Journal of Natural Products
Vol. 52, No. 3, pp. 652-654, May-Jun 1989

(+)-*N*-FORMYLNORNANTENINE, A NEW APORPHINE ALKALOID FROM *CYCLEA ATJEHENSIS*

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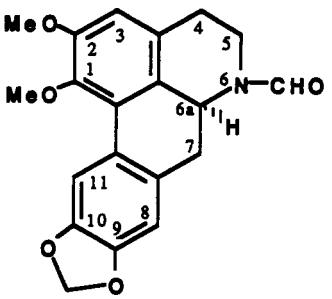
ABSTRACT.—*Cyclea atjehensis* (Menispermaceae), of Thai origin, has yielded the new aporphine (+)-*N*-formylnornantenine [**1**] which in $CDCl_3$ solution exists as a mixture of isomers **1a** and **1b**.

Cyclea atjehensis Forman (Menispermaceae) is a vine native to Thailand where its extracts are sometimes used in folk medicine for the treatment of stomach disorders.[3]

Presently, an investigation of the alkaloidal contents of this plant has yielded a number of monomeric and dimeric bases. It is the monomeric bases that will be dealt with in this paper.

Five alkaloidal monomers were isolated, which proved to be the pavinanes (−)-norargemonine and (−)-argemonine (1), and the aporphines (+)-laurotetanine, (+)-nornantenine, and (+)-*N*-formylnornantenine (2). This represents the first recorded occurrence of pavines within a member of the Menispermaceae. Of the five alkaloids, only (+)-*N*-formylnornantenine is new.



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(+)-*N*-Formylnornantenine [**1**], $C_{20}H_{19}NO_5$, was obtained as colorless crystals, λ max (MeOH) 240, 283, 309, 320 sh nm (log ε 4.30, 4.02, 4.12, 4.05), an absorption pattern characteristic of a 1,2,9,10-substituted aporphine (2). The ir spectrum, with peaks at 1660 and 1615 cm^{-1}, was suggestive of an amidic function.

The mass spectrum showed a strong molecular ion, *m/z* 353, and base peak *m/z* 295 due to loss of (CH_2-N-CHO + H) from the molecular ion. It followed that the amidic function was in the shape of an *N*-formyl group.

An important conclusion immediately derived from the nmr spectrum at 500 MHz was that two species were actually present in solution, due to isomerism about the amidic bond. Broad downfield singlets at δ 8.27 and 8.38 represented the *N*-formyl proton. The integrals of these peaks indicated that the isomers were present in a ratio of 2:1.

The spectra for the two isomers could be clearly differentiated, even though the two isomers could not be separated. While the differences in chemical shifts were minimal in the case of the methoxyl and methylenedioxy signals, they were clearly noticeable for the aromatic protons, with signals at δ 6.62, 6.77, and 7.98 for the major isomer **1a**, and at δ 6.65, 6.75, and 7.99 for the minor isomer **1b**.

The divergences between the two isomers were quite prominent in the aliphatic range. Some of the more salient

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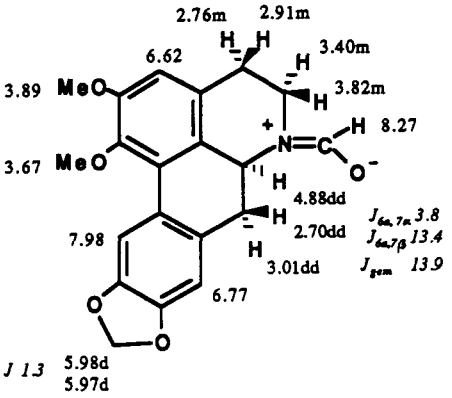
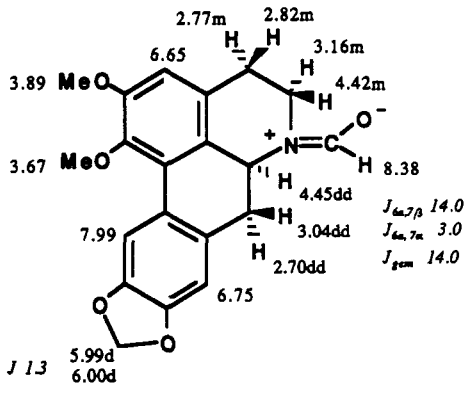
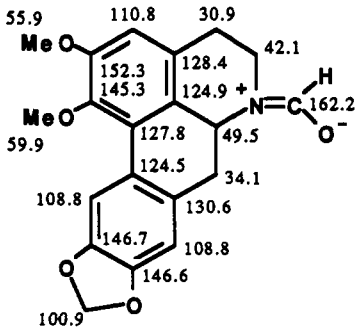
[3]B. Tantisewie, personal observation.



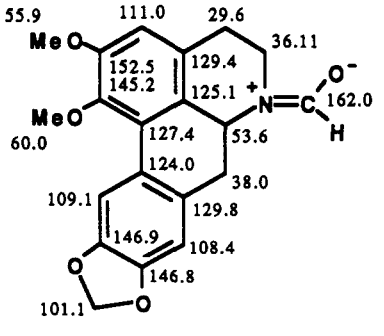
1a



1b



2a



2b

differences in chemical shifts occurred in the resonances for the hydrogens bonded to C-5, C-6a, and C-7. For the dominant isomer **1a**, H-5β appeared at δ3.82 and H-5α at 3.40. For the subordinate isomer, the corresponding protons were found at δ 4.42 and 3.16, respectively. Also, for the major isomer **1a**, the signals for H-6a and H-7α were downfield at δ 4.88 and 3.01, respectively. On the other hand, for **1b**, these two protons are relatively upfield at δ 4.45 and 2.70, respectively. For both isomers, the H-7α signals were characterized by small coupling constants with H-6a (ca. 3.5 Hz), but the H-7β signals were denoted by large constants (ca. 14 Hz).

The disparity in geometry between the two isomers also came to the fore when nmr nOe measurements were obtained at 500 MHz. In particular, the proximity of the formyl proton to H-5β (δ 3.82) in the major isomer and to H-6a (δ 4.45) in the minor isomer was clearly evident (see Experimental). With both isomers, a strong nOe could be observed between H-7α and H-8.

Turning now to the ^{13}C-nmr spectrum of *N*-formylnornantenine [**1**], again two sets of peaks were in evidence. Complete assignments as shown in expression **2a** for the major isomer and expression **2b** for the minor component were made possible through hetero-COSY and COLOC experiments (3).

It is very likely that geometrical isomerism such as presently observed obtains with all amidic aporphines (4). This isomerism was clearly evident in the ^{1}H nmr spectrum of *N*-formylnornantenine [**1**] because of the resolution possible at 500 MHz.

EXPERIMENTAL

PLANT MATERIAL.—*C. atjehensis* was collected in Somchitra tin mine, Kanchanaburi Prov-

ince, near the Burmese border, in January 1987. A sample was deposited in the herbarium of the Faculty of Pharmaceutical Sciences, Chulalongkorn University.

PLANT EXTRACTION AND ALKALOID ISOLATION.—The powdered plant material (2.5 kg) was extracted with petroleum ether and then with EtOH. Following solvent evaporation, the EtOH extracts were treated with 10% HOAc. The aqueous acidic solution was filtered, basified with NH_4OH, and extracted with $CHCl_3$. Evaporation of the organic layer afforded the crude alkaloids (55.4 g). Separation of the alkaloids was achieved by cc on Si gel, using a $CHCl_3$/MeOH gradient. Final purification was carried out by cc using Si gel for tlc and also by tlc on Si gel glass plates. The following alkaloids were thus obtained: (−)-norargemonine (313 mg), (−)-argemonine (356 mg), (+)-laurotetanine (5 mg), (+)-nornantenine (40 mg), and (+)-*N*-formylnornantenine (93 mg).

(+)-*N*-FORMYLNORNANTENINE [**1**].—$C_{20}H_{19}NO_5$; mp 232° (MeOH); eims *m/z* $[M]^+$ 353 (61), 308 (9), 295 (100), 281 (16), 251 (12); hreims $[M]^+$ calcd for $C_{20}H_{19}NO_5$ *m/z* 353.1263, found 353.1260; calcd for $C_{18}H_{15}O_4$ *m/z* 295.0970, found 295.0962; ir ($CHCl_3$) 3020, 2980, 1660, 1615, 1585 cm^{-1}; uv λ max (MeOH) 240, 283, 309, 320 sh nm (log ε 4.30, 4.02, 4.12, 4.05); $[\alpha]_D$ +315° (*c* = 0.13, $CHCl_3$); $[\alpha]_D$ +292° (*c* = 0.13, MeOH).

Nmr spectra were obtained at 500 MHz in $CDCl_3$ solution. Important nOe's are: for isomer **1a**, H-3 to 2-OMe (10%), 2-OMe to H-3 (18%), H-11 to 1-OMe (8%), 1-OMe to H-11 (20%), CHO to H-5β (2%), H-5β to CHO (2%), H-6a to H-7α (2%), H-7α to H-6a (5%), H-7α to H-8 (12%), H-8 to H-7α (2%), H-7β to H-8 (4%); for isomer **1b**, H-3 to 2-OMe (9%), 2-OMe to H-3 (18%), H-11 to 1-OMe (5%), 1-OMe to H-11 (20%), CHO to H-6a (3%), H-6a to CHO (1%), H-7α to H-6a (2%), H-7α to H-8 (5%).

ACKNOWLEDGMENT

This research was supported by National Science Foundation grant INT-8515317.

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Received 7 November 1988