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ANDRACHCINE, AN ALKALOID FROM *ANDRACHNE ASPERA*

VIQAR UDDIN AHMAD and M. AJMAL NASIR

H. E. J. Research Institute of Chemistry, University of Karachi, Karachi-32, Pakistan

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Key Word Index— *Andrachne aspera*, Euphorbiaceae; dehydropiperidine alkaloid.

Abstract—A new dehydropiperidine alkaloid, andrachcine, was isolated from the medicinal plant *Andrachne aspera*. Its structure was determined by spectroscopic methods.

INTRODUCTION

The plant *Andrachne aspera* Spreng is a small perennial under-shrub commonly found in Karachi [1]. In the local system of medicine, this plant is used as a treatment for eye sores and to improve eyesight [2, 3]. It is also reported as a substitute for *Polygala senega* [4]. The crude alkaloidal mixture has been reported to show activity in various biological tests and to be antibacterial [5]. In this paper, we report the isolation of a new alkaloid, andrachcine (**1**) from this plant.

RESULTS AND DISCUSSION

Andrachcine was obtained by repeated chromatography of alkaloidal mixture isolated from the plant as described in the Experimental. The high-resolution mass spectrum showed a molecular ion peak at *m/z* 255.22048, corresponding to the molecular formula $C_{15}H_{29}NO_2$ (calculated 255.21981). The IR spectrum ($CHCl_3$) revealed a broad peak at 3100–3200 cm^{-1} (–OH). The UV spectrum showed only end absorption at 220 nm. In the ^1H NMR spectrum a sharp triplet centred at δ0.98 (3H, J = 7.4 Hz) and a distorted triplet at δ0.91 (3H, J = 6.7 Hz) were present which were assigned to two methyl groups adjacent to methylenes. A singlet at δ2.52 (3H) indicated the presence of an N–Me group. A broad signal at δ3.77 (2H) was assigned to two protons geminal to hydroxyl groups and another signal at δ3.48 was due to H-2 and H-6 of the piperidine ring. The presence of a double bond was indicated by two signals at δ5.63 (1H, H-3) and 5.88 (1H H-4). The coupling constants of these signals became clear through the decoupling experiments. On irradiation at δ3.48 (H-2 and H-6), the H-3 signal changed into a clear doublet with $J_{3,4}$ = 10.3 Hz, whereas the H-4 signal was a *ddd* ($J_{3,4}$ = 10.3, $J_{4,5A}$ = 4.7, $J_{4,5B}$ = 2.2 Hz). Irradiation at δ5.88 (H-4) converted the broad H-3 signal into a doublet with a very small coupling constant (J = 1 Hz). The mass spectrum exhibited a $[M]^+$ at *m/z* 255 and other important fragments were observed at *m/z* 240, 226, 212, 196, 182, 168, 130, 110, 96 and 56. The fragments at *m/z* 240, 226, 196, 182 indicate loss of CH_3, C_2H_5, C_3H_7O and $C_4H_{10}O$ (Me–CH_2–CHOH–CH_2), respectively. On the other hand, the fragments at *m/z* 212 and 168 show loss of C_3H_7 and $C_5H_{11}O$ (Me–CH_2–CH_2–CHOH–CH_2) from the molecular ion (Fig. 1). This signifies that one alkyl side chain is C_4 and other is C_5, and both have a hydroxyl group the C_2 position of the alkyl side chain. The fragment of *m/z* 96 on peak matching was found to be 96.082098 (calculated for $C_6H_{10}N$: 96.081320) $C_6H_{10}N$ which could be a protonated species having the structure shown in Fig. 2. The ion at *m/z* 130, formed as a result of retro-Diels–Alder fragmentation, shows that the C_4H_9O chain is attached to C-2. The attachment of the $C_5H_{11}O$ chain to C-2 would have led to the formation of an ion at *m/z* 115, which was, however, not observed (Fig. 3).

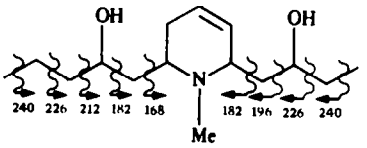


Fig. 1.

The published (60 MHz) NMR spectrum of sedenine (**2**) [6] shows a very broad signal due to H-6 with $W_{1/2}$ = 15 Hz. This is due to the presence of *trans*-diaxial coupling between H-6 and the axial H-5. We observed the same type of broad signal, with $W_{1/2}$ = 12 Hz. Hence in the case of andrachcine both alkyl side chains are *trans* to each other at the C_2 and C_6 positions on the dihydropiperidine ring, which is also consistent with its biogenesis. The *trans* configuration of sedenine has already been confirmed by X-ray crystallography [7]. The assigned ^{13}C (75 MHz) values are: N–Me (34.68), C_2 (63.12), C_3 (126.03), C_4 (124.67), C_5 (24.92) C_6 (51.02), $C_{1'}$ (40.74), $C_{2'}$ (73.30), $C_{3'}$ (30.83), $C_{4'}$ (9.6), $C_{1''}$ (38.2), $C_{2''}$ (69.9), $C_{3''}$ (38.9), $C_{4''}$ (18.7), $C_{5''}$ (14.13).

Application of the Horeau method led to the isolation of (+)-phenylbutyric acid. If we assume that the (±)-phenylbutyric anhydride reacts with the hydroxyl groups at 2′ and 2″ with equal optical yields because of the similar

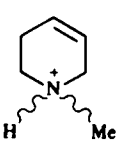


Fig. 2.

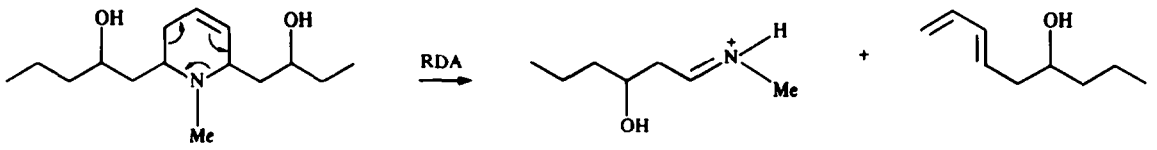
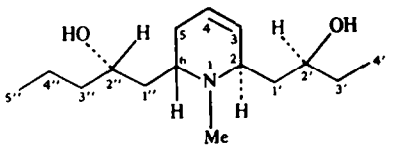
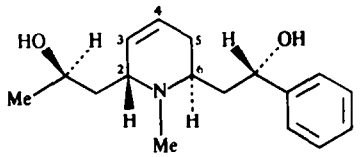


Fig. 3.



Andrachcine (**1**)



Sedenine (**2**)

environment, then it may be concluded that the absolute configuration at both of these centres is *S*.

EXPERIMENTAL

The UV spectrum was measured in MeOH with a Shimadzu UC-240 graphicord spectrometer. The IR spectrum was scanned in $CHCl_3$ on a Jasco IRA-I spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker AM-300 spectrometer, using $CHCl_3$ as internal standard. Mass spectra were recorded on a Fingan MAT 312 double focusing mass spectrometer connected to a PDP 11/34 computer.

Plant material. The plant *Andrachne aspera* was collected from hills near the University campus and was identified by the Department of Botany. A voucher specimen has been deposited at the Herbarium, Department of Botany, University of Karachi.

Isolation. The plant material was crushed in EtOH and the filtrate obtained was evaporated under red. pres. The residue thus obtained was partitioned between EtOAc and H_2O. The aq. layer was neutralized with NH_3 (pH 9.0) and extracted repeatedly. On evaporation under red. pres. it yielded a crude alkaloidal mixture. This mixture was chromatographed on a column of silica gel using a flash chromatograph. This step gave us 5 fractions. Fraction II was rechromatographed on a column of silica gel using $CHCl_3$–MeOH 3:1 as the mobile phase. The fraction showed one major spot together with two minor compounds on TLC. This fraction was further purified by low pres. liquid chromatography using a Lobar column Lichroprep Si 60 (40–63 μm) (Merck) with $CHCl_3$–MeOH (4:1) as the mobile phase. This step afforded andrachcine in pure form as a gum $[\alpha]_D^{25}$ −87° (MeOH; c 1.2). The purity of the alkaloid was checked by TLC (silica gel) using $CHCl_3$–MeOH (8:2 and 9:1) as the mobile phase.

Application of Horeau's method. Andrachcine 2 mg was dissolved in *ca* 0.2 ml dry pyridine and 2 M equiv. of ± 2-phenylbutanoic anhydride were added. After standing for 1 hr at room temp., H_2O (3 ml) was added to the reaction mixture and it was allowed to stand for 3 hr at room temp. The mixture was neutralized with 0.1 M NaOH and extracted × 3 with $CHCl_3$ to remove the ester formed; the aq. phase was then acidified with 1 M HCl and extracted with C_6H_6. The extract was dried (Na_2SO_4), filtered and the vol. adjusted to 10 ml. Reading at the D-line afforded + 1.399°.

Mass spectrum. $[M]^+$ *m/z* 225; other important fragments were at *m/z* 240 $[M-Me]^+$, 226 $[M-C_2H_5]^+$, 212 $[M-C_3H_7]^+$, 196 $[M-C_3H_7O]^+$, 182 $[M-C_4H_9O]^+$, 168 $[M-C_5H_{11}O]^+$, 130 $[M-C_7H_{16}NO$, RDA fragment$]^+$, 110 $[M-C_8H_{18}O_2]^+$, 96 $[M-C_9H_{20}O_2]^+$, 58 $[M-C_{12}H_{22}NO]^+$. For ^1H NMR and ^{13}C NMR: see Discussion.

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