

hulls by the Freudenberg and Harder modification of Urban's method, and in the distillate of the lignin from spruce wood prepared by the same method. The result so far as the lignin from spruce wood is concerned is in agreement with that recorded by Freudenberg and Harder.

The results obtained are discussed from the standpoint of the probable presence of the methylene dioxide group in the lignin molecule.

WASHINGTON, D. C.

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

ROTENONE. XXIII. THE STRUCTURE OF ROTENONONE

BY F. B. LAFORGE

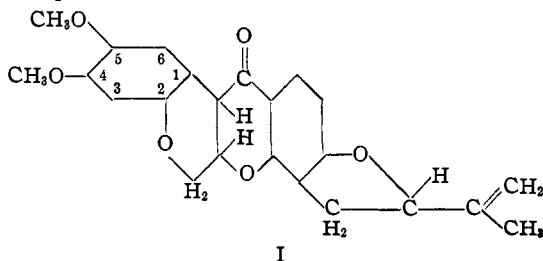
RECEIVED APRIL 21, 1932

PUBLISHED AUGUST 5, 1932

Rotenonone is obtained from rotenone by chromic acid oxidation, or by the action of nitrous acid. Butenandt assumed the compound to be a 1,2-diketone of formula $C_{23}H_{20}O_7$ arising from the oxidation of a methylene group adjacent to the carbonyl group present in rotenone. It is converted by the action of strong alkali, with the addition of one mole of water, into an acid of the supposed formula $C_{23}H_{22}O_8$, a reaction which was interpreted by Butenandt as a benzylic acid rearrangement.¹

In a previous article² we have shown that the analogs of rotenonone are obtained not only from dihydrorotenone, isorotenone and rotenonic acid, but even more readily from the corresponding dehydro derivatives and that all derivatives of the rotenonone type belong to the dehydro series. Therefore rotenonone should be represented by the formula $C_{23}H_{18}O_7$, rotenonic acid by $C_{23}H_{20}O_8$, and corresponding formulas should be applied to the other derivatives. These formulas in fact correspond more closely to the analytical figures obtained for the respective compounds.

After the complete formula for rotenone (I) had been established,³



it became evident that the formula for rotenonone proposed by Butenandt was untenable.

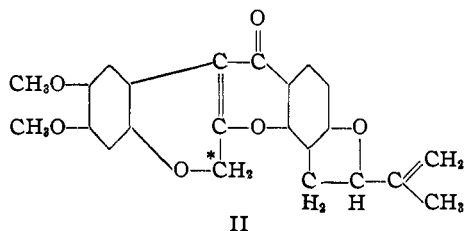
¹ Butenandt, *Ann.*, **464**, 253 (1929).

² LaForge and Smith, *THIS JOURNAL*, **52**, 1091 (1930).

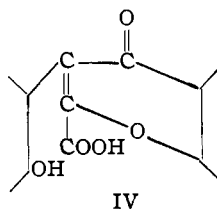
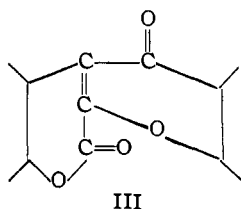
³ LaForge and Haller, *ibid.*, **54**, 810 (1932).

In a previous article⁴ we have described the oxidation of dihydro-rotenononic acid to dihydrotubaic acid, and also the reconversion of dihydrotubaic acid to dihydrorotenonone. The last-mentioned reaction is best explained by the assumption that dihydrorotenonone and hence rotenonone are lactones.

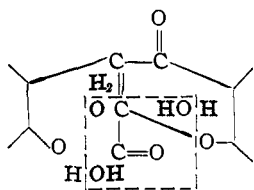
It is apparent from consideration of the formula of dehydrorotenone II



that a lactone would be formed on oxidation of the methylene group indicated by the asterisk. Consequently rotenonone would be represented by the formula III and rotenononic acid by IV.



A compound of formula III, like rotenone, might be expected to undergo alkaline hydrolysis with the formation of derritol. The experiment showed that this reaction does in fact take place. A small yield of derritol was obtained from rotenonone under the same conditions that were employed for the preparation of derritol from rotenone.⁵ The main product, however, was an acid which failed to crystallize.



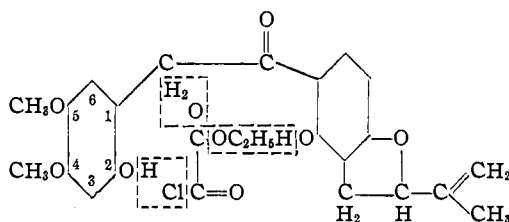
Rotenononic acid gives a positive test for phenol with ferric chloride and is easily methylated by dimethyl sulfate to the methyl ester of methylrotenononic acid, which separates in crystalline form from the alkaline solution. The corresponding acid is obtained from the ester. The ester is also easily hydrogenated to the tetrahydro derivative, which is alkali soluble.

Contrary to expectations, methyltetrahydrorotenononic acid is not cleaved by hydrogen peroxide to asaronic acid. The resistance of rotenononic acid toward strong alkali is also quite remarkable and indicates an unusual stability of the complex represented by formula IV.

⁴ LaForge and Smith, THIS JOURNAL, **52**, 3603 (1930).

⁵ LaForge and Smith, *ibid.*, **51**, 2574 (1929).

If formula III is a correct expression for rotenonone, it should be possible to effect the synthesis of rotenonone from derritol by substitution of the oxalyl ethyl ester radical on the free phenol group in position 2 followed by saponification and dehydration, as in the formation of dehydrorotenone from derrisic acid. The reaction is represented below.



Derritol was therefore allowed to react with chloro-oxalyl ethyl ester in pyridine solution. It was expected that the oxalyl ethyl ester would result, which could subsequently be saponified and dehydrated to rotenonone. However, under the conditions of the experiment all three reactions took place spontaneously, and there resulted a nearly quantitative yield of rotenonone. In view of the small yield of rotenonone obtained by oxidation of rotenone, this method is probably the most convenient one for its preparation.

There can be no further doubt that rotenonone is represented by formula III.⁶

Experimental

Rotenonic Acid.¹—Two grams of rotenonone was added to a boiling solution of 2 g. of solid potassium hydroxide in 2 cc. of water to which 6 cc. of alcohol had been added. The solution was boiled for five minutes, then diluted with water and acidified. The amorphous precipitate crystallized directly, and the product was purified by dissolving in a large quantity of hot alcohol, filtering if necessary from a small residue of rotenonone and concentrating to a small volume. The compound crystallized slowly. The yield was about 1.7 g. It melted at 250°.

Methylrotenonic Acid Methyl Ester.—Four grams of rotenonic acid dissolved in 35 cc. of 5% potassium hydroxide was methylated with 7 g. of dimethyl sulfate. The reaction was carried out with mechanical stirring over a period of two hours.

The product separated crystalline and was recrystallized from methyl alcohol. It melted at 138°. The yield was 3.5 g.

Anal. Subs., g. 0.0790, 0.0207, 0.0198: CO₂, 0.1906; H₂O, 0.0386. Thiosulfate solution (1 cc. = 0.000520 CH₃O), 10.7, 10.15. Calcd. for C₂₈H₂₄O₈: C, 66.37; H, 5.32; 4CH₃O, 27.43. Found: C, 65.80; H, 5.43; CH₃O, 26.90; 26.68.

The corresponding acid was obtained by saponification of the ester. It was recrystallized from a small quantity of methyl alcohol. It melted at 179–180°.

Anal. Subs., 0.0777, 0.0272 g.: CO₂, 0.1864; H₂O, 0.0374. Thiosulfate (1 cc. =

⁶ An article by Butenandt and McCartney [*Ann.*, **494**, 17 (1932)] has just reached us, April 20, as the foregoing article is being submitted for publication in which the authors have expressed the formula for rotenonone by a formula identical with III.

0.000520 CH_3O), 11.00. Calcd. for $\text{C}_{24}\text{H}_{22}\text{O}_8$: C, 65.75; H, 5.02; $3\text{CH}_3\text{O}$, 21.23. Found: C, 65.43; H, 5.34; CH_3O , 21.04.

Tetrahydromethylrotenononic Acid.—Two grams of methylrotenononic acid methyl ester was reduced with platinum catalyst in acetic ester solution until the required four atoms of hydrogen were absorbed. The solution was extracted with cold dilute alkali, and, after standing for some time to allow the ester to saponify, the aqueous solution was acidified and the product recrystallized from dilute alcohol. A small sample was recrystallized from very little methyl alcohol. The melting point was $184\text{--}186^\circ$.

Anal. Subs., 3.542, 3.149 mg.: CO_2 , 8.495, 7.588; H_2O , 1.949, 1.712. Calcd. for $\text{C}_{24}\text{H}_{26}\text{O}_8$: C, 65.18; H, 5.88. Found: C, 65.42, 65.71; H, 6.11, 6.04.

Derritol from Rotenonone.—Three grams of rotenonone was boiled with zinc and alcoholic potassium hydroxide under the same conditions as for the preparation of derritol from rotenone.⁵

The solution was filtered and acidified, and the precipitate was dissolved in ether. The ether solution was extracted with aqueous carbonate solution, which removed a considerable quantity of an acid which was recovered by acidifying the solution and extracting with ether. The material remaining after evaporation of the ether represented by far the larger part of the reaction product, but it could not be made to crystallize.

The first ether solution was then extracted with dilute potassium hydroxide solution. The alkaline solution was acidified and extracted with ether. The ether solution gave on evaporation 0.06 g. of derritol. It was recrystallized and compared with an authentic sample by the mixed melting point and crystal form. It melted at 161° .

Anal. Subs., 2.989 mg.: CO_2 , 7.388; H_2O , 1.654. Calcd. for $\text{C}_{21}\text{H}_{22}\text{O}_8$: C, 68.07; H, 5.99. Found: C, 67.41; H, 6.15.

Synthesis of Rotenonone from Derritol.—Two grams of derritol was dissolved in 5 cc. of pyridine. The solution was cooled in an ice-bath and 2.5 g. of chloro-oxalyl ethyl ester⁷ was slowly added. The reaction mixture was allowed to stand for forty-eight hours, after which time the contents of the flask had become a semi-solid mass of fine yellow crystals. Alcohol was added and the solid material filtered off. The product was recrystallized by dissolving in chloroform and adding hot alcohol. It formed yellow needles and possessed all the characteristic properties of rotenonone. The melting point was 298° ; mixed melting point $298\text{--}300^\circ$. The yield was 1.6 g. of pure material.

Anal. Subs., 0.0257, 0.0249: thiosulfate (1 cc. = 0.000520 CH_3O) 7.30, 7.05. Calcd. for $\text{C}_{23}\text{H}_{18}\text{O}_7$: $2\text{CH}_3\text{O}$, 15.27. Found: CH_3O , 14.77, 14.69.

Summary

Rotenonone is partially converted into derritol by zinc alkali hydrolysis. Rotenononic acid is methylated by dimethyl sulfate to the methyl ester of methylrotenononic acid. Methylrotenononic acid is hydrogenated to a tetrahydro compound.

Rotenonone is the lactone corresponding to rotenononic acid.

The synthesis of rotenonone from derritol was accomplished by the substitution of the oxalyl ethyl ester groups on the reactive phenolic group in pyridine solution. Complete condensation to rotenonone took place in one operation with the formation of rotenonone.

WASHINGTON, D. C.

⁷ Anschütz, *Ann.*, **254**, 27 (1889).