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ON THE STRUCTURE OF AILANTHONE, A BITTER PRINCIPLE FROM *AILANTHUS ALTISSIMA*

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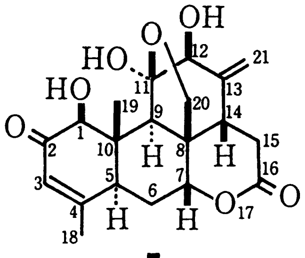
The structure of ailanthone has been revised and shown to be 11β,20-epoxy-1β,11α,12α-trihydroxypicrasa-3,13(21)-diene-2,16-dione by X-ray diffraction analysis.

Ailanthone is a main bitter principle with amoebicidal toxity[1] isolated from *Ailanthus altissima* SWINGLE (=*A. glandulosa* DESF.)[2a] and the chemical structure (1) has been proposed by spectral and chemical evidence.[3] Although the configuration of the $C_{(12)}$-OH was proposed to be an α-axial orientation in a $C_{(11)}$-keto form (2) by Casinovi,[2b] it has been assigned to be β-equatorial in a hemiacetal form (1) by spectral examination and correlation of ailanthone with chaparrinone.[3] Recently we investigated bitter constituents of *A. altissima* (Japanese name: Shinju or Niwaurushi) grown in Japan[4] and obtained ailanthone (mp 234-235 °C, $[\alpha]_D^{20}$ +9.2° (EtOH))[5] as a main bitter principle[6] together with shinjulactones A (3)[7], B,[8] and C,[9] and shinjudilactone.[6] During the structure investigation on these picrasane derivatives, a question arose in regard to the configuration of the $C_{(12)}$-OH group of ailanthone; a preliminary NOE experiment[10] in the ^{1}H NMR measurement of ailanthone in pyridine-d_5 suggested that the $C_{(12)}$-H would be in β-equatorial disposition; that is the $C_{(12\alpha)}$-OH configuration.

Unambiguous proof for this configuration was provided by X-ray diffraction analysis of ailanthone. Ailanthone was crystallized from chloroform-methanol solution as a thin plate. The crystal belongs to an orthorhombic space group $P2_12_12_1$ with the cell parameters of $a = 17.067(8)$, $b = 16.608(8)$, and $c = 6.594(2)$ Å. Four ailanthone molecules and four water molecules are contained in a unit cell, to give the calculated density of 1.40 g·cm^{-3}. A total of 1874 independent intensity data were collected on a Philips PW1100 diffractometer as above the 2σ(I) level using Cu Kα radiation monochromated by a graphite plate. The structure was solved by the direct method using MULTAN program. An E-map based on the phase set with the lowest R-value revealed the whole skeleton. Hydrogens were located on a difference electron map, except for those of O(3) hydroxyl and water molecule. The structure was refined by the block-diagonal least-squares method assuming anisotropic thermal motions for non-hydrogen atoms and isotropic ones for hydrogens. The final R-value was 4.3%. Figure 1 shows a computer-generated perspective drawing of the ailanthone molecule, indicating the $C_{(12\alpha)}$-OH configuration.[11]

Molecules are infinitely linked by the intermolecular hydrogen bond between O(2) (carbonyl) and O(4) (hydroxyl) with a distance of 2.843(4) Å. The water molecule is strongly hydrogen-bonded to O(1) (hydroxyl), O(3) (hydroxyl), and O(6) (lactone carbonyl) of the three different ailanthone molecules, with the distances of 2.709(3), 2.861(4), and 3.007(4) Å, respectively.

Thus the structure of ailanthone has been shown to be revised to 11β,20-epoxy-1β,11α,12α-trihydroxypicrasa-3,13(21)-diene-2,16-dione (4).



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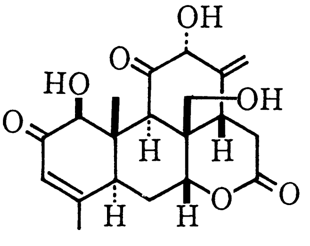

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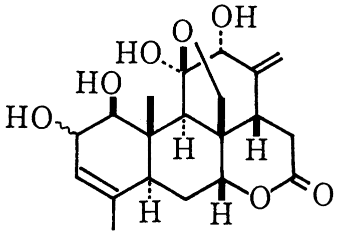

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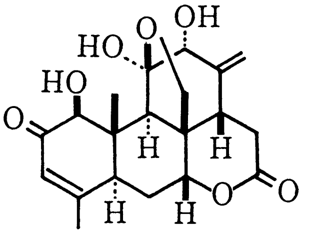

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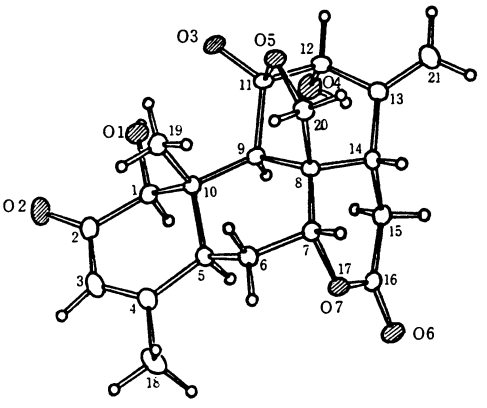

Figure 1. A computer-generated perspective drawing of ailanthone, shaded circles indicating oxygen atoms

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4) The plant was collected at the Botanical Gardens, Faculty of Science, The University of Tokyo.

5) This sample was shown to be completely identical with the authentic ailanthone[3)] by ^{1}H NMR (400 MHz) measurement.

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10) On irradiation at δ 4.44 ($C_{(12)}$-H), a signal at δ 5.27 (one of the two $C_{(21)}$-H's) showed an increase by 6% and the reverse irradiation afforded an increase by 10%.

11) Numbering of picrasane refers to the nomenclature described in the Chemical Abstracts.

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