[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

The Relation of Fabacein to Cucurbitacin B[1]

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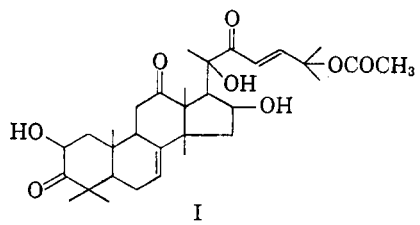
Fabacein is a diacetate of the composition $C_{34}H_{48}O_9$. The products of catalytic hydrogenation of fabacein and the oxidation products of acetylated fabacein indicate that fabacein has the same structure as cucurbitacin B, $C_{32}H_{46}O_8$, except that one additional hydroxyl group is acetylated. However, acetylation of cucurbitacin B gives a product different from that obtained by the acetylation of fabacein. Accordingly a further difference between fabacein and cucurbitacin B must exist, possibly a difference in the configuration of a portion of the molecule.

Two crystalline compounds have been isolated from *Echinocystis fabacea*,[2] cucurbitacin B and fabacein. Our analyses indicated the molecular formula $C_{30}H_{44}O_8$ for both compounds. Cucurbitacin B, however, appears to have the molecular formula $C_{32}H_{46}O_8$,[3] and a complete structural formula (I) has been proposed for it.[4] Our analyses of cucurbitacin B and of several acetylated derivatives can be reconciled with this formula if it is assumed that our products contain one-half mole of water.[5]



I

Further work on fabacein has shown that it has the same structure as cucurbitacin B except that one additional hydroxyl group is acetylated. Hence it has the molecular formula $C_{34}H_{48}O_9$. The original analyses[2] agree almost as well with this formula. (Calcd. for $C_{30}H_{44}O_8$: C, 67.64; H, 8.33; for $C_{34}H_{48}O_9$: C, 67.98; H, 8.05. Found: C, 67.56; H, 8.23; average of ten analyses.) Comparison of the NMR spectra of cucurbitacin B and fabacein to be reported later, shows that the second acetoxy group in fabacein occurs at C-16.

Like cucurbitacin B, fabacein contains an α,β-unsaturated carbonyl group, a hindered carbonyl group, and an allylic acetoxyl group.[2] Small absorption peaks in the infrared spectra of fabacein and certain derivatives at 12.15–12.35 μ (823–810 cm.$^{-1}$) indicate the presence of a trisubstituted double bond,[6] a conclusion that has been confirmed by the NMR spectra.

Fabacein in ethanol in the presence of palladium-on-carbon catalyst absorbs 1.4 moles of hydrogen to give two products which can be separated readily on a Celite-formamide column.[5] One product is dihydrofabacein in which the conjugated double bond of fabacein has been reduced. The other product could not be crystallized, but its paper chromatogram indicated that it was homogeneous. Analysis showed that it is a dihydromonodeacetoxyfabacein in which the acetoxy group in the side chain has been removed by hydrogenolysis and the conjugated double bond has been reduced. These products are analogous to those obtained by the hydrogenation of cucurbitacin B.[5]

The presence of the second acetoxy group in fabacein is shown by the fact that dihydromonodeacetoxyfabacein still absorbs in the infrared at 8.05 μ (1242 cm.$^{-1}$), whereas this peak is absent in dihydrodeacetoxycucurbitacin B. Moreover, a quantitative comparison showed that the infrared absorption at 8.05 μ of dihydrofabacein is twice that of dihydrocucurbitacin B.

Acetylation of fabacein and its hydrogenation products gave only amorphous products which were purified by chromatography on a Celite-formamide column. Analyses indicated that acetylated fabacein and dihydrofabacein contained either four acetyl groups, or three acetyl groups and one half mole of water. Analyses of acetylated dihydromonodeacetoxyfabacein indicated three acetyl groups, or two acetyl groups and one half mole of water. As was true for the acetylated products from curcurbitacin B and its derivatives[5], the inconsistency of acetyl determinations did not permit a differentiation of these two possibilities. However, the analyses of other derivatives forces the conclusion that these acetylated products contain one half mole of water. The presence of an absorption band at 2.95 μ in their infrared spectra probably is due to an unacetylated tertiary hydroxyl group.

Catalytic hydrogenation of acetylated fabacein gives two products which are identical with acetylated dihydrofabacein and acetylated dihydromonodeacetoxyfabacein. This behavior is in contrast to that of acetylated cucurbitacin B which is

(1) A preliminary report of this work was published in *Tetrahedron Letters*, No. 13, p. 16 (1959).

(2) W. O. Eisenhut and C. R. Noller, *J. Org. Chem.*, **23**, 1984 (1958).

(3) D. Lavie, Y. Shvo, D. Willner, P. R. Enslin, J. M. Hugo, and K. B. Norton, *Chem. and Ind. (London)*, 951 (1959).

(4) D. Lavie and Y. Shvo, *Chem. and Ind. (London)*, 403 (1960).

(5) W. Schlegel, A. Melera, and C. R Noller, *J. Org. Chem.*, **26**, 1206 (1961).

(6) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley, 2nd ed., New York, 1958, p. 51

hydrogenated to a product isomeric with that obtained by the acetylation of dihydrocucurbitacin B.[5] Moreover, comparative paper chromatograms show that none of acetylation products of fabacein or its hydrogenated derivatives is identical with the corresponding products derived from cucurbitacin B. It thus appears that acetylation of cucurbitacin B and its hydrogenated derivatives leads to rearrangement, but acetylation of fabacein and its derivatives does not.

Oxidation of acetylated fabacein with chromium trioxide in acetic acid gives the same mixture of neutral products obtained from acetylated cucurbitacin B, namely, chiefly the ketones A and B.[5] Thus it appears that fabacein and cucurbitacin B differ also in the side chain, possibly in the configuration at C_{20}.

EXPERIMENTAL

Hydrogenation of fabacein. A solution of 1.025 g. of fabacein[5] dissolved in 15 cc. of ethanol and 50 cc. of ethyl acetate was hydrogenated over 10% palladium on carbon (Baker and Company). The absorption of hydrogen was 55 cc. (1.44 moles), and titration of the solution after removal of the catalyst indicated the production of 50 mg. (0.49 mole) of acetic acid. After evaporation of the ethanol, the residue was combined with a previous 550-mg. run and separated on a Celite-formamide column,[5] using hexane-benzene (3v.: 1v.) as elutant and collecting 50-cc. fractions. Fractions 1–3 gave small amounts of oil which were discarded. Fractions 4–13 weighed 617 mg. All attempts to crystallize this material were unsuccessful but its paper chromatogram indicated that it was homogeneous; $[\alpha]_D^{25}$ +17.6° (*c* 1.42)[7]; ultraviolet λ_{max} 286 mμ, log ε 2.32[7]; infrared 2.90 (OH) 5.78 (OAc), 5.85 and 5.89 (C=O), 8.05 (OAc), 12.30 w (R_2C=CHR).[7] Analysis indicated this product to be a *dihydromonodeacetoxyfabacein.*

Anal. Calcd. for $C_{32}H_{48}O_7$: C, 70.56; H, 8.88. Found: C, 70.26, 8.83.

Fractions 14–16 gave 29 mg. of a mixture. Fractions 17–25 (687 mg.) were eluted with hexane-benzene (1v.: 1v.). Crystallization from acetone-hexane gave 538 mg. of prisms, m.p. 170–175°. Further recrystallization raised the melting point to 177–179°; $[\alpha]_D^{25}$ +24.0° (*c* 1.35); ultraviolet λ_{max} 285 mμ, log ε 2.39; infrared 2.90 (OH), 5.75 and 5.79 (OAc), 5.85 (C=O), 8.05 (OAc), 12.30 w (R_2C=CHR). Analysis indicated this product to be *dihydrofabacein.*

Anal. Calcd. for $C_{34}H_{50}O_9$: C, 67.75; H, 8.36. Found: C, 67.70; H, 8.33.

Acetylations. Acetylations were carried out with acetic anhydride in pyridine at room temperature and worked up in the usual way. All of the products were amorphous, but paper chromatograms showed only a single spot for each. Fabacein gave a product with $[\alpha]_D^{25}$ −2.0° (*c* 1.76); ultraviolet λ_{max} 229 mμ, log ε 4.10 and 289 mμ, log ε 2.31;[8] infrared 2.95 (OH), 5.80 (OAc), 5.92, 6.15 (C=C—C=O), 8.15 (OAc), 12.35 w (R_2C=CHR).

Anal. Calcd. for $C_{38}H_{52}O_{11}$ (4 OAc): C, 66.65; H, 7.66; for $C_{36}H_{50}O_{10}\cdot{}^1/_2\ H_2O$ (3 OAc): C, 66.34; H, 7.89. Found: C, 66.52, 8.05.

Dihydrofabacein gave a product with $[\alpha]_D^{25}$ −8.0° (*c* 1.35); ultraviolet λ_{max} 282 mμ, log ε 2.49; infrared 2.95 (OH), 5.80 (OAc), 5.90 (C=O), 8.10 (OAc).

Anal. Calcd. for $C_{38}H_{54}O_{11}$ (4 OAc): C, 66.45; H, 7.92; for $C_{36}H_{52}O_{10}\cdot{}^1/_2\ H_2O$ (3 OAc): C, 66.13; H, 8.17. Found: C, 66.08; H, 8.19.

Dihydromonodeacetoxyfabacein gave a product with $[\alpha]_D^{25}$ +13° (*c* 1.15); ultraviolet λ_{max} 287 mμ, log ε 2.37; infrared 2.95 (OH), 5.80 (OAc), 5.90 (C=O), 8.10 (OAc).

Anal. Calcd. for $C_{36}H_{52}O_9$ (3 OAc): C, 68.76; H, 8.34; for $C_{34}H_{50}O_8\cdot 0.5\ H_2O$ (2 OAc): C, 68.54; H, 8.63. Found: C, 68.72; H, 8.70.

Oxidations. Oxidations of acetylated fabracein, dihydrofabacein, and dihydrodeacetoxyfabacein were carried out by the same procedure described for the oxidation of acetylated cucurbitacin B and its hydrogenation products.[5] The neutral products were identical in all cases and consisted chiefly of the ketones A and B. The acidic products of the oxidation of acetylated fabacein and dihydrofabacein could not be positively identified. Isocaproic acid was isolated and identified by gas chromatography as a product of oxidation of acetylated dihydrodeacetoxyfabacein just as was true in the oxidation of dihydrodeacetoxycucurbitacin B. One difference was noted, however. During the oxidation of the latter, carbon dioxide was evolved, but no carbon dioxide could be detected as a product of the oxidation of acetylated dihydrodeacetoxyfabacein.

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(7) All rotations and infrared spectra are in chloroform and all ultraviolet spectra in ethanol.

(8) The previously reported values for log ε of 4.24 and 2.49 (Ref. 1) are in error.