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Photochemical Reaction of Isocoumarin and Related Compounds

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The effect of irradiation with ultraviolet ray for methanol solution of 2-carboxystyrenes and 3,4-dihydroisocoumarins were examined.

Irradiation of 2-carboxystyrene and its β-(4′-methoxyphenyl), β-methyl, β,β-dimethyl, and β-cyclohexylidenemethyl derivatives gave the corresponding cyclized compounds.

Some of these reactions were reversible since styrene derivatives were obtained from 3,4-dihydroisocoumarins in the same manner.

In the case of ring closed reactions of β-alkyl substituted 2-carboxystyrenes, such as β-methyl, β,β-dimethyl, and β-cyclohexylidenemethyl derivatives, the rearranged products were obtained. These products agreed with each of an authentic sample which was synthesized by another, method.

Keywords——photo-cyclization; photo-cleavage; photo-rearrangement; 3,4-dihydroisocoumarins; 2-carboxystilbenes; 2-carboxystyrenes

Since 1972, Yamato has reported syntheses of isocoumarin derivatives, and on the relationship between the chemical structure of isocoumarins and sweet taste. Isocoumarin derivatives do not have toxicity, or little, if any, and hence, it seems worth to design a drug using isocoumarin ring as a carrier. The object of the present experiment was to synthesize 3,4-dihydroisocoumarins by irradiation of styrenecarboxylic acid and its derivatives.

A number of papers have been published on the photoreaction of coumarins and their related compounds such as the photodimerization of coumarins,[2] formation of 3-methyl-4-phenylisocoumarin from 2,3-epoxy-2-methyl-3-phenylindanone,[3] and preparation of 3,4-diphenyl-6-methoxyisocoumarin from 2-phenyl 7-methoxyisoflavon[4] by irradiation of ultraviolet (UV) rays. Although *cis-trans* isomerization[5] and photoxidation[6] of styrenes and stilbenes, which were used as the starting materials in the present work, are known, there is no report on the attempted synthesis of 3,4-dihydroisocoumarins by irradiation of 2-carboxystyrene derivatives.

Irradiation of a methanol solution of 2-carboxy-4′-methoxystilbene (I)[7] with 100-W high-pressure mercury lamp gave two products; *cis*-2-carboxy-4′-methoxystilbene (I′) and 3-(4-methoxyphenyl)-3,4-dihydroisocoumarin (II). The compound I′ had a lower melting point and showed its UV absorption maximum at a lower region than those of I. As a whole, δ-values of I′ in nuclear magnetic resonance (NMR) spectrum shifted to a higher magnetic field. Therefore, I′ seems to be *cis*-form of I. The compound II showed no depression in mixed melting point measurement with the authentic sample of II, prepared by heating 2-carboxy-α-ethoxycarbonyl-4′-methoxystilbene with hydrochloric acid in acetic acid.

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[1] Location: *Tsushima-naka, 1-1-1, Okayama, 700, Japan.*

[2] G.S. Hamond, C.A. Stout, and A.A. Lamole, *J. Am. Chwm. Soc.*, 86, 3103 (1964); H. Morrison, H. Curtis, and T. McDowell, *J. Am. Chem. Soc.*, **88**, 5415 (1966).

[3] H.E. Zimmerman and R.D. Simkin, *Tetrahedron Lett.*, **1964**, 1847.

[4] N. Ishibe and S. Yutaka, *Tetrahedron,* **32**, 1331 (1964).

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[7] M. Yamato, K. Hashigaki, Y. Kuwano, and T.Koyama, *Yakugaku Zasshi*, **92**, 535 (1972).

NMR and mass spectral data of II suggested that it has a lactone ring in its molecule. For the formation of II, introduction of a new proton into the ethylene moiety of I will be necessary. The use of isopropanol instead of methanol in the above photoreaction, however, failed to increase the yield of II.

The same photoreaction was carried out with esters of I, such as 2-methoxycarbonyl-4′-methoxystilbene (III), 2-ethoxycarbonyl-4′-methoxystilbene (IV), and 2-benzyloxycarbonyl-4′-methoxystilbene (V). A small amount of II and a large amount of *cis*-form compound (III′) were separated from the reaction mixture of III, while in the reaction with IV, the formation of II was detected only by thin-layer chromatography (TLC), and a mixture of *trans* and *cis* forms of IV, in a ratio of 1: 3, was obtained. In the reaction with V, II was not detected at all and a mixture of *trans* and *cis* forms of V, in a ratio of 1: 3 was obtained.

Irradiation of 2-carboxystilbene (VI) with a high-pressure mercury lamp gave *cis*-2-carboxystilbene (VI′) but the cyclized 3-phenyl-3,4-dihydroisocoumarin (VII) was not obtained. The same result was obtained when a 30-W low-pressure mercury lamp was used instead of the high-pressure mercury lamp. From these facts, it can be presumed that the methoxyl group in the 4′-position of stilbenes must have some effect on this photocyclization.

The same reaction was carried out on 2,α-dicarboxy-4′-methoxystilbene (VIII) but only the starting material was recovered, and neither the cyclized compound nor the *cis*-form compound was obtained.

Irradiation of methanol solution of II with high-pressure mercury lamp gave the ring opening compound I′. The formation of VII by cyclization of VI did not progress, but the ring opening of VII proceeded to give VI′. Based on these results, it may be concluded that photocyclization of 2-carboxystilbenes is a reversible reaction. The photoreaction between I and II is reversible, and hence, it was considered preferrable to measure the convertible substance by using gas chromatography (GC). The alternation from I to the equilibrium mixture of I and II was attained in about 5 hr by irradiation of a methanol solution and, according to the assay by GC (OV-1, 1.5 m; N_2, 40 ml/min; column temp., 210°; internal standard, 0.1% pyrene; retention time, 7.5 min) the yield of II reached 53%.

I: R_1, R_2=H, R_3=OCH_3
III: R_1=CH_3, R_2=H, R_3=OCH_3
IV: R_1=C_2H_5, R_2=H, R_3=OCH_3
V: R_1=CH_2-C_5H_6, R_2=H, R_3=OCH_3
VI: R_1, R_2, R_3=H
VIII: R_1=H, R_2=COOH, R_3=OCH_3

II: R_2=H, R_3=OCH_3
VII: R_2, R_3=H

Chart 1

For the mechanism of photocyclization, two pathways can be presumed; namely, ionic mechanism similar to cyclization in an acidic medium and bi-radical mechanism. If it were an ionic mechanism, it cannot explain the fact that while both I and VI undergo cyclization with the aid of a mineral acid, VI did not undergo cyclization by irradiation. When it comes to taking up the bi-radical pathway, as shown in Chart 2, 3,4-dihydroisocoumarins must be produced by passing through route (A) and benzylphthalides through route (B). Berti⁸⁾ actually obtained a mixture of VII and 3-benzylphthalide by the reaction of VI with benzyl peroxide. However, phthalides were not obtained by irradiation of I and VI in the present work. Therefore, the mechanism of photocyclization is still uncertain.

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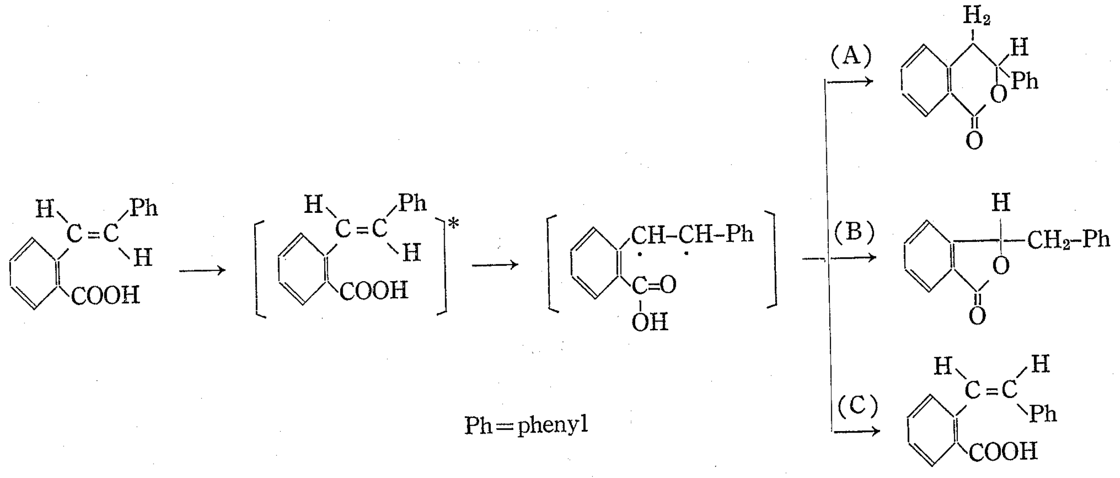

Chart 2

The ring opening reaction seems to have been initiated with pulling out of hydrogen in γ-position. As benzylphthalides have hydrogen in γ-position, a ring opening reaction may occur if the hydrogen was extruded, and presumably 2-carboxystilbenes will be produced. 3-(4-Methoxybenzyl)phthalide (X)[9] and 3-(2-carboxybenzyl)phthalide (XI)[10] were irradiated, but isocoumarins and 2-carboxystilbenes were not obtained and almost all of the starting materials were recovered. This is probably due to the resistance of phthalides to irradiation.

Irradiation of 2-carboxystyrene (XII),[11] which was synthesized as a sample of simple styrene derivatives, was carried out in methanol solution by using low-pressure mercury lamp. 3,4-Dihydroisocoumarin (XIII) was obtained in about 6% yield and it agreed with analytical data of an authentic sample obtained by another method. In this reaction, colorless powder was recovered with the starting material. According to Sakaguchi's report,[11] polymer-A was obtained by the reaction of XII with benzoyl peroxide in benzene solution. The infrared (IR) spectrum of the colorless powder agreed with the polymer-A.

The photoreactions of β-substituted styrenes were examined. Irradiation of 2-carboxy-β,β-dimethylstyrene (XIV) in methanol solution gave three products; mixture-A, compound-B, and the starting material. The mixture-A seemed to consist of two species from its NMR spectrum and it was separated by GC to A-1 and A-2 in 1:3 ratio. The GC-mass spectrometry (GC–MS) of A-1 showed a parent peak at m/e 176 (M^+) and a base peak at m/e 118 ($M^+-CH_3COCH_3$), while the signal of $\delta=3.0$ (2H, s) appeared in its NMR spectrum. Since these data agreed very closely with the authentic sample of 3,3-dimethyl-3,4-dihydroisocoumarin (XV), which was obtained by the usual method, it was established that the structure of A-1 was the same as XV. The compound A-2 showed m/e 176 (M^+) and m/e 146 (M^+-30) in GC–MS. Therefore, the compound A-2 is the isomer of XV which could be 1,1-dimethylisochroman-4-one (XVI)[12] or 4,4-dimethyl-3,4-dihydroisocoumarin (XVII), because the presence of fragment peak at m/e 147 suggests that H_2CO was released from the parent peak. Each of these compounds were synthesized by another pathway and it was proved that A-2 was identical to XVII. These facts indicate that this reaction also gave a rearranged compound, XVII, besides the normal cyclized compound, XV. The compound-B seemed to have one hydroxyl group from its NMR spectrum. The compound XV was produced by catalytic hydrogenation of compound-B over palladium-carbon. From these facts, the

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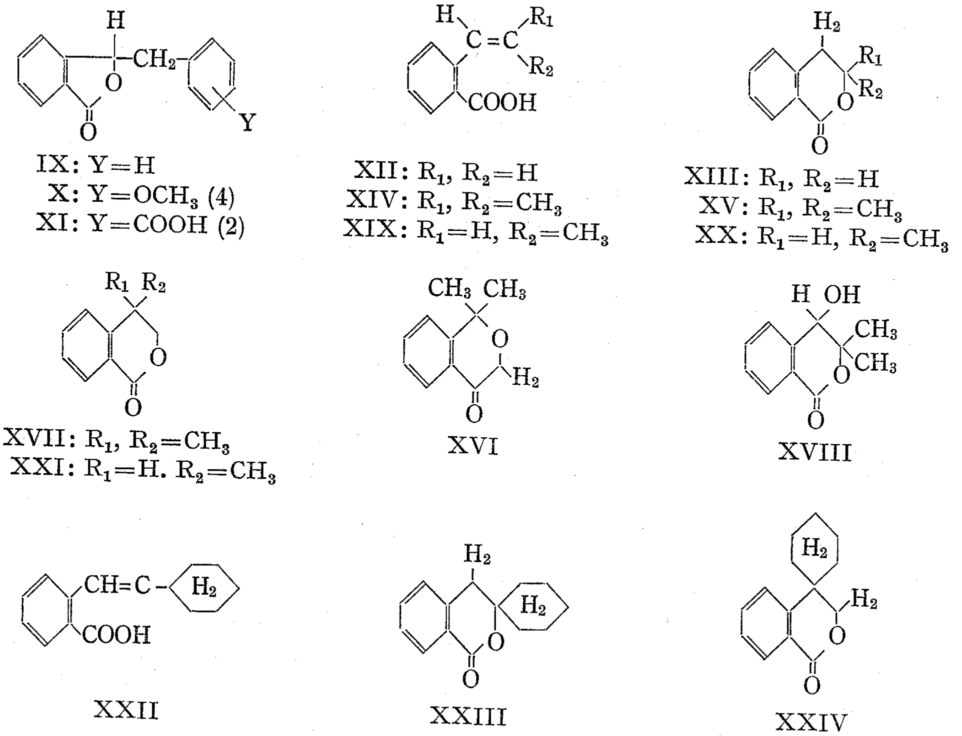

IX: $Y=H$
X: $Y=OCH_3$ (4)
XI: $Y=COOH$ (2)

XII: $R_1, R_2=H$
XIV: $R_1, R_2=CH_3$
XIX: $R_1=H, R_2=CH_3$

XIII: $R_1, R_2=H$
XV: $R_1, R_2=CH_3$
XX: $R_1=H, R_2=CH_3$

XVII: $R_1, R_2=CH_3$
XXI: $R_1=H. R_2=CH_3$

XVI

XVIII

XXII

XXIII

XXIV

Chart 3

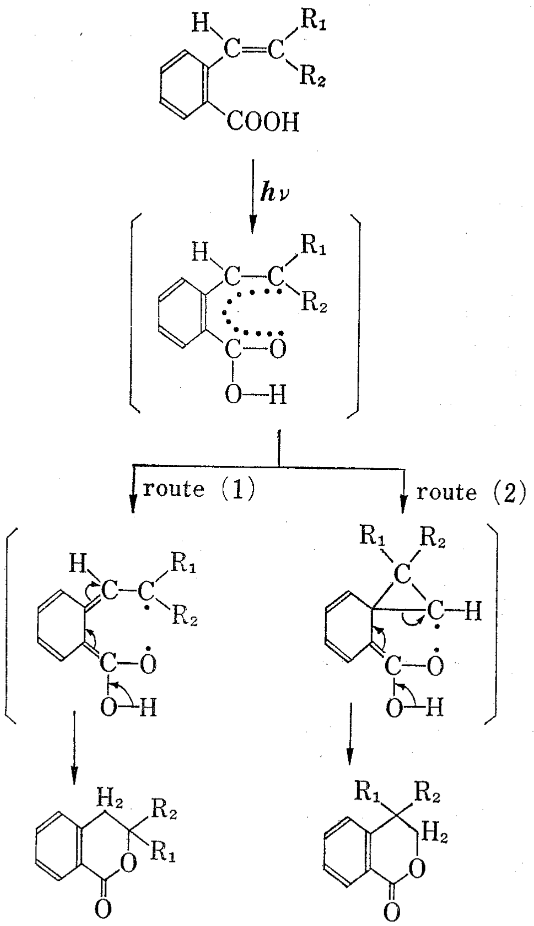

Chart 4

Table I. The Conditions and Results of Photoreactions

React. No.	Reactant	Lamp	React. time (hr)	Product
1	I	HPML	5	I′, II
2	I	HPML	5	I′, II
3	III	HPML	5	III′, II
4	IV	HPML	15	IV′
5	V	HPML	15	V′
6	VI	HPML	10	VI′
7	VI	LPML	10	VI′
8	VIII	HPML	10	—
9	X	HPML	40	—
10	XI	HPML	10	—
11	XI	LPML	15	—
12	XII	LPML	25	XIII, Polymer
13	XIV	HPML	15	XV, XVII, XVIII
14	XIX	LPML	10	XIX′, XXI
15	XXII	LPML	10	XXIII, XXIV
16	II	HPML	5	I′
17	VII	LPML	5	VI′
18	XIII	LPML	25	XII
19	XV	LPML	20	—
20	XVII	LPML	30	—
21	XX	LPML	10	XIX′
22	XXI	LPML	10	—
23	XXIII	LPML	10	XXII
24	XXIV	LPML	10	—

compound-B seems to be 3,3-dimethyl-4-hydroxy-3,4-dihydroisocoumarin (XVIII), formed by photo-oxidation of XIV in the presence of a small amount of oxygen.

As other example of photorearrangement, irradiation of 2-allylbenzoic acid (XIX) was carried out. Normal cyclized 3-methyl-3,4-dihydroisocoumarin (XX)[13] was not obtained but the rearrangement product, 4-methyl-3,4-dihydroisocoumarin (XXI), was isolated. The *cis*-form of the starting material was also isolated in this reaction, which changed gradually to the *trans*-form during purification. These photorearrangements occurred with 2-carboxy-β-alkylstyrenes, but not with β-aryl derivatives. Irradiation of 2-cyclohexylidenemethylbenzoic acid (XXII), which has a bulky group in β-position of styrene, gave both the normal cyclized 3-spiro-cyclohexane-3,4-dihydroisocoumarin (XXIII) and the rearranged 4-spiro-cyclohexane-3,4-dihydroisocoumarin (XXIV).

The ring opening reactions of these 3,4-dihydroisocoumarin derivatives without a phenyl group in their 3-position were examined. Irradiation of XIII, XX, and XXIII gave the corresponding ring-opened derivatives but XV, XVII, XXI, and XXIV did not undergo any reaction. If the ring opening reaction initiate with pulling out of hydrogen in γ-position, it is natural that XVII and XXIV do not react by irradiation. However, XV and XXI did not react even though they have hydrogen in their γ-position. It was presumed that, if these products were recycled after the ring opening reaction of XX and XXIII, there is a possibility that rearranged compounds XXI and XIV might be produced under the same condition, but they were not isolated.

As shown in Chart 4, two routes of photorearrangement can be considered; if the photoreaction passes through route (1), normal reaction may occur. When it passes through route (2), rearrangement reaction may take place. In the latter pathway, a 3-membered ring compound may temporarily form as an intermediate. There is no way to prove positively that this photoreaction passes through either of these two routes.

Results of the present photoreaction are summarized in Table I. As stated above, the photoreaction of 2-carboxystyrenes unexpectedly gave rearranged products.

Experimental

All melting points were measured on a micro hot stage apparatus and uncorrected. NMR spectra were obtained on a Hitachi Model R-22 spectrometer at 90 MHz in the $CDCl_3$ solution employing tetramethylsilane as an internal standared. Mass spectra were measured by a Shimadzu Model LKB-9000 spectrometer. IR spectra were obtained on a Nipponbunko Model DS-301 spectrometer. UV spectra were measured on a Hitachi EPS-2 spectrometer. Gas chromatograph was employed Shimadzu GC-6AM.

3-(4-Methoxyphenyl)-3,4-dihydrocoumarin (II)——A suspension of 2-carboxy-α-ethoxycarbonyl-4′-methoxy-stilbene (1 g), acetic acid (6 ml), and H_2O (7.5 ml) was refluxed for 7 hr. The solvent was distilled off under reduced pressure, and the residue was recrystallized from EtOH. Colorless plates (0.6 g, 76.9%). mp 109—110°, MS *m/e*: 254 (M^+). *Anal.* Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.50; H, 5.52. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 273, 279.5, 287.

2-Methoxycarbonyl-4′-methoxystilbene (III)——The compound I (2.1 g) dissolved in mixture of 70 ml of ether and 30 ml of $CHCl_3$. This solution was treated with diazomethane. After standing for 6 hr, 20 ml of 2 N H_2SO_4 was added into the reaction mixture. The organic layer was separated and washed with 10% $KHCO_3$ solution and water. The solvent was removed and recrystallization of the residue from cyclohexane gave III as colorless plates. (1.58 g, 72.0%) mp 81—82.5°. MS *m/e*: 268 (M^+), 237 (M^+-OCH_3), 209 ($M^+-COOCH_3$). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 322.5, 300.

2-Ethoxycarbonyl-4′-methoxystilbene (IV)——To a mixture of I (2 g) and diethylsulfate (1.04 ml), 20% NaOH solution (2 ml) was added dropwise and heated at 100° for 2 hr. After cooling, the mixture was poured into 100 ml of ice-water and was extracted with ether. After removal of solvent, the residue was purified on a column (silica gel) with benzene to give a pale yellow oil (1.34 g, 60.5%). MS *m/e*: 282 (M^+). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 323, 300, 250.

2-Benzylcarbonyl-4′-methoxystilbene (V)——To a solution of KOH (0.5 g) and abs.EtOH (70 ml), I (2 g) was dissolved. The EtOH was evaporated, and the residue was dissolved in dimethylformamide (80 ml). To this solution, a mixture of dimethylformamide (20 ml) and benzylalcohol (19 ml) was added

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13) R.B. Tirodkar and R.N. Usganokar, *J. Indian Chem. Soc.*, 46, 935 (1969).

dropwise at 40° during 10 min. The reaction mixture was refluxed for 6 hr. After cooling, the mixture was poured into 100 ml of ice-water and extracted with ether. The solvent was distilled off, and the residue was purified by column chromatography (silica gel) with benzene. The pale yellow oil of V was obtained 0.9 g, 58.8%). MS *m/e*: 344 (M^+). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 319, 297.

3,4-Dihydroisocoumarin (XIII)——To a solution of isochroman (9.12 g)[14] in 100 ml of glacial acetic acid, a mixture of CrO_3 (250 g) in 60% acetic acid (350 ml) was added dropwise at 30°. After stirring for 1 hr at room temperature, the mixture was diluted with water (500 ml) and extracted with CH_2Cl_2. The organic layer was washed with 10% $KHCO_3$ solution and water. Removal of the solvent gave colorless oil of XIII, which was distilled under reduced pressure (6,59 g, 65.6%). bp 149—154°/13 mmHg. MS *m/e*: 148 (M^+), 118 (M^+-CH_2O). *Anal.* Calcd. for $C_9H_8O_2$: C, 72.96; H, 5.44. Found: C, 72.81; H, 5.35. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 334, 278.

2-Carboxy-β,β-dimethylstyrene (XIV)——A mixtire of 2-α-dicarboxy-β,β-dimethylstyrene (12.6 g), dimethyl-formamide (100 ml), H_2O (20 ml), and KOH (3.21 g) was refluxed for 7 hr at 150—160°. After cooling, the mixtute was diluted with 500 ml of water and was acidified with dil. HCl and then extracted with ethyl acetate. The solvent was distilled off, and the residue was dissolved with 10% KOH solution. After shaking with ethyl acetate, the basic aqueous layer was neutralized with dil. HCI, and extracted with ethyl acetate. The solvent was distilled off, and recrystallization of residue from benzene gave XIV as colorless needles (2.25 g, 25.3%). mp 65—67°, *Anal.* Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.85; H, 6.99. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 292, 247. In this treatment, 3,3-dimethyl-3,4-dihydroisocoumarin X was obtained from the ethyl acetate, which was obtained as extract from the acidic reaction mixture (2.81 g, 27.9%) Colorless oil. bp 153—154°/11 mmHg. MS *m/e*: 176 (M^+), 118 $(M^+-CH_3COCH_3)$. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 288, 282.

4,4-Dimethyl-3,4-dihydrosiocoumarin (XVII)——It was obtained from 4,4-dimethylisochroman[15] (8.1 g) and CrO_3 (17.15 g) by the method as in XIII. The colorless oil was obtained (6.9 g, 78.4%). bp 131—133°/2 mmHg. MS *m/e*: 176 (M^+), 146 (M^+-CH_2O). *Anal.* Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.82: H, 6.78. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 287, 280.

2-Allyl-benzoic Acid (XIX)——A mixture of 2-allyl-bromobenzene (3.5 g), dry ether (40 ml), and Mg (0.86 g) was refluxed 4 hr with trace of iodine. After cooling, the solution was poured into a large amount of dry-ice, acidified with 10% H_2SO_4 and extracted with ether. The organic layer was washed with saturated NaCl solution and extracted with 5% KOH solution (50 ml × 5). The crude product was obtained by acidified the basic aqueous layer with 10% H_2SO_4. It was recrystallized from 70% EtOH (1.52 g, 52.8%). Colorless needles. mp 80—82°. MS *m/e*: 162 (M^+). *Anal.* Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.43; H, 6.22. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 297.

4-Methyl-3,4-dihydroisocoumarin (XXI)——It was obtained from 4-methylisochroman (11 g) and CrO_3 (25.5 g) by the same method as in XIII. The colorless oil was obtained (9.5 g, 78.9%). bp 154—156°/8 mmHg. MS *m/e*: 162 (M^+), 132 (M^+-CH_2O). *Anal.* Calcd. for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 74.28; H, 6.19. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 288, 282.

2-Cyclohexylidenemethylbenzoic Acid (XXII) and 3-Spiro-cyclohexane-3,4-dihydroisocoumarin (XXIII)——A mixture of α-cyclohexylidenehomophthalic acid[16] (11.2 g), 10% KOH (25 ml) and dimethylformamide (80 ml) was heated at 160—170° for 8 hr in a stream of nitrogen. After cooling, 300 ml of water was poured into the reaction mixture, acidified with 10% H_2SO_4, and extracted with ether. The ether layer was washed with saturated NaCl solution and the solvent was distilled off. The residue was purified by column chromatography using silica gel and CH_2Cl_2. The earlier elution was distilled under reduce pressure. The compound XXIII was obtained as colorless oil (3.1 g, 33.3%). bp 172—173°/3 mmHg. MS *m/e*; 216 (M^+). 118 $(M^+-C_6H_{10}O)$. *Anal.* Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.54; H, 7.38. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 282.5, 290. The solid that obtained from the latter elution was rechromatographed with silica gel using CH_2Cl_2. The crude product of XXII was obtained. It was recrystallized from large quantity of pet. ether (1.6 g, 17.2%). Colorless plates. mp 97—98° MS *m/e*: 216 (M^+). *Anal.* Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.71; H, 7.52. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 239.

4-Spiro-cyclohexaneisochroman——1-Hydroxymethyl-1-phenylcyclohexane[17] (6.5 g) was added to the mixture of paraldehyde (1.4 g) and ether (40 ml). A stream of hydrogen chloride was passed through the mixture at a temperature between 0° and 10° till saturation and subsequently for 6 hr at a temperature of about 35—40°. After cooling, the ice water was added into the reaction mixture, and extracted with benzene. The benzene layer was heated under reflux with NaOH (4 g) in H_2O (20 ml). The organic layer was separated, washed with water, and distilled *in vaccuo* (3.2 g, 46.4%). Colorless oil bp 145—146°/5 mmHg. NMR (in $CDCl_3$) δ: 1.05—2.18 (10H, m, protons of cyclohexane ring), 3.82 (2H, s, C_3-H), 4.69 (2H, s, C_1-H), 6.80—7.37 (4H, m, aromatic-H). MS *m/e*: 202 (M^+), 172 (M^+-CH_2O).

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15) C. Van der Stelt, P.S. Hofmann, and W.T. Naute, *Rec. Trav. Chem.*, **84**, 633 (1965).
16) H.J.E. Loewenthal and R. Pappo, *J. Chem. Soc.*, **1952**, 4799.
17) J.W. Wilt and D.D. Roberts, *J. Org. Chem.*, **27**, 3434 (1962).

4-Spiro-cyclohexane-3,4-dihydroisocoumarin (XXIV)——It was obtained from 4-spiro-cyclohexane-isochroman (3.2 g) and CrO_3 (5 g) by the same method as in XIII (2.4 g, 70.2%). bp 194—196°/5 mmHg. Colorless oil. *MS m/e*: 216 (M^+), 186 (M^+-CH_2O). *Anal.* Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.86; H, 7.43. UV λ_{max}^{MeOH} nm: 282.5, 290.

Photoreactions——General Method: A solution of the compound (1 g) in MeOH (1000 ml) was irradiated with 100-W high-pressure mercury lamp (HPML) or 30-W low-pressure mercury lamp (LPML) under nitrogen at room temperature. The solvent was distilled off *in vaccuo* at room temperature and purified by column chromatography (silica gel). The conditions of the reactions were shown in Table I.

React. No. 1——The compound I′ and II were obtained from the elution of CH_2Cl_2. II was recrystallized from EtOH (232 mg, 23.2%). Colorless plates. This compound showed no depression in mixed melting point with definite sample and NMR, MS spectra, and elemental analysis data agreed with the authentic sample. I′ was recrystallized from EtOH (73 mg, 7.3%). Colorless plates. mp 129—130.5°. MS *m/e*: 254 (M^+). UV λ_{max}^{MeOH} nm: 296.5, 277, 228. The δ-values of NMR spectrum of I showed as in Table II, and the melting point and UV spectrum of I showed as follows; mp 196°, UV λ_{max}^{MeOH} nm: 307, 318. Since the compound I′ seems to be *cis*-form of I.

React. NO. 2——It was treated by the same method as in react. No. I. The compound II (70 mg, 7.0%) and I′ (204 mg, 20.4%) was obtained.

React No. 3——The compound III′ was obtained from the fraction of benzene and II (32 mg, 3.2%) was also obtained from the fraction of CH_2Cl_2. Recrystallization of benzene elution from 50% EtOH, gave III′ as colorless needles. mp 44—46.5°. UV λ_{max}^{MeOH} nm: 306, 278.5, 233. This compound seems to be *cis*-form of III.

React. No. 4——It was treated by the same method as in React. No. 3. The pale yellow oily product (650 mg, 65.0%) was obtained from the benzene fraction. UV λ_{max}^{MeOH} nm: 304.5, 273, 235. This compound seems to be *cis*-form of IV. The compound II was observed only on the TLC (silica gel, developer: toluene/ethyl formate/formic acid =5/4/1).

React. No. 5——It was treated as above. Only *cis*-form of V was obtained (673 mg, 67.3%) as pale yellow oil.

React. No. 6 and 7——They were treated as in React No.3. Only *cis*-form of VI was obtained with the yield of about 80%. Colorless plates. mp 151—152°.

React. No 8. 9, 10, and 11——They were treated by the usual method but the starting materials were removed with in high proportion.

React. No. 12——The solvent of the reaction mixture was distilled off and the residue dissolved with CH_2Cl_2. Then, the insoluble substance was obtained as colorless powder (230 mg). The IR spectrum (cm^{1-}: 1695) of this powder agreed with Sakaguchi's polymer-A. The CH_2Cl_2 soluble substance was purified with chromatography to give XIII as pale yellow oil (58 mg, 5.8%). Its analytical data agreed with authentic sample.

React. No. 13——It was treated by the same way as in React. No. 3. First, it was eluted with benzene and next with CH_2Cl_2. From the benzene fraction mixture-A (earlier elution) and starting material (later elution) were obtained, and then, it was attempted to separate the mixture-A using alumina column chromatography ($CHCl_3$). But it was not successful in isolation, and pale yellow oil was obtained (40 mg). According to the gas chromatography (OV-1, 1.5 m, N_2 gas 40 ml/min, column temp. 120°), the pale yellow oil was divided two peaks such as peak-I (retention time 7.3 min) and peak-II (retention time 7.8 min), and ratio of area of the peaks showed 1: 3. GC–MS *m/e*: peak-I; 176 (M^+), 118 ($M^+-CH_3COCH_3$). Peak-II; 176 (M^+), 146 (M^+-CH_2O). From these data and NMR spectrum, the substance peak-I seems to be XV and the peak-II seems to be XVII. The oily product was obtained from the CH_2Cl_2 fraction. It was rechromatographed using silica gel and $CHCl_3$. The compound-B was obtained as pale yellow oil (160 mg). A solution of compound-B in MeOH was hydrogenated over 10% palladium-carbon. The solvent was distilled off, and purified on column (silica gel/$CHCl_3$). XIV was obtained as colorless oil (20 mg).

React. No. 14——It was treated by the same way as above. The rearranged compound XXI and mixture of *trans*-form XIX and *cis*-form XIX′ were obtained. The compound XXI was rechromatographed (silica gel) with benzene (205 mg, 20.5%). Colorless oil. MS *m/e*: 162 (M^+), 132 (M^+-CH_2O). UV λ_{max}^{MeOH} nm: 288, 282. The mixture of XIX and XIX′ was recrystallized from 70% MeOH but XIX′ cannot be separated, because it changed gradually to *trans*-form with laps of time.

React. No 15——It was treated as above. The oily product was obtained from the benzene fraction (270 mg). According to the gas chromatography (OV-17, 2m, N_2 gas 40 ml/min, column temp. 250 °), the product was divided two peaks such as peak-I (retention time 3.8 min) and peak-II (retention time 5.0 min) and ratio of peak area showed 1: 3. GC–MS *m/e*: peak-I; 216 (M^+), 118 ($M^+-C_6H_{10}O$). peak-II; 216 (M^+), 186 (M^+-CH_2O). The δ-values of NMR spectrum of peak-I agreed with that of XXIII, and peak-II also agreed with that of XXIV.

React. No. 16——It was treated by usual way. The compound I′ was obtained from CH_2Cl_2 fraction as colorless plates (97 mg, 9.7%). Its analytical data agreed with that of the sample which was obtained in React. No. 1.

React No. 17——It was treated as above. VI′ (164 mg, 16.4%) was obtained. Its analytical data agreed with that of the sample which was obtained in React. No. 6.

React. No. 18——It was treated as above. XII (124 mg, 12.4%) was obtained. Its analytical data agreed with that of the authentic sample.

React. No. 21——It was treated as above. From the CH_2Cl_2 fraction, mixture of XIX and 20 mg of XIX′ was obtained.

Table II. NMR Spectra of Related Compounds

No.	NMR (δ) in $CDCl_3$
I	3.78 (3H, s, $OC\underline{H}_3$), 6.81—8.19 (10H, m, vinyl and aromatic-H)
I′	3.68 (3H, s, $OC\underline{H}_3$), 6.55—7.50 (9H, m, vinyl and aromatic-H), 7.95—8.20 (1H, m, C_3–H)
Ⅱ	3.78 (3H, s, $OC\underline{H}_3$), 3.05—3.25 (2H, m, C_4–H), 5.50 (1H, dd, $J_1=4$ Hz, $J_2=16.5$ Hz, C_3–H), 6.70—7.90 (7H, m, aromatic-H), 8.13 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
Ⅲ	3.77 (3H, s, $OC\underline{H}_3$), 3.87 (3H, s, $OC\underline{H}_3$), 6.80—7.97 (10H, m, vinyl and aromatic-H)
Ⅲ′	3.68 (3H, s, $OC\underline{H}_3$), 3.83 (3H, s, $OC\underline{H}_3$), 6.50 (1H, d, $J=12$ Hz, vinyl-H), 6.61 (2H, dd, $J_1=8$ Hz, $J_2=2$ Hz, $C_{3',5'}$–H), 6.88 (1H, d, $J=12$ Hz, vinyl-H), 6.95 (2H, dd, $J_1=8$ Hz, $J_2=2$ Hz, $C_{2',6'}$–H), 6.70—7.78 (3H, m, aromatic-H), 7.80—8.00 (1H, m, C_3–H)
IV	1.36 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 3.77 (3H, s, $OC\underline{H}_3$), 4.33 (2H, q, $J=7$ Hz, $COOC\underline{H}_2CH_3$), 6.70—8.00 (10H, m, vinyl and aromatic-H)
IV′	1.32 (3H, t, $J=7$ Hz, $COOCH_2C\underline{H}_3$), 3.67 (3H, s, $OC\underline{H}_3$), 4.27 (2H, q, $J=7$ Hz, $COOC\underline{H}_2CH_3$), 6.48 (1H, d, $J=12$ Hz, vinyl-H), 6.66 (2H, dd, $J_1=8$ Hz, $J_2=2$ Hz, $C_{3',5'}$ –H), 6.87 (1H, d, $J=12$ Hz, vinyl-H), 7.94 (2H, dd, $J_1=8$ Hz, $J_2=2$ Hz, $C_{2',6'}$–H), 7.05—7.78 (3H, m, aromatic-H), 7.79—8.00 (1H, m, (C_3–H)
V	3.82 3H, s, $OC\underline{H}_3$), 5.40 (2H, s, $C\underline{H}_2C_6H_5$), 6.60—8.13 (15H, m, vinyl and aromatic-H)
V′	3.68 (3H, s, $OC\underline{H}_3$), 5.32 (2H, s, $C\underline{H}_2C_6H_5$), 6.53 (1H, d, $J=12$ Hz, vinyl-H), 6.64 (2H, dd, $J_1=8$ Hz, $J_2=12$ Hz, vinyl-H), 6.98 (2H, dd, $J_1=8$ Hz, $J_2=2$ Hz, $C_{2',6'}$–H), 7.10—7.78 (8H, m, aromatic-H), 7.80—8.13 (1H, m, C_3–H)
VI′	6.62 (1H, d, $J=12$ Hz, vinyl-H), 7.08 (1H, d, $J=12$ Hz, vinyl-H), 6.80—7.50 (8H, m, aromatic-H), 7.84—8.20 (1H, m, C_3–H), 10.66—11.65 (1H, very broad, $COO\underline{H}$)
X	1.45 (6H, s, $C\underline{H}_3\times 2$), 3.00 (2H, s, C_4–H), 7.19—7.64 (3H, m, aromatic-H), 8.13 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
XⅢ	3.01 (2H, t, $J=6$ Hz, C_4–H), 4.48 (2H, t, $J=6$ Hz, C_3–H), 7.05 (3H, m, aromatic-H), 8.02 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
XIV	1.70 (3H, s, $C\underline{H}_3$), 1.92 (3H, s, $C\underline{H}_3$), 6.77 (1H, broad, vinyl-H), 7.25—7.63 (3H, m, aromatic-H), 8.09 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_3–H), 10.73 (1H, broad, $COO\underline{H}$)
XV	1.44 (6H, s, $C\underline{H}_3\times 2$), 3.00 (2H, s, C_4–H), 7.18—7.70 (3H, m, aromatic-H), 8.12 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
XVⅡ	1.33 (6H, s, $C\underline{H}_3\times 2$), 4.16 (2H, s, C_3–H), 7.24—7.68 (3H, m, aromatic-H), 8.08 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
XVⅢ	1.42 (6H, s, $C\underline{H}_3\times 2$), 2.45 (1H, broad, $O\underline{H}$), 4.68 (1H, s, C_4–H), 7.28—7.74 (3H, m, aromatic-H), 8.05 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
XIX	1.82 (3H, dd, $J_1=6$ Hz, $J_2=1$ Hz, $C\underline{H}_3$), 5.87—6.15 (1H, m, vinyl-H), 6.95—7.40 (4H, m, vinyl and aromatic-H), 7.79 (1H, d, with shoulder, $J=6$ Hz, C_6–H), 10.30 (1H, very broad, $COO\underline{H}$)
XIX′	1.71 (3H, dd, $J_1=6$ Hz, $J_2=1$ Hz, CH_3), 5.72—6.23 (1H, m, vinyl-H), 6.93 (1H, d, with shoulder, $J=12$ Hz, vinyl-H), 6.96—7.60 (3H, m, aromatic-H), 7.95 (1H, d, with shoulder, $J=6$ Hz, C_6–H), 9.67 (1H, broad, $COO\underline{H}$)
XXI	1.34 (3H, d, $J=8$ Hz, $C\underline{H}_3$), 2.90—3.26 (1H, m, C_4–H), 4.16 (1H, dd, $J_1=7$ Hz, $J_2=12$ Hz, C_3–H_a), 4.45 (1H, dd, $J_1=5$ Hz, $J_2=12$ Hz, C_3–H_b), 7.09—7.58 (3H, m, aromatic-H), 8.00 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_8–H)
XXⅡ	1.35—2.38 (10H, m, protons of cyclohexane ring), 6.59 (1H, broad, vinyl-H), 7.15—7.52 (3H, m, aromatic-H), 7.98 (1H, dd, $J_1=8$ Hz, $J_2=2$ Hz, C_6–H)
XXⅢ	1.10—2.37 (10H, m, protons of cyclohexane ring), 2.96 (2H, s, C_4–H), 7.10—7.54 (3H, m, aromatic-H), 8.00 (1H, dd, $J_1=7$ Hz, $J_2=2$ Hz, C_8–H)
XXIV	1.05—2.23 (10H, m, protons of cyclohexane ring), 4.35 (2H, s, C_3–H), 7.12—7.69 (3H, m, aromatic-H), 8.00 (1H, dd, $J_1=7$ Hz, $J_2=2$ Hz, C_8–H)

React. No 23——The pale yellow product was obtained from the CH_2Cl_2 fraction. This product was dissolved with ether and extracted with 10% KOH solution. The extract was acidified with CH_3COOH and the crystal was obtained. It was recrystallized from pet-ether (54 mg, 5.4%). mp 96—98°. Colorless plates. The analytical data of this crystal agreed with that of authentic sample of XXII.

React. No. 19, 20, 22, and 24——They were treated as above but the corresponding starting materials were recovered.

The NMR spectra of related compounds were shown in Table II.