Synthesis of Thioflavanone and Flavanone Derivatives by Cyclization of Chalcones

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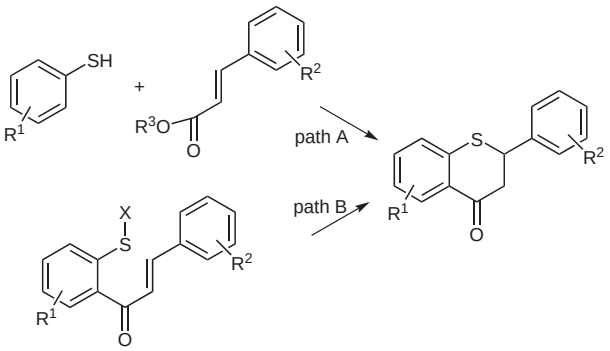
Abstract: Chalcones bearing suitably positioned protected 2′-sulfanyl or 6′-hydroxy groups cyclize to form the corresponding thioflavanones and flavanones, respectively. The thioflavanones were prepared by a new method involving deprotection of the sulfanyl group under alkaline conditions. These reactions provide a route to new biologically interesting molecules.

Key words: chalcone cyclization, thioflavanone synthesis, benzoxathiolone ring opening, flavanones

Flavonoids are a well-known source of inspiration in the search for new medicines.[1] Surprisingly, however, the biological activity of their sulfur analogues has been relatively little explored,[2–8] even though it has been found that replacement of the oxygen atom by sulfur does not deprive the compounds of activities,[3a,6,8] and sometimes can even improve it.

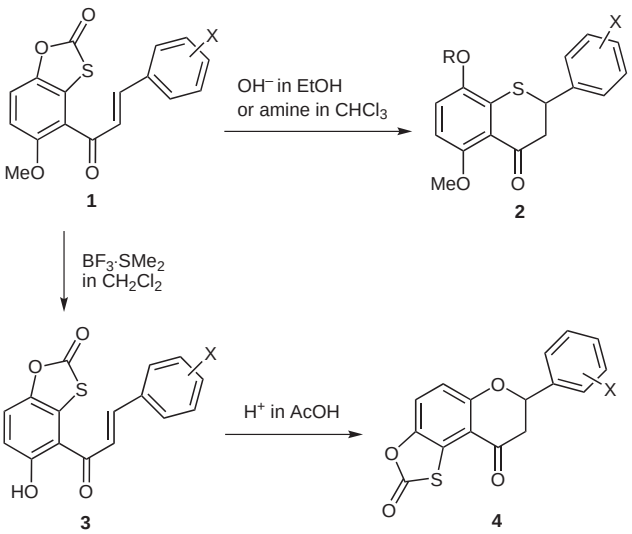
There are two general methods for the synthesis of thioflavanone derivatives (Scheme 1).



Scheme 1 General methods for the synthesis of thioflavanones

The first method (path A) is by far the most popular, and depends on the Michael addition of a thiophenol to a suitable cinnamic acid derivative, followed by Friedel–Crafts cyclization.[2,4,9] The second method (path B) involves intramolecular ring closure to form the thiopyranone ring, and closely resembles the synthesis of flavanones from 2′-hydroxychalcones. The approach has been converted into a practical synthetic method by Taylor and Dean, who used *S*-(4-methoxybenzyl)-protected substrates (Scheme 1, X = CH_2-4-$MeOC_6H_4$). Deprotection and subsequent cyclization were performed as a one-pot reaction in the presence of formic acid.[10,11] The reaction conditions were found to be inappropriate for synthesis of 5-methoxythioflavanones, because the methoxy group was partially cleaved in the presence of formic acid.[12] However, 5-methoxy derivatives could be prepared if silver nitrate in ethanol was used to deprotect the 4-methoxybenzyl sulfides.[12] The Taylor–Dean method is acid specific, and replacement of the formic acid with trifluoroacetic acid led to thioaurones.[10]

To overcome the problems associated with the Taylor–Dean acid-induced deprotection–cyclization sequence, we examined the use of thiophenols protected with base-cleavable groups. We report the synthesis of thioflavanones **2** from chalcones **1** (Scheme 2), which can be conveniently obtained[13] from 4-acetyl-5-methoxy-1,3-benzoxathiol-2-one. Treatment of chalcones **1a–c** with sodium hydroxide in aqueous ethanol gave the 8-hydroxythioflavanone derivatives 2**a–c**, respectively (Table 1, entries 1–3). Alternatively, the transformation could be achieved with amines (preferably piperidine) in chloroform (entries 4–6). The second approach appears to be more convenient, especially if protection of the newly formed 8-hydroxy group with a base-cleavable group is required. A suitable method of cleavage of the piperidin-1-ylcarbonyl (PPCO) group has already been described.[14]



Scheme 2 Synthesis of thioflavanones **2**, chalcones **3**, and flavanones **4**

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Table 1 Synthesis of Thioflavanones **2**

Entry	Substrate	Cond.[a]	Product	Yield (%)
1	**1a** (X = H)	A	**2a** (X = H; R = H)	50
2	**1b** (X = 4-Br)	A	**2b** (X = 4-Br; R = H)	51
3	**1c** (X = 4-OMe)	A	**2c** (X = 4-OMe; R = H)	64
4	**1a** (X = H)	B	**2d** (X = H; R = PPCO[b])	70
5	**1d** (X = 4-Cl)	B	**2e** (X = 4-Cl; R = PPCO[b])	59
6	**1b** (X = 4-Br)	B	**2f** (X = 4-Br; R = PPCO[b])	30

[a] A: NaOH, EtOH–H_2O; B: piperidine, $CHCl_3$.
[b] PPCO = piperidin-1-ylcarbonyl.

Interestingly, chalcones **1** can also be transformed into flavanones **4** by a two-step procedure involving deprotection of the methoxy group with boron trifluoride–dimethyl sulfide complex to give the related hydroxy derivatives **3**, which undergo acid-induced cyclization to form the flavanones **4** (Scheme 2). The resulting compounds are listed in Table 2.

Table 2 Preparation of Hydroxychalcones **3** and Flavanones **4**

Entry	Substrate	Cond.[a]	Product	Yield (%)
1	**1a** (X = H)	A	**3a**	49
2	**1b** (X = 4-Br)	A	**3b**	78
3	**1c** (X = 4-OMe)	A	**3c**	41
4	**1e** (X = 4-NO_2)	A	**3d**	68
5	**1f** (X = 3-Cl)	A	**3e**	42
6	**3a** (X = H)	B	**4a**	52
7	**3b** (X = 4-Br)	B	**4b**	89
8	**3e** (X = 3-Cl)	B	**4c**	50

[a] A: $BF_3 \cdot Me_2S$; B: H_2SO_4 in AcOH.

These reactions appear to be of interest from the point of view of medicinal chemistry, as they open a way to flavanones with the same pattern of potential pharmacophores in ring A (two *para*-positioned oxygen atoms, and a sulfur atom *ortho* to one of the oxygens), but with different spatial arrangement of the pharmacophoric atoms. In this context, this is a continuation of our work on similarly substituted thioaurones.[15] Possible modifications of the pharmacophoric atoms aimed at optimization of such pharmacologically important parameters as bulkiness, rigidity, lipophilicity, and solubility have already been demonstrated for thioaurones.[14]

Melting points are uncorrected. IR spectra were obtained from KBr pellets by using a Thermo Mattson Satellite instrument. The NMR spectra were recorded on a 500-MHz spectrometer (Varian Unity Plus). Elemental analyses were performed on a Carlo-Erba 1108 instrument.

8-Hydroxy-5-methoxy-2-phenyl-2,3-dihydro-4*H*-1-benzothiopyran-4-one (2a)

A suspension of 1,3-benzoxathiol-2-one **1a** (X = H; 156 mg, 0.5 mmol) in MeOH (5 mL) was deoxygenated with N_2 and mixed with 2 M aq NaOH (2 mL). The mixture was stirred at reflux for 2 h, cooled, and acidified with 2 M HCl. The resulting precipitate was filtered off, washed with MeOH, and crystallized [$MeO(CH_2)_2OH$] to give thioflavanone **2a** as a yellow solid; yield: 72 mg (50%); mp 206–209 °C.

IR (KBr): 3300, 1639, 1573, 1466, 1288, 1246, 1040 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 9.79 (s, 1 H, OH), 7.47 (d, J = 7.3 Hz, 2 H, H-2′, H-6′), 7.32–7.40 (m, 3 H, H-3′, H-4′, H-5′), 6.96 (d, = 8.8 Hz, 1 H, H-7), 6.74 (d, J = 8.8 Hz, 1 H, H-6), 4.74 (dd, J_1 = 2.9 Hz, J_2 = 13.1 Hz, 1 H, H-2), 3.71 (s, 3 H, OCH_3), 3.30 (dd, J_1 = 13.1 Hz, J_2 = 15.1 Hz, 1 H, H-3), 2.93 (dd, J_1 = 2.9 Hz, J_2 = 15.1 Hz, 1 H, H-3).

Anal. Calcd for $C_{16}H_{14}O_3S$: C, 67.11; H, 4.93; S, 11.20. Found: C, 66.73; H, 4.95; S, 11.05.

2-(4-Bromophenyl)-8-hydroxy-5-methoxy-2,3-dihydro-4*H*-1-benzothiopyran-4-one (2b)

A suspension of 1,3-benzoxathiol-2-one **1b** (X = 4-Br; 150 mg, 0.383 mmol) in MeOH (4 mL) was deoxygenated with N_2 and mixed with 2 M aq NaOH (2 mL). The mixture was stirred at reflux for 2 h, cooled, and acidified with dil HCl. The product was extracted with $CHCl_3$ (2 × 30 mL), washed with H_2O (3 × 10 mL), and dried ($MgSO_4$). The solvent was evaporated, and the residue was crystallized (MeOH) to give thioflavanone **2b** as an orange solid; yield: 71 mg (51%); mp 206–210 °C.

IR (KBr): 3136, 1640, 1570, 1276, 1241, 1042 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 9.83 (s, 1 H, OH), 7.58 (d, J = 8.5 Hz, 2 H, H-3′, H-5′), 7.42 (d, J = 8.5 Hz, 2 H, H-2′, H-6′), 6.95 (d, J = 8.9 Hz, 1 H, H-7), 6.74 (d, J = 8.9 Hz, 1 H, H-6), 4.75 (dd, J_1 = 12.3 Hz, J_2 = 3.3 Hz, 1 H, H-2), 3.70 (s, 3 H, OCH_3), 3.23 (dd, J_1 = 12.3 Hz, J_2 = 15.3 Hz, 1 H, H-3), 2.93 (dd, J_1 = 15.3 Hz, J_2 = 3.3 Hz, 1 H, H-3).

Anal. Calcd for $C_{16}H_{13}BrO_3S$: C, 52.61; H, 3.59; S, 8.78. Found: C, 52.48; H, 3.60; S, 8.63.

8-Hydroxy-5-methoxy-2-(4-methoxyphenyl)-2,3-dihydro-4*H*-1-benzothiopyran-4-one (2c)

A suspension of 1,3-benzoxathiol-2-one **1c** (X = 4-OMe; 171 mg, 0.5 mmol) in MeOH (5 mL) was deoxygenated with N_2, and 2 M aq NaOH (2 mL) was added. The mixture was stirred at reflux for 2 h, cooled, and acidified with dil HCl. The resulting precipitate was filtered off, washed with MeOH, and crystallized (MeOH) to give thioflavanone **2c** as an orange solid; yield: 101 mg (64%); mp 197–201 °C.

IR (KBr): 3263, 1643, 1572, 1513, 1256, 1046 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 9.77 (s, OH, 1 H), 7.40 (d, J = 8.7 Hz, 2 H, H-2′, H-6′), 6.93–6.98 (m, 3 H, H-3′, H-5′, H-7), 6.74 (d, J = 8.7 Hz, 1 H, H-6), 4.68 (dd, J_1 = 3.0 Hz, J_2 = 13.0 Hz, 1 H, H-2), 3.76 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 3.28 (dd, J_1 = 13.0 Hz, J_2 = 15.1 Hz, 1 H, H-3), 2.88 (dd, J_1 = 3.0 Hz, J_2 = 15.1 Hz, 1 H, H-3).

Anal. Calcd for $C_{17}H_{16}O_4S$: C, 64.54; H, 5.10; S, 10.14. Found: C, 64.43; H, 5.05; S, 10.05.

5-Methoxy-4-oxo-2-phenyl-3,4-dihydro-2*H*-1-benzothiopyran-8-yl 1-Piperidinecarboxylate (2d)

A suspension of 1,3-benzoxathiol-2-one **1a** (X = H; 100 mg, 0.32 mmol) in CH_2Cl_2 (5 mL) was deoxygenated with N_2, and piperidine (0.3 mL, 3 mmol) was added. The mixture was stirred at r.t. for 1 h and then concentrated. The residue was crystallized ($CHCl_3$–MeOH) to give thioflavanone **2d** as a colorless solid; yield: 89 mg (70%); mp 165–166 °C.

IR (KBr): 1722, 1670, 1417, 1215 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.48 (d, *J* = 7.3 Hz, 2 H, H-2′, H-6′), 7.42–7.29 (m, 4 H, H-3′, H-4′, H-5′, H-7), 6.93 (d, *J* = 9.3 Hz, 1 H, H-6), 4.84 (dd, J_1 = 2.9 Hz, J_2 = 12.9 Hz, 1 H, H-2), 3.81 (s, 3 H, OCH_3), 3.52 (br s, 2 H, piperidine), 3.3–3.4 (m, H-3, piperidine, H_2O), 2.97 (dd, J_1 = 2.9 Hz, J_2 = 15.6 Hz, 1 H, H-3), 1.43–1.6 (m, 6 H, piperidine).

Anal. Calcd for $C_{22}H_{23}NO_4S$: C, 66.48; H, 5.83; N, 3.52; S, 8.07. Found: C, 66.22; H, 5.83; N, 3.61; S, 8.04.

2-(4-Chlorophenyl)-5-methoxy-4-oxo-3,4-dihydro-2*H*-1-benzothiopyran-8-yl 1-Piperidinecarboxylate (2e)

A suspension of 1,3-benzoxathiol-2-one **1d** (X = 4-Cl; 108 mg, 0.3 mmol) in $CHCl_3$ (4 mL) was deoxygenated with argon, and piperidine (0.2 mL, 2 mmol) was added. The mixture was stirred at r.t. for 1 h and then concentrated. The residue was crystallized ($CHCl_3$–MeOH) to give thioflavanone **2e** as a colorless solid; yield: 80 mg (59%); mp 172–173 °C.

IR (KBr): 1717, 1678, 1420, 1217 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.51 (d, *J* = 8.4 Hz, 2 H, H-3′, H-5′), 7.46 (d, *J* = 8.4 Hz, 2 H, H-2′, H-6′), 7.32 (d, *J* = 9.0 Hz, 1 H, H-7), 6.93 (d, *J* = 9.0 Hz, 1 H, H-6), 4.88 (dd, J_1 = 2.8 Hz, J_2 = 12.3 Hz, 1 H, H-2), 3.81 (s, 3 H, OCH_3), 3.52 (br s, 2 H, piperidine), 3.3–3.4 (m, H-3, piperidine, H_2O), 2.98 (dd, J_1 = 2.8 Hz, J_2 = 15.0 Hz, 1 H, H-3), 1.4–1.6 (m, 6 H, piperidine).

Anal. Calcd for $C_{22}H_{22}ClNO_4S$: C, 61.18; H, 5.13; N, 3.24; S, 7.42. Found: C, 61.07; H, 5.09; N, 3.37; S, 7.46.

2-(4-Bromophenyl)-5-methoxy-4-oxo-3,4-dihydro-2*H*-1-benzothiopyran-8-yl 1-Piperidinecarboxylate (2f)

A suspension of 1,3-benzoxathiol-2-one **1b** (X = 4-Br; 100 mg, 0.25 mmol) in $CHCl_3$ (5 mL) was deoxygenated with N_2, and piperidine (3 mmol, 0.3 mL) was added. The mixture was stirred at r.t. for 1 h, and then concentrated. The residue was purified on a silica gel column ($CHCl_3$–EtOAc, 3:1), and crystallized (MeOH) to give thioflavanone **2f** as a cream solid; yield: 36 mg (30%); mp 156–160 °C.

IR (KBr): 1717, 1678, 1420, 1217 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.60 (d, *J* = 8.3 Hz, 2 H, H-3′, H-5′), 7.44 (d, *J* = 8.3 Hz, 2 H, H-2′, H-6′), 7.33 (d, *J* = 9.3, 1 H, H-7), 6.93 (d, *J* = 9.3 Hz, 1 H, H-6), 4.87 (dd, J_1 = 12.2 Hz, J_2 = 2.9 Hz, 1 H, H-2), 3.81 (s, 3 H, OCH_3), 3.50 (br s, 2 H, piperidine), 3.25–3.4 (m, H-3, piperidine, H_2O), 2.96 (dd, J_1 = 15.1 Hz, J_2 = 2.9 Hz, 1 H, H-3).

Anal. Calcd for $C_{22}H_{22}BrNO_4S$: C, 55.47; H, 4.65; N, 2.94; S, 6.73. C, 55.16; H, 4.55; N, 3.02; S, 6.72.

Cleavage of the 5-Methoxy Group in Chalcones 1: General Procedure

$BF_3{\cdot}Me_2S$ (21 mmol) was added to a soln of a 5-methoxychalcone **1** (2 mmol) in CH_2Cl_2 (12 mL), and the mixture was stirred at r.t., cooled in ice, and quenched with H_2O (40 mL). The CH_2Cl_2 was evaporated under vacuum, and the precipitate was filtered off, and washed with H_2O to give a crude product that was crystallized.

5-Hydroxy-4-[(2*E*)-3-phenylprop-2-enoyl]-1,3-benzoxathiol-2-one (3a)

Substrate: **1a** (X = H); reaction time: 2.5 h; crystallization: $MeO(CH_2)_2OH$; orange solid; yield: 49%; mp 165–168 °C.

IR (KBr): 3292, 1744, 1595, 1551, 1339, 1282, 1047 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.35 (s, 1 H, OH), 8.13 (d, *J* = 16.1 Hz, 1 H, H-β), 7.80 (d, *J* = 16.1 Hz, 1 H, H-α), 7.72 (m, 2 H, H-2′, H-6′), 7.60 (d, *J* = 8.8 Hz, 1 H, H-7), 7.47 (m, 3 H, H-3′, H-4′, H-5′), 7.08 (d, *J* = 8.8 Hz, 1 H, H-6).

Anal. Calcd for $C_{16}H_{10}O_4S$: C, 64.42; H, 3.38; S, 10.75. Found: C, 64.36; H, 3.39; S, 10.76.

4-[(2*E*)-3-(4-Bromophenyl)prop-2-enoyl]-5-hydroxy-1,3-benzoxathiol-2-one (3b)

Substrate: **1b** (X = 4-Br); reaction time: 1 h; crystallization: $MeO(CH_2)_2OH$; yellow solid; yield: 78%; mp 153–155 °C.

IR (KBr): 3280, 1691, 1598, 1428 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.36 (br s, 1 H, OH), 8.12 (d, *J* = 16.6 Hz, 1 H, H-β), 7.75 (d, *J* = 16.6 Hz, 1 H, H-α), 7.66 (s, 4 H, H-2′, H-3′, H-5′, H-6′), 7.58 (d, *J* = 8.8 Hz, 1 H, H-7), 7.07 (d, *J* = 8.8 Hz, 1 H, H-6).

Anal. Calcd for $C_{16}H_9BrO_4S$: C, 50.95; H, 2.40; S, 8.50. Found: C, 50.93, H, 2.46, S, 8.32.

5-Hydroxy-4-[(2*E*)-3-(4-methoxyphenyl)prop-2-enoyl]-1,3-benzoxathiol-2-one (3c)

Substrate: **1c** (X = 4-OMe); reaction time: 1 h; crystallization: $MeO(CH_2)_2OH$; red solid; yield: 41%; mp 190–193 °C.

IR (KBr): 3123, 1754, 1551, 1252, 823 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.28 (br s, 1 H, OH), 8.03 (d, *J* = 15.6 Hz, 1 H, H-β), 7.79 (d, *J* = 15.6 Hz, 1 H, H-α), 7.70 (d, *J* = 8.3 Hz, 2 H, H-2′, H-6′), 7.59 (d, *J* = 8.8 Hz, 1 H, H-7), 7.18 (d, *J* = 8.8 Hz, 1 H, H-6), 7.05 (d, *J* = 8.3 Hz, 2 H, H-3′, H-5′), 3.83 (s, 3 H, OCH_3).

Anal. Calcd for $C_{17}H_{12}O_5S$: C, 62.19; H, 3.68; S, 9.77. Found: C, 62.08; H, 3.70; S, 9.47.

5-Hydroxy-4-[(2*E*)-3-(4-nitrophenyl)prop-2-enoyl]-1,3-benzoxathiol-2-one (3d)

Substrate: **1e** (X = 4-NO_2); reaction time: 1 h; crystallization: $MeO(CH_2)_2OH$; yellow solid; yield: 68%; mp 228–232 °C.

IR (KBr): 3285, 1751, 1692, 1602, 1431, 1345 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11, 46 (br s, 1 H, OH), 8.31 (d, *J* = 6.5 Hz, 2 H, H-3′, H-5′), 8.23 (d, *J* = 15.6 Hz, 1 H, H-β), 8.00 (d, *J* = 6.5 Hz, 2 H, H-2′, H-6′), 7.86 (d, *J* = 15.6 Hz, 1 H, H-α), 7.64 (d, *J* = 8.8 Hz, 1 H, H-7), 7.10 (d, *J* = 8.8 Hz, 1 H, H-6).

Anal. Calcd for $C_{16}H_9NO_6S{\cdot}0.5H_2O$: C, 54.54; H, 2.86; N, 3.97; S, 9.10. Found: C, 54.17; H, 2.93; N, 3.86; S, 9.02.

4-[(2*E*)-3-(3-Chlorophenyl)prop-2-enoyl]-5-hydroxy-1,3-benzoxathiol-2-one (3e)

Substrate: **1f** (X = 3-Cl); reaction time: 2 h; crystallization: $CHCl_3$–MeOH; yellow solid; yield: 42%; mp 175–179 °C.

IR (KBr): 3319, 1749, 1631, 1596, 1430 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.40 (br s, 1 H, OH), 8.14 (d, *J* = 15.8 Hz, 1 H, H-β), 7.81 (s, 1 H, H-2′), 7.77 (d, *J* = 15.8 Hz, 1 H, H-α), 7.72 (d, *J* = 6.0 Hz, 1 H, H-6′), 7.63 (d, *J* = 8.7 Hz, 1 H, H-7), 7.51 (m, 2 H, H-4′, H-5′), 7.09 (d, *J* = 8.7 Hz, 1 H, H-6).

Anal. Calcd for $C_{16}H_9ClO_4S$: C, 57.75; H, 2.73; S, 9.64. Found: C, 57.50; H, 2.74; S, 9.70.

7-Phenyl-7*H*-[1,3]oxathiolo[4,5-*f*][1]benzopyran-2,9(8*H*)-dione (4a)

A suspension of benzothiazolone **3a** (X = H; 180 mg, 0.6 mmol) in AcOH (2 mL) and H_2SO_4 (0.2 mL) was stirred at 60 °C for 4 h, then cooled and diluted with H_2O. The resulting precipitate was filtered off, dried, and crystallized ($CHCl_3$–MeOH) to give oxathioloflavanone **4a** as a colorless solid; yield: 94 mg (52%); mp 181–182 °C.

IR (KBr): 1763, 1676, 1599, 1451, 1284 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.76 (d, J = 8.8 Hz, 1 H, H-7), 7.55 (d, J = 7.3 Hz, 2 H, H-2′, H-6′), 7.47–7.38 (m, 3 H, H-3′, H-4′, H-5′), 7.18 (d, J = 8.8 Hz, 1 H, H-8), 5.78 (dd, J_1 = 12.9 Hz, J_2 = 2.4 Hz, 1 H, H-2), 3.41 (dd, J_1 = 17.1 Hz, J_2 = 12.9 Hz, 1 H, H-3), 2.97 (dd, J_1 = 17.1 Hz, J_2 = 2.4 Hz, 1 H, H-3).

Anal. Calcd for $C_{16}H_{10}O_4S$: C, 64.42; H, 3.38; S, 10.75. Found: C, 64.48; H, 3.44; S, 10.52.

7-(4-Bromophenyl)-7*H*-[1,3]oxathiolo[4,5-*f*][1]benzopyran-2,9(8*H*)-dione (4b)

A suspension of benzothiazolone **3b** (X = 4-Br; 400 mg, 1.02 mmol) in AcOH (1.5 mL) and H_2SO_4 (0.2 mL) was stirred at 80 °C for 1.5 h, then cooled and diluted with H_2O. The resulting precipitate was filtered off, dried, and crystallized [$MeO(CH_2)_2OH$] to give oxathioloflavanone **4b** as a beige solid; yield: 356 mg (89%); mp 229–231 °C.

Anal. Calcd for $C_{16}H_9BrO_4S$: C, 50.95; H, 2.40; S, 8.50. Found: C, 50.94; H, 2.43; S, 8.39.

IR (KBr): 1754, 1675, 1603, 1457, 1284 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.77 (d, J = 9.1 Hz, 1 H, H-7), 7.66 (d, J = 8.4 Hz, 2 H, H-3′, H-5′), 7.52 (d, J = 8.4 Hz, 2 H, H-2′, H-6′), 7.20 (d, J = 9.1 Hz, 1 H, H-8), 5.80 (dd, J_1 = 12.9 Hz, J_2 = 3.0 Hz, 1 H, H-2), 3.38 (dd, J_1 = 17.2 Hz, J_2 = 12.9 Hz, 1 H, H-3), 3.00 (dd, J_1 = 1 7.2 Hz, J_2 = 2.9 Hz, 1 H, H-3).

7-(3-Chlorophenyl)-7*H*-[1,3]oxathiolo[4,5-*f*][1]benzopyran-2,9(8*H*)-dione (4c)

A suspension of benzothiazolone **3e** (X = 3-Cl; 166 mg, 0.5 mmol) in AcOH (2 mL) and H_2SO_4 (0.2 mL) was stirred at 80 °C for 2.5 h, then cooled and diluted with H_2O. The resulting precipitate was filtered off, dried, purified on a silica gel column ($CHCl_3$–cyclohexane, 2:1), and crystallized ($CHCl_3$–MeOH) to give oxathioloflavanone **4c** as a colorless solid; yield: 84 mg (50%); mp 155–157 °C.

IR (KBr): 1753, 1680, 1602, 1457, 1287 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.80 (d, J = 8.8 Hz, 1 H, H-7), 7.68 (s, 1 H, H-2′), 7.51, (m, 3 H, H-4′, H-5′, H-6′), 7.24 (d, J = 8.8 Hz, 1 H, H-8), 5.83 (dd, J_1 = 12.9 Hz, J_2 = 2.0 Hz, 1 H, H-2), 3.43 (dd, J_1 = 17.0 Hz, J_2 = 12.9 Hz, 1 H, H-3), 3.04 (dd, J_1 = 1 7.0 Hz, J_2 = 2.0 Hz, 1 H, H-3).

Anal. Calcd for $C_{16}H_9ClO_4S$: C, 57.75; H, 2.73; S, 9.64. Found: C, 57.73; H, 2.74; S, 9.53.

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