3. Oxidation of toxicarol with ferricyanide yields dehydrotoxicarol involving the loss of two hydrogen atoms from the mother substance.

4. Dehydrotoxicarol is also formed by the oxidation of toxicarol with iodine in an alcoholic potassium acetate solution. In this reaction an intermediate iododehydrotoxicarol is formed which can be dehalogenated with zinc dust and acetic acid.

5. Reduction of dehydrotoxicarol or its acetyl derivative not only results in the reduction of the double bond, demonstrated by the dihydro formation, but it also regenerates the structure responsible for the dehydro formation.

6. It seems possible that the second acetyl group introduced into toxicarol is the result of some reaction brought about by the reagents involved in the acetylation process.

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

ROTENONE. XII. SOME NEW DERIVATIVES OF ROTENOL

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When rotenone ($C_{23}H_{22}O_6$) is refluxed with zinc and alkali in alcohol solution, two products are obtained, derritol, which is soluble in alkali, and rotenol, which is alkali insoluble. Rotenol is a white compound which possesses two hydrogen atoms more than rotenone, and Butenandt[1] assumes that it is formed by the reduction of the carbonyl group to a secondary alcohol group because, unlike rotenone, it does not yield an oxime and because it liberates one mole of methane with the Grignard reagent. The presence of an hydroxyl group in rotenol has not been satisfactorily demonstrated, however, as all attempts to obtain acyl derivatives have failed, and we have lately found several new facts which contradict the assumption that it is an alcohol.

In the course of our work on the structure of rotenone it has been found that rotenol readily yields isotubaic acid on alkali fusion[2] and that dihydrorotenolic acid is readily cleaved with alkaline hydrogen peroxide, forming netoric acid[3] ($C_{12}H_{14}O_5$), which contains the original methoxyl groups.

Both these reactions are best explained by the assumption of cleavage at a carbonyl group, as is generally assumed for other derivatives of rotenone. An attempt was made, therefore, to determine whether or not rotenol possesses a ketone group or whether this group has been reduced as suggested by Butenandt.

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[1] Butenandt, *Ann.*, **464**, 253 (1928).

[2] Haller and LaForge, THIS JOURNAL, **52**, 4505 (1930).

[3] Smith and LaForge, *ibid.*, **52**, 4595 (1930).

We have, in fact, confirmed the observations of Butenandt in that we have been unable to form an oxime from rotenol and have not been successful in preparing an acetyl derivative. On the other hand, we have found in one important reaction an indication of the presence of a ketone group. With Clemmensen's reagent (amalgamated zinc) isorotenol ($C_{23}H_{24}O_6$) yields a compound having the empirical formula $C_{23}H_{26}O_5$, thus indicating the reduction of a carbonyl group. Rotenol and dihydrorotenol on the other hand are not reduced with this reagent but are recovered unchanged. Rotenol, however, can be isomerized to isorotenol identical with the isorotenol obtained from isorotenone, and there is no reason to assume that the carbonyl group is involved in the process of isomerization.

As it has been shown that rotenone contains two asymmetric centers, one of which disappears when rotenone and its derivatives are isomerized with sulfuric acid to isorotenone and its derivatives, and the other in the formation of the dehydro derivatives, it would be expected that isorotenol would be optically active, especially as a new asymmetric center would be formed in the conversion of the carbonyl group to the secondary alcohol group. The fact that isorotenol is optically inactive whereas rotenol is optically active is an additional argument against its supposed alcoholic nature.

On oxidation with ferricyanide and alkali, rotenol and dihydrorotenol yield dehydro derivatives isomeric with rotenone and dihydrorotenone. Unlike all the other dehydro derivatives of rotenone, which are yellow, dehydrorotenol and dehydrodihydrorotenol are white. Molecular weight determination shows that dehydrorotenol is not a dimolecular compound. It does not yield an oxime nor an acetyl derivative. On catalytic hydrogenation dehydrorotenol yields a mixture of a dihydro compound which is identical with the dehydro derivative obtained from dihydrorotenol and an acid which has been termed dehydrodihydrorotenolic acid. This acid is quite stable to alkali and is not cleaved in alkaline solution with hydrogen peroxide as are most of the rotenonic acid derivatives. With zinc and alkali, dehydrorotenol does not add water as do other dehydro derivatives of rotenone but is reduced quantitatively to rotenol.

Dihydrorotenol also yields a dehydro derivative. This substance, dehydrodihydrorotenol, is not reduced with catalytic hydrogen, but on boiling with zinc and alkali in alcohol solution it is quantitatively reduced to dihydrorotenol.

On boiling with zinc and alkali in alcohol solution, dihydrorotenonic acid yields dihydrorotenolic acid. There is no evidence that dihydroderritolic acid is formed, as might be expected from the analogy in the case of rotenone itself.

Experimental

Dehydrodihydrorotenol.—One-half gram of dihydrorotenol was dissolved in 25 cc. of 95% alcohol and 0.9 g. of potassium ferricyanide, and 0.135 g. of potassium hydroxide in 7.5 cc. of water was added to the hot solution. The reaction mixture was allowed to stand overnight and then diluted with about 400 cc. of water. The precipitated substance was filtered off, washed with water and dried. Recrystallized from 95% alcohol, it melted at 171°.

Anal. Subs., 0.0870, 0.0912: CO_2, 0.2220, 0.2328; H_2O, 0.0472, 0.0499. 0.1770 subs. in 12.3 g. benzene; $\Delta T = 0.191°$. Calcd. for $C_{23}H_{24}O_6$: C, 69.69; H, 6.06; mol. wt., 396. Found: C, 69.59, 69.62; H, 6.07, 6.12; mol. wt., 376.7.

Dehydrodihydrorotenol did not yield an oxime when refluxed with hydroxylamine hydrochloride and sodium acetate in absolute alcohol. When boiled with acetic anhydride and sodium acetate it was recovered unchanged.

Dehydrorotenol.—Dehydrorotenol was obtained when rotenol was treated with alkali and potassium ferricyanide in the same manner that was described for the preparation of dehydrodihydrorotenol. It was purified by crystallization from 95% alcohol. It melted at 124°.

Anal. Subs., 0.0936: CO_2, 0.2402; H_2O, 0.0465. Calcd. for $C_{23}H_{22}O_6$: C, 70.03; H, 5.63. Found: C, 69.99; H, 5.56.

Reduction of Dehydrorotenol with Catalytic Hydrogen.—1.86 g. of dehydrorotenol dissolved in 25 cc. of ethyl acetate was added to 25 cc. of ethyl acetate containing about 0.3 g. of platinum oxide catalyst, previously saturated with hydrogen, and the solution was shaken in an atmosphere of hydrogen. About 200 cc. of hydrogen was absorbed in two or three minutes, after which absorption practically ceased. The solution was decanted from the catalyst, most of the ethyl acetate was distilled off, and the concentrated solution was dissolved in ether. The ether solution was extracted with 5% sodium hydroxide, then with water. It was dried over sodium sulfate. After the ether was removed the remaining product was crystallized from 95% alcohol. It melted at 171°. When mixed with an equal quantity of dehydrodihydrorotenol, no depression in melting point was noted.

The aqueous alkaline extract was acidified with dilute sulfuric acid 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 95% alcohol. It melted at 206°. It was named dehydrodihydrorotenolic acid.

Anal. Subs., 0.0839: CO_2, 0.2129; H_2O, 0.0474. *Titration.* Subs., 0.0328: 0.85 cc. of $N/10$ KOH. Calcd. for $C_{23}H_{26}O_6$: C, 69.31; H, 6.58. Found: C, 69.21; H, 6.32. Acid number calcd., 398; found, 386.

The potassium and sodium salts of dehydrodihydrorotenolic acid are relatively quite insoluble in dilute alkaline solution. In an attempt to oxidize this acid in alkaline solution with hydrogen peroxide by the procedure usually employed, only the unchanged material was recovered. Unchanged starting material was also obtained when the acid was treated with alkaline permanganate, although some oxidation took place.

The acid was also found to be stable on prolonged boiling in strong alcoholic potash solution.

Mixed Anhydride of Dehydrodihydrorotenolic Acid and Acetic Acid.—One-half gram of dehydrodihydrorotenolic acid was refluxed with 20 cc. of acetic anhydride and 1 g. of anhydrous sodium acetate for two hours. The solution was poured into water, the precipitate was filtered off, washed with water and dried. It was then recrystallized from 95% alcohol. It melted at 136°.

Anal. Subs., 0.0770: CO_2, 0.1919; H_2O, 0.0428. Calcd. for $C_{25}H_{28}O_7$: C, 68.15; H, 6.41. Found: C, 67.97; H, 6.22.

The substance is insoluble in cold dilute alkali and is quite stable in boiling methyl alcohol. When it is decomposed with cold alcoholic alkali, dehydrodihydrorotenolic acid can be recovered.

Reduction of Dehydrodihydrorotenol to Dihydrorotenol.—Five-tenths of a gram of dehydrodihydrorotenol was refluxed for two hours with 20 cc. of 95% alcohol, 5 cc. of 40% potassium hydroxide, and 2 g. of zinc. The hot solution was then filtered into ice cold dilute sulfuric acid. The precipitate was filtered off, washed with water and dissolved in ether. The ether solution was washed with water and dried over sodium sulfate. After the removal of the ether the substance was crystallized from 95% alcohol. It crystallized in fine needles which melted at 131–132°. The yield was 0.5 g. When mixed with an equal quantity of dihydrorotenol, the melting point was 129°. It was further identified as dihydrorotenol by an optical examination of the crystals.

Anal. Subs., 0.0785: CO_2, 0.1994; H_2O, 0.0462. Calcd. for $C_{23}H_{26}O_6$: C, 69.31; H, 6.58. Found: C, 69.28; H, 6.59.

Reduction of Dehydrorotenol to Rotenol.—The procedure employed was the same as that described above for the reduction of dehydrodihydrorotenol. The product obtained was recrystallized from 95% alcohol. It melted at 120° and was identified as rotenol.

Desoxyisorotenol.—Two grams of isorotenol dissolved in 80 cc. of glacial acetic acid was added to 12 g. of amalgamated zinc followed by 10 cc. of concentrated hydrochloric acid. The reaction mixture was then refluxed for two hours. The hot solution was decanted from the zinc and slowly poured into 500 cc. of water. After cooling, the precipitate was filtered off, washed with water and dissolved in ether. The ethereal solution was washed with water and dried over sodium sulfate. On removal of most of the ether the substance readily crystallized. It was recrystallized from 95% alcohol. It melted at 149°. It does not give a color with ferric chloride.

Anal. Subs., 0.0825: CO_2, 0.2189; H_2O, 0.0525. Calcd. for $C_{23}H_{26}O_5$: C, 72.25; H, 6.86. Found: C, 72.35; H, 7.07.

Isorotenol from Rotenol.—Three grams of rotenol (melting point 119°) was dissolved in a solution of 36 cc. of glacial acetic acid and 9 cc. of concentrated sulfuric acid. The solution was heated to 100° for five minutes, cooled and poured into 600 cc. of water. A little sodium sulfate was added, and the precipitate was filtered off and washed twice with water. The precipitate was dissolved in ether, and was washed twice with 5% potassium carbonate solution and then with water. After it was dried over sodium sulfate, the ether was removed, when the substance crystallized. The yield was 2.2 g. After repeated crystallization from 95% alcohol, it was obtained pure. It melted at 131°. It gave the same color in alcohol solution with ferric chloride as does isorotenol prepared from isorotenone. It was further identified as isorotenol by an optical examination of the crystals.

Reduction of Dihydrorotenonic Acid with Zinc and Alkali.—Two grams of dihydrorotenonic acid was refluxed for four hours in a solution of 60 cc. of 95% alcohol and 20 cc. of 15% potassium hydroxide to which had been added 4 g. of zinc. The hot solution was decanted from the zinc and filtered into cold dilute sulfuric acid. The precipitate was filtered off, washed with water, and dissolved in ether. The ethereal solution was washed with water and dried over sodium sulfate. On removal of the ether the substance readily crystallized. It was recrystallized from methyl alcohol and melted at about 90°. It was identified as dihydrorotenolic acid.

When 45% potassium hydroxide was employed, dihydrorotenonic acid also yielded dihydrorotenolic acid. There was no indication of the formation of dihydroderritolic acid.

Summary

Rotenol and dihydrorotenol on oxidation with alkaline ferricyanide yield dehydro derivatives.

Dehydrorotenol is reduced with catalytic hydrogen to a mixture of dehydrodihydrorotenol and dehydrodihydrorotenolic acid.

Dehydrodihydrorotenolic acid is not cleaved with alkaline hydrogen peroxide.

With zinc and alkali dehydrorotenol and dehydrodihydrorotenol are reduced quantitatively to rotenol and dihydrorotenol.

Isorotenol ($C_{23}H_{24}O_6$) on reduction with Clemmensen reagent (amalgamated zinc) yields a compound of formula $C_{23}H_{26}O_5$, indicating the reduction of a carbonyl group.

Dihydrorotenonic acid is reduced with zinc and alkali to dihydrorotenolic acid.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

THE MUTAROTATION OF THE ALCOHOLATE AND ALDEHYDROL OF ALDEHYDO-GALACTOSE PENTAACETATE

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The open chain or aldehydo sugar acetates synthesized in this Laboratory show mutarotation in alcohol but not in such non-hydroxylated solvents as acetylene tetrachloride. The mutarotation in alcohol is indicative of chemical combination of some kind between the solvent and the carbonyl group of the sugar acetate. In the case of galactose,[1] well-defined crystalline compounds with ethanol and water were isolated. At the time of the isolation of these two compounds, we were interested only in determining their initial rotation in chloroform and the U. S. P. grade of this solvent was used. The rotations were thus determined in chloroform containing an appreciable amount of ethanol. In both cases mutarotation curves which passed through a minimum were obtained. The unusual nature of these mutarotation curves has been pointed out to us by Professor T. M. Lowry and we have accordingly repeated the experiments using alcohol-free chloroform. In this solvent we find a minimum only in the curve for the ethanol compound (Fig. 1). Data for two experiments with the ethanol compound are given in Table I. The actual speeds for the two experiments are widely different but values identical within the limits of experimental error are obtained for the minimum and final rotations. This variation in speed is probably due to the catalytic effect of hydrogen chloride produced by the slight photochemical decomposition of the alcohol-free chloroform used, the amount of acidity present being apparently different in the two cases.

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[1] M. L. Wolfrom, THIS JOURNAL, 52, 2464 (1930).