

[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

## ROTENONE.

## XI. THE RELATION BETWEEN ISOROTENONE AND ROTENONE

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Rotenone on catalytic hydrogenation with one mole of hydrogen yields a mixture of dihydrorotenone and rotenonic acid.<sup>1</sup> Rotenonic acid on hydrogenation is reduced to dihydrorotenonic acid, which can also be obtained by the hydrogenation of dihydrorotenone.<sup>1</sup>

Isorotenone,<sup>2</sup> an isomer of rotenone, is obtained by dissolving rotenone in a solution of glacial acetic acid and concentrated sulfuric acid and then adding the resulting cherry red solution to water. In its chemical behavior isorotenone exhibits most of the typical reactions of rotenone. It yields a dehydro derivative, a diketone, isoderritol and isotubaic acid. The only marked difference is in its behavior on catalytic hydrogenation. Whereas rotenone is readily reduced with catalytic hydrogen to an acid, and a dihydro derivative, isorotenone is reduced only with great difficulty and so far it has not been possible to obtain from it an acid corresponding to rotenonic acid.

Isoderritol and isorotenol are not reduced to acids under the conditions employed for the reduction of derritol and rotenol.

Tubaic acid,<sup>3</sup> which is obtained on boiling an alcoholic potassium hydroxide solution of rotenone, is readily reduced to a dihydro derivative.

Isotubaic acid<sup>4</sup> (rotenic acid), which is obtained on isomerization of tubaic acid, is not easily hydrogenated but can be reduced under certain conditions, as has been shown by Butenandt and Hildebrandt<sup>5</sup> and by Takei, Koide and Miyajima.<sup>6</sup>

Tubaic acid is optically active, whereas isotubaic acid is optically inactive. Dihydroisotubaic acid is a racemic mixture. It has been resolved<sup>5,6</sup> into its enantiomorphs and the levo form has been found to be identical with dihydrotubaic acid. Thus it is definitely established that the isomerization of tubaic acid into isotubaic acid is due to the migration of a double bond.

The facts that isorotenone yields isotubaic acid under the same conditions that rotenone yields tubaic acid and that tubaic acid can be isomerized

<sup>1</sup> F. B. LaForge and L. E. Smith, *THIS JOURNAL*, **51**, 2574 (1929).

<sup>2</sup> S. Takei, *Biochem. Z.*, **157**, 1 (1925); *Ber.*, **61**, 1003 (1928).

<sup>3</sup> T. Kariyone, Y. Kimura and K. Kondo, *J. Pharm. Soc. (Japan)*, **514**, 1094 (1924); *ibid.*, **518**, 377 (1925); S. Takei, *Ber.*, **61**, 1003 (1928).

<sup>4</sup> S. Takei, *Biochem. Z.*, **157**, 1 (1925); A. Butenandt and F. Hildebrandt, *Ann.*, **477**, 245 (1930); H. L. Haller and F. B. LaForge, *THIS JOURNAL*, **52**, 3207 (1930).

<sup>5</sup> A. Butenandt and F. Hildebrandt, *Ann.*, **477**, 245 (1930).

<sup>6</sup> S. Takei, M. Koide and S. Miyajima, *Ber.*, **63**, 1369 (1930).

to isotubaic acid, lead to the conclusion that the same groupings are involved in the isomerization of rotenone into isorotenone as in the transformation of tubaic acid into isotubaic acid.

On oxidation with permanganate, tubaic acid yields acetic acid, whereas isotubaic and dihydrotubaic acid give isobutyric acid.<sup>7</sup> Takei and Koide<sup>8</sup> have obtained a methyl ketone on ozonization of tubaic acid. The presence of an isoallyl group in tubaic acid and in rotenone is therefore definitely established; isotubaic acid, dihydrotubaic acid and isorotenone, on the other hand, contain the isopropyl group.

As it has been shown that the double bond in tubaic acid which is readily reduced is in the isoallyl group and that isotubaic acid does not reduce readily, it appears fairly well established that the double bond from the isopropylene group in tubaic acid is the one which migrates on isomerization.

The fact that rotenone readily yields an acid on catalytic hydrogenation, whereas isorotenone does not, indicates that there is a close relation between the lactone ring and the migratory double bond, and that the cleavage of the lactone ring by hydrogenation depends upon the position of the unsaturated bond. It has not yet been possible to fix the position of the lactone ring, but in a recent paper it has been shown that acid derivatives obtained by hydrogenation of rotenone do not yield tubaic acid, but that the hydroxyl group resulting from the hydrolytic opening of the lactone ring is necessary for its formation.<sup>9</sup>

In an attempt to isomerize rotenonic acid to isorotenonic acid with glacial acetic and sulfuric acids, a product insoluble in alkali was obtained. It is not a mixed anhydride since it was recovered unchanged on refluxing in methyl alcohol solution, but is isomeric with rotenonic acid and dihydrototenone. It will be called  $\beta$ -dihydrototenone. It is probably a saturated lactone formed by the migration of a double bond with subsequent ring closure. As is well known, unsaturated acids can be transformed into saturated lactones by means of acid.

The formation of  $\beta$ -dihydrototenone is further evidence that there is a close association between the lactone ring and the migratory double bond.

Jacobs and Scott<sup>10</sup> have recently shown that  $\gamma$ - and  $\delta$ -lactones which contain a double bond in the  $\beta$ ,  $\gamma$ - or  $\gamma,\delta$ -position readily yield desoxy acids on catalytic hydrogenation. When the double bond is in the  $\alpha,\beta$ -position the ring is not opened but, instead, saturated lactones are obtained.

It is possible that when rotenone is isomerized to isorotenone, the double bond from the isopropylene group migrates to an  $\alpha,\beta$ -position to the lactone

<sup>7</sup> S. Takei and M. Koide, *Bull. Inst. Phys. Chem. Res.*, **8**, 64 (1929); *Ber.*, **62**, 3030 (1929); Takei and Miyajima, *Bull. Inst. Phys. Chem. Res.*, **8**, 61 (1929).

<sup>8</sup> S. Takei and M. Koide, *Ber.*, **62**, 3030 (1929).

<sup>9</sup> H. L. Haller and F. B. LaForge, *THIS JOURNAL*, **52**, 4505 (1930).

<sup>10</sup> W. A. Jacobs and A. B. Scott, *J. Biol. Chem.*, **87**, 601 (1930).

group and that the double bond becomes part of a conjugated system, which rearrangement might explain why isorotenone does not yield an acid on hydrogenation and why it is reduced only with difficulty.

The isomerization of rotenonic acid to a saturated lactone may be explained by rearrangement, accompanied by the disappearance of the double bond. No such change is possible in the case of dihydrorotenonic acid because the double bond in the isoallyl group has been reduced.

$\beta$ -Dihydrorotenone is optically active. In alcohol solution it reduces Fehling's solution. It is not reduced with platinum oxide and hydrogen in ethyl acetate solution. On refluxing in alcoholic potash solution, an acid isomeric with dihydrotubaic acid is obtained. The same acid is obtained on fusion with potassium hydroxide. Like rotenone,  $\beta$ -dihydrorotenone yields a yellow dehydro compound on mild oxidation, and with stronger oxidizing agents, a diketone. Dehydro- $\beta$ -dihydrorotenone on boiling with alcoholic potash and zinc adds two moles of water to form an acid corresponding to dihydro-dehydrodihydroxyrotenonic acid (dihydro-derris säure, Butenandt) which has been termed dehydrodihydroxy- $\beta$ -dihydrorotenonic acid. This acid also yields derric acid on oxidation with hydrogen peroxide in alkaline solution.

### Experimental

**$\beta$ -Dihydrorotenone.**—Five grams of rotenonic acid was dissolved with gentle heating in a solution of 16.5 cc. of concentrated sulfuric acid and 60 cc. of acetic acid. The cherry red solution was slowly poured into 500 cc. of water with constant stirring. The precipitate was filtered off, washed with water and dissolved in ether. The ether solution was washed with 5% potassium hydroxide, then with water and then dried over sodium sulfate. The substance readily crystallized after most of the ether was distilled off. It melted at 156°. In alcohol solution it reduced Fehling's solution; in chloroform,  $[\alpha]_D^{25} -26.5^\circ$  ( $C = 5.86$ ).

*Anal.* Subs., 0.0790, 0.0782, 0.0987:  $\text{CO}_2$ , 0.2000, 0.1984, 0.2522;  $\text{H}_2\text{O}$ , 0.0432, 0.0416, 0.0531. Subs., 0.0220, 0.0214;  $\text{AgI}$ , 0.0268, 0.0261. Calcd. for  $\text{C}_{23}\text{H}_{24}\text{O}_6$ : C, 69.69; H, 6.06,  $2\text{OCH}_3$ , 15.65. Found: C, 69.08, 69.20, 69.68; H, 6.08, 5.92, 5.96;  $\text{OCH}_3$ , 16.08, 16.09.

One gram of  $\beta$ -dihydrorotenone was dissolved in 50 cc. of methyl alcohol, and the solution was refluxed for three hours. It was then concentrated to about half its volume and cooled. The substance which readily crystallized proved to be unchanged  $\beta$ -dihydrorotenone. The melting point was 156°.  $\beta$ -Dihydrorotenone in ethyl acetate solution with platinum oxide catalyst absorbed no hydrogen.

**$\beta$ -Dihydrotubaic Acid.**—Five grams of  $\beta$ -dihydrorotenone was dissolved in a solution of 5 g. of potassium hydroxide in 50 cc. of alcohol and 5 cc. of water. The solution was refluxed for three hours and then poured into 500 cc. of water. The acid was isolated by the procedure described for the preparation of tubaic acid.<sup>11</sup> It melted at 175–176° with decomposition. In alcohol it gave a purple color with ferric chloride. It contained no methoxyl.

*Anal.* Subs., 0.0844, 0.0827:  $\text{CO}_2$ , 0.2002, 0.1946;  $\text{H}_2\text{O}$ , 0.0467, 0.0469. Calcd.

<sup>11</sup> H. L. Haller and F. B. LaForge, *THIS JOURNAL*, 52, 3207 (1930).

for  $C_{12}H_{14}O_4$ : C, 64.86; H, 6.31. Found: C, 64.70, 64.16; H, 6.15, 6.31. 0.0245 g. of subs. required 1.10 cc. of N/10 KOH; 0.242 g. of subs. required 1.10 cc. of N/10 KOH. Calcd. mol. wt., 222. Found: 223, 220.

**Alkali Fusion of  $\beta$ -Dihydrototenone.**—Two grams of  $\beta$ -dihydrototenone was intimately mixed with 18 g. of powdered potassium hydroxide and 1 cc. of water in a nickel crucible. The reaction mixture was heated with constant stirring in a metal-bath at  $225^\circ$  for twenty-five minutes. After cooling, the fusion mass was dissolved in water and the acid isolated by the procedure previously described.<sup>10</sup> The acid proved to be identical with the acid obtained by the action of alcoholic potash on  $\beta$ -dihydrototenone.

**$\beta$ -Dihydrototenone.**—Four grams of  $\beta$ -dihydrototenone was dissolved in 120 cc. of glacial acetic acid, and the solution was heated to boiling under a reflux condenser. During the course of three hours, 8 g. of chromium trioxide in 200 cc. of glacial acetic acid was added. The solution was then concentrated to half its volume. On cooling fine yellow needles crystallized out which decomposed at about  $310^\circ$ .

*Anal.* Subs., 0.0808, 0.0804:  $CO_2$ , 0.1982, 0.2001;  $H_2O$ , 0.0351, 0.0349. Subs., 0.0223, 0.0223: AgI, 0.0247, 0.0248. Calcd. for  $C_{23}H_{26}O_7$ : C, 67.61; H, 4.93;  $2OCH_3$ , 15.20. Found: C, 66.90, 67.88; H, 4.83, 4.82;  $OCH_3$ , 14.62, 14.68.

From the mother liquors obtained in the oxidation described above a minute quantity of acid was isolated which was found to be identical with the acid obtained by the action of alcoholic potash on  $\beta$ -dihydrototenone.

**Dehydro- $\beta$ -dihydrototenone.**—One gram of  $\beta$ -dihydrototenone was dissolved in 50 cc. of boiling 95% alcohol. A solution of 1.8 g. of potassium ferricyanide and 0.27 g. of potassium hydroxide in 15 cc. of water was added to the boiling solution. The reaction mixture was allowed to stand overnight. Water was then added and the resulting crystalline precipitate was filtered off, washed with water and then with alcohol. It melted at  $269^\circ$ .

*Anal.* Subs., 0.0823, 0.0884:  $CO_2$ , 0.2100, 0.2250;  $H_2O$ , 0.0419, 0.0441. Calcd. for  $C_{23}H_{22}O_8$ : C, 70.00; H, 5.58. Found: C, 69.62, 69.47; H, 5.70, 5.58.

**$\beta$ -Dihydrototenolone.**—One gram of  $\beta$ -dihydrototenone was dissolved in a solution of 2.5 g. of potassium acetate in 50 cc. of absolute alcohol. To the hot solution 0.8 g. of iodine dissolved in 50 cc. of absolute alcohol was slowly added. On cooling, a cream-colored product crystallized. It was recrystallized from chloroform-ethyl alcohol. It melted at  $274^\circ$ . The compound was a hydroxy derivative of  $\beta$ -dihydrototenone.

*Anal.* Subs., 0.0855, 0.1009:  $CO_2$ , 0.2109, 0.2495;  $H_2O$ , 0.0441, 0.0511. Subs., 0.0212, 0.0219: AgI, 0.0248, 0.0255. Calcd. for  $C_{23}H_{24}O_7$ : C, 67.00; H, 5.82;  $2OCH_3$ , 15.05. Found: C, 67.27, 67.44; H, 5.73, 5.63;  $OCH_3$ , 15.45, 15.37.

On boiling with alcoholic sulfuric acid,  $\beta$ -dihydrototenolone yielded a yellow compound which was identical with the dehydro compound obtained by oxidation of  $\beta$ -dihydrototenone with potassium ferricyanide.

The filtrate from the  $\beta$ -dihydrototenolone was concentrated to dryness and water was added. The undissolved substance was filtered off, dried and recrystallized from 95% alcohol. It melted at  $224^\circ$ . Analysis indicated it to be the acetyl derivative of the hydroxy compound obtained above.

*Anal.* Subs., 0.0945, 0.0907:  $CO_2$ , 0.2288, 0.2195;  $H_2O$ , 0.0473, 0.0464. Calcd. for  $C_{25}H_{26}O_8$ : C, 66.08; H, 5.75. Found: C, 66.03, 66.00; H, 5.56, 5.68.

**Dehydrodihydroxy- $\beta$ -dihydrototenonic Acid.**—Eight-tenths gram of dehydro- $\beta$ -dihydrototenone was refluxed with 5 cc. of 40% potassium hydroxide, 20 cc. of ethyl alcohol and 2 g. of zinc dust for one and one-half hours. The zinc was removed by filtration and the solution was acidified with dilute sulfuric acid. After adding water to

the solution it was cooled and extracted with ether. The ether extract was washed with water and dried over sodium sulfate. The ether was removed and the substance was crystallized from butyl ether. It melted at 149°.

*Anal.* Subs., 0.0927: CO<sub>2</sub>, 0.2177; H<sub>2</sub>O, 0.0506. Calcd. for C<sub>21</sub>H<sub>25</sub>O<sub>8</sub>: C, 64.16; H, 6.09. Found: C, 64.05; H, 6.11.

**Oxidation of Dehydrodihydroxy- $\beta$ -Dihydrorotenonic Acid to Derric Acid.**—One gram of acid was dissolved in 12 cc. of 5% sodium hydroxide solution. The solution was gently heated and 3 cc. of 30% hydrogen peroxide was gradually added. The solution was finally heated to boiling for a few minutes, then cooled and acidified with dilute sulfuric acid. The solution was extracted with ether, the ether extract was washed with water and dried over sodium sulfate. After removal of the ether the substance was crystallized from butyl ether. It melted at 167° and was found to be identical with derric acid.

### Summary

Rotenonic acid in glacial acetic acid and sulfuric acid is isomerized to a substance which is insoluble in alkali and appears to be a saturated lactone. This compound has been named  $\beta$ -dihydrorotenone.

$\beta$ -Dihydrorotenone gives the typical reactions of rotenone. It yields a dehydro compound which adds two moles of water to form an acid. It gives a diketone. With potassium hydroxide it yields an acid isomeric with dihydrotubaic acid.

A possible explanation is given of the fact that rotenone is readily reduced and isorotenone is not, and a relation between the two is indicated.

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## THE SPECTROCHEMISTRY OF FURAN AND ITS DERIVATIVES<sup>1</sup>

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Absorption spectra and molecular refraction have proved to be of considerable value in attacking chemical problems from a physical standpoint. In the furan series no extensive study has been made of these optical properties, although a number of observations are reported in the literature. The present work was undertaken with the object of making a rather extensive study of furan derivatives with the idea of discovering any general relationships which might prove useful in elucidating the structure and behavior of furan and its derivatives.

Preliminary observations of absorption spectra showed that furan and its simpler derivatives do not exhibit selective absorption in the visible and ultraviolet regions (to 2200 Å.). It was hoped that there would be a difference in the absorption spectra of the isomeric alpha- and beta-sub-

<sup>1</sup> This article is an abstract of a thesis submitted to the Faculty of the Graduate School of Cornell University by Everett C. Hughes, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1930.