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STRUCTURAL STUDIES OF ALOENIN; THE CRYSTAL STRUCTURE OF ITS AGLYCONE

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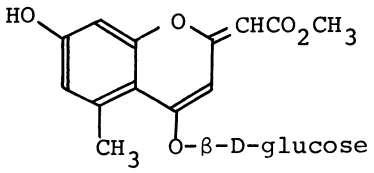
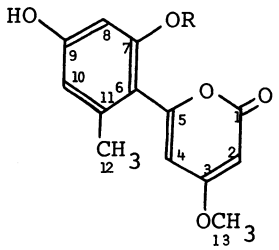
The recently proposed structure of aloenin (II) has remained uncertain due to difficulty in interpreting the NMR spectra. The structure of its aglycone has now been determined by X-ray crystallography to be as in formula III, and aloenin has therefore been unambiguously confirmed to correspond to structure II.

The structure of aloenin,** isolated from the leaves of *Aloe arborescens* Mill. var. *natalensis* Berger, was reported as I.[1,2] However, nuclear Overhauser effect (NOE) studies of aloenin raised doubt about the reported structure. The structure,



I



II: R=β-D-glucosyl
III: R=H

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** Nishioka et al.[2] also isolated independently the identical compound from the *Aloe* and named as "aloearbonaside." The authors (T.H. and T.S.) have now obtained their consent of making the name uniform hereafter by the adoption of "aloenin" proposed by Suga et al.[1]

after re-examination[3] by a combination of chemical and spectroscopic methods, was proposed as II.[4] However, it has remained uncertain due to some ambiguous points in the assignment of its ^{13}C-NMR spectra[3,5~7] and in the explanation of the anomalous intensity enhancement of C-2 and C-4 proton signals by 33% and 4%, respectively, in the NOE as saturating the 13-methoxyl group of aloenin penta-acetate.[3] Hence, we now have examined the structure of an aglycone of the aloenin by X-ray crystallography to confirm the structure of the aloenin.[8]

Hydrolysis of aloenin with aqueous MeOH-HCl (3%) produced the aglycone III,[3] which was crystallized from a mixture of EtOAc, $CHCl_3$, and MeOH (9:1:1 in volume) to give the single crystals. Crystal data are: $C_{13}H_{12}O_5$; M=248.23; monoclinic (space group $P2_1/c$); four molecular units per unit cell with dimensions a=7.422(2), b=10.719(4), c=14.392(4), β=99.54(2); V=1129.1 Å^3; D_c=1.46 g·cm^{-3}. A total of 2292 reflections were collected on a Syntex $P2_1$ diffractometer using the ω-scan technique with Cu Kα radiation and a Ni-filter; 198 reflections were smaller than 1.96 times of the standard deviations in intensities and were recorded as "unobserved." All non-hydrogen atoms were found by direct methods based on 153 reflections with $|E|>1.85$, using the program MULTAN.[9] The structure was refined by full-matrix least-squares method. Four cycles of anisotropic refinement for carbon atoms and oxygen atoms and isotropic refinement for hydrogen atoms reduced the R index to 0.073. The final atomic coordinates of the non-hydrogen atoms are given in Table 1 and the molecular structure is shown in Fig. 1.[10] This result demonstrates that the structure of aloenin corresponds to formula II unambiguously.

TABLE 1. Atomic parameters of aglycone III.

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
C(1)	0.6099(5)*	0.1251(3)	0.1062(2)	C(10)	0.2029(4)	0.5496(3)	-0.0306(2)
C(2)	0.5120(5)	0.0190(3)	0.1261(2)	C(11)	0.2727(4)	0.4448(3)	0.0194(2)
C(3)	0.3272(5)	0.0134(3)	0.0950(2)	C(12)	0.3541(5)	0.4571(4)	0.1216(2)
C(4)	0.2339(5)	0.1148(4)	0.0436(3)	C(13)	0.3049(6)	-0.1883(4)	0.1592(3)
C(5)	0.3301(4)	0.2153(3)	0.0252(2)	O(1)	0.5157(3)	0.2206(2)	0.0555(2)
C(6)	0.2608(4)	0.3284(3)	-0.0262(2)	O(2)	0.7755(3)	0.1420(3)	0.1296(2)
C(7)	0.1785(4)	0.3207(3)	-0.1214(2)	O(3)	0.2201(4)	-0.0833(3)	0.1084(2)
C(8)	0.1097(4)	0.4264(3)	-0.1718(2)	O(4)	0.1782(4)	0.2059(3)	-0.1626(2)
C(9)	0.1237(4)	0.5396(3)	-0.1250(2)	O(5)	0.0559(5)	0.6423(3)	-0.1743(2)

* E.s.d. are in parentheses (×10^4).

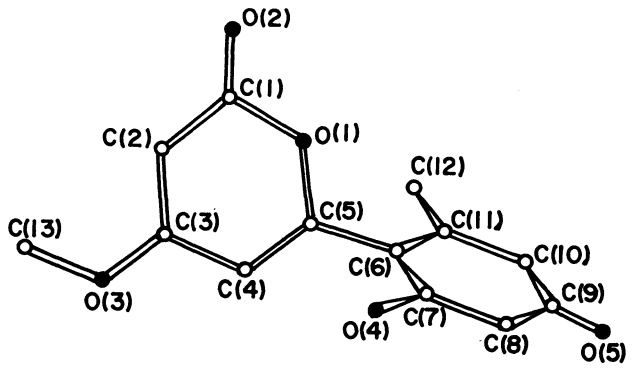

Fig. 1. The molecular structure of aglycone III. The atoms indicated with o and ● denote carbon and oxygen atoms, respectively.

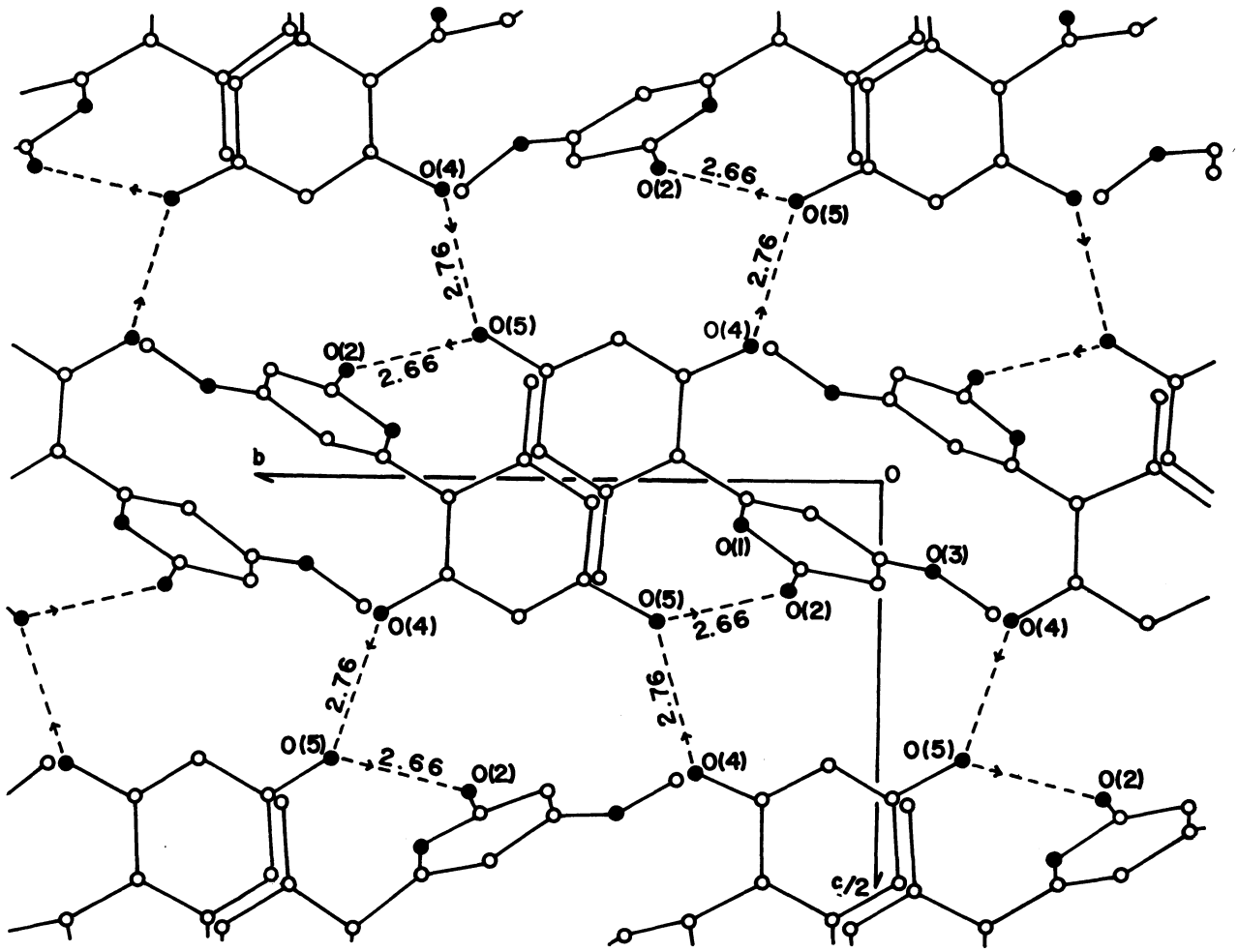

Fig. 2. The projection of aglycone III viewed along the a-axis. Hydrogen bonds are shown by a broken line. The atoms indicated with o and ● denote carbon and oxygen atoms, respectively.

The molecular arrangement and the hydrogen-bond networks in the crystal are shown in Fig. 2. The crystal structure is composed of two stackings of the planes of phenyl and pyrone groups, which are packed along the a- and the c-axes, respectively. A dihedral angle between the planes is 117 degrees. One carbonyl and two hydroxyl groups participate in the formation of the intermolecular hydrogen bond. One chain is formed through O(2)-carbonyl and O(5)-hydroxyl groups. The other chains link O(4)- and O(5)-hydroxyl groups belonging to the neighboring molecules related by a 2_1 screw axis. The crystal structure is stabilized by these networks of hydrogen bonds.

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References and Notes

1) T. Suga, T. Hirata, and M. Odan, Chem. Lett., 547 (1972).
2) K. Makino, A. Yagi, and I. Nishioka, Chem. Pharm. Bull., 21. 149 (1973).
3) T. Suga, T. Hirata, and K. Tori, Chem. Lett., 715 (1974).
4) In this paper, for convenience, the carbon atoms of aloenin are numbered as shown in formula II as related to the molecular structure of aglycone III shown in Fig. 1.
5) M. Tanabe, H. Seto, and L. Johnson, J. Amer. Chem. Soc., 92, 2157 (1970).
6) W. V. Turner and W. H. Pirkle, J. Org. Chem. 39, 1935 (1974).
7) The signal assignment problems in the C-13 NMR spectra of 4-methoxy-2-pyrones have been solved now, and the results will be reported eleswhere.
8) For lack of the formation of a good single crystal of aloenin, the X-ray crystallographic analysis was performed on its aglycone.
9) G. Germain, P. Main, and M. M. Woolfson, Acta Crystallogr., A27, 368 (1971).
10) The results described in this paper was obtained on a Syntex $P2_1$ diffractometer, but we (T.H., Y.K., and T.S.) have already reached the same conclusion as in this paper by means of photographic techniques. However, the R index was only 0.128.

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