396, 1377, 1227, 1180, 1026, 810, 752; EI-MS (70 eV) m/z (% int.): 278 (M^+, 100), 277 (M^+–H, 54), 263 (M^+–CH_3, 28), 250 (M^+–CO, 6), 245 (M^+–CH_3– H_2O, 18), 235 (M^+–CH_3– CO, 15), 208 (29), 194 (47), 165 (72), 152 (13), 139 (10), 128 (12), 115 (7). Anal. calcd. for $C_{19}H_{18}O_2$, %: C, 82.01; H, 6.48. Found, %: C, 81.96; H, 6.53.

3-(1-Adamantyl)-9,9-dimethyl-8,9,10,12-tetrahydro-1*H*-benzo[*a*]xanthen-11-one (5b). Pink crystals; ^1H NMR, δ, ppm: 1.16 [s, 6H, $C(CH_3)_2$], 1.78–1.85 (m, 6H, $3CH_{2Ad}$), 2.02 (s, 6H, $3CH_{2Ad}$), 2.14 (br. s, 3H, $3CH_{Ad}$), 2.38 (s, 2H, CH_2), 2.49 (s, 2H, CH_2), 3.78 (s, 2H, CH_2-Ar), 7.13 (d, $J = 8.8$ Hz, 1H, $H_{arom.}$), 7.67 (d, $J = 8.8$ Hz, 2H, $H_{arom.}$), 7.70 (s, 1H, H-4), 7.87 (d, $J = 8.8$ Hz, 1H, $H_{arom.}$); ^{13}C NMR, δ, ppm: 18.98 (CH_2), 28.59 (CH_3), 29.02 (CH), 32.29 (C), 36.31 (C), 36.90 (CH_2), 41.49 (CH_2), 43.19 (CH_2), 50.81 (CH_2), 108.80 (C), 113.34 (C), 116.90 (CH), 122.98 (CH), 123.46 (CH), 125.29 (CH), 128.35 (CH), 130.32 (C), 130.98 (C), 146.59 (C), 148.09 (C), 164.91 (C), 198.42 (C); IR, ν, cm^{-1}: 3070, 3060 ($CH_{arom.}$), 2955, 2901, 2847 ($CH_{aliph.}$), 1647 (C=O), 1624, 1601 (C=C), 1396, 1231, 1188, 1173, 1150, 1018, 976, 887, 806; EI-MS (70 eV) m/z (% int.): 412 (M^+, 100), 397 (M^+–CH_3, 14), 384 (M^+–CO, 4), 379 (M^+–CH_3– H_2O, 4), 369 (M^+–CH_3– CO, 5), 342 (12), 328 (8), 178 (6), 135 (Ad^+, 6). Anal. calcd. for $C_{29}H_{32}O_2$, %: C, 84.46; H, 7.77. Found, %: C, 84.40; H, 7.82.

3,6-Di(1-adamantyl)-9,9-dimethyl-8,9,10,12-tetrahydro-1*H*-benzo[*a*]xanthen-11-one (5c). Pink crystals; ^1H NMR, δ, ppm: 1.21 [s, 6H, $C(CH_3)_2$], 1.84 (br. s, 12H, H_{Ad}), 2.02 (br. s, 6H, H_{Ad}), 2.16 (br. s, 6H, H_{Ad}), 2.21 (br. s, 6H, H_{Ad}), 2.42 (s, 2H, CH_2), 2.58 (s, 2H, CH_2), 3.81 (s, 2H, CH_2-Ar), 7.60 (s, 1H, H-5), 7.63 (d, $J = 8.1$ Hz, 1H, H-2), 7.70 (s, 1H, H-4), 7.84 (d, $J = 8.1$ Hz, 1H, H-1); ^{13}C NMR, δ, ppm: 19.13 (CH_2), 28.68 (CH_3), 29.04 (CH), 29.15 (CH), 32.35 (C), 36.30 (C), 36.93 (CH_2), 37.20 (CH_2), 37.50 (C), 41.35 (CH_2), 43.23 (CH_2), 50.87 (CH_2), 108.50 (C), 113.83 (C), 122.49 (CH), 123.46 (CH), 124.59 (CH), 125.18 (CH), 128.93 (C), 130.65 (C), 137.59 (C), 146.63 (C), 148.08 (C), 164.05 (C), 198.25 (C); IR, ν, cm^{-1}: 2901, 2847 ($CH_{aliph.}$), 1655 (C=O), 1597 (C=C), 1450, 1396, 1223, 1180, 1134, 1030, 976, 899, 802; EI-MS (70 eV) m/z (% int.): 546 (M^+, 8), 411 (M^+–Ad, 6), 246 ($M^+ - 2Ad - 2CH_3$, 10), 135 (Ad^+, 100). Anal. calcd. for $C_{39}H_{46}O_2$, %: C, 85.67; H, 8.48. Found, %: C, 85.72; H, 8.41.

9,9-Dimethyl-12-phehyl-8,9,10,12-tetrahydro-1*H*-benzo[*a*]xanthen-11-one (5d). Colorless crystals; ^1H NMR, δ, ppm: 0.94 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.20–2.31 (m, 2H, CH_2), 2.55 (s, 2H, CH_2), 5.70 (s, 1H, CHPh), 7.04 (dd, $J = 7.4$ Hz, $J = 7.3$ Hz, 1H, $H_{arom.}$), 7.16 (t, $J = 7.5$ Hz, 2H, $H_{arom.}$), 7.30–7.36 (m, 4H, $H_{arom.}$), 7.41 (dd, $J = 8.2$ Hz, $J = 1.2$ Hz, 1H, $H_{arom.}$), 7.73–7.76 (m, 2H, $H_{arom.}$), 7.99 (d, $J = 8.3$ Hz, 1H, $H_{arom.}$); ^{13}C NMR, δ, ppm: 27.26 (CH_3), 29.42 (CH_3), 32.36 (C), 34.82 (CH), 41.50 (CH_2), 51.00 (CH_2), 114.36 (C), 117.16 (CH), 117.80 (C), 123.78 (CH), 125.01 (CH), 126.35 (CH), 127.12 (CH), 128.36 (CH), 128.50 (CH), 128.54 (CH), 128.95 (CH), 131.50 (C), 131.59 (C), 144.87 (C), 147.84 (C), 163.99 (C), 197.00 (C); IR, ν, cm^{-1}: 3055, 3024 ($CH_{arom.}$), 2955, 2885 ($CH_{aliph.}$), 1651

(C=O), 1630, 1597 (C=C), 1450, 1373, 1227, 1184, 1169, 1142, 1030, 806, 748, 698; EI-MS (70 eV) m/z (% int.): 354 (M^+, 23), 277 (M^+–C_6H_5, 100), 269 (4), 239 (4), 221 (22), 193 (14), 165 (25). Anal. calcd. for $C_{25}H_{22}O_2$, %: C, 84.75; H, 6.22. Found, %: C, 84.68; H, 6.27.

6,6-Dimethyl-1,5,6,7,8,9,10,11,12,13-decahydrochromeno[3,2-*g*]β-carboline-8,13-dione (7). A mixture of 0.63 g (3.8 mmol) of **1b** and 1 g (3.8 mmol) of **6** in DMF (10 ml) was refluxed for 1 h. After completion, the reaction mixture was cooled to room temperature, the precipitate that formed was filtered, washed in ice-cold ethylacetate, and purified by recrystallization from DMF to give 0.93 g (73%) of pink crystals, mp > 300 °C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.07 [s, 6H, $C(CH_3)_2$], 2.26 (s, 2H, CH_2), 2.87 (s, 2H, CH_2), 3.15 (t, $J = 6.9$ Hz, 2H, CH_2), 3.52 (td, $J = 6.9$ Hz, $J = 2.3$ Hz, 2H, CH_2), 3.73 (s, 2H, CH_2-Ar), 6.88 (d, $J = 8.7$ Hz, 1H, $H_{arom.}$), 7.09 (br. s, 1H, NH_{amide}), 7.23 (d, $J = 8.70$ Hz, 1H, $H_{arom.}$), 11.24 (br. s, 1H, NH_{indole}); ^{13}C NMR (DMSO-d_6), δ, ppm: 19.79 (CH_2), 22.72 (CH_2), 28.43 (CH_3), 32.16 (C), 41.61 (CH_2), 41.86 (CH_2), 50.98 (CH_2), 107.81 (C), 112.40 (CH), 112.87 (C), 114.71 (CH), 119.10 (C), 123.91 (C), 129.19 (C), 134.94 (C), 143.68 (C), 161.99 (C), 165.12 (C), 196.83 (C); IR, ν, cm^{-1}: 3398, 3224 (NH), 2955, 2927, 2870 ($CH_{aliph.}$), 1651 (C=O), 1636 (C=O), 1612 (C=C), 1497, 1427, 1396, 1369, 1342, 1227, 1207, 1173, 1076, 1026, 806, 775; EI-MS (70 eV) m/z (% int.): 336 (M^+, 100), 335 (M^+–H, 55), 321 (M^+–CH_3, 20), 279 (10), 252 (22). Anal. calcd. for $C_{25}H_{22}O_2$, %: C71.43; H, 5.95; N, 8.32. Found, %: C, 71.37; H, 5.99; N, 8.36.

2,2,11,11-Tetramethyl-1,2,3,4,5,8,9,10,11,12-decahydrochromeno[3,2-*c*]-xanthene-4,9-dione (9). A mixture of 2.07 g (6.7 mmol) of **8**[31] and 2.23 g (13.4 mmol) of **1b** in DMF (15 ml) was refluxed for 10 h. After completion, the reaction mixture was cooled to room temperature, and the precipitate that formed was filtered, washed in ethanol, and purified by recrystallization from DMF to give 1.72 g (68%) of yellow crystals, mp 276–278 °C. ^{1}H NMR, δ, ppm: 1.12 (s, 12H, $6CH_3$), 2.32 (s, 4H, $2CH_2$-3,10), 2.50 (s, 4H, $2CH_2$-1,12), 3.45 (s, 4H, $2CH_2$-Ar), 6.82 (s, 2H, $H_{arom.}$); ^{13}C NMR, δ, ppm: 20.90 (CH_2), 28.49 (CH_3), 32.29 (C), 41.44 (CH_2), 50.70 (CH_2), 108.90 (C), 120.29 (C), 124.53 (CH), 138.27 (CH), 164.64 (CH), 197.96 (CH); IR, ν, cm^{-1}: 2959, 2927, 2874 ($CH_{aliph.}$), 1655 (C=O), 1574, 1462, 1385, 1285, 1226, 1207, 1126, 1061, 814; EI-MS (70 eV) m/z (% int.): 378 (M^+, 100), 377 (M^+–H, 24), 363 (M^+–CH_3, 23), 335 (M^+–CH_3–CO, 15), 294 (23), 256 (32), 115 (32). Anal. calcd. for $C_{24}H_{26}O_4$, %: C, 76.17; H, 6.92. Found, %: C, 76.23; H, 6.88.

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