# *Notes*

## A Convenient Method for Synthesizing 2-Aryl-3-hydroxy-4-oxo-4*H*-1-benzopyrans or Flavonols

André Fougerousse, Emmanuel Gonzalez, and Raymond Brouillard*

*Laboratoire de Chimie des Polyphénols, UMR 7509 du CNRS, Université Louis Pasteur, 4, rue Blaise Pascal, 67008 Strasbourg, France*

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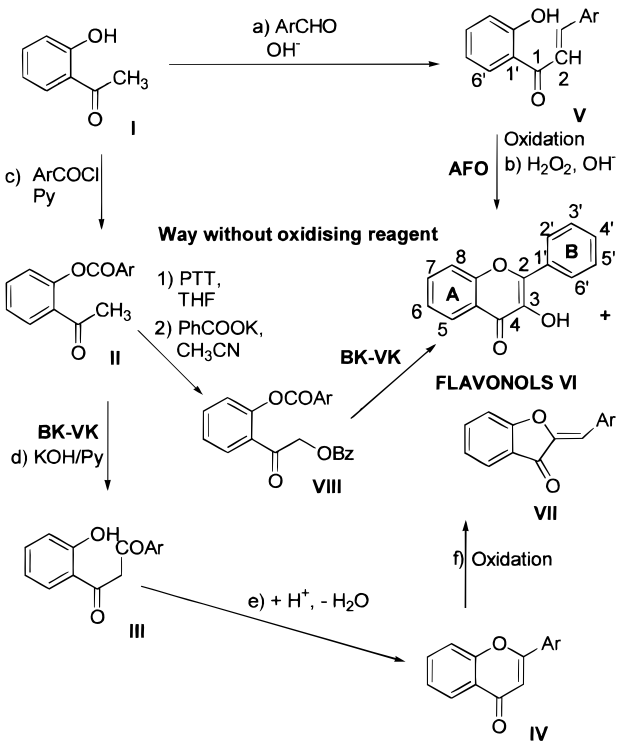
It has recently been demonstrated that flavonols possess antiviral, antitumoral, and/or antibiotic effects.[1,2] They are also known for their good antioxidant properties, rendering the consumption of foods (fruits, vegetables) and beverages (tea, wine) containing these compounds highly recommended.[3,4] Commercial flavonol samples are scarce, and to evaluate their antioxidant properties, one must efficiently synthesize pure molecules in high yields. Like the natural ones, the synthetic flavonols must contain different substituents on rings A and B (see structure **VI**, Scheme 1).

Two main methods of obtaining flavonols of type **VI** have been described (Scheme 1): the oxidative cyclization of chalcone **V** according to the Algar−Flynn−Oyamada reaction (AFO)[5,6]and the cyclization of dibenzoylmethanes **III**, obtained from the Baker−Venkataraman rearrangement (BK−VK), followed by the oxidation of the flavone **IV**.[7,8]

Both methods have some disadvantages. With the AFO method, if the chalcone **V** has a substituent in position 6′, the resulting yields are low. This is due to some strain in the C1−C1′ bond that leads to steric hindrance, and therefore, the opening of the intermediate epoxide (Scheme 1, step b) occurs essentially on the C2 carbon. Consequently, type **VII** aurones are the main products.[9−11] Recent flavonol syntheses contained substrates without substituents at the chalcone 6′ site, in contrast to natural flavonols.[12−15] This observation, therefore, restricts the interest of the AFO method.

**Scheme 1**




The Baker−Venkataraman rearrangement (Scheme 1, step d) is followed by a quick cyclization−dehydration step that leads to flavones of type **IV**. It works well in reactions that afford 5-substituted flavones.[16,17] However, the last step before reaching **VI** features strong oxidizing reagents, like dimethyldioxirane or hypervalent iodine derivatives.[18−21] Some sensitive substituents, like glycosyl and isoprenyl groups, are incompatible with such reagents. Therefore, it is essential to suggest a new approach that avoids the use of any oxidizing reagents (Scheme 1).

(1) Bognar, R.; Rakosi, M. *Proc. 5th Hung. Bioflavonoid Symp. Matrafured, Hungary* **1977**, 138.
(2) (a) Cody, V., Middleton, E., Jr., Harborne, J. B., Eds. *Plant Flavonoids in Biology and Medicine; Biochemical, Pharmacological, and Structure−Activity Relationships*; Alan R. Liss: New York, 1986. (b) Cody, V., Middleton, E., Jr., Harborne, J. B., Beretz, A., Eds. *Plant Flavonoids in Biology and Medicine II; Biochemical, Cellular, and Medicinal Properties*; Alan R. Liss: New York, 1988. (c) Bors, W. *Methods Enzymol.* **1990**, *186*, 343.
(3) Vercauteren, J., Chèze, C., Dumon, M. C., Weber, J. F., Eds. *Polyphenols Communications 96*; Université Bordeaux 2: Bordeaux, 1996.
(4) Charbonnier, F., Delacotte, J. M., Rolando, C., Eds. *Polyphenols Communications 98*; Université Bordeaux 2: Bordeaux, 1998.
(5) Algar, J.; Flynn, J. P. *Proc. R. Irish Acad.* **1934**, *42b*, 1.
(6) (a) Oyamada, T. *J. Chem. Soc. Jpn.* **1934**, *55*, 1256. (b) Oyamada, T. *Bull. Chem. Soc. Jpn.* **1935**, *10*, 182.
(7) Baker, W. *J. Chem. Soc.* **1933**, 1381.
(8) (a) Mahal, H. S.; Venkataraman, K. *Curr. Sci.* **1933**, *4*, 214. (b) Mahal, H. S.; Venkataraman, K. *J. Chem. Soc.* **1934**, 1767.
(9) Cummins, B.; Donnely, D. M. X.; Eades, J. F.; Fletcher, H.; O'Cinneide, F.; Philbin, E. M.; Swirski, J.; Wheeler, T. S.; Wilson, R. K. *Tetrahedron* **1963**, *19*, 499.
(10) Gormley, T. R.; O'Sullivan, W. I. *Tetrahedron* **1973**, *29*, 369.
(11) Adams, C. J.; Main, L. *Tetrahedron* **1991**, *47*, 4979.
(12) Fringuelli, F.; Pani, G.; Piermatti, O.; Pizzo, F. *Tetrahedron* **1994**, *50*, 11499.
(13) Gupta, S. C.; Saini, A.; Kumar, D.; Yadav, N. S.; Chand, K.; Mor, S.; Dhawan, S. N. *J. Chem. Soc., Perkin Trans. 1* **1995**, *2*, 177.
(14) Bhatti, S. P.; Garg, C. P.; Kapoor, R. P. *Indian J. Chem., Sect. B* **1995**, *34*, 879.
(15) Zwaagstra, M. E.; Korthouver, R. E. M.; Timmerman, H.; Zhang, M. Q. *Eur. J. Med. Chem.* **1998**, *33*, 95.
(16) Ares, J. J.; Outt, P. E.; Kakodkar, S. V.; Buss, R. C.; Geiger, J. C. *J. Org. Chem.* **1993**, *58*, 7903.
(17) Nishinaga, A.; Ando, H.; Maruyama, K.; Mashino, T. *Synthesis* **1992**, 839.
(18) Adam, W.; Hadjiarapoglou, L.; Levai, A. *Synthesis* **1992**, 436.
(19) (a) Horie, T.; Kawamura, Y.; Yamamoto, H.; Yamashita, K. *Chem. Pharm. Bull.* **1995**, *43*, 2054. (b) Horie, T.; Kitou, T.; Kawamura, Y.; Yamashita, K. B*ull. Chem. Soc. Jpn.* **1996**, *69*, 1033. (c) Horie, T.; Shibata, K.; Yamashita, K.; Kawamura, Y.; Tsukayama, M. *Chem. Pharm. Bull.* **1997**, *45*, 446.
(20) Prakash, O.; Pahuja, S.; Tanwar, M. P. *Indian J. Chem., Sect. B* **1994**, *33*, 272.
(21) Burke, A. J.; O'Sullivan, W. I. *Tetrahedron* **1997**, *53*, 8491.

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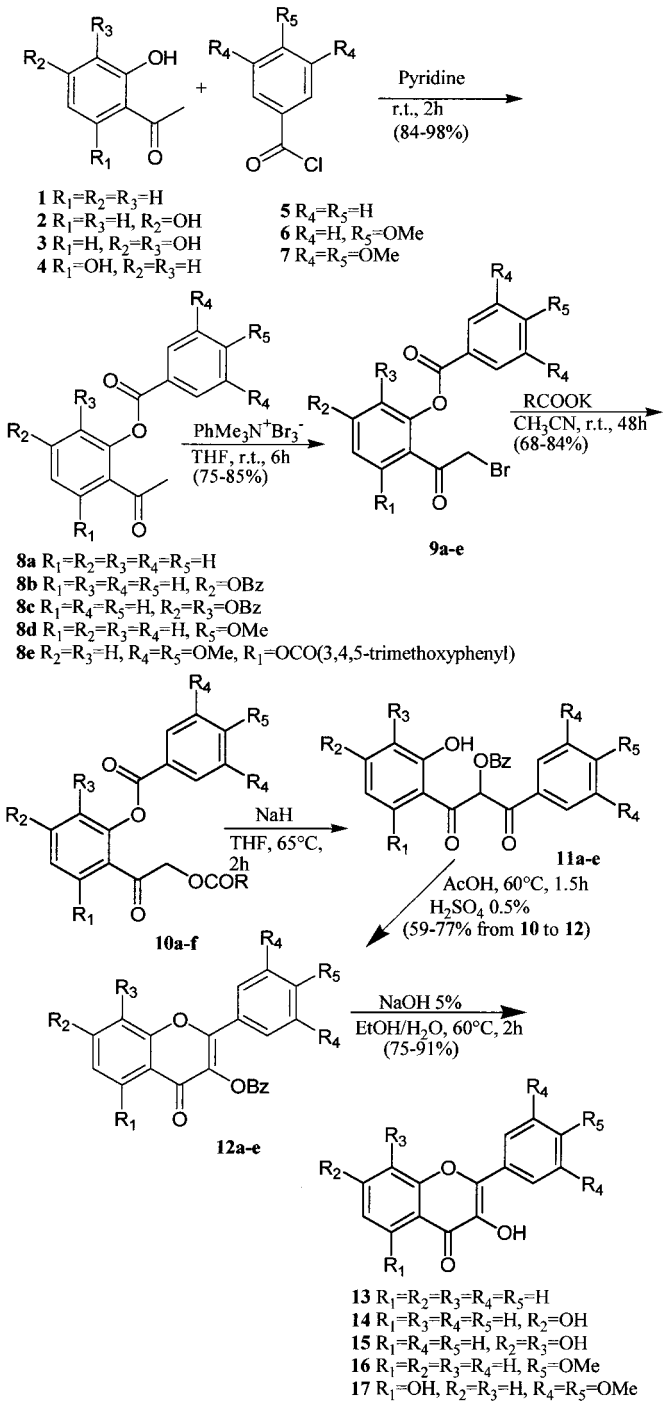
**Scheme 2**




To be able to use mild conditions, we modified the oxidation state of the C2 carbon of the acylated acetophenones **II** via a selective bromination. Substitution of the bromine atom by a benzoate group (**VIII**) introduces the oxygen atom, then the Baker−Venkataraman rearrangement, followed by a cyclization−dehydration step and saponification of the benzoate group, yields the hydroxyl group in position 3 of the flavonol.

## Results and Discussion

Commercially available hydroxyacetophenones **1**−**4** and aroyl chlorides **5**−**7** were used as starting materials (Scheme 2).

Acylation of the hydroxyacetophenones took place in pyridine solution at room temperature for 2 h. Yields for **8a**−**e** ranged from 84 to 98%. Selective bromination of the α position of the carbonyl group was obtained by using phenyltrimethylammonium tribromide (PTT). This reagent is known for selectively brominating acetophenones at the *ω* position, without attacking the aromatic rings.[22] After recrystallization, the yields ranged from 75 to 85%. In the next step, we introduced the functional flavonol oxygen atom. The substitution of the bromine by an alkoxide ion cannot be performed as such, because alkoxides act as strong bases. Epoxyether formation, Favorskii rearrangement, and aldol condensation originated several products that were of no interest for this present work.

As we have already reported, carboxylate ions react readily with α-halogenated aldehydes.[23] Because the acetate was too labile, we chose to use potassium benzoate and cinnamate in a polar solvent (acetonitrile). Potassium *p*-methoxybenzoate and potassium cinnamate are especially well suited for the $^1$H NMR elucidation of the different structures appearing in Scheme 2. Although potassium benzoate and potassium cinnamate are poorly soluble in acetonitrile, the substitution is still possible after long and vigorous stirring (48 h) at room temperature. Yields of pure products **10** vary from 68 to 84%.

The Baker−Venkataraman rearrangement was done with a nonnucleophilic base, sodium hydride in tetrahydrofuran, under reflux for 2 h. The mixture was then poured in acidified water, which led to the precipitation of dibenzoylcarbinol benzoates **11**. The products **11** were washed with water and immediately used in the cyclization step, which took place in a 0.5% concentrated sulfuric acid solution in glacial acetic acid. After recrystallization, overall yields of steps transforming **10** into **12** ranged from 59 to 77%.

Finally, the hydroxyl groups were deprotected by saponification; the compounds **12** were dissolved in a 10/90 hydro-alcoholic solution with 5% sodium hydroxide, for 2 h at 60 °C. After extraction, the pure flavonols **13**−**17** were isolated.

If starting materials (acetophenones and aroyl chlorides) are well chosen, our synthetic approach constitutes a simple and high yielding way to synthesize diverse flavonols.

## Experimental Section

**General.** All starting materials were commercially available, ≥98% purity, and used without further purification. $^1$H and $^{13}$C NMR spectra were referenced to internal standards TMS ($\delta_H$ = 0.00, $\delta_C$ = 0.0), $CDCl_3$ ($\delta_H$ = 7.26, $\delta_C$ = 77.0), $CD_3OD$ ($\delta_H$ = 4.87, $\delta_C$ = 49.2), or DMSO-$d_6$ ($\delta_H$ = 2.50, $\delta_C$ = 39.4).

**General Procedure for 8: 2′-Benzoyloxyacetophenone (8a).** A mixture of **1** (8.20 g, 60.2 mmol) and **5** (10.67 g, 75.9 mmol) was stirred in dry pyridine (25 mL) at room temperature for 2 h. The reaction mixture was then poured into a mixture of crushed ice (120 mL) and concentrated HCl (5 mL), extracted twice with dichloromethane, washed three times with aqueous $Na_2CO_3$, and then washed three times with water. The solvent was removed under reduced pressure. The residue was recrystallized from ethanol to give **8a** (13.68 g, 95%) as white solid. $^1$H NMR: $\delta_H$ 8.25−8.20 (2H, m), 7.90−7.85 (1H, m), 7.67−7.22 (6H, m), 2.55 (3H, s). $^{13}$C NMR: $\delta_C$ 197.4, 165.1, 149.3, 133.7, 133.3, 131.3, 130.2, 129.2, 128.6, 126.1, 123.9, 29.7.

(22) (a) Brulé, D.; Mentzer, C. *C. R. Acad. Sci.* **1960**, *250*, 365. (b) Jacques, J.; Marquet, A. *Organic Syntheses;* Wiley & Sons: New York, 1988, VI, p175.

(23) Riehl, J. J.; Fougerousse, A. *Bull. Soc. Chim. France* **1968**, *10*, 4083.

**2′,4′-Dibenzoyloxyacetophenone (8b).** White solid (2.33 g, 98%). $^1$H NMR: $\delta_H$ 8.24−8.17 (4H, m), 7.98 (1H, d, $J$ = 8.5 Hz), 7.71−7.49 (6H, m), 7.33−7.22 (2H, m), 2.57 (3H, s).$^{13}$C NMR: $\delta_C$ 196.3, 164.9, 164.3, 154.4, 150.3, 134.1, 131.5, 130.4, 129.1, 128.8, 119.6, 117.7, 29.9.

**2′,3′,4′-Tribenzoyloxyacetophenone (8c).** Colorless needles (6.02 g, 89%). $^1$H NMR: $\delta_H$ 8.12−7.89 (7H, m), 7.56−7.24 (10 H, m), 2.58 (3H, s). $^{13}$C NMR: $\delta_C$ 195.7, 163.6, 163.3, 147.3, 143.6, 136.4, 134.0, 130.4, 130.3, 128.7, 128.5, 128.4, 127.9, 127.4, 120.8, 29.8.

**2′-(4-Methoxybenzoyloxy)-acetophenone (8d).** White solid (3.88 g, 98%). $^1$H NMR: $\delta_H$ 8.17 (2H, d, $J$ = 9 Hz), 7.85 (1H, dd, $J$ = 7.7, 1.7 Hz), 7.58 (1H, m), 7.35 (1H, m), 7.23 (1H, dd, $J$ = 8.1, 1.1 Hz), 7.00 (2H, d, $J$ = 9 Hz), 3.90 (3H, s), 2.54 (3H, s). $^{13}$C NMR: $\delta_C$ 197.8, 164.8, 164.2, 149.6, 133.3, 132.5, 131.6, 130.2, 126.1, 124.0, 121.6, 114.1, 55.6, 30.0.

**2′,6′-Di(3,4,5-trimethoxybenzoyloxy)-acetophenone (8e).** White solid (1.53 g, 84%). $^1$H NMR: $\delta_H$ 7.51 (1H, d, $J$ = 8.2 Hz), 7.40 (4H, s), 7.21 (2H, d, $J$ = 8.2 Hz), 3.94−3.91 (18H, m), 2.47 (3H, s). $^{13}$C NMR: $\delta_C$ 198.3, 164.2, 153.2, 148.2, 143.4, 131.0, 128.4, 123.5, 120.6, 107.6, 61.0, 56.4, 31.4.

**General Procedure for 9: 2′-Benzoyloxy-2-bromoacetophenone (9a).** To a solution of **8a** (5.00 g, 20.8 mmol) in anhydrous tetrahydrofuran (25 mL) was added PTT (7.80 g, 20.8 mmol) in portions over a period of 10 min. The reaction mixture was stirred at room temperature for 6 h, poured into water (110 mL), and stirred until a colorless precipitate was formed. The residue was recrystallized from ethanol to give **9a** (5.57 g, 84%) as colorless needles. $^1$H NMR: $\delta_H$ 8.24−8.19 (2H, m), 7.89 (1H, m), 7.68−7.22 (6H, m), 4.41 (2H, s).$^{13}$C NMR: $\delta_C$ 190.9, 164.9, 149.7, 134.2, 134.1, 130.6, 130.4, 129.0, 128.9, 128.5, 126.3, 124.2, 34.1.

**2′,4′-Dibenzoyloxy-2-bromoacetophenone (9b).** Colorless needles (547 mg, 75%). $^1$H NMR: $\delta_H$ 8.25−8.17 (4H, m), 8.01 (1H, d, $J$ = 8.3 Hz), 7.69−7.29 (8H, m), 4.42 (2H, s).

**2′,3′,4′-Tribenzoyloxy-2-bromoacetophenone (9c).** Colorless needles (5.25 g, 77%). $^1$H NMR: $\delta_H$ 8.11−7.91 (7H, m), 7.59−7.24 (10H, m), 4.45 (2H, s).

**2′-(4-Methoxybenzoyloxy)-2-bromoacetophenone (9d).** Colorless needles (1.10 g, 85%). $^1$H NMR: $\delta_H$ 8.17 (2H, d, $J$ = 9 Hz), 7.89 (1H, dd, $J$ = 7.8, 1.6 Hz), 7.63 (1H, m), 7.42−7.30 (2H, m), 7.02 (2H, d, $J$ = 9 Hz), 4.41 (2H, s), 3.91 (3H, s). $^{13}$C NMR: $\delta_C$ 190.9, 164.5, 164.4, 149.8, 134.1, 132.6, 130.6, 128.7, 126.2, 124.2, 121.2, 114.2, 55.7, 34.6.

**2′,6′-Di(3,4,5-trimethoxybenzoyloxy)-2-bromoacetophenone (9e).** Colorless needles (904 mg, 79%). $^1$H NMR: $\delta_H$ 7.60 (1H, d, $J$ = 8.2 Hz), 7.39 (4H, s), 7.30 (2H, d, $J$ = 8.2 Hz), 4.35 (2H, s), 3.99−3.93 (18H, m). $^{13}$C NMR: $\delta_C$ 191.3, 164.0, 153.3, 148.6, 143.5, 131.9, 123.2, 120.6, 107.7, 61.1, 56.5, 35.6.

**General Procedure for 10: 2,2′-Dibenzoyloxyacetophenone (10a).** A mixture of **9a** (1.45 g, 4.55 mmol) and potassium benzoate (1.10 g, 6.87 mmol) was stirred in acetonitrile (20 mL) at room temperature for 48 h. The salts were filtered off, and the solvent was removed under reduced pressure. The residue was taken up in dichloromethane, washed with aqueous sodium carbonate, and then washed with water. The solvent was removed under reduced pressure, and the residue was recrystallized from ethanol to give **10a** (1.38 g, 84%) as colorless needles. $^1$H NMR: $\delta_H$ 8.25−8.19 (2H, m), 8.07−8.01 (2H, m), 7.94 (1H, dd, $J$ = 7.7, 1.7 Hz), 7.69−7.34 (8H, m), 7.29 (1H, dd, $J$ = 8.1, 1.1 Hz), 5.38 (2H, s). $^{13}$C NMR: $\delta_C$ 192.3, 165.9, 164.9, 149.7, 134.2, 134.1, 133.3, 130.5, 130.1, 130.0, 129.4, 128.9, 128.7, 128.4, 126.4, 123.9, 68.4.

**2,2′,4′-Tribenzoyloxyacetophenone (10b).** Colorless needles (669 mg, 79%). $^1$H NMR: $\delta_H$ 8.27−8.04 (7H, m), 7.69−7.31 (11H, m), 5.40 (2H, s). $^{13}$C NMR: $\delta_C$ 191.1, 165.9, 164.5, 164.2, 154.9, 150.7, 134.3, 134.1, 133.4, 131.3, 130.5, 130.4, 130.0, 129.4, 129.0, 128.8, 128.5, 126.1, 119.9, 117.7, 68.4.

**2,2′,3′,4′-Tetrabenzoyloxyacetophenone (10c).** Colorless needles (3.53 g, 73%). $^1$H NMR: $\delta_H$ 8.13−7.92 (9H, m), 7.61−7.23 (13H, m), 5.43 (2H, s). $^{13}$C NMR: $\delta_C$ 190.5, 164.8, 163.7, 163.2, 163.0, 148.0, 143.9, 136.3, 134.2, 134.1, 134.0, 133.3, 130.5, 130.3, 130.2, 130.0, 129.3, 128.7, 128.6, 128.4, 128.2, 127.9, 127.7, 127.6, 127.2, 121.3, 68.1.

**2-Benzoyloxy-2′-(4-methoxybenzoyloxy)-acetophenone (10d).** Colorless needles (865 mg, 77%). $^1$H NMR: $\delta_H$ 8.20 (2H, d, $J$ = 9 Hz), 8.07 (2H, m), 7.97 (1H, dd, $J$ = 7.7, 1.6 Hz), 7.60−7.27 (6H, m), 7.01 (2H, d, $J$ = 9 Hz), 5.38 (2H, s), 3.91 (3H, s). $^{13}$C NMR: $\delta_C$ 192.3, 166.0, 164.6, 164.5, 149.9, 134.0, 133.3, 132.7, 130.2, 130.0, 129.4, 128.8, 128.4, 126.2, 124.0, 121.1, 114.3, 68.6, 55.6.

**2-Benzoyloxy-2′,6′-di(3,4,5-trimethoxybenzoyloxy)-acetophenone (10e).** Colorless needles (467 mg, 68%). $^1$H NMR: $\delta_H$ 7.94−7.88 (2H, m), 7.61−7.38 (8H, m), 7.30 (2H, d, $J$ = 8.2 Hz), 5.21 (2H, s), 3.95−3.93 (18H, m). $^{13}$C NMR: $\delta_C$ 194.1, 165.8, 164.1, 153.2, 148.9, 143.4, 133.4, 131.8, 129.8, 129.1, 128.4, 124.6, 123.3, 120.6, 107.8, 69.0, 61.0, 56.4.

**2′-Benzoyloxy-2-cinnamoyloxyacetophenone (10f).** Colorless needles (417 mg, 69%). $^1$H NMR: $\delta_H$ 8.27−8.22 (2H, m), 7.94 (1H, dd, $J$ = 7.7, 1.7 Hz), 7.78−7.29 (12H, m), 6.50 (1H, d, $J$ = 16 Hz), 5.27 (2H, s). $^{13}$C NMR: $\delta_C$ 192.6, 166.2, 164.9, 149.7, 146.1, 134.2, 134.0, 130.5, 130.1, 128.9, 128.3, 126.4, 124.0, 117.0, 68.1.

**General Procedure for 12: 2-Phenyl-3-benzoyloxy-4-oxo-*4H*-1-benzopyran (3-Benzoyloxyflavone) (12a).** To a suspension of sodium hydride (60% dispersion in oil, washed three times with dry hexane) (48 mg, 2.0 mmol) in dry tetrahydrofuran (10 mL) was added **10a** (250 mg, 0.7 mmol) in THF (10 mL). The reaction mixture was refluxed for 90 min with stirring, and then the cooled mixture was poured into a mixture of ice (120 g) and concentrated HCl (2 mL). The crude $\beta$-diketone **11a** precipitated, was washed with water, and was used in the following ring closure step without further purification.

To a solution of the crude $\beta$-diketone **11a** in acetic acid (10 mL) was added, dropwise, concentrated sulfuric acid (0.25 mL). The reaction mixture was heated at 60 °C for 90 min with stirring, and the solution was poured over ice (60 g). The precipitate was filtered, washed with water, and recrystallized from ethanol to yield the pure **12a** (150 mg, 63%) as colorless needles. $^1$H NMR: $\delta_H$ 8.28 (1H, dd, $J$ = 8.1, 1.6 Hz), 8.19 (2H, m), 7.93 (2H, m), 7.78−7.32 (9H, m). $^{13}$C NMR: $\delta_C$ 172.2, 164.0, 156.4, 155.8, 134.1, 133.9, 131.3, 130.6, 130.1, 128.8, 128.7, 128.4, 126.2, 125.3, 123.8, 118.2. HRMS $(M + H)^+$: calcd for $C_{22}H_{14}O_4$, 343.0970; found, 343.0967.

**2-Phenyl-3,7-dibenzoyloxy-4-oxo-*4H*-1-benzopyran (3,7-Dibenzoyloxyflavone) (12b).** Colorless solid (274 mg, 59%). $^1$H NMR: $\delta_H$ 8.33 (1H, d, $J$ = 8.7 Hz), 8.26−8.19 (4H, m), 7.95 (2H,m), 7.70−7.46 (10H, m), 7.33 (1H, dd, $J$ = 8.7, 2 Hz). $^{13}$C NMR: $\delta_C$ 171.6, 164.3, 163.8, 156.9, 156.2, 155.2, 134.2, 133.9, 131.4, 130.6, 130.3, 129.9, 128.8, 128.6, 128.3, 127.6, 121.5, 119.7, 111.3. HRMS $(M + H)^+$: calcd for $C_{29}H_{18}O_6$, 463.1182; found, 463.1183.

**2-Phenyl-3,7,8-tribenzoyloxy-4-oxo-*4H*-1-benzopyran (3,7,8-Tribenzoyloxyflavone) (12c).** Colorless solid (451 mg, 77%). $^1$H NMR: $\delta_H$ complex spectrum. $^{13}$C NMR: $\delta_C$ 171.9, 163.8, 156.8, 147.8, 134.0, 130.6, 130.5, 130.0, 129.6, 128.8, 128.3, 123.8, 120.6. HRMS $(M + H)^+$: calcd for $C_{36}H_{22}O_8$, 583.1393; found, 583.1384.

**2-(4-Methoxyphenyl)-3-benzoyloxy-4-oxo-*4H*-1-benzopyran (3-Benzoyloxy-4′-methoxyflavone) (12d).** Colorless solid (357 mg, 75%). $^1$H NMR: $\delta_H$ 8.30−8.20 (3H, m), 7.93 (2H, d, $J$ = 9 Hz), 7.75−7.40 (6H, m), 6.97 (2H, d, $J$ = 9 Hz), 3.83 (3H, s). $^{13}$C NMR: $\delta_C$ 172.1, 163.9, 162.0, 156.3, 155.7, 133.8, 133.4, 130.6, 130.2, 128.9, 128.7, 126.2, 125.1, 123.8, 122.4, 118.1, 114.3, 55.5. HRMS $(M + H)^+$: calcd for $C_{23}H_{16}O_5$, 373.1076; found, 373.1078.

**2-(3′,4′,5′-Trimethoxyphenyl)-3-benzoyloxy-5-hydroxy-4-oxo-*4H*-1-benzopyran (3-Benzoyloxy-5-hydroxy-3′,4′,5′-trimethoxyflavone) (12e).** Yellow solid (240 mg, 59%). $^1$H NMR: $\delta_H$ 12.06 (1H, s, 5-OH), 8.25−8.19 (2H, m), 7.69−7.46 (4H, m), 7.16 (2H, s), 7.01 (1H, dd, $J$ = 8.4, 0.7 Hz), 6.82 (1H, dd, $J$ = 8.4, 0.7 Hz), 3.88 (3H, s), 3.75 (6H, s). $^{13}$C NMR: $\delta_C$ 176.9, 163.7, 160.8, 157.0, 155.7, 153.3, 141.2, 135.8, 134.4, 131.8, 130.5, 128.9, 128.2, 124.4, 111.4, 110.8, 107.3, 106.0, 61.0, 56.2. HRMS $(M + H)^+$: calcd for $C_{25}H_{20}O_8$, 449.1236; found, 449.1231.

**General Procedure for Flavonols: 2-Phenyl-3-hydroxy-4-oxo-*4H*-1-benzopyran (Flavonol) (13).** Compound **12a** (150 mg, 0.438 mmol) was hydrolyzed with 5% aqueous sodium hydroxide solution (2.5 mL) in ethanol (20 mL) at 60 °C for 2 h. The reaction mixture was poured into a mixture of crushed ice (60 g) and concentrated HCl (1 mL). It was then extracted with ethyl acetate and washed with aqueous sodium hydrogen carbonate and water. The solvent was removed under reduced pressure, and the residue was recrystallized from aqueous ethanol to give the flavonol **13** (83 mg, 80%) as colorless needles. $^1$H NMR ($CDCl_3$): $\delta_H$ 8.27−8.20 (3H, m), 7.73−7.34 (6H, m), 6.97

(1H, s). $^{13}$C NMR: $\delta_C$ 173.5, 155.5, 145.0, 138.6, 133.7, 131.2, 130.3, 128.7, 127.8, 125.5, 124.6, 120.7, 118.3. HRMS $(M + H)^+$: calcd for $C_{15}H_{10}O_3$, 239.0708; found, 239.0717.

**2-Phenyl-3,7-dihydroxy-4-oxo-*4H*-1-benzopyran (7-Hydroxyflavonol) (14).** Colorless needles (72 mg, 87%). $^1$H NMR (DMSO-$d_6$): $\delta_H$ 10.81 (1H, s), 9.35 (1H, s), 8.17 (2H, dd, $J$ = 8.4, 1.6 Hz), 7.96 (1H, d, $J$ = 8.5 Hz), 7.59−7.42 (3H, m), 6.96−6.90 (2H, m). $^{13}$C NMR: $\delta_C$ 172.3, 162.5, 156.5, 144.0, 138.4, 131.4, 129.4, 128.4, 127.3, 126.5, 114.8, 114.2, 101.9. HRMS $(M + H)^+$: calcd for $C_{15}H_{10}O_4$, 255.0657; found, 255.0655.

**2-Phenyl-3,7,8-trihydroxy-4-oxo-*4H*-1-benzopyran (7,8-Dihydroxyflavonol) (15).** Yellow needles (105 mg, 91%). $^1$H NMR ($CD_3OD$): $\delta_H$ 8.30 (2H, dd, $J$ = 8.3, 1.4 Hz), 7.59−7.24 (4H, m), 6.93 (1H, d, $J$ = 8.9 Hz). $^{13}$C NMR (DMSO-$d_6$): $\delta_C$ 172.7, 150.0, 145.8, 143.9, 138.0, 132.6, 131.5, 129.5, 128.4, 127.5, 115.2, 115.0, 114.1. HRMS $(M + H)^+$: calcd for $C_{15}H_{10}O_5$, 271.0606; found, 271.0604.

**2-(4′-Methoxyphenyl)-3-hydroxy-4-oxo-*4H*-1-benzopyran (4′-Methoxyflavonol) (16).** Yellow solid (145 mg, 88%). $^1$H NMR (DMSO-$d_6$): $\delta_H$ 9.48 (1H, s), 8.21 (2H, d, $J$ = 9.0 Hz), 8.10 (1H, m), 7.85−7.73 (2H, m), 7.46 (1H, m), 7.13 (2H, d, $J$ = 9.0 Hz), 3.85 (3H, s). $^{13}$C NMR: $\delta_C$ 172.5, 160.2, 137.9, 133.4, 129.4, 124.7, 124.4, 123.2, 121.0, 118.3, 114.0, 55.3. HRMS $(M + H)^+$: calcd for $C_{16}H_{12}O_4$, 269.0814; found, 269.0794.

**2-(3′,4′,5′-Trimethoxyphenyl)-3,5-dihydroxy-4-oxo-*4H*-1-benzopyran (5-Hydroxy-3′,4′,5′-trimethoxyflavonol) (17).** Yellow needles (97 mg, 75%). $^1$H NMR (DMSO-$d_6$): $\delta_H$ 12.23 (1H, s), 9.84 (1H, s), 7.64−7.49 (3H, m), 7.14 (1H, m), 6.72 (1H, m), 3.85 (6H, s), 3.76 (3H, s). $^{13}$C NMR: $\delta_C$ 177.1, 159.1, 154.5, 152.6, 146.6, 139.5, 137.4, 135.1, 125.9, 109.2, 107.5, 105.7, 60.1, 56.0. HRMS $(M + H)^+$: calcd for $C_{18}H_{16}O_7$, 345.0974; found, 345.0974.

**Supporting Information Available:** $^1$H NMR and/or $^{13}$C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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