gemacht und mit $CHCl_3$ ausgezogen. Die Chloroform-Lösung wurde nach dem Trocknen mit Na_2SO_4 eingedampft und 0.58 g amorphe Base erhalten. 80 mg davon wurden in 10 ccm EtOH gelöst und unter Zusatz von 0.4 ccm 4% iger Natronlauge und 100 mg Raney-Nickel katalytisch reduziert. Die H_2-Aufnahme : 20 ccm (10°, ca. 4.2 mol). Die vom Katalysator abfiltrierte Lösung wurde im Vakuum eingedampft, ammoniak-alkalisch gemacht und ausgeäthert. Der Ätherextrakt (50 mg) wurde in $CHCl_3$ gelöst und durch eine Alumina-Säule chromatographisch gereinigt. Der mit $CHCl_3$ entwickelte Teil wurde als Bromhydrat aus EtOH-Äther umkristallisiert. Nadeln vom Schmp. 296~299° (u. Zers.) (25 mg). $C_{22}H_{33}ON \cdot HBr$—Ber. : C, 64.7; H, 8.3. $C_{21}H_{31}ON \cdot HBr$—Ber. : C, 63.9; H, 8.1. Gef. : C, 64.82; H, 7.69. $[\alpha]_D^8$: $-62.2°$ ($l=1$ dm, c=0.516% in H_2O). UV: λ_{max}^{EtOH} 285 mμ ($\log \epsilon = 1.69$). IR : 1707 cm^{-1} (CO).

Zusammenfassung

Shimoburobase I ist dem Songorin sehr ähnlich. Die 3 Sauerstoffe in ihnen bestehen aus 2 Hydroxylgruppen und einer Carbonylgruppe. Sie enthält noch eine ungesättigte Doppelbindung, die beim Ozon-Abbau das Formaldehyd gibt. Eine Atomgruppierung $-CH(OH)-C=CH_2$ in ihnen wird angenommen, die sichbeim Behandeln mit Pd-Katalysator in $CH_3-CH-C=O$ umlagert. Desoxybase von (I) wurde hergestellt.

(Eingegangen am 14. Oktober, 1955)

U.D.C. 547.565.2'462.3

4. **Ken'ichi Takeda, Keizo Kitahonoki, and Kikuo Igarashi** :

Diels-Alder Reaction. III.[1,2] The Reaction of Hydroquinone and Maleic Anhydride.

(*Research Laboratory, Shionogi & Co., Ltd.**)

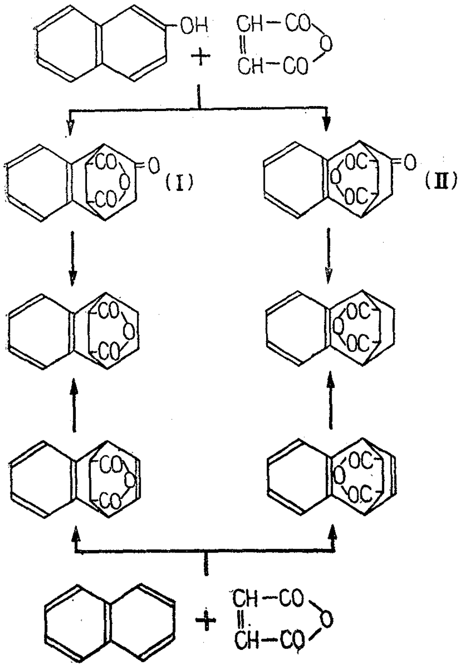

Chart 1.

Previously we reported[2] on the reaction of β-naphthol and maleic anhydride by heating a mixture of these substances at 220~240°, and the two addition products obtained, (I), m.p. 193~194°, and (II), m.p. 194~195°, were clarified as the *endo*- and *exo*-type isomers of the normal Diels-Alder addition, where β-naphthol reacts as a conjugated diene. The confirmation of the structure of each isomer was carried out by the route shown in Chart 1.

It appeared of interest, therefore, to extend this investigation to a benzenoid compound, and the present paper is concerned with the reaction of hydroquinone and maleic anhydride.

By heating hydroquinone and maleic anhydride at 200~220° in carbon dioxide atmosphere without any solvent, a crystalline product, m.p. 251~253° (decomp.), is obtained. The yield of this product is about 10% of the theoretical

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* Imafuku, Amagasaki, Hyogo-ken (武田健一, 北朴木馨三, 五十嵐喜九男).

[1] The outline of this paper was read at the 14th International Congress of Pure and Applied Chemistry in Zürich, Switzerland, July 26, 1955.

[2] Part I : K. Takeda, K. Kitahonoki : J. Pharm. Soc. Japan, **73**, 280 (1953); Part II : K. Takeda, K. Kitahonoki : This Bulletin, **1**, 135 (1953).

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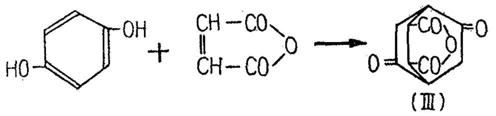
amount. Its free acid and dimethyl ester melt at 248~253°(decomp.) and 181~182.5°, respectively. The analytical values of these compounds are all in good agreement with the formula $C_{10}H_8O_5$ for the reaction product. This product shows a negative color reaction with ferric chloride and is not affected by catalytic reduction using palladium-charcoal as a catalyst and it is also negative to the tetranitromethane unsaturation test.

The infrared and ultraviolet absorption spectra of this substance (Ⅲ) (Figs. 1 and 2) exhibit a distinct carbonyl absorption band at 5.79 μ in the infrared and 286 mμ (ϵ 59.2) (free acid) in the ultraviolet spectra, but no band corresponding to the hydroxyl group absorption (cf. infrared spectrum) nor aromatic ring absorption (cf. ultraviolet spectrum).

The three absorption bands at 5.43, 5.56, and 8.23 μ in the infrared absorption spectrum correspond to those of an acid anhydride. Attempts to crystallize the carbonyl derivatives of (Ⅲ), e. g. the oxime, *p*-nitrophenylhydrazone, or 2,4-dinitrophenylhydrazone, were unsuccessful.



(Ⅲ)

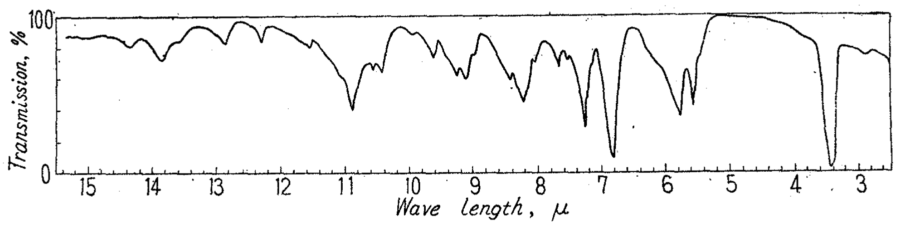


Fig. 1. Infrared Spectrum of the Hydroquinone-Maleic Anhydride Adduct (Ⅲ) (Baird Double-beam Infrared Spectrophotometer) (in Nujol)

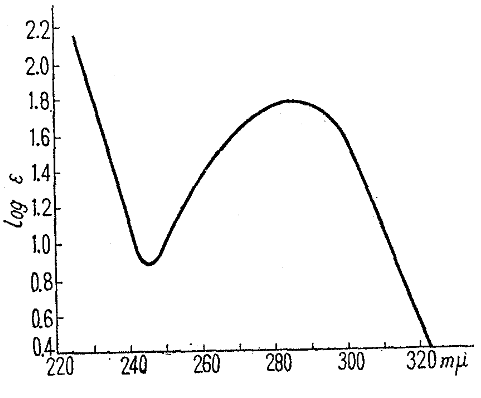


Fig. 2. Ultraviolet Spectrum of the Hydroquinone-Maleic Anhydride Adduct (Ⅲ) (free acid) (Beckman Model DU Spectrophotometer) (in water)

From these facts the most probable structure of the reaction product was assumed to be (Ⅲ).

If the reaction product can be represented by the structure (Ⅲ), then the desoxo derivative should correspond to the compound (V) previously prepared by Diels and Alder.[3] According to this assumption, then, an effort was made to relate the two compounds by the Raney nickel desulfurization of the bisthioketal of (Ⅲ), which was formed by the condensation with ethanedithiol. The bisthioketal derivative (Ⅳ), m.p. 235~237°, of (Ⅲ), possessing the formula $C_{14}H_{16}O_3S_4$, resulted easily from the

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[3] O. Diels, K. Alder: Ann., **460**, 115(1928); **478**, 137(1930).

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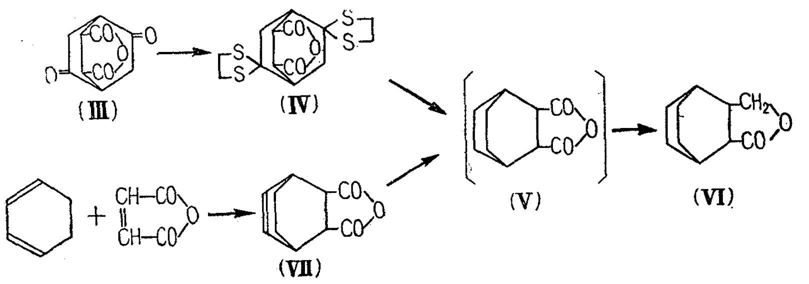
condensation of ethanedithiol with (III) in the presence of boron trifluoride. The Raney nickel reduction of the foregoing thioketal (IV) in boiling dioxane gave a sublimable substance, m.p. 147°, corresponding to the formula $C_{10}H_{14}O_2$. This reduction product possesses no acid anhydride group but has lactonic properties. The infrared absorption spectrum (Fig. 3) also indicated the presence of a five-membered lactone ring (absorption band at 5.68 μ and no band corresponding to an acid anhydride). Thus, it is obvious that this compound is not identical with the anticipated anhydride (V), reported by Diels and Alder.[3]

For further confirmation of the structure of this lactone (VI), we next turned to the synthesis of this compound by another route.

Following the method of Diels and Alder,[3] *endo*-ethylenetetrahydrophthalic anhydride (VII) was prepared by the reaction of cyclohexadiene with maleic anhydride. When this unsaturated anhydride was treated with freshly prepared Raney nickel in boiling dioxane for 8 hours, there was obtained the anticipated lactone in a good yield.

This substance is apparently identical with the lactone obtained from our Diels-Alder adduct as evidenced by its mixed melting point behavior, and the infrared absorption spectrum of each substance also gave the identical results (Figs. 3 and 4).



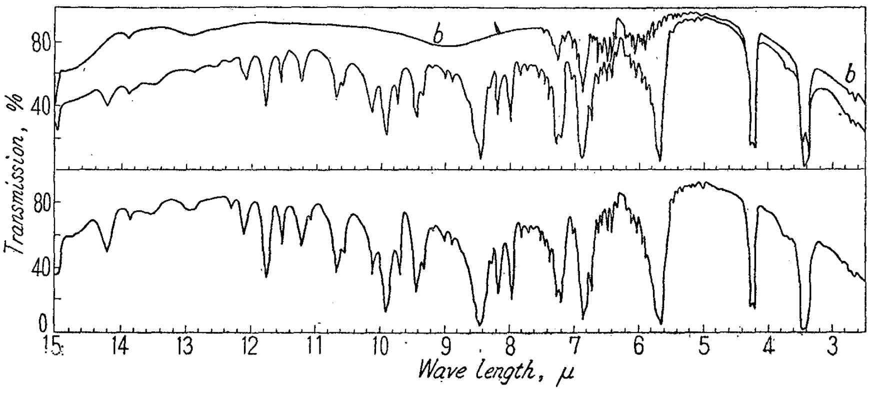


Fig. 3.
(VI), obtained from (III)

Fig. 4.
(VI), obtained from (VII)
(Curve b : back ground +Nujol)

Infrared Spectra of *endo*-Ethylenehexahydrophthalide (VI) (in Nujol)

Here again, it is seen that the partial reduction of the acid anhydride occurs by the Raney nickel reduction under the above-mentioned conditions with simultaneous reduction of the double bond.

Summarizing the above, it can be concluded that maleic anhydride undergoes an addition reaction at the 2- and 5-positions of hydroquinone in the usual manner of the Diels-Alder reaction. In this case there exists theoretically no *endo*- or *exo*-type isomer and this fact also agrees well with the experimental data.

It is of interest to note that a benzene derivative undergoes such a Diels-Alder reaction as a normal conjugated diene system. The reaction of maleic anhydride with other phenolic derivatives is now under investigation in this Laboratory.

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Our thanks are tendered to Dr. K. Kuratani of the University of Tokyo and to Messrs. Y. Matsui, M. Narisada, and T. Kubota of our laboratory for the measurements of the ultraviolet and infrared spectra. We wish also to thank Messrs. T. Iyeki and K. Miyahara and Miss N. Morita of our laboratory for the microanalyses.

Experimental[4)]

Hydroquinone-Maleic Anhydride Adduct (III) (Bicyclo[2,2,2]octane-2,5-dioxo-7,8-dicarboxylic Anhydride)—A mixture of 10 g. of hydroquinone and 20 g. of maleic anhydride was heated in CO_2 atmosphere at 200∼220°(bath temp.) for 1.5 hrs. To the brown reaction product was added ca. 100 cc. of ether and the insoluble solid was filtered and washed well several times with ether. Three recrystallizations of this substance (1.9 g.) from anhyd. acetone gave the pure adduct (Ⅲ) as colorless plates, m.p. 251∼253°(decomp.). *Anal.* Calcd. for $C_{10}H_8O_5$: C, 57.69; H, 3.87. Found: C, 57.51; H, 3.99.

This compound is sparingly soluble in ether, AcOEt and $CHCl_3$ and soluble in dioxane and acetone. It shows a negative color reaction with $FeCl_3$ solution and tetranitromethane, and also it is not reduced with H_2 over Pd-C in acetone. I.R. : 5.43, 5.56, 8.23 μ (acid anhydride); 5.79 μ (C=O). U.V. (free acid) : $\lambda_{max}^{H_2O}$ 286 mμ (ϵ 59.2) (Figs. 1 and 2).

Dimethyl Ester of the Hydroquinone-Maleic Anhydride Adduct (III)—For hydrolysis of the adduct (Ⅲ), 50 mg. of the sample was dissolved in 5 cc. of water with warming. Evaporation of the solvent *in vacuo* left a crystalline residue (dicarboxylic acid), m.p. 248∼253°(decomp.), easily soluble in a cold $NaHCO_3$ solution with effervescence. This substance was dissolved in 10 cc. of dioxane and methylated with an ether solution of CH_2N_2 to give 60 mg. of a dimethyl ester, m.p. 180∼182°. Recrystallization from MeOH gave colorless prisms, m.p. 181∼182.5°. *Anal.* Calcd. for $C_{12}H_{14}O_6$: C, 56.69; H, 5.55. Found : C, 56.91 ; H, 5.80.

Bisthioketal (IV) of the Hydroquinone-Maleic Anhydride Adduct (III)—To a suspension of 4 g. of the hydroquinone-maleic anhydride adduct (Ⅲ) in 12 cc. of ethanedithiol was added 5 cc. of BF_3(45%) in ether. The mixture was allowed to stand for 2 days at room temperature. The resulting crystals were filtered and washed with ether and MeOH to yield 2.5 g. of needles, m.p. 225∼235°. Recrystallization from acetone gave bisthioketal (Ⅳ) as colorless needles, m.p. 235∼237°. *Anal.* Calcd. for $C_{14}H_{16}O_3S_4$: C, 46.64; H, 4.47; S, 35.58. Found : C, 46.67; H, 4.42; S, 35.52. I. R. : 5.43, 5.64, 8.15 μ (acid anhydride; no carbonyl).

3,6-*endo*-Ethylenehexahydrophthalide (VI)—The above bisthioketal (1.5 g.) was dissolved in 100 cc. of dioxane and 15 g. of freshly prepared Raney Ni[5)] was added. The mixture was refluxed for 8 hrs. After removal of Ni, the solvent was evaporated at reduced pressure to give a sublimable crystalline residue. Recrystallization from ether-petr. ether gave colorless rods, m.p. 147°. *Anal.* Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found : C, 72.47; H, 8.50. I. R. : 5.68 μ (lactone; no acid anhydride) (Fig. 3).

3,6-*endo*-Ethylene-Δ^4-tetrahydrophthalic Anhydride (VII)—This was prepared from cyclohexa-$\Delta^{1,3}$-diene and maleic anhydride by the procedure of Diels and Alder.[3)] I. R. : 5.45, 5.64, and 8.20 μ (acid anhydride).

3,6-*endo*-Ethylenehexahydrophthalide (VI) from 3,6-*endo*-Ethylene-Δ^4-tetrahydrophthalic Anhydride (VII)—To the solution of 1 g. of (Ⅶ) in 25 cc. of dioxane was added 10 g. of freshly prepared Raney Ni[5)] and the mixture was heated under reflux for 8 hrs. Ni was filtered off and the solvent was distilled under reduced pressure. To the residue was added petr. ether and the resulting crystals were recrystallized from ether-petr. ether to colorless rods, m.p. 147°, which depressed to 142° on admixture with the starting adduct (Ⅶ). No depression in m.p. was observed on admixture with the lactone, obtained from the hydroquinone-maleic anhydride adduct. *Anal.* Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found : C, 72.08; H, 8.48. I. R. : 5.68 μ (lactone; no acid anhydride) (Fig. 4).

Summary

An addition compound of hydroquinone and maleic anhydride was obtained by heating a mixture of these substances at 200∼220°. It was found that this compound is the *endo*-ethylenecyclohexane derivative (Ⅲ), and that such a benzenoid compound can react with maleic anhydride as in the case of the usual Diels-Alder reaction.

(Received October 29, 1955).

[4)] All melting points were determined in soft-glass capillary tubes, and are uncorrected. Infrared spectra, except (Ⅲ), were measured with a Perkin-Elmer Single-beam Infrared Spectrophotometer, Model 12C, in Nujol.

[5)] Org. Syntheses, **21**, 15 (1941).

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