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A FACILE SYNTHESIS OF NEW TROPONOID-BEARING FLAVONOID-LIKE COMPOUNDS

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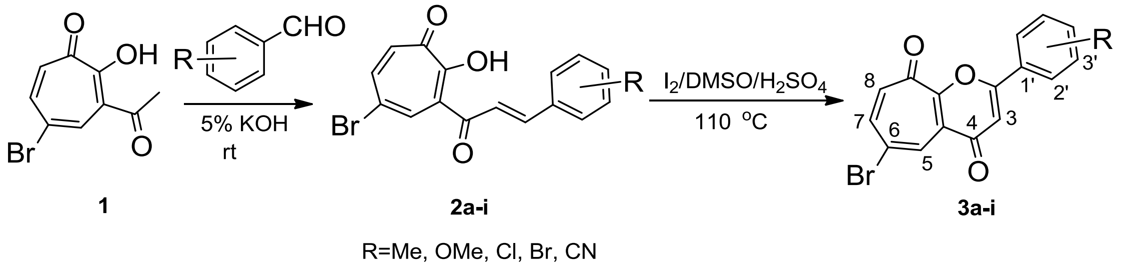
Abstract – A facile synthesis of a series of new flavonoid-like troponoid compounds, namely 3-(3-arylacryloyl)-5-bromotropolones (**2a-i**) and 2-aryl-6-bromocyclohepta[*b*]pyran-4,9-diones (**3a-i**) is described, involving the Claisen-Schmidt condensation reaction of 3-acetyl-5-bromotropolone **(1)** with various substituted benzaldehydes followed by the intramolecular oxidation cyclization reaction through the treatment with I_2/DMSO/H_2SO_4 system.

Flavonoids (chalcones and flavones) are an important class of naturally occurring compounds present in all vascular plants and exhibiting a wide spectrum of biological activities. The average human diet contains about 1 g of flavonoids per day, assimilated through fruits, vegetables, red wine, tea etc.[1] Currently, there is considerable interest in the synthesis of chalcone and flavone derivatives due to a wide range of biological activities including anti-oxidative,[2,3] anti-inflammatory,[4-6] cancer suppressing[7-10] and anti-viral (anti-HIV)[11-13] activities. Especially, some brominated flavonoids such as 8-bromoflavonoid analogs have been reported to exhibit strong activities against human gastric adenocarcinoma cell lines (SGC-7901) and colorectal adenocarcinoma (HT-29) cells[14,15] and also be used for the synthesis of biologically active natural products such as vitexin and aciculatin.[16] The complex pharmacological activities together the easy synthetic reproduction and derivatization of the core structure have solicited considerable interest towards the exploitation of the unique flavonoid template for the discovery of prospective lead compounds.[17-19]

On the other hand, it is well known that numerous natural products and several synthetic compounds bearing troponoid nucleus exhibit remarkable pharmacological effects such as antitumor, inhibitory ribonucleotide reductase and antimalarial activities.[20-25] In particular, the introduction of bromo moiety to troponoid nucleus exhibit important biological activities such as the inhibition of Hepatitis C virus.[26] In addition, the troponoid moiety also plays an important role in molecular assemblies for a faster and efficient lead generation towards the new drug discovery. Despite featuring only seven ring carbon atoms and no stereocentres, the synthesis of structurally novel troponoids continues to be a considerable synthetic challenge as troponoid derivatives are scarce in nature,[27] occurring only in lower plants and fungi,[28] and limited information is available on these compounds.

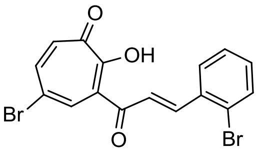
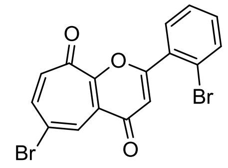
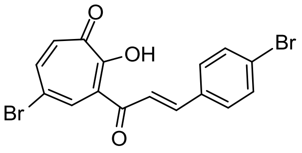
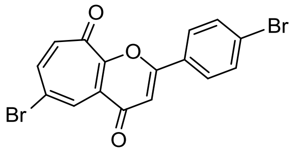
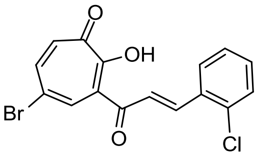
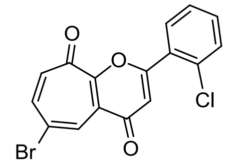
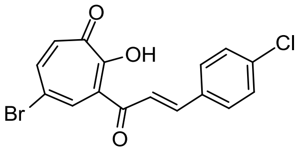
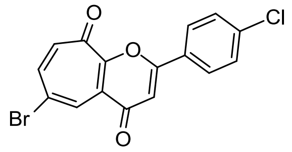
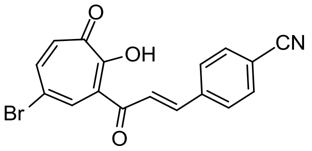
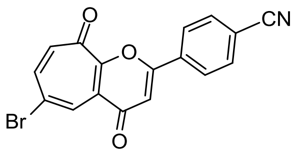
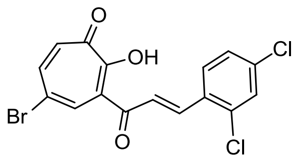
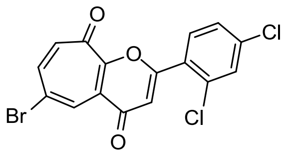
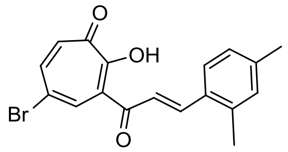
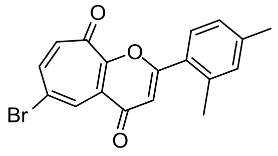
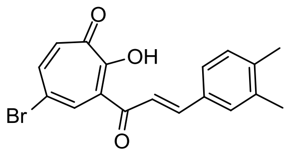
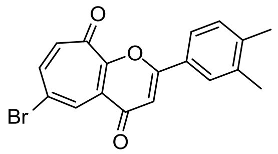
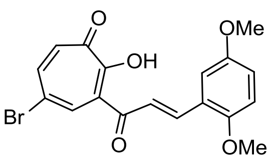
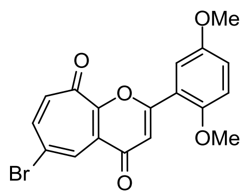
Although the synthesis of substituted chalcones and flavones are among the most extensively reports in recent years due to their potential as valuable templates for medicinal chemistry, to the best of our knowledge, there are few reports on the synthesis of troponoid-bearing flavonoid-like compounds.[29-32] In this regard, we have reported recently on the synthesis of troponoid-[33] and 5,7-dibromotroponoid-bearing[34] flavonoid-like compounds. Therefore, in the context of our ongoing studies on troponoid chemistry and in diversifying our work on the synthesis of new troponoid compounds,[35-37] herein, we wish to report herein the synthesis of a series of monobromo-troponoid-bearing flavonoid-like compounds employing 3-acetyl-5-bromotropolone as the starting compound. As far as we know, 3-acetyl-5-bromotropolone has been synthesized conveniently for many years, but the further modification of it is very limit.[38]

The synthetic route for eighteen new chalcone-like (*E*)-3-(3-arylacryloyl)-5-bromo-2-hydroxy cyclohepta-2,4,6-trienones (**2a-i)** and flavone-like 2-aryl-6-bromocyclohepta[*b*]pyran-4,9-diones (**3a-i**) is illustrated in Scheme 1 and the results are summarized in Table 1. The Claisen-Schmidt condensation reaction of 3-acetyl-5-bromotropolone **(1)** with appropriate aromatic aldehyde (1.5 molar equv.) applying 5% aqueous KOH as catalyst in 50% aqueous methanol solvent at room temperature furnished 3-cinnamoyl-5,7-dibromotropolones (**2**) in high yields and high purities as well. Then the resulting chalcone-like **2** were converted to flavone-like **3** *via* oxidation cyclization reaction in good yields of 53-62% by treating with I_2/DMSO/H_2SO_4 system. The oxidation cyclization reaction is performed in the presence of 10 mol% I_2 as catalyst, DMSO as solvent, and concentrated H_2SO_4 as additive at 110 °C for 10-15 hours. In this reaction, to ensure the formation of solid a minimal amount of DMSO was used. In addition, we also attempted to conduct the oxidation cyclization reaction using the DMSO-I_2 reagent in the absence of concentrated H_2SO_4 according to the method reported by Lokhande *et al.*[39] The reaction also proceeds smoothly, but plagued by poor yields.



Scheme 1. Synthetic route of the title compounds **2a-i** and **3a-i**

Table 1. Synthesis of chalcone-like and flavone-like troponoids **2a-i** and **3a-i**

Entry	Compd. **2**		Yield (%)[a]	Compd. **3**		Yield (%)[a]
1		**2a**	78		**3a**	57
2		**2b**	83		**3b**	62
3		**2c**	81		**3c**	61
4		**2d**	76		**3d**	56
5		**2e**	74		**3e**	62
6		**2f**	77		**3f**	60
7		**2g**	80		**3g**	58
8		**2h**	82		**3h**	60
9		**2i**	75		**3i**	53

[a] Isolated yield.

Compounds **2a-i** and **3a-i** are new and their structures were confirmed by spectral data and elemental analysis. For example, the IR spectrum of **2a** shows a wide absorption at 3183 cm^{-1} for the O-H stretching, two stretching vibration bands at 1603 and 1544 cm^{-1} due to the carbonyl and C=C absorptions of tropolone moiety, and a typical absorption at 1646 cm^{-1} due to the α,β-unsaturated carbonyl group. The main features of its ^1H NMR data are the resonances of the two vinylic protons appearing as two doublets at δ 7.16 and 7.69 with a coupling constant J=16.0 Hz, which indicated the *E*-configuration of these vinylic systems. As reported by chalcone literatures, to yield only *E*-stereoisomers is a prerogative of the Claisen-Schmidt condensation reaction. Further, the structure assigned for this reaction product is fully supported by its ESI-MS (positive-ion mode) spectrum, which exhibits a characteristic quasi-molecular ion peak cluster $(M+H)^+$ at *m/z* 409.3, 411.3, 413.3 with a ratio of 1:2:1, suggesting the presence of two Br-atoms in **2a**. Finally, the structure assigned for this reaction product is fully supported by its elemental analysis, which establishes its molecular formula in accordance with its suggested molecular structure. Similarly, the IR spectrum of **3a** exhibits the absence of hydroxyl group at about 3183 cm^{-1} and the presence of two typical carbonyl absorptions for the tropone and nascent γ-pyrone moieties at 1656 and 1649 cm^{-1}. Particularly characteristic was the presence of one C=C absorptions of γ-pyrone at 1617 cm^{-1}. Its ^1H NMR spectrum also exhibits no signals attributable to both hydroxy OH proton signal and two vinylic protons resonances. The main feature of the spectrum shows the presence of a distinct singlet, integrating for one proton resonating at δ 6.94, assignable to be the proton attached on pyrone ring moiety along with the signals for seven aromatic protons exactly matching its structure in the range of aromatic region. Further, the structure assigned for this reaction product is fully supported by its mass spectrum, which shows a characteristic quasi-molecular ion peak cluster $(M+H)^+$ at *m/z* 406.9, 408.9, 410.9 and matches the expected molecular weight of **3a**.

It can be concluded that the present investigation has demonstrated a facile synthesis of a series of new chalcone-like (*E*)-3-(3-arylacryloyl)-5-bromotropolones (**2a-i**) and flavone-like 2-aryl-6-bromo cyclohepta[*b*]pyran-4,9-dione (**3a-i**). The molecules we have synthesized should allow us, in the future, to investigate structure-activity relationships over various biotests. Moreover, all these synthesized molecules can be used for the synthesis of more complex troponoid compounds since a bromo group on troponoid ring can be further elaborated to a variety of other functional groups, for example, *via* metal-catalyzed coupling reactions.

EXPERIMENTAL

The melting points were measured on WRS-1B digital melting points apparatus and are uncorrected. The progress of the reaction was monitored by TLC. Infrared spectra were recorded on KBr pellets on an FT/IR-430 spectrophotometer. ^1H NMR spectra were determined on a Bruker AVANCE 400 NMR spectrometer at 400 MHz using TMS as internal standard. Elemental analyses were estimated on an Elementar Vario EL-III element analyzer. The Mass spectra were determined using a MSD VL ESI1 spectrometer. The reaction process was monitored by thin-layer chromatography (TLC) on silica gel GF254 using EtOAc/petroleum ether (1/1).

General procedure for the synthesis of (*E*)-3-(3-arylacryloyl)-5-bromo-2-hydroxycyclohepta-2,4,6-trienones (2a-i). To a stirred solution of 3-acetyl-5-bromotropolone **1** (1 mmol, 0.243 g) and substituted benzaldehyde (1.5 mmol) in 50% aqueous MeOH (8 mL) was added 5 mL of 5% potassium hydroxide aqueous solution at room temperature. The resulting solution was stirred at room temperature for 24 h. The reaction mixture was then quenched by addition of 5 mL H_2O and acidification with 1 N HCl. The precipitated chalcone-like tropolone **2a-i** was collected and recrystallized from MeOH to yield pure product in 74-83% yields.

(*E*)-5-Bromo-3-[3-(2-bromophenyl)acryloyl]tropolone (2a). This compound was obtained as yellow crystals, mp 221-223 °C. IR (KBr) *v*/cm^{-1}: 3183 (OH), 1646 (C=O), 1603 (C=O), 1544 (C=C), 1451, 1379, 1298, 1222; ^{1}H NMR (DMSO-d_6) δ (ppm): 7.00 (d, 1H, *J*=10.4 Hz, tropolone-H), 7.16 (d, 1H, *J*=16.0 Hz, =CH), 7.22-7.35 (m, 2H, ArH), 7.61 (d, 1H, *J*=8.0 Hz, ben-H), 7.69 (d, 1H, *J*=16.0 Hz, =CH), 7.73-7.81 (m, 3H, ArH), 10.71 (s, br, 1H, OH); ESI-MS *m/z*: 409.3, 411.3, 413.3 $(M+1)^+$. Anal. Calcd for $C_{16}H_{10}Br_2O_3$: C, 46.86; H, 2.46. Found: C, 46.74; H, 2.65.

(*E*)-5-Bromo-3-[3-(4-bromophenyl)acryloyl]tropolone (2b). This compound was obtained as yellow crystals, mp 223-224 °C. IR (KBr) *v*/cm^{-1}: 3191 (OH), 1652 (C=O), 1602 (C=O), 1545 (C=C), 1450, 1381, 1356, 1274, 1237; ^{1}H NMR (DMSO-d_6) δ (ppm): 7.01 (d, 1H, *J*=10.4 Hz, tropolone-H), 7.17 (d, 1H, *J*=16.0 Hz, =CH), 7.44 (d, 1H, *J*=16.0 Hz, =CH), 7.50-7.62 (m, 5H, ben-H and tropolone-H), 7.73 (d, 1H, *J*=10.4 Hz, tropolone-H), 10.78 (s, br, 1H, OH); ESI-MS *m/z*: 409.3, 411.3, 413.3 $(M+1)^+$. Anal. Calcd for $C_{16}H_{10}Br_2O_3$: C, 46.86; H, 2.46. Found: C, 46.68; H, 2.52.

(*E*)-5-Bromo-3-[3-(2-chlorophenyl)acryloyl]tropolone (2c). This compound was obtained as orange crystals, mp 228-229 °C. IR (KBr) ν/cm^{-1}: 3181 (OH), 1654 (C=O), 1590 (C=O), 1547 (C=C), 1424, 1344, 1262, 1219, 1195; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.05 (d, 1H, *J*=10.0 Hz, tropolone-H), 7.18 (d, 1H, *J*=16.0 Hz, =CH), 7.30 (d, 1H, *J*=8.0 Hz, ben-H), 7.39 (dd, 1H, *J*=10.4, 2.1 Hz, tropolone-H), 7.58 (d, 1H, *J*=2.1 Hz, tropolone-H), 7.62-7.66 (m, 1H, ben-H), 7.71 (d, 1H, *J*=16.0 Hz, =CH), 7.96-8.02 (m, 2H, ben-H), 10.69 (s, br, 1H, OH); ESI-MS *m/z*: 364.9, 366.9, 368.9 $(M+1)^+$. Anal. Calcd for $C_{16}H_{10}BrClO_3$: C, 52.56; H, 2.76. Found: C, 52.74; H, 2.82.

(*E*)-5-Bromo-3-[3-(4-chlorophenyl)acryloyl]tropolone (2d). This compound was obtained as yellow crystals, mp 230-231 °C. IR (KBr) ν/cm^{-1}: 3192 (OH), 1653 (C=O), 1637 (C=O), 1559 (C=C), 1445, 1387, 1351, 1287, 1199; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.11 (d, 1H, *J*=10.4 Hz, tropolone-H), 7.21 (d, 1H, *J*=15.8 Hz, =CH), 7.26-7.32 (m, 2H, ben-H), 7.42 (dd, 1H, *J*=10.4, 2.1 Hz, tropolone-H), 7.51 (d, 1H, *J*=2.1 Hz, tropolone-H), 7.72 (d, 1H, *J*=16.0 Hz, =CH), 7.8-8.08 (m, 2H, ben-H), 10.92 (s, br, 1H, OH); ESI-MS *m/z*: 364.9, 366.9, 368.9 $(M+1)^+$. Anal. Calcd for $C_{16}H_{10}BrClO_3$: C, 52.56; H, 2.76. Found: C, 52.70; H, 2.67.

(*E*)-5-Bromo-3-[3-(4-cyanophenyl)acryloyl]tropolone (2e). This compound was obtained as orange crystals, mp 273-274 °C. IR (KBr) ν/cm^{-1}: 3211 (OH), 2240 (CN), 1663 (C=O), 1597 (C=O), 1546 (C=C), 1454, 1382, 1303, 1252, 1220; ^{1}H NMR ($CDCl_3$) *δ* (ppm): 7.16-7.21 (m, 2H, ArH), 7.38 (d, 1H, *J*=16.0 Hz, =CH), 7.44 (d, 1H, *J*=10.0 Hz, tropolone-H), 7.52-7.57 (m, 3H, ArH), 7.67 (d, 1H, *J*=16.0 Hz, =CH), 7.82 (d, 1H, *J*=10.0 Hz, tropolone-H), 11.01 (s, br, 1H, OH); ESI-MS *m/z*: 356.4, 358.4 $(M+1)^+$. Anal. Calcd for $C_{17}H_{10}BrNO_3$: C, 57.33; H, 2.83. Found: C, 57.47; H, 2.89.

(*E*)-5-Bromo-3-[3-(2,4-dichlorophenyl)acryloyl]tropolone (2f). This compound was obtained as orange crystals, mp 233-235 °C. IR (KBr) ν/cm^{-1}: 3190 (OH), 1642 (C=O), 1602 (C=O), 1546 (C=C), 1450, 1382, 1235, 1207; ^{1}H NMR (DMSO-d_6) *δ* (ppm): 7.14-7.19 (m, 1H, ArH), 7.34 (d, 1H, *J*=16.0 Hz, =CH), 7.36 (s, 1H, ben-H), 7.50 (d, 1H, *J*=10.0 Hz, tropolone-H), 7.57-7.63 (m, 2H, ArH), 7.74 (d, 1H, *J*=16.0 Hz, =CH), 7.97 (d, 1H, *J*=8.0 Hz, ben-H), 10.69 (s, br, 1H, OH); ESI-MS *m/z*: 398.9, 400.9, 402.9, 404.9 $(M+1)^+$. Anal. Calcd for $C_{16}H_9BrCl_2O_3$: C, 48.04; H, 2.27. Found: C, 47.91; H, 2.34.

(*E*)-5-Bromo-3-[3-(2,4-dimethylphenyl)acryloyl]tropolone (2g). This compound was obtained as pale yellow crystals, mp 189-190 °C. IR (KBr) ν/cm^{-1}: 3186 (OH), 1651 (C=O), 1607 (C=O), 1559 (C=C), 1507, 1458, 1346, 1259, 1187; ^{1}H NMR ($CDCl_3$) *δ* (ppm): 2.36 (s, 3H, Me), 2.42 (s, 3H, Me), 7.12-7.14 (m, 2H, ArH), 7.18 (d, 1H, *J*=16.0 Hz, =CH), 7.26-7.39 (m, 2H, ArH), 7.48 (d, 1H, *J*=10.0 Hz, tropolone-H), 7.61 (d, 1H, *J*=16.0 Hz, =CH), 7.68 (d, 1H, *J*=10.0 Hz, tropolone-H), 10.64 (s, br, 1H, OH); ESI-MS *m/z*: 359.1, 361.1 $(M+1)^+$. Anal. Calcd for $C_{18}H_{15}BrO_3$: C, 60.18; H, 4.21. Found: C, 60.09; H, 4.39.

(*E*)-5-Bromo-3-[3-(3,4-dimethylphenyl)acryloyl]tropolone (2h). This compound was obtained as pale yellow crystals, mp 182-184 °C. IR (KBr) ν/cm^{-1}: 3192 (OH), 1644 (C=O), 1625 (C=O), 1545 (C=C), 1508, 1400, 1345, 1256, 1183; ^{1}H NMR ($CDCl_3$) *δ* (ppm): 2.38 (s, 3H, Me), 2.43 (s, 3H, Me), 7.12-7.26 (m, 3H, ArH and =CH), 7.40-7.52 (m, 3H, ArH), 7.64 (d, 1H, *J*=16.0 Hz, =CH), 7.67 (d, 1H, *J*=10.0 Hz, tropolone-H), 10.65 (s, br, 1H, OH); ESI-MS *m/z*: 359.0, 361.0 $(M+1)^+$. Anal. Calcd for $C_{18}H_{15}BrO_3$: C, 60.18; H, 4.21. Found: C, 59.93; H, 4.35.

(*E*)-5-Bromo-3-[3-(2,5-dimethoxylphenyl)acryloyl]tropolone (2i). This compound was obtained as yellow crystals, mp 193-194 °C. IR (KBr) ν/cm^{-1}: 3190 (OH), 1642 (C=O), 1602 (C=O), 1545 (C=C), 1510, 1450, 1382, 1271, 1207; ^{1}H NMR ($CDCl_3$) *δ* (ppm): 3.79 (s, 3H, OMe), 3.82 (s, 3H, OMe), 6.86-6.90 (m, 2H, ArH), 7.08 (d, 1H, *J*=16.0 Hz, =CH), 7.18 (d, 1H, *J*=10.4 Hz, tropolone-H), 7.55-7.59 (m, 2H, ArH), 7.61 (d, 1H, *J*=16.0 Hz, =CH), 7.76 (d, 1H, *J*=10.0 Hz, tropolone-H), 10.88 (s, br, 1H, OH); ESI-MS *m/z*: 391.2, 393.2 $(M+1)^+$. Anal. Calcd for $C_{18}H_{15}BrO_5$: C, 55.26; H, 3.86. Found: C, 55.40;

H, 3.77.

General procedure for the synthesis of flavone-like tropone compounds 6-Bromo-2-(2-aryl) cyclohepta[*b*]pyran-4,9-diones (3a-i). To a stirred solution of each 5-bromotropolone **2** in 8 mL of DMSO was added 3-4 drops of concd. H_2SO_4. After 15 min of magnetic stirring at 110 °C, I_2 was added carefully and the resulting reaction mixture was reacted under the temperature for 10-15 h. The completion of the reaction was monitored by TLC. The reaction mixture was cooled to room temperature and added with 5 mL of H_2O slowly. And then the resulting precipitate was collected by filtration and crystallized from 1,4-dioxane to give **3a-i** in 53-62% yields.

6-Bromo-2-(2-bromophenyl)cyclohepta[*b*]pyran-4,9-dione (3a). This compound was obtained as pale yellow crystals, mp 245-246 °C. IR (KBr) ν/cm^{-1}: 1656 (C=O), 1649 (C=O), 1617 (C=C), 1586, 1560, 1492, 1424, 1370, 1346, 1303, 1220; ^{1}H NMR($CDCl_3$) δ (ppm): 6.94 (s, 1H, H-3), 7.01 (d, 1H, *J*=12.8 Hz, H-8), 7.38-7.41 (m, 1H, ben-H), 7.47-7.50 (m, 1H, ben-H), 7.52 (dd, 1H, *J*=12.8, 2.1 Hz, H-7), 7.68-7.70 (m, 1H, ben-H), 7.73-7.75 (m, 1H, ben-H), 8.41 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 406.9, 408.9, 410.9 (M+1)$^+$. Anal. Calcd for $C_{16}H_8Br_2O_3$: C, 47.10; H, 1.98. Found: C, 46.94; H, 2.11.

6-Bromo-2-(4-bromophenyl)cyclohepta[*b*]pyran-4,9-dione (3b). This compound was obtained as yellow crystals, mp 281-282 °C. IR (KBr) ν/cm^{-1}: 1653 (C=O), 1646 (C=O), 1615 (C=C), 1587, 1560, 1490, 1422, 1378, 1350, 1315, 1217; ^{1}H NMR ($CDCl_3$) δ (ppm): 6.97 (s, 1H, H-3), 7.03 (d, 1H, *J*=12.8 Hz, H-8), 7.53 (dd, 1H, *J*=12.8, 2.1 Hz, H-7), 7.68 (d, 2H, *J*=8.7 Hz, ben-H), 7.87 (d, 2H, *J*=8.7 Hz, ben-H), 8.40 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 407.0, 408.9, 411.0 (M+1)$^+$. Anal. Calcd for $C_{16}H_8Br_2O_3$: C, 47.10; H, 1.98. Found: C, 47.26; H, 2.08.

6-Bromo-2-(2-chlorophenyl)cyclohepta[*b*]pyran-4,9-dione (3c). This compound was obtained as light yellow crystals, mp 232-233 °C. IR (KBr) ν/cm^{-1}: 1652 (C=O), 1647 (C=O), 1617 (C=C), 1584, 1485, 1373, 1345, 1264, 1217; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.01 (d, 1H, *J*=12.8 Hz, H-8), 7.05 (s, 1H, H-3), 7.43-7.55 (m, 4H, H-7 and ben-H), 7.81 (m, 1H, ben-H), 8.41 (d, 1H, *J*=2.0 Hz, H-5); ESI-MS *m/z*: 362.9, 364.9, 366.8 (M+1)$^+$. Anal. Calcd for $C_{16}H_8BrClO_3$: C, 52.85; H, 2.22. Found: C, 52.73; H, 2.41.

6-Bromo-2-(4-chlorophenyl)cyclohepta[*b*]pyran-4,9-dione (3d). This compound was obtained as yellow crystals, mp 254-255 °C. IR (KBr) ν/cm^{-1}: 1654 (C=O), 1647 (C=O), 1618 (C=O), 1583, 1560, 1542, 1473, 1430, 1370, 1340, 1252, 1220; ^{1}H NMR ($CDCl_3$) δ (ppm): 6.94 (s, 1H, H-3), 7.04 (d, 1H, *J*=12.8 Hz, H-8), 7.23 (d, 2H, *J*=8.7 Hz, ben-H), 7.53 (dd, 1H, *J*=12.8, 2.1 Hz, H-7), 8.02 (d, 2H, *J*=8.7 Hz, ben-H), 8.41 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 362.9, 364.9, 366.9 (M+1)$^+$. Anal. Calcd for $C_{16}H_8BrClO_3$: C, 52.85; H, 2.22. Found: C, 52.97; H, 2.28.

6-Bromo-2-(4-cyanophenyl)cyclohepta[*b*]pyran-4,9-dione (3e). This compound was obtained as orange crystals, mp 227-228 °C. IR (KBr) ν/cm^{-1}: 2210 (CN), 1667 (C=O), 1652 (C=O), 1620 (C=C), 1582, 1561, 1481, 1403, 1369, 1342, 1277, 1221; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.07 (s, 1H, H-3), 7.13 (d, 1H, *J*=12.8 Hz, H-8), 7.25-7.32 (m, 2H, ben-H), 7.58 (dd, 1H, *J*=12.8, 2.1 Hz, H-7), 8.08-8.14 (m, 2H, ben-H), 8.49 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 354.1, 356.1 $(M+1)^+$. Anal. Calcd for $C_{17}H_8BrNO_3$: C, 57.65; H, 2.28. Found: C, 52.52; H, 2.35.

6-Bromo-2-(2,4-dichlorophenyl)cyclohepta[*b*]pyran-4,9-dione (3f). This compound was obtained as yellow crystals, mp 267-268 °C. IR (KBr) ν/cm^{-1}: 1658 (C=O), 1644 (C=O), 1606 (C=C), 1584, 1559, 1490, 1431, 1374, 1346, 1186; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.02 (d, 1H, *J*=12.8 Hz, H-8), 7.06 (s, 1H, H-3), 7.44 (dd, 1H, *J*=8.5, 2.0 Hz, ben-H), 7.53 (dd, 1H, *J*=12.8, 2.0 Hz, H-7), 7.57 (d, 1H, *J*=2.0 Hz, ben-H), 7.79 (d, 1H, *J*=8.5 Hz, ben-H), 8.40 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 396.9, 398.8, 400.9, 402.8 $(M+1)^+$. Anal. Calcd for $C_{16}H_7BrCl_2O_3$: C, 48.28; H, 1.77. Found: C, 48.08; H, 1.81.

6-Bromo-2-(2,4-dimethylphenyl)cyclohepta[*b*]pyran-4,9-dione (3g). This compound was obtained as pale yellow crystals, mp 244-245 °C. IR (KBr) ν/cm^{-1}: 1652 (C=O), 1642 (C=O), 1619 (C=C), 1583, 1560, 1489, 1412, 1370, 1343, 1317, 1289, 1187; ^{1}H NMR ($CDCl_3$) δ (ppm): 2.39 (s, 3H, Me), 2.54 (s, 3H, Me), 6.69 (s, 1H, H-3), 6.99 (d, 1H, *J*=12.8 Hz, H-8), 7.12-7.15 (m, 2H, ben-H), 7.48 (d, 1H, *J*=8.9 Hz, ben-H), 7.52 (dd, 1H, *J*=12.8, 2.0 Hz, H-7), 8.42 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 357.2, 359.2 $(M+1)^+$. Anal. Calcd for $C_{18}H_{13}BrO_3$: C, 60.52; H, 3.67. Found: C, 60.40; H, 3.86.

6-Bromo-2-(3,4-dimethylphenyl)cyclohepta[*b*]pyran-4,9-dione (3h). This compound was obtained as pale yellow crystals, mp 271-272 °C. IR (KBr) ν/cm^{-1}: 1651 (C=O), 1640 (C=O), 1622 (C=C), 1585, 1560, 1491, 1421, 1379, 1324, 1299, 1173; ^{1}H NMR ($CDCl_3$) δ (ppm): 2.35 (s, 3H, Me), 2.36 (s, 3H, Me), 6.96 (s, 1H, H-3), 7.02-7.05 (m, 2H, H-8 and ben-H), 7.29-7.33 (m, 2H, ben-H), 7.52 (dd, 1H, *J*=12.8, 2.1 Hz, H-7), 8.41 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 357.1, 359.1 $(M+1)^+$. Anal. Calcd for $C_{18}H_{13}BrO_3$: C, 60.52; H, 3.67. Found: C, 60.61; H, 3.55.

6-Bromo-2-(2,5-dimethoxyphenyl)cyclohepta[*b*]pyran-4,9-dione (3i). This compound was obtained as golden crystals, mp 259-261 °C. IR (KBr) ν/cm^{-1}: 1651 (C=O), 1642 (C=O), 1612 (C=O), 1566, 1491, 1451, 1379, 1300, 1250, 1184; ^{1}H NMR ($CDCl_3$) δ (ppm): 3.89 (s, 3H, OMe), 3.94 (s, 3H, OMe), 6.54 (d, 1H, *J*=2.3 Hz, ben-H), 6.68 (dd, 1H, *J*=8.9, 2.3 Hz, ben-H), 7.01 (d, 1H, *J*=12.8 Hz, H-8), 7.43 (s, 1H, H-3), 7.52 (dd, 1H, *J*=12.8, 2.1 Hz, H-7), 8.21 (d, 1H, *J*=8.9 Hz, ben-H), 8.42 (d, 1H, *J*=2.1 Hz, H-5); ESI-MS *m/z*: 389.0, 390.9 $(M+1)^+$. Anal. Calcd for $C_{18}H_{13}BrO_5$: C, 55.55; H, 3.37. Found: C, 55.75; H, 3.49.

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