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ORIGINAL PAPER

Non-catalytic multicomponent rapid and efficient approach to 10-(2,4,6-trioxohexahydropyrimidin-5-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-ones from salicylaldehydes, dimedone, and barbituric acids

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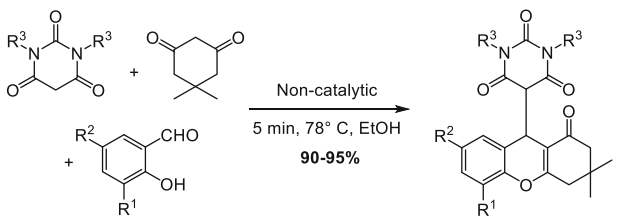
Abstract Non-catalytic multicomponent reaction of salicylaldehydes, dimedone, and barbituric acids initiated by reflux in ethanol results in the fast (5 min) and efficient formation of substituted tetrahydro-1*H*-xanthen-1-ones in 90–95 % yields. The developed fast multicomponent approach to the substituted tetrahydro-1*H*-xanthen-1-ones, which are known as medicinally relevant substances such as antibiotics, enzyme inhibitors, and anticancer drugs, is beneficial from the viewpoint of diversity-oriented multigram-scale processes and represents fast, efficient, and environmentally benign synthetic concept for multicomponent reaction strategy.

Graphical abstract



Keywords Non-catalytic · Carbanions · Cyclizations · Heterocycles · Green chemistry

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Introduction

Multicomponent reactions are valuable tools for the preparation of structurally diverse drug-like heterocyclic compounds [1]. MCR designed to produce biologically active compounds has become an important area of research in organic, combinatorial, and medicinal chemistry [2].

Xanthenes (tricyclic dibenzopyrans) are one of the most widely distributed classes of natural compounds and possess diverse pharmacological properties, such as antiviral [3], anti-inflammatory [4], and anti-cancer [5, 6] activity. They are also used as antagonists for paralyzing the action of zoxazolamine [7], in photodynamic therapy (PDT) [8], and as antagonists for drug resistant leukemia lines [9]. 9-(2-Hydroxy-4,4-dimethyl-6-oxo-1-cyclohexen-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-ones are well-known as orally active and selective Y5 antagonists [10]. Correlations between the in vitro function and the binding activity of different peptide agonists and their potent stimulation of food intake have found the Y5 receptor as a major feeding receptor [11].

2,4,6-Trioxohexahydropyrimidine or barbituric acid is a type of privileged medicinal scaffold also called barbiturates. Barbiturates are the famous class of drugs that act as central nervous system depressants, and by virtue of this produce a wide spectrum of effects, from mild sedation to anesthesia [12]. They are also effective as anxiolytics and as anticonvulsants [13]. The current interest in barbiturates arises from their pharmacological potential as analeptics, immunomodulating and anti-AIDS agents, and also as anticancer remedies [14].

Thus, the 10-(2,4,6-trioxohexahydropyrimidin-5-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one system

appears to be of the interest because it incorporates a tetrahydro-1*H*-xanthen-1-one and a 2,4,6-trioxohexahydropyrimidine heterocyclic ring, which are both promising with respect to biological responses. Recently two catalytic methods were suggested for 10-(2,4,6-trioxohexahydropyrimidin-5-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one synthesis from salicylaldehydes, dimedone, and barbituric acid under different catalytic conditions. Among these catalysts are known L-prolin (10 mol%) [15] and TH amino acid catalyst [16] (20 % by weight of salicylaldehyde), which was specially obtained by tedious hydrolysis of bovine tendon [16]. In the case of L-prolin as catalyst only one example of this multicomponent reaction is known. From salicylaldehyde, dimedone, and barbituric acid (80 °C, 6 h) 2,4,6-trioxohexahydropyrimidine substituted tetrahydro-1*H*-xanthen-1-one **1** was obtained in 87 % yield [15]. The similar reaction with TH amino acid catalyst resulted in only 56 % yield of **1** after 24 h heating at 80 °C [16] (Scheme 1).

Both these catalytic methods are characterized by heating at 80 °C during long reaction time (6–24 h), and resulted in moderate yields of tetrahydro-1*H*-xanthen-1-one **1** [15, 16]. Moreover, from the position of 'green chemistry' one could formulate that 'the best catalyst is no catalyst' [17, 18]. Thus, the two known procedures for the synthesis of tetrahydro-1*H*-xanthen-1-ones **1** have its merits, but the fast, simple, and efficient non-catalytic method for this tandem Knoevenagel–Michael process with further cyclization has yet to be developed.

Recently, we have found non-catalytic fast and efficient multicomponent transformation of isatin, cyclic C–H acids, and malononitrile into spirooxoindoles [19], general non-catalytic approach to spiroacenaphthylene heterocycles from acenaphthenequinone, cyclic CH-acids, and malononitrile [20], and also non-catalytic efficient approach to substituted 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones from salicylaldehydes and dimedone [21].

Considering our results on the non-catalytic multicomponent and cascade transformation of C–H acids and salicylaldehydes [19–21] as well as the certain biomedical application of 10-(2,4,6-trioxo-hexahydropyrimidin-5-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-ones mentioned above, we were prompted to design a convenient fast and facile non-catalytic methodology for the efficient synthesis of substituted tetrahydro-1*H*-xanthen-1-ones based on multicomponent reaction of salicylaldehydes, dimedone, and barbituric acids.

Results and discussion

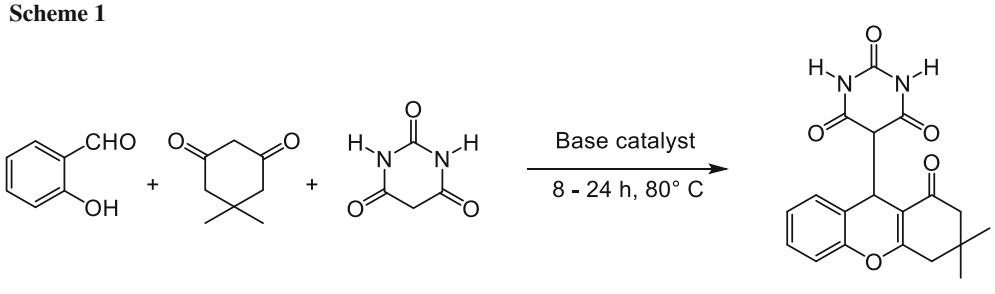
As it follows from introduction, we were interested in designing a fast, convenient, and facile non-catalytic methodology for the efficient synthesis of functionalized tetrahydro-1*H*-xanthen-1-one system based on multicomponent reaction of salicylaldehydes **2a–2g**, dimedone, and barbituric acids **3a–3c** (Scheme 2; Tables 1, 2).

On the first step of this investigation the transformation of salicylaldehyde (**2a**), dimedone, and *N*′,*N*′-dimethylbarbituric acid (**2a**) into tetrahydro-1*H*-xanthen-1-one **4a** was studied (Table 1). In ethanol as a solvent under reflux (78 °C) in the presence of NaOAc or KF as catalyst in only 5 min reaction time tetrahydro-1*H*-xanthen-1-one **4a** was obtained in 85–92 % yield (Table 1, entries 1–4). The more interesting was the fact that just the same result (93 % yield) was achieved in ethanol without any catalyst (Table 1, entry 5). Somewhat lower yields of 75–91 % were found when multicomponent reaction was carried out in water, methanol, *n*-propanol, or even under solvent-free conditions without catalyst under heating (Table 1, entries 5–9). The best yield 95 % of tetrahydro-1*H*-xanthen-1-one **4a** was obtained in ethanol with the minimal quantity of solvent (Table 1, entry 10).

Under the optimal conditions thus found, salicylaldehydes **2a–2f**, dimedone, and barbituric acids **3a–3c** were transformed into corresponding substituted tetrahydro-1*H*-xanthen-1-ones **4a–4h** in 90–95 % yields (Table 2).

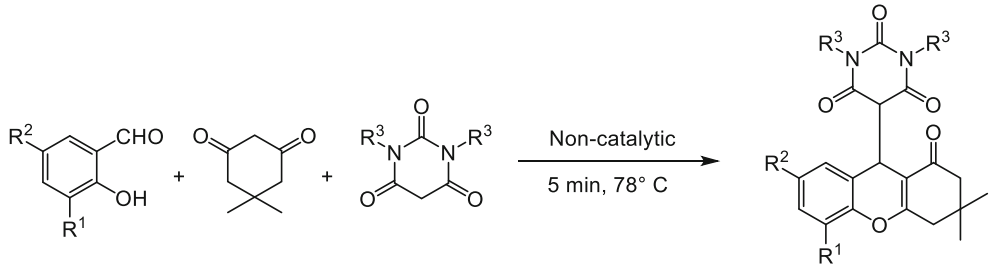
With the above results taken into consideration and the mechanistic data on non-catalytic multicomponent

Scheme 1



1

Scheme 2



2a-2f

2a: $R^1 = R^2 = H$
2b: $R^1 = H$, $R^2 = Me$
2c: $R^1 = OEt$, $R^2 = H$
2d: $R^1 = OMe$, $R^2 = Br$
2e: $R^1 = H$, $R^2 = Cl$
2f: $R^1 = H$, $R^2 = Br$

3a-3c

3a: $R^3 = Me$
3b: $R^3 = Et$
3c: $R^3 = H$

4a-4h

4a: $R^1 = R^2 = H$, $R^3 = Me$
4b: $R^1 = H$, $R^2 = Me$, $R^3 = Me$
4c: $R^1 = OEt$, $R^2 = H$, $R^3 = Me$
4d: $R^1 = OMe$, $R^2 = Br$, $R^3 = Me$
4e: $R^1 = H$, $R^2 = Cl$, $R^3 = Me$
4f: $R^1 = H$, $R^2 = Br$, $R^3 = Me$
4g: $R^1 = R^2 = H$, $R^3 = Et$
4h: $R^1 = R^2 = R^3 = H$

Table 1 Multicomponent transformation of salicylaldehyde (**2a**), dimedone, and *N*,*N*′-dimethylbarbituric acid (**3a**) into tetrahydro-1*H*-xanthen-1-one **4a**

Entry	Catalyst	Solvent	Quantity of solvent/cm^3	Temp./°C	Time/min	Yield/%[a]
1	NaOAc	EtOH	5	78	5	85
2	KF	EtOH	5	78	5	88
3	NaOAc	EtOH	2	78	5	89
4	KF	EtOH	2	78	5	92
5	–	EtOH	2	78	5	93
6	–	H_2O	2	80	5	76
7	–	MeOH	2	65	5	85
8	–	PrOH	2	80	5	91
9	–	–	–	80	5	75
10	–	EtOH	1	78	5	95
11	–	EtOH	1	78	3	87

5 mmol of aldehyde **2a**, 5 mmol of dimedone, 5 mmol of *N*,*N*′-dimethyl-barbituric acid (**3a**), heating 3–5 min

[a] Isolated yield

Table 2 Non-catalytic multicomponent transformation of salicylaldehydes **2a–2f**, dimedone, and barbituric acids **3a–3c** into substituted tetrahydro-1*H*-xanthen-1-ones **4a–4h**

Entry	Aldehyde	R^1	R^2	Barbituric acid	R^3	Tetrahydro-1*H*-xanthen-1-one	Yield/%[a]
1	**2a**	H	H	**3a**	Me	**4a**	95
2	**2b**	H	Me	**3a**	Me	**4b**	91
3	**2c**	OEt	H	**3a**	Me	**4c**	96
4	**2d**	OMe	Br	**3a**	Me	**4d**	92
5	**2e**	H	Cl	**3a**	Me	**4e**	90
6	**2f**	H	Br	**3a**	Me	**4f**	93
7	**2a**	H	H	**3b**	Et	**4g**	90
8	**2a**	H	H	**3c**	H	**4h**	92

5 mmol of aldehyde **2a–2f**, 5 mmol of dimedone, 5 mmol of barbituric acid **3a–3c**, 1 mL of EtOH, 5 min heating at 78 °C

[a] Isolated yield

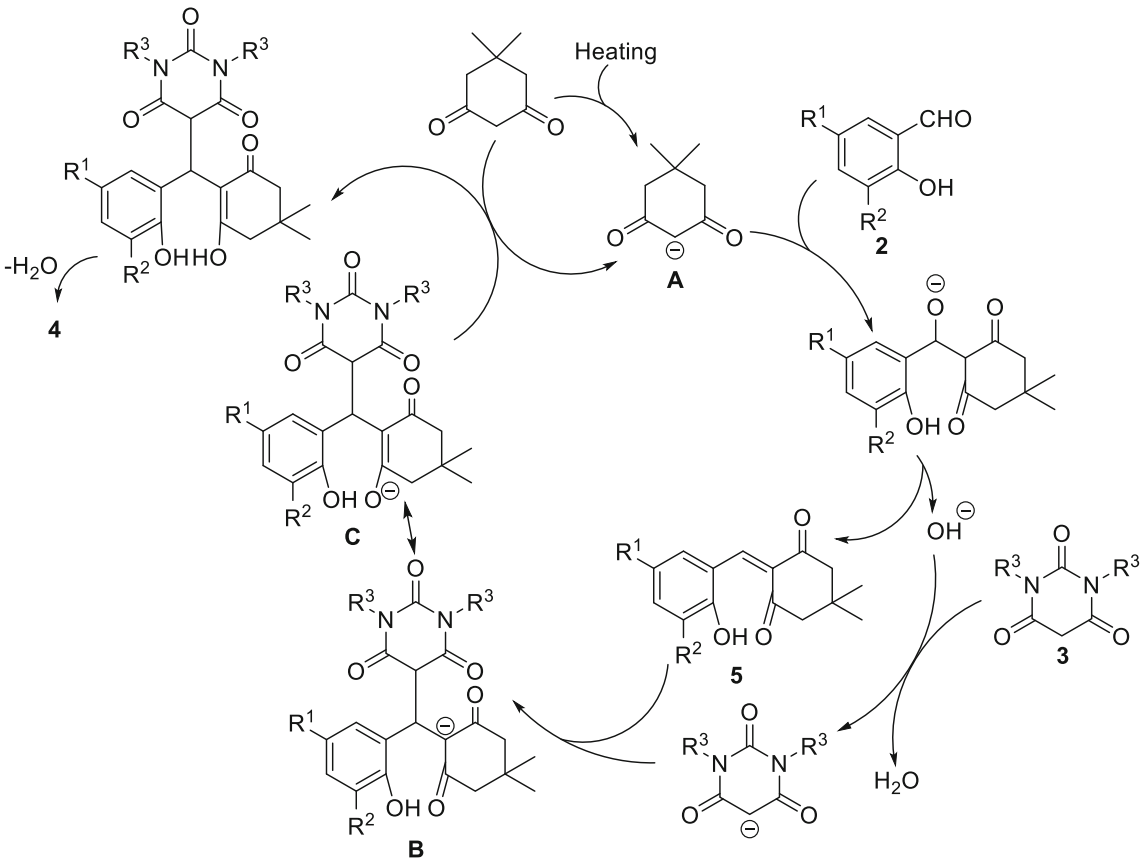
processes [19–21], the following mechanism for the non-catalytic multicomponent transformation of salicylaldehydes **2**, dimedone, and barbituric acids **3** into substituted tetrahydro-1*H*-xanthen-1-ones **4** is proposed. The initiation step of the catalytic cycle begins with the thermal deprotonation of a molecule of dimedone, which leads to the dimedone anion **A** formation (Scheme 3). The following process represents a typical multicomponent reaction. Knoevenagel condensation of the anion **A** with salicylaldehyde **2** takes place with the elimination of a hydroxide anion and formation of Knoevenagel adduct **5** [22]. The subsequent hydroxide-promoted Michael addition of barbituric acids **3** to electron-deficient Knoevenagel adduct **5** results in anions **B** and **C** formation. Protonation of anion **C** with the next molecule of dimedone leads to the corresponding tetrahydro-1*H*-xanthen-1-one **4** formation with the regeneration of anion **A** at the last step of the catalytic cycle (Scheme 3).

Thus, the simple non-catalytic procedure can produce a fast (5 min), efficient, and selective multicomponent transformation of salicylaldehydes, dimedone, and barbituric acids into substituted tetrahydro-1*H*-xanthen-1-ones in excellent 90–95 % yields. This new process opens an efficient and convenient multicomponent way to create substituted tetrahydro-1*H*-xanthen-1-ones, the pharmacologically active substances with known antiviral, anti-inflammatory, anticancer activity and promising compounds for different biomedical applications. This non-catalytic multicomponent procedure utilizes simple equipment; it is easily carried out and is valuable from the viewpoint of environmentally benign diversity-oriented large-scale processes.

Experimental

All melting points were measured with a Gallenkamp melting-point apparatus. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker Avance II 300 spectrometer at ambient temperature. Chemical shift values are relative to Me_4Si. IR spectra were recorded with a Bruker ALPHA-T FT-IR spectrometer in KBr pellets. Mass-spectra (EI, 70 eV) were obtained directly with a Kratos MS-30 spectrometer. High-resolution mass spectrometry (HRMS) (electrospray ionization, ESI) was measured on a Bruker microTOF II instrument; external or internal calibration was done with an electrospray calibrant solution

Scheme 3



(Fluka). All chemicals used in this study were commercially available.

General procedure

A solution of salicylaldehyde (5 mmol), barbituric acid (5 mmol), and 0.7 g dimedone (5 mmol) in 1 cm^3 ethanol was stirred under reflux for 5 min. Then the precipitated product was filtered off, rinsed with 2 cm^3 ice-cold ethanol–water solution (1:1), and dried under reduced pressure.

5-(3,3-Dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-1,3-dimethyl-pyrimidine-2,4,6(1H,3H,5H)-trione (**4a**, $C_{21}H_{22}N_2O_5$)
Yield 95 %; m.p.: 212–213 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 2.24 (s, 2H, CH_2), 2.47 (d, J = 17.7 Hz, 1H, CH_2), 2.57 (d, J = 17.7 Hz, 1H, CH_2), 3.07 (s, 3H, N–CH_3), 3.22 (s, 3H, N–CH_3), 3.86 (d, J = 2.7 Hz, 1H, CH), 4.87 (d, J = 2.7 Hz, 1H, CH), 7.03 (d, J = 8.1 Hz, 1H, Ar), 7.07–7.12 (m, 2H, Ar), 7.19–7.29 (m, 1H, Ar) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.3, 28.3, 28.4, 29.4, 32.1, 36.4, 41.6, 50.7, 55.1, 109.0, 116.8, 120.6, 125.1, 128.0, 129.1, 150.5, 151.3, 167.1, 167.3, 168.1, 197.3 ppm; IR (KBr): $\bar{\nu}$ = 3428, 3412, 2962, 2951, 1690, 1676, 1643, 1391, 1376, 1229 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 382 ($[M]^+$, 6), 298 (5), 227 (100), 171 (96), 143 (19), 115 (84), 69 (30), 58 (32), 42 (56), 28 (61); HRMS (ESI): *m/z* calcd for $C_{21}H_{24}N_2NaO_5$ $[M+Na]^+$ 405.1421, found 405.1412.

1,3-Dimethyl-5-(3,3,7-trimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-pyrimidine-2,4,6(1H,3H,5H)-trione (**4b**, $C_{22}H_{24}N_2O_5$)
Yield 91 %; m.p.: 179–180 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.33 (s, 2H, CH_2), 2.45 (d, J = 17.7 Hz, 1H, CH_2), 2.55 (d, J = 17.7 Hz, 1H, CH_2), 3.08 (s, 3H, N–CH_3), 3.22 (s, 3H, N–CH_3), 3.84 (d, J = 2.7 Hz, 1H, CH), 4.81 (d, J = 2.7 Hz, 1H, CH), 6.91 (d, J = 8.3 Hz, 2H, Ar), 7.04 (dd, J_1 = 8.3 Hz, J_2 = 2.0 Hz, 1H, Ar) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8, 27.4, 28.3 (2C), 29.4, 32.1, 36.8, 41.7, 50.7, 55.1, 108.7, 116.4, 120.2, 128.3, 129.8, 134.9, 148.5, 151.4, 167.2, 167.5, 168.3, 197.3 ppm; IR (KBr): $\bar{\nu}$ = 2959, 2877, 2888, 1695, 1678, 1631, 1458, 1388, 1229, 1111 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 396 ($[M]^+$, 1), 241 (100), 225 (7), 185 (35), 157 (14), 128 (29), 115 (14), 69 (24), 58 (36), 42 (55); HRMS (ESI): *m/z* calcd for $C_{22}H_{24}N_2NaO_5$ $[M+Na]^+$ 419.1577, found 419.1564.

5-(5-Ethoxy-3,3-dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4c**, $C_{23}H_{26}N_2O_6$)
Yield 96 %; m.p.: 164–165 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.45 (t, J = 7.0 Hz, 3H, CH_3), 2.34 (s, 2H, CH_2), 2.54 (d, J = 17.7 Hz, 1H, CH_2), 2.65 (d, J = 17.7 Hz, 1H, CH_2), 3.08 (s, 3H, N–CH_3), 3.21 (s, 3H, N–CH_3), 3.86 (d, J = 2.6 Hz, 1H, CH), 3.96–4.19 (m, 2H, CH_2), 4.86 (d, J = 2.6 Hz, 1H, CH), 6.64 (d, J = 7.7 Hz, 1H, Ar), 6.82 (d, J = 7.7 Hz, 1H), 7.00 (t, J = 8.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 27.4, 28.3, 28.4, 29.4, 32.2, 36.7, 41.6, 50.8, 55.0, 64.8, 108.8, 112.9, 119.3, 121.6, 124.8, 140.6, 147.3, 151.4, 167.1, 167.3, 168.1, 197.5 ppm; IR (KBr): $\bar{\nu}$ = 2957, 1676, 1648, 1469, 1421, 1388, 1287, 1225, 1194, 1075 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 426 ($[M]^+$, 8), 410 (4), 326 (8), 271 (100), 255 (9), 215 (11), 187 (12), 159 (5), 115 (8), 69 (8); HRMS (ESI): *m/z* calcd for $C_{23}H_{26}N_2NaO_6$ $[M+Na]^+$ 449.1683, found 449.1665.

5-(7-Bromo-5-methoxy-3,3-dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4d**, $C_{22}H_{23}BrN_2O_6$)
Yield 92 %; m.p.: 188–189 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.29 (d, J = 16.3 Hz, 1H, CH_2), 2.35 (d, J = 16.3 Hz, 1H, CH_2), 2.52 (d, J = 17.7 Hz, 1H, CH_2), 2.61 (d, J = 17.7 Hz, 1H, CH_2), 3.16 (s, 3H, N–CH_3), 3.24 (s, 3H, N–CH_3), 3.87 (s, 3H, CH_3), 3.83 (d, J = 2.6 Hz, 1H, CH), 4.82 (d, J = 2.6 Hz, 1H, CH), 6.89 (d, J = 1.8 Hz, 1H, Ar), 6.94 (d, J = 1.8 Hz, 1H, Ar) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.3, 28.4, 28.5, 29.3, 32.2, 35.8, 41.5, 50.7, 55.1, 56.4, 108.6, 114.8, 117.2, 122.2, 123.6, 139.5, 148.6, 151.3, 166.9, 167.1, 167.7, 197.4 ppm; IR (KBr): $\bar{\nu}$ = 2964, 2955, 1676, 1646, 1575, 1483, 1422, 1382, 1225, 1191 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 492 ($[M]^+$, 2), 490 ($[M]^+$, 3), 337 (5), 335 (6), 279 (2), 172 (4), 156 (3), 115 (7), 69 (18), 28 (100); HRMS (ESI): *m/z* calcd for $C_{22}H_{23}BrN_2NaO_6$ $[M+Na]^+$ 513.0632, found 513.0622.

5-(7-Chloro-3,3-dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4e**, $C_{21}H_{21}ClN_2O_5$)
Yield 90 %; m.p.: 207–208 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.29 (d, J = 16.2 Hz, 1H, CH_2), 2.35 (d, J = 16.2 Hz, 1H, CH_2), 2.47 (d, J = 17.8 Hz, 1H, CH_2), 2.54 (d, J = 17.8 Hz, 1H, CH_2), 3.16 (s, 3H, N–CH_3), 3.24 (s, 3H, N–CH_3), 3.85 (d, J = 2.5 Hz, 1H, CH), 4.85 (d, J = 2.5 Hz, 1H, CH), 6.98 (d, J = 8.7 Hz, 1H, Ar), 7.16 (d, J = 2.3 Hz, 1H, Ar), 7.21 (dd, J_1 = 8.7 Hz, J_2 = 2.3 Hz, 1H, Ar) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2, 28.4, 28.5, 29.4, 32.1, 35.6, 41.5, 50.7, 55.2, 108.6, 118.1, 123.0, 128.0, 129.1, 130.2, 149.1, 151.2, 166.9, 167.1, 167.9, 197.4 ppm; IR (KBr): $\bar{\nu}$ = 2961, 2883, 1678, 1633, 1684, 1678, 1633, 1456, 1386, 1235 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 418 ($[M]^+$, 2), 416 ($[M]^+$, 5), 332

(4), 261 (99), 245 (12), 205 (97), 149 (78), 114 (30), 83 (33), 42 (100); HRMS (ESI): *m/z* calcd for $C_{21}H_{21}ClN_2NaO_5$ $[M+Na]^+$ 439.1031, found 439.1023.

5-(7-Bromo-3,3-dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4f**, $C_{21}H_{21}BrN_2O_5$)

Yield 93 %; m.p.: 209–210 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.13$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.28 (d, $J = 16.3$ Hz, 1H, CH_2), 2.35 (d, $J = 16.3$ Hz, 1H, CH_2), 2.47 (d, $J = 18.0$ Hz, 1H, CH_2), 2.54 (d, $J = 18.0$ Hz, 1H, CH_2), 3.16 (s, 3H, N–CH_3), 3.25 (s, 3H, N–CH_3), 3.84 (d, $J = 2.5$ Hz, 1H, CH), 4.84 (d, $J = 2.5$ Hz, 1H, CH), 6.92 (d, $J = 8.6$ Hz, 1H, Ar), 7.31 (d, $J = 1.9$ Hz, 1H, Ar), 7.35 (dd, $J_1 = 8.6$ Hz, $J_2 = 1.9$ Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 27.2$, 28.4, 28.5, 29.4, 32.2, 35.7, 41.6, 50.7, 55.2, 108.7, 117.5, 118.5, 123.4, 131.0, 132.0, 149.6, 151.2, 166.9, 167.1, 167.9, 197.4 ppm; IR (KBr): $\bar{\nu} = 2960$, 2877, 1679, 1634, 1455, 1416, 1386, 1234, 1187, 1111, 1037 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 462 ($[M]^+$, 7), 460 ($[M]^+$, 8), 307 (100), 305 (93), 251 (4), 249 (4), 142 (9) 114 (12), 58 (28), 42 (45); HRMS (ESI): *m/z* calcd for $C_{21}H_{21}BrN_2NaO_5$ $[M+Na]^+$ 483.0526, found 483.0516.

1,3-Diethyl-5-(3,3-dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)-pyrimidine-2,4,6(1H,3H,5H)-trione (**4g**, $C_{23}H_{26}N_2O_5$)

Yield 90 %; m.p.: 115–116 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.90$ (t, $J = 7.0$ Hz, 3H, CH_3), 1.13 (s, 3H, CH_3), 1.21 (t, $J = 7.0$ Hz, 3H, CH_3), 1.22 (s, 3H, CH_3), 2.35 (s, 2H, CH_2), 2.47 (d, $J = 17.6$ Hz, 1H, CH_2), 2.59 (d, $J = 17.6$ Hz, 1H, CH_2), 3.56–3.78 (m, 2H, CH_2), 3.82–3.94 (m, 2H, CH_2), 3.86 (d, $J = 2.5$ Hz, 1H, CH), 4.91 (d, $J = 2.5$ Hz, 1H, CH), 7.01 (d, $J = 8.3$ Hz, 1H, Ar), 7.07 (t, $J = 6.3$ Hz, 2H, Ar), 7.19–7.29 (m, 1H, Ar) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 12.7$, 13.1, 27.6, 29.2, 32.3, 36.4, 36.9, 37.3, 41.7, 50.8, 54.4, 109.3, 117.0, 120.4, 125.0, 128.2, 129.1, 150.5, 150.6, 166.7, 167.2, 168.0, 197.3 ppm; IR (KBr): $\bar{\nu} = 2980$, 2953, 1677, 1652, 1458, 1406, 1387, 1310, 1231, 1125 cm^{-1}; MS (EI, 70 eV): *m/z* (%) = 410 ($[M]^+$, 5), 326 (2), 267 (4), 227 (100), 211 (8), 171 (35), 115 (28), 69 (14), 44 (14), 29 (34); HRMS (ESI): *m/z* calcd for $C_{23}H_{26}N_2NaO_5$ $[M+Na]^+$ 433.1734, found 433.1724.

*5-(3,3-Dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-xanthen-9-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (**4h**)*

Yield 92 %; m.p.: 166–167 °C (Ref. [15] m.p.: 150–152 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.13$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.35 (s, 2H, CH_2), 2.48 (d, $J = 17.6$ Hz, 1H, CH_2), 2.56 (d, $J = 17.6$ Hz, 1H, CH_2), 3.88 (d, $J = 2.3$ Hz, 1H, CH), 4.94 (d, $J = 2.3$ Hz, 1H, CH), 7.02 (d, $J = 8.0$ Hz, 1H, Ar), 7.10 (t, $J = 7.2$ Hz, 1H, Ar), 7.23 (d, $J = 7.2$ Hz, 1H, Ar), 8.76 (s, 1H, NH), 8.94 (s, 1H, NH) ppm.

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