BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 51 (6), 1784—1787 (1978) [Vol. 51, No. 6

The Synthesis of New Flavones with a 4*H*,10*H*-Benzo[1,2-*b*: 3,4-*b*′]dipyran-4,10-dione Skeleton and the Light Resistannce of These Compounds

Makoto KANETA, Hiroshi HIKICHI, Seiichi ENDO, and Noboru SUGIYAMA*
Fukushima Technical College, Iwaki-shi, Fukushima 970
**Department of Chemistry, Tokyo Kyoiku University, Otsuka, Bunkyo-ku, Tokyo 112*

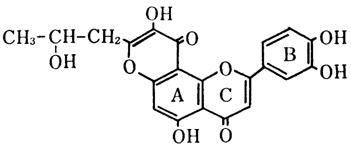
(Received August 16, 1977)

Six analogous new flavones with a skeleton similar to arthraxin, which is a light-stable, natural, new flavone, have been synthesized by the use of a modification of Allan-Robinson's flavone synthesis. The structures of these compounds were elucidated by means of the Gibbs reaction, NMR, and mass spectrometry. The light resistance of these flavones was then examined by means of UV spectrometry. The results indicate that these flavones, with a 4*H*,10*H*-benzo[1,2-*b*: 3,4-*b*′] dipyran-4,10-dione skeleton, in contrast with natural common flavonol and arthraxin, show a high resistance to light.

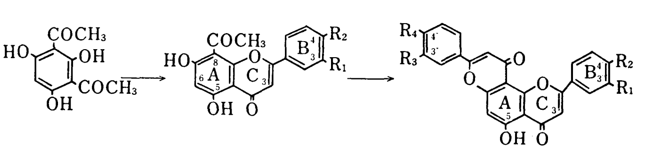
In a previous paper,[1] we reported the isolation and structure of a new flavone arthraxin (**1**) from the grass *Arthraxon hispidus*, which had been used as a source of natural dyestuff for the light-stable, yellow coloring "Kihachijo," produced on Hachijo Island, Japan. In our succesive studies,[2,3] arthraxin, in contrast with flavonol, was found to show a high resistance to light. This result suggests that the flavones which have a skeleton similar to arthraxin's 4*H*,10*H*-benzo[1,2-*b*: 3,4-*b*′]dipyran-4,10-dione skeleton will be stable to light. To make clear this problem, we have synthesized a series of new flavones with skeletons similar to arthraxin and have examined the light resistance of these compounds by UV spectrometry.

*Synthesis of Six Analogous New Flavones with a 4*H*,10*H*-Benzo[1,2-*b*: 3,4-*b*′]dipyran-4,10-dione Skeleton.* These compounds, **6**, **7**, **8**, **9**, **10**, and **11**, have been synthesized according to the annexed scheme.

2,4-Diacetylphloroglucinol (**2**) was prepared by saturating a glacial acetic acid solution of phloroglucinol with boron trifluoride gas.[4] The condensation of **2** with potassium benzoate and benzoic anhydride yielded 8-acetyl-5,7-dihydroxyflavone (**3**). By using potassium *p*-anisate and *p*-anisic anhydride or potassium veratrate and veratric anhydride instead, 8-acetyl-5,7-dihydroxy-4′-methoxyflavone (**4**) or 8-acetyl-5,7-dihydroxy-3′,4′-dimethoxyflavone (**5**) was obtained respectively. The alternative structures, 6-acetyl-5,7-dihydroxyflavone (**3b**), 6-acetyl-5,7-dihydroxy-4′-methoxyflavone (**4b**), and 6-acetyl-5,7-dihydroxy-3′,4′-dimethoxyflavone (**5b**), were rejected after a study of the NMR spectra of Compounds **3**, **4**, and **5** indicated the presence of the C-6 proton and because the negative Gibbs reaction[5] indicated the presence of C substitution in the C-8 position. The signals at 6.40, 6.41, and 6.43 ppm of **3**, **4**, and **5** can be assigned to the C-6 proton in the A-ring, because the C-6 and C-8 protons of the 5,7-disubstituted flavones appear in the regions of 6.25—6.5 ppm for the C-6 proton and 6.5—6.9 ppm for the C-8 proton.[6,7] The Gibbs reaction with *N*-chloro-2,6-dichloro-*p*-benzoquinone 4-imine has been used for the



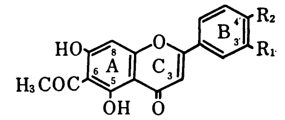
1 Arthraxine



2

3 $R_1=R_2=H$
4 $R_1=H$, $R_2=OCH_3$
5 $R_1=R_2=OCH_3$

6 $R_1=R_2=R_3=R_4=H$
7 $R_1=R_2=R_3=H$, $R_4=OCH_3$
8 $R_1=R_2=H$, $R_3=R_4=OCH_3$
9 $R_1=R_3=H$, $R_2=R_4=OCH_3$
10 $R_1=H$, $R_2=R_3=R_4=OCH_3$
11 $R_1=R_2=R_3=R_4=OCH_3$



3b $R_1=R_2=H$
4b $R_1=H$, $R_2=OCH_3$
5b $R_1=R_2=OCH_3$

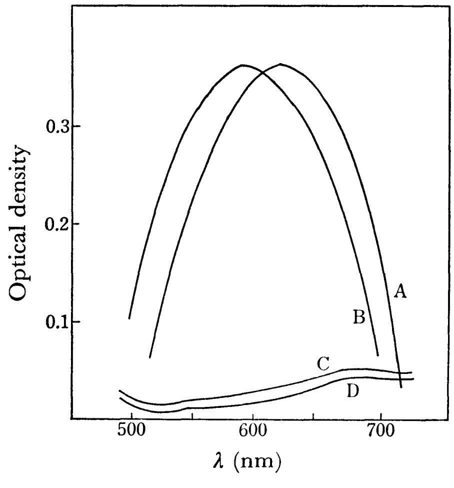


Fig. 1. UV spectra of the compounds treated with the Gibbs reagent.
A: Phenol, B: *o*-cresol, C: Compd **3**, D: Compd **4**.

detection of unsubstituted CH para to a phenolic hydroxyl group at the C-5 position. On treatment with the Gibbs reagent, a phenolic compound which is unsubstituted in the para position to the phenolic hydroxyl group gives the blue-green color of the indophenol derivative, with an absorption peak at 500—900 nm.[5] Compounds **3**, **4**, and **5** showed negative Gibbs reactions. This constitutes further evidence that **3**, **4**, and **5** do not have the C-8 proton which is in the para position to the C-5 hydroxyl group.

Heating **3** with potassium *p*-anisate and *p*-anisic anhydride yielded a new flavone, 2-phenyl,8-(4-methoxyphenyl)-4*H*, 10*H*-benzo[1,2-*b*: 3,4-*b*′] dipyran-4, 10-dione (**7**). By using potassium benzoate and benzoic anhydride or potassium veratrate and veratric anhydride instead, 2,8-diphenyl-4*H*, 10*H*-benzo[1,2-*b* : 3,4-*b*′] dipyran-4,10-dione (**6**) or 2-phenyl,8-(3,4-dimethoxyphenyl)-4*H*,10*H*-benzo[1,2-*b*: 3,4-*b*′] dipyran-4,10-dione (**8**) was obtained. When **4** was used for the condensation with potassium veratrate and veratric anhydride, 2-(4-methoxyphenyl)-8-(3,4-dimethoxyphenyl)-4*H*, 10*H*-benzo[1,2-*b*: 3,4-*b*′]dipyran-4,10-dione (**10**) was obtained.

According to the usual Allan-Robinson's flavone synthesis, Compound **6** is synthesized by heating a mixture of **3** which has been synthesized from **2**, potassium benzoate, and benzoic anhydride in a ratio of about 1 : 2 : 4 mol for several hours. However, we could synthesize **6** directly from **2** by heating a mixture of **2**, potassium benzoate, and benzoic anhydride in a ratio of about 1: 4: 8 mol for 10—12 h. In this way, Compounds (**9**) and (**11**) were also synthesized. The NMR and mass spectral data as well as the negative Gibbs reaction support the **6**, **7**, **8**, **9**, **10**, and **11** structures.

*Light Resistance of New Synthesized Flavones with a 4*H*,10*H*-Benzo[1,2-*b*: 3,4-*b*′]dipyran-4,10-dione Skeleton.* The light resistance of the following flavones, has been examined by means of the UV spectra; quercetin, morin, arthraxin (**1**), **7**, **9**, and **11**. The methanol solution of a sample prepared at a constant concentration was irradiated with a 200 W high-pressure mercury lamp

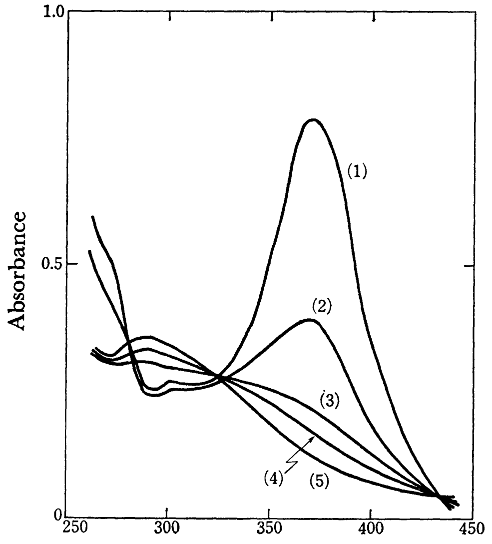


Fig. 2. Time change during irradiation of the spectrum of quercetin in methanol.
(1) : 0 h irradiation, (2) : 3 h, (3) : 5 h, (4) : 8 h, (5) : 15 h.

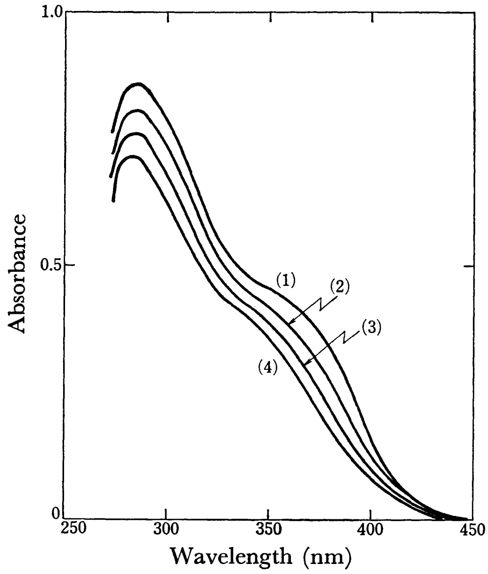


Fig. 3. Time change during irradiation of the spectrum of Compound **9** in methanol.
(1): 0 h irradiation, (2): 3 h, (3): 5 h, (4): 8 h, (5): 15 h.

Table 1. Decrease ratio of the concentration calculated from the intensity of Band 1

	Flavonol		Flavone with a 4*H*,10*H*-benzo[1,2-*b*: 3,4-*b*′]-dipyran-4,10-dione skeleton			
			Natural	Synthesized		
	Quercetin[a] (370 nm)	Morin (370)	Arthraxin (340)	Compound **7** (358)	Compound **9** (355)	Compound **11** (356)
0 h						
3	50.2	69.2	8.8	8.4	8.0	2.8
5	71.7	80.8	13.3	13.2	11.9	3.7
8	78.8	86.5	18.0	15.7	15.9	4.5
15	83.5	92.0	23.5	18.1	21.1	6.4
22	84.5	94.2	27.6	20.5	24.1	8.8
50			36.4	24.7	27.9	16.1

a) λ_{max} of Band 1 of the samples are shown in the respective parentheses.

through a quartz glass tube, with a water-cooled jacket, under bubbling air. The UV spectrum of an aliquot portion was then recorded at intervals of 3, 5, 8, 15, 22, and 50 h. The resistance to light was measured in terms of the decrease ratio of the concentration calculated from the intensity of Band 1, defined as the peak absorption intensity in the 350—450 nm region.

The results tabulated in Table 1 indicate that the synthesized flavones with a 4*H*,10*H*-benzo[1,2-*b*: 3,4-*b*′]dipyran-4,10-dione skeleton, in contrast with flavonol and arthraxin, show a high resistance to light when air is bubbled into the methanol solution.

Experimental

The melting points are uncorrected. The NMR spectra were taken at 60 MHz with a Hitachi high-resolution nuclear magnetic resonance spectrometer, R-24 A. All the samples were run as 5—10% solutions in deuteriochloroform. The mass spectra were determined by a direct sample introduction using a Hitachi mass spectrometer, model RMU-6MG, under the following conditions: ionizing voltage; 70 eV, Samples **3**, **4**, and **5**; 20 eV, Samples **6**, **7**, **8**, **9**, **10**, and **11**; accelerating voltage; 3 kV, Samples **3**, **4**, and **5**; 3.2 kV, Samples **6**, **7**, **8**, **9**, **10**, and **11**; ion-source temperature; 170 °C, Samples **6**, **8**, and **10**, 200 °C, Samples **3**, **4**, and **5**; 220 °C, Samples **7**, **9**, and **11**.

2,4-Diacetylphloroglucinol (2). A solution of phloroglucinol (25 g) in warm glacial acetic acid (150 ml) was saturated with boron trifluoride gas and was then set aside for 1 h. The reaction mixture was poured into water (1300 ml), and the orange solid which separated was collected and recrystallized from aqueous ethanol to give nearly colorless needles (17 g); mp 164 °C (lit,[4]) mp 168 °C).

8-Acetyl-5,7-dihydroxyflavone (3). A mixture of **2** (20 g), benzoic anhydride (88 g), and potassium benzoate (32 g) was heated at 170—175 °C for 6 h. The product was boiled for a short time with a mixture of ethanol (750 ml), water (90 ml), and potassium hydroxide (60 g). After the subsequent evaporation of the solvent under reduced pressure, the residue was redissolved in water (1000 ml). The solution was saturated with carbon dioxide, and the brown precipitate which separated was collected, washed, and dried (14 g). The product was purified on a silica gel column by eluting it successively with benzene, benzene–ethyl acetate (1: 1), and ethyl acetate. The fraction which was eluted with benzene–ethyl acetate was evaporated to dryness, and the residue was recrystallized from ethanol to give **3** (4.15 g) as yellow needles; mp 210 °C; NMR ($CDCl_3$), 2.81 (s, 3H, $COCH_3$), 6.40 (s, 1H, H-6), 6.66 (s, 1H, H-3), 7.4—8.0 (m, 5H, H-2′, 3′, 4′ 5′, 6′); M(mass spectrum), 296. $C_{17}H_{12}O_5$ requires M, 296.

The Gibbs Reaction. A small quantity (about 1 mg) of Samples **3**, **4**, **5**, **6**, **7**, **8**, **9**, **10**, and **11** was placed in a measuring cylinder and dissolved in pyridine (1 ml). To the solution we then added 5 ml of a freshly prepared Gibbs reagent solution (*N*-chloro-2,6-dichloro-*p*-benzoquinone diimine (10 mg) in pyridine (5 ml)), after which the mixture was diluted to 20 ml with a sodium borate buffer (pH 9.2). The absorption spectrum was determined between 10 and 20 min. All the samples, **3**—**11**, showed negative Gibbs reactions.

8-Acetyl-5,7-dihydroxy-4′-methoxyflavone (4). Compound **4** (15 g) was synthesized from **2** (18.7 g), *p*-anisic anhydride (90 g), and potassium *p*-anisate (35 g) by a way similar to that used in synthesizing **3**. Compound **4** was obtained as yellow needles; mp 181 °C; NMR ($CDCl_3$), 2.75 (s, 3H, $COCH_3$), 3.82 (s, 3H, OCH_3), 6.41 (s, 1H, H-6), 6.73 (s, 1H, H-3), 6.93, 7.09 (d, 2H, 3′, 5′-H), 7.79, 7.94 (d, 2H, 2′, 6′-H); M(mass spectrum), 326. $C_{18}H_{14}O_6$ requires M, 326.

8-Acetyl-5,7-dihydroxy-3′,4′-dimethoxyflavone (5). Compound **5** (7.5 g) was synthesized from **2** (8 g), veratric anhydride (35 g), and potassium veratrate (13 g) by a way imilar to that used in synthesizing **3**. Compound **5** was obtained as yellow needles; mp 251 °C; NMR ($CDCl_3$), 2.75 (s, 3H, $COCH_3$). 3.70 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.43 (s, 1H, H-6), 6.66 (s, 1H, H-3), 6.73—6.88 (m, 1H, H-5′), 7.40—7.58 (m, 2H, H-2′, 6′); M (mass spectrum), 356. $C_{19}H_{16}O_7$ requires M, 356.

*2-Phenyl-8-(4-methoxylhenyl)-4*H, *10*H-*benzo[1,2-*b: *3,4-*b′*]-dipyran-4,10-dione (7).* A mixture of **3** (1 g), *p*-anisic anhydride (17 g), and potassium *p*-anisate (3 g) was heated at 170 °C for 8 h. The product was boiled for 30 min with a mixture of ethanol (125 ml), water (30 ml), and potassium hydroxide (10 g). After the evaporation of the solvent, the residue was redissolved in water. The solution was saturated with carbon dioxide, and the precipitate which was thus separated was collected, washed, and dried (450 mg). The product was purified on a silica gel column by eluting it successively with benzene, benzene–ehytl acetate (15: 1), benzene–ethyl acetate (1: 1), and benzene–ethyl acetate (1: 5). The fraction which was eluted with benzene–ethy acetate (15: 1) was evaporated to dryness, and, the residue was recrystallzed from ethanol to give **7** (*ca.* 40 mg) as yellow needles; mp 139 °C; NMR ($CDCl_3$), 3.87 (s, 3H, OCH_3), 6.45 (s, 1H, H-6), 6.72 (s, 1H, H-3), 7.3—7.8 (m, 10H); M (mass spcetrum), 412. $C_{25}H_{16}O_6$ requires M, 412.

*2-Phenyl-8-(3,4-dimethoxyphenyl)-4*H,*10*H-*benzo[1,2-*b*:3,4-*b′*]-dipyran-4,10-dione (8).* Compound **8** (850 mg) was synthesized from **3** (1 g), veratric anhydride (20 g), and potassium veratrate (4 g) by a way similar to that used in synthesizing **7**. Compound **8** was obtained as yellow needles, mp 151 °C; NMR ($CDCl_3$), 3.85 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.45 (s, 1H, H-6), 6.73 (s, 1H, H-3), 6.9—7.9 (m, 9H); M (mass spectrum), 442. $C_{26}H_{18}O_7$ requires M, 442.

*2-(4-Methoxyphenyl)-8-(3,4-dimethoxyphenyl)-4*H,*10*H-*benzo[1,2-*b*: 3,4-*b′*]dipyran-4,10-doine (10).* Compound **10** (700 mg) was syntheized from **4** (1.3 g), veratric anhydride (23.5 g), and potassium veratrate (4.1 g) by a way similar to that used in synthesizing **7**. Compound **10** was obtained as yellow needles; mp 168 °C; NMR ($CDCl_3$), 3.82 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.42 (s, 1H, H-6), 6.70 (s, 1H, H-3), 6.9—8.0 (m, 8H); M (mass spectrum), 472. $C_{27}H_{20}O_8$ requires M, 472.

*2,8-Diphenyl-4*H, *10*H-*benzo[1,2-b: 3,4-b′] dipyran-4,10-dione (6).* A mixture of **2** (3 g), benzoic anhydride (25 g), and potassium benzoate (9 g) in a ratio of about 1: 4: 8 mol was heated at 170 °C for 11 h. The product was boiled for 30 min with a mixture of ethanol (200 ml), water (70 ml), and potassium hydroxide (43 g). After the evaporation of the solvent under reduced pressure, the residue was redissolved in water. The solution was saturated with carbon dioxide, and the precipitate which was thus separated was collected, washed, and dried (2.9 g). The product was purified on a silica gel column by eluting it successively with benzene–ethyl acetate (1: 1), ethyl acetate, ethyl acetate–acetone (1: 1), acetone, acetone–methanol (1: 1), and methanol. The fraction which was eluted with acetone was evaporated to dryness, and the residue was recrystallized from ethanol to give (**6**) as pale yellow needles; mp 272 °C; NMR ($CDCl_3$), 6.76 (s, 1H), 6.94 (s, 1H), 7.30—7.62 (m, 7H), 7.81—8.05 (m, 4H); M (mass spectrum), 382. $C_{24}H_{14}O_5$ requires M, 382.

*2-(4-Methoxyphenyl)-8-(4-methoxyohenyl)-4*H,*10*H-*benzo[1,2-*b*:

*3,4-*b′]*dipyran-4,10-dione* (**9**). Compound **9** (1.2 g) was synthesized from **2** (1 g), *p*-anisic anhydride (11 g), and potassium *p*-anisate (3.7 g) by a way similar to that used in synthesizing **6**. Compound **9** was thus obtained as yellow needles; mp 286 °C; NMR ($CDCl_3$), 3.71 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.40 (s, 1H), 6.80 (s, 1H), 6.9—8.1 (m, 9H); M (mass spectrum), 442. $C_{26}H_{18}O_7$ requires M, 442.

*2-(3,4-Dimethoxyphenyl)-8-(3,4-dimethoxyphenyl)-4*H, *10*H*-benzo[1,2-*b: *3,4-*b′]*dipyran-4,10-dione (11).* Compound **11** (600 mg) was synthesized from **2** (1 g), veratric anhydride (13.5 g), and potassium veratrate (4.3 g) in a way similar to that used in synthesizing **6**. Compound **11** was thus obtained as yellow needles; mp 225 °C; NMR ($CDCl_3$), 3.65, 3.73, 3.88, 3.95 (all s, 3H, OCH_3), 6.43 (s, 1H), 6.70 (s, 1H), 6.9—8.1 (m, 7H); M (mass spectrum), 502. $C_{28}H_{22}O_9$ requires M, 502.

References

1) M. Kaneta and N. Sugiyama, *J. Chem. Soc., C,* **1971**, 1982.

2) M. Kaneta and N. Sugiyama, *Bull. Chem. Soc. Jpn.*, **44**, 3211 (1971).

3) M. Kaneta and N. Sugiyama, *Bull. Chem. Soc. Jpn.*, **46**, 2265 (1973).

4) T. W. Campbell and G. M. Coppinger, *J. Am. Chem. Soc.*, **73**, 2708 (1951).

5) F. E. King and L. C. Manning, *J. Chem. Soc.*, **1957**, 563.

6) J. Massicot and J. P. Marthe, *Bull. Soc. Chim. Fr.*, **1962**, 1962.

7) J. Massicot, J. P. Marthe, and S. Heitz, *Bull. Soc. Chim. Fr.*, **1963**, 2712.