

THE CRYSTAL AND MOLECULAR STRUCTURE OF
A BROMINATION PRODUCT OF (+)TETRAHYDRORUGULOSIN

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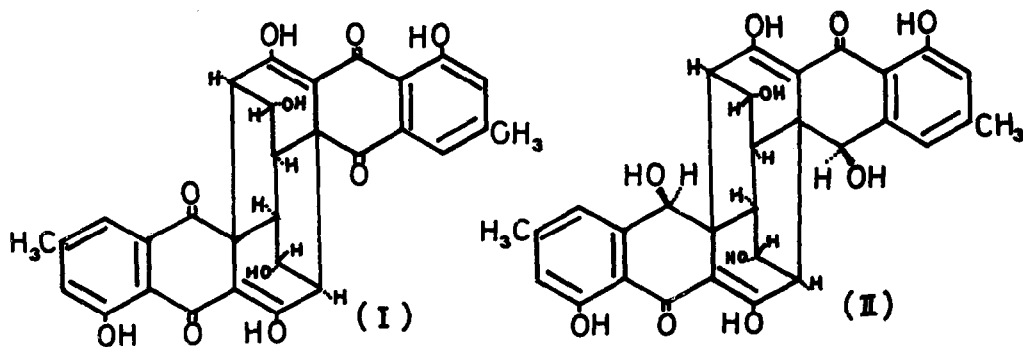
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As described in the previous paper(1), a new structures of (+)rugulosin (I), a colouring matter of Penicillium rugulosum Thom and some other fungi was forwarded mainly on the basis of the NMR-spectral analysis. (+)Rugulosin has intimate structural correlations with (-)luteoskyrin, (-)rubroskyrin and (-)flavoskyrin, the colouring metabolites of P.islandicum Sopp. Therefore the establishment of the structure and the absolute configuration of (+)rugulosin by X-ray crystallography would be of fundamental importance.

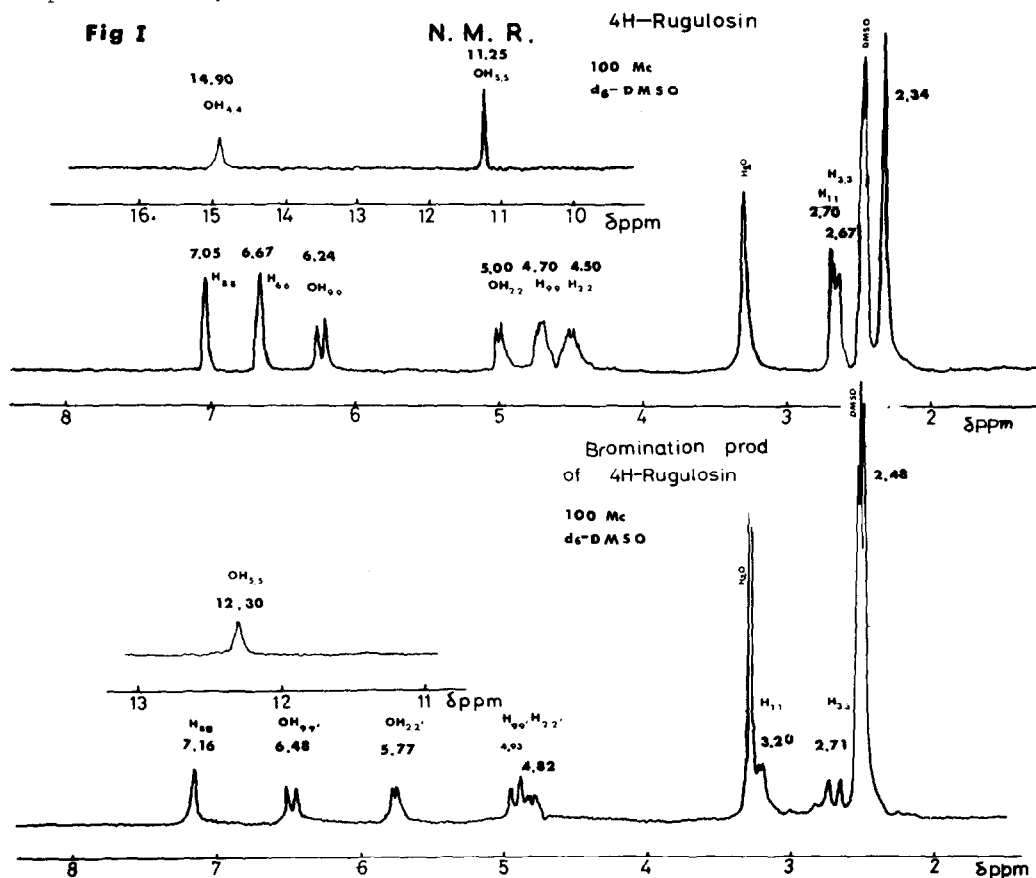
After several unsuccessful trials, we found that a bromination product of (+)tetrahydrorugulosin formed crystals which could only be used for the X-ray crystallographical analysis under a special caution.

(+)Tetrahydrorugulosin, $C_{30}H_{26}O_{10}$, m.p.295°(decomp.) $[\alpha]_D^{25} +172^{\circ}$ (Me_2CO) (II) prepared by catalytic reduction of (+)rugulosin was treated with dioxane dibromide with a few drop of pyridine in tetrahydrofuran under ice-cooling.



The bromination product thus obtained which should be named (+)dibromo-dehydro-tetrahydro-rugulosin gave a molecular formula, $C_{30}H_{22}O_{10}Br_2$, m.p. $> 270^\circ$ and $[\alpha]_D^{25.5} +345^\circ$ (dioxane). This compound revealed NMR signals which almost correspond to those of tetrahydro-rugulosin except the exclusion of an aromatic proton signal by the replacement with bromine atom, its effect to the neighbouring protons and the disappearance of the proton signal corresponding to the enolic \underline{OH} .

It is however noticeable that the appearance of an IR absorption at 1755 cm^{-1} in the bromination product besides the preexisting chelated $C=O$ absorption at 1605 cm^{-1} .



Dibromodehydro-tetrahydro-rugulosin was recrystallized from a mixed solution of methanol, acetone and water to form transparent yellow plates elongated along the c-axis containing methanol and water as the solvents of crystallization. The crystals are easily damaged on leaving in air to give a sticky

yellow powder presumably due to loss of the solvent molecules. The X-ray photographs were taken with the crystals sealed in thinwalled glass capillaries together with the mother liquor of crystallization.

The crystal belongs to the monoclinic system, space group $P 2_1$ with the lattice constants, $a=9.78\pm 0.02 \text{ \AA}$, $b=17.04\pm 0.04 \text{ \AA}$, $c=9.45\pm 0.02 \text{ \AA}$, $\beta=98.0\pm 0.2^\circ$, which were determined from the precession photographs of $hk0$ and $h0l$ using $\text{CuK}\alpha$ radiation. The density measured by flotation in the mixed solution of dibromomethane and chloroform was 1.68_4 g.cm^{-3} and that in dibromomethane and methanol was 1.64_1 g.cm^{-3} . The density calculated by assuming two structural units in a cell each consisting of 1:1:1 molar ratios of dibromodehydro-tetrahydrorugulosin, water and methanol was 1.602 g.cm^{-3} , and that of 1:1:2 composition was 1.671 g.cm^{-3} . The difference Fourier map calculated at the final stage of the structure determination showed two methanol molecules in an asymmetric unit indicating the 1:1:2 composition.

Three-dimensional intensity data were collected from the equi-inclination Weissenberg photographs. The layers $hk0 \sim hk6$ about the c -axis and $h0l \sim h3l$ about the b -axis were taken by $\text{CuK}\alpha$ radiation using the multiple film technique. The intensities were estimated visually with the aid of calibrated intensity scales to give a total of 1482 independent non-zero observed structure factors.

The crystal structure was solved by the heavy atom method on the basis of the contributions of the two bromine atoms involved in the molecule of (+) dibromodehydro-tetrahydrorugulosin. Successive use of Fourier and difference Fourier syntheses enabled us to assign the structure (Fig II) for this compound. Refinement of the structural parameters was carried out by the blockmatrix least-squares calculations including anisotropic thermal parameters for each atom. The presence of the solvent molecules, one water and two methanol in the asymmetric unit, was revealed on the difference Fourier map which was calculated using the refined atomic parameters of (+)dibromodehydro-tetrahydrorugulosin. The final R factor for 1482 reflexions was 0.128 including the molecules of solvation.

The absolute configuration was determined by the anomalous dispersion method. Taking into account of the dispersion correction of the bromine atoms for $\text{CuK}\alpha$ radiation, the intensities of the pairs of the $hk\bar{l}$ and $h\bar{k}l$ reflexions

were calculated and compared with those observed in the various layers of the c-axis Weissenberg photographs. Sixteen out of seventeen pairs of reflexion for which the intensity differences were expected to be discernible, showed significant differences to lead conclusively the absolute configuration of (+)dibromodehydro-tetrahydrorugulosin as formulated in (III).

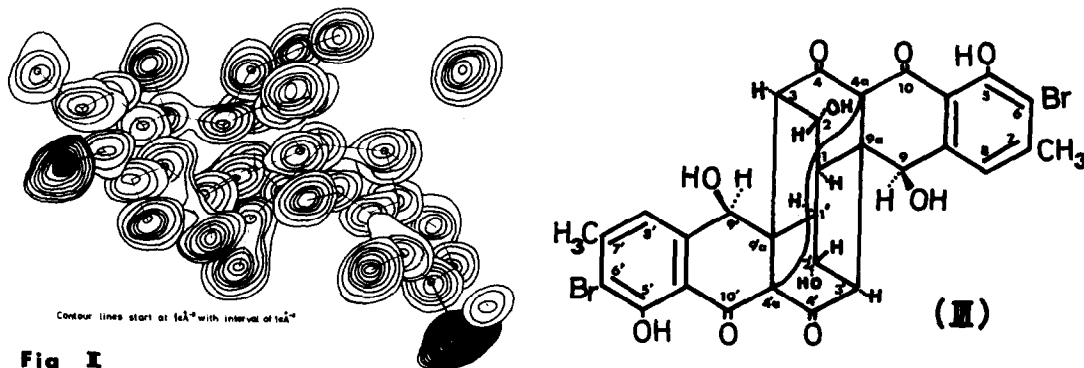


Fig 1

A dehydration resulting a bond formation between 4a and 4'a occurred during the process of bromination of tetrahydrorugulosin. On the basis of the established absolute configuration of (+)dibromodehydro-tetrahydrorugulosin the structures and their stereochemistry of (+)rugulosin, (-)luteoskyrin and (-)rubroskyrin have now unequivocally been established.

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REFERENCE

1. U. Sankawa, S. Seo, N. Kobayashi, Y. Ogihara and S. Shibata: Tetrahedron Letters, No.53 (1968) (in press).