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

DEGUELIN. II. RELATIONSHIPS BETWEEN DEGUELIN AND ROTENONE

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Recently¹ attention has been directed to a relationship between deguelin and rotenone in which the following facts were involved. Upon mild oxidation rotenone is converted to dehydrorotenone, $C_{23}H_{20}O_6$, which when boiled with alcoholic potassium hydroxide and zinc dust yields an hydroxy acid, $C_{23}H_{24}O_{8.2}$ When this acid is oxidized in alkaline solution with hydrogen peroxide, the molecule is ruptured, and derric acid, $C_{12}H_{14}O_{7,3}$ is obtained. Derric acid contains the two methoxyl groups originally in rotenone and represents one-half of the rotenone molecule.

In an analogous manner deguelin is oxidized with potassium ferricyanide to dehydrodeguelin, $C_{23}H_{20}O_{6}$,⁴ which upon boiling with alcoholic potassium hydroxide yields a phenolic monocarboxylic acid, $C_{23}H_{24}O_{8}$, known as deguelic acid. When this acid is oxidized with hydrogen peroxide, as was the acid from dehydrorotenone, it also yields derric acid.

It thus follows that in deguelin as in rotenone derric acid constitutes one-half of the molecule, and hence the structural differences between deguelin and rotenone must be sought either in the second half of the molecule or in the linkages between the two parts.

Another set of experiments showing the same relationship has been performed more recently. Takei, Miyajima and Ono⁵ described an acid, $C_{11}H_{12}O_7$, which they called risic acid (Rissäure). The compound was obtained by permanganate oxidation of the hydroxy acid, $C_{23}H_{24}O_8$, derived from dehydrorotenone through the action of alcoholic alkali. LaForge and Smith⁶ originally obtained this acid by permanganate oxidation of derric acid, and as derric acid is a part of the deguelin molecule, risic acid should be expected as an oxidation product of deguelic acid. This experiment was performed, and risic acid was obtained, having the properties recorded for it by the Japanese investigators.

The purpose of the present report is to record the experimental data obtained in establishing the relationship mentioned above and also to describe some experiments the results of which show that these two insecticides are even more closely related than was demonstrated in the first instance.

Dehydrodeguelin was catalytically reduced with hydrogen to dihydro-

¹ Clark, Science, 73, 17 (1931).

- ² Butenandt, Ann., 464, 272 (1928).
- ³ LaForge and Smith, THIS JOURNAL, 52, 1091 (1930).
- ⁴ Clark, *ibid.*, **53**, 313 (1931).
- ⁵ Takei, Miyajima and Ono, Ber., 64, 248 (1931).
- ⁶ LaForge and Smith, THIS JOURNAL, 52, 2878 (1930).

dehydrodeguelin, C₂₃H₂₂O₆. This material was found to be identical with the compound recently described by Haller⁷ as dehydro- β -dihydrorotenone. Mild oxidation of dihydrodehydrodeguelin with chromic acid under the conditions described in the experimental part vielded oxydehydrodeguelin, $C_{23}H_{20}O_8$. Dihydrodehydrodeguelin when treated with alcoholic alkali in the manner by which deguelic acid was obtained from dehydrodeguelin yielded dihydrodeguelic acid, C23H26O8. The same substance was also prepared by catalytically reducing deguelic acid. This reduced deguelic acid was found to be identical with the compound described by Haller as dehydrodihydroxy-8-dihydrorotenoic acid.7

When dihydrodeguelic acid was subjected to alkaline oxidation with hydrogen peroxide, the yield of derric acid was essentially the same as that given by deguelic acid.

In the first communication of this series⁴ it was shown that deguelic acid reverts to dehydrodeguelin when an attempt is made to acetylate the phenolic hydroxyl group in the acid with acetic anhydride and sodium acetate. However, it has been found that if the acid is treated with a large excess of acetic anhydride in pyridine, a monoacetyldeguelic acid is formed which no longer gives a phenolic reaction with ferric chloride.

The reactions under discussion are summarized diagrammatically in Chart I.



CHART I-DERIVATIVES OF DEGUELIN

The observations just recorded show that there exist structural relationships common to the entire molecule of both rotenone and deguelin. However, the information now available is so fragmentary that it seems best to present the facts now at hand and await further developments before attempts at correlation are made.

Experimental

Derric Acid from Deguelic Acid.—An aqueous solution of 2 g. of deguelic acid in $25~{\rm cc.}$ of 5% potassium hydroxide solution, warmed to $60\,^{\circ}$, was treated portionwise with

⁷ Haller, This Journal, 53, 733 (1931).

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6 cc. of 30% hydrogen peroxide. After the reagent was added the mixture was gently boiled until foaming ceased. The liquid was then cooled, acidified with sulfuric acid and thoroughly extracted with ether. The extract was dried with sodium sulfate, concentrated to 20 cc. and allowed to crystallize. After several hours 0.5 g. of derric acid separated. This was removed from the mother liquor, washed with a small quantity of ether and dried. Its melting point was 167–168°.

The acid was recrystallized from boiling *n*-butyl ether, from which it separated as colorless rods and needles that melted at 168° (corr.).

The crystals had both straight and inclined extinction and positive elongation: η_{α} , 1.525 (on rods crosswise showing straight extinction); η_{β} , 1.565 (common on fragments not extinguishing sharply); and η_{γ} , 1.640 (usually on irregular-shaped fragments).⁸

These properties are the same as those possessed by derric acid prepared according to the directions of LaForge and Smith³ from rotenone and recrystallized from n-butyl ether.

Risic Acid from Deguelic Acid.—Two grams of deguelic acid, dissolved in 40 cc. of 1% potassium hydroxide was treated portionwise with a warm aqueous solution of 15 g. of potassium permanganate. After the reaction was completed, the liquid was filtered from the manganese dioxide and concentrated to 15 cc. The solution was then acidified with sulfuric acid and allowed to crystallize. The yield was 0.25 g. or 21%. Recrystallization of the acid from boiling *n*-butyl alcohol yielded colorless sheathes of fine needles and rods which melted at 256° with decomposition. A sample of the acid which Dr. LaForge obtained by the oxidation of derric acid had the same melting point upon recrystallization from *n*-butyl alcohol, and a mixture of the two acids showed no melting point depression.

Dihydrodeguelic Acid from Deguelic Acid.—A solution of 2 g. of deguelic acid in 100 cc. of alcohol was reduced at atmospheric pressure with hydrogen and the platinum catalyst of Voorhees and Adams.⁹ After the reaction was completed the solution was filtered and heated to boiling. An equal volume of hot water was then added. As the solution cooled long colorless needles separated. These began to soften at 70° and melted at 80°, apparently with the loss of vapor. Upon further heating the melt solidified and then remelted at 144°. When the acid was recrystallized from boiling *n*-butyl ether, it separated as colorless rods showing inclined extinction and having a melting point of 147° (corr.); η_{α} , 1.490; η_{β} , indeterminate and η_{γ} , higher than 1.740. It also possesses two intermediate indices, η_i , 1.605, and η_i' 1.740, which are useful diagnostic values.

Anal. Caled. for $C_{23}H_{26}O_6$: C, 64.17; H, 6.09; OCH₃ (2), 14.4. Found (material recryst. from butyl ether): C, 64.13; H, 6.24; OCH₃, 14.6.

Dihydrodeguelic acid and the compound described by Haller⁷ as dehydrodihydroxy- β -dihydrorotenonic acid were shown to be identical when it was found that both materials possess the same optical properties and melting point and that when the two substances were mixed no melting point depression occurred.

Derric Acid from Dihydrodeguelic Acid.—Two grams of dihydrodeguelic acid was treated with alkali and hydrogen peroxide according to the directions given before for the preparation of derric acid from deguelic acid. The yield of crystalline product was 0.55 g. This material, recrystallized from *n*-butyl ether, had a melting point of $167-168^{\circ}$ and it showed no depression of the melting point when mixed with derric acid. It also had the optical properties that are characteristic of derric acid.

⁸ The optical data recorded in this communication were determined by George L. Keenan of the Food and Drug Administration of the U. S. Department of Agriculture. Appreciation is gratefully acknowledged for this coöperation.

⁹ Voorhees and Adams, THIS JOURNAL, 44, 1397 (1922).

Monoacetyldeguelic Acid.—Two grams of deguelic acid was dissolved in 12 cc. of pyridine, and the solution was treated with 16 cc. of acetic anhydride. The mixture was allowed to stand at room temperature for three hours, and then one volume of acetic acid and four volumes of water were added. The liquid was made acid to Congo red with 10% sulfuric acid and set aside to crystallize. The yield was 1.85 g. The material was recrystallized by dissolving it in acetic acid and adding hot water until a slight turbidity was produced. Upon standing the acetyl derivative separated as colorless crystals which melted at 128–129°. It gave no color reaction with ferric chloride as did the free acid.

For analysis it was necessary to heat the material to its melting point in a high vacuum to remove an indefinite quantity of solvent which could not be completely eliminated otherwise.

Anal. Caled. for $C_{26}H_{26}O_{9}$: C, 63.82; H, 5.57; OCH₃ (2), 13.2. Found: C, 63.85; H, 5.6; OCH₃, 13.1.

Dihydrodehydrodeguelin.—Five grams of dehydrodeguelin dissolved in 200 cc. of hot acetic acid was reduced at atmospheric pressure and approximately 75° with hydrogen and the platinum catalyst of Voorhees and Adams.⁹ After the reaction was completed and the solution cooled to room temperature, a product crystallized from the acetic acid. This was removed by filtration, and dissolved in 40 cc. of chloroform. The solution was filtered through norit, again heated to boiling, and five volumes of boiling ethanol was then added. Crystallization began at once, yielding 1.9 g. of long yellow rods and needles which melted at 267°. Their extinction was inclined and in convergent polarized light (crossed nicols) biaxial interference figures were common. 2E was small and the double refraction was very strong. The only index of refraction determinable was the minimum value η_{cr} 1.498; η_{γ} is greater than 1.74.

A comparison of dihydrodehydrodeguelin and the compound dehydro- β -dihydrorotenone described by Haller showed the two substances to be identical, as their melting points and optical properties were the same, and when the two substances were mixed the melting point was not depressed.

Anal. Caled. for $C_{23}H_{22}O_6$: C, 70.03; H, 5.63; OCH₃ (2), 15.7. Found: C, 69.86; H, 5.79; OCH₃, 15.5.

Oxydehydrodeguelin.—Two grams of dihydrodehydrodeguelin dissolved in the minimum quantity of boiling acetic acid was oxidized with 15 cc. of a 10% acetic acid solution of crystalline sodium dichromate. The mixture was allowed to stand until the next day. The oxydehydrodeguelin was then removed by filtration. The yield was 0.36 g. It was recrystallized by dissolving 0.3 g. of the crystals in 20 cc. of boiling chloroform and adding to the solution 60 cc. of boiling ethanol. The substance melted at 303°, and the yield was almost quantitative. It consisted of small yellow needles and rods with square ends. The extinction was straight, and the elongation was negative. Only faint partial biaxial interference figures were shown in convergent polarized light (crossed nicols); η_{α} , 1.490 (frequently shown lengthwise on rods), η_{β} , 1.595 (crosswise), and η_{γ} , >1.740.

Anal. Caled. for C₂₈H₂₀O₈: C, 65.08; H, 4.75; OCH₃ (2) 14.6. Found: C, 64.81; H, 4.85; OCH₃, 14.2.

Dihydrodeguelic Acid from Dihydrodehydrodeguelin.—A mixture of 0.5 g. of dihydrodehydrodeguelin, 1 g. of zinc dust, 12 cc. of ethanol and 3 cc. of a 50% aqueous potassium hydroxide solution was refluxed for thirty minutes. The reaction mixture was cooled by the addition of crushed ice and diluted with water to a volume of 75 cc. The zinc was removed by decantation, and the alkaline solution was made acid to Congo red with sulfuric acid. The acid solution was extracted with ether. The ethereal ex-

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tract was dried over sodium sulfate and evaporated to dryness. The residue was dissolved in hot *n*-butyl ether. Upon cooling 0.36 g. of dihydrodeguelic acid separated which had the properties recorded for the acid obtained by catalytically reducing deguelic acid.

Summary

1. Derric and risic acids have been obtained from deguelic acid by methods analogous to those used in preparing these acids from derivatives of rotenone. This shows that in deguelin as in rotenone, derric acid constitutes one-half of the molecule.

2. Reduction of dehydrodeguelin yields dihydrodehydrodeguelin, which is identical with dehydro- β -dihydrorotenone.

3. Upon treatment with alcoholic alkali, dihydrodehydrodeguelin gives dihydrodeguelic acid. This acid is also obtained by catalytically reducing deguelic acid.

4. Dihydrodeguelic acid has been found to be identical with dehydrodihydroxy- β -dihydrorotenonic acid described by Haller.

5. These facts show that there exist structural relationships common to the entire molecule of both rotenone and deguelin.

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THE SYNTHESIS OF POLYPORIC ACID AND ATROMENTIN DIMETHYL ETHER

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Two of the important coloring matters found in fungi are polyporic acid (I) obtained from *Polyporous nidulans* and atromentin (II) from *Paxillus atrotomentosus*. Kögl² determined the structures of these two compounds to be derivatives of diphenylquinone.



Moreover, he synthesized each of these compounds in two ways. The first method was that devised by Fichter.³ For the polyporic acid, ethyl phenylacetate and ethyl oxalate² were condensed together with sodium;

¹ This communication is an abstract of a portion of a thesis submitted by P. R. Shildneck in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

- ² Kögl, Ann., 447, 78 (1926).
- ⁸ Fichter, *ibid.*, **361**, 363 (1908).