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The Structure of Hamayne, a New Alkaloid from *Crinum asiaticum* L. *var. japonicum* Baker

Masamitsu OCHI, Hitoshi OTSUKI, and Kosho NAGAO

Faculty of Arts and Sciences, Kochi University, Asakura, Kochi 780

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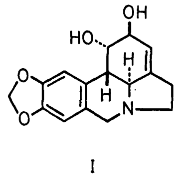
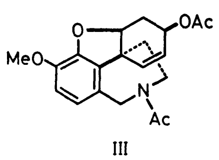
Synopsis. The structure of hamayne isolated from the fruit of *Crinum asiaticum* L. *var. japonicum* Baker was established to be *O*-demethylcrinamine (IV) on the basis of spectral and chemical evidence.

Kutani and Matsumoto have reported the isolation of lycorine (I) from the fruit (or seed) of *Crinum asiaticum* L. *var. japonicum* Baker.[1] Reinvestigation of the alkaloidal components in the fruit of this plant led to the isolation of three additional alkaloids, crinamine (II), *O,N*-diacetyl-*N*-demethylgalanthamine (III),[2] and a new alkaloid. In this paper, we will deal with the structural elucidation of the new alkaloid designated as hamayne.

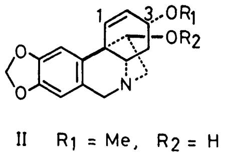
Hamayne (IV), $C_{16}H_{17}O_4N$, mp 79—80 °C, $[\alpha]^{12}_{D}$ +43° (*c* 0.1, EtOH), was obtained in a 0.002% yield from fresh fruit by partitioning and careful column chromatography. IV shows a hydroxylic absorption in the IR (KBr) spectrum at 3400 cm^{-1} and forms a diacetate (V), $C_{20}H_{21}O_6N$, mp 77.5—78 °C, the IR spectrum of which no longer exhibits a hydroxyl group. The NMR spectrum of V shows signals due to two acetyl groups at δ 2.01 and 2.07 (3H each, s), a benzyl methylene group linked to a nitrogen atom at δ 3.66 and 4.32 (1H each, AB q, J=18 Hz), a methylenedioxy group at δ 5.89 (2H, s), and two aromatic protons at δ 6.46 and 6.84 (1H each, s). In addition, the NMDR data of V indicate the presence of two groupings, $-CH(OAc)-CH_2-N<$[δ 3.40 (2H, d, J=6 Hz) and 4.95 (1H, t, J=6 Hz)] and $-CH_A=CH_B-CH_C(OAc)-$[δ_A 6.21 (1H, dd), δ_B 5.87 (1H, dd), and δ_C 5.44 (1H, m); J_{AB}=10 Hz, $J_{AC}=J_{BC}$=2 Hz]. These facts suggest that IV has a structure analogous to that of crinamine (II), in which the methoxyl group is replaced by a hydroxyl group. This was confirmed by the conversion of IV into apohaemanthamine (VI).[4] Thus, the treatment of IV with 6 M hydrochloric acid gave VI, which was also obtained by a similar treatment from II.[4] The configuration at C-3 was proven as follows. In the NMR spectrum of V, the signal due to C-1 proton appears as a doublet of doublets at δ 6.21 as a result of the coupling with the C-2 and C-3 protons, the allylic coupling constant ($J_{1,3}$=2 Hz) of which corresponds to that of C-3 equatorial (α-oriented) acetate.[5] This observation indicates that IV and II have the same configuration at C-3. Therefore, hamayne (IV) must be *O*-demethylcrinamine.



I



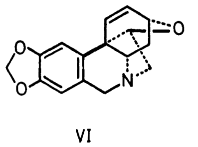
III



II R_1 = Me, R_2 = H

IV $R_1 = R_2$ = H

V $R_1 = R_2$ = Ac



VI

Experimental

All mps are uncorrected. The IR and UV spectra were recorded on a JASCO model IR-S and a Hitachi EPS-3T spectrophotometer, respectively. The NMR spectra were determined, using a JEOL PS-100 spectrometer, in $CDCl_3$ solutions with TMS as an internal standard unless otherwise stated. A Rex Optical Works apparatus, model NEP-2, was used for the measurement of the rotations.

Isolation. Fresh fruit of *Crinum asiaticum* L. *var. japonicum* Baker (19.2 kg), collected in the garden of the Usa Marine Biological Station, Kochi University, in August 1974, were chopped up and extracted with 20 l of methanol for 2 months. The methanol extract was concentrated up to about 2 l, leaving an aqueous solution. This solution, after filtration, was basified with solid Na_2CO_3 and extracted with 3 l of chloroform. The chloroform insoluble alkaloids containing lycorine were deposited between two layers. These alkaloids (16.5 g) were collected by filtration. The chloroform layer was washed with water, dried over Na_2SO_4 and evaporated to dryness. The residue (5.08 g) was repeatedly subject to chromatography over silicic acid. Elution with $CHCl_3$–AcOEt–MeOH (5: 5: 1) gave crinamine (II) (0.684 g) (mp and IR) and the fractions eluted with $CHCl_3$–AcOEt–MeOH (5: 5: 2) yielded hamayne (IV) (0.371 g): plates from acetone; mp 79—80 °C, $[\alpha]^{12}_{D}$ +43° (*c* 0.1, EtOH); UV (EtOH) nm (ε) 240 (4380) and 296 (7010). Found: C, 64.42; H, 6.47; N, 4.32%. Calcd for $C_{16}H_{17}O_4N \cdot 2/3H_2O$: C, 64.20; H, 6.17; N, 4.68%.

The more polar fractions eluted with $CHCl_3$–AcOEt–MeOH (1: 1: 1) were combined and evaporated to dryness. The residue (1.07 g) was acetylated with acetic anhydride (15 ml) and pyridine (30 ml) by heating under reflux for 3 h and worked up in the usual way. The resulting precipitates were chromatographed over silicic acid, with $CHCl_3$–MeOH (99: 1) as the eluent, to give *O,N*-diacetyl-*N*-demethylgalanthamine (III) (0.784 g) (mp, IR, NMR, and chemical properties).[6]

Acetylation of IV. A solution of IV (50 mg) in acetic anhydride (1 ml) and pyridine (2 ml) was refluxed for 3 h and then worked up in the usual way to afford V (34 mg): needles from methanol; mp 77.5—78 °C; IR (Nujol) 1730 cm^{-1}. Found: C, 64.70; H, 5.70; N, 3.61%. Calcd for $C_{20}H_{21}O_6N$: C, 64.88; H, 5.70; N, 3.77%.

Formation of VI. The procedure of Fales and Wildman[4] was followed: a solution of IV (76 mg) in 2.5 ml of 6 M hydrochloric acid was heated at 100 °C for 1 h. The solution was poured into 75 ml of water, basified with aqueous ammonia and extracted with chloroform. The chloroform layer was washed with water, dried with Na_2SO_4 and concentrated. The residual oil (69 mg) was subject to chromatography over silicic acid, and the elution with benzene–AcOEt (9: 1) gave VI (28 mg) (mp, IR, and NMR).

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References

1) N. Kutani and Y. Matsumoto, *Yakugaku Zasshi*, **64**, 239 (1944).

2) *N*-Demethylgalanthamine may be the plant constituent. See also Ref. 6.

3) This signal was observed in C_6D_6.

4) H. M. Fales and W. C. Wildman, *J. Am. Chem. Soc.*, **82**, 197 (1960).

5) R. D. Haugwitz, P. W. Jeffs, and E. Wenkert, *J. Chem. Soc.*, **1965**, 2001.

6) S. M. Laiho and H. M. Fales, *J. Am. Chem. Soc.*, **86**, 4434 (1964).