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THE STRUCTURE OF LOGANIN

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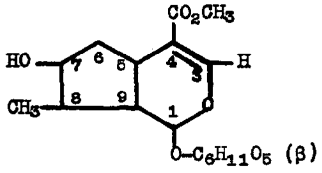
IN this communication we wish to report that loganin ($C_{17}H_{26}O_{10}$), a glycoside isolated from Strychnos nux-vomica[1,2,3] and other Strychnos species,[4,5] has the constitution represented by formula (I).



I

The glucosidic nature and the presence of one additional free hydroxyl group in loganin, m.p. 222-223°,* as suggested by previous investigators,[2,4] was confirmed by the production of glucose on enzymatic hydrolysis with

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* This loganin was isolated from the fruit pulp of Strychnos nux-vomica. The authors are thankful to S.B. Penick and Company, and to Mr. Shanti Sheth, Bombay, for supplying the pulp.

[1] W.R. Dunston and F.W. Short, Pharm.J.Trans. 14, 1025 (1883).

[2] K.W. Merz and K.G. Krebs, Arch.Pharm. 275, 217 (1937).

[3] K.W. Merz and H. Lehmann, Arch.Pharm. 290, 543 (1957).

[4] A.J. Birch and E. Smith, Austr.J.Chem. 9, 234 (1956).

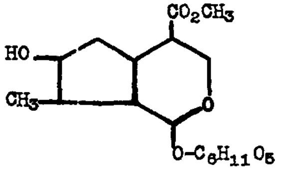
[5] A.J. Birch and J. Grimshaw, J.Chem.Soc. 1407 (1961).

emulsin and by the formation of a pentaacetate derivative, m.p. 139-140°.

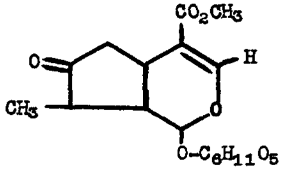
Loganin consumed one equivalent of sodium hydroxide on heating and gave methanol and norloganin, m.p. ca. 110°, λ_{max} 234 mμ (ε 9360), characterized as its penaacetate derivative, m.p. 99° and 160-162°, λ_{max} 231 mμ (ε 12,300). Norloganin displayed a broad, weak band at 2500-2700 cm^{-1} characteristic of the hydrogen-bonded hydroxyl group of a carboxylic acid. The sodium salt of norloganin lacked a carbonyl peak at 1695 cm^{-1}, but showed new peaks at 1522 and 1380 cm^{-1} which are assigned to a carboxylate anion. The fact that loganin is the methyl ester of norloganin was deduced from the formation of loganin pentaacetate by the action of diazomethane on norloganin pentaacetate.

The presence of an enol-ether group conjugated with the carbomethoxyl function in loganin was indicated by bands in the infrared at 1722 cm^{-1} ($-CO_2CH_3$) and 1660 cm^{-1} ($-C{=}C-O-$) and by absorption in the ultraviolet at 236 mμ (ε 10,940). This structural feature was confirmed by the facile uptake of one equivalent of hydrogen by the use of platinum oxide as a catalyst and acetic acid as a solvent. Dihydrologanin (II), m.p. 160-162°, does not absorb in the ultraviolet above 210 mμ and lacks the enol-ether band at 1660 cm^{-1}.

Diagnostically, the two most significant signals in the NMR spectra of loganin and loganin pentaacetate, determined at 56.4 mc in deuterium oxide and carbon tetrachloride respectively and related to tetramethylsilane as a standard, proved to be the ones at -470 and -56 c.p.s. The former is assigned to the conjugated olefinic proton at C-3 and the unusually large shift to lower magnetic field confirms the location of the oxygen atom of the enol-ether as adjacent to it. The signal at -56 c.p.s., appearing as a doublet, is assigned to a single methyl group spin coupled with an adjacent proton. It should be noted that similar peaks are exhibited by verbenalin.



II



III

The presence of a pyran ring finds support from a comparison of the ultraviolet spectrum of loganin with model compounds[6,7] and with the spectra of the closely related verbenalin,[8] genepin,[9] asperuloside,[10] and plumieride.[11] The presence of a furan ring is excluded since it would be expected to absorb at 251 m ,[12] higher than the values of 234-237 m found for loganin and its derivatives.

The placement of the glucose radical at C-1 was deduced from the positive Tollens and 2,4-dinitrophenylhydrazine reactions given by the aglycone (R_f 0.85[*]) of loganin (R_f 0.48) and *the aglycone* (R_f 0.81) *of dihydrologanin* (R_f 0.45).

Of the remaining four carbon atoms, one of which is a methyl group, three must take the form of another ring since the presence of a second double bond is eliminated by the hydrogenation data and by ozonolysis experiments with loganin and its derivatives, which all gave trace amounts

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[*] Solvent system: butanol-acetic acid-water (4:1:1), paper: Whatman No. 1.

[6] L.N. Owen, *J.Chem.Soc.* 385 (1945).

[7] F. Korte and K. Buchel, *Ber.* **92**, 877 (1959).

[8] G. Buchi and R.E. Manning, *Tetrahedron Letters* No. 26, 5 (1960).

[9] C. Djerassi, T. Nakano, A.N. James, L.H. Zalkow, E.J. Eisenbraun and J.H. Shoolery, *J.Org.Chem.* **26**, 1192 (1961).

[10] J. Grimshaw, *Chem. & Ind.* 403 (1961).

[11] O. Halpern and H. Schmid, *Helv.Chim.Acta* **41**, 1109 (1958).

[12] F. Korte, K. Buchel, D. Scharf and A. Zschocke, *Ber.* **92**, 884 (1959).

of formaldehyde but no other carbonyl compounds. The three carbon atoms are attached in the form of a cyclopentane ring at C-5 and C-9 and the methyl group is located at C-8 for biogenetic reasons.

Oxidation of loganin by the Jones procedure[13] yielded a crystalline ketone (III), $C_{17}H_{24}O_{10}$, m.p. 189-191°, which displayed absorption at 234 mμ (ε 11,100) and 1650, 1700 and 1751 cm^{-1} (cyclopentanone). The fact that the hydroxyl groups of the glucosyl radical were not affected was indicated by the formation of glucose on hydrolysis with emulsin. The ketone (III) was stable toward traces of sodium methoxide and sodium carbonate and was not identical with verbenalin. The low intensity $n\text{-}\pi^*$ transition in the ultraviolet spectrum of (III), $\lambda_{max}^{H_2O}$ 290 mμ (ε 44) as compared with $\lambda_{max}^{H_2O}$ 290 mμ (ε 160) for verbenalin suggests that the carbonyl group in (III) is located at C-7 and that loganin is best represented by formula (I).

Structure I is also consistant with the formation of succinic, methyl succinic and oxalic acids by alkaline permanganate oxidation of the aglycone of loganin.

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[13] K. Bowden, I.M. Heilbron, E.R.H. Jones and B.C.L. Weedon, J.Chem.Soc. 39 (1946).