

THE CRYSTAL AND MOLECULAR STRUCTURE OF
HELICHRYSOSIDE, A NEW ACYLATED FLAVONOID
GLYCOSIDE FROM HELICHRYSUM KRAUSSII

H.A. Candy, M. Laing* and C.M. Weeks**

(Chemistry Department, University of Natal, Durban 4001)

G.J. Kruger,

(National Physical Research Laboratory, C.S.I.R., Pretoria 0001)

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Helichrysum kraussii Sch. Bip. is a compact, herbaceous shrub¹ which grows in profusion in the sandy soil along the coastal belt of Natal. Because little is known of the chemical taxonomy of this plant, a detailed investigation was undertaken².

The golden yellow flower heads were milled and extracted, in turn, with hexane, ether, acetone and methanol. From the hexane extract 3,5-dihydroxy-6,7,8-trimethoxyflavone was isolated. In addition to L(-)-2-O-methylinositol and 3-O-methylquercetin the acetone extract yielded a new acylated flavonoid glucoside, helichrysoside. This was soluble in acetone, methanol and ethanol but could not be satisfactorily crystallised from any of these anhydrous solvents. Ready crystallisation was accomplished, however, by adding water dropwise to a solution of the solid in either boiling acetone or methanol. On cooling, small bright yellow hexagonal plates were obtained; m.p. 181-184⁰, $[\alpha]_D^{21} - 44^0$ (MeOH); λ_{\max} (MeOH) 223sh, 260sh, 265, 302sh, 312, 353sh nm; λ_{\max} (MeOH-NaOMe) 271, 312sh, 365, 405sh nm; λ_{\max} (MeOH-AlCl₃) 226sh, 276, 308, 440 nm. (Loss on drying in vacuo over P₂O₅ at room temp. for 16 hr 11.1%; found C = 56.5, H = 4.6%; calc. for C₃₀H₂₆O₁₄ · 1.5 H₂O; C = 56.50; H = 4.55%; calc. for loss of 4.5 H₂O 10.7%). The dehydrated material melted between 260-270⁰ with decomposition.

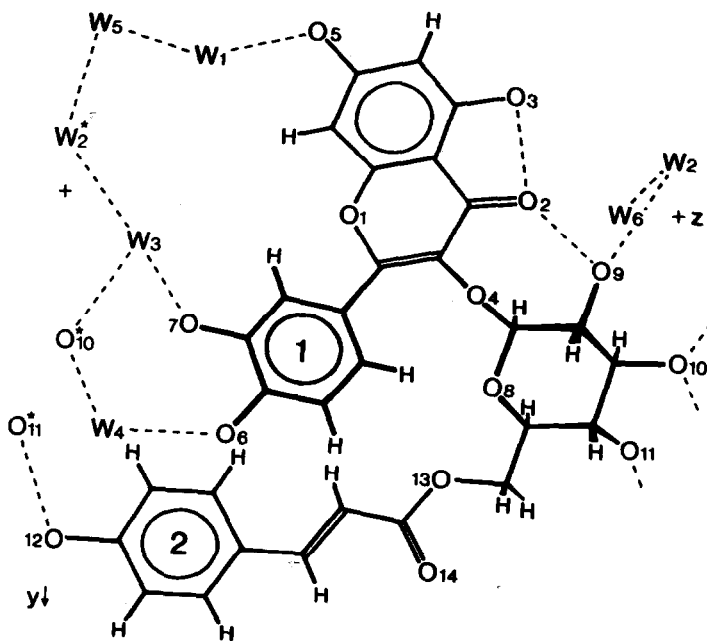
The crystals (from acetone and water) were orthorhombic, space group P2₁2₁2; $a = 7.51$, $b = 31.49$, $c = 13.81$ (± 0.01) Å, Vol = 3266 Å³, $d_{\text{meas}} = 1.45$ (± 0.01) gcm⁻³, Z = 4,

** Visiting Lecturer; permanent address:-

Medical Foundation of Buffalo, Research Laboratories, New York 14203.

Mol. Wt. = 710 (± 5), equivalent to $C_{30}H_{26}O_{14} \cdot 5.5 H_2O$ per asymmetric unit. Intensity data were collected on a Philips 4-circle diffractometer with graphite-monochromated Mo-K α radiation to $\theta = 30^\circ$. The overall B and scale factor, obtained by a Wilson plot from the 5375 measured data, were used to generate E's only for those data with $\sin \theta/\lambda < 0.6$ (3210). The 400 largest E's were then processed with programs PHASE and MULTAN³ and the E map yielded the 44 atoms of the molecule. An observed Fourier map revealed the positions of six water molecules, five in general positions and one on the 2-fold axis. The structure has been refined isotropically by block diagonal least squares to $R = 0.18$ (2715 observed data with $\theta < 20^\circ$). Further anisotropic refinement is continuing, and details of the structure elucidation will be published elsewhere.

The structure is shown in projection down a .



Helichrysoide is thus quercetin-3- β -D-(6-p-coumaroyl)glucoside. There are $5\frac{1}{2}$ molecules of water per molecule of glycoside in the crystal. The waters of crystallisation link the molecules of helichrysoide together by a complex network of hydrogen bonds which results in a very densely packed structure. The strong hydrogen bonds ($O \cdots O$ separations

of 3\AA or less) in the asymmetric unit are shown as dashed lines in the figure. There are additional hydrogen bonds to other molecules in the crystal: the acyl oxygen O(14) is involved in hydrogen bonding with O(6) of an adjacent molecule. This accounts for the necessity of adding water to the acetone solution before crystallisation could be achieved. The very high density of 1.45 g cm^{-3} is unusual and the cell volume yields a value of 16.5\AA^3 per non-hydrogen atom: these values differ considerably⁴ from the usual 1.3 g cm^{-3} and 18\AA^3 for typical organic compounds, and show that the structure is very tightly packed indeed.

The bond lengths and angles throughout the molecule are normal. The only significant distortion from regularity involves the torsion angles associated with O(11) on the glucose ring: O(10)-CH-CH-O(11) 71° , O(11)-CH-CH-CH₂ 80° . These enlarged angles are presumably caused by packing forces associated with the hydrogen bonding involving O(11).

The molecule is compactly folded, with the p-coumaroyl system coiled to place phenyl ring 2 parallel to and in contact with ring 1. Oxygen O(9) on the glucose ring is hydrogen bonded to O(2) on the flavonone nucleus: O(9)···O(2) = 2.65\AA . It is possible that this intramolecular hydrogen bond is retained in solution and may well account for the relative inertness of the glycoside linkage in quercetin-3- β -D-glucoside to base hydrolysis. Similar intramolecular hydrogen bonds were observed in crystals of the flavanone obtusifolin⁵. It is also probable that in solution there is relatively free rotation about the acyl-glucose link which results in the p-coumaroyl system "uncoiling" to give an effectively larger and more flexible molecule.

Several compounds similar to helichryoside have been reported in the past: QGC⁶, petunoside⁷, bignonoside⁸ and tiliroside⁹; and a discussion of the general class of acylated flavonoid glycosides has been given¹⁰. Based on this unequivocal structure of helichryoside, it should now be possible to determine with certainty the structures of those related compounds which have been only partly characterised.

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References.

1. J.C. Willis, "Flowering Plants and Ferns", 7th Ed., 1966, Cambridge University Press, p.527; J.M. Watt and M.G. Breyer-Brandwijk, "The Medicinal and Poisonous Plants of Southern and Eastern Africa", Livingstone, London, 1962, 2nd Edition, p.238.
2. H.A. Candy and W. Wright, J.S.A. Chem. Inst., 1974, submitted for publication.
3. PHASE, a set of programs for direct phasing by C.M. Weeks; MULTAN, a program by P. Main and M.M. Woolfson, University of York, and G. Germain, University of Louvain.
4. C.J.E. Kempster and H. Lipson, Acta Cryst., 1972, B28, 3674;
A.I. Kitaigorodsky, "Molecular Crystals and Molecules", Academic Press, New York, 1973, p.18-21;
M. Laing, "The Packing of Molecules in Crystals", Le Bel - Van't Hoff Centenary Symposium, Johannesburg, August 1974.
5. P. Narayanan, K. Zechmeister, M. Röhrl and W. Hoppe, Acta Cryst., 1971, B27, 718.
6. M. Furuya and A.W. Galston, Phytochem., 1965, 4, 285.
7. L. Birkofer, C. Kaiser and H. Kosmol, Zeits. für Naturforsch., 1965, 20b, 605.
8. L. Birkofer, C. Kaiser and F. Becker, Zeits. für Naturforsch., 1965, 20b, 923.
9. J.B. Harborne, Phytochem., 1964, 3, 151.
10. J.B. Harborne, "Comparative Biochemistry of the Flavonoids", Academic Press, London, 1967, p.73; von H. Wagner in "Progress in the Chemistry of Organic Natural Products", ed. L. Zechmeister, Vol. 31, 1974; p.174-177.