ABSOLUTE STRUCTURE OF (+)-13β-HYDROXYMAMANINE, A POSSIBLE METABOLITE OF (-)-BAPTIFOLINE

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The absolute structure of (+)-13β-hydroxymamanine (**1**), isolated from an alkaloidal component of *Maackia amurensis* (Leguminosae), has been established as (7*R*, 9*S*, 11*R*, 13*R*) by the X-ray analysis of its hydrobromide. The absolute stereochemistry of **1** is the same as that of the structure corresponding to an oxidative product derived from (-)-baptifoline (7*R*, 9*R*, 11*R*, 13*R*) coexisting in the same plant. It was strongly suggested that **1** might be an oxidative metabolite of (-)-baptifoline.

KEYWORDS lupin alkaloid; quinolizidine alkaloid; *Maackia amurensis*; absolute configuration; X-ray analysis; (+)-13β-hydroxymamanine

As a result of screening plants belonging to the Genus *Maackia* (Leguminosae) for lupin alkaloid,[1,2] (+)-13β-hydroxymamanine (**1**) was isolated from the aerial parts of *Maackia amurensis* as a colorless crystal $[\alpha]_D$ +31.2 (*c*=0.107, MeOH), together with (-)-cytisine, (-)-anagyrine, (-)-*N*-methylcytisine, (-)-lupanine, (-)-baptifoline, *N*-formylcytisine, ammodendrine, and camoensidine. Its structure has been proposed to be **1** or its enantiomer from spectroscopic data.[3]

(+)-13β-Hydroxymamanine (**1**) can be structurally correlated with the unusual lupin alkaloids (+)-mamanine (**2**),[4] (-)-pohakuline (**3**),[4] and (+)-kuraramine (**4**)[5] (Fig. 1).

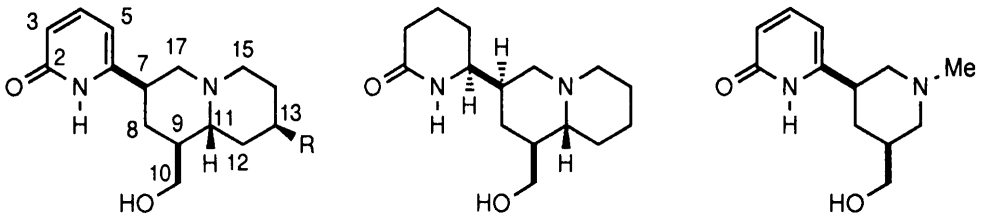

Fig. 1

The structures of **1**-**4** correspond to oxidative products derived from the N1-C10 bond cleavage of the usual tetra and tricyclic lupin alkaloids (-)-baptifoline (**5**), (-)-anagyrine (**6**), (-)-lupanine (**7**), and (-)-*N*-methylcytisine (**8**), respectively (Fig. 2).

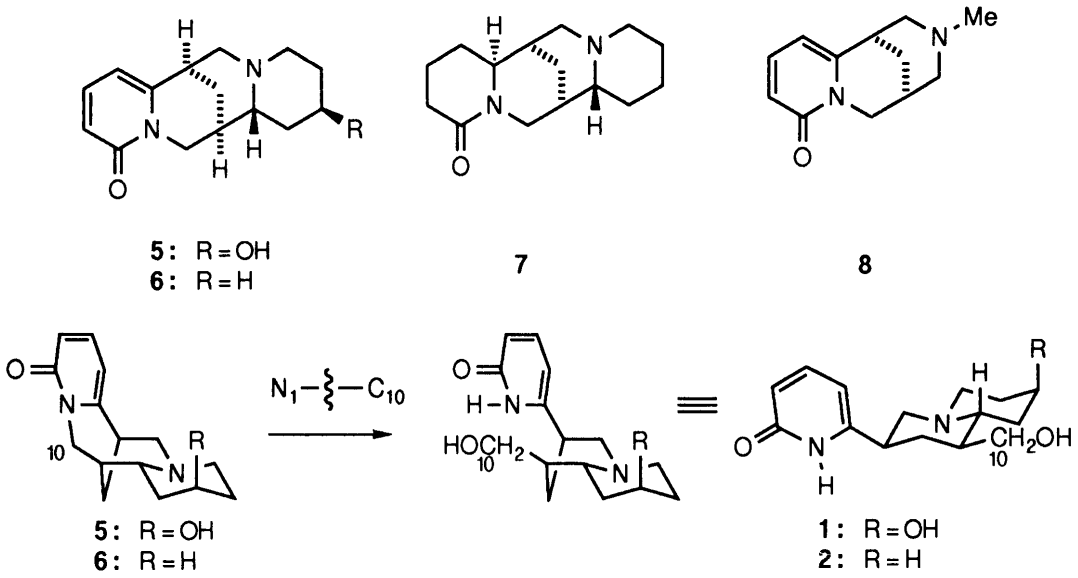

Fig. 2

The factoring of absolute configuration into the structural relationship between the unbridged alkaloids (**1**-**4**) and the bridged alkaloids (**5**-**8**) is of interest in connection with their biosynthetic correlations. However, absolute configurations of the unbridged alkaloids (**1**-**4**) have not been determined because they were minor components in the plants, though those of the bridged alkaloids (**5**-**8**) are known.

In order to confirm the structure of **1**, an X-ray structure analysis of **1** hydrobromide hydrate was undertaken. Crystals of **1** hydrobromide hydrate (mp 168°C) suitable for X-ray analysis were grown by the slow evaporation of ethanol containing 1%-H_2O. The molecular structure of **1** hydrobromine hydrate is illustrated in Fig. 3. Thus absolute configuration of (+)-13β-hydroxymamanine (**1**) (7*R*, 9*S*, 11*R*, 13*R*) was confirmed by heavy-atom anomalous dispersion of its hydrobromide hydrate.

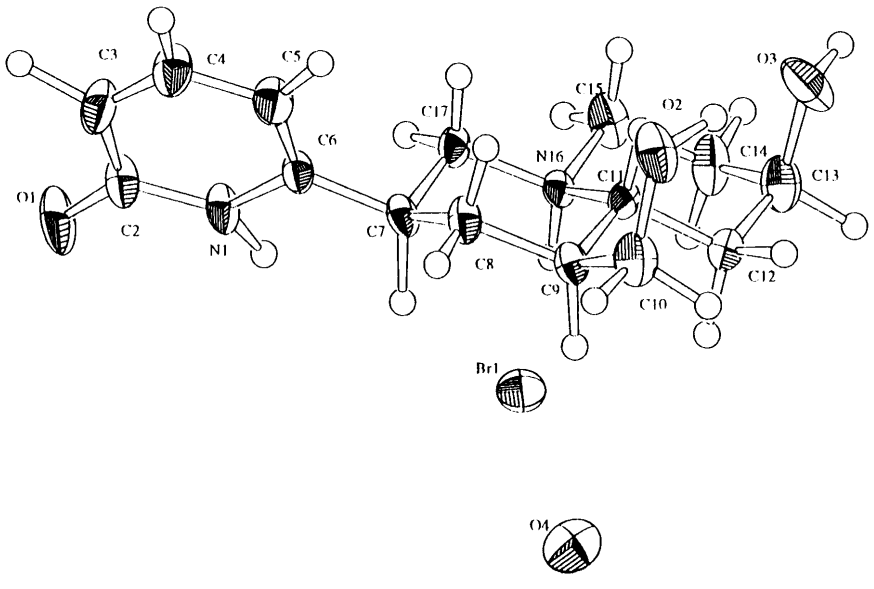

Fig. 3

The absolute configuration of **1** is the same as that of the oxidative product derived from (-)-baptifoline(**5**), coexisting in the same plant. The absolute configurations of the other unbridged alkaloids(**2-4**) are expected to be the same as that of (-)-anagyrine (**6**; 7*R*, 9*R*, 11*R*), (-)-lupanine (**7**; 6*S*, 7*R*, 9*R*, 11*R*), and (-)-*N*-methylcytisine (**8**; 7*R*, 9*S*), respectively.

From the stereochemical point of view among the lupin alkaloids, it can therefore be presumed that (+)-13β-hydroxymamanine is a metabolite of (-)-baptifoline. From the same standpoint, (+)-mamanine (**2**), (-)-pohakuline (**3**), and (+)-kuraramine (**4**) are suggested to be metabolites of (-)-anagyrine (**6**), (-)-lupanine (**7**), and (-)-*N*-methylcytisine (**8**), respectively.

X-Ray Structure Analysis

Crystal Data: $C_{15}H_{22}N_2O_3$ HBr H_2O (mp 168°C); M=377.28; monoclinic; $P2_1$(#4) ; a=10.901(3), b=7.440(3), c=11.232(3)Å, β=114.10(2)°; V=835.0(4)Å^3; Z= 2; D_c=1.501 g/cm^3; F(000)=392.00.

The diffraction intensities were collected from a (+)-13β-hydroxymamanine hydrobromide hydrate with a crystal with dimensions of 0.20 × 0.20 × 0.30mm on a Rigaku AFC7R diffractometer with graphite monochromated Cu-Kα radiation (λ=1.54178Å). A total of 2868 reflections were measured within a 2θ range of 120° as above the $3.00\sigma(I)$ level. These were used in the solution and refinement of the structure.

Determination of the structure: The structure was resolved by direct methods using SAPI91[6] and refined by the full-matrix least-squares method.

In the final refinement, anisotropic thermal parameters were used for non-hydrogen atoms. The contribution of hydrogen atoms of hydrate was ignored. The final R factor was 0.040.[7]

REFERENCES AND NOTES

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7) Lists of *Fo* and *Fc* values, tables of final atomic parameters, bond length and angles, anisotropic thermal parameters, and atomic fractional parameters are available from one of the authors(H.K.) upon request.

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