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GARDNERIA ALKALOIDS – IX

STRUCTURES OF CHITOSENINE AND THREE OTHER MINOR BASES FROM Gardneria multiflora Makino

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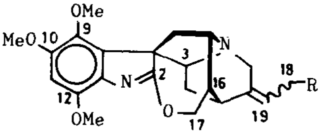
A Japanese Loganiaceae plant, Gardneria multiflora, has been found to be a rich source of indolic alkaloids,1) and the structure of the main base, gardneramine(I), was fully elucidated by us.2,3) This paper deals with the isolation and structure elucidation of four new alkaloids of this plant. The structure of cooccurring novel dimeric indole alkaloid, gardmultine, is to be published elsewhere.5)

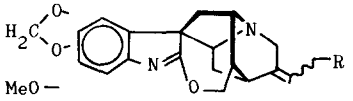
The crude base obtained by methanol extraction of this plant was roughly fractionated by Al_2O_3 column chromatography. As examination of a gardneramine fraction by TLC revealed coexistence of three minor bases, they were isolated by the use of preparative TLC (Silicagel GF_{254} (Merck), acetone-$CHCl_3$ 4:5 as a developer). The fastest moving base (II) was crystallyzed from acetone to give colorless prisms, $C_{22}H_{24}O_5N_2 \cdot 1/2\ H_2O$, mp.159-160°, $[\alpha]_D$ -248°. Its spectral data are as follows; λ_{max}^{MeOH} (log ε), 239(4.33) and 296(3.49) nm, and $\nu_{max}^{CHCl_3}$ 1580 cm^{-1} (C=N-), m/e 396(M^+, base peak). A signal due to a methylene dioxyl group appeared as a 2H-singlet at δ 5.87 in its NMR spectrum and color reaction for this group using gallic acid and sulfuric acid (Labat test) was positive (blue) to II. Other NMR signals are at δ 3.33 (3H,s.)(aliph.-OMe), 4.05(3H,s.)(arom.-OMe), 4.45(2H,br.s.)($C_{(17)}H_2$), 5.40(1H,m.)($C_{(19)}H$) and 6.55(1H,s.)(arom. H). These findings showed that this base is a gardneramine analogue with a methylene dioxyl and a methoxyl group on its aromatic ring instead of the three methoxyl groups of I. The name, gardfloramine, is given to this new base.

The second base (III), $C_{22}H_{26}O_4N_2$, mp160-161.5°, $[\alpha]_D$ -147°, was crystallized from acetone. Its UV spectrum is superimposable to that of I, and the characteristic C=N- absorption was observed at 1588 cm^{-1} in the IR spectrum. Its NMR spectrum showed the presence of an ethylidene side chain by a methyl signal at δ 1.61(3H,d.t.,J=7 and 1.5 Hz)($=C{<}^{Me}_{H}$) and an olefinic proton signal at δ 5.13(1H,q.t.,J=7 and 1.5 Hz)($=C{<}^{Me}_{\underline{H}}$), while the signal due to an allylic methoxyl group of I is lacking. Thus the structure of III was deduced to be 18-desmethoxy gardneramine (III). The geometry of the Δ^{19} double bond of this alkaloid has been determined to be E configuration. Detail of this part of our work has been published separately.[4)]

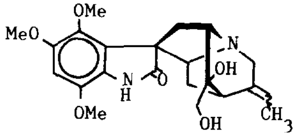
The third base (IV) was obtained in only a minor amount as an amorphous powder, whose UV spectrum is similar to that of II suggesting the presence of a methylene dioxyl group in its aromatic ring. This assumption was supported by its positive reaction to Labat test. The mass spectrum of IV showed the molecular ion peak at m/e 366 as the base peak, which proved this base to be a demethoxy analogue of II. Its NMR spectrum showed the signals due to an ethylidene side chain (δ 1.65,3H,d.J=7 Hz, $=C{<}^{\underline{Me}}_{H}$; δ5.17,1H,m., $=C{<}^{Me}_{\underline{H}}$), together with those due to an aromatic methoxy (δ 4.07,3H,s.), a methylene dioxy (δ 5.86,2H,s.) and an aromatic proton (δ 6.54,1H,s.). Therefore IV was proved to be 18-desmethoxy gardfloramine (IV).



I R= OMe Δ^{19} Z config.
III R= H Δ^{19} E config.



II R= OMe
IV R= H

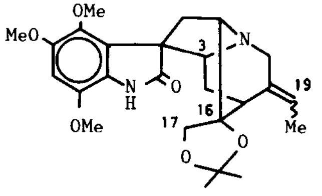


V

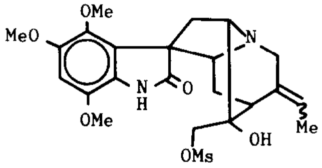
A few years ago we reported the isolation of a new alkaloid with a tentative name of alkaloid F from the same plant.[1)] This base (V), now named chitosenine after the Japanese name of this plant "Chitose-kazura", has been elucidated to possess the structure shown above. Brief explanation of the structural work will be given here.

Chitosenine (V) is an amorphous base with a molecular formula of $C_{22}H_{28}O_6N_2$, which is evidenced by the molecular ion peak at m/e 416 in its mass spectrum and the correct elemental analysis of its hydrochloride, mp.173-174°. The UV spectrum of V (λ_{max}^{MeOH} 259(sh) and 314 nm) showed that the basic skeleton is 7-spiro oxindole with three methoxyl groups at 9,10 and 12 positions (indole alkaloid numbering), and IR absorptions due to oxindolic NH and C=O groups are found at 3420 and 1705 cm^{-1}, respectively. Its NMR spectrum showed the following signals; δ 1.61 (3H,d.J=6.5 Hz)($=C{<}^{H}_{\underline{Me}}$), 3.73 (3H,s) and 3.80(6H,s.)(arom.-OMe x 3), 3.92,4.08(AB type doublets,J=10.3 Hz)($C_{(17)}H_2$), 5.37(1H,q.J=6.5 Hz)($=C{<}^{\underline{H}}_{Me}$), 6.42(1H,s.)($C_{(11)}H$) and 7.21(1H,br.

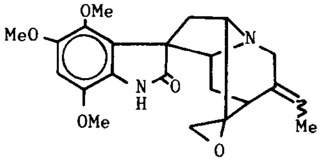
s.)(NH). The α glycol system of V at $C_{(16)}$ and $C_{(17)}$ was proved by consumption of one molar equivalent of periodic acid at room temperature and formation of an acetonide (VI), $C_{25}H_{32}N_2O_6 \cdot C_6H_6$ (from benzene),mp.105-110°, by heating in acetone containing p-TsOH. The NMR spectrum of VI showed the following characteristic signals; δ 1.35 and 1.40 (each 3H,s.)($\begin{matrix}\text{-O}\\ \text{-O}\end{matrix}\!\!>\!\text{C}\!<\!\begin{matrix}\text{Me}\\ \text{Me}\end{matrix}$),1.59 (3H,d.J=6.3 Hz)($=\text{C}\!<\!\begin{matrix}\text{H}\\ \underline{\text{Me}}\end{matrix}$), 3.77(3H,s),3.84(6H,s.)(arom.-OMe x 3), 4.35(1H,d.J=9 Hz)($C_{(17)}$H), 5.20 (1H,q.J=6.3 Hz)($=\text{C}\!<\!\begin{matrix}\underline{\text{H}}\\ \text{Me}\end{matrix}$), 6.42(1H,s.)($C_{(11)}$H) and 7.58(1H,s.)(NH). The mother base (V) was regenerated from VI on heating in dilute hydrochloric acid. When treated with mesyl chloride in pyridine, V gave a mono mesylate (VII), mp.161-167°. In its NMR spectrum a 3H-singlet signal due to a methyl group of the methane sulfonate residue appeared at δ 3.13 and the signals due to $C_{(17)}$ methylene which was deshielded by this group were observed as AB type doublets centred at δ 4.73 and 4.90 with the coupling constant of 10 Hz. An oxilane derivative (VIII) was formed from VII on treatment with anhydrous K_2CO_3 in absolute DMF at room temperature. In its NMR spectrum the methylene protons on the oxilane ring appeared as a 2H-singlet at δ 2.96.



VI



VII



VIII

These structures were further supported by the mass spectral evidences. Thus, in the mass spectrum of V a strong fragment peak was observed at m/e 357(76%) together with the molecular ion peak at m/e 416(57%) and a weak but characteristic peak at m/e 248(28%) which has great diagnostic value for the basic skeleton of this series of oxindoles.[2)] On the other hand, in the spectra of VI and VIII, the most prominent fragment peak was that of m/e 356. These fragments are depicted as shown below, supporting the proposed structures. (Chart 3).

The gross skeleton and the absolute configuration of chitosenine (V) was finally confirmed by the conversion of VII to an iminoether (IX), whose UV absorption curve was superimposable to that of gardneramine (I).[2)] A strong IR absorption of C=N- group which is characteristic to an iminoether system of the gardneramine analogues was observed at 1591 cm^{-1}. In its NMR spectrum the signals due to $C_{(17)}$ methylene group were shown as AB type doublets centred at δ 4.13

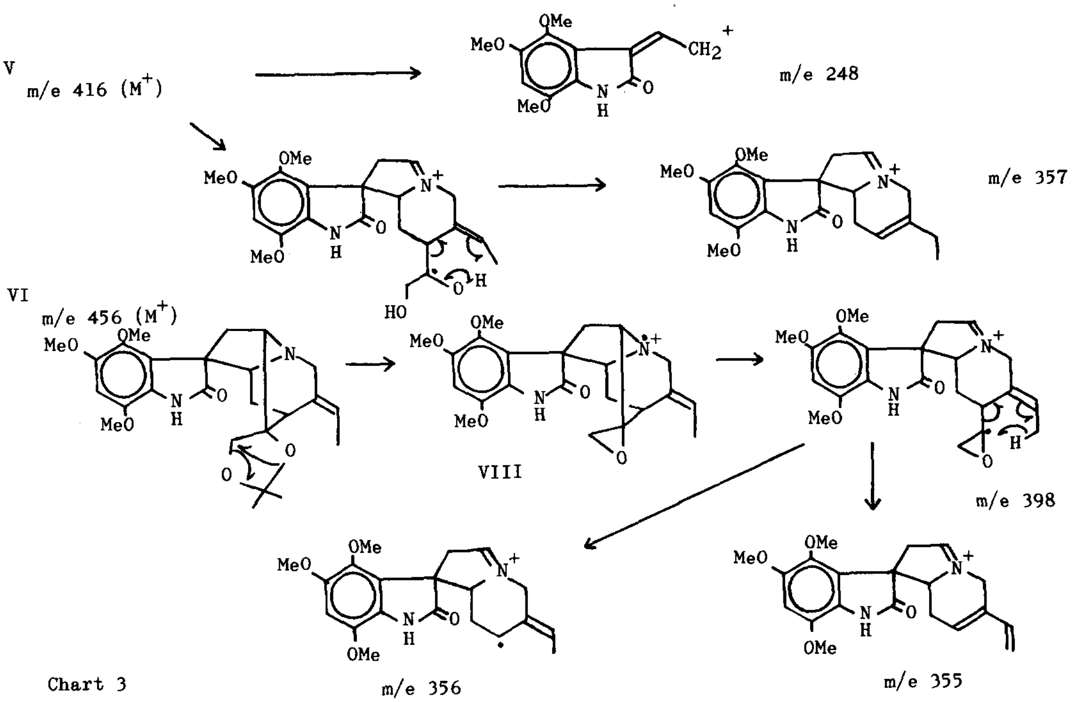
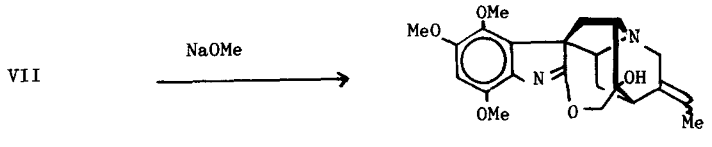


Chart 3

and 4.42 with a coupling constant of 13 Hz. The CD spectrum of IX was superimposable to that of gardneramine (I) whose absolute configuration is known.



IX

Chart 4

ACKNOWLEDGEMENT : The authors are grateful to Hōan-sha for financial support.

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