*Chinese Journal of Chemistry*, **2009**, *27*, 2073—2078 **Full Paper**

# Synthesis of Novel Bromo-substituted Flavone-like Troponoid Compounds from Oxidation Cyclization of 3-Cinnamoyl-5,7-dibromotropolones Using $I_2$/DMSO/$H_2SO_4$ System

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A convenient method to obtain a series of bromo-substituted flavone-like troponoid compounds 6,8-dibromo-2-arylcyclohepta[*b*]pyran-4,9-diones **3a—3s** by oxidation cyclization of the readily available intermediates 3-cinnamoyl-5,7-dibromotropolones **2a—2s** using $I_2$/DMSO/$H_2SO_4$ system was realized. Compounds **2a—2s** were obtained from the aldol reaction of 3-acetyl-5,7-dibromotropolone **1** with various benzaldehydes. Compounds **2a—2s** and **3a—3s** are novel and their structures were supported by IR, $^1$H NMR, MS and elemental analyses.

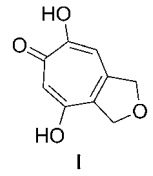
**Keywords** flavone-like, troponoid, aldol reaction, oxidation cyclization

## Introduction

It is well known that the chromones, flavones and related compounds are widely distributed in nature and have been found to play an important role in a number of biological processes. Synthesis of flavones and their derivatives have attracted considerable attention due to a wide range of biological activities including anti-oxidative,[1,2] anti-inflammatory,[3-5] cancer suppressing[6-8] and anti-viral (anti-HIV)[9-11] activities. The average human diet contains about 1 g of flavonoids per day, assimilated through fruits, vegetables, red wine, tea and so on.[12] The incorporation of electronegative elements, such as halogens and nitro groups, in the flavonoid structure usually introduces new patterns of biological properties. Halogenated flavones are considered potential benzodiazepine receptor ligands. Indeed, 6-bromoflavone and 6-bromo-3'-nitroflavone showed activities close to or higher than diazepam;[13] 8-bromo flavone analogs exhibit strong activities against human gastric adenocarcinoma cell lines (SGC-7901) and colorectal adenocarcinoma (HT-29) cells.[8]

On the other hand, compounds containing a troponoid nucleus exhibit remarkable pharmacological effects such as antitumor, inhibiting ribonucleotide reductase and antimalarial activities.[14,15] For instance, a new tropolone, namely cordytropolone (**I**) discovered in the culture broth of *Cordyceps* sp. BCC 1681 exhibits the especial antimalarial activities.[16]

The introduction of bromo moieties to troponoid nucleus was reported to inhibit the hepatitis C virus.[17] However, tropolone derivatives are scarce in nature,[18] occurring only in lower plants and fungi[19] and very limited information is available on these compounds.




I

**Figure 1** Structure of cordytropolone (**I**).

In light of these findings and in view of structural diversity playing a prominent role in medicinal and combinatorial chemistry for a faster and efficient lead generation towards the new drug discovery,[20] the synthesis of novel bromo-substituted flavone-like troponoid compounds which involved the substitution of the corresponding benzenoid by the troponoid would be much more attractive if a facile, and broadly applicable synthetic approach could be used. As far as we know, only two methods about the synthesis of this type of compounds have been reported. One is oxidation and cyclization of 3-cinnamoyltropolones using $SeO_2$ or DDQ as oxidative reagent.[21] The other is based on the reaction of 3-acetyltropolone with methoxyl- and/or hydroxy- substituted benzaldehydes in the presence of triethyl orthoformate and with perchloric acid as the oxidant.[22] However, both have restriction regarding the choice of substrates and the generality, compatibility, and usefulness have not been appreciated. Because of this initial observation, it seemed advantageous to find a new and more suitable way to the synthesis of bromo-substituted flavone-like troponoid compounds.

Therefore, we report, herein, a convenient and gen-

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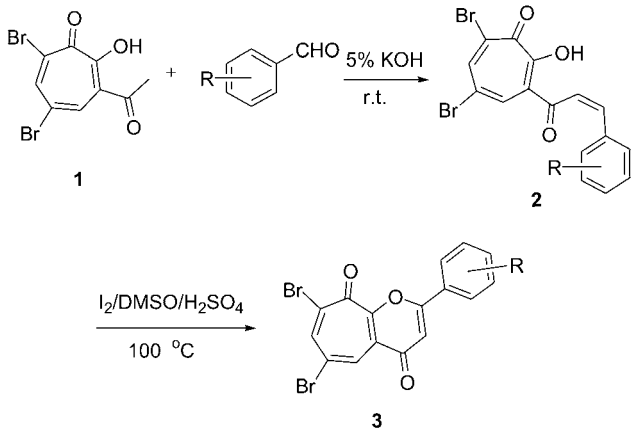
Received March 6, 2009; revised April 24, 2009; accepted June 4, 2009.
Project supported by the Foundation of Liaoning Province Key Laboratory of Applied Chemistry (No. 2008s001).

eral method for the synthesis of 6,8-dibromo-2- arylcyclohepta[*b*]pyran-4,9-diones from 3-acetyl-5,7- dibromotropolone using $I_2$/DMSO/$H_2SO_4$ system,[23] which, to the best of our knowledge, has never been reported in any literature.

## Results and discussion

Scheme 1 outlined the synthetic sequence employed in our laboratories for preparation of the heterocycle-fused flavone-like troponoid compounds **3**.

**Scheme 1**




The aldol condensation reaction of 3-acetyl-5,7-dibromotropolone (**1**) with benzaldehydes using aqueous KOH ($w$=5%) as the base, methanol as solvent furnished 3-cinnamoyl-5,7-dibromotropolones **2** in high yields and high purities as well. Then the resulting intermediates **2** were subjected to oxidation cyclization reaction under treatment with $I_2$/DMSO/$H_2SO_4$ system and thus were smoothly converted to the corresponding flavone-like troponoid compounds 6,8-dibromo-2-arylcyclohepta[*b*]pyran-4,9-diones **3** in moderate to good yields. The results are summarized in Table 1.

In fact, our own initial investigation towards the synthesis of **3a** was conducted by treating **2a** with $SeO_2$ or 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) under the conditions reported in literature 21 giving a complex mixture with several products (TLC). After purification by flash chromatography, it was only possible to isolate and identify traces (3%) of **3a**. The very low yield of **3a** was probably due to the formation of the corresponding aurone-like product. In addition, we have ever reported that 3-cinnamoyltropolone could be oxidized in acetic acid by 3 equiv. of bromine to 6,8-dibromo-2-phenylcyclohepta[*b*]pyran-4,9-dione.[24] We applied this reaction condition to the synthesis of **3a**. However, no product was formed using excess of bromine.

Considering these problems, the use of $I_2$/DMSO/$H_2SO_4$ system can be expected to be an advantageous alternative to synthesize the desired flavone-like troponoid compounds. To our delight, the oxidation cyclization reaction of **2a** conducted under teatment of $I_2$/DMSO/$H_2SO_4$ system led to the formation of flavone-like troponoid compound **3a** as the only isolable product. Through an effort to optimize the reaction conditions, such as reaction temperature and the amount of the $I_2$/DMSO/$H_2SO_4$ system, we found that the best results were achieved when the reactions were conducted at a temperature of 100 ℃ with a ratio of 1 mmol 3-cinnamoyl-5,7-dibromotropolone to 8 mL DMSO, 10 mg $I_2$ and 3—4 drops of concentrated $H_2SO_4$.

**Table 1** Yields and physical properties of the compounds **2** and **3**

| Entry | R | Compound **2** | Yield/% | m.p./℃ | Compound **3** | Yield/% | m.p./℃ |
|---|---|---|---|---|---|---|---|
| 1 | 2-Me | **2a** | 70 | 193—195 | **3a** | 65 | 233—234 |
| 2 | 3-Me | **2b** | 74 | 196—197 | **3b** | 61 | 241—242 |
| 3 | 4-Me | **2c** | 78 | 209—211 | **3c** | 45 | 236—237 |
| 4 | 4-Et | **2d** | 88 | 179—181 | **3d** | 34 | 234—235 |
| 5 | 2-OMe | **2e** | 76 | 189—190 | **3e** | 49 | 229—231 |
| 6 | 3-OMe | **2f** | 75 | 220—221 | **3f** | 70 | 262—263 |
| 7 | 4-OMe | **2g** | 85 | 199—200 | **3g** | 72 | 268—269 |
| 8 | 2-OEt | **2h** | 71 | 187—188 | **3h** | 40 | 245—246 |
| 9 | 4-OEt | **2i** | 82 | 178—180 | **3i** | 49 | 221—224 |
| 10 | 3-OPh | **2j** | 61 | 204—205 | **3j** | 58 | 229—231 |
| 11 | 2-Cl | **2k** | 77 | 186—187 | **3k** | 59 | 246—247 |
| 12 | 3-Cl | **2l** | 87 | 211—212 | **3l** | 70 | 282—283 |
| 13 | 4-Cl | **2m** | 78 | 222—223 | **3m** | 64 | 260—261 |
| 14 | 2-Br | **2n** | 69 | 187—188 | **3n** | 41 | 244—245 |
| 15 | 3-Br | **2o** | 81 | 204—206 | **3o** | 77 | 301—302 |
| 16 | 4-Br | **2p** | 85 | 221—222 | **3p** | 50 | 264—265 |
| 17 | 3-CN | **2q** | 74 | 215—217 | **3q** | 40 | 271—272 |
| 18 | 4-CN | **2r** | 82 | 238—239 | **3r** | 53 | 251—253 |
| 19 | 3-$CF_3$ | **2s** | 88 | 222—223 | **3s** | 55 | 236—237 |

We also found that addition of increased amounts of $I_2$ or $H_2SO_4$ lowered the purity and yield of products. As solvent, DMSO appeared to give the best results.

To establish the generality and applicability of this method, a wide variety of 3-cinnamoyl-5,7-dibromotropolones containing electron-donating (such as alkyl or alkoxyl group) and electron-withdrawing (such as halo, cyano, or trifluoromethyl group) substituents were subjected to the same set of experiments to furnish the corresponding flavone-like troponoid compounds. The results summarized in Table 1 indicated the scope and generality of the oxidation cyclization reaction with respect to various 3-cinnamoyl-5,7-dibromotropolones.

It seems that the effect of substitution groups is not very strong; both the electron-donating (Entries 1—10) and electron-withdrawing (Entries 11 — 19) groups worked well, showing little distinction. For example, 3-cinnamoyl-5,7-dibromotropolones **2a**, **2d**, **2g** and **2j** (Entries 1, 4, 7 and 10) bearing electron-donating groups on the benzene ring were reacted to give the corresponding flavone-like products **3a**, **3d**, **3g** and **3j** in 65%, 34%, 72% and 58% yields, respectively. On the other hand, 3-cinnamoyl-5,7-dibromotropolones **2l**, **2o**, **2q** and **2s** (Entries 12, 15, 17 and 19) bearing electron-withdrawing groups gave the corresponding **3l**, **3o**, **3q** and **3s** in 70%, 77%, 40% and 55% yields, respectively. The ease of isolation of compounds **3** was notable; after aqueous workup, compounds **3** were isolated as the main products and their structures were analyzed. When the compounds **3** were developed on TLC (silica gel: GF254, developing agent: ethyl acetate), there was only one main spot with no tailing. The compounds **3** had the negative coloring test with iron(III) chloride in methanol solution. The IR spectra exhibited the absence of hydroxyl group at about 3180 $cm^{-1}$ which appeared in 3-cinnamoyl-5,7-dibromotropolones and the presence of two typical carbonyl absorptions for the tropone and pyrone moieties at about 1640 and 1600 $cm^{-1}$, respectively. The $^1H$ NMR spectra showed the absence of a hydroxy OH signal and the presence of one signal attributable to the proton of the pyrone ring, in addition to the signals of other groups. Moreover, the structures assigned for the reaction products were fully supported by their mass spectra and elemental analyses. The mass spectra displayed the corresponding ($M^+ + 1$) peak, which is consistent with the title compounds. All these facts showed that the hydroxyl group in the tropolone ring had taken part in the oxidation cyclization reaction.

In conclusion, the present investigation has demonstrated that the use of $I_2$/DMSO/$H_2SO_4$ offers a simple, facile and effective method for the conversion of wide varieties of 3-cinnamoyl-5,7-dibromotropolones to the corresponding flavone-like troponoid compounds. And the numerous molecules we have synthesized should allow us, in the future, to investigate structure-activity relationships over various biotests. In addition, as bromo-substituted tropolone and troponoid derivatives these molecules also constitute functional entities liable to be employed in Suzuki-Miyaura cross-coupling reaction,[25] and thus will be used as synthons in troponoid chemistry.

## Experimental

Melting points (uncorrected) were determined by using a WRS-1B melting points apparatus. $^1H$ NMR (400 MHz) spectra were recorded with a Varian Inova 400 NMR spectrometer at 400 MHz, with the reported chemical shifts being against TMS. Mass spectra were determined using an MSD VL ESI1 spectrometer. Elemental analyses were performed for C, H using an Elementar Vario EL-III element analyzer and found within $\pm$0.4%. The progress of reactions was monitored by thin-layer chromatography (TLC) on silica gel GF254 using ethyl acetate as eluent.

### General procedure for the preparation of 3-cinnamoyl-5,7-dibromotropolones 2a—2s

To a stirred solution of 3-acetyl-5,7-dibromotropolone (**1**, 1 mmol, 0.322 g) and 1.5 equimolar amount of the corresponding substituted benzaldehyde in methanol (5 mL) were added dropwise 5 mL of 5% aqueous KOH over 5 min. After the addition was complete, the reaction mixture was magnetically stirred for 48 h at room temperature. After completion of the reaction, the reaction was quenched with 5 mL of $H_2O$ and acidified with 1 mol•$L^{-1}$ HCl solution. The resulting precipitate was collected by filtration and crystallized from methanol to give **2**. Yields and melting points are indicated in Table 1.

5,7-Dibromo-3-(3-*o*-tolylacryloyl)tropolone (**2a**): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$: 2.43 (s, 3H, $CH_3$), 7.09 (d, $J$=15.9 Hz, 1H, =CH), 7.21—7.32 (m, 3H, ArH), 7.61—7.64 (m, 1H, ArH), 7.90 (s, 1H, ArH), 8.01 (d, $J$=16.1 Hz, 1H, =CH), 8.51 (s, 1H, ArH); IR (KBr) $v$: 3190 (OH), 1653 (C=O), 1636 (C=O) $cm^{-1}$; ESI-MS *m/z*: 424.1 ($M^+$). Anal. calcd for $C_{17}H_{12}Br_2O_3$: C 48.15, H 2.85; found C 48.25, H 2.87.

5,7-Dibromo-3-(3-*m*-tolylacryloyl)tropolone (**2b**): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$: 2.37 (s, 3H, $CH_3$), 7.05 (d, $J$=16.0 Hz, 1H, =CH), 7.22—7.28 (m, 2H, ArH), 7.32 (d, $J$=15.9 Hz, 1H, =CH), 7.36—7.41 (m, 1H, ArH), 8.51 (s, 1H, ArH); IR (KBr) $v$: 3181 (OH), 1654 (C=O), 1624 (C=O) $cm^{-1}$; ESI-MS *m/z*: 424.4 ($M^+$). Anal. calcd for $C_{17}H_{12}Br_2O_3$: C 48.15, H 2.85; found C 48.13, H 2.94.

5,7-Dibromo-3-(3-*p*-tolylacryloyl)tropolone (**2c**): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$: 2.29 (s, 3H, $CH_3$), 6.99 (d, $J$=16.0 Hz, 1H, =CH), 7.18—7.21 (m, 2H, ArH), 7.41—7.50 (m, 3H, ArH), 7.57 (d, $J$=15.9 Hz, 1H, =CH), 8.35 (s, 1H, ArH); IR (KBr) $v$: 3192 (OH), 1653 (C=O), 1637 (C=O) $cm^{-1}$; ESI-MS *m/z*: 424.0 ($M^+$). Anal. calcd for $C_{17}H_{12}Br_2O_3$: C 48.15, H 2.85; found C 48.21, H 2.89.

5,7-Dibromo-3-(3-(4-ethylphenyl)acryloyl)tropolone (**2d**): $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$: 1.23 (t, $J$=7.6 Hz, 3H, $CH_2CH_3$), 2.70 (q, $J$ = 6.8 Hz, 2H, $CH_2CH_3$),

7.11—7.29 (m, 3H, ArH, =CH), 7.47—7.59 (m, 2H, ArH), 7.61 (d, $J$=15.9 Hz, 1H, =CH), 7.73 (s, 1H, ArH), 8.39 (s, 1H, ArH); IR (KBr) $\nu$: 3179 (OH), 1642 (C=O), 1622 (C=O) $cm^{-1}$; ESI-MS *m/z*: 438.4 ($M^+$). Anal. calcd for $C_{18}H_{14}Br_2O_3$: C 49.35, H 3.22; found C 49.41, H 3.27.

5,7-Dibromo-3-(3-(2-anisyl)acryloyl)tropolone (**2e**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 3.87 (s, 3H, $OCH_3$), 6.88—7.04 (m, 2H, ArH), 7.21 (d, $J$=16.1 Hz, 1H, =CH), 7.36—7.46 (m, 1H, ArH), 7.52—7.61 (m, 1H, ArH), 7.82 (s, 1H, ArH), 7.92 (d, $J$=16.0 Hz, 1H, =CH), 8.52 (s, 1H, ArH); IR (KBr) $\nu$: 3187 (OH), 1658 (C=O), 1609 (C=O) $cm^{-1}$; ESI-MS *m/z*: 440.0 ($M^+$). Anal. calcd for $C_{17}H_{12}Br_2O_4$: C 46.40, H 2.75; found C 46.35, H 2.81.

5,7-Dibromo-3-(3-(3-anisyl)acryloyl)tropolone (**2f**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 3.76 (s, 3H, $OCH_3$), 6.84—6.90 (m, 3H, ArH), 7.41 (d, $J$=15.9 Hz, 1H, =CH), 7.56—7.59 (m, 3H, ArH and =CH), 8.39 (s, 1H, ArH); IR (KBr) $\nu$: 3180 (OH), 1657 (C=O), 1626 (C=O) $cm^{-1}$; ESI-MS *m/z*: 439.9 ($M^+$). Anal. calcd for $C_{17}H_{12}Br_2O_4$: C 46.40, H 2.75; found C 46.45, H 2.82.

5,7-Dibromo-3-(3-(4-anisyl)acryloyl)tropolone (**2g**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 3.75 (s, 3H, $OCH_3$), 6.86—7.01 (m, 3H, ArH), 7.45 (d, $J$=16.1 Hz, 1H, =CH), 7.51—7.64 (m, 3H, ArH and =CH), 8.40 (s, 1H, ArH); IR (KBr) $\nu$: 3197 (OH), 1646 (C=O), 1616 (C=O) $cm^{-1}$; ESI-MS *m/z*: 440.2 ($M^+$). Anal. calcd for $C_{17}H_{12}Br_2O_4$: C 46.40, H 2.75; found C 46.39, H 2.69.

5,7-Dibromo-3-(3-(2-ethoxyphenyl)acryloyl)tropolone (**2h**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 1.47 (t, $J$=7.0 Hz, 3H, $CH_3$), 4.10 (q, $J$=6.8 Hz, 2H, $OCH_2$), 6.90—6.99 (m, 1H, ArH), 7.26 (s, 1H, ArH), 7.31 (d, $J$=15.9 Hz, 1H, =CH), 7.35—7.40 (m, 1H, ArH), 7.55—7.58 (m, 1H, ArH), 7.83 (s, 1H, ArH), 7.91 (d, $J$=16.1 Hz, 1H, =CH), 8.51 (1H, s, ArH); IR (KBr) $\nu$: 3178 (OH), 1667 (C=O), 1593 (C=O) $cm^{-1}$; ESI-MS *m/z*: 454.0 ($M^+$). Anal. calcd for $C_{18}H_{14}Br_2O_4$: C 47.61, H 3.11; found C 47.63, H 3.17.

5,7-Dibromo-3-(3-(4-ethoxyphenyl)acryloyl)tropolone (**2i**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 1.47 (t, $J$=6.8 Hz, 3H, $CH_3$), 4.08 (q, $J$=7.0 Hz, 2H, $OCH_2$), 6.90—6.94 (m, 2H, ArH), 7.01 (d, $J$=16.1 Hz, 1H, =CH), 7.51—7.57 (m, 3H, ArH and =CH), 7.80 (s, 1H, ArH), 8.49 (s, 1H, ArH); IR (KBr) $\nu$: 3205 (OH), 1655 (C=O), 1601 (C=O) $cm^{-1}$; ESI-MS *m/z*: 454.4 ($M^+$). Anal. calcd for $C_{18}H_{14}Br_2O_4$: C 47.61, H 3.11; found C 47.59, H 3.15.

5,7-Dibromo-3-(3-(3-phenoxyphenyl)acryloyl)tropolone (**2j**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 6.89—7.04 (m, 3H, ArH), 7.12—7.20 (m, 1H, ArH), 7.32—7.49 (m, 5H, ArH), 7.41 (d, $J$=16.1 Hz, 1H, =CH,), 7.50—7.55 (m, 1H, ArH), 7.67 (d, $J$=16.1 Hz, 1H, =CH), 8.45 (s, 1H, ArH); IR (KBr) $\nu$: 3181 (OH), 1651 (C=O), 1598 (C=O) $cm^{-1}$; ESI-MS *m/z*: 502.2 ($M^+$). Anal. calcd for $C_{22}H_{14}Br_2O_4$: C 52.62, H 2.81; found C 52.58, H 2.88.

5,7-Dibromo-3-(3-(2-chlorophenyl)acryloyl)tropolone (**2k**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.12 (d, $J$=15.9 Hz, 1H, =CH), 7.29—7.43 (m, 3H, ArH), 7.64 (s, 1H, ArH), 7.73—7.79 (m, 1H, ArH), 7.85 (d, $J$=16.1 Hz, 1H, =CH), 8.35 (s, 1H, ArH); IR (KBr) $\nu$: 3191 (OH), 1679 (C=O), 1602 (C=O) $cm^{-1}$; ESI-MS *m/z*: 444.9 ($M^+$). Anal. calcd for $C_{16}H_9Br_2ClO_3$: C 43.23, H 2.04; found C 43.28, H 2.19.

5,7-Dibromo-3-(3-(3-chlorophenyl)acryloyl)tropolone (**2l**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.10 (d, $J$=16.0 Hz, 1H, =CH), 7.35 (s, 2H, ArH), 7.48 (d, $J$=15.9 Hz, 1H, =CH), 7.51—7.62 (m, 3H, ArH), 8.34 (s, 1H, ArH); IR (KBr) $\nu$: 3175 (OH), 1654 (C=O), 1627 (C=O) $cm^{-1}$; ESI-MS *m/z*: 445.2 ($M^+$). Anal. calcd for $C_{16}H_9Br_2ClO_3$: C 43.23, H 2.04; found C 43.26, H 2.07.

5,7-Dibromo-3-(3-(4-chlorophenyl)acryloyl)tropolone (**2m**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.07 (d, $J$=16.0 Hz, 1H, =CH), 7.32—7.36 (m, 2H, ArH), 7.49 (d, $J$=16.0 Hz, 1H, =CH), 7.58—7.61 (m, 3H, ArH), 8.35 (s, 1H, ArH); IR (KBr) $\nu$: 3183 (OH), 1651 (C=O), 1608 (C=O) $cm^{-1}$; ESI-MS *m/z*: 444.9 ($M^+$). Anal. calcd for $C_{16}H_9Br_2ClO_3$: C 43.23, H 2.04; found C 43.25, H 2.11.

5,7-Dibromo-3-(3-(2-bromophenyl)acryloyl)tropolone (**2n**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.11 (d, $J$=16.0 Hz, 1H, =CH), 7.24—7.36 (m, 2H, ArH), 7.58—7.63 (m, 2H, ArH), 7.72—7.78 (m, 1H, ArH), 7.81 (d, $J$=16.1 Hz, 1H, =CH), 8.35 (s, 1H, ArH); IR (KBr) $\nu$: 3188 (OH), 1680 (C=O), 1611 (C=O) $cm^{-1}$; ESI-MS *m/z*: 489.2 ($M^+$). Anal. calcd for $C_{16}H_9Br_3O_3$: C 39.30, H 1.86; found C 39.31, H 1.88.

5,7-Dibromo-3-(3-(4-bromophenyl)acryloyl)tropolone (**2o**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.09 (d, $J$=16.0 Hz, 1H, =CH), 7.21—7.30 (m, 5H, ArH), 7.32 (d, $J$=15.9 Hz, 1H, =CH), 8.34 (s, 1H, ArH); IR (KBr) $\nu$: 3186 (OH), 1651 (C=O), 1607 (C=O) $cm^{-1}$; ESI-MS *m/z*: 488.9 ($M^+$). Anal. calcd for $C_{16}H_9Br_3O_3$: C 39.30, H 1.86; found C 39.28, H 1.91.

5,7-Dibromo-3-(3-(3-bromophenyl)acryloyl)tropolone (**2p**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.10 (d, $J$=16.0 Hz, 1H, =CH), 7.28 (s, 2H, ArH), 7.45 (d, $J$=15.9 Hz, 1H, =CH), 7.52—7.64 (m, 3H, ArH), 8.36 (s, 1H, ArH); IR (KBr) $\nu$: 3197 (OH), 1682 (C=O), 1610 (C=O) $cm^{-1}$; ESI-MS *m/z*: 489.1 ($M^+$). Anal. calcd for $C_{16}H_9Br_3O_3$: C 39.30, H 1.86; found C 39.33, H 1.85.

5,7-Dibromo-3-(3-(3-cyanophenyl)acryloyl)tropolone (**2q**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.14—7.22 (m, 3H, ArH and =CH), 7.42 (d, $J$=16.0 Hz, 1H, =CH), 7.48—7.61 (m, 3H, ArH), 8.41 (s, 1H, ArH); IR (KBr) $\nu$: 3216 (OH), 2340 (CN), 1672 (C=O), 1611 (C=O) $cm^{-1}$; ESI-MS *m/z*: 435.4 ($M^+$). Anal. calcd for $C_{17}H_9Br_2NO_3$: C 46.93, H 2.09; found C 47.01, H 2.17.

5,7-Dibromo-3-(3-(4-cyanophenyl)acryloyl)tropolone (**2r**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.15—7.27 (m, 3H, ArH and =CH), 7.44 (d, $J$=16.0 Hz, 1H, =CH), 7.51—7.63 (m, 3H, ArH), 8.44 (s, 1H, ArH); IR (KBr) $\nu$: 3192 (OH), 2337 (CN), 1675 (C=O), 1609 (C=O) $cm^{-1}$; ESI-MS *m/z*: 435.3 ($M^+$). Anal. calcd for $C_{17}H_9Br_2NO_3$: C 46.93, H 2.09; found C 46.98, H 2.11.

5,7-Dibromo-3-(3-(3-(trifluoromethyl)phenyl)acryloyl)tropolone (**2s**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.11—7.13 (m, 1H, ArH), 7.30 (d, $J$=16.0 Hz, 1H, =CH), 7.69 (d, $J$=16.0 Hz, 1H, =CH), 7.72—7.89 (m, 4H, ArH), 8.59 (s, 1H, ArH); IR (KBr) $v$: 3216 (OH), 1672 (C=O), 1611 (C=O) cm$^{-1}$; ESI-MS *m/z*: 478.4 ($M^+$). Anal. calcd for $C_{17}H_9Br_2F_3O_3$: C 42.71, H 1.90; found C 42.68, H 1.97.

**General procedure for the preparation of 6,8-dibromo-2-(2-aryl)cyclohepta[*b*]pyran-4,9-diones 3a—3s**

To a solution of each 5,7-dibromo-3-cinnamoyltropolone **2** in 8 mL of DMSO at 100 ℃ were added 3—4 drops of concd. $H_2SO_4$. After 15 min of magnetical stirring, $I_2$ was added carefully and the resulting reaction mixture was stirred under the temperature of 100 ℃ 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 **3**. Yields and melting points are indicated in Table 1.

6,8-Dibromo-2-(2-tolyl)cyclohepta[*b*]pyran-4,9-dione (**3a**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 2.41 (s, 3H, $CH_3$), 7.05 (s, 1H, H-3), 7.31—8.47 (m, 6H, ArH); IR (KBr) $v$: 1652 (C=O), 1621 (C=O) cm$^{-1}$; ESI-MS *m/z*: 423.1 ($M^+$+1). Anal. calcd for $C_{17}H_{10}Br_2O_3$: C 48.38, H 2.39; found C 48.28, H 2.41.

6,8-Dibromo-2-(3-tolyl)cyclohepta[*b*]pyran-4,9-dione (**3b**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 2.39 (s, 3H, $CH_3$), 7.20 (s, 1H, H-3), 7.38—8.49 (m, 6H, ArH); IR (KBr) $v$: 1653 (C=O), 1623 (C=O) cm$^{-1}$; ESI-MS *m/z*: 422.9 ($M^+$+1). Anal. calcd for $C_{17}H_{10}Br_2O_3$: C 48.38, H 2.39; found C 48.43, H 2.47.

6,8-Dibromo-2-(4-tolyl)cyclohepta[*b*]pyran-4,9-dione (**3c**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 2.44 (s, 3H, $CH_3$), 6.96—6.99 (m, 1H, H-3), 7.33—8.50 (m, 6H, ArH); IR (KBr) $v$: 1651 (C=O), 1619 (C=O) cm$^{-1}$; ESI-MS *m/z*: 423.2 ($M^+$ + 1). Anal. calcd for $C_{17}H_{10}Br_2O_3$: C 48.38, H 2.39; found C 48.49, H 2.35.

6,8-Dibromo-2-(4-ethylphenyl)cyclohepta[*b*]pyran-4,9-dione (**3d**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 1.38 (t, $J$=6.2 Hz, 3H, $CH_3$), 2.72 (dd, $J$=7.6, 14.8 Hz, 2H, $CH_2$), 6.91—6.93 (m, 1H, H-3), 7.26—8.47 (m, 6H, ArH); IR (KBr) $v$: 1648 (C=O), 1601 (C=O) cm$^{-1}$; ESI-MS *m/z*: 437.2 ($M^+$ + 1). Anal. calcd for $C_{18}H_{12}Br_2O_3$: C 49.57, H 2.77; found C 49.61, H 2.71.

6,8-Dibromo-2-(2-anisyl)cyclohepta[*b*]pyran-4,9-dione (**3e**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 3.96 (s, 3H, $OCH_3$), 7.03—7.06 (m, 1H, H-3), 7.11—8.50 (m, 6H, ArH); IR (KBr) $v$: 1667 (C=O), 1595 (C=O) cm$^{-1}$; ESI-MS *m/z*: 438.9 ($M^+$ + 1). Anal. calcd for $C_{17}H_{10}Br_2O_4$: C 46.61, H 2.30; found C 46.58, H 2.35.

6,8-Dibromo-2-(3-anisyl)cyclohepta[*b*]pyran-4,9-dione (**3f**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 3.91 (s, 3H, $OCH_3$), 6.99—7.02 (m, 1H, H-3), 7.11—8.51 (m, 6H, ArH); IR (KBr) $v$: 1644 (C=O), 1624 (C=O) cm$^{-1}$; ESI-MS *m/z*: 439.1 ($M^+$ + 1). Anal. calcd for $C_{17}H_{10}Br_2O_4$: C 46.61, H 2.30; found C 46.61, H 2.31.

6,8-Dibromo-2-(4-anisyl)cyclohepta[*b*]pyran-4,9-dione (**3g**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 3.93 (s, 3H, $OCH_3$), 7.04—7.06 (m, 1H, H-3), 7.34—8.52 (m, 6H, ArH); IR (KBr) $v$: 1649 (C=O), 1617 (C=O) cm$^{-1}$; ESI-MS *m/z*: 439.2 ($M^+$ + 1). Anal. calcd for $C_{17}H_{10}Br_2O_4$: C 46.61, H 2.30; found C 46.69, H 2.27.

6,8-Dibromo-2-(2-ethoxyphenyl)cyclohepta[*b*]-pyran-4,9-dione (**3h**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 1.42 (t, $J$=6.9 Hz, 3H, $CH_3$), 4.09 (q, $J$=6.9 Hz, 2H, $OCH_2$), 7.02—7.04 (m, 1H, H-3), 7.46—8.48 (m, 6H, ArH); IR (KBr) $v$: 1648 (C=O), 1620 (C=O) cm$^{-1}$; ESI-MS *m/z*: 453.0 ($M^+$ + 1). Anal. calcd for $C_{18}H_{12}Br_2O_4$: C 47.82, H 2.68; found C 47.89, H 2.75.

6,8-Dibromo-2-(4-ethoxyphenyl)cyclohepta[*b*]-pyran-4,9-dione (**3i**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 1.43 (t, $J$=6.9 Hz, 3H, $CH_3$), 4.08 (q, $J$=6.9 Hz, 2H, $OCH_2$), 7.01—7.04 (m, 1H, H-3), 7.43—8.50 (m, 6H, ArH); IR (KBr) $v$: 1652 (C=O), 1636 (C=O) cm$^{-1}$; ESI-MS *m/z*: 453.2 ($M^+$ + 1). Anal. calcd for $C_{18}H_{12}Br_2O_4$: C 47.82, H 2.68; found C 47.77, H 2.61.

6,8-Dibromo-2-(3-phenoxyphenyl)cyclohepta[*b*]-pyran-4,9-dione (**3j**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 6.95—6.97 (m, 1H, H-3), 7.33—8.51 (m, 11H, ArH); IR (KBr) $v$: 1651 (C=O), 1616 (C=O) cm$^{-1}$; ESI-MS *m/z*: 501.4 ($M^+$+1). Anal. calcd for $C_{22}H_{12}Br_2O_4$: C 52.83, H 2.42; found C 52.91, H 2.52.

6,8-Dibromo-2-(2-chlorophenyl)cyclohepta[*b*]-pyran-4,9-dione (**3k**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.12 (s, 1H, H-3), 7.54—8.50 (m, 6H, ArH); IR (KBr) $v$: 1657 (C=O), 1639 (C=O) cm$^{-1}$; ESI-MS *m/z*: 443.2 ($M^+$+1). Anal. calcd for $C_{16}H_7Br_2ClO_3$: C 43.43, H 1.59; found C 43.44, H 1.51.

6,8-Dibromo-2-(3-chlorophenyl)cyclohepta[*b*]-pyran-4,9-dione (**3l**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.24 (s, 1H, H-3), 7.61—8.58 (m, 6H, ArH); IR (KBr) $v$: 1653 (C=O), 1630 (C=O) cm$^{-1}$; ESI-MS *m/z*: 443.4 ($M^+$+1). Anal. calcd for $C_{16}H_7Br_2ClO_3$: C 43.43, H 1.59; found C 43.50, H 1.64.

6,8-Dibromo-2-(4-chlorophenyl)cyclohepta[*b*]pyran-4,9-dione (**3m**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.27 (s, 1H, H-3), 7.51—8.49 (m, 6H, ArH); IR (KBr) $v$: 1652 (C=O), 1621 (C=O) cm$^{-1}$; ESI-MS *m/z*: 443.0 ($M^+$+ 1). Anal. calcd for $C_{16}H_7Br_2ClO_3$: C 43.43, H 1.59; found C 43.34, H 1.56.

6,8-Dibromo-2-(2-bromophenyl)cyclohepta[*b*]pyran-4,9-dione (**3n**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 6.88 (s, 1H, H-3), 7.42—8.48 (m, 6H, ArH); IR (KBr) $v$: 1656 (C=O), 1624 (C=O) cm$^{-1}$; ESI-MS *m/z*: 487.9 ($M^+$+ 1). Anal. calcd for $C_{16}H_7Br_3O_3$: C 39.47, H 1.45; found C 39.51, H 1.55.

6,8-Dibromo-2-(3-bromophenyl)cyclohepta[*b*]-pyran-4,9-dione (**3o**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 6.92 (s, 1H, H-3), 7.59—8.50 (m, 6H, ArH); IR (KBr) $v$: 1654 (C=O), 1629 (C=O) cm$^{-1}$; ESI-MS *m/z*: 488.0 ($M^+$+ 1). Anal. calcd for $C_{16}H_7Br_3O_3$: C 39.47, H 1.45; found C 39.45, H 1.51.

6,8-Dibromo-2-(4-bromophenyl)cyclohepta[*b*]pyran-

4,9-dione (**3p**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 6.98 (s, 1H, H-3), 7.68—8.52 (m, 6H, ArH); IR (KBr) *v*: 1652 (C=O), 1619 (C=O) $cm^{-1}$; ESI-MS *m/z*: 488.0 ($M^+$ + 1). Anal. calcd for $C_{16}H_7Br_3O_3$: C 39.47, H 1.45; found C 39.52, H 1.39.

6,8-Dibromo-2-(3-cyanophenyl)cyclohepta[*b*]pyran-4,9-dione (**3q**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.04—7.06 (m, 1H, H-3), 7.52—8.48 (m, 6H, ArH); IR (KBr) *v*: 2360 (CN), 1651 (C=O), 1620 (C=O) $cm^{-1}$; ESI-MS *m/z*: 434.0 ($M^+$ + 1). Anal. calcd for $C_{17}H_7Br_2NO_3$: C 47.15, H 1.63; found C 47.11, H 1.65.

6,8-Dibromo-2-(4-cyanophenyl)cyclohepta[*b*]pyran-4,9-dione (**3r**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.08—7.10 (m, 1H, H-3), 7.53—8.49 (m, 6H, ArH); IR (KBr) *v*: 2320 (CN), 1652 (C=O), 1620 (C=O) $cm^{-1}$; ESI-MS *m/z*: 434.2 ($M^+$ + 1). Anal. calcd for $C_{17}H_7Br_2NO_3$: C 47.15, H 1.63; found C 47.22, H 1.67.

6,8-Dibromo-2-[3-(trifluoromethyl)phenyl]cyclohepta[*b*]pyran-4,9-dione (**3s**): $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$: 7.05—7.08 (m, 1H, H-3), 7.80—8.52 (m, 6H, ArH); IR (KBr) *v*: 1644 (C=O), 1624 (C=O) $cm^{-1}$; ESI-MS *m/z*: 477.1 ($M^+$ + 1). Anal. calcd for $C_{17}H_7Br_2F_3O_3$: C 42.89, H 1.48; found C 43.00, H 1.57.

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(E0903066 Zhao, C.)