[Chem. Pharm. Bull. 14(2) 121~128 (1966)]

UDC 547.816.04

20. Akira Ueno: Studies on Benzochromones. VIII.*1 Ring Isomerization of γ-Pyrone Ring condensed with Naphthoquinone.

(*Shizuoka College of Pharmacy*2)*)

In the preceding paper,[1] formation of 2-methyl-5,8-dihydroxy-6,7-benzochromone (I) from 2-methyl-8-hydroxy-6,7-benzochromone and that of 2-methyl-5,6-dihydroxy-7,8-benzochromone (II) from 2-methyl-6-hydroxy-7,8-benzochromone were described. These facts demonstrated that I had a linear structure (anthracene type) and II, an angular structure (phenanthrene type). In this connection, formation of I from 2-methyl-5-hydroxy-6,7-benzochromone (III) and that of II from 2-methyl-5-hydroxy-7,8-benzochromone (IV) were investigated, and it was found that Elbs oxidation of III and IV produced 2-methyl-4*H*-naphtho[2,3-*b*]pyran-4,5,10(5*H*,10*H*)-trione (V) in both cases. The present paper deals with the mechanism of abnormal reaction in the formation of V through the step of Elbs oxidation of III and IV, and the synthesis of I from II and of 2-methyl-3-acetyl-5,8-dihydroxy-6,7-benzochromone (VI) from 2-methyl-3-acetyl-5,6-dihydroxy-7,8-benzochromone (VII) in the application of novel reaction established herein.

First, Elbs oxidation of IV was carried out through the procedure described in the Experimental section, and I was unexpectedly formed. This fact could not be explained from the structure of IV elucidated in the preceding paper,[2] and suggested that either this structure of IV was wrong or that a ring isomerization had occurred during this oxidation. It is difficult to deny this structure of IV and, if such a ring isomerization could occur during the reaction step, it would be reverse of the Wessely-Moser type ring isomerization, such as the formation of II from I.

As is well known, Elbs oxidation involves a few steps such as formation of potassium aryl sulfate and its hydrolysis. In an attempt to examine where such ring isomerization is involved in the reaction step, synthesis of potassium 2-methyl-5-hydroxy-6,7-benzochromon-8-yl sulfate (VIII) and potassium 2-methyl-5-hydroxy-7,8-benzochromon-6-yl sulfate (IX) was tried.

Treatment of I with equimolar chlorosulfonic acid in the presence of chloroform and pyridine, and that of the resulting pyridine aryl sulfate with potassium acetate in ethanol, gave VIII as yellow needles. IX was also obtained from II by the same procedure. This method used in the preparation of VIII and IX seems to be useful for the synthesis of potassium salt of partially sulfated polyphenolic compounds.

The established structure of VIII and IX was based on the following facts: (1) The analytical values of VIII and IX corresponded to $C_{14}H_9O_7KS$; (2) their aqueous solution showed a stable green color with ferric chloride; (3) hydrolysis of VIII and IX gave I and II, respectively. However, both VIII and IX were insoluble in alkaline water and did not undergo ring isomerization.

On the other hand, a mild demethylation of 2-methyl-5-methoxy-6,7-benzochromone with "magnesium iodide etherate"[3] gave III, which was assumed to have

*1 This paper constitutes Part VIII of a series entitled "Studies on Benzochromones" by S. Fukushima. Part VII: This Bulletin, **12**, 316 (1964).

*2 Oshika, Shizuoka (上野 明).

1) S. Fukushima, A. Ueno, Y. Akahori: This Bulletin, **12**, 307 (1964).
2) S. Fukushima, A. Ueno, Y. Akahori: This Bulletin, **12**, 312 (1964).
3) V. Arkley, *et al.*: J. Chem. Soc., **1962**, 1260; B. W. Bycoft, J. Roberts: *Ibid.*, **1963**, 4868.

Table I. Ultraviolet Spectra of 2-Methyl-6,7-benzochromone Derivatives

Compounds	$\lambda_{max}^{99\% EtOH}$ (log ε)			
Ⅲ	219 (4.19)	257 (4.59)	265 (4.60)	294 (3.42)
	307 (3.45)	319[a] (2.94)	390 (3.57)	
XIV	214 (4.29)	253 (4.65)	282[a] (3.99)	307 (3.59)
	320 (3.47)	365 (3.66)	379 (3.61)	
XV	213 (4.33)	260 (4.65)	311 (3.53)	325 (3.45)
	376 (3.68)			
Ⅵ	256[a] (4.31)	276 (4.42)	353 (3.64)	425 (3.50)

a) Inflexion point

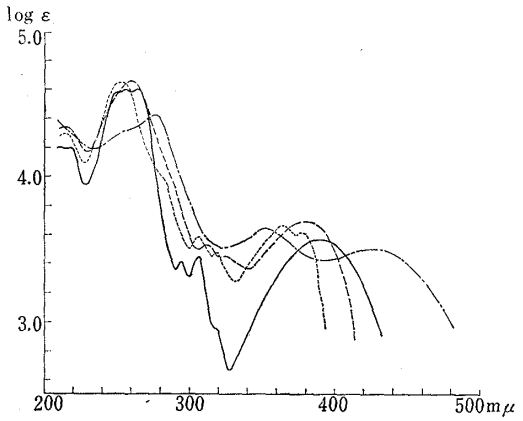
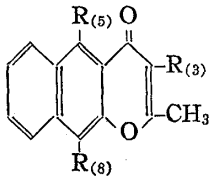


Fig. 1. Ultraviolet Spectra of 2-Methyl-6,7-benzochromone Derivatives



Compound		$R_{(3)}$	$R_{(5)}$	$R_{(8)}$
Ⅲ :	———	H	OH	H
XIV :	·····	$COCH_3$	O-$COCH_3$	O-$COCH_3$
XV :	– – – –	$COCH_3$	OCH_3	OCH_3
Ⅵ :	– – – – –	$COCH_3$	OH	OH

a linear structure from their ultraviolet spectra[4] as shown in Fig. 1 and Table I. The Elbs oxidation of Ⅲ gave a product by extraction of the reaction mixture with chloroform which was confirmed to be Ⅴ, and I was smoothly obtained from the reaction mixture by the addition of sodium acetate and sodium hydrosulfite. These results suggested that the product expected to be obtained by the Elbs oxidation of Ⅳ might be Ⅴ, and I might have been formed by the reduction of Ⅴ with sodium hydrosulfite used for decolorization of the product during recrystallization. Indeed, this assumption was demonstrated by the following Elbs oxidation of Ⅳ, in which the experimental result was identical with that of the Elbs oxidation of Ⅲ. These facts indicated that the Elbs oxidation of Ⅲ and Ⅳ involves an abnormal reaction step, and does not give the expected I or Ⅱ. The reaction product (Ⅴ) was anticipated from the oxidation of I, but could not be assumed to be obtained by the oxidation of Ⅱ, and 2-methyl-4*H*-naphtho-[1,2-*b*]pyran-4,5,6(5*H*,6*H*)-trione (X) was produced from Ⅱ by Yamaguchi, Fukushima, and Yamada,[5] The compound expected to be obtained from the Elbs oxidation of Ⅳ might be Ⅱ, but the product actually obtained was Ⅴ, and Ⅱ or X, which should be the oxidation product of Ⅱ, was not obtained.

In an attempt to clarify the reason why Ⅱ or X could not be obtained and Ⅴ was obtained by the Elbs oxidation of Ⅳ, action of alkali on Ⅴ and X was investigated, considering that the Elbs oxidation was usually carried out in an alkaline solution.

Ⅴ and X dissolved in a cold aqueous potassium hydroxide, forming a red solution, and acidification of this solution gave yellow needles, m.p. 126°, from both. This substance was unstable and colored deep red with ferric chloride in ethanolic solution, and its analytical values corresponded to $C_{14}H_{10}O_5$. It was easily converted into Ⅴ by heating in the presence of a trace of hydrochloric acid in methanol. These facts indicated that this substance is 2-acetoacetyl-3-hydroxy-1,4-naphthoquinone (Ⅺ).

4) S. Fukushima, Y. Akahori, A. Ueno : This Bulletin, **12**, 316 (1964).
5) K. Yamaguchi, S. Fukushima, H. Yamada : This Bulletin, 8, 1028 (1960).

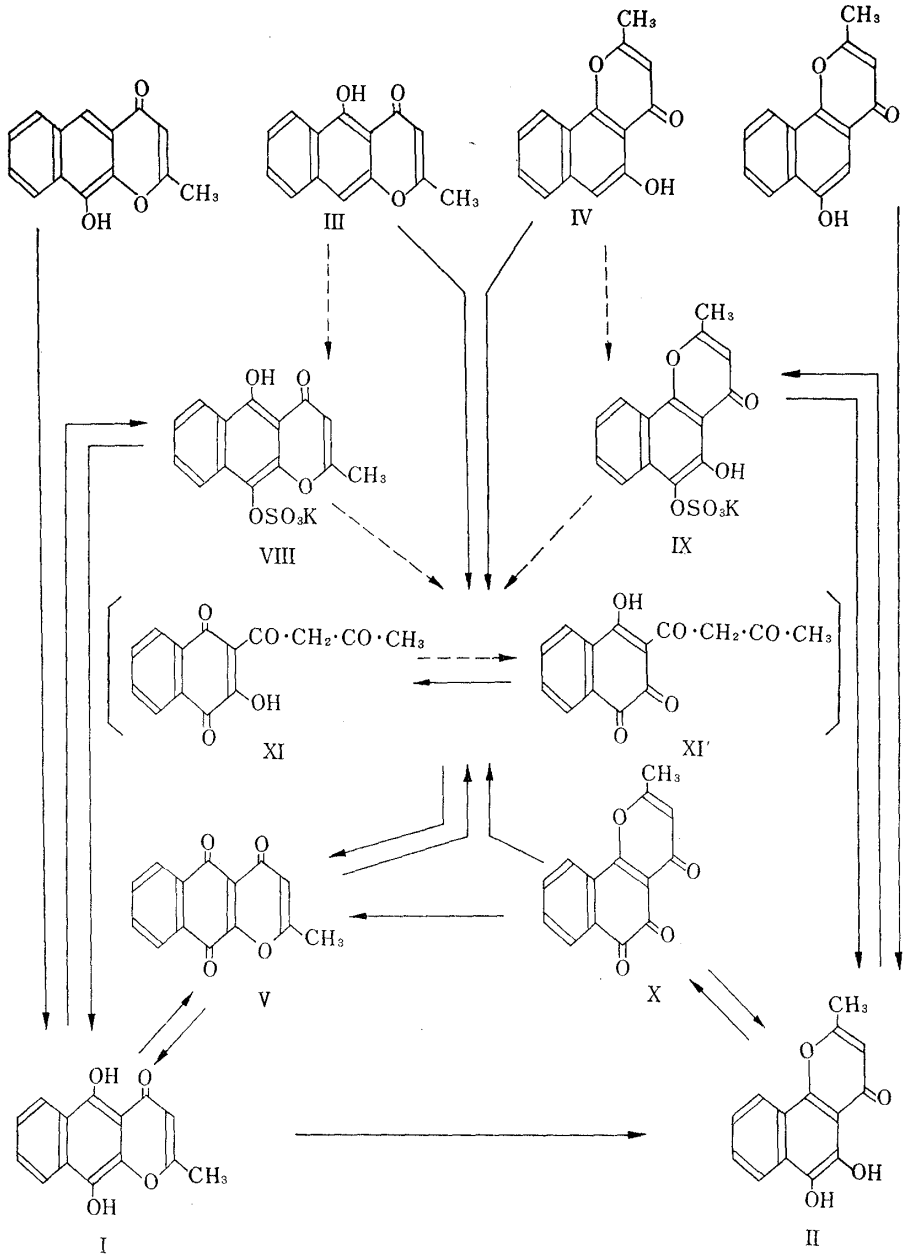


Chart 1.

Consequently, these facts indicate that X is converted into V through XI as an intermediate. XI is tautomeric with 3-acetoacetyl-4-hydroxy-1,2-naphthoquinone (XI'). In an alkaline solution, V and X might exist in the form of a salt of XI, of XI', or in the mixture of salt of XI and XI', as a result of a cleavage of γ-pyrone ring in V and X, and XI could not be isolated by acidification of the alkaline solution to the extent of acidity to congo-red. When XI or XI' exists as a free form, XI is assumed to predominate in the equilibrium mixture, and it is easily converted into V by cyclization in an acidic medium. Such a ring opening and ring closing are similar to that of α-pyrone derivative such as coumarin. This kind of ring isomerization in naphthoquinone derivatives, like X→XI→V, had beed reported in the case of naphthoquinones condensed with dihydropyrane ring (α,β-lapachone)[6] or dihydrofurane (α,β-dun-

6) S.C. Hooker: J. Chem. Soc., **61**, 611 (1892); *Ibid.*, **69**, 1355 (1896); J. Am. Chem. Soc., **58**, 1181 (1936); *Ibid.*, **58**, 1190 (1936).

nione)[7] in which the rearrangement progresses in a different direction under a variety of conditions.

An attempt to obtain X from V or XI was unsuccessful. Further, V was obtained on heating a solution of X in acetic acid with hydrochloric acid for 3 minutes. This fact indicates that the ring isomerization also occurred between X and V, and this behavior is similar to that of Wessely-Moser type, the structure of V being more stable than that of X in this case.

The formation of II from I by the Wessely-Moser type ring isomerization was reported in the previous paper.[1] It was shown that a benzochromone, like I (linear type) having a unit of *p*-dihydroxyl group underwent ring isomerization to form benzochromone, II (angular type) having the unit of *o*-dihydroxyl group. However, the ring isomerization occurred in an opposite direction in the case of quinones such as X (angular type; *o*-quinone) forming V (linear type; *p*-quinone). These facts are very interesting concerning the direction of ring isomerization.

These facts revealed that the ring isomerization from angular to linear type was able to take place in the course of the Elbs oxidation of IV.

It is reasonable that the first product of the Elbs oxidation of IV is presumed to be IX, because the ring opening of chromone derivatives could not be found under the condition of the reaction, and the ring opening of α-pyrone derivatives has been noted in literature.[8] IX was insoluble in the alkaline solution used for oxidation of IV, and IX suspended in such an alkaline solution scarcely underwent degeneration under cooling and stirring. IX dissolved in the solution in the presence of potassium persulfate, and V was obtained from this solution by the same treatment as the Elbs oxidation. This fact suggested that IX, presumed as the intermediate, was oxidized further to quinone in the course of the Elbs oxidation of IV in the presence of potassium persulfate. This behavior is assumed more easily in the case of VIII which forms a *p*-quinone, though the mechanism of this oxidation could not be clarified. Consequently, the product exists in the state of an alkali salt of XI, of XI′, or of the mixture of XI and XI′, and the final reaction product is V in the Elbs oxidation of either IV or III.

The formation of I from II is considered to be significant, because it is more difficult to synthesize a compound that undergoes Wessely-Moser type ring isomerization as I than the compound that does not undergo ring isomerization. For this synthetic purpose, the synthesis of X and I from II was investigated.

X is prepared from II by its oxidation with chromic acid,[5] but it was more effectively obtained in an excellent yield (95%) from II using a small amount of sodium nitrite in acetic acid. This oxidation was of use for the formation of V from I, and the experimental condition and amount of sodium nitrite used in this method suggest that the oxidation is caused by oxygen in air and by the catalytic action of oxides of nitrogen.

I was produced from X through the steps of the ring opening by dilute alkali in the presence of methanol, a cyclization in a different way by acidification, and by the reduction of the resulting V by sodium hydrosulfite under continuous operation, in 57% overall yield from II. This method established for the synthesis of I from II is assumed to be applicable not only to benzochromones, but also to other compounds having a similar structure, *i.e.* furochromones, chromones, flavones, xanthones, etc.

The synthesis of 2-methyl-3-acetyl-5,8-dimethoxy-6,7-benzochromone (XV) has attracted a considerable interest because of its physiological activity for the same

7) R.G. Cooke: Nature, **162**, 178 (1948); R.G. Cooke, J.C. Somer: Austral. J. Sci. Res., **A3**, 481 (1950); C.A., **45**, 7086 (1951).
8) S.M. Sethna: Chem. Revs., **49**, 91 (1951), and literature cited therein.

reason as 2-methyl-5,8-dimethoxy-6,7-benzochromone, and it was investigated by several methods.

Ⅶ and its derivatives have been synthesized from the derivatives of 2-acetyl-1,3,4-naphthalenetriol by several methods by Fukushima.[9] 2-Acetyl-4-acetoxy-1,3-naphthalenediol, 2-acetyl-3,4-diacetoxy-1-naphthol, and 2-acetyl-1,3,4-triacetoxynaphthalene all gave 2-methyl-3-acetoxy-5,6-diacetoxy-7,8-benzochromone (Ⅻ) on heating with acetic anhydride and sodium acetate. In the expectation of obtaining 2-methyl-3-acetyl-5-methoxy-8-acetoxy-6,7-benzochromone, 2-acetyl-1-methoxy-3,4-diacetoxynaphthalene was treated with acetic anhydride and sodium acetate, but the product was found to be Ⅻ. These facts indicate that angular structure is more stable than linear structure in these benzochromones.

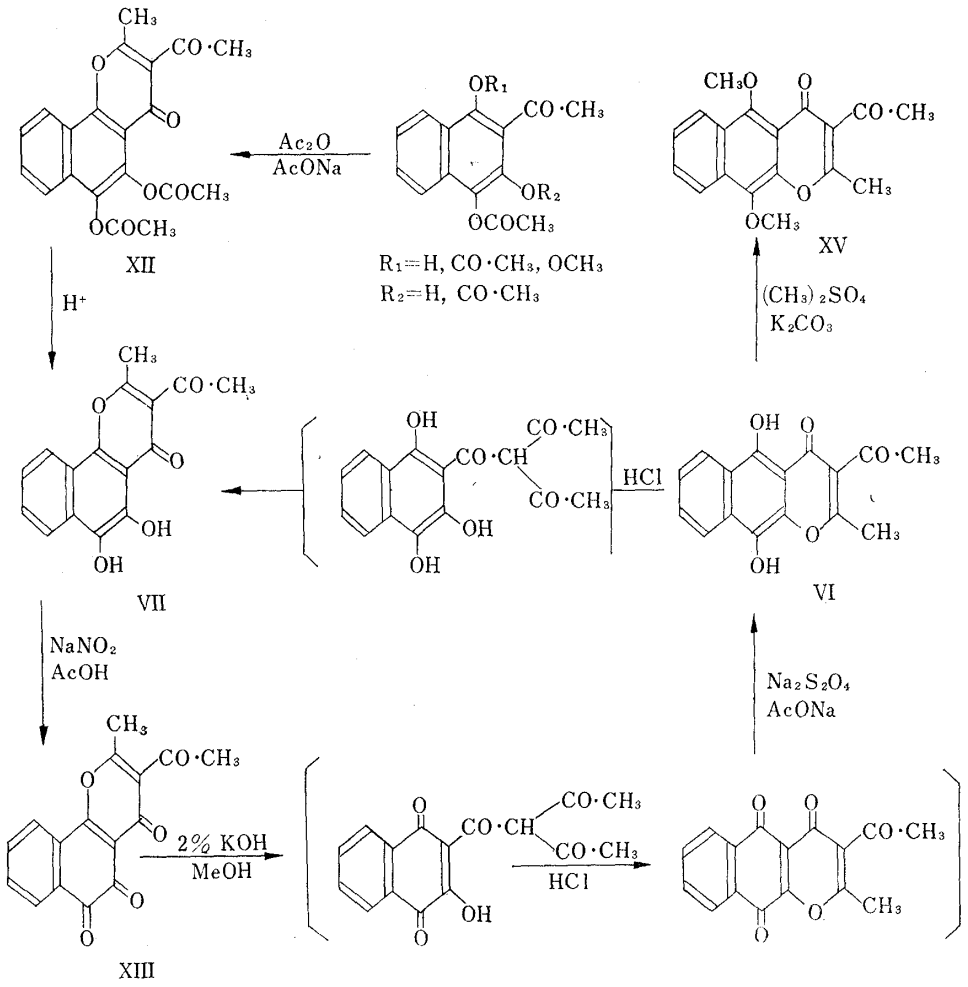


Chart 2.

Ⅶ was conveniently prepared by the hydrosis of Ⅻ, and formation of Ⅵ from Ⅶ was tried by the application of the method for synthesis of I from Ⅱ.

Ⅶ was oxidized to 2-methyl-3-acetyl-4*H*-naphtho[1,2-*b*]pyran-4,5,6(5*H*,6*H*)-trione (XIII) with sodium nitrite in acetic acid. The treatment of XIII by the same method as described for the synthesis of I from Ⅱ gave yellow plates, m.p. 216° (decomp.), expected to be Ⅵ. This product gave a diacetate (XIV) by acetylation, produced 2-methyl-3-acetyl-5,8-dimethoxy-6,7-benzochromone (XV) by methylation with dimethyl

9) S. Fukushima : This Bulletin, 8, 1036 (1960).

sulfate, and reconverted to VII by heating with hydrochloric acid in dioxane solution. The ultraviolet spectra of XIV and XV exhibited the characteristic absorption bands[4] for linear benzochromone, as shown in Table I and Fig. 1. These facts demonstrated that the product is VI and formation of VI from XIII may follow the route shown in Chart 2, by the same behavior as established in the formation of I from X.

In addition, these results indicate that two ring isomerizations occurred in the formation of VII from VI, and in the synthesis of VI from VII, these rearrangements progress without elimination of acetyl groups at 3-position in XIII and VI, and that introduction of acetyl group at 3-position in 2-methyl-6,7-benzochromone shows no change in ultraviolet spectra.

Experimental*3

2-Methyl-5,8-dihydroxy-6,7-benzochromone (I) and 2-Methyl-5,6-dihydroxy-7,8-benzochromone (II)——These compounds were prepared by the methods described in the preceding paper[1,5] and proved to be identical with authentic samples by a mixed fusion and comparison of their IR spectra.

Potassium 2-Methyl-5-hydroxy-6,7-benzochromon-8-yl Sulfate (VIII)——To a solution of I (120 mg.) in pyridine (1 ml.), 0.5 ml. of $ClSO_3H$ solution containing 1 g. of $ClSO_3H$ in 10 ml. of $CHCl_3$ was added dropwise with stirring under chilling to below 0° and the stirring was continued at 0° for 2 hr. The mixture was poured into a cold solution of AcOK (0.5 g.) in EtOH (7 ml.) and left to stand overnight at room temperature. After adding ether (20 ml.) to the mixture, the resulting precipitate was collected, washed with ether, and recrystallized from H_2O to deep yellow needles (70 mg.), m.p. 200° (decomp.). This product was insoluble in organic solvents, sparingly soluble in alkaline H_2O, and soluble in H_2O, and its aqueous solution showed a stable green color with $FeCl_3$. This product was reconverted into I by heating with dil. HCl. *Anal.* Calcd. for $C_{14}H_9O_7KS$: C, 46.66; H, 2.50; K, 10.85. Found : C, 46.52; H, 2.78; K, 10.74. IR ν_{max}^{KBr} cm^{-1} : 1635 (C=O), 745 (v. s.), 720 (v. s.).

Potassium 2-Methyl-5-hydroxy-7,8-benzochromon-6-yl Sulfate (IX)——This compound (100 mg.) was obtained from II (120 mg.) by the same method as described above as yellow needles (from H_2O), m.p. 200° (decomp.). Its aqueous solution colored a stable green with $FeCl_3$. *Anal.* Calcd. for $C_{14}H_9O_7KS$: C, 46.66; H, 2.50; K, 10.85. Found : C, 46.32; H, 2.85; K, 11.06. IR ν_{max}^{KBr} cm^{-1} : 1668 (C=O), 742 (v. s.), 720 (s.).

2-Methyl-5-hydroxy-6,7-benzochromone (III)——A solution of 2-methyl-5-methoxy-6,7-benzochromone[2] (0.7 g), in dry benzene (50 ml.) was mixed with ether-benzene solution of MgI_2, prepared from I_2 (1.5 g.), Mg (0.3 g.) in ether (10 ml.) and benzene (10 ml.), and the mixture was refluxed for 3 hr. The mixture was treated with excess of 0.5*N* HCl and then extracted with ether. The ether extract was washed with H_2O, 1% $NaHSO_3$, and H_2O, and dried over Na_2SO_4. Removal of the solvent and two recrystallizations of the residue from EtOH gave 0.44 g. (67%) of yellow needles, m.p. 141°, whose ethanolic solution showed a green color with $FeCl_3$. *Anal.* Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.46. Found : C, 74.33; H, 4.63. IR ν_{max}^{KBr} cm^{-1} : 1635 (C=O).

Elbs Oxidation of III and 2-Methyl-5-hydroxy-7,8-benzochromone (IV)—— a) To a solution of IV (200 mg.) in H_2O (30 ml.) containing KOH (0.3 g.) and pyridine (6 ml.), a solution of $K_2S_2O_8$ (0.3 g.) in H_2O (6 ml.) was slowly added at 0° with stirring. After standing overnight in a refrigerator, the mixture was acidified to congo-red with dil. HCl, filtered to remove the resulting precipitate, and the filtrate was shaken with ether. The aqueous layer was heated with conc. HCl (1 ml.) on a boiling water bath for 10 min., cooled, and extracted with ether. The ether extract was washed with H_2O, dried over Na_2SO_4, and evaporated to dryness. Recrystallization of the residue from EtOH containing a small amount of $Na_2S_2O_4$ gave red prisms (10 mg.), m.p. 250° (decomp.), which was identified as I.

b) To a solution of III (200 mg.) in pyridine (5 ml.), a solution of KOH (0.3 g.) in H_2O (30 ml.) was added at once, and then a solution of $K_2S_2O_8$ (0.3 g.) in H_2O (6 ml.) was added dropwise at 0° under stirring, and the stirring was continued for 6 hr. at 0°. After standing overnight in a refrigerator, the mixture was filtered, the filtrate was acidified to congo-red, and then filtered. The filtrate was heated with conc. HCl (1 ml.) on a boiling water bath for 10 min., cooled, and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with H_2O, dried over Na_2SO_4, and evaporated to dryness, Recrystallization of the residue from MeOH gave golden yellow needles (20 mg.), m.p. 165° (decomp.), which was identified as V.

In this operation, addition, of AcONa (0.5 g.) and $Na_2S_2O_4$ (0.5 g.) to the forgoing filtrate without extraction with $CHCl_3$, orange red precipitate separated out. This precipitate was recrystallized from EtOH to red prisms (30 mg.), m.p. 250° (decomp.), which was identified as I.

c) IV (200 mg.) was oxidized by the same procedure as in (b). From the reaction mixture, V was obtained by extraction with $CHCl_3$, as golden yellow needles (20 mg.), m.p. 164° (decomp.), and I was also obtained as red prisms, m.p. 250° (decomp.) by addition of $Na_2S_2O_4$ and AcONa to the reaction mixture.

*3 All melting points are uncorrected.

d) Action of potassium persulfate on Ⅸ : To a solution of Ⅸ (100 mg.) dissolved in H_2O (20 ml.) containing pyridine (5 ml.), a solution of KOH (0.3 g.) in H_2O (10 ml.) was added at once, and the resulting suspension of amorphous precipitate was stirred for 5 hr. at 0° The mixture was allowed to stand overnight in a refrigerator, but the reaction mixture showed no change and the hydrolysis of precipitate with dil. HCl gave yellow needles, m.p. 225°, which was found to be identical with an authentic sample of Ⅱ.

A solution of $K_2S_2O_8$ (0.1 g.) in H_2O (2 ml.) was added to the foregoing suspension, the mixture was stirred for 5 hr. at 0°, and then left to stand overnight in a refrigerator. During this operation, the suspended precipitate dissolved into solution, and the resulting red solution was treated by the same method as in (b). From the reaction mixture, Ⅴ was obtained as golden yellow needles, m.p. 164° (decomp.), and Ⅰ as red prisms, m.p. 249° (decomp.).

Ⅴ and Ⅰ obtained by these methods were proved identical with their authentic samples by a mixed fusion and comparison of their IR spectra.

2-Methyl-4*H*-naphtho[1,2-*b*]pyran-4,5,6(5*H*,6*H*)-trione (Ⅹ)——Pulverized Ⅱ (240 mg.) was suspended in AcOH (6 ml.) in an Erlenmeyer flask and crystals of $NaNO_2$ were added with shaking in three portions (total 10 mg.). The mixture was left to stand with occasional shaking at room temperature for 1 hr., resulting red crystals were collected, washed with AcOH, EtOH, and ether, and dried. The product (227 mg.) was recrystallized from AcOH to red prisms (170 mg., 70%), m.p. 234° (decomp.), which was identified with an authentic sample of Ⅹ by a mixed fusion and comparison of their IR spectra.

2-Acetoacetyl-3-hydroxy-1,4-naphthoquinone (Ⅺ)——Ⅴ or Ⅹ (120 mg.) was dissolved in cold 2% KOH solution (30 ml.), the resulting red solution was allowed to stand for 10 min. under cooling, and then filtered. The filtrate was acidified with 5% HCl under cooling, the separated precipitate was collected, washed with H_2O, and dried. The crude product (120 mg.) was recrystallized cautiously from acetone to yellow needles, m.p. 126°, whose ethanolic solution colored deep red with $FeCl_3$. *Anal.* Calcd. for $C_{14}H_{10}O_5$: C, 65.12; H, 3.90. Found : C, 65.34; H, 3.85. IR ν_{max}^{KBr} cm^{-1} : 1685, 1650 (C=O).

2-Methyl-4*H*-naphtho[2,3-*b*]pyran-4,5,10(5*H*,10*H*)-trione (Ⅴ)——a) Ⅺ (50 mg.) was heated with MeOH (1 ml.) and conc. HCl (1 drop) under reflux for 10 min., and the mixture was cooled. The resulting crystals were recrystallized from MeOH to golden yellow needles, m.p. 165° (decomp.).

b) To a solution of Ⅹ (50 mg.) dissolved in AcOH (5 ml.) with heating, conc. HCl (2 drop) was added, the mixture was boiled for 3 min., and then cooled. The resulting solution was diluted with $CHCl_3$ (100 ml.) and poured into H_2O (300 ml.). The separated $CHCl_3$ layer was washed with H_2O, dried over Na_2SO_4, and evaporated to dryness. Recrystallization of the residue from MeOH gave golden yellow needles, m.p. 165° (decomp.).

c) A suspension of pulverized Ⅰ (50 mg.) in AcOH (2 ml.) and $CHCl_3$ (2 ml.) was shaken with $NaNO_2$ (5 mg.) in the same way as described for the preparation of Ⅹ from Ⅱ. The resulting yellow solution was diluted with H_2O (20 ml.) and extracted with $CHCl_3$. After washing with H_2O and drying over Na_2SO_4, the $CHCl_3$ extract was evaporated to dryness, and the residue was recrystallized from MeOH to golden yellow needles, m.p. 165° (decomp.).

Three products by these methods were proved to be Ⅴ by mixed fusion and comparison of their IR spectra with that of authentic sample of Ⅴ.

Reduction of Ⅹ——To a cold solution of Ⅹ (50 mg.) dissolved in AcOH (5 ml.) with heating, a solution of $Na_2S_2O_4$ (50 mg.) in H_2O (1 ml.) was added at once, and the mixture was diluted with H_2O (10 ml.). The resulting precipitate was collected, washed with H_2O, and recrystallized from EtOH to yellow needles, m.p. 224°, which was identified with an authentic sample of Ⅱ by a mixed fusion and comparison of their IR spectra.

Synthesis of Ⅰ from Ⅱ——Ⅱ (0.3 g.) was suspended in AcOH (8 ml.) and oxidized with catalytic amount of $NaNO_2$ to give Ⅹ (280 mg.) by the same method as described above.

This product was dissolved in 2% KOH solution (40 ml.) and MeOH (30 ml.) was added to the solution. After filtration, the resulting red solution was acidified with dil. HCl (5%), heated at 60° for 10 min., and cooled. A small amount of precipitate that formed was filtered off, and AcONa (1 g.) and $Na_2S_2O_4$ (0.5 g.) were added to the filtrate. The mixture was diluted with H_2O (80 ml.) and left to stand overnight in a refrigerator. Resulting orange precipitate was collected, washed with H_2O, and dried. Recrystallization from EtOH gave red prisms (170 mg., 57% from Ⅱ), m.p. 250° (decomp.), which was identified with an authentic sample of Ⅰ by a mixed fusion and comparison of their IR spectra.

2-Methyl-3-acetyl-5,6-diacetoxy-7,8-benzochromone (Ⅻ)——A mixture of 2-acetyl-1,3,4-triacetoxynaphthalene (8 g.), Ac_2O (40 g.), and AcONa (16 g.) was refluxed for 8 hr. in an oil bath (180°). When cooled, the mixture was poured into H_2O, the separated solid was collected, washed with H_2O, and dried. Two recrystallizations from benzene gave pale yellow plates (5 g., 53%), m.p. 234°. *Anal.* Calcd. for $C_{20}H_{16}O_7$: C, 65.21; H, 4.38. Found : C, 65.26; H, 4.43. IR ν_{max}^{KBr} cm^{-1} : 1762 (O-C=O), 1685, 1640 (C=O).

This compound was also obtained from 2-acetyl-4-acetoxy-1,3-naphthalenediol, 2-acetyl-3,4-diacetoxy-1-naphthol, or 2-acetyl-1-methoxy-3,4-diacetoxynaphthalene by the same method.

2-Methyl-3-acetyl-5,6-dihydroxy-7,8-benzochromone (VII)——XII (1.2 g.) was dissolved in conc. H_2SO_4 (10 ml.), the solution was left to stand for 10 min., and then poured into cold H_2O (500 ml.). The separated precipitate was collected, washed with H_2O, and dried. Two recrystallizations from EtOH gave yellow needles (0.5 g.), m.p. 226° (decomp.). This compound was identified with an authentic sample of VII by a mixed fusion and comparison of their IR spectra.

2-Methyl-3-acetyl-4*H*-naphtho[1,2-*b*]pyran-4,5,6(5*H*,6*H*)-trione (XIII)——VII (140 mg.) was suspended in AcOH (3 ml.) and oxidized with $NaNO_2$ (5 mg.) by the same manner as described in the case of X. The crude product (130 mg.) was recrystallized from AcOH to red prisms (100 mg., 72%), m.p. 229° (decomp.), which was proved identical with an authentic sample of XIII by a mixed fusion and comparison of their IR spectra.

2-Methyl-3-acetyl-5,8-dihydroxy-6,7-benzochromone (VI)——XIII (200 mg.) was dissolved in a cooled mixture of 2% KOH solution (20 ml.) and MeOH (20 ml.), the solution was left to stand for 5 min. under cooling, and then filtered. The filtrate was acidified with dil. HCl (5%), heated at 60° for 5 min., and then cooled. The precipitate thereby formed was filtered off, and AcONa (1 g.) and $Na_2S_2O_4$ (0.5g.) were added to the filtrate and the mixture was diluted with H_2O (40 ml.). After standing the mixture for 2 hr. under cooling, separated precipitate was collected, washed with H_2O, and dried. Two recrystallizations from EtOH gave yellow plates (70 mg., 35%), m.p. 210° (decomp.). *Anal.* Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.26. Found : C, 67.37; H, 4.34. IR ν_{max}^{KBr} cm^{-1} : 3350 (O-H), 1684, 1640 (C=O).

2-Methyl-3-acetyl-5,8-diacetoxy-6,7-benzochromone (XIV)——A mixture of VI (30 mg.), Ac_2O (1 ml.), and pyridine (1 drop) was left to stand overnight and then poured into ice-water. The separated precipitate was collected, washed with H_2O, and dried. Two recrystallizations from EtOH gave pale yellow needles, m.p. 198°. *Anal.* Calcd. for $C_{20}H_{16}O_7$: C, 65.21; H, 4.38. Found : C, 65.09; H, 4.35. IR ν_{max}^{KBr} cm^{-1} : 1776 (O-C=O), 1684, 1650 (C=O).

2-Methyl-3-acetyl-5,8-dimethoxy-6,7-benzochromone (XV)——A mixture of VI (100 mg.), Me_2SO_4 (0.1 ml.), acetone (5 ml.), and K_2CO_3 (0.5 g.) was refluxed for 3 hr. with stirring and then filtered to remove inorganic salt. The filtrate was diluted with H_2O (100 ml.) and extracted with ether. The ether extract was washed with dil. KOH solution and dried over Na_2SO_4. After removal of the solvent, the residue was recrystallized once from CCl_4 and twice from EtOH-H_2O (1:1) to pale yellow needles, m.p. 162.5°. *Anal.* Calcd. for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found : C, 69.13; H, 5.02. IR ν_{max}^{KBr} cm^{-1} : 1684, 1648 (C=O).

Ring Isomerization of VI——A mixture of VI (40 mg.), dioxane (2 ml.), and conc. HCl (2 ml.) was heated on a boiling water bath for 1 hr. When cooled, the mixture was diluted with H_2O (50 ml.), the separated precipitate was collected, washed with H_2O, and dried. Recrystallization from EtOH gave yellow needles, m.p. 226° (decomp.), which was identified with an authentic sample of VII by a mixed fusion and comparison of the IR spectra.

The author wishes to express his deep gratitude to Prof. T. Okamoto of Tokyo University for his helpful guidance, to Dr. T. Ukai, the President of this College, for his kind encouragement, and to Dr. Y. Saiki and Dr. Y. Akahori of this laboratory for valuable advice, during the course of this work. Thanks are due to Mr. K. Narita, Miss N. Yamazaki, and Mrs. K. Yamamoto of this College for elemental analyses and measurement of ultraviolet spectra.

Summary

Potassium 2-methyl-5-hydroxy-6,7-benzochromon-8-yl sulfate (VIII) and potassium 2-methyl-5-hydroxy-7,8-benzochromon-6-yl sulfate (IX) were synthesized from 2-methyl-5,8-dihydroxy-6,7-benzochromone (I) and 2-methyl-5,6-dihydroxy-7,8-benzochromone (II). Hydroxylation of 2-methyl-5-hydroxy-6,7-benzochromone (III) and 2-methyl-5-hydroxy-7,8-benzochromone (IV) gave 2-methyl-4*H*-naphtho[2,3-*b*]pyran-4,5,10(5*H*,10*H*)-trione (V) from both, and the mechanisms of the abnormal reaction were investigated. It was found that V is also obtained from IX in the same condition as hydroxylation, and that 2-methyl-4*H*-naphtho[1,2-*b*]pyran-4,5,6(5*H*,6*H*)-trione (X) underwent ring isomerization to V directly or through a diketone, 2-acetoacetyl-3-hydroxy-1,4-naphthoquinone (XI), as an intermadiate.

Synthesis of I from II and that of 2-methyl-3-acetyl-5,8-dihydroxy-6,7-benzochromone (VI) from 2-methyl-3-acethyl-5,6-dihydroxy-7,8-benzochromone (VII) was accomplished by the application of a novel reaction together with a new oxidation method using sodium nitrite. VI also underwent ring isomerization to VII. Thus, it was found that acetyl group at 3-position in VI or 2-methyl-3-acetyl-4*H*-naphtho[1,2-*b*]pyran-4,5,6(5*H*,6*H*)-trione (XIII) was not eliminated during two kinds of ring isomerization described.

(Received June 1, 1965)