[Chem. Pharm. Bull. 25(3) 523—524 (1977)]

UDC 547.913.6.02 : 581.192

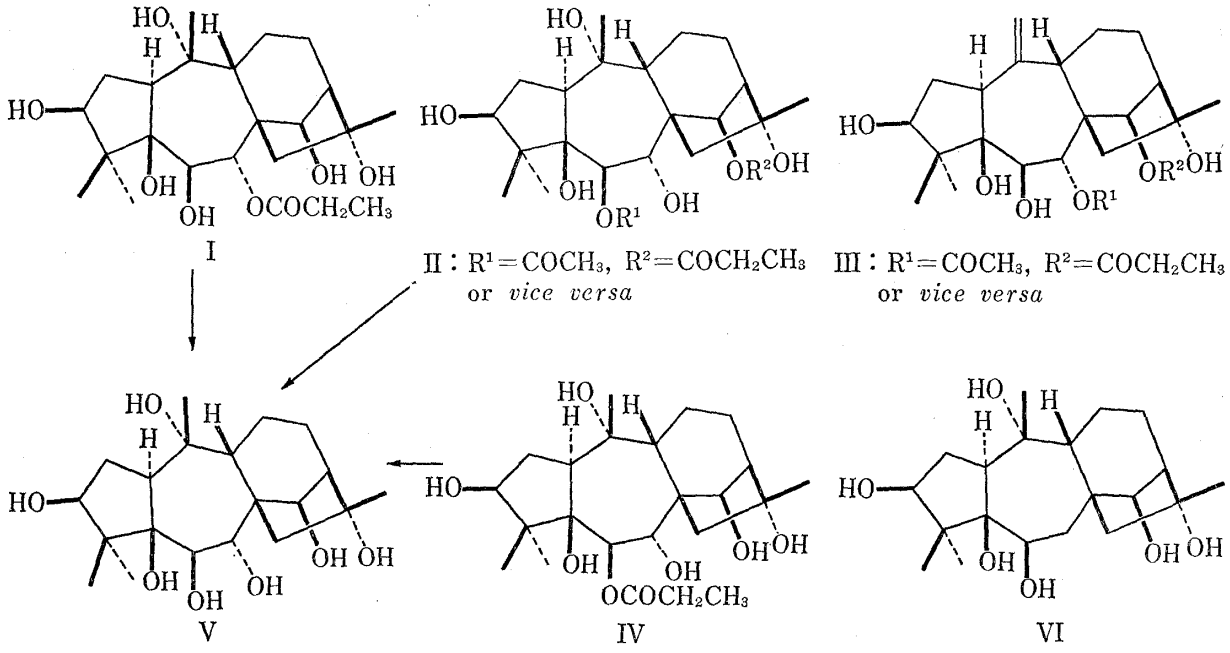
# Stereostructure of Asebotoxin VI, VIII, and IX, Toxins of *Pieris japonica*

From the flowers of *Pieris japonica* (Ericaceae), three new diterpenoids, now designated as asebotoxin VI, VIII, and IX (A–VI, A–VIII, and A–IX), have been isolated. Chemical and spectroscopic examinations have led to the conclusion that A–VI, A–VIII, and A–IX are represented by formulas I, II, and III, respectively.

**Keywords**——asebotoxin; andromedane skeleton; diterpenoid; toxin; *Pieris japonica*

From the flowers of *Pieris japonica* D. Don (Ericacea), a famous poisonous tree in Japan, we have hitherto isolated six diterpenic toxins, asebotoxin I—V and VII and elucidated their stereostructures.[1–4] Further survey has led to the isolation of three new diterpenoids which are designated as asebotoxin VI, VIII, and IX (A–VI, A–VIII, and A–IX).

A–VI, $C_{23}H_{38}O_8$, mp 105—106°, was shown by its spectral properties to have four tertiary methyls (0.95, 1.34, 1.54, 1.54 ppm), hydroxyls (3300 $cm^{-1}$) three of which are secondary (3.92, 4.58, 5.20 ppm), and a secondary O-propionyl (1703, 1185 $cm^{-1}$, 1.17, 2.38, 5.94 ppm). Thus A–VI was found to be similar in functional groups and $^1H$ nuclear magnetic resonance (NMR) parameters to A–IV (IV), suggesting that the former was an isomer of the latter. A–VI was then subjected to alkaline hydrolysis to give the depropionyl-derivative which was identified as depropionyl-A–IV (V). In the $^1H$ NMR spectrum of A–VI, the two signals at 4.58 and 5.94 ppm were spin-coupled only to each other, a fact which demonstrates that they are attributed to the C-6 and C-7 carbinyl hydrogens either of which is acylated. Since 6-O-propionyl derivative of the heptaol (V) is known (*i.e.* A–IV (IV)), A–VI is consequently concluded to be 7-O-propionyl derivative (I). This conclusion was confirmed by the observation that A–IV consumed the reagent on periodate oxidation (A–IV consumed no periodate[3]).

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A–VIII, $C_{25}H_{40}O_9$, mp 203—204°, was shown to contain four tertiary methyls (1.06, 1.48, 1.48, 1.76 ppm), hydroxyls (3420 $cm^{-1}$) two of which are secondary (3.88, 4.17 ppm), a secondary O-acetyl and a secondary O-propionyl (1710, 1230 $cm^{-1}$, 2.08, 1.17, 2.47, 5.50, 6.30 ppm). In the $^1H$ NMR spectrum, the two carbinyl hydrogen signals at 4.17 and 5.50 ppm appeared as two doublets in an AB spectrum ($J$=7 Hz) and another carbinyl hydrogen signal at 6.30 ppm occurred as a singlet. On the basis of the above evidence, A–VIII was assumed to be a deacyl-A–IV derivative in which the C-6 or C-7 hydroxyl and the C-14 hydroxyl were esterified by acetic acid and propionic acid. In support of this supposition, alkaline hydrolysis of A–VIII then performed gave deacyl-A–IV (V). Treatment of A–VIII with periodate resulted in consumption of no reagent, demonstrating that the C-6 hydroxyl was acylated. In order to elucidate the respective location of the acetyl and propionyl groups, partial hydrolysis of A–VIII was carried out to afford only the starting materials, A–VIII and the completely hydrolyzed product (V) but no monoacylated derivatives under conditions attempted. Accumulated data indicate that A–VIII is represented by formula II.

A–IX, $C_{25}H_{38}O_8$, mp 186—187°, was indicated to possess three tertiary methyls (0.85, 1.20, 1.45 ppm), a vinylidene (3100, 1620, 898 $cm^{-1}$, 5.05, 5.09 ppm), hydroxyls (3460, 3310 $cm^{-1}$) two of which are secondary (3.80, 4.19 ppm), a secondary O-acetyl and a secondary O-propionyl (1728, 1690, 1236 $cm^{-1}$, 1.99, 1.06, 2.36, 5.45, 5.71 ppm). The $^1H$ NMR parameters, which were well rationalized as those for an anhydro-derivative of the heptaol (V)bearing an acetyl and a propionyl group, together with the circumstantial evidence, demonstrated that A–IX was similar in structure to A–VIII (possibly an anhydro-derivative). The carbinyl hydrogen singlet assigned to the C-14 hydrogen appeared at a lower-field region showing that the C-14 hydroxyl was acylated. From the chemical shifts of the other signals at 4.19 and 5.71 ppm for the C-6 and C-7 carbinyl hydrogens constituting as AB spectrum, it was concluded that either of the hydroxyls at C-6 and C-7 was acylated. A–IX on periodate oxidation consumed the reagent, indicating that the C-6 hydroxyl was free and the remaining C-7 hydroxyl acylated. All attempts to clarify the respective location of the acetyl and the propionyl groups by partial hydrolysis failed because no monoacylated derivatives were obtained also in this case. The location of the vinylidene moiety (at C-10: C-20 or C-16: C-17) was next examined. In the $^1H$ NMR spectrum, the absence of the C-20 methyl hydrogen signal, which showld occur at a lower-field region, showed that the C-10 and C-20 carbons constituted a vinylidene groupings. In an andromedane congener, dehydration of a 10-hydroxyl to a C-10: C-20 vinylidene group (G–III (VI)→G–II) brings about a down field and an upfield shift (+0.15 and −0.24 ppm) of the C-1 and C-14 hydrogen signals, respectively, while dehydration of a 16-hydroxyl to a C-16: C-17 vinylidene group (G–II→G–VIII) results in practically no shifts (−0.01 and −0.02 ppm) of the C-1 and C-14 hydrogen signals. On the other hand, displacement of an acyl group from C-6 to C-7 in the 6,7-glycol system (A–IV→A–VI) causes a downfield and a slight upfield shift (+0.33 and −0.04 ppm) of the C-1 and C-14 hydrogen signals, respectively. The observed differences of the C-1 and C-14 hydrogen resonances (+0.25 and −0.59 ppm, respectively) between A–VIII and A–IX also demonstrated that the vinylidene was situated at C-10: C-20. Combined evidence has led to the conclusion that the stereostructure of A–IX is as shown in formula III.

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Received November 19, 1976