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STRUCTURE OF CUCURBITACIN B

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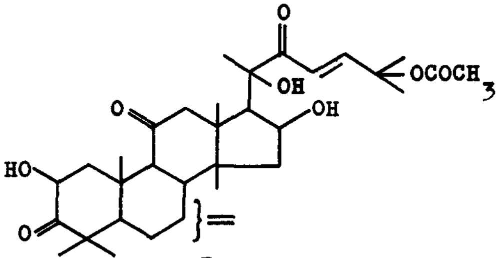
STRUCTURE I has been proposed for cucurbitacin B.[1] *We wish to report* the results of experiments which provide evidence against this structure and suggest alternative structures.



I

Optical rotatory dispersion curves have been reported for compounds having carbonyl groups in various positions of the steroid and tetracyclic and pentacyclic triterpene nuclei and such curves have been correlated with structure.[2] Hence the rotatory dispersion curve of a derivative of cucurbitacin B in which all of the carbonyl

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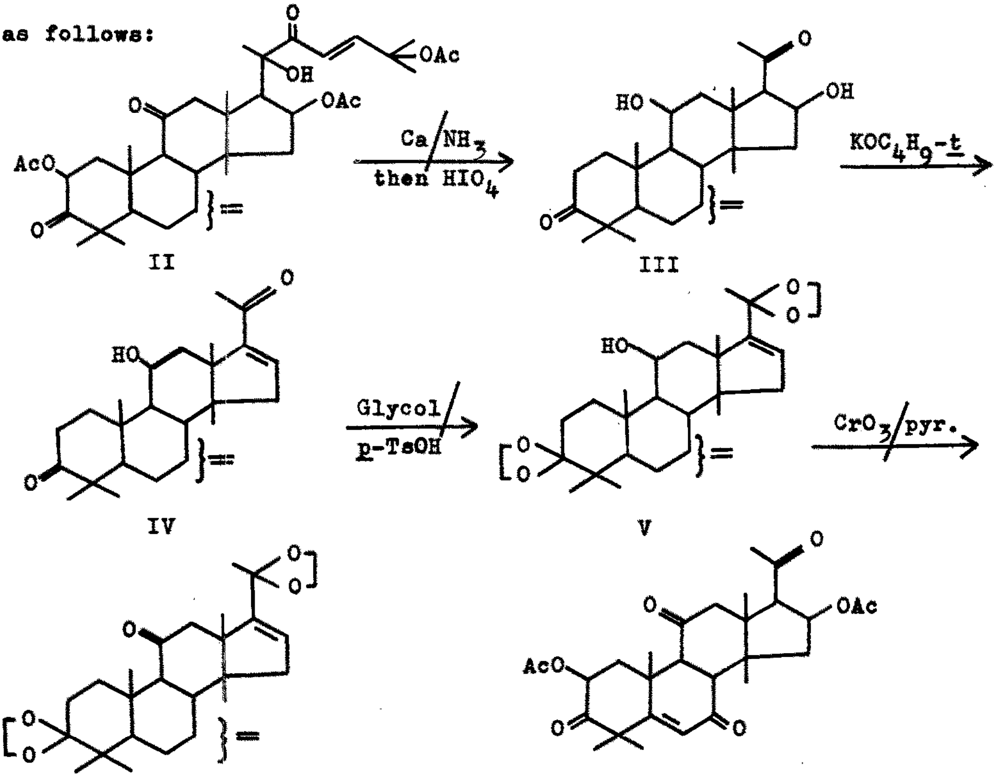
[1] D. Lavie, Y. Shvo, D. Willner, P.R. Enslin, J.M. Hugo and K.B. Norton, Chem. and Ind. (London), 951 (1959).

[2] C. Djerassi, Optical Rotatory Dispersion. McGraw Hill, New York, 1960.

groups except that which is hindered are either eliminated or masked should provide information concerning the location of the hindered group. To prepare such a compound, a series of reactions was carried out, which, on the basis of formula I, may be represented as follows:



Acetylated fabacein[3] as well as acetylated cucurbitacin B was used for the preparation of compound III. Obviously the above reactions apply also for other possible positions of the hindered carbonyl group and of the unreactive double bond. The physical and analytical

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[3] W. Schlegel and C.R. Noller, Tetrahedron Letters No. 13, p. 16 (1959).

data (C, H, O) of the products are: III, m.p. 200-201°; IR 2.80, 2.90, 5.86; Calcd. for $C_{24}H_{36}O_4$: 74.19, 9.34, 16.47; Fd.: 74.47, 8.95, 16.73. IV, m.p. 221-222°; IR 2.86, 5.88, 6.00, 6.28; UV 244 (8600); Calcd. for $C_{24}H_{34}O_3$; 77.80, 9.25, 12.96; Fd.: 77.48, 9.25, 12.84. V, m.p. 195-197°; IR 2.78, 2.86, 6.21; Calcd. for $C_{28}H_{42}O_5$: 73.32, 9.23, 17.44; Fd.: 73.14, 9.07, 17.93. VI, m.p. 215-216°; IR 5.91, 6.21; Calcd. for $C_{28}H_{40}O_5$: 73.65, 8.83, 17.52; Fd.: 73.48, 8.96, 17.58.

These reactions in themselves gave useful information. For example an attempt to eliminate the carbonyl group from VI by the usual Huang-Minlon procedure failed, and only unchanged VI was recovered. Hence if the carbonyl group is at C-11, the double bond must be at the 5,6 position. If it were at the 7,8 position, it would have migrated into conjugation with a carbonyl group at C-11 under the conditions of the Huang-Minlon procedure.

A double bond at the 5,6 position and carbonyl at C-11 would require structure VII for ketone A.[4] However, the 60-mc NMR spectrum of ketone A has two distinct peaks at -375 and -378 cps using deuterochloroform as solvent and tetramethylsilane as an internal reference. The splitting of the band in this region indicates interaction of the proton on the conjugated double bond with a second nearby proton which can be accounted for by either partial structure VIII or IX but not by structure VII, and suggests partial structure X or XI for cucurbitacin B.

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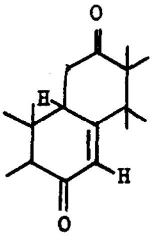
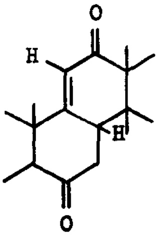
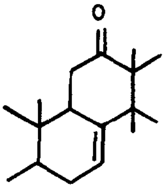
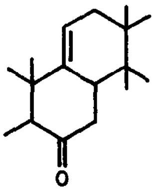
[4] A. Melera, W. Schlegel and C.R. Noller, J. Org. Chem. **24**, 291 (1959).


VIII


IX


X


XI

That the double bond in cucurbitacin B is trisubstituted is indicated by weak absorption in the infrared at 12.1 μ (825 cm $^{-1}$) and a broad flat band in the NMR spectrum at -350 cps, the broadening being caused by the adjacent methylene group.

The rotatory dispersion curve of VI is positive with a maximum $[\alpha]_{322}$ +2813° and a minimum $[\alpha]_{275}$ -2062° (c = 0.089 in dioxane). The magnitude of these rotations, among compounds having only an oxo group in ring B or C, for which RD curves have been reported, is approached only by 6-oxocoprostane and its curve is negative, $[\alpha]_{312}$ -2240° and $[\alpha]_{270}$ +2695°.[5] The curves for VI and 6-oxocoprostane are practically mirror images, and suggest a mirror image relationship in structure and configuration,[6] i.e., structure XI for cucurbitacin B with the α configuration at C-10 and

at C-5. However, chemical evidence for structure X recently

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[5] C. Djerassi and W. Closson, J. Am. Chem. Soc. 78, 3768 (1956). The magnitude of the minimum given in the experimental part as $[\alpha]_{312}$ -224° is a misprint (Private communication from Dr. C. Djerassi).

[6] cf. W. Klyne, J. Chem. Soc. 2916 (1952).

has been obtained by D. Lavie and Y. Shvo.[7] On the basis of either structure X or XI, it is difficult to understand why ketone A (VIII or IX) did not oxidize further with chromium trioxide in acetic acid to the conjugated dienedione or why we have been unable to bring about the further oxidation of ketone A with mercuric acetate, cupric acetate, or selenium dioxide.

We wish to report also that by a series of nine steps, compound IV has been converted into a product, m.p. 280-281°, IR 5.86, 5.88, 5.91, tetranitromethane test negative. This compound, if cucurbitacin B had structure I with a configuration corresponding to lanostane or euphane, should be identical with either 7,11,20-trioxohexanorlanostane or 7,11,20-trioxohexanoreuphane. The latter compound is eliminated because it melts at 229°.[8] A mixture of our product with 7,11,20-trioxohexanorlanostane, m.p. 281-282°,[9] melted at 245-255°.

Acknowledgments. We are indebted to Dr. E.J. Eisenbraun and Mrs. T. Nakano for determining the rotatory dispersion curve of compound IV, and to Dr. O. Jeger for samples of the lanostane and

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[7] We wish to thank Dr. Lavie for a copy of a Communication submitted to Chemistry and Industry (London) in which this structure is proposed.

[8] M. Dünnenberger, Dissertation, Eidg. Tech. Hochschule, Zürich, 1955.

[9] W. Voser, M.V. Mijović, O. Jeger and L. Ruzicka, Helv. Chim. Acta **34**, 1585 (1951), report an uncorrected melting point of 269-271°.

euphane derivatives. This work was supported in part by a research grant, RG-5076, from the National Institutes of Health, U.S. Public Health Service.