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24. **Seigo Fukushima**: Studies on Benzochromones. IV.1) The Mechanism of Novel Cyclization of 1,3,4-Triacetoxy-2-acetylnaphthalene to 2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone.

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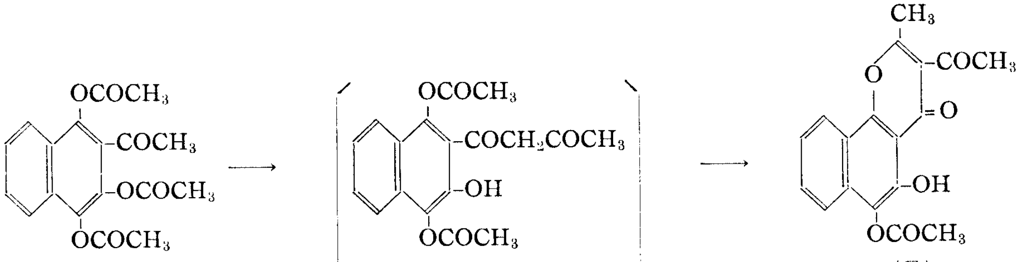
Previously2) it was reported that 1,3,4-triacetoxy-2-acetylnaphthalene (I) was converted to 2-methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (II) on heating (I) at 160~180° with equimolar amount of sodium amide in toluene.

The present paper describes the result of ^{14}C-tracer experiments which were carried out in order to examine the mechanism of this reaction.

The mechanism of the reaction from (I) to (II) was assumed as the rearrangement of acetyl from acetoxyl group in 3-position to the ω-carbon atom of methyl-ketone group in 2-position, immediately followed by cyclization to form (II).



(I) (I′) (II)

In order to confirm this assumption, following experiments were carried out: First, 1,3-diacetoxy-2-acetyl-4-acetoxy[*carbonyl*-^{14}C]-naphthalene (Ia and Ia′), 1,4-diacetoxy-2-acetyl-3-acetoxy[*carbonyl*-^{14}C]-naphthalene (Ib and Ib′), and 1-acetoxy[*carbonyl*-^{14}C]-2-acetyl-3,4-diacetoxynaphthalene (Ic and Ic′) were prepared in two different acetylating conditions and each of them was converted to the radioactive 2-methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromones (IIa, IIa′, IIb, IIb′, IIc, and IIc′). They were then hydrolysed with sulfuric acid to 2-methyl-3-acetyl-5,6-dihydroxy-7,8-benzochromones (IIIa, IIIa′, IIIb, IIIb′, IIIc, and IIIc′).

(Ia), (Ib), and (Ic) were prepared by boiling the mixture of corresponding material and acetic anhydride for a short time. (Ia′), (Ib′), and (Ic′) were prepared by mechanically shaking a mixture of corresponding material with a trace of sodium acetate and acetic anhydride for a long time at room temperature.

The radioactivity of completely purified samples of (IIa), (IIIa), (IIb), (IIIb), (IIc), (IIIc), (IIa′), (IIIa′), (IIb′), (IIIb′), (IIc′), and (IIIc′) was measured with Windowless-type, Low-background 2π-Q-Gas Flow Counter and their specific activity (c.p.m./mM) was compared with each other. The results of these experiments are shown in Table I.

Table I.

Compd. No.	c.p.m./mM × 10^{-3}	%	Compd. No.	c.p.m./mM × 10^{-3}	%
(IIa)	18.7	100	(IIa′)	21.7	100
(IIIa)	7.31	39	(IIIa′)	6.45	33
(IIb)	4.89	100	(IIb′)	5.51	100
(IIIb)	3.44	70	(IIIb′)	4.21	76
(IIc)	37.6	100	(IIc′)	3.22	100
(IIIc)	29.1	77	(IIIc′)	2.66	83

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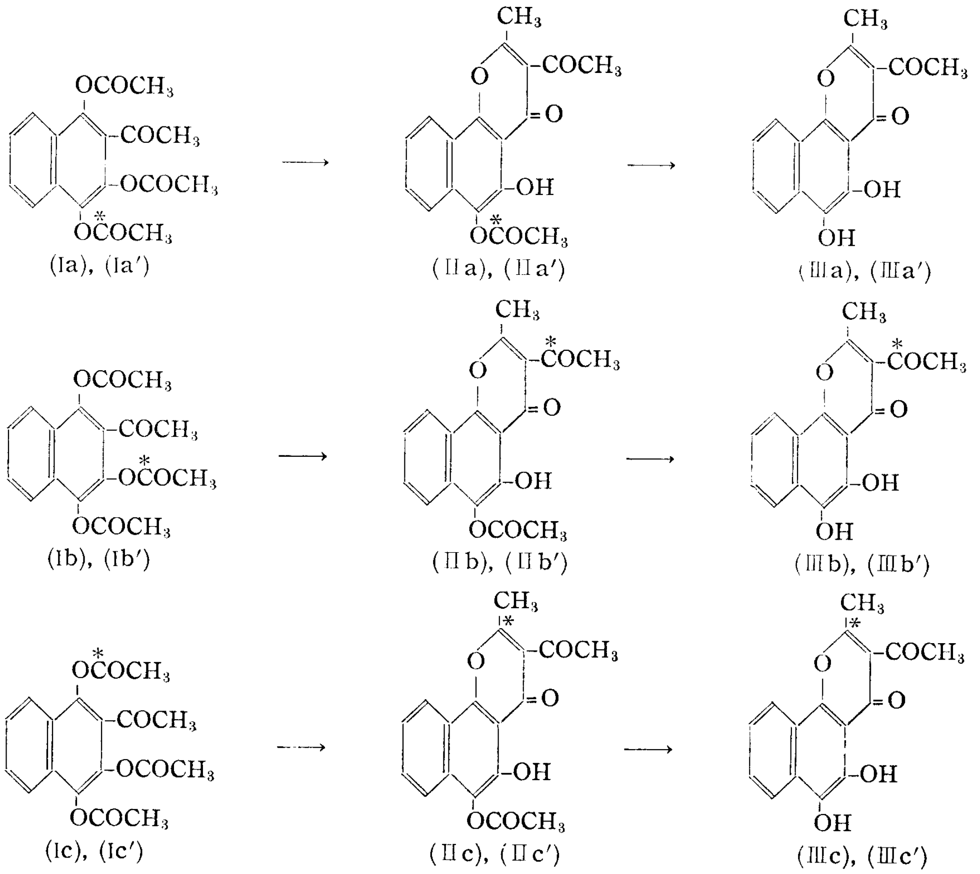
1) Part III: This Bulletin, **9**, 124 (1961).

2) Part II: *Ibid.*, 8, 1036 (1960).



* represents ^{14}C

If the reaction in question exclusively followed the route (I)→(I')→(II), the radioactivity of (IIIa) and (IIIa') would be nil and the specific activity of (IIIb), (IIIc), (IIIb'), and (IIIc') would be equal to those of (IIb), (IIc), (IIb'), and (IIc'), respectively. However, as is apparent from Table I, marked discrepancy is observed between actually determined values of specific activity and expected values, especially in the case of (IIIa), (IIIb), and (IIIc), the discrepancy was more marked than in the case of (IIIa'), (IIIb'), and (IIIc').

In order to investigate the cause of such a marked discrepancy, the following experiments were carried out : A mixture of inactive 1,3,4-triacetoxy-2-acetylnaphthalene (I) and acetic[*carbonyl*-^{14}C] anhydride, with sodium acetate or pyridine, was shaken for a long time at room temperature or boiled for a short time, chemically pure 1,3,4-triacetoxy-2-acetylnaphthalene was separated, and its radioactivity was measured. If no interchange of acetyl groups between (I) and radioactive acetic anhydride takes place, there must be no radio-

TABLE II.

Expt. No.	1	2	3
Inactive (I)	0.10 g.	0.20 g.	0.10 g.
Acetic[*carbonyl*-^{14}C] anhydride (1.13×10^6 c.p.m./g.)	6.0 g.	8.0 g.	4.0 g.
Addition	AcONa 25 mg.	AcONa 50 mg.	Pyridine 10 drops.
Condition	Shaken for 6 hr. and stood for 20 hr. at room temp.	Boiled for 4 min.	Boiled for 4 min.
Total activity of Ac_2O used (c.p.m.)	6.78×10^6	9.04×10^6	4.52×10^6
Calcd. total activity of (I) when 100% interchange of acetyl groups takes place (c.p.m.)	4.99×10^4	9.95×10^4	4.97×10^4
Found total activity of (I) (c.p.m.)	30	2.46×10^4	1.33×10^4
Migration ratio of radioactivity (%)	0.06	25	27

activity in the samples separated. The results of these experiments are shown in Table II. As is evident from Table II, under the condition of Expt. 1, which is equivalent to that used in preparation of (Ia′), (Ib′), and (Ic′), migration of radioactivity is negligible. This fact suggests that mutual interchange of acetyl groups would not take place during acetylation process to form (Ia′), (Ib′), and (Ic′).

On the other hand, under the conditions of Expt. 2, which is almost equal to that used in preparation of (Ia), (Ib), and (Ic), a marked migration of radioactivity is observed. This fact indicates that mutual interchange of acetyl groups takes place to a certain degree during acetylation process to form (Ia), (Ib), and (Ic), and such interchange of acetyl groups might be the reason for the discrepancy between determined values of specific activity and expected values being more prominent in the case of (IIIa), (IIIb), and (IIIc), than that observed in the case of (IIIa′), (IIIb′), and (IIIc′). Under the conditions of Expt. 3, namely, when the mixture is boiled for 4 minutes with 10 drops of pyridine, which is a kind of a base, a marked migration of radioactivity is also observed and this fact suggests indirectly that base-catalysed interchange of acetyl groups might take place to a certain degree when (I) is heated at 160~180° for about 10 minutes with equimolar amount of sodium amide in toluene.

In all, about 70~80% of this reaction seems to follow the route of (I)→(I′)→(II), but, complicated intra- and/or inter-molecular rearrangement of acetyl in acetoxyl group at 4-position to the ω-carbon atom in the methyl-ketone group at 2-position, involving mutual interchange of acetyl in acetoxyl groups, might take part in this reaction to about 30%.

Experimental*[2]

1,3-Diacetoxy-2-acetyl-4-acetoxy[*carbonyl*-^{14}C]-naphthalene (Ia)—A mixture of 380 mg. of 1,3-dihydroxy-2-acetyl-4-acetoxy[*carbonyl*-^{14}C]-naphthalene,$^{1)}$ 15.2 g. of Ac_2O, and 30 mg. of AcONa was boiled for 1 min. Resulting pale yellow solution was poured into ice water, the precipitated crystals were collected, washed thoroughly with H_2O, and dried. Four recrystallizations from EtOH gave (Ia) as almost colorless prisms, m.p. 135°. Yield, 107 mg.

1,4-Diacetoxy-2-acetyl-3-acetoxy[*carbonyl*-^{14}C]-naphthalene (Ib)—A mixture of 109 mg. of 2-acetyl-3-acetoxy[*carbonyl*-^{14}C]-4-acetoxy-1-naphthol,$^{1)}$ 4.4 g. of Ac_2O, and 8 mg. of AcONa was boiled for 1 min., the mixture was treated by the same procedure as above, and 27 mg. of (Ib), m.p. 135°, was obtained.

1-Acetoxy[*carbonyl*-^{14}C]-2-acetyl-3,4-diacetoxynaphthalene (Ic)—A mixture of 0.5 g. of 2-acetyl-3,4-diacetoxy-1-naphthol, 20 g. of $(CH_3{}^{14}CO)_2O$, and 40 g. of AcONa was boiled for 1 min., the mixture was treated by the same procedures as above, and 158 mg. of (Ic), m.p. 135°, was obtained.

1,3-Diacetoxy-2-acetyl-4-acetoxy[*carbonyl*-^{14}C]-naphthalene (Ia′)—A mixture of 390 mg. of 1,3-dihydroxy-2-acetyl-4-acetoxy[*carbonyl*-^{14}C]-naphthalene,$^{1)}$ 24 g. of Ac_2O, and 33 mg. of AcONa was shaken mechanically for 6 hr., allowed to stand for 20 hr. at room temperature, the mixture was treated by the same procedure as above, and 125 mg. of (Ia′), m.p. 135°, was obtained.

1,4-Diacetoxy-2-acetyl-3-acetoxy[*carbonyl*-^{14}C]-naphthalene (Ib′)—A mixture of 115 mg. of 2-acetyl-3-acetoxy[*carbonyl*-^{14}C]-4-acetoxy-1-naphthol,$^{1)}$ 6.9 g. of Ac_2O, and 9 mg. of AcONa was shaken mechanically for 6 hr. at room temperature, allowed to stand for 20 hr., the mixture was treated by the same procedure as above, and 30 mg. of (Ib′), m.p. 135°, was obtained.

1-Acetoxy[*carbonyl*-^{14}C]-2-acetyl-3,4-diacetoxy-naphthalene (Ic′)—A mixture of 2-acetyl-3,4-diacetoxy-1-naphthol, 6.0 g. of $(CH_3{}^{14}CO)_2O$, and 8 mg. of AcONa was shaken mechanically for 6 hr., allowed to stand for 20 hr. at room temperature, the mixture was treated by the same procedure as above, and 20 mg. of (Ic′) was obtained.

2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (IIa)—A mixture of 103 mg. of (Ia), 270 mg. of inactive 1,3,4-triacetoxy-2-acetylnaphthalene (I), 42 mg. of powdered $NaNH_2$, and 3.0 cc. of dehyd. toluene was heated in an oil bath at 160~180° for about 10 min., the reaction mixture was treated as previously reported,$^{2)}$ and 70 mg. of (IIa), m.p. 205°, was obtained.

2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (IIb)—From a mixture of 20 mg. of (Ib), 300 mg. of (I), 37 mg. of powdered $NaNH_2$, and 2.6 cc. of dehyd. toluene, 70 mg. of (IIb), m.p. 205°, was obtained by the same procedure as above.

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*[2] All m.p.s of radioactive samples were not depressed on admixture with authentic inactive samples.

2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (IIc)—From a mixture of 150 mg. of (Ic), 230 mg. of (I), 44 mg. of powdered $NaNH_2$, and 3.0 cc. of dehyd. toluene, 85 mg. of (Ic), m.p. 205°, was obtained by the same procedure as above.

2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (IIa')—From a mixture of 120 mg. of (Ia'), 253 mg. of (I), 43 mg. of powdered $NaNH_2$, and 3.0 cc. of dehyd. toluene, 73 mg. of (IIa'), m.p. 205°, was obtained by the same procedure as above.

2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (IIb')—From a mixture of 25 mg. of (Ib'), 305 mg. of (I), 37 mg. of powdered $NaNH_2$, and 2.6 cc. of dehyd. toluene, 78 mg. of (IIb'), m.p 205°, was obtained by the same procedure as above.

2-Methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (IIc')—From a mixture of 18 mg. of (Ic'), 270 mg. of (I), 33 mg. of powdered $NaNH_2$, and 2.4 cc. of dehyd. toluene, 64 mg. of (IIc'), m.p. 205°, was obtained by the same procedure as above.

2-Methyl-3-acetyl-5,6-dihydroxy-7,8-benzochromones (IIIa, IIIb, IIIc, IIIa', IIIb', and IIIc')—A solution of 50 mg. of (IIa), (IIb), (IIc), (IIa'), (IIb'), or (IIc') dissolved in 1.0 g. of ice-cold H_2SO_4, which colored deep red, was allowed to stand for 10 min. at room temperature and ice water was added to the solution. The separated yellow precipitate was collected, washed thoroughly with H_2O, and recrystallized twice from EtOH to afford about 20 mg. of (IIIa), (IIIb), (IIIc), (IIIa'), (IIIb'), or (IIIc'), m.p. 226°.

Analysis of radioactivity and correction of self-absorption were carried out as previously reported.[1]

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Summary

The mechanism of novel cyclization of 1,3,4-triacetoxy-2-acetylnaphthalene (I) to 2-methyl-3-acetyl-5-hydroxy-6-acetoxy-7,8-benzochromone (II) was investigated by the ^{14}C-tracer method and it was found that about 70~80% of the reaction followed the route of $(I)\rightarrow(I')\rightarrow(II)$.

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