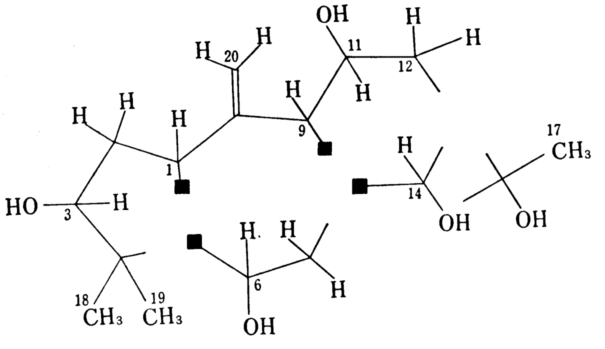
[Chem. Pharm. Bull. 20(2) 422—423 (1972)]

UDC 547.597.02 : 581.192 : 582.912.4

Stereostructure of Grayanotoxin XII and XIII, Toxins of *Leucothoe grayana*

From the leaves of *Leucothoe grayana* Maximowicz (Ericaceae), a famous poisonous shrub in Japan, eleven toxic diterpenoids, grayanotoxin I, II, III,[1,2] IV,[3] V,[3,4] VI, VII,[4] VIII, IX, X, and XI,[5] have been isolated. In continuation of our survey, we have further isolated two novel diterpenoids for which the names grayanotoxin XII and XIII (G-XII and G-XIII) are given.

G-XII, $C_{20}H_{32}O_6$, mp 208—209°, was indicated to contain two tertiary methyls (1.12, 1.57 ppm), a tertiary methyl on a hydroxyl-bearing carbon (1.61 ppm), a vinylidene (3100, 1634, 880 cm^{-1}, 5.41 ppm), hydroxyls (3540, 3410 cm^{-1}), four of which are secondary (3.88, 4.23, 4.68, 5.21 ppm). nucler magnetic double resonance (NMDR) experiments demonstrated the presence of the partial structure A in G-XII. *Inter alia*, intramolecular nuclear Overhauser effects (NOE) were ovserved between the C-1 and C-14 hydrogens, the C-3 and C-18 hydrogens, the C-3 and C-19 hydrogens, the C-6 and C-18 hydrogens, the C-9 and one of the C-20 hydrogens, the C-9 and C-11 hydrogens, and the C-11 and C-17 hydrogens. Acetylation afforded the triacetate (III) and the pentaacetate (IV). On chromic acid oxidation the triacetate (III) furnished the ketone (V) whose infrared (IR) spectrum showed the formation of a cyclopentanone (1727 cm^{-1}). The optical rotatory dispersion (ORD) and circuear dichroism (CD) curves of the ketone (V) (a—59, $[\theta]_{299}$ —3589) are similar to those of the ketone (IX) derived from G-11 3,6-diacetate (VIII) (a —49, $[\theta]_{300}$ —2940). Further on ozonolysis G-XII yielded the norketone (VI), whose IR spectrum indicated the formation of a cycloheptanone (1689 cm^{-1}). The ORD and CD curves of the norketone (VI) (a —185, $[\theta]_{294}$ —13700) resemble those of the norketone (X) prepared from G-II (VII) (a —168, $[\theta]_{294}$ —12100). Accumulated data show that G-XII possesses the andromedane skeleton. The α-configuration of the C-II hydroxyl was deduced by the findings that 1) the $J_{9,11}$, $J_{11,12\alpha}$, and $J_{11,12\beta}$ are 7,6, and 6 Hz, respectively, 2) NOE's were observed between the C-11 and C-9 hydrogens and between the C-11 and C-17 hydrogens, and 3) the C-1 and C-14 hydrogens are considerably deshielded (0.56 and 0.84 ppm) as compared with those of G-II (VII). On the basis of the above evidence, it is concluded that G-XII is represented by stereoformula I.

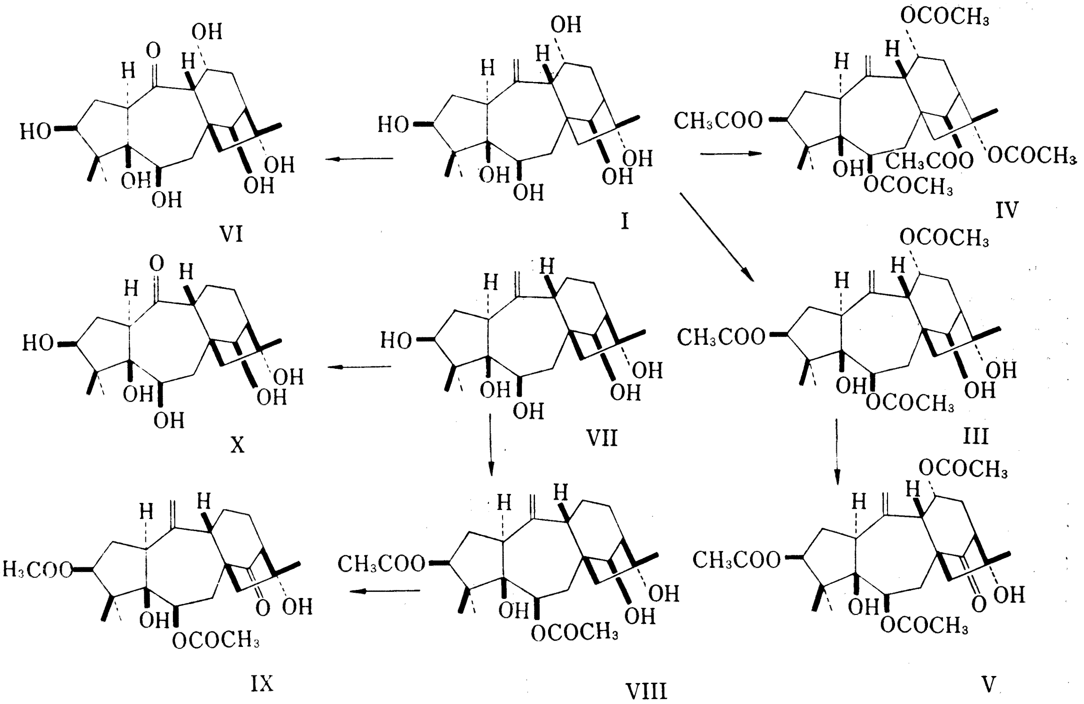


A

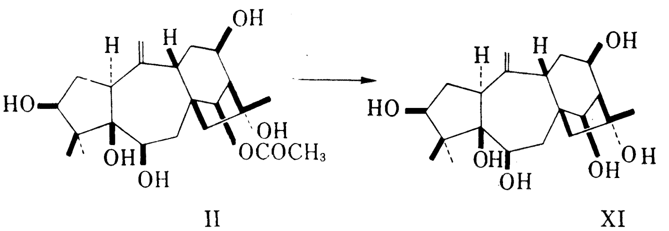
G-XIII, $C_{22}H_{34}O_7$, mp 150—151°, was shown to have two tertiary methyls (0.91, 1.33 ppm), a tertiary methyl on a hydroxyl-carrying carbon (1.93 ppm), a vinylidene (3200, 1625,

---

1) *cf.* H. Kakisawa, T. Kozima, M. Yanai, and K. Nakanishi, *Tetrahedron*, **21**, 3091 (1965).
2) H. Hikino, M. Ogura, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 1071 (1970).
3) T. Okuno, N. Hamanaka, H. Miyakoshi, and T. Matsumoto, *Tetrahedron*, **26**, 4765 (1970).
4) H. Hikino, N. Shoji, S. Koriyama, T. Ohta, Y. Hikino, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 2357 (1970).
5) H. Hikino, T. Ohta, S. Koriyama, Y. Hikino, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 1289 (1971).



895 cm^{-1}, 5.07, 5.18 ppm), a secondary O-acetyl (1703, 1268 cm^{-1}, 2.05, 5.24 ppm), and hydroxyls (3400 cm^{-1}). three of which are secondary (3.81, 4.22, 4.50 ppm). Since G-XIII contains an ester moiety, alkaline hydrolysis was carried out to give deacetyl-G-XIII which was identified as G-XI (XI). The C-14 hydrogen signal in the NMR spectrum of G-XIII occures at a lower-field region (5.24 ppm), indicating that the C-14 hydroxyl is acetylated. Therefore, G-XIII is concluded to possess the stereostructure II.



II XI

Acknowledgement We are indebted to Analytical Laboratory, Department of Chemistry, this University, for NMR spectra.

Pharmaceutical Institute,
Tohoku University
Aoba-yama, Sendai

Hiroshi Hikino
Shinji Koriyama
Tomihisa Ohta
Tsunematsu Takemoto

Received October 28, 1971