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THE ISOLATION AND STRUCTURE OF ISOASATONE

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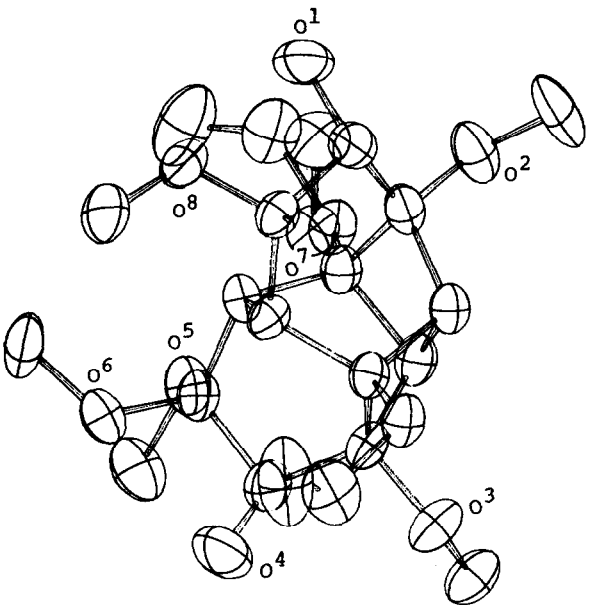
In the previous paper,[1] we reported the isolation and structure of asatone, a main component of Asarum taitonense Hayata. We further examined chemical constituents of the same plant, and could isolate a new compound, named "isoasatone", the novel structure of which was elucidated by X-ray analysis of the corresponding dihydroxy-compound. In the present paper, we wish to describe the isolation and structure of isoasatone (I). In addition, the biogenesis of I will be also discussed.

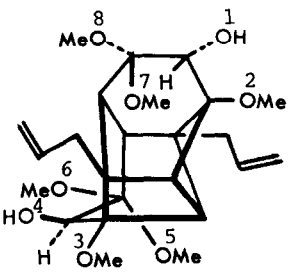
As described in the previous paper,[1] a sample of pulverized material of the whole herb was extracted with n-hexane to give asatone. The residue was further extracted with $CHCl_3$ for 3hr., and then filtered. The filtrates were concentrated under reduced pressure to give a dark green jelly, which was chromatographed on silica gel and eluted with n-hexane-EtOAc (8 : 1) to give white crystals of isoasatone (I) in ca. 0.001% yield, m.p. 156.5-158° (from n-hexane); $C_{24}H_{32}O_8$(m/e 448(M^+), 416, 384, 343 and 224); $[\alpha]_D^{20°} = \pm 0°$ (MeOH); ν_{max}(KBr) 1735 and 1640cm^{-1}; λ_{max}(MeOH) 221nm (ε, 2010); δ($CDCl_3$) 2.56(2H, q, J= 14.3, 8.6Hz), 2.80(2H, s), 2.85(2H, br.q, J= 14.3, 7.5Hz), 3.00(2H, s), 3.25(6H, s), 3.27(6H, s), 3.38(6H, s), 5.00(2H, br.d, J= 15Hz), 5.03(2H, br.d, J= 11.5Hz) and 5.35-5.80ppm(2H, m).

Isoasatone (I) is a racemic or meso-compound ($[\alpha]_D^{20°} = \pm 0°$) having a molecular formula ($C_{24}H_{32}O_8$). As described above, only half of the total protons are observed in the NMR spectrum. Accordingly, isoasatone has two allyl groups (δ2.56, 2.85, 5.00, 5.03 and 5.35-5.80ppm). In fact, catalytic hydrogenation of I was carried out over 10% Pd-C in EtOAc (room temp., overnight) to afford tetrahydroisoasatone (II), m.p. 161-162°; $C_{24}H_{36}O_8$ (m/e 452(M^+) and 226); ν_{max}(Nujol) 1735cm^{-1}; λ_{max}(MeOH) 222nm (ε, 2070). The NMR spectrum of II has a methyl triplet at δ0.90ppm(3 x 2H, t, J= 5.5Hz) and complex signals at 1.70-2.30ppm(8H, complex). Furthermore, the presence of two carbonyl groups is also supported by chemical evidences: treatment of I with $LiAlH_4$ in THF (room temp., 3hr.) gave dihydroxyisoasatone (III), m.p. 153-154°; $C_{24}H_{36}O_8$(m/e 452(M^+) and 226); ν_{max}(Nujol) 3500, 3430, 3060, 1635 and 908cm^{-1}; no UV absorption maximum; $\delta(CDCl_3)$ 2.39(2H, br.q, J= 14.3, 8.5Hz), 2.41(2H, s), 2.49(2H, s), 2.55(2H, br.q, J= 14.3, 7.5Hz), 3.24(6H, s), 3.30(6H, s), 3.35(6H, s), 3.71[2H, s (H-C(-OH)-)], 5.01(2H, br.d, J=~11Hz), 5.03(2H, br.d, J= 15Hz) and 5.70-6.20ppm(2H, m). From the above chemical and spectral data of isoasatone, this compound seemed to have a simple molecular structure with a mirror plane of symmetry. Finally, the complex structure of isoasatone (I) was elucidated by X-ray analysis of the corresponding dihydroxy-compound (III), as follows.

Recrystallization of III from n-hexane-Et_2O afforded colourless needles elongated along the b-axis, which were shown to be monoclinic with unit cell dimensions of a = 10.478, b = 17.746, c = 14.525Å, β = 119.76° and belong to space group $P2_1/C$. The density measured by the flotation method using calcium chloride solution is 1.279$g \cdot cm^{-3}$, which agreed with the calculated value of 1.282$g \cdot cm^{-3}$ based on the presence of four molecules in a unit cell. Lattice constant and intensities were measured on a Hilger and Watts four-circle automatic diffractometer Y-290 with Cu-Kα radiation. A total 2440 independent non-zero intensities were collected in the range, $\theta \leq 75°$. The structure was solved by direct methods, applying the program MULTAN of Germain, Main and Woolfson.[2] Refinement of the structural parameters was

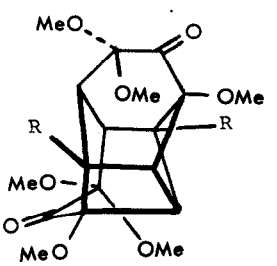
carried out by the block-diagonal least-squares calculation with anisotropic thermal parameters, and the R factor was 0.083. The molecular shape of III is shown in Fig.1. The structure (III) thus obtained is in good agreement with the physical data of dihydroxyisoasatone. Therefore, the structure of isoasatone should be represented by I, in which the UV absorption maximum at 221nm may be due to the conjugative overlap of the cyclobutane ring with the carbonyl group. The carbon skeleton of isoasatone (I)





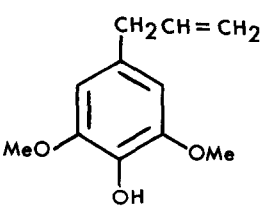
(III)

FIG. 1. MOLECULAR STRUCTURE OF DIHYDROXYISOASATONE (III).



(I) R = $CH_2CH=CH_2$

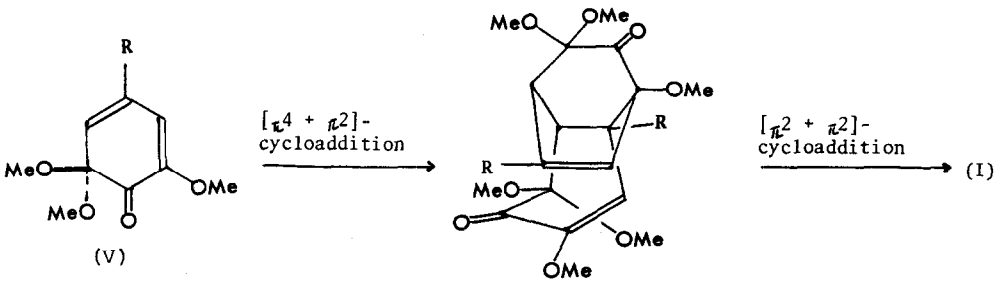
(II) R = n-Pr



(IV)

consists of two C_6-C_3 units. From a biogenetic point of view, 2,6-dimethoxy-4-allylphenol (IV) or its further oxygenated compound (V) is regarded as the original precursor of isoasatone (I): probably, isoasatone (I) is formed from V through the possible intermediate (VI), as shown below. In the last step (VI⟶I), photochemical [$_{\pi}2 + _{\pi}2$]cycloaddition may take place, leading to the formation of cyclobutane system. Furthermore, in connection with the biogenesis of I, the tentative structure of asatone[1] will be re-examined.

All compounds gave satisfactory physical data and elemental analyses.



(V)

R = $CH_2CH{=}CH_2$

(VI)

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