An Effective Synthesis of 5,4′-Disubstituted Flavones *via* a Cesium Enolate Assisted Intramolecular *ipso*-Substitution Reaction

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A variety of 5,4′-disubstituted flavones, which are anticipated to be androgen receptor antagonists to treat diseases mediated by the androgen receptor, were synthesized. It was found that an intramolecular *ipso*-substitution reaction *via* cesium enolate using 2-fluoro-6-hydroxyacetophenone and various benzoyl chlorides was effective in the preparation of 5-hydroxy-4′-alkylflavones.

Key words flavone; *ipso*-substitution; androgen; antagonist

The androgen receptor (AR), which is activated by androgenic hormones, functions as a DNA binding transcription factor that regulates gene expression.[1,2] The androgen-regulated genes are important for the development and maintenance of the male sexual phenotype. It is known that isoflavones are similar to the estrogen hormone, and several studies using flavones as AR antagonists have been reported.[3,4] We have already reported that some flavonoids act as a novel androgen receptor ligand which interacts with the receptor in a different manner from known androgen receptor ligands.[5] We also disclosed that 5-hydroxyflavone have extremely high AR antagonistic activity, and that the hydroxyl group at the 5-position plays an important role in the interaction with the AR. Furthermore, the introduction of hydroxyl group at the 4′-position increases AR antagonistic activity as well. We report herein the syntheses of various 5,4′-disubstituted flavones, which are expected to be AR antagonist, using a novel intramolecular *ipso*-substitution method to construct the flavone-skeleton.

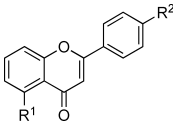
Results and Discussion

We planned to prepare a number of 5,4′-disubstituted flavones, shown in Table 1, and assay them for AR antagonistic activity. The compounds with asterisk are novel flavones and the others are flavones, with unknown AR antagonistic activity. These compounds were chosen because of the variation in the substituent constant[6] and STERIMOL parameter[7,8] of the 4′-position substituent as shown in Table 2.

At the outset, 5-hydroxyflavones (**3a**—**h**) in Table 3 were prepared according to the known method[9] using 2,6-dihydroxyacetophenone and the corresponding benzoyl chlorides under basic conditions in acetone.[10] The yields were low except for the 5-hydroxy-4′-trifluoromethylflavone (**3e**). The ^{1}H-NMR of the crude products showed significant contamination with by-products. More importantly, the desired reaction did not proceed at all, when 4-alkylbenzoyl chlorides were used as substrate (Table 1, entries 9, 10). In this case, the major product was **4** even under high dilution conditions (Fig. 1).[11]

Thus finding a new method to prepare 4′-alkylflavones was imperative. To prevent the double benzoylation of the alkylbenzoyl chloride to 2,6-dihydroxyacetophenone, 2-fluoro-6-hydroxyacetophenone **5** was used as an alternative substrate. We hypothesized that the electron-withdrawing effect of the fluoro-group on the aromatic ring would decrease the electron density of the corresponding phenoxy anion intermediate. And the various 5-hydroxyflavones would be

Table 1. Flavones Pointing for AR Antagonist



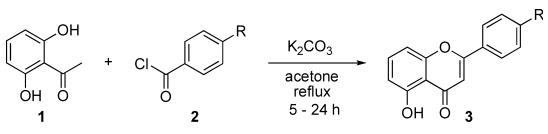
Entry	R^1	R^2	Entry	R^1	R^2
1	OH	F	10	OH	*t*Bu
2	OH	Cl	11[a]	OH	NH_2
3[a]	OH	CN	12[a]	OH	NHAc
4	OH	NO_2	13[a]	OH	NAc_2
5[a]	OH	CF_3	14	OMe	F
6[a]	OH	SMe	15	OMe	CF_3
7[a]	OH	NMe_2	16[a]	F	F
8	OH	Ph	17[a]	F	Cl
9	OH	Me	18[a]	F	CN

a) Novel flavones.

Table 2. Substituent Constant[4] and STERIMOL Parameter[5]

R^2	Substituent constants (σ)	STERIMOL	R^2	Substituent constants (σ)	STERIMOL
NMe_2	−0.83	3.53	SMe	0	4.3
NH_2	−0.66	2.93	NHAc	0	5.15
OH	−0.37	2.74	NAc_2	0	7.15
OMe	−0.27	3.98	F	0.06	2.65
*t*Bu	−0.2	4.11	Cl	0.23	4.3
Me	−0.17	3	CF_3	0.54	3.3
Ph	−0.01	—	CN	0.66	4.23
H	0	2.06	NO_2	0.78	3.44

Table 3. Synthesis of 5-Hydroxyflavones (**3a**—**h**)



Entry	R	Yield (%)[a]	Entry	R	Yield (%)[a]
1	F: **3a**	22	6	SMe: **3f**	9
2	Cl: **3b**	23	7	NMe_2: **3g**	10
3	CN: **3c**	34	8	Ph: **3h**	15
4	NO_2: **3d**	37	9	Me: **3i**	0[b]
5	CF_3: **3e**	78	10	*t*Bu: **3j**	0[c]

a) Isolated yield after recrystallization from ethyl acetate. *b*) The major product was **4i**. *c*) The major product was **4j**

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obtained *via* the plausible mechanism shown in Fig. 2, if an intramolecular *ipso*-substitution reaction[12] of an enolate proceeds.

Although there had been no report of flavone synthesis using intramolecular *ipso*-substitution reaction, we found that the treatment of 2-fluoro-6-hydroxyacetophenone **5**, benzoyl chloride **2k**, and potassium carbonate provided 5-hydroxyflavone in good yield (78% recryst. from ethyl acetate) (Table 4, entry 1). After exploring a variety of reaction conditions, we found that cesium carbonate was better as the base than other carbonates (Li_2CO_3, Na_2CO_3, and K_2CO_3) in terms of reaction rate, and either acetone or *N*,*N*-dimethylformamide (DMF) was suitable as solvent. We then tried to prepare 5-hydroxyflavones (**3i**, **3j**, **3f**, **3g**), which were difficult to obtain in good yields with the reported method.[9] The yields were improved as shown in Table 4 and enough amount of the target flavones were obtained for the assay. We believe that the *ipso*-substitution method will be one of the most effective synthetic methods for various 5-hydroxyflavones, if suitable substrates are available.

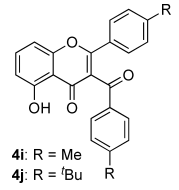


Fig. 1. By-products Dibenzoylated

Attempts to utilize the intramolecular *ipso*-substitution method to prepare 5-fluoroflavones proved futile. Therefore we had to apply the known synthetic method[13,14] to prepare the novel 5-fluoroflavones (**7a**—**c**) (Fig. 3). Similarly, 5-methoxyflavones (**10a**, **b**) were also prepared using another known method[15] because the corresponding substrates for the intramolecular *ipso*-substituted protocol were difficult to obtain (Fig. 4).

Finally, novel 5-hydroxy-4′-aminoflavone derivatives (**3l**—**n**) were prepared from 5-hydroxy-4′-nitroflavone (**3d**) as shown in Fig. 5. The prepared novel flavones (**3c**, **3e**, **3f**, **3g**, **3l**—**n**) and the other flavones, which have not been examined for AR antagonist activity (**3a**,[9] **3b**,[16] **3d**,[9] **3h**,[17] **3i**,[16] **3j**,[18] **3k**,[19] **10a**,[20] **10b**[20]), will be tested in an *in-vitro* reporter gene assay in the near future.

Experimental

Melting points are uncorrected. Infrared absorption spectra were recorded on a Bibby Scientific Ltd. Stuart® SMP 30. ^{1}H-NMR spectra were measured in $CDCl_3$ on JNM-EX270 (270 MHz) spectrometers with tetramethylsilane as the internal standard. Mass spectra were recorded on a Shimadzu Corp.,

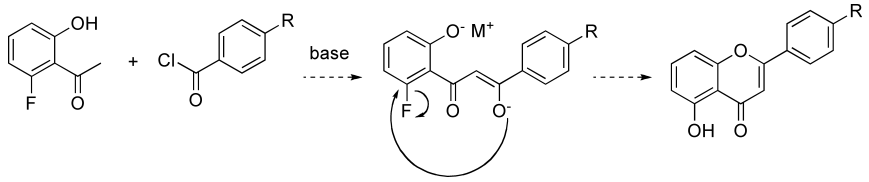
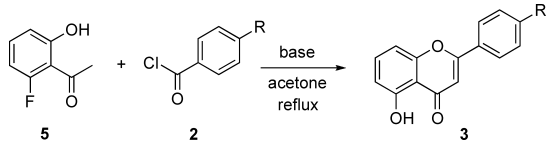


Fig. 2. Synthetic Strategy for Flavone Synthesis *via* Intramolecular *ipso*-Substitution of an Enolate

Table 4. Flavone Synthesis *via* Intramolecular *ipso*-Substitution



Entry	R	Base	Time (h)	Yield (%)
1	H: **3k**	K_2CO_3	24	78[a]
2	Me: **3i**	Cs_2CO_3	3	68[b]
3	CN: **3c**	Cs_2CO_3	4	68[a]
4	^{t}Bu: **3j**	Cs_2CO_3	2	54[b]
5	SMe: **3f**	Cs_2CO_3	3	44[b]
6	NMe_2: **3g**	Cs_2CO_3	4	47[b]

a) Isolated yield after recrystallization from ethyl acetate. *b*) Isolated yield after column chromatography.

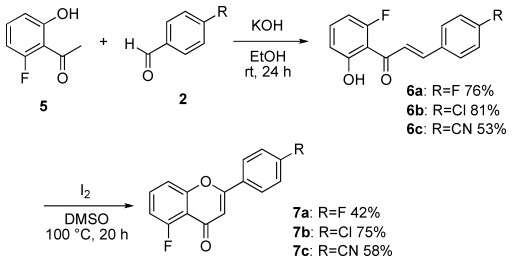


Fig. 3. Synthesis of Novel 5-Fluoroflavones

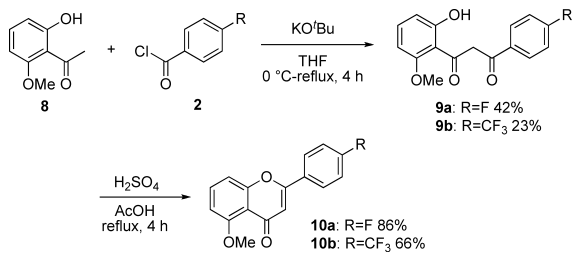


Fig. 4. Synthesis of 5-Methoxyflavones, Which Were Not Examined for AR Antagonist

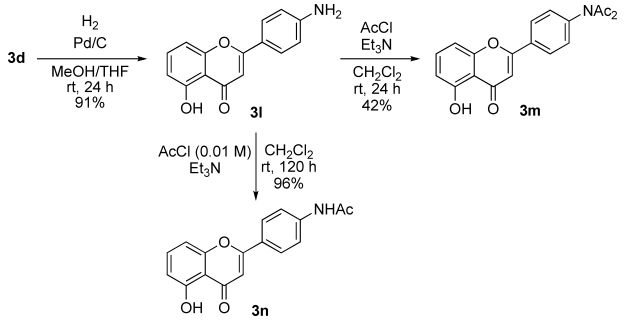


Fig. 5. Synthesis of Novel 5-Hydroxy-4′-aminoflavone Derivatives

Ltd. QP5050A mass spectrometer. Wakogel® C-300 (45—75 μm) was used for column chromatography and flash column chromatography. The chemicals used, were purchased from Sigma-Aldrich Co., Wako Pure Chemical Industries, Ltd., Tokyo Chemical Industry Co., Ltd., and Apollo Scientific Ltd. companies.

Typical Procedure for the Intramolecular *ipso*-Substitution Reaction To a stirred suspension of 2-fluoro-6-hydroxyacetophenone **5** (98 mg, 0.64 mmol) and 4-methylbenzoyl chloride **2i** (120 mg, 0.78 mmol) in acetone (10 ml), was added cesium carbonate (635 mg, 1.95 mmol) at room temperature. The reaction mixture was stirred at 70 °C for 3 h, and quenched with 1 M HCl, then extracted with AcOEt. The organic layer was washed with brine, dried with sodium sulfate and concentrated *in vacuo*. The residue was purified by recrystallization from ethyl acetate to give 5-hydroxy-4′-methylflavone **3i**[16] (110 mg, 68% yield) as yellow crystals; mp 172.0—173.0 °C. ^{1}H-NMR δ: 2.45 (3H, s), 6.71 (1H, s), 6.81 (1H, d, J=7.6 Hz), 7.00 (1H, d, J=7.8 Hz), 7.31 (2H, d, J=8.6 Hz), 7.54 (1H, t, J=8.4 Hz), 7.82 (2H, d, J=8.6 Hz), 12.62 (1H, s). MS m/z: 252 (M^+), 136.

5-Hydroxy-4′-fluoroflavone 3a[9] Yellow crystals; mp 158.0—160.0 °C. ^{1}H-NMR δ: 6.69 (1H, s), 6.83 (1H, d, J=8.1 Hz), 7.00 (1H, d, J=10.8 Hz), 7.22 (2H, d, J=8.1 Hz), 7.56 (1H, t, J=8.1 Hz), 7.91—7.96 (2H, m), 12.53 (1H, s). *Anal.* Calcd for $C_{15}H_9O_3F$: C, 70.31; H, 3.54. Found: C, 70.41; H, 3.73.

5-Hydroxy-4′-chloroflavone 3b[16] Yellow crystals; mp 175.0—176.0 °C. ^{1}H-NMR δ: 6.72 (1H, s), 6.84 (1H, d, J=7.6 Hz), 6.92 (1H, m), 7.49—7.60 (3H, m), 7.84—7.89 (2H, m), 12.50 (1H, s). MS m/z: 272 (M^+), 274 (M^+)+2, 136, 108.

5-Hydroxy-4′-cyanoflavone 3c Yellow crystals; mp 195.0—196.0 °C. ^{1}H-NMR δ: 6.79 (1H, s), 6.86 (1H, d, J=8.4 Hz), 7.03 (1H, d, J=8.1 Hz), 7.60 (1H, t, J=8.1 Hz), 7.85 (2H, d, J=8.1 Hz), 8.04 (2H, d, J=8.1 Hz), 12.37 (1H, s). MS m/z: 263 (M^+), 136, 108. *Anal.* Calcd for $C_{16}H_9O_3N$: C, 73.00; H, 3.45; N, 5.32. Found: C, 72.64; H, 3.41; N, 5.28.

5-Hydroxy-4′-nitroflavone 3d[9] Yellow crystals; mp 226.0—227.0 °C. ^{1}H-NMR δ: 6.83 (1H, s), 6.88 (1H, d, J=8.1 Hz), 7.04 (1H, d, J=7.6 Hz), 7.61 (1H, t, J=8.1 Hz), 8.10 (2H, d, J=7.0 Hz), 8.40 (2H, d, J=7.0 Hz), 12.34 (1H, s). MS m/z: 283 (M^+), 237, 108.

5-Hydroxy-4′-trifluoromethylflavone 3e Yellow crystals; mp 138.0—139.0 °C. ^{1}H-NMR δ: 6.79 (1H, s), 6.85 (1H, d, J=8.1 Hz), 7.03 (1H, d, J=10.8 Hz), 7.59 (1H, t, J=8.1 Hz), 7.81 (2H, d, J=8.1 Hz), 8.04 (2H, d, J=8.1 Hz), 12.43 (1H, s). *Anal.* Calcd for $C_{16}H_9O_3F_3$: C, 62.75; H, 2.96. Found: C, 62.81; H, 3.09.

5-Hydroxy-4′-methylthioflavone 3f Yellow crystals; mp 166.0—167.0 °C. ^{1}H-NMR δ: 2.56 (3H, s), 6.71 (1H, s), 6.82 (1H, d, J=8.4 Hz), 6.98—7.01 (1H, m), 7.34—7.37 (2H, m), 7.55 (1H, t, J=8.4 Hz), 7.81—7.85 (2H, m), 12.61 (1H, s). MS m/z: 284 (M^+), 148. *Anal.* Calcd for $C_{16}H_{12}O_3S$: C, 67.60; H, 4.25. Found: C, 67.30; H, 4.20.

5-Hydroxy-4′-dimethylaminoflavone 3g Yellow crystals; mp 184.0—185.0 °C. ^{1}H-NMR δ: 3.09 (6H, s), 6.59 (1H, s), 6.75 (3H, t, J=8.1 Hz), 6.96 (1H, d, J=8.1 Hz), 7.49 (1H, d, J=9.5 Hz), 7.80 (2H, d, J=8.9 Hz), 12.87 (1H, s). MS m/z: 281 (M^+), 207. *Anal.* Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.46; H, 5.41; N, 5.00.

5-Hydroxy-4′-phenylflavone 3h[17] Pale yellow crystals; mp 177.0—178.0 °C. ^{1}H-NMR δ: 6.78 (1H, s), 7.01 (1H, d, J=10.8 Hz), 7.37—7.57 (4H, m), 7.64 (2H, d, J=8.1 Hz), 7.65 (2H, d, J=8.1 Hz), 7.98 (2H, d, J=8.1 Hz), 12.57 (1H, s). MS m/z: 314 (M^+), 178.

5-Hydroxy-4′-*tert*-butylflavone 3j[18] Yellow crystals; mp 155.0—156.0 °C. ^{1}H-NMR δ: 1.37 (9H, s), 6.72 (1H, s), 6.82 (1H, d, J=8.4 Hz), 7.00 (1H, d, J=7.8 Hz), 7.52—7.58 (3H, m), 7.86 (2H, d, J=8.4 Hz), 12.63 (1H, s). MS m/z: 294 (M^+), 279.

5-Hydroxyflavone 3k[9] Yellow crystals; mp 145.0—146.0 °C. ^{1}H-NMR δ: 6.75 (1H, s), 6.83 (1H, d, J=8.1 Hz), 7.01 (1H, d, J=8.6 Hz), 7.53—7.59 (4H, m), 7.90—7.94 (2H, m), 12.57 (1H, s). MS m/z: 238 (M^+), 136, 108.

5-Hydroxy-4′-aminoflavone 3l Yellow crystals; mp 195.0—196.0 °C. ^{1}H-NMR δ: 4.13—4.23 (2H, m), 6.60 (1H, s), 6.77 (3H, t, J=8.5 Hz), 6.96 (1H, d, J=8.1 Hz), 7.51 (1H, t, J=8.5 Hz), 7.75 (2H, d, J=8.6 Hz), 12.78 (1H, s). MS m/z: 253 (M^+), 207, 117.

5-Hydroxy-4′-*N*,*N*-diacetylaminoflavone 3m Yellow crystals; mp 202.0—203.0 °C. ^{1}H-NMR δ: 2.05 (3H, s), 2.30 (3H, s), 6.72 (1H, s), 6.82 (1H, d, J=8.1 Hz), 7.00 (1H, d, J=8.1 Hz), 7.56 (1H, t, J=8.1 Hz), 7.63—7.68 (2H, m), 7.92—7.97 (2H, m), 12.51 (1H, s). MS m/z: 295+42 (M^+), 253, 117.

5-Hydroxy-4′-*N*-acetylaminoflavone 3n Yellow crystals; mp 230.0—231.0 °C. ^{1}H-NMR δ: 2.24 (3H, s), 6.70 (1H, s), 6.82 (1H, d, J=8.1 Hz), 7.00 (1H, d, J=8.1 Hz), 7.31 (1H, s), 7.55 (1H, t, J=8.1 Hz), 7.70 (2H, d, J=8.1 Hz), 7.90 (2H, d, J=8.1 Hz), 12.61 (1H, s). MS m/z: 295 (M^+), 253, 207.

5,4′-Difluoroflavone 7a Colorless crystals; mp 190.0—191.0 °C. ^{1}H-NMR δ: 6.71 (1H, s), 7.05—7.12 (1H, m), 7.20—7.26 (2H, m), 7.37 (1H, d, J=8.6 Hz), 7.60—7.67 (1H, m), 7.88—7.94 (2H, m). MS m/z: 258 (M^+), 110. *Anal.* Calcd for $C_{15}H_8O_2F_2$: C, 69.77; H, 3.12. Found: C, 69.56; H, 3.21.

5-Fluoro-4′-chloroflavone 7b Colorless crystals; mp 195.0—196.0 °C. ^{1}H-NMR δ: 6.74 (1H, s), 7.05—7.12 (1H, m), 7.38 (1H, d, J=8.6 Hz), 7.50—7.53 (2H, m), 7.60—7.68 (1H, m), 7.83—7.86 (2H, m), MS m/z: 274 (M^+), 138, 110.

5-Fluoro-4′-cyanoflavone 7c Colorless crystals; mp 201.8—202.0 °C. ^{1}H-NMR δ: 6.81 (1H, s), 7.08—7.15 (1H, m), 7.38—7.42 (1H, m), 7.63—7.72 (1H, m), 7.82—7.85 (2H, m), 8.00—8.04 (2H, m). MS m/z: 265 (M^+), 237, 138, 110.

5-Methoxy-4′-fluoroflavone 10a[20] Pale yellow crystals; mp 149.0—150.0 °C. ^{1}H-NMR δ: 4.01 (3H, s), 6.68 (1H, s), 6.84 (1H, d, J=8.1 Hz), 7.11—7.23 (3H, m), 7.58 (1H, t, J=8.1 Hz), 7.87—7.94 (2H, m). *Anal.* Calcd for $C_{16}H_{11}O_3F$: C, 71.11; H, 4.10. Found: C, 71.35; H, 4.26.

5-Methoxy-4′-trifluoromethylflavone 10b[20] Yellow crystals; mp 171.0—172.0 °C. ^{1}H-NMR δ: 4.02 (3H, s), 6.79 (1H, s), 6.86 (1H, d, J=8.1 Hz), 7.16 (1H, d, J=10.8 Hz), 7.61 (1H, t, J=8.1 Hz), 7.78 (2H, d, J=8.1 Hz), 8.02 (2H, d, J=8.1 Hz), *Anal.* Calcd for $C_{17}H_{11}O_3F_3$: C, 63.75; H, 3.46. Found: C, 63.49; H, 3.60.

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References and Notes

1) Cohen M. B., Rokhlin O. W., *J. Cell. Biochem.*, **3**, 363—371 (2006).
2) Mooradian A. D., Morley J. E., Korenman S. G., *Endocr. Rev.*, **8**, 1—28 (1987).
3) Kao Y. C., Zhou C., Sherman M., Laughton C. A., Chen S., *Environ. Health Perspect.*, **106**, 85—92 (1998).
4) Bovee Toine F. H., Schoonen Willem G. E. J., Hamers Astrid R. M., Bento Marta J., Peijnenburg Ad A. C. M., *Anal. Bioanal. Chem.*, **390**, 1111—1119 (2008).
5) Nishizaki Y., Ishimoto Y., Hotta Y., Hosoda A., Yoshikawa H., Akamatsu M., Tamura H., *Bioorg. Med. Chem. Lett.*, **19**, 4706—4710 (2009).
6) Hammett L. P., *Chem. Rev.*, **17**, 125—136 (1935).
7) Hansch C., Leo A., Unger S. H., Kim K. H., Nikaitani D., Lien E. J., *J. Med. Chem.*, **16**, 1207—1216 (1973).
8) Hansch C., Rockwell S. D., Jow P. Y. C., Leo A., Steller E. E., *J. Med. Chem.*, **20**, 304—306 (1977).
9) Bois F., Beney C., Mariotte A., Boumendjel A., *Synlett*, **9**, 1480—1482 (1999).
10) Typical Experimental Procedure; Preparation of 5-hydroxy-4′-fluoroflavone **3a**: To a stirred suspension of 2,6-dihydroxyacetophenone **1a** (229 mg, 1.5 mmol) and 4-fluorobenzoyl chloride **2a** (357 mg, 2.25 mmol) in acetone (10 ml), was added potassium carbonate (2.1 g, 15.2 mmol) at room temperature. The reaction mixture was stirred at 70 °C for 24 h, and quenched with 1 M HCl, then extracted with AcOEt. The organic layer was washed with brine, dried with sodium sulfate and concentrated *in vacuo*. The residue was purified by recrystallization from ethyl acetate/*n*-hexane to give 5-hydroxy-4′-fluoroflavone **3a** (86 mg, 22% yield) as yellow crystals.
11) 5-Hydroxy-3-(4-methylbenzoyl)-2-*p*-tolyl-4*H*-chromen-4-one (**4i**)[16]: Pale yellow crystals; mp 223.0—224.0 °C. ^{1}H-NMR δ: 2.34 (3H, s), 2.39 (3H, s), 6.85 (1H, d, J=8.1 Hz), 7.02 (1H, d, J=7.6 Hz), 7.15—7.26 (4H, m), 7.53—7.63 (3H, m), 7.84 (2H, d, J=8.4 Hz), 12.23 (1H, s). MS m/z: 370 (M^+), 341. 2-(4-*tert*-Butylphenyl)-5-hydroxy-3-(4-methylbenzoyl)-4*H*-chromen-4-one (**4j**): Pale yellow crystals; mp 228.0—229.0 °C. ^{1}H-NMR δ: 1.28 (9H, s), 1.33 (9H, s), 6.85 (1H, d, J=8.4 Hz), 7.02 (1H, d, J=8.6 Hz), 7.39 (2H, d, J=7.8 Hz), 7.47 (2H, d, J=8.6 Hz), 7.59—7.61 (3H, m), 7.90 (2H, d, J=8.4 Hz), 12.22 (1H, s). MS m/z: 454 (M^+), 397, 207. *Anal.* Calcd for $C_{30}H_{32}O_4$: C, 78.92; H, 7.06. Found: C, 78.73; H, 6.58.
12) Moodie R. B., Schofield K., *Accounts of Chemical Research*, **9**, 287—292 (1976).
13) Kagawa H., Shigematsu A., Ohta S., Harigaya Y., *Chem. Pharm. Bull.*,

53, 547—554 (2005).
14) Dao T. T., Chi Y. S., Kim J., Kim H. P., Kim S., Park H., *Bioorg. Med. Chem. Lett.*, **14**, 1165—1167 (2004).
15) Ares J. J., Outt P. E., Kakodkar S. V., Buss R. C., Geiger J. C., *J. Org. Chem.*, **58**, 7903—7905 (1993).
16) Pinto D. C. G. A., Silva A. M. S., Almeida L. M. P. M., Cavaleiro J. A. S., Elguero J., *Eur. J. Org. Chem.*, **22**, 3807—3815 (2002).
17) Baston D. S., Nagy S. R., Nantz M., Kurth M., Springsteel M., Denison M. S., *Organohalogen Compounds*, **65**, 142—145 (2003).
18) Beutner S., Frixel S., Ernst H., Haremza S., Hoffmann T., Hernandez-Blanco I., Kiesendahl N., Mayer B., Noack P., Ruck C., Scherrers R., Schmidt M., Schuelke I., Martin H. D., *Advances in Colour Science and Technology*, **5**, 103—112 (2002).
19) Fitzmaurice R. J., Etheridge Z. C., Jumel E., Woolfson D. N., Caddick S., *Chem. Commun.*, **46**, 4814—4816 (2006).
20) Ares J. J., Outt P. E., Randall J. L., Murray P. D., Weisshaar P. S., O'Brien L. M., Ems B. L., Kakodkar S. V., Kelm G. R., Kershaw W. C., Werchowski K. M., Parkinson A., *J. Med. Chem.*, **38**, 4937—4943 (1995).