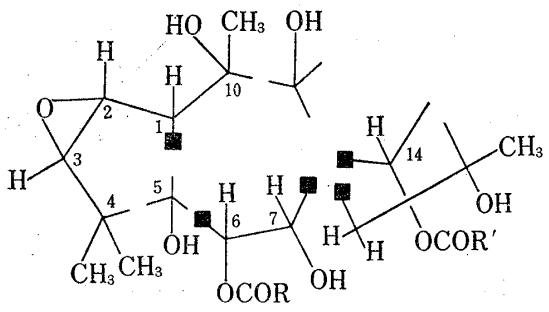
[Chem. Pharm. Bull. 19(9)1980—1981(1971)]

UDC 547.913.6.02 : 581.192 : 582.912.4

Stereostructure of Asebotoxin VII, Toxin of *Pieris japonica*

From the flowers of *Pieris japonica* D. Don (Ericaceae), a famous poisonous tree in Japan, we have recently isolated five toxins, asebotoxins I, II, III, IV, and V and elucidated their stereostructures.[1-4] Further survey has resulted in the isolation of a new toxic diterpenoid for which the term asebotoxin VII is given.

A-VII, $C_{25}H_{38}O_{10}$, was shown by its spectral properties to have tertiary methyls (1.14, 1.22 ppm), two tertiary methyls on hydroxyl-carrying carbons (1.28, 1.57 ppm), an epoxide (3.21, 3.83 ppm (J=2.5 Hz)), hydroxyls (3430 cm^{-1}) one of which is secondary (3.55 ppm), an O-acetyl (1725, 1237 cm^{-1}, 2.13 ppm) and an O-propionyl (1.17, 2.40 ppm), the two O-acyl groups being both secondary (5.26, 5.96 ppm). Alkaline hydrolysis of A-VII gave the heptaol (II), mp 299—300°, which on acetylation yielded the monoacetate (III) and the diacetate (IV). Analysis of the nuclear magnetic resonance (NMR) spectra of A-VII and the diacetate (IV) with the aid of double resonance experiments indicated the presence of the partial structure A in A-VII. Inter alia, intramolecular nuclear Overhauser effects were observed between the C-1 and C-2 hydrogens, the C-1 and C-6 hydrogens, the C-1 and C-14 hydrogens, the C-3 and C-18 hydrogens, and the C-6 and C-18 hydrogens. When A-VII was treated with phosphorus oxychloride in pyridine gave the dehydration product (V), mp 211—213°, having a vinylidene group (3090, 1660, 890 cm^{-1}, 4.83 ppm), which on ozonolysis have the norketone (VI), mp 123—125°, whose spectral properties demonstrated the formation of a cyclopentanone (1730 cm^{-1}, $[\theta]_{284}$—1900). Taking into account the simultaneous occurrence of A-VII with the other diterpenoids having the andromedane skeleton in the same plant, the above data demonstrate that A-VII also possesses the same carbon skeleton, the remaining problem being the location of the unaccommodated tertiary hydroxyl which must be at C-9 or C-13, and the situation of the two different acyl groups. While A-VII consumes no periodate, the monoacetate (III) on periodate oxidation afforded the hemiacetal-hemiketal (VII), mp 112—114°, exhibiting no circular dichroism (CD) maximum in the region 250—300 nm. Since four-membered hemiketal ring formation between the C-5 carbonyl and the C-10 hydroxyl is thought to be improbable, the tertiary hydroxyl grop which can be linked to the C-5 carbonyl, must be located at C-9. In consistent with this deduction, the C-20 methyl hydrogen signal (2.07 ppm) in the NMR spectrum of bisdeacyl-A-VII(II) suffered from a considerable downfield shift (—0.20 ppm) as compared with the corresponding signal (1.87 ppm) in the spectrum of the reference substance, rhodojaponin III.[2] A-VII on partial hydrolysis gave the depropionhl-derivative (VIII), mp 263—264°, retaining the O-acetyl group (1.94 ppm) woich was not identical with the 14-acetate (III) and was not reacted with periodate.



A: R=$COCH_3$, R'=$COCH_2CH_3$ or *vice versa*
■ denotes a quaternary carbon

The accumulated data have led to the conclusion that A-VII is represented by stereoformula I.

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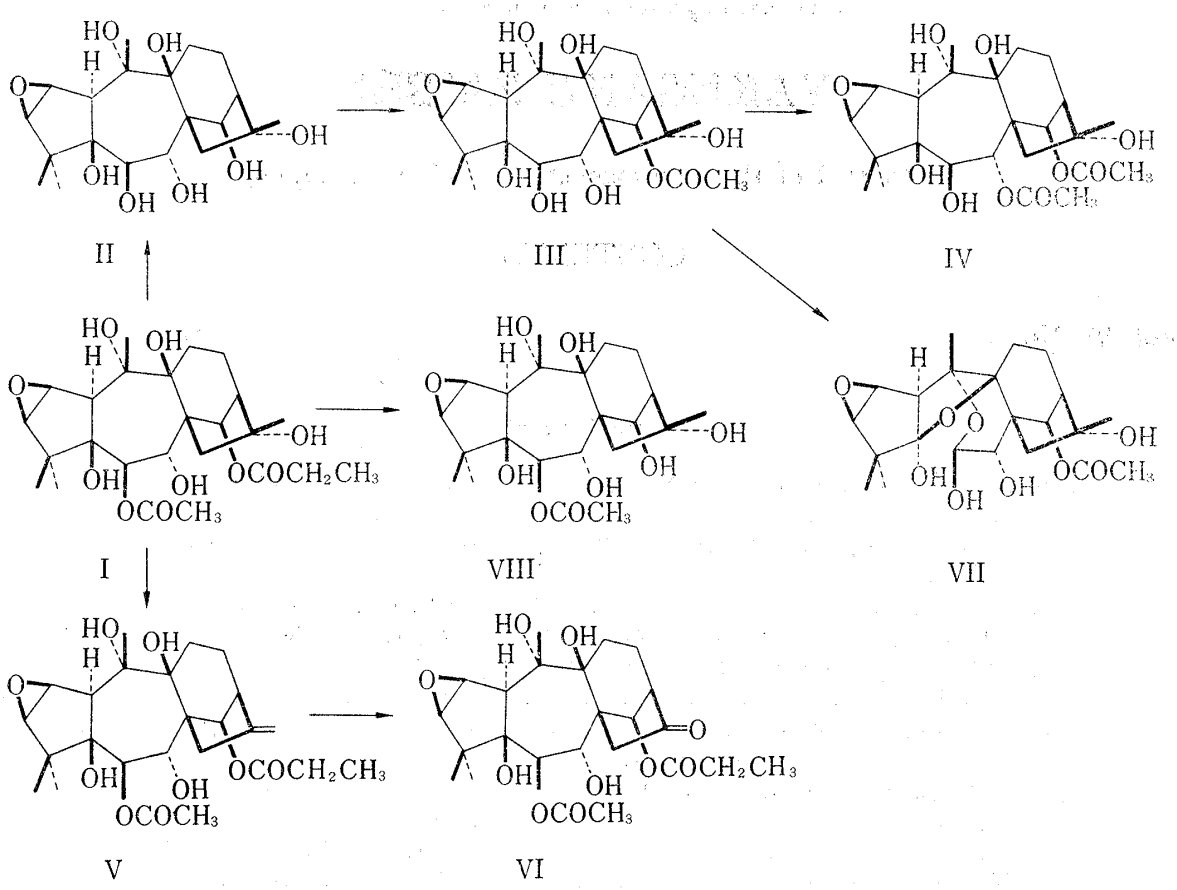
3) H. Hikino, M. Ogura, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 1071 (1970).
4) H. Hikino, M. Ogura, M. Fuzita, K. Ito, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 856 (1971).



Acknowledgement We thank Mr. K. Ito, this laboratory, for the preliminary experiments. Thanks are also due to Research Laboratory, Yoshitomi Pharmaceutical Co., Ltd., for the mass spectra, and Research Laboratories, Takeda Chemical Industries, Ltd., and Department of Chemistry, this University, for the NMR spectra.

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Received June 22, 1971