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STRUCTURE OF CORIANIN

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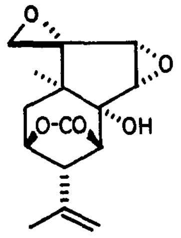
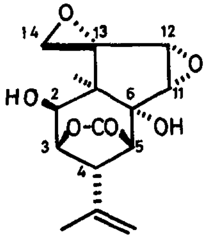
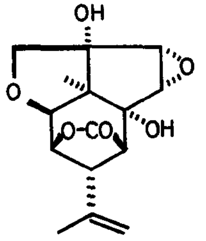
The absolute structures of coriamyrtin $C_{15}H_{18}O_5$ and tutin $C_{15}H_{18}O_6$, the main toxic principles of Coriaria japonica A. Gray, were previously determined as I (1) and II (2). Another constituent, whose melting point is 183.5° (3) or 184° (4) had been isolated in 1884 and 1931. Later, this compound was analyzed as $C_{15}H_{18}O_6$, and hence was named pseudotutin (5). Pseudotutin has now been found to be constituted by two equimolar constituents, tutin and its isomer, which has been named corianin.



I



II



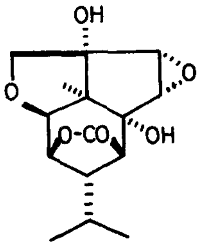
III

Although pseudotutin shows m.p. 184° when recrystallized from water, it has been fractionated into two constituents on recrystallization from chloroform. The one crystallized first from the chloroform solution was identified as tutin. Another constituent, corianin, m.p. 215-216°, was deposited from the mother liquor and analyzed as $C_{15}H_{18}O_6$ (M^+ 294).

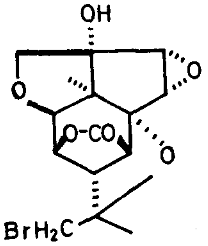
The IR spectrum (KBr) of corianin shows a hydroxyl group (3450 cm^{-1}), a γ-lactone (1760 and 1740 cm^{-1}), and a double bond (1640 cm^{-1}). The NMR spectrum (60 MHz, $CDCl_3$) shows a singlet of a quaternary methyl group at 8.40τ, and also a singlet at 7.90τ and a diffused doublet at 5.05τ, which are assignable to an isopropenyl group. An AB quartet at 6.16 and 5.57τ (J=2.5 Hz), which is analogous to the epoxide protons at C_{11} and C_{12} of tutin, and a doublet (J=4 Hz) at 5.35τ and a triple doublet at 4.70τ (J=4 and 1 Hz) which are similar to C_2 and C_3 protons in tutin are shown. A multiplet at 6.64τ and a double doublet (J=5 and 1 Hz) at 6.55τ in the 90 MHz NMR spectrum are also analogous to C_4 and C_5 protons in tutin.

The isopropenyl signals were replaced by a doublet at 9.08τ (J=6 Hz) and 8.84τ (J=6 Hz) of an isopropyl group after the hydrogenation over Adams catalyst leading to dihydrocorianin IV, $C_{15}H_{20}O_6$, m.p. 239° (decomp.). On the treatment of corianin with bromine water, monobromocorianin V, $C_{15}H_{17}O_6Br$ (M^+ 373), m.p. 135-137° was produced. The NMR spectrum of V shows two methyl singlets at 8.24 and 8.39τ, and a singlet at 6.15τ assignable to the protons of the bromomethyl group. It is presumable that the formation of these groups on the bromination is accompanied by the ether ring formation between the isopropenyl and a hydroxyl group in the original compound as found on the bromination of tutin. Such analogy of corianin to tutin in the chemical behaviors and in the most part of the spectra leads to the assumption that the carbon skeleton of corianin is the same as that of tutin.

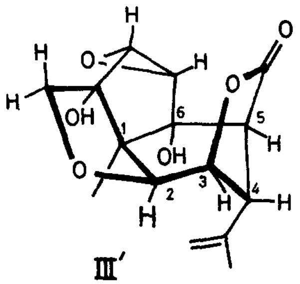
The difference between corianin and tutin is observed at the part corresponding to the terminal epoxide and C_2-oxygen function in tutin: The AB quartet (J=6 Hz) of the terminal epoxide at 5.29 and 6.90τ observed in tutin is absent in corianin, and an AB quartet (J=10 Hz) at 5.50 and 5.70τ, which is assignable to a methyleneoxy group in a five-membered or a larger ring is observed in the latter. The NMR spectrum of corianin measured in dimethylsulfoxide shows two singlets at 4.86 and 4.91τ, which disappear on addition of D_2O, while that of tutin shows a singlet at 4.40τ and a doublet at 4.84τ. Corianin, therefore, should have two tertiary hydroxyl groups, presumably at C_6 and C_{13}. This presumption is chemically supported by the fact that corianin is fairly resistant to acetylation and oxidation with chromium trioxide. As an oxygen function should be present at C_2, while there would be no hydroxyl group, the oxygen at C_2 should be an ethereal oxygen. Unlike tutin (2), corianin does not show in the NMR spectrum measured in pyridine, the large downfield shift of the angular methyl and C_{14} protons. This is in accord with the above presumption since the large downfield shift would be observed if corianin has a hydroxyl group at C_2.



IV



V



III′

The result of the bromination shows that C_6-hydroxyl group and the isopropenyl group are present on the same side of the cyclohexane ring, and that the lactone ring is located on the opposite side. The structure of corianin is thus shown as III. In the conformation of corianin shown by III', H_3-C_3-C_4-C_5-H_5 are in the "M" arrangement (6). The fine splitting of each peak in the H_3 triplet in the NMR spectrum therefore should be due to the long-range coupling with H_5.

Structure III is further supported by NMDR (90 MHz, pyridine-d_5): Irradiation of H_2 (5.40τ), H_3 (4.77τ), H_4, and H_5 respectively caused conversion of H_3, H_2, H_3, and H_3 to a double doublet (J=4 and 1), a singlet, a doublet (with a fine splitting of each peak), and a triplet (J=4). Irradiation of a doublet (6.15τ) in the AB quartet of H_{11} and H_{12} converted the other doublet (5.72τ) to a singlet.

The ORD curve of corianin, $[M]^{23}_{237}$ +4185° (c=0.078, MeOH), is almost superposable on that of tutin. The absolute configuration of corianin is accordingly represented by III.

The melting point and the IR spectrum of the crystals obtained on evaporation of the aqueous solution of 1:1 mixture of corianin and tutin have been found identical with those of pseudotutin, while the mixtures of different ratios 2:3 ~ 3:2 showed lower melting points. These results indicate that pseudotutin is a molecular compound composed by 1:1 ratio of corianin and tutin.

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