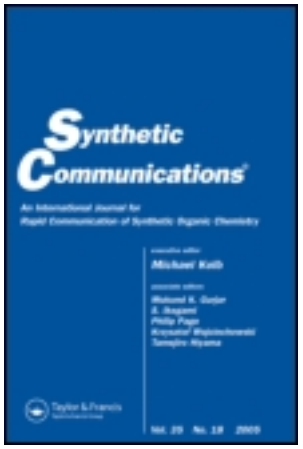

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Efficient One-Pot Synthesis of Some New Xanthene Derivatives Based on the Reaction of Dimedone with α,α′-Bis(substituted-benzylidene) Cycloalkanones Using Catalytic Amount of $_p$TSA

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EFFICIENT ONE-POT SYNTHESIS OF SOME NEW XANTHENE DERIVATIVES BASED ON THE REACTION OF DIMEDONE WITH α,α′-BIS(SUBSTITUTED-BENZYLIDENE) CYCLOALKANONES USING CATALYTIC AMOUNT OF $_P$TSA

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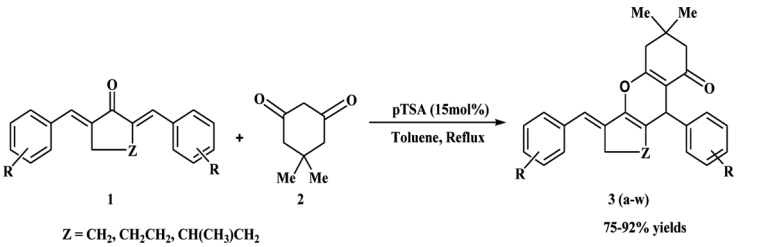
GRAPHICAL ABSTRACT



Abstract *A one-pot synthesis of a series of new xanthene derivatives has been achieved for the first time based on an application of Michael reaction between dimedone (5,5-dimethylcyclohexan-1,3-dione) and α,α′-bis(substituted-benzylidene)cycloalkanones using catalytic amount of p-toluene sulfonic acid as catalyst. The xanthenes were achieved efficiently via intramolecular cyclization of the Michael adduct.*

Keywords α,α′-Bis(substituted-benzylidene)cycloalkanones; dimedone; Michael addition; p-toluenesulfonic acid; xanthenes

INTRODUCTION

Xanthenes and benzoxanthenes are important heterocycles that are known to possess multiple biological activities. Although not widely found in nature, xanthenes and compounds based on these core templates exhibit a broad spectrum of pharmaceutical activities such as antibacterial,[1] anti-inflammatory,[2] and antiviral[3] activities. In addition, these compounds have been employed as dyes[4] and pH-sensitive fluorescent materials for visualization of biomolecular assemblies[5] and utilized in laser technologies.[6] Therefore, the synthesis of various xanthene

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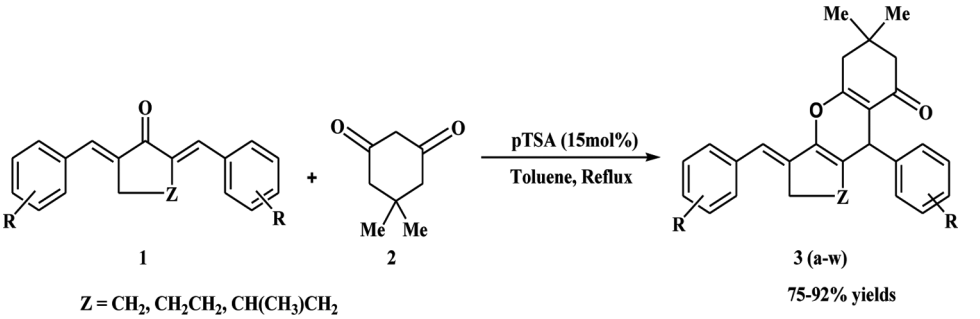


Scheme 1. Reaction of α,α′-bis(substituted-benzylidene) cycloalkanones (**1**) with dimedone.

derivatives is of great importance. A broad utility range has made xanthenes prime synthetic candidates, thereby accentuating the need to develop newer synthetic routes for scaffold manipulation of xanthene derivatives.

The α,α′-bis(substituted-benzylidene)cycloalkanones are very important materials used commonly as precursors of some important organic compounds. 2-Amino-3-cyano-4H-pyran derivatives were synthesized by one-step reaction of bisarylidenecycloalkanones with malononitrile.[7] Also, bisbenzylidenecyclohexanone derivatives have been efficiently used as trapping dipolarophiles for the synthesis of several spiro[pyrrolidine2,30-oxindole] derivatives.[8] In 2005, Ahmed *et al.* reported synthesis of the fused spiroketal skeleton by an application of Michael reaction between dimedone and diarylideneacetone using anhydrous $ZnCl_2$ as catalyst.[9] Herein we report the reaction of dimedone with α,α ′-bis(substituted-benzylidene) cycloalkanones for the synthesis of xanthene derivatives using *p*-toluene sulfonic acid (pTSA) as catalyst for the first time (Scheme 1).

The use of solid acid catalysts has gained vast importance in organic synthesis because of their several advantages such as operationally simplicity, nontoxicity, reusability, low cost, and easy isolation after completion of the reaction. In recent years pTSA has been considered as an efficient, inexpensive, and readily available catalyst for several organic transformations.[10]

RESULTS AND DISCUSSION

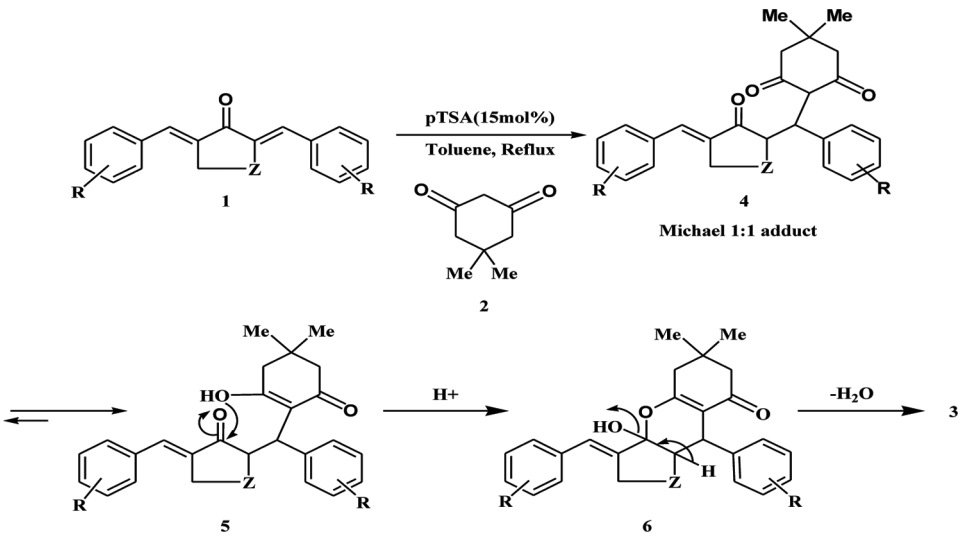
Initially, the reaction of α,α′-bis benzylidene cyclohexanone (**1**) with dimedone (**2**) was used as a model reaction. Reactions at different conditions and various molar ratios of substrates in the presence of pTSA revealed that acceptable yield (80%) of the desired product (**3j**) was obtained in toluene under reflux conditions after 6 h and a molar ratio of α,α′-bis benzylidene cyclohexanone/dimedone/pTSA of 1:1.2:0.15. After completion of the reaction, the catalyst (pTSA) can be separated from the reaction mixture by extraction with water.

We then investigated the reaction scope of this catalytic system and its tolerance of functional groups in the case of other α,α′-bis(substituted-benzylidene) cycloalkanones. Under the optimized reaction conditions, a wide range of α,α′-bis (substituted-benzylidene)cycloalkanones were investigated, and the results are shown

Table 1. Synthesis of new xanthene derivatives (**3a–w**) under reflux in toluene[a]

Entry	Z	R	Product	Time (h)	Yield (%)[b]	Mp (°C)
1	CH_2	H	**3a**	5	85	204–206
2	CH_2	4-Me	**3b**	4	87	230–232
3	CH_2	4-OMe	**3c**	6	92	174–176
4	CH_2	3- OMe	**3d**	9	87	159–161
5	CH_2	4-Cl	**3e**	7	90	233–234
6	CH_2	2-Cl	**3f**	5	83	235–237
7	CH_2	2,4-Cl_2	**3g**	4	85	223–226
8	CH_2	4-Br	**3h**	5	80	250–252
9	CH_2	4-F	**3i**	3	78	198–199
10	CH_2-CH_2	H	**3j**	6	80	166–168
11	CH_2-CH_2	4-Me	**3k**	6	83	165–167
12	CH_2-CH_2	4-OMe	**3l**	6	85	158–160
13	CH_2-CH_2	4-Cl	**3m**	9	90	156–159
14	CH_2-CH_2	4-Br	**3n**	9	75	165–167
15	CH_2-CH_2	4-F	**3o**	4	75	149–152
16	CH_2-CH_2	3-NO_2	**3p**	12	85	176–179
17	CH_2-CH_2	4-NO_2	**3q**	15	85	175–178
18	$CH(CH_3)CH_2$	H	**3r**	8	75	145–146
19	$CH(CH_3)CH_2$	4-Me	**3s**	8	80	191–192
20	$CH(CH_3)CH_2$	4-OMe	**3t**	5	78	161–163
21	$CH(CH_3)CH_2$	4-Cl	**3u**	13	75	159–161
22	$CH(CH_3)CH_2$	2-Cl	**3v**	11	80	223–225
23	$CH(CH_3)CH_2$	4-F	**3w**	5	75	169–171

[a]Reaction conditions: α,α′-bis(substituted-benzylidene) cycloalkanones **1** (2 mmol), dimedone **2** (2.4 mmol), pTSA (0.3 mmol, 15 mol %), toluene (15 mL), reflux.
[b]Isolated yields.



Scheme 2. Proposed mechanism.

in Table 1. In all these cases, the corresponding xanthene derivatives were obtained in good yields. The results (Table 1) indicated that substrates **1** bearing both electron-donating groups and electron-withdrawing groups can be involved in this reaction to afford desired products **3** with good yields. It is concluded that the electronic nature of the substituents has no significant effect on this reaction. It is important to note that the synthesis of desired products could not be achieved in the absence of catalyst (pTSA).

The mechanism of this reaction is believed to involve Michael addition of dimedone with α,α′-bis(substituted-benzylidene)cycloalkanones in the presence of pTSA. The acid catalyst (pTSA) activated the carbonyl group of the proposed intermediate **5**, which presumably underwent cyclization to form xanthene derivatives, accompanied by loss of H_2O as shown in Scheme 2 **(4→5→6→3)**[9]

The structures of all products **3a–w** were confirmed by infrared (IR), ^{1}H NMR, ^{13}C NMR, and elemental analysis.

CONCLUSION

In conclusion, this article describes an efficient method for the reaction of dimedone with α,α′-bis(substituted-benzylidene)cycloalkanones using a catalytic amount of pTSA as catalyst under reflux in toluene. Thus a series of new xanthene derivatives were synthesized in good yields.

EXPERIMENTAL

α,α′-Bis(substituted-benzylidene)cycloalkanones have been synthesized through cross-aldol condensation of cycloalkanones and aldehydes using our reported method.[11]

General Procedure for the Synthesis of New Xanthene Derivatives (3a–w)

A mixture of α,α′-bis(substituted-benzylidene)cycloalkanones **1** (2 mmol), dimedone **2** (2.4 mmol), and 15 mol% pTSA (0.3 mmol) in dry toluene (15 mL) was refluxed for the appropriate time indicated in Table 1. After completion of the reaction, as indicated by thin-layer chromatography (TLC, ethyl acetate / n-hexane 1/4), the reaction mixture was allowed to cool at room temperature. Water (10 ml) was added (to dissolve the catalyst) and then extracted. The toluene extract was dried over anhydrous sodium sulfate and evaporated in vacuo. The crude product was purified by recrystallization from ethanol to afford pure products.

3-Benzylidene-6,6-dimethyl-9-phenyl-2,3,6,7-tetrahydrocyclopenta [b]chromen-8(1H,5H,9H)-one (Entry 1, 3a)

White powder, IR (KBr): 3026, 2957, 1663, 1617, 1450, 1369, 1212, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.12$ (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 2.23–2.32 (m, 3H, CH_2, CH), 2.38–2.44 (m, 1H, CH), 2.63 (dd, 2H, $J = 17.2$, 17.2 Hz, CH_2), 2.82–2.96 (m, 2H, CH_2), 4.50 (s, 1H, CH), 6.52 (s, 1H, =CH), 7.20–7.24 (m, 2H,

ArH), 7.29–7.30 (m, 4H, ArH), 7.35–7.43 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 27.11$, 27.78, 28.17, 28.98, 32.18, 38.58, 41.71, 51.07, 112.72, 116.70, 125.17, 126.27, 126.56, 127.84, 128.10, 128.15, 128.34, 128.50, 137.71, 137.74, 143.39, 164.97 and 197.47. Anal. calcd. for $C_{27}H_{26}O_2$: C, 84.78; H, 6.58. Found: C, 84.52; H, 6.40.

3-(4-Methylbenzylidene)-9-(4-methylphenyl)-6,6-dimethyl-2,3,6,7-tetrahydrocyclopenta[b]chromen- 8(1H,5H,9H)-one (Entry2, 3b)

White powder, IR (KBr): 2923, 1659, 1617, 1370, 1047, 876 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.12$ (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.23–2.27 (m, 3H, CH_2, CH), 2.28–2.32 (m, 1H, CH), 2.33 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.62 (dd, 2H, $J = 17.6$, 17.6 Hz, CH_2), 2.80–2.95 (m, 2H, CH_2), 4.47 (s, 1H, CH), 6.50 (s, 1H, =CH), 7.11 (d, 2H, $J = 7.6$ Hz, ArH), 7.16–7.20 (m, 4H, ArH), 7.33 (d, 2H, $J = 7.6$ Hz, Hz, ArH); ^{13}CNMR (100 MHz, $CDCl_3$): $\delta = 21.11$, 21.23, 27.09, 27.80, 28.17, 28.99, 32.18, 38.15, 41.72, 51.10, 112.86, 116.45, 124.82, 127.98, 128.08, 129.06 129.24, 134.94, 136.01, 136.02, 136.85, 140.53, 146.74, 164.87, and 197.52. Anal. calcd. for $C_{29}H_{30}O_2$: C, 84.84; H, 7.37. Found: C, 84.91; H, 7.40.

3-(4-Methoxybenzylidene)-9-(4-methoxyphenyl)-6,6-dimethyl-2,3,6, 7-tetrahydrocyclopenta[b]chromen-8(1H,5H,9H)-one (Entry 3, 3c)

White crystals, IR (KBr): 2956, 1661, 1616, 1509, 1369, 1250, 1175, 1037, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.21–2.30 (m, 3H, CH_2, CH), 2.35–2.42 (m, 1H, CH), 2.60 (dd, 2H, $J = 17.2$, 17.2 Hz, CH_2), 2.83–2.88 (m, 2H, CH_2), 3.79 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.44 (s, 1H, CH), 6.46 (s, 1H, =CH), 6.83 (d, 2H, $J = 8.8$ Hz, ArH), 6.92 (d, 2H, $J = 8.4$ Hz, ArH), 7.19 (d, 2H, $J = 8.4$ Hz, ArH), 7.36 (d, 2H, $J = 8.8$ Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 26.97$, 27.77, 28.10, 28.98, 32.18, 37.61, 41.69, 51.09, 55.20, 55.30, 112.97, 113.68, 113.98, 115.98, 124.20, 129.07, 129.35, 130.58, 135.58, 135.79, 146.77, 158.03, 158.15, 164.76 and 197.64. Anal. calcd. for $C_{29}H_{30}O_4$: C, 78.71; H, 6.83. Found: C, 78.91; H, 6.90.

3-(3-Methoxybenzylidene)-9-(2-methoxyphenyl)-6,6-dimethyl-2,3,6, 7-tetrahydrocyclopenta[b]chromen-8(1H,5H,9H)-one (Entry 4, 3d)

White crystals, IR (KBr): 2956, 2835, 1663, 1617, 1598, 1369, 1243, 1047, 885, 778, 693 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.13$ (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.26–2.32 (m, 3H, CH_2, CH), 2.34–2.39 (m, 1H, CH), 2.62 (dd, 2H, $J = 17.6$, 17.2 Hz, CH_2), 2.86–2.91 (m, 2H, CH_2), 3.80 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.47 (s, 1H, CH), 6.48 (s, 1H, =CH), 6.73–6.81 (m, 2H, CH, ArH), 6.82 (s, 1H, ArH), 6.87 (d, 1H, $J = 7.6$ Hz, ArH) 6.96 (s, 1H, ArH), 7.02 (d, 1H, $J = 8$ Hz, Hz, ArH), 7.21 (t, 1H, $J = 8$ Hz, ArH),7.29 (t, 1H, $J = 8$ Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 27.13$, 27.84, 28.20, 28.97, 32.18, 38.59, 41.69, 51.06, 55.17, 55.21, 111.66, 111.75, 112.52, 113.68, 114.06, 116.63, 120.59, 120.87, 125.29, 129.26, 129.42, 138.11, 139.09, 145.07, 146.67, 159.64, 159.66, 165.06 and 197.50. Anal. calcd. for $C_{29}H_{30}O_4$: C, 78.71; H, 6.83. Found: C, 78.99; H, 6.94.

3-(4-Chlorobenzylidene)-9-(4-chlorophenyl)-6,6-dimethyl-2,3,5, 6-tetrahydrocyclopenta[b]chromen-7(1H, 8H, 9H)-one (Entry 5, 3e)

White powder, IR (KBr): 2959, 2926, 1654, 1616, 1489, 1370, 1090, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.21–2.31 (m, 3H, CH_2, CH), 2.34–2.44 (m, 1H, CH), 2.60 (dd, 2H, $J = 18.4$, 18.4 Hz, CH_2), 2.82–2.88 (m, 2H, CH_2), 4.47 (s, 1H, CH), 6.47 (s, 1H, =CH), 7.20–7.33 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 27.03$, 27.73, 28.11, 28.95, 32.21, 38.04, 41.46, 50.99, 112.41, 115.87, 124.99, 128.54, 128.69, 129.29, 131.88, 132.32, 136.05, 138.02, 141.81, 146.92, 165.04 and 197.47. Anal. calcd. for $C_{27}H_{24}Cl_2O_2$: C, 71.84; H, 5.36. Found: C, 71.94; H, 5.10.

3-(2-Chlorobenzylidene)-9-(2-chlorophenyl)-6,6-dimethyl-2,3,6, 7-tetrahydrocyclopenta[b]chromen-8(1H,5H,9H)-one (Entry 6, 3f)

White powder, IR (KBr): 2941, 2920, 1656, 1616, 1439, 1372, 1048, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.15$ (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 2.18–2.24 (m, 1H, CH), 2.28–2.29 (m, 2H, CH_2), 2.48–2.54 (m, 1H, CH), 2.61–2.68 (m, 2H, CH_2), 2.76–2.78 (m, 1H, CH), 2.82–2.85 (m, 1H, CH), 5.08 (s, 1H, CH), 6.83 (s, 1H, =CH), 7.11–7.35 (m, 5H, ArH), 7.36 (d, 1H, $J = 7.6$ Hz, ArH), 7.42 (dd, 1H, $J = 1.6$, 1.2 Hz, ArH), 7.51 (dd, 1H, $J = 1.6$, 1.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 26.67$, 27.89, 27.97, 28.94, 32.21, 35.31, 41.67, 50.97, 111.90, 112.98, 125.45, 126.55, 127.09, 127.46, 127.74, 128.42, 129.50, 129.76, 130, 133.45, 133.56, 135.39, 139.54, 140.71, 146.76, 166.01 and 197.16. Anal. calcd. for $C_{27}H_{24}Cl_2O_2$: C, 71.84; H, 5.36. Found: C, 71.90; H, 5.40.

3-(2,4-Dichlorobenzylidene)-9-(2,4-dichlorophenyl)-6,6-dimethyl-2,3, 6,7-tetrahydrocyclopenta[b]chromen-8(1H,5H,9H)-one (Entry 7, 3g)

White powder, IR (KBr): 2923, 2853, 1657,1616, 1467, 1373, 1046, 868, 807, 657 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.15$ (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.16–2.32 (m, 3H, CH_2, CH), 2.45–2.51 (m, 1H, CH), 2.59–2.85 (m, 4H, CH_2, CH_2), 5.0 (s, 1H, CH), 6.74 (s, 1H, =CH), 7.08–7.23 (m, 3H, ArH), 7.37–7.43 (m, 3H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 26.65$, 27.84, 27.93, 28.40, 28.88, 32.21, 41.62, 50.90, 111.54, 112.29, 126.90, 127.47, 128.98, 129.10, 129.27, 129.35, 129.55, 132.13, 132.29, 132.37, 132.73, 133.86, 134.05, 134.11, 139.78, 166.12 and 197.12. Anal. calcd. for $C_{27}H_{22}Cl_4O_2$: C, 62.33; H, 4.26. Found: C, 62.29; H, 4.22.

3-(4-Bromobenzylidene)-9-(4-bromophenyl)-6,6-dimethyl-2,3,6, 7-tetrahydrocyclopenta[b]chromen-8(1H,5H,9H)-one (Entry 8, 3h)

Pale pink powder, IR (KBr): 2956, 2924, 1653, 1615, 1485, 1369, 1114, 1048, 843 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.20–2.24 (m, 4H, CH_2, CH_2), 2.55–2.65 (m, 2H, CH_2), 2.77–2.85 (m, 2H, CH_2), 4.46 (s, 1H, CH), 6.45 (s, 1H, =CH), 7.09–7.20 (m, 2H, ArH), 7.26–7.32 (m, 2H, ArH), 7.40–7.43 (m, 2H, ArH), 7.46–7.52 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 27.05$, 27.74, 28.12, 28.94, 32.20, 38.14, 41.64, 50.98, 112.34, 115.95,

120.03, 120.48, 125.01, 129.61, 129.87, 131.48, 131.63, 136.48, 138.19, 142.31, 146.96, 165.04 and 197.40. Anal. calcd. for $C_{27}H_{24}Br_2O_2$: C, 60.02; H, 4.48. Found: C, 60.09; H, 4.52.

3-(4-Fluorobenzylidene)-9-(4-fluorophenyl)-6,6-dimethyl-2,3,6, 7-tetrahydrocyclopenta[b]chromen-8(1H,5H,9H)-one (Entry 9, 3i)

White crystals, IR (KBr): 2927, 2827, 1662, 1618, 1506, 1369, 1218, 1156, 1047, 851 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.22–2.31 (m, 3H, CH_2, CH), 2.38–2.42 (m, 1H, CH), 2.56–2.65 (m, 2H, CH_2), 2.86–2.88 (m, 2H, CH_2), 4.48 (s, 1H, CH), 6.48 (s, 1H, =CH), 6.95–7.08 (m, 4H, ArH), 7.22–7.39 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 26.90$, 27.72, 28.04, 28.94, 32.18, 37.80, 41.66, 51.03, 112.68, 115.05, 115.30 (d, $J = 36$ Hz), 115.78, 124.64, 129.54 (d, $J = 24$ Hz), 129.61 (d, $J = 20$ Hz), 133.78 (d, $J = 12$ Hz), 137.04 (d, $J = 8$ Hz), 139.09 (d, $J = 12$ Hz), 146.84, 160.19 (d, $J = 132$ Hz), 162.63 (d, $J = 124$ Hz), 164.90 and 197.48. Anal. calcd. for $C_{27}H_{24}F_2O_2$: C, 77.49; H, 5.78. Found: C, 77.44; H, 5.75.

5-Benzylidene-3,3-dimethyl-9-phenyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 10, 3j)

White powder, IR (KBr): 3026, 2929, 1662, 1627, 1491, 1451, 1379, 1223, 1142, 1062, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.05$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.60–1.69 (m, 2H, CH_2), 2.06–2.09 (m, 2H, CH_2), 2.24 (dd, 2H, $J = 16.4$, 16.4 Hz, CH_2), 2.57 (s, 2H, CH_2), 2.59–2.63 (m, 1H, CH), 2.73–2.75 (m, 1H, CH), 4.24 (s, 1H, CH), 6.98 (s, 1H, =CH), 7.18–7.40 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 22.45$, 27.12, 27.42, 27.67, 29.34, 32.15, 40.32, 41.34, 50.83, 112.57, 118.22, 122.05, 126.56, 128.13, 128.25, 128.31, 129.25, 130.27, 137.40, 141.84, 144.15, 164 and 197.18. Anal. calcd. For $C_{28}H_{28}O_2$: C, 84.81; H, 7.11. Found: C, 84.57; H, 6.90.

5-(4-Methylbenzylidene)-9-(4-methylphenyl)-3,3-dimethyl-3,4,5,6,7, 8-hexahydro-2H-xanthen-1(9H)-one (Entry 11, 3k)

White powder, IR (KBr): 2955, 1661, 1627, 1510, 1377, 1220, 1141, 815 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.07$ (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 1.60–1.69 (m, 2H, CH_2), 2.08 (t, 2H, $J = 6$ Hz, CH_2), 2.25 (dd, 2H, $J = 16.4$, 16.4 Hz, CH_2), 2.33 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.57 (s, 2H, CH_2), 2.59–2.63 (m, 1H, CH), 2.73–2.79 (m, 1H, CH), 4.21 (s, 1H, CH), 6.96 (s, 1H, =CH), 7.10–7.12 (m, 2H, ArH), 7.19–7.29 (m, 6H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.13$, 21.26, 22.52, 27.22, 27.51, 27.68, 29.40, 32.20, 39.94, 41.39, 50.90, 112.70, 118.04, 121.89, 128.23, 128.91, 129.02, 129.24, 129.72, 134.56, 136, 136.36, 141.30, 141.82, 163.96 and 197.27. Anal. calcd. for $C_{30}H_{32}O_2$: C, 84.87; H, 7.60. Found: C, 84.93; H, 7.64.

5-(4-Methoxybenzylidene)-9-(4-methoxyphenyl)-3,3-dimethyl3,4,5,6, 7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 12, 3l)

White crystals, IR (KBr): 2932, 2834, 1660, 1626, 1509, 1377, 1250, 1174, 1036, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.05$ (s, 3H, CH_3), 1.14 (s, 3H, CH_3),

1.62–1.65 (m, 2H, CH_2), 2.07 (t, 2H, $J = 6$ Hz, CH_2), 2.23 (dd, 2H, $J = 16.4$, 16 Hz, CH_2), 2.55 (s, 2H, CH_2), 2.57–2.63 (m, 1H, CH), 2.71–2.75 (m, 1H, CH), 3.79 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.18 (s, 1H, CH), 6.82–6.85 (m, 2H, ArH), 6.92–6.93(m, 2H, ArH), 6.94 (s, 1H, =CH), 7.23–7.25 (m, 2H, ArH), 7.28–7.30 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 22.53$, 27.22, 27.46, 27.63, 29.39, 32.19, 41.37, 50.88, 55.19, 55.30, 112.77, 113.64, 117.71, 121.48, 128.84, 129.28, 130, 130.55, 131.37, 136.53, 141.86, 158.18, 158.29, 163.91 and 197.39. Anal. calcd. for $C_{30}H_{32}O_4$: C, 78.92; H, 7.06. Found: C, 78.65; H, 6.98.

5-(4-Chlorobenzylidene)-9-(4-chlorophenyl)-3,3-dimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 13, 3m)

White powder, IR (KBr): 2957, 1662, 1627, 1488, 1377, 1222, 1061, 1014, 834 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.04$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.58–1.74 (m, 2H, CH_2), 1.98–2.12 (m, 2H, CH_2), 2.24 (dd, 2H, $J = 16.4$, 16 Hz, CH_2), 2.52–2.60 (m, 3H,CH_2, CH), 2.68–2.76 (m, 1H, CH), 4.22 (s, 1H, CH), 6.92 (s, 1H, =CH), 7.25–7.29 (m, 6H, ArH), 7.33–7.36 (m, 2H, ArH); ^{13}C NMR(100 MHz, $CDCl_3$): $\delta = 22.35$, 27.10, 27.41, 27.61, 29.35, 32.21, 39.82, 41.32, 50.79, 112.26, 118.09, 121.21, 128.38, 128.48, 129.70, 130.53, 130.63, 132.30, 132.41, 135.74, 141.94, 142.62, 164.07 and 197.15. Anal. calcd. for $C_{28}H_{26}Cl_2O_2$: C, 72.26; H, 5.63. Found: C, 72.19; H, 5.59.

5-(4-Bromobenzylidene)-9-(4-bromophenyl)-3,3-dimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 14, 3n)

Pale pink powder, IR (KBr): 2924, 2868, 1658, 1623, 1484, 1378, 1223, 831 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.04$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.62–1.64 (m, 2H, CH_2), 1.99–2.09 (m, 2H, CH_2), 2.24 (dd, 2H, $J = 16$, 16.4 Hz, CH_2), 2.50–2.60 (m, 3H, CH_2, CH), 2.68–2.72 (m, 1H, CH), 4.20 (s, 1H, CH), 6.90 (s, 1H, =CH), 7.19–7.21 (m, 4H, ArH), 7.40–7.42 (m, 2H, ArH), 7.49–7.51 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 22.34$, 27.11, 27.43, 27.62, 29.35, 32.21, 39.91, 41.32, 50.79, 112.18, 118.07, 120.47, 120.59, 121.27, 130.10, 130.71, 130.85, 131.33, 131.43, 136.19, 141.96, 143.13, 164.08 and 197.14. Anal. calcd. for $C_{28}H_{26}Br_2O_2$: C, 60.67; H, 4.73. Found: C, 60.76; H, 4.80.

5-(4-Fluorobenzylidene)-9-(4-fluorophenyl)-3,3-dimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 15, 4o)

White crystals, IR (KBr): 2957, 1662, 1628, 1506, 1378, 1222, 1157, 843 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.05$ (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.61–1.70 (m, 2H, CH_2), 2.04–2.10 (m, 2H, CH_2), 2.24 (dd, 2H, $J = 16$, 16 Hz, CH_2), 2.55–2.58 (m, 3H, CH_2, CH), 2.68–2.73 (m, 1H, CH), 4.23 (s, 1H, CH), 6.93 (s, 1H, =CH), 6.98 (t, 2H, $J = 8.8$ Hz, ArH), 7.07 (t, 2H, $J = 8.8$ Hz, ArH), 7.27–7.32 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 22.40$, 27.07, 27.39, 27.60, 29.34, 32.19, 39.59, 41.33, 50.38, 112.52, 115.0 (d, $J = 20$ Hz), 115.22 (d, $J = 20$ Hz), 117.97, 121.20, 129.75(d, $J = 36$ Hz), 130.01, 130.83 (d, $J = 32$ Hz), 133.35 (d, $J = 12$ Hz), 139.87 (d, $J = 12$ Hz), 141.91, 160.35 (d, $J = 40$ Hz), 162.79 (d, $J = 32$ Hz),

163.98 and 197.21. Anal. calcd. for $C_{28}H_{26}F_2O_2$: C, 77.76; H, 6.06. Found: C, 77.85; H, 7.02.

5-(3-Nitrobenzylidene)-3,3-dimethyl-9-(3-nitrophenyl)-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 16, 3p)

Pale yellow powder, IR (KBr): 2957, 1661, 1627, 1528, 1378, 1349, 808, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.06$ (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.66–1.73 (m, 2H, CH_2), 1.99–2.07 (m, 1H, CH), 2.10–2.17 (m, 1H, CH), 2.25 (dd, 2H, $J = 16$, 19.4 Hz, CH2), 2.56–2.66 (m, 3H, CH2, CH), 2.72–2.78 (m, 1H, CH), 4.39 (s, 1H, CH), 7.03 (s, 1H, =CH), 7.48 (t, 1H, $J = 8$ Hz, ArH), 7.56 (t, 1H, $J = 8$ Hz, ArH), 7.65 (d, 1H, $J = 7.6$ Hz, ArH), 7.71 (d, 1H, $J = 7.6$ Hz, ArH), 8.08–8.13 (m, 2H, ArH), 8.15 (s, 1H, ArH), 8.20 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 22.16$, 29.97, 27.49, 27.63, 28.26, 29.26, 32.30, 40.37, 50.70, 111.59, 118.13, 120.78, 121.53, 122.01, 122.95, 123.90, 129.16, 129.21, 132.16, 134.79, 135.15, 138.84, 142.08, 146.08, 148.22, 148.57, 164.56 and 197.09. Anal. calcd. for $C_{28}H_{26}N_2O_6$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.47; H, 5.35; N, 5.68.

5-(4-Nitrobenzylidene)-3,3-dimethyl-9-(4-nitrophenyl)-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 17, 3q)

Yellow powder, IR (KBr): 2957, 1661, 1625, 1517, 1342, 856 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.04$ (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.64–1.74 (m, 2H, CH_2), 1.98–2.04 (m, 1H, CH), 2.19–2.32 (m, 3H, CH_2, CH), 2.60–2.63 (m, 3H, CH_2, CH), 2.74–2.78 (m, 1H, CH), 4.39 (s, 1H, CH), 7.04 (s, 1H, =CH), 7.49 (t, 4H, $J = 8.4$ Hz, ArH), 8.17 (d, 2H, $J = 8{,}4$ Hz, ArH), 8.24(d, 2H, $J = 8{,}4$ Hz, ArH); ^{13}C NMR(100 MHz, $CDCl_3$): $\delta = 22.20$, 27.21, 27.41, 27.71, 29.28, 32.26, 40.55, 41.30, 50.68, 111.61, 118.80, 121.11, 123.58, 123.77, 129.21, 129.87, 133.13, 142.20, 143.97, 146.20, 146.86, 151.25, 164.42 and 196.94. Anal. calcd. for $C_{28}H_{26}N_2O_6$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.20; H, 5.43; N, 5.76.

5-Benzylidene-3,3,7-trimethyl-9-phenyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 18, 3r)

White crystals, IR (KBr): 3025, 2956, 1663, 1628, 1377, 1221, 1141, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.92$ (d, 3H, $J = 6.4$ Hz, CH_3), 1.12 (S, 3H, CH_3), 1.15 (S, 3H, CH_3), 1.67–1.74 (m, 1H, CH), 1.77–1.90 (m, 1H, CH), 2.04–2.18 (m, 1H, CH), 2.20–2.25 (m, 3H, CH_2, CH), 2.57 (d, 2H, $J = 12.4$ Hz, CH_2), 2.86–2.90 (m, 1H, CH), 4.25 (s, 1H, CH), 7.0 (s, 1H, =CH), 7.20–7.42 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): 21.08, 21.14, 27.49, 29.14, 32.18, 35.25, 39.80, 40.76, 41.40, 50.86, 112.58, 112.67, 117.47, 122.23, 126.56, 128.20, 128.31, 128.56, 129.33, 130.13, 137.45, 142, 144.11, 164.21 and 197.20. Anal. calcd. for $C_{29}H_{30}O_2$: C, 84.84; H, 7.37. Found: C, 8475; H, 7.31.

5-(4-Methylbenzylidene)-9-(4-methylphenyl)-3,3,7-trimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 19, 3s)

White crystals, IR (KBr): 2956, 2828, 1662, 1628, 1377, 1221, 1142, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.94$ (d, 3H, $J = 6$ Hz, CH_3), 1.09 (S, 3H, CH_3),

1.18 (S, 3H, CH_3), 1.78–1.88 (m, 2H, CH_2), 2.04–2.19 (m, 2H, CH_2), 2.21–2.31 (m, 2H, CH_2), 2.33 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.58 (d, 2H, $J = 12.4$ Hz, CH_2), 2.89–2.93 (m, 1H, CH), 4.21 (s, 1H, CH), 6.99 (s, 1H, =CH), 7.11 (d, 2H, $J = 7.1$ Hz, Hz, ArH), 7.22–7.30 (m, 6H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): 21.19, 21.31, 27.42, 27.54, 29.20, 29.46, 34.95, 36.43, 39.39, 40.37, 41.38, 50.92, 112.68, 112.77, 117.30, 122.04, 128.14, 128.96, 129.06, 129.56, 134.55, 136.03, 141.25, 141.50, 163.84, 164.17 and 197.29. Anal. calcd. for $C_{31}H_{34}O_2$: C, 84.89; H, 7.81. Found: C, 84.93; H, 7.83.

5-(4-Methoxybenzylidene)-9-(4-methoxyphenyl)-3,3,7-trimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 20, 3t)

White crystals, IR (KBr): 29.55, 28.33, 1661, 1627, 15.09, 1377, 1250, 1174, 1036, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.93$ (d, 3H, $J = 6.4$ Hz, CH_3), 1.06 (S, 3H, CH_3), 1.15 (S, 3H, CH_3), 1.77–1.88 (m, 2H, CH_2), 2.0–2.11 (m, 2H, CH_2), 2.18–2.30 (m, 2H, CH_2), 2.55 (d, 2H, $J = 11.2$ Hz, CH_2), 2.85–2.89 (m, 1H, CH), 3.80 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.15 (s, 1H, CH), 6.82–6.86 (m, 2H, ArH), 6.92–6.93 (m, 2H, ArH), 6.95 (s, 1H, =CH), 7.22–7.26 (m, 2H, ArH), 7.28–7.31 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.17$, 21.33, 27.37, 27.49, 28.78, 29.12, 38.85, 39.83, 41.36, 50.90, 55.19, 55.30, 112.74, 112.82, 116.91, 117.10, 121.60, 128.70, 128.94, 129.17 129.97, 130.56, 141.99, 158.19, 163.74, 164.09 and 197.37. Anal. calcd. for $C_{31}H_{34}O_4$: C, 79.12; H, 7.28. Found: C, 79.06; H, 7.31.

5-(4-Chlorobenzylidene)-9-(4-chlorophenyl)-3,3,7-trimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 21, 3u)

White crystals, IR (KBr): 2957, 2828, 1662, 1628, 1488, 1376, 1221, 1090, 1014, 837 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.93$ (d, 3H, $J = 6.4$ Hz, CH_3), 1.02 (S, 3H, CH_3), 1.14 (S, 3H, CH_3), 1.61–1.80 (m, 1H, CH), 1.86–1.88 (m, 1H, CH), 1.98–2.01 (m, 1H, CH), 2.16–2.29 (m, 3H, CH_2, CH), 2.55 (d, 2H, $J = 11.2$ Hz, CH_2), 2.79–2.83 (m, 1H, CH), 4.21 (s, 1H, CH), 6.92 (s, 1H, =CH), 7.25–7.28 (m, 6H, ArH), 7.34–7.37 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.04$, 21.10, 27.44, 29.0, 29.39, 34.89, 36.27, 40.20, 41.35, 50.80, 112.22, 112.30, 117.27, 121.36, 128.40, 128.50, 129.89, 130.55, 132.43, 135.74, 142.03, 142.62, 163.93, 164.26 and 197.16. Anal. calcd. for $C_{29}H_{28}Cl_2O_2$: C, 72.65; H, 5.89. Found: C, 72.62; H, 5.91.

5-(2-Chlorobenzylidene)-9-(2-chlorophenyl)-3,3,7-trimethyl-3,4,5,6,7,8-hexahydro-2H-xanthen-1(9H)-one (Entry 22, 3v)

White crystals, IR (KBr): 2956, 2926, 1664, 1629, 1439, 1376, 1222, 1115, 1046, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.88$ (d, 3H, $J = 6.4$ Hz, CH_3), 1.05 (S, 3H, CH_3), 1.17 (S, 3H, CH_3), 1.64–1.71 (m, 1H, CH), 1.88–1.89 (m, 1H, CH), 2.02–2.05 (m, 1H, CH), 2.18–2.31 (m, 3H, CH_2, CH), 2.55–2.66 (m, 3H, CH_2, CH), 4.85 (s, 1H, CH), 7.03 (s, 1H, =CH), 7.21–7.30 (m, 6H, ArH), 7.36 (d, 1H, $J = 7.2$ Hz, ArH), 7.44 (d, 1H, $J = 7.2$ Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.99$, 27.58, 28.50, 28.93, 29.39, 35.22, 35.67, 37.25, 41.69, 50.78, 111.85, 117.58, 119.74, 119.84, 126.23, 127.05, 127.70, 128.09, 129.48, 130.23, 130.75,

131.35, 131.57, 133.67, 134.12, 135.64, 141.27, 164.56 and 196.97. Anal. calcd. for $C_{29}H_{28}Cl_2O_2$: C, 72.65; H, 5.89. Found: C, 72.59; H, 5.84.

5-(4-Fluorobenzylidene)-9-(4-fluorophenyl)-3,3,7-trimethyl-3,4,5,6,7, 8-hexahydro-2H-xanthen-1(9H)-one (Entry 23, 3w)

White crystals, IR (KBr): 2957, 2829, 1663, 1629, 1505, 1377, 1222, 1157, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.94$ (d, 3H, $J = 6.8$ Hz, CH_3), 1.02 (S, 3H, CH_3), 1.14 (S, 3H, CH_3), 1.68–1.77 (m, 1H, CH), 1.82–1.89 (m, 1H, CH), 1.99–2.19 (m, 1H, CH), 2.21–2.30 (m, 3H, CH_2, CH), 2.55 (d, 2H, $J = 11.6$ Hz, CH_2), 2.80–2.83 (m, 1H, CH) 4.22 (s, 1H, CH), 6.94 (s, 1H, =CH), 6.95–7.0 (m, 2H, ArH), 7.06–7.10 (m, 2H, ArH), 7.26–7.33 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.12$, 27.43, 28.74, 29.0, 29.38, 32.18, 35.15, 36.27, 39.97, 50.81, 112.52 (d, $J = 32$ Hz), 115.01 (d, $J = 36$ Hz), 115.22 (d, $J = 36$ Hz), 117.14, 117.35, 121.37 (d, $J = 20$ Hz), 129.65 (d, $J = 32$ Hz), 129.94 (d, $J = 32$ Hz), 130.85(d, $J = 32$ Hz), 133.33, 139.84, 141.54, 160.35 (d, $J = 32$ Hz), 167.17 and 197.22. Anal. calcd. for $C_{29}H_{28}F_2O_2$: C, 78.0; H, 6.32. Found: C, 79.01; H, 6.37.

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