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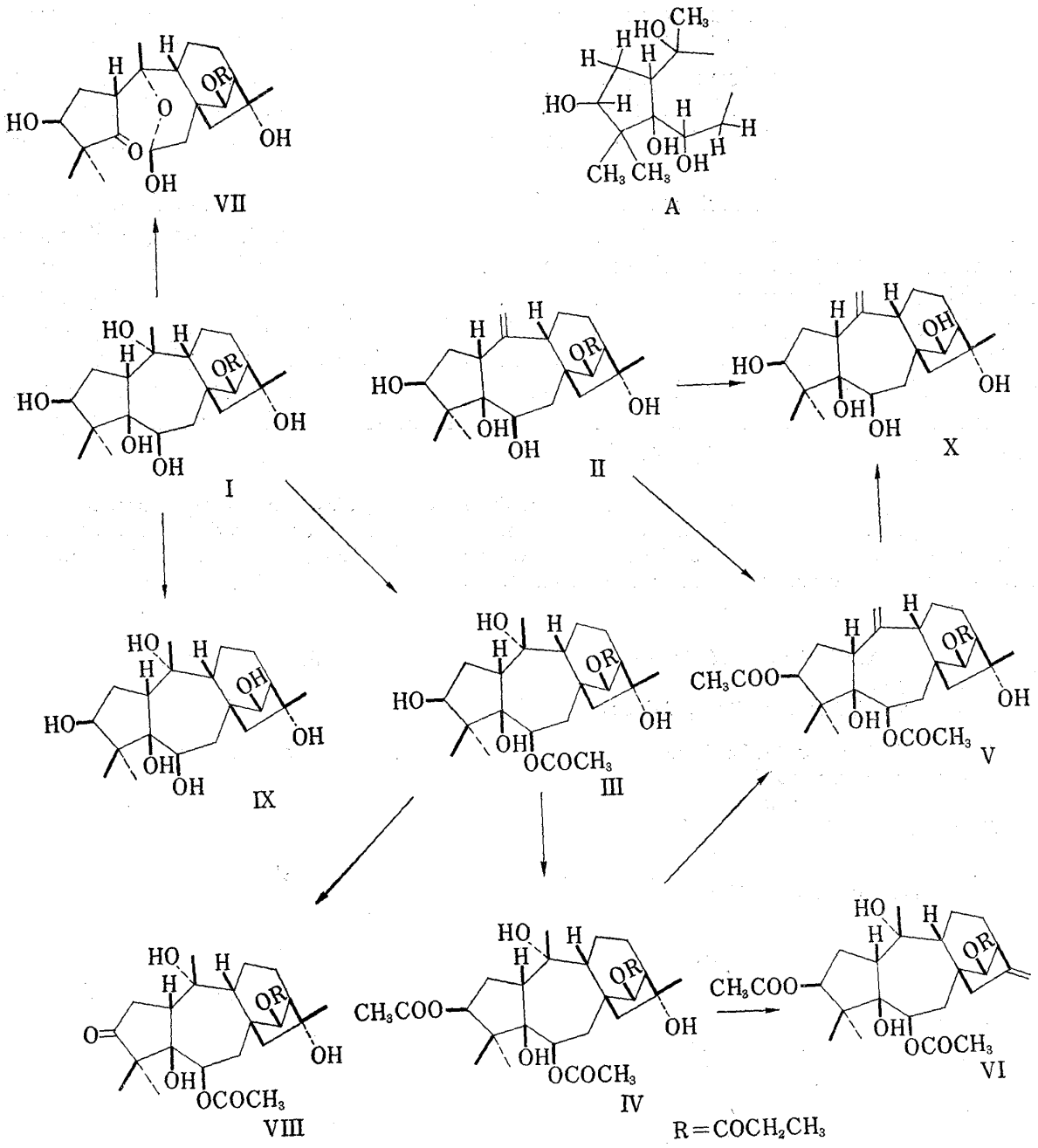
Stereostructure of Asebotoxin I and II, Toxins of *Pieris japonica*

Since the first investigation by Eykman,[1] the toxic constituents of *Pieris japonica* D. Don (Ericaceae), a famous poisonous tree in Japan, have been the subject of numerous investigations.[2] However, the only toxic principle whose structure has been elucidated is grayanotoxin III isolated from the leaves.[3]



1) J.F. Eykman, *Rec. Trav. Chim.*, **1**, 225 (1882).
2) For the historical backgroud of the researches, see T. Takemoto and H. Meguri, *Yakugaku Kenkyu*, **29**, 588 (1957).
3) H. Meguri, *Yakugaku Zasshi*, **79**, 1059 (1959).

From the flowers, we have recently isolated two new toxic diterpenoids for which the names asebotoxin I (A-I) and asebotoxin II (A-II) have been proposed.

A-I, $C_{23}H_{38}O_7$, has mp 196—198° and was shown by its spectral properties to possess a geminal dimethyl (1386, 1363 cm^{-1}, 0.95, 1.15 ppm), two tertiary methyls on hydroxyl-carrying carbons (1.31, 1.37 ppm), hydroxyls (3410 cm^{-1}), and an O-propionyl (1720, 1240 cm^{-1}, 1.15, 2.40 ppm). A-I was acetylated to give the monoacetate (III) and the diacetate (IV). Dehydration of the diacetate (IV) afforded the two dehydro-derivatives (V and VI), each of which contained a vinylidene group, confirming that two tertiary hydroxyls on two methyl-carrying carbons are present in A-I. On periodate oxidation, A-I gave the cyclopentanone (VII), ν_{max} 1725 cm^{-1}, while the acetate (III) recovered the starting material (III), a fact which indicates the presence of a >C(OH)–CH(OH)– system where the quaternary carbon is located in a five-membered ring. The NMDR analysis of the monoacetate (III) showed the presence of a $-C(CH_3)_2-CH(OH)-CH_2-CH(C\lessdot)_2$ system, which is involved in a five-membered ring, since chromic acid oxidation of the acetate (III) gave the cyclopentanone (VIII), ν_{max} 1735 cm^{-1}. The signal due to the corresponding methine hydrogen in the $-CH_2-CH(C\lessdot)-C=CH_2$ system of the dehydro-derivative (V) was spin-coupled to one of the vinyl hydrogen signals. The combined evidence together with the deshielded line position of the methine proton (2.95 ppm) in the acetate (III) led to the postulate that A-I has the part-structure A. This partial structure is consistent with the A, B ring of, for instance, grayanotoxin I.[4] A-I was then hydrolyzed to furnish the depropionyl-derivative which was found identical with grayanotoxin III (IX).[4] The accumulated data show that A-I is represented by stereoformula I.

A-II, $C_{23}H_{36}O_6$, is amorphous and was shown by its spectral properties to have a geminal dimethyl (1385, 1368 cm^{-1}, 0.95, 1.16 ppm), a tertiary methyl on a carbon attached to a hydroxyl (1.38 ppm), a vinylidene (1631, 890 cm^{-1}, 5.01, 5.12 ppm), hydroxyls (3450 cm^{-1}), and an O-propionyl (1730, 1230 cm^{-1}, 1.17, 2.21 ppm). The NMR spectrum was quite similar to that of A-I except that a tertiary methyl on a hydroxyl-bearing carbon in A-I was replaced by a vinylidene in A-II. A-II diacetate and depropionyl-A-II were then prepared and identified as the diacetate (V) and grayanotoxin II (X),[4] respectively. These results have established the stereostructure of A-II to be as shown in formula II.

Addendum in Proof (Received April 22, 1969): Asebotoxin II has been recently crystallized, mp 142—144°.

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cf., H. Kakisawa, T. Kozima, M. Yanai, and K. Nakanishi, *Tetrahedron*, **21**, 3091 (1965).