—To a solution of 3 g. of isodione in 275 cc. of absolute ethyl alcohol was added 2 cc. of *n*-butyl mercaptan. The solution was refluxed for sixteen hours during which time dry hydrogen chloride was bubbled through continuously. Evaporation to 50 cc. and precipitation by pouring into ice and water gave 1.87 g. of amorphous material which was washed repeatedly with hot water. Five crystallizations from methanol including decolorization with Norite gave a product melting at 236–242°; $[\alpha]^{25}_{\mathrm{D}}$ +45.3°; $[\alpha]^{26}_{546}$ +56.1° in chloroform. *Anal.* Calcd. for $C_{29}H_{44}O_2$: C, 82.02; H, 10.44. Found: C, 82.01; H, 10.74.

A strong positive test for unsaturation was obtained with tetranitromethane. The compound contained no sulfur as was shown by testing for sulfide ion after fusion with sodium. Treatment with cold acetic anhydride and pyridine or refluxing four hours with acetic anhydride and potassium acetate gave only the unchanged conjugated dione.

An **oxime** was prepared by refluxing 0.96 g. of conjugated dione, 0.49 g. of hydroxylamine hydrochloride, and 1.23 g. of fused potassium acetate in 125 cc. of methanol for five hours. On cooling 0.61 g. of crystalline material was obtained which, after four crystallizations from methyl alcohol, melted with decomposition at 269–271° when placed in a heated bath at 250°; $[\alpha]^{25}_{\mathrm{D}}$ −23.4° in dioxane. Although there is no depression in decomposition point on mixing with the oxime of isodione, the rotation of the latter compound is $[\alpha]^{26}_{\mathrm{D}}$ +22.0°, $[\alpha]^{26}_{546}$ +28.2° in dioxane. *Anal.* Calcd. for a monoxime, $C_{29}H_{45}O_2N$: C, 79.22; H, 10.32; N, 3.18. Found: C, 79.00; H, 10.16; N, 3.90.

Treatment of 0.52 g. of nordione in 60 cc. of absolute ethyl alcohol and 1 cc. of *n*-butyl mercaptan with hydrogen chloride as described previously for the isodione gave a product which melted at 236–242°, $[\alpha]^{22}_{\mathrm{D}}$ +42.7° in dioxane, and showed no depression in melting point when mixed with conjugated dione.

Refluxing 1 g. of isodione with 1 cc. of *n*-butyl mercaptan in 100 cc. of 95% ethyl alcohol for sixteen hours without the addition of hydrogen chloride yielded material on concentration which melted at 219–225° and showed no melting point depression on mixing with isodione. The mother liquors gave only isodione.

A solution of 0.110 g. of conjugated dione and 0.3 g. of potassium hydroxide in 30 cc. of 95% ethyl alcohol was refluxed for four hours. Water was added to the hot solution to turbidity, and on cooling a white crystalline product was obtained which after two crystallizations from methyl alcohol melted at 234–242° and showed no melting point depression on mixing with the starting material.

Absorption Spectra.—The absorption spectrum of the conjugated dione was determined first by Dr. R. Norman Jones in the Chemical Laboratory of Harvard University, using a quartz spectrograph in conjunction with a Hilger Spekker photometer and we wish to express our appreciation of his help. This work has been duplicated and the other spectra obtained using a Beckman quartz photoelectric spectrophotometer.

Summary

1. Treatment of isonorechinocystenedione with either alcoholic hydrogen chloride, acetic anhydride and potassium acetate, or alcoholic potassium hydroxide leads to isomerization to norechinocystenedione. Prolonged action of alcoholic potassium hydroxide on pure norechinocystenedione gives some isonorechinocystenedione indicating that the conversion of isodione to nordione is reversible

2. Prolonged treatment of either isodione or nordione with alcoholic hydrogen chloride in the presence of butyl mercaptan gives a new isomer designated as "conjugated norechinocystenedione" in which the double bond has become conjugated with one of the carbonyl groups as shown by the ultraviolet absorption spectrum.

3. The abnormally high absorption and the second maximum reported previously for the nordione are due to an impurity. That this impurity is not conjugated nordione is indicated by the fact that the absorption curve of the impure compound cannot be duplicated by mixtures of nordione and conjugated nordione.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

Saponins and Sapogenins. XXVI. The Conversion of Echinocystic Acid into Oleanolic Acid

BY DAVID FRAZIER AND C. R. NOLLER

While it has been possible to show that echinocystic acid and oleanolic acid have the same carbon skeleton,[1] attempts to interrelate the compounds more closely were unsuccessful.[2] The indications, however, are that echinocystic acid differs from oleanolic acid in having an additional hydroxyl group β to the carboxyl group. If it were possible to replace the β-hydroxyl group in echinocystic acid by hydrogen under conditions which did not involve rearrangement, one would expect to obtain oleanolic acid. Among various procedures which have been tried to bring this about, an attempt was made to replace the β-hydroxyl group by iodine using the series of reactions worked out by Helferich[3] for the sugars, namely, formation of the methanesulfonyl (mesyl) derivative and reaction with sodium iodide to replace the methanesulfonate group by iodine. It was expected that it would be possible to remove the iodine from an iodo derivative by reduction.

For this purpose the monoacetyl derivative of methyl echinocystate prepared by direct esterification with acetic acid was used as a starting point. In this compound the hydroxyl group which is not β to the carboxyl group is acetylated while the β-hydroxyl group is free.[4] Reaction with methanesulfonyl chloride in pyridine gave methyl acetylmesylechinocystate. When this

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(1) Todd, Harris and Noller, THIS JOURNAL, **62**, 1624 (1940).

(2) Harris and Noller, *ibid.*, **66**, 1005 (1944).

(3) Helferich, *Ber.*, **71**, 712 (1938).

(4) White and Noller, THIS JOURNAL, **61**, 983 (1939).

compound was heated with sodium iodide in acetone solution at 100° a product was obtained which was free of iodine and sulfur. Analyses showed it to be methyl acetylanhydroechinocystate formed by loss of methanesulfonic acid. No other crystalline product could be isolated. When methyl acetylmesylechinocystate was heated with methyl alcohol in the absence of sodium iodide at 140° or refluxed with acidified methyl alcohol, methyl anhydroechinocystate was obtained. Methyl acetylanhydroechinocystate and the deacetylated product were transparent to ultraviolet light, proving that the newly introduced double bond was not conjugated with the double bond originally present in methyl echinocystate.

Catalytic reduction of methyl anhydroechinocystate gave a product having the same melting point and optical rotation as methyl oleanolate and the melting point was not depressed on mixing with an authentic sample of methyl oleanolate. Acetylation gave a product which had the same properties as methyl acetyloleanolate and which did not depress the melting point of the latter compound on mixing. The conversion of echinocystic acid into oleanolic acid by the above series of reactions has an important bearing on the structure of oleanolic acid.[4a]

Experimental

Methyl Acetylmesylechinocystate.—Methyl monoacetylechinocystate was prepared by direct esterification of methyl echinocystate with acetic acid.[4] To a solution of 1.75 g. of vacuum dried product in 10 cc. of dry pyridine was added 1 cc. of methanesulfonyl chloride. After standing for forty-eight hours, a few drops of water were added to destroy the excess acid chloride, and the solution was poured into 50 cc. of distilled water. The gummy precipitate solidified on standing and was crushed, washed, filtered and crystallized from methanol to give 1.7 g. of product. For analysis it was recrystallized several times from 60–70° ligroin and dried at 110° and 5 mm. Like all the mesyl derivatives studied, the compound did not have a satisfactory melting point. It decomposed at approximately 165° with the evolution of gas and the formation of a deep red liquid. *Anal.* Calcd. for $C_{34}H_{54}O_7S$: C, 67.3. Found: C, 67.2, 67.4.[5]

Other Mesyl Derivatives of Echinocystic Acid.—Subjecting methyl echinocystate to the above procedure gave **methyl dimesylechinocystate.** After crystallization from methyl alcohol it decomposed at approximately 132°. *Anal.* Calcd. for $C_{33}H_{54}O_8S_2$: C, 61.6; S, 10.0. Found: C, 61.5, 61.7[5]; S, 10.4.

When echinocystic acid was treated in the same way a product was obtained which could be crystallized from methyl alcohol or ligroin and presumably was **dimesylechinocystic acid.** It was unstable, however, and changed to a red oil even on standing in an evacuated desiccator.

Methyl Acetylanhydroechinocystate.—A solution of 0.2 g. of methyl acetylmesylechinocystate and 0.5 g. of fused sodium iodide in 10 cc. of dry acetone was heated in a sealed tube at 100° for ten hours. A crystalline water soluble precipitate, presumably sodium methanesulfonate, was formed and the solution turned red. Evaporation of the acetone gave a residue which was washed thoroughly with distilled water and crystallized from methanol. The yield was only 50% of the calculated amount but no other crystalline product could be isolated. Three recrystallizations gave fluffy rosets, m. p. 192–193°, $[\alpha]^{23}_D$ +19.5°, $[\alpha]^{23}_{546}$ +22.2° in chloroform. *Anal.* Calcd. for $C_{33}H_{50}O_4$: C, 77.59; H, 9.86. Found[6]: C, 77.47, 77.42; H, 9.89, 9.86.

Methyl Anhydroechinocystate.—A solution of 1.2 g. of methyl acetylmesylechinocystate in 75 cc. of methanol containing 5 cc. of concentrated hydrochloric acid was refluxed for forty-eight hours. On cooling 0.7 g. of long transparent needles separated. After two recrystallizations from methanol and drying in air at room temperature, the crystals melted at 177°, then slowly solidified and remelted at 192–193°. Crystals dried at 110° lose their transparency and melt initially at 192–193°; $[\alpha]^{23}_D$ +18.3° in chloroform. *Anal.* Calcd. for $C_{31}H_{48}O_3$: C, 79.43; H, 10.32. Found[6]: C, 79.30, 79.27; H, 10.31, 10.35.

The same compound was obtained by heating methyl acetylmesylechinocystate with methyl alcohol alone in a sealed tube for four hours at 140°.

Acetylation of methyl anhydroechinocystate gave methyl acetylanhydroechinocystate identical with the product obtained by the action of sodium iodide in acetone on methyl acetylmesylechinocystate.

Catalytic Reduction of Methyl Anhydroechinocystate to Methyl Oleanolate.—A solution of 0.134 g. of methyl anhydroechinocystate in 15 cc. of glacial acetic acid was stirred with 0.120 g. of Adams platinum oxide catalyst in a hydrogen atmosphere.[7] After one mole of hydrogen was absorbed, the solution was filtered and poured into 50 cc. of water. The precipitate was filtered, washed with water and crystallized twice from methanol. It melted at 199–200°; $[\alpha]^{25}_D$ +73.2°; $[\alpha]^{25}_{546}$ +86.7° in chloroform. *Anal.* Calcd. for $C_{31}H_{50}O_3$: C, 79.09; H, 10.71. Found[6]: C, 79.34, 79.22; H, 10.83, 10.71. No depression in melting point was observed on mixing with an authentic sample of methyl oleanolate, m. p. 199–200°; $[\alpha]^{18}_D$ +74.9° in chloroform.[8]

When 0.066 g. of the product of catalytic reduction was reacted with 5 cc. of acetic anhydride in 5 cc. of pyridine, the acetate was obtained which was crystallized from methanol; m. p. 219–220°, $[\alpha]^{24}_D$ +69.7°, $[\alpha]^{24}_{546}$ +84.7° in chloroform. *Anal.* Calcd. for $C_{33}H_{52}O_4$: C, 77.30; H, 10.22. Found: C, 77.24, 77.16; H, 10.26, 10.21. No depression in melting point was observed on mixing with methyl acetyloleanolate, m. p. 219–220°, $[\alpha]^{18}_D$ +70.4° in chloroform.[8]

The same product was obtained on catalytic reduction of a sample of methyl acetylanhydroechinocystate.

Summary

Methyl echinocystate has been converted under mild conditions into methyl oleanolate, thus proving the assumption that echinocystic acid differs from oleanolic acid only in that the former has an additional hydroxyl group β to the carboxyl group.

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[4a] See paper XXVII, THIS JOURNAL, **66**, 1269 (1944).

[5] Carbon analyses by the manometric procedure of Van Slyke and Folch, *J. Biol. Chem.*, **136**, 509 (1940).

[6] Carbon–hydrogen analyses by Dr. E. W. D. Huffman, Denver, Colorado.

[7] Noller and Barusch, *Ind. Eng. Chem.*, *Anal. Ed.*, **14**, 907 (1942).

[8] Winterstein and Stein, *Z. physiol. Chem.*, **199**, 71 (1931).