one of the two bromine atoms substituted at 5-position in 5,5-dibromobarbituric acid is so unstable that it is capable of a nonspecific intermolecular bromination of co-existing compounds. On the other hand, since the compounds of the 5-phenylcarbamoyl derivatives do not have such a reactive chemical group in their structure, the *in vivo* anti-tumor activity of No. 26 should be attributed to some unknown specific affinity responsible for its anti-tumor activity.

The authors are deeply indebted to Dr. D. Mizuno and his collaborators at the National Institute of Health, Tokyo, and to Dr. K. Kajiwara of Research Laboratories, Takeda Pharmaceutical Industries, Ltd., for carrying out a part of the anti-tumor tests.

## Summary

5-Halo, 5-acyl, 5-benzylidene, and 5-phenylcarbamoyl derivatives of 1-hydrogen, 1-methyl, and 1-phenyl-barbituric acids were synthesized and examined for their antidehydrogenase activity against ascites tumor cells by the cylinder agar plate (CAP) method (A), for their growth inhibitory activity in cell-culture of AH-130 (B), and for their anti-tumor activity against Ehrlich ascites carcinoma in mice (C). Among the compounds tested, sodium 5-phenylcarbamoylbarbiturate showed potent anti-tumor activity, both *in vitro* and *in vivo* biological tests (B) and (C), to reveal its promising properties as a cancer chemotherapeutic.

(Received August, 13 1960)

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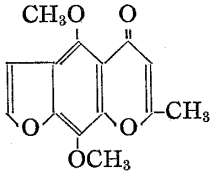
*UDC 547.816.07*

## *172.* Kazutaka Yamaguchi, Seigo Fukushima, and Hiroshi Yamada: Studies on Benzochromones. I. Synthesis of 2-Methyl-5,6-dimethoxy-7,8-benzochromone.

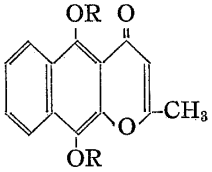
(*National Institute of Hygienic Sciences*[*1])

The natural product khellin (I) has attracted considerable attention as a potent vasodilator and an antispasmodic agent, and great many variants of khellin have been prepared in an effort to find derivatives with greater activity than that of khellin.[1,2]

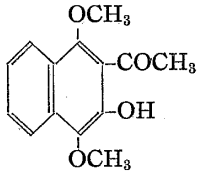
This paper deals with some investigations on the attempted synthesis of a compound in which the furan ring of khellin is replaced by a benzenoid ring, such as 2-methyl-5,8-dimethoxy-6,7-benzochromone (II).




(I)




(II) R=$CH_3$
(II′) R=H




(III)

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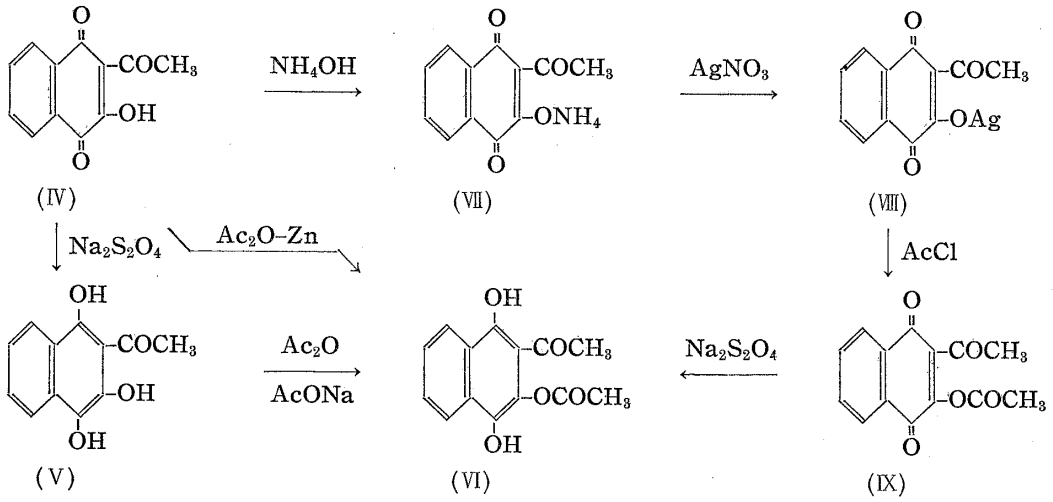
*1 Tamagawa-yoga-machi, Setagaya-ku, Tokyo (山口一孝, 福島清吾, 山田 裕).

1) J. Schmitz, H. Lauener, R. Hirt, M. Sanz: Helv. Chim. Acta, **34**, 767(1951).
2) A. Schönberg, A. Sina: J. Am. Chem. Soc., **72**, 1611, 3396(1950).

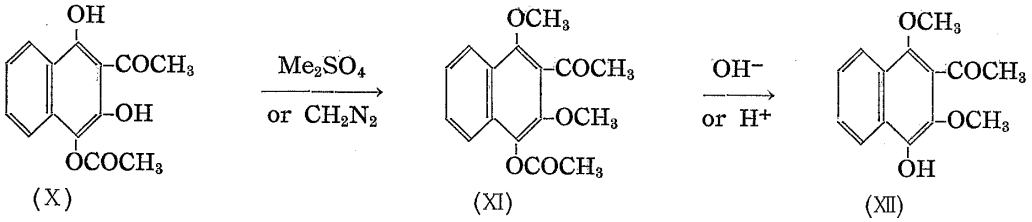
Spruit[3] reported that 2-acetyl-3-acetoxy-1,4-naphthohydroquinone (VI), m.p. 187°, was obtained by reductive acetylation of 2-acetyl-3-hydroxy-1,4-naphthoquinone (IV). On the other hand, Cram[4] claimed that the same substance (VI), m.p. 196~197°, was obtained by either reduction of 2-acetyl-3-acetoxy-1,4-naphthoquinone (IX) or partial acetylation of 1,3,4-trihydroxy-2-acetylnaphthalene (V).




(IV) (VII) (VIII) (V) (VI) (IX)

In an attempt to obtain 1,4-dimethoxy-2-acetyl-3-hydroxynaphthalene (III) as the starting material of (II), all the procedures mentioned above were followed. Reductive acetylation of 2-acetyl-3-hydroxy-1,4-naphthoquinone (IV) and partial acetylation of 1,3,4-trihydroxy-2-acetylnaphthalene (V) afforded the same yellow needles (X), m.p. 192~193°, whose analytical values agreed with those of monoacetoxy-dihydroxy-acetylnaphthalene, $C_{14}H_{12}O_5$, in either case, and 2-acetyl-3-acetoxy-1,4-naphthoquinone (IX) was not obtained from the silver salt of 2-acetyl-3-hydroxy-1,4-naphthoquinone (VIII), by any means. This substance (X) was proved to be identical with authentic sample of (VI) of Spruit by admixture*2 and comparison of their infrared spectra, but its structure was proved to be 1,3-dihydroxy-2-acetyl-4-acetoxynaphthalene (X) and not 2-acetyl-3-acetoxy-1,4-naphthohydroquinone (VI), because of many supporting reasons to be discussed later.

Methylation of the substance (X) with either dimethyl sulfate and potassium carbonate or diazomethane produced a monoacetoxy-dimethoxy-acetylnaphthalene (XI), m.p. 68°, which was hydrolysed with alcoholic potassium hydroxide or sulfuric acid to produce a monohydroxy-dimethoxy-acetylnaphthalene (XII), m.p. 114~115°.




(X) (XI) (XII)

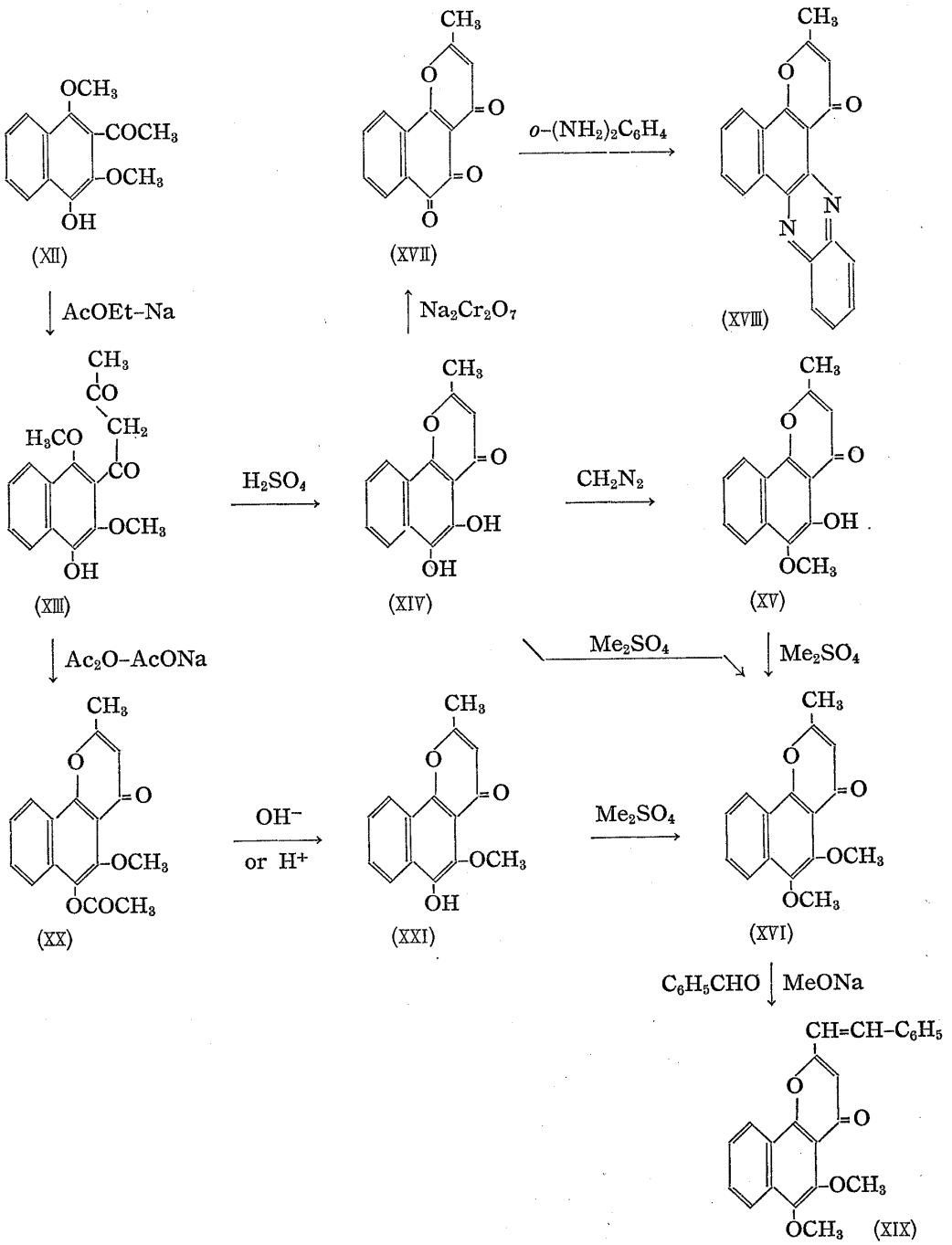
The infrared spectrum of (XII) shows a sharp absorption band at 3568 $cm^{-1}$, which can be attributed to the presence of a free hydroxyl group, and a carbonyl absorption at 1700 $cm^{-1}$, which remains unchanged from (XI). There is no hydroxyl group in (XI) and therefore, the carbonyl group of (XII) must be a non-chelated one. The only structure of

*2 Sample of Spruit, m.p. 186°; mixed sample, m.p. 187°; the present sample, m.p. 192~193°.

3) C. J. P. Spruit: Rec. trav. chim., **1947**, 665.
4) D. J. Cram: J. Am. Chem. Soc., **71**, 3953(1949).

(XII) consistent with these facts is 1,3-dimethoxy-2-acetyl-4-hydroxynaphthalene. Since the fact that (XI) can be obtained from (X) with the mildest methylating agent (diazomethane) seems to reject the possibility of migration of acetyl group during the reaction from (X) to (XI), the structure of (XI) must be 1,3-dimethoxy-2-acetyl-4-acetoxynaphthalene. Consequently, it is concluded that the structure of monoacetate of 1,3,4-trihydroxy-2-acetylnaphthalene is 1,3-dihydroxy-2-acetyl-4-acetoxynaphthalene (X) and not 2-acetyl-3-acetoxy-1,4-naphthohydroquinone (VI). Further support of this conclusion will be discussed later.

The condensation of (XII) with ethyl acetate using metallic sodium led to a diketone, 1,3-dimethoxy-2-acetoacetyl-4-hydroxynaphthalene (XIII), m.p. 104~105°, ethanol solution of which showed a deep red color with ferric chloride reagent.



Treatment of (XIII) with 10 parts of cold sulfuric acid gave yellow needles, m.p. 224~225°, whose analytical values agreed with $C_{14}H_{10}O_4$, and assay of methoxyl group proved that it had no methoxyl group. It was found to have a 2-methylchromone structure, because its dimethyl ether (XVI) underwent condensation with benzaldehyde to produce a styryl derivative (XIX), m.p. 184°, as do other 2-methylchromones.[5]

Then, the substance was assumed to have a structure of either 2-methyl-5,8-dihydroxy-6,7-benzochromone (II') or 2-methyl-5,6-dihydroxy-7,8-benzochromone (XIV).

Oxidation of (XIV) with sodium dichromate gave a brick-red quinone (XVII), $C_{14}H_8O_4$, m.p. 234° (decomp.), which was condensed with *o*-phenylenediamine to afford a quinoxaline derivative (XVIII), $C_{20}H_{12}O_2N_2$, m.p. 250° (decomp.). This fact demonstrates that (XVII) is an *o*-quinone and consequently the yellow needles obtained from (XIII) were proved to be 2-methyl-5,6-dihydroxy-7,8-benzochromone (XIV).

Methylation of 2-methyl-5,6-dihydroxy-6,7-benzochromone (XIV) with diazomethane produced yellow needles (XV), m.p. 168°, and its analytical values agreed with those of monomethyl ether of (XIV). Infrared spectrum of (XV) exhibits broad and weak hydroxyl band from 3400 to beyond 2600 $cm^{-1}$, which can be attributed to the presence of a chelated hydroxyl group,[6] and (XV) is almost insoluble in alkali and resists further methylation with diazomethane. These characteristics have also been observed in similar cases, such as in *o*-hydroxyacetophenone, 5-hydroxyflavones, 1-hydroxyanthraquinones, etc., and have been believed to be due to the formation of a chelated ring system.[7,8]

These facts suggest that the position of hydroxyl group of (XV) is 5-position which is capable of forming a chelated ring system and, therefore, the structure of (XV) is 2-methyl-5-hydroxy-6-methoxy-7,8-benzochromone.

Methylation of (XIV) or (XV) with dimethyl sulfate and potassium carbonate in acetone led to 2-methyl-5,6-dimethoxy-7,8-benzochromone (XVI), m.p. 130°, in each case.

Cyclization of (XIII) with acetic anhydride and sodium acetate gave colorless needles of m.p. 186°, whose infrared spectrum showed the absence of hydroxyl group and the presence of acetoxyl group. This substance has the molecular formula, $C_{17}H_{14}O_5$ and assay of methoxyl group showed the presence of one methoxyl group. Hydrolysis of this substance (XX) with 1% potassium hydroxide or sulfuric acid gave pale yellow needles (XXI), m.p. 212°, whose infrared spectrum exhibited a sharp absorption band at 3550 $cm^{-1}$, due to the presence of a free hydroxyl group, and this substance (XXI) could be easily converted to a dimethyl ether, which was identified with above-mentioned 2-methyl-5,6-dimethoxy-7,8-benzochromone (XVI) by admixture and comparison of infrared spectra.

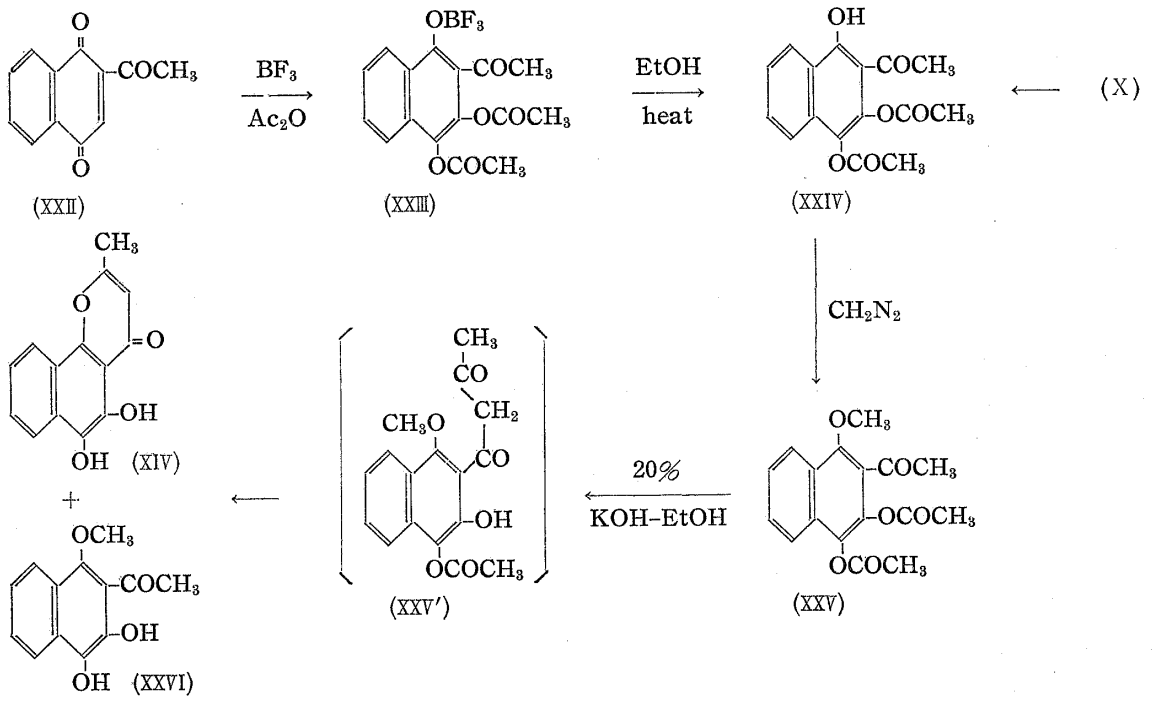
It was, therefore, proved that (XXI) is 2-methyl-5-methoxy-6-hydroxy-7,8-benzochromone and consequently, (XX) is 2-methyl-5-methoxy-6-acetoxy-7,8-benzochromone.

As the 5-position of (XX) was proved to have the methoxyl group, the 3-position in (XIII), (XII), and (XI) must carry methoxyl group and therefore, 3-position of (X) must have hydroxyl group, not acetoxyl group.

Thus, it was demonstrated again that the monoacetate of 1,3,4-trihydroxy-2-acetylnaphthalene could not be 2-acetyl-3-acetoxy-1,4-naphthohydroquinone (VI), but 1,3-dihydroxy-2-acetyl-4-acetoxynaphthalene (X).

Cram[4] obtained 2-acetyl-3,4-diacetoxy-1-naphthol (XXIV) from 2-acetyl-1,4-naphthoquinone (XXII) through boron trifuloride derivative of 2-acetyl-3,4-diacetoxy-1-naphthol (XXIII) and identified it with the diacetate obtained by preferential acetylation of the monoacet-

5) I. M. Heilbron, H. Barnes, R. A. Morton : J. Chem. Soc., **1923**, 2559.
6) L. J. Bellamy : "The Infra-red Spectra of Complex Molecules," 2nd Ed., 96 (1958). Methuen and Co., Ltd., London.
7) A. Schönberg : J. Chem. Soc., **1946**, 746.
8) V. N. Gupta, T. R. Seshadri : *Ibid.*, **1954**, 2350.




ate*3 of 1,3,4-trihydroxy-2-acetylnaphthalene. When he tried hydrolysis of methyl ether of (XXIV), 1-methoxy-2-acetyl-3,4-diacetoxynaphthalene (XXV), with alcoholic potassium hydroxide, light yellow needles were obtained in better yield than that of the anticipated 1-methoxy-2-acetyl-3,4-dihydroxynaphthalene (XXVI) but the substance was not identified. Its analytical values agreed with $C_{14}H_{10}O_4$ and the characteristics described were very similar to those of (XIV) obtained in the present experiment.

Under the assumption that the substance obtained by him might be identical with (XIV), the same procedure was followed and yellow needles, m.p. 224~225°, were obtained, which were identified with (XIV) by admixture and infrared spectral determination. It was, therefore, proved that the unknown substance is 2-methyl-5,6-dihydroxy-7,8-benzochromone (XIV), but (XXVI) was not obtained.

The mechanism of this novel reaction was assumed to be a rearrangement of acetyl group at 3-position to the $\omega$-carbon atom of methyl ketone group in (XXV), forming an intermediate (XXV'), followed by cyclization to (XIV).

Such kind of base-catalysed rearrangement as formation of 2-hydroxy-$\omega$-acylacetophenone derivatives from 2-acyloxyacetophenone derivatives is well known as Baker-Venkataraman transformation[9,10] but the solvent used for this object has been completely water-free without exception, and only a few cases[11,12] are known, in which aliphatic acyl group caused such a rearrangement.

It is therefore very interesting that the acetyl group easily underwent rearrangement followed by cyclization, in such a solvent containing about 20% of water. Further details of mechanism of this reaction will be reported later.

*3 D. J. Cram[4] insisted that the structure of this monoacetate is 2-acetyl-3-acetoxy-1,4-naphthohydroquinone, but the authors propose a new formula of 1,3-dihydroxy-2-acetyl-4-acetoxynaphthalene.

9) W. Baker : J. Chem. Soc., **1933**, 138.
10) K. Venkataraman, *et al.* : *Ibid.*, **1934**, 1767.
11) T. S. Wheeler, *et al.* : *Ibid.*, **1939**, 1679.
12) T. S. Wheeler, *et al.* : *Ibid.*, **1950**, 1252.

## Experimental

**2-Acetyl-3-hydroxy-1,4-naphthoquinone (IV)**—Starting from 29 g. of 2-acetyl-4-amino-1-naphthol hydrochloride, 13 g. of golden yellow plates, m.p. 132~133°, were obtained by the method given by Spruit.[3] Its dilute EtOH solution gave a red color with $FeCl_3$. *Anal.* Calcd. for $C_{12}H_8O_4$: C, 66.67; H, 3.73. Found: C, 66.51; H, 3.74.

**1,3,4-Trihydroxy-2-acetylnaphthalene (V)**—To a mixture of 20 g. of (IV) and 300 cc. of EtOH warmed on a water bath, a solution of 20 g. of sodium hydrosulfite (about 1.1 equiv.) in 300 cc. of $H_2O$ was added and the mixture was warmed for several minutes to form deep red-brown clear solution. The solution was cooled, separated crystals were collected, and recrystallized from dil. EtOH containing a little hydrosulfite to yield 15 g. (74%) of orange-red needles, m.p. 185°. A dil. EtOH solution of it gave a green color with $FeCl_3$. *Anal.* Calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.83. Found: C, 65.95; H, 4.55.

**1,3-Dihydroxy-2-acetyl-4-acetoxynaphthalene (X)**—a) A mixture of 10 g. of (V) and 75 g. of $Ac_2O$ was warmed to 60~70° on a water bath to form an orange-red solution, when yellow needles began to separate. After cool, the crystals were collected, washed with a small amount of cold AcOH, and recrystallized twice from EtOH to yield 6 g. (46%) of yellow needles, m.p. 192~193°. Its dil. EtOH solution showed a green color with $FeCl_3$ changing immediately to an orange-red color. *Anal.* Calcd. for $C_{14}H_{12}O_5$: C, 64.61; H, 4.65. Found: C, 64.58; H, 4.60.

b) A mixture of 2 g. of (IV), 2 g. of zinc dust, and 40 cc. of $Ac_2O$ was boiled for several seconds, filtered while hot, cooled, and poured into ice-water. Separated crystals were recrystallized twice from EtOH to yield 0.8 g. (34%) of (X).

c) According to the method of Cram,[4] a mixture of 0.5 g. of (V), about 10 mg. of AcONa, and 20 g. of $Ac_2O$ was allowed to stand for 10 hr. at room temperature. To the reaction mixture, 200 cc. of $H_2O$ was added and recrystallization of separated crystals gave 0.2 g. (34%) of (X).

The substances obtained by these methods were confirmed to be identical with each other by admixture and infrared spectral determination.

**1,3-Dimethoxy-2-acetyl-4-acetoxynaphthalene (XI)**—a) A mixture of 13 g. of (X), 26 g. of $K_2CO_3$, 13 g. of $Me_2SO_4$, and 260 cc. of $Me_2CO$ was heated for 3 hr. on a boiling water bath. After cool, $Me_2CO$ was evaporated under a reduced pressure. The oil that separated on adding $H_2O$ solidified after cooling in ice-salt mixture. Two recrystallizations of the solid from dil. EtOH gave 12 g. (83%) of colorless prisms, m.p. 68°. A dil. EtOH solution showed no color with $FeCl_3$. *Anal.* Calcd. for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59; $CH_3O$, 21.53. Found: C, 67.14; H, 5.57; $CH_3O$, 22.23. IR $\nu_{max}^{CHCl_3}$: 1700 $cm^{-1}$ (C=O).

b) To a solution of 2.0 g. of (X) in 150 cc. of dry benzene and 3 cc. of MeOH, an $Et_2O$ solution of $CH_2N_2$ prepared from 5 g. of N-methyl-N-nitrosourea was added. The mixture, after standing overnight at room temperature, was evaporated to leave an oil, which showed a green color with $FeCl_3$. Its $CHCl_3$ solution was passed through alumina column and the first eluate, which showed no color with $FeCl_3$, was evaporated to dryness. Two recrystallizations from dil. EtOH afforded 0.2 g. (9%) of (XI). Two substances obtained by these methods were proved to be identical with each other, by admixture and infrared spectral determination.

**1,3-Dimethoxy-2-acetyl-4-hydroxynaphthalene (XII)**—a) To a warm solution of 10 g. of (XI) in 120 cc. of EtOH, 20 cc. of 30% KOH solution was added in $N_2$ atmosphere. After standing for 30 min. in $N_2$, excess of AcOH and 600 cc. of $H_2O$ were added. Separated solid was recrystallized twice from dil. EtOH to yield 7.5 g. (88%) of colorless needles, m.p. 114~115°. An EtOH solution of the substance showed a red color with $FeCl_3$. *Anal.* Calcd. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73; $CH_3O$, 25.16. Found: C, 68.13; H, 5.70; $CH_3O$, 24.78. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3568 (OH) 1700 (C=O).

b) A mixture of 1.0 g. of (XI) and 10 g. of cold $H_2SO_4$, forming a deep red solution, was allowed to stand for 10 min. and poured into ice-water. Separated solid was recrystallized several times to yield 0.6 g. (70%) of (XII).

These substances were confirmed to be identical with each other by admixture.

**1,3-Dimethoxy-2-acetoacetyl-4-hydroxynaphthalene (XIII)**—To a solution of 6 g. of (XII) dissolved in 24 g. of AcOEt, 3 g. of metallic Na was gradually added in small pieces. When the initial vigorus reaction subsided, the mixture was refluxed on a water bath for 3 hr. and left overnight. The reaction mixture was treated with 5 cc. of MeOH to destroy unchanged Na, 100 cc. of $H_2O$ was added, and acidified with AcOH. Separated oil solidified on cooling and scratching. On recrystallization of the substance once from dil. EtOH and twice from $Me_2CO$-petr. benzine gave 3.2 g. (45%) of slightly yellow prisms, m.p. 104~105°. Its dil. EtOH solution showed a deep red color with $FeCl_3$. *Anal.* Calcd. for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59; $CH_3O$, 21.53. Found: C, 66.52; H, 5.97; $CH_3O$, 21.35. IR $\nu_{max}^{CHCl_3}$: 3566 $m^{-1}$ (OH).

**2-Methyl-5,6-dihydroxy-7,8-benzochromone (XIV)**—a) A deep red solution of 1.0 g. of (XIII) in 10 g. of cold $H_2SO_4$ was allowed to stand for 10 min. and poured into ice-water. Separated yellow-brown

precipitate was collected, washed thoroughly with $H_2O$, and dried. Two recrystallizations of the substance from EtOH, gave yellow needles, m.p. 224~225°; yield, 0.7 g. (83%). A dil. EtOH solution showed an instantaneous green color with $FeCl_3$, changing to orange-red. *Anal.* Calcd. for $C_{14}H_{14}O_4$ : C, 69.42; H, 4.16; $CH_3O$, 0. Found : C, 69.57; H, 4.00; $CH_3O$, 0.23. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$ : 3575 (OH), 1670 (C=O).

b) To a solution of 2.2 g. of (XXV) in 30 cc. of EtOH, 7.5 cc. of 20% KOH solution was added in $N_2$ atmosphere, to separate a red-brown solid. The reaction mixture was allowed to stand for 4 min. in $N_2$ and acidified with AcOH. Separated crystals were collected, washed with a small amount of cold EtOH, and dried. Recrystallization twice from EtOH afforded 0.7 g. (38%) of (XIV).

The substances obtained by these two methods were proved to be identical with each other by admixture and infrared spectral determination.

**2-Methyl-5-hydroxy-6-methoxy-7,8-benzochromone (XV)**—To a suspension of 1.0 g. of (XIV) in 60 cc. of dry benzene and 1.2 cc. of MeOH, an $Et_2O$ solution of $CH_2N_2$, prepared from 3.0 g. of N-methyl-N-nitrosourea, was added. Suspended crystals disappeared once and then light yellow needles began to separate out. After the mixture was allowed to stand overnight, separated crystals were collected, the mother liquor was concentrated to a small volume, and separated crystals were collected. All the crystals were combined and recrystallized form MeOH to yield 0.8 g. (76%) of light yellow needles, m.p. 168°. A dil. EtOH solution showed a blue-green color with $FeCl_3$. *Anal.* Calcd. for $C_{15}H_{12}O_4$ : C, 70.30; H, 4.72; $CH_3O$, 12.11. Found : C, 70.70; H, 5.19; $CH_3O$, 11.80. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$ : 3400~2600 (chelated OH), 1667 (C=O).

**2-Methyl-5,6-dimethoxy-7,8-benzochromone (XVI)**—a) A mixture of 0.5 g. of (XV), 0.5 g. of $Me_2SO_4$, 2.0 g. of $K_2CO_3$, and 20 cc. of $Me_2CO$ was refluxed for 6 hr. on a water bath. After removal of $K_2CO_3$, $Me_2CO$ was evaporated to a small volume in vacuum and 50 cc. of $H_2O$ was added. Separated solid was purified through alumina with benzene and recrystallized twice from dil. EtOH to yield 0.23 g. (22%) of colorless needles, m.p. 130°. *Anal.* Calcd. for $C_{16}H_{14}O_4$ : C, 71.10; H, 5.22; $CH_3O$, 22.95. Found : C, 70.90; H, 5.31; $CH_3O$, 23.27. IR : 1660 $cm^{-1}$ (C=O).

b) A mixture of 0.5 g. of (XIV), 1.0 g. of $Me_2SO_4$, 4 g. of $K_2CO_3$, and 20 cc. of $Me_2CO$ was refluxed for 16 hr. Treatment of the reaction mixture as above gave 0.12 g. (21%) of (XVI).

c) Refluxing of 0.3 g. of (XXI), 0.3 g. of $Me_2SO_4$, 1.5 g. of $K_2CO_3$, and 12 cc. of $Me_2CO$ for 30 min. afforded 0.25 g. (69%) of (XVI).

The substances obtained by these three methods were proved to be identical with each other by admixture and infrared spectral determination.

**2-Methyl-4*H*-naphtho[1,2-*b*]pyran-4,5,6-trione (XVII)**—A mixture of 0.5 g. of (XIV), 10 cc. of AcOH, 2 cc. of 30% $H_2SO_4$, and 4 cc. of 30% $Na_2Cr_2O_7$ solution was shaken vigorously for 30 min. Resulting solid was collected, washed, and dried. Two recrystallizations from AcOH afforded 0.23 g. of brick-red prisms, m.p. 234° (decomp.). *Anal.* Calcd. for $C_{14}H_8O_4$ : C, 70.00; H, 3.36. Found : C, 69.79; H, 3.58.

**3-Methyl-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazin-1-one (XVIII)**—A mixture of 0.2 g. of (XVII), 0.14 g. of *o*-phenylenediamine, and 4 cc. of AcOH was heated for several min. on a water bath and allowed to stand for 1 hr. at room temperature. The solid that separated on adding $H_2O$ was recrystallized once from dil. AcOH and once from EtOH to yield 0.08 g. of orange-yellow crystals, m.p. 250° (decomp.). *Anal.* Calcd. for $C_{20}H_{12}O_2N_2$ : C, 76.91; H, 3.87; N, 8.97. Found : C, 76.40; H, 4.21; N, 9.31.

**2-Styryl-5,6-dimethoxy-7,8-benzochromone (XIX)**—A mixture of 0.2 g. of (XVI), 0.5 g. of BzH, and MeONa in MeOH (0.1 g. of Na in 8 cc. of MeOH) was refluxed for 10 min. on a water bath. The crystals that separated after allowing to stand in a refrigerater for 18 hr. were recrystallized from EtOH to yield 0.15 g. of colorless needles, m.p. 184°. *Anal.* Calcd. for $C_{23}H_{18}O_4$ : C, 77.08; H, 5.06. Found : C, 77.25; H, 5.06. IR $\nu_{max}^{CHCl_3}$ : 1636 $cm^{-1}$ (C=O).

**2-Methyl-5-methoxy-6-acetoxy-7,8-benzochromone (XX)**—A mixture of 1.0 g. of (XIII), 1.0 g. of AcONa, and 15 cc. of $Ac_2O$ was heated for 6 hr. on a boiling water bath. After cool, $H_2O$ was added to the mixture, the resulting red-brown solid was washed with a small amount of ice-cold ether, and recrystallized 3 times from dil. $Me_2CO$ to yield 0.31 g. (30%) of colorless needles, m.p. 186°. *Anal.* Calcd. for $C_{17}H_{14}O_5$ : C, 68.45; H, 4.73; $CH_3O$, 10.40. Found : C, 68.55; H, 5.21; $CH_3O$, 10.85. IR $\nu_{max}^{HCl_3}$ $cm^{-1}$ : 1763 (phenolic acetate C=O), 1659 (C=O).

**2-Methyl-5-methoxy-6-hydroxy-7,8-benzochromone (XXI)**—a) A mixture of 0.2 g. of (XX) and 20 cc. of 1% KOH was shaken vigorously and formed a yellow solution. Precipitate that separated on acidification with HCl was recrystallized from EtOH to yield 0.13 g. (76%) of pale yellow needles, m.p. 212°. A dil. EtOH solution showed a red-brown color with $FeCl_3$. *Anal.* Calcd. for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72; $CH_3O$, 12.11. Found : C, 70.38; H, 5.10; $CH_3O$, 12.48. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$ : 3550 (OH), 1658 (C=O).

b) A yellow solution of 0.25 g. of (XX) dissolved in 2.5 g. of cold $H_2SO_4$ was allowed to stand for 10 min. and poured into ice-water. Separated slightly yellow crystals were collected and washed with $H_2O$. Recrystallization from EtOH yielded 0.17 g. (79%) of (XXI).

These two substances were identical with each other by admixture and infrared spectral determination.

**2-Acetyl-1,4-naphthoquinone (XXII)**—Starting from 10 g. of 2-acetyl-4-amino-1-naphthol hydrochloride, 0.8 g. of light brown prisms (IX), m.p. 84°, were obtained, according to method given by Spruit.[3]

**$BF_3$ Derivative of 2-Acetyl-3,4-diacetoxy-1-naphthol (XXIII)**—A mixture of 0.8 g. of (XXII), 2.5 g. of $Ac_2O$ and 0.5 g. of $BF_3 \cdot Et_2O$ solution was allowed to stand for 24 hr. Separated light-yellow long needles were collected and recrystallized from AcOH, and 0.3 g. of crystals, m.p. 224~225°, were obtained.

**2-Acetyl-3,4-diacetoxy-1-naphthol (XXIV)**—a) A mixture of 1.0 g. of (X) and 20 cc. of $Ac_2O$ was boiled for 4 min. and after cooling, added with ice-water, was shaken vigorously. Separated solid was recrystallized 3 times from EtOH to yield 0.3 g. (26%) of light yellow needles, m.p. 184°. A dil. EtOH solution of it showed a blue-green color with $FeCl_3$. *Anal.* Calcd. for $C_{16}H_{14}O_6$: C, 63.57; H, 4.67. Found: C, 63.21; H, 4.78. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1775 (phenolic acetate C=O), 1622 (chelated C=O).

b) A solution of 0.3 g. of (XXIII) in 3 cc. of 90% EtOH was refluxed for 30 min. on a water bath. The mixture was cooled, the separated crystals were collected, and recrystallized to yield 0.1 g. of (XXIV), m.p. 184°. Admixture of the substance with the sample from method (a) did not depress the m.p.

**1-Methoxy-2-acetyl-3,4-diacetoxynaphthalene (XXV)**—To a suspension of 2.0 g. of (XXIV) in 150 cc. of dehyd. benzene and 3 cc. of MeOH, an $Et_2O$ solution of $CH_2N_2$ prepared from 5 g. of N-methyl-N-nitrosourea was added. The reaction mixture, after standing for 3 hr. was evaporated in vacuum to an oil, which solidified on cooling and scratching. Two recrystallizations from hydr. $Me_2CO$ gave 1.3 g. (62%) of almost colorless prisms, m.p. 104~106°. *Anal.* Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10; $CH_3O$, 9.81. Found: C, 64.17; H, 5.11; $CH_3O$, 9.96. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1772 (phenolic acetate C=O), 1690 (C=O).

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## Summary

Monoacetate of 1,3,4-trihydroxy-2-acetylnaphthalene has been believed to be 2-acetyl-3-acetoxy-1,4-naphthohydroquinone, but a new formula 1,3-dihydroxy-2-acetyl-4-acetoxynaphthalene was proposed with many supporting reasons. Cyclization of 1,3-dimethoxy-2-acetyl-4-hydroxynaphthalene with sulfuric acid gave 2-methyl-5,6-dihydroxy-7,8-benzochromone, which was identified with the unknown substance obtained by hydrolysis of 1-methoxy-2-acetyl-3,4-diacetoxynaphthalene.

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