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STRUCTURE OF AMORPHIGENIN

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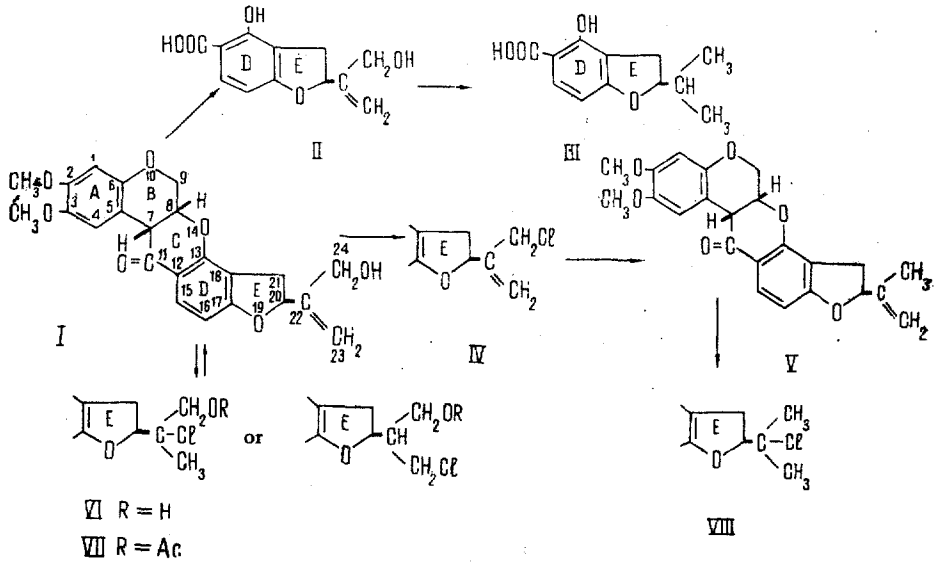
We have shown previously [1] that amorphigenin (the aglycone of the rotenoid glycoside amorphin from plants of the genus Amorpha) has the ring system of rotenone. The position of the hydroxy group, which we consider must be attached to the dihydrofuran ring, remained obscure.

Claisse, Crombi, and Peace have made a study of the structure of amorphin [2]. By using various physical methods, mainly NMR spectroscopy, and by interpreting certain chemical reactions somewhat differently, the British authors came to the conclusion that amorphigenin possesses not only the cyclic structure of rotenone but also a side chain. In contrast to rotenone, this side chain contains a primary hydroxy group attached in amorphin to the disaccharide vicianose. In this paper we give direct experimental results confirming the structure of amorphigenin as 24-hydroxyrotenone.

When heated with alkalies, amorphigenin (I), like rotenone [3], undergoes extensive degradation, forming a hydroxy acid with the composition $C_{12}H_{12}O_5$ (II), the catalytic hydrogenation of which leads to dihydrotubaic acid (III), which has been described in the literature [3, 5].

The processes taking place in the reduction of hydroxytubaic acid (II) to dihydrotubaic acid (III) are similar to those observed on passing from amorphigenin to deoxydihydroamorphigenin [1]. The production of III unambiguously established the structure of the benzofuran moiety of amorphigenin and of the side chain.

We have also carried out a direct transition from I to rotenone (V), showing both the structure and the stereochemistry of the former compound. For this purpose, the hydroxy group of amorphigenin was replaced by chlorine through the action of thionyl chloride. The reduction of the 24-chlororotenone (IV) with zinc gave a substance with physical (UV and IR spectra, specific rotation) and chemical properties of which were identical with those of natural rotenone (V) and which gave no depression of the melting point with the latter. Its hydrochloride (VIII) had the same melting point as rotenone hydrochloride. Thus, amorphigenin is 24-hydroxyrotenone and has the configuration I.



In addition to this (in connection with other matters), we also studied the action of hydrogen chloride on amorphigenin. Like rotenone [4], amorphigenin adds hydrogen chloride at the double bond of the side chain to form the hydrochloride of the latter (VI) with the composition $C_{23}H_{23}ClO_7$. However, here a fundamental difference is observed. When hydrogen chloride is split off from rotenone hydrochloride (VIII) the double bond migrates from the side chain into the furan nucleus and forms isorotenone, but in the case of amorphigenin hydrochloride (VI) the normal reaction takes place with the appearance of a double bond at its original position in the side chain. Dehydroamorphigenin behaved similarly under the action of hydrogen chloride.

Experimental

Hydroxytubaic acid (II) from amorphigenin (I). A mixture of 10 g of amorphigenin and 5 g of caustic potash in 5 ml of water and 100 ml of ethanol was heated at the boil for 3 hr. The mixture was poured into 500 ml of water and acidified with 20% hydrochloric acid, and the reaction products were extracted with ether. The ethereal solution was extracted with 10% sodium hydrogen carbonate solution, and the alkaline extract was again acidified with hydrochloric acid and extracted with ether. The ether was evaporated off to dryness, and the dry residue was recrystallized from benzene and water. This gave 400 mg of slightly brownish needles with mp 120°–121° C, $[\alpha]_D^{20}$ −80.8± 2.5° (c 3.7; methanol). With ferric chloride the substance gave a violet-red coloration.

IR spectrum: 3390 cm^{-1}, 3300 (phenolic OH), 3000–2700 (carboxylic OH), 1668, 1653, 1633 (carboxylic C=O), 1598, 1500 (aromatic C—C), 1270 (alcoholic OH), and 785 cm^{-1} (C—H of a 1, 2, 3, 4-substituted benzene).

Found, %: C 60.63, 60.81; H 5.01, 5.20; mol. wt. 234, 237 (potentiometric). Calculated for $C_{12}H_{12}O_5$, %: C 60.92; H 5.12; mol. wt. 236.23.

Dihydrotubaic acid (III) from (II). 100 mg of hydroxytubaic acid (II) was hydrogenated in 5 ml of glacial acetic acid over Adams platinum. After the absorption of hydrogen had ceased, the solution was filtered and poured into 100 ml of water. The precipitate that deposited was recrystallized from 70% methanol. This yielded fine needles with mp 166°–167° C, $[\alpha]_D^{20}$ −85 ± 3° (c 0.5; chloroform). Literature: mp 166° C, $[\alpha]_D$ −82° [3]; mp 168° C, $[\alpha]_D$ −89° [5].

Found, %: C 64.65, 64.80; H 6.07, 6.21. Calculated for $C_{12}H_{14}O_4$, %: C 64.85; H 6.34.

24-Chlororotenone (IV) from (I). A mixture of 1 g of amorphigenin, 0.2 ml of thionyl chloride, and 50 ml of benzene was heated to the boil. After half an hour, 0.1 ml of thionyl chloride in 5 ml of benzene was added to the reaction mixture and after another half hour a further 0.5 ml of thionyl chloride, after which the mixture was heated for another 1 hr. The cooled solution was washed with water to neutrality, dried, passed through a column of 30 g of alumina, and evaporated to dryness, and the residue was crystallized successively from methanol and ethyl acetate and again from methanol. The IR spectrum lacked a hydroxyl absorption band.

Found, %: C 64.13, 64.10; H 4.92, 4.84; Cl 8.46, 8.37. Calculated for $C_{23}H_{21}ClO_6$, %: C 64.40; H 4.93; Cl 8.26.

Rotenone (V) from (IV). One gram of rotenone was heated at 100° C in a mixture of acetic acid, ethanol, and water (1:1:1) for 6 hr with the gradual addition of 2 g of zinc dust. The hot solution was filtered and poured into 120 ml of water. The precipitate that deposited was dissolved in benzene and the solution was dried and passed through a column of alumina (10 g). The benzene was evaporated off and the residue was twice recrystallized from methanol. Needles with mp 162° C deposited. A mixture with an authentic sample of rotenone melted at 161° C, $[\alpha]_D^{20}$ −225° (c 1.37; benzene); $[\alpha]_D^{20}$ −120° (c 1.39; chloroform). Literature: $[\alpha]_D^{20}$ −227° (c 1.62; benzene); $[\alpha]_D^{20}$ −122° (c 1.7; chloroform) [6].

The UV and IR spectra of the rotenone obtained from chlorotenone and of an authentic sample were identical.

Rotenone hydrochloride (VIII) was prepared by a published method [4] from the rotenone that we had synthesized. White crystals with mp 186°–187° C were formed. Literature: mp 188° C [4]. A mixture with chlororotenone (IV) melted at 165° C.

Amorphigenin hydrochloride (VI) from (I). Obtained similarly to rotenone hydrochloride [4]. After successive recrystallizations from acetic acid, benzene, and 50% methanol, it formed white needles with mp 171°–172° C, $[\alpha]_D^{20}$ −87° (c 0.92; chloroform).

Found, %: C 61.63, 62.01; H 5.15, 5.34; Cl 8.18, 8.27. Calculated for $C_{23}H_{23}ClO_7$, %: C 61.81; H 5.18; Cl 7.93.

Amorphigenin hydrochloride acetate (VII) from (VI). A mixture of 100 mg of amorphigenin hydrochloride, 1.5 ml of acetic anhydride, 0.2 ml of glacial acetic acid, and 0.2 g of anhydrous sodium acetate was heated at 100° C for half an hour and was then left at room temperature for a day. The reaction mixture was poured into 10 ml of water and the precipitate that deposited was recrystallized from methanol. Crystals with mp 184°–186° C were obtained.

The IR spectrum lacked the absorption band of a hydroxy group.

Amorphigenin acetate from amorphigenin hydrochloride (VI). A mixture of 0.5 g of amorphigenin hydrochloride and 5 ml of glacial acetic acid was heated at the boil for 2 hr with the gradual addition of 2 g of zinc dust to the reaction mixture. Then heating was continued for another 2 hr. The filtered reaction mixture was poured into water and the precipitate that deposited was recrystallized from 50% acetic acid and from methanol. Needles with mp 155°–156° C were formed. A mixture with authentic amorphigenin acetate melted at 155° C.

Dehydroamorphigenin hydrochloride. The substance was obtained similarly to rotenone hydrochloride [4]. After recrystallization from 50% acetic acid and a mixture of chloroform and methanol, yellow needles were obtained with

mp 209°–212° C (decomp.).

Found, %: C 61.93, 62.18; H 4.59, 4.73; Cl 8.15, 8.11. Calculated for $C_{23}H_{21}ClO_7$, %: C 62.09; H 4.75; Cl 7.97.

The acetate of dehydroamorphigenin hydrochloride had mp 178°–180° C (decomp.).

Summary

The alkaline cleavage of amorphigenin has given hydroxytubaic acid and amorphigenin has been converted directly to rotenone. The hydrochlorination of amorphigenin has been studied.

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