ALKALOIDS FROM *Strempeliopsis strempelioides* K. SCHUM.

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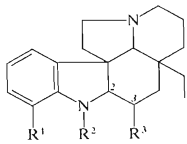
From the leaves of *Strempeliopsis strempelioides* K. SCHUM. (*Apocynaceae*), an indigenous species from Cuba, the following alkaloids were isolated: (+)-Demethylaspidospermine, (—)-aspidosine. (+)-tubotaiwine, (—)-vallesine, (+)-condylocarpine and (+)-eburnamonine. From stem bark of the plant the following alkaloids were isolated: (—)-Aspidospermine, (+)-deacetylaspidospermine, (+)-vincadifformine, (—)-apparicine, (+)-tubotaiwine, (+)-condylocarpine and (+)-demethylaspidospermine. All the structures were proposed on the basis of spectral evidence and chemical reactions.

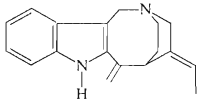
The Cuban flora is rich in indigenous species from a number of plant families[1]. In the present investigation we focused our attention on the indole alkaloid content of the leaves and the stem bark of *Strempeliopsis strempelioides* K. SCHUM., an indigenous Cuban plant of the *Apocynaceae* family. This family is the richest one with respect to the content and the diversity of the structures of indole alkaloids. The *Strempeliopsis* genus belongs to the *Alstonieae* tribe of the subfamily *Plumerioideae*[2]. In a recent publication[3] a phytochemical study of the mayor bases from the leaves of this plant has been described.

From the stem bark, as well as from the leaves[3], (+)-aspidospermine (*I*) was isolated as the principal alkaloid. Its skeleton is common in this family. This alkaloid was isolated from the leaves of *Aspidosperma quebracho blanco* by Fraude[4]. The same skeleton as aspidospermine was also found in: (+)-deacetylaspidospermine (*II*), and (+)-vincadifformine (*III*) from the stem bark; in (−)-aspidosine (*IV*) and (−)-vallesine (*V*) from the leaves and in (+)-demethylaspidospermine (*VI*) from both parts of the plant. The alkaloids *II*, *IV*, and *VI* were isolated for the first time from plants of the *Aspidosperma* genus[5–7], *III* was isolated for the first time from *Rhazya stricta*[8] and *V* from *Vallesia dichotoma* RUIZ et PAV[9]. (−)-Apparicine (*VII*), isolated from the stem bark of *S. strempelioides* was also isolated from four different species of *Aspidosperma*[10], while (+)-eburnamonine (*VIII*), isolated from the leaves, was for the first time isolated from *Hunteria eburnea* PICHON[11].

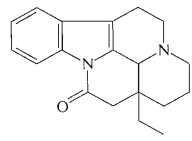
The two last alkaloids, isolated both from the leaves and the stem bark of the plant, (+)-tubotaiwine (*IX*) and (+)-condylocarpine (*X*), have a very characteristic skeleton[12], *i.e.* that of aspidopermatidine group and tetrahydro derivative of condylocarpine.



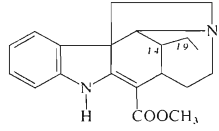
	R^1	R^2	R^3
I	OCH_3	$COCH_3$	H
II	OCH_3	H	H
III	H	H	$COOCH_3$, $\Delta^{2,3}$
IV	OH	H	H
V	OCH_3	COH	H
VI	OH	$COCH_3$	H



VII



VIII



IX

X, $\Delta^{14,19}$

EXPERIMENTAL

The melting points were determined on a Leitz Wetzlar instrument and the samples were also compared by mixed melting points. Optical rotation was measured on a Polartronic I apparatus. The UV spectra recorded on a Unicam SP-1800 spectrophotometer in methanol and the IR spectra on a Carl Zeiss UR-20 instrument in KBr discs. The ^{1}H-NMR spectra were taken on a Varian 60 MHz machine in deuteriochloroform, using tetramethylsilan as internal reference. The mass spectra were measured on a Hitachi RMU-6D spectrometer and the high-resolution measurements were done with an AEI-MS 902 instrument. Alumina (Merck) for column chromatography was of activity II according to Brockmann. Silica gel G 60 (Merck) of 70—230 mesh ASTM was used for column chromatography while Silicagel G (Merck) Type 60 was used for thin-layer chromatography.

Extraction and Isolation of Alkaloids

The plant was collected in March 1977 in a selvatic region of Imias, a zone of the Guantanamo's province in Cuba. The plant material was dried in a drying cabinet at temperatures not exceeding 45°C. The dried material was treated with ammonia–methanol mixture (1 : 2) and the free bases were extracted using the method described previously[3]. From 1000 g of either leaves or stem bark of the plant 27·2 g and 19·8 g, respectively, of crude extract of alkaloids were obtained. The crude extracts were chromatographed on columns of Alumina (in both cases sample to adsorbent ratio 1 : 35). Elution was carried out with light petroleum, benzene, chloroform and methanol. From column chromatography of the crude extract of the leaves. (+)-demethylaspidospermine and (+)-vallesine were eluted with light petroleum–benzene 1 : 1. In the fractions eluted with chloroform–benzene 1 : 1, four alkaloids were present which were purified by column chromatography on silica gel and by preparative thin-layer chromatography. (+)-Tubotaiwine and (+)-condylocarpine were isolated using a column of silica gel and ethyl acetate as eluent. (—)-Aspidosine and (+)-eburnamonine were purified by preparative thin-layer chromatography with diethyl ether–methanol 99 : 1 as solvent. From column chromatography of the crude extract of the stem bark, (+)-vincadifformine and (+)-demethylaspidospermine were eluted using light petroleum–benzene 1 : 1. They were purified by preparative thin-layer chromatography. With benzene three alkaloids were eluted; one of them, (—)-aspidospermine, was crystallized from methanol and the other two were separated using a column of silica gel and chloroform–methanol as eluent. They were identified as (+)-desacetylaspidospermine and (—)-apparicine. (+)-Tubotaiwine and (+)-condylocarpine were isolated from the fraction eluted with benzene–chloroform 1 : 1 from the main column. They were further purified by preparative thin-layer chromatography.

Characterization of the Alkaloids

Aspidospermine (I): M.p. 206—208°C; $[\alpha]_D^{20}$ —95·5° (methanol); UV spectrum: 223 (4·56), 255 nm (4·09) and 282—290 sh. IR spectrum: 2950, 1665, 1460, 1395, 800 and 625 cm^{-1}. ^{1}H-NMR spectrum: 0·7 t, 1·75 q, 2·20 q, 3·00 s, 3·75 s and 6·80 m ppm. Mass spectrum (*m/z*): 354 (M^+, $C_{22}H_{30}N_2O_2$), 339, 326, 311, 174, 160, 152 and 124 (100%, $C_8H_{14}N$).

Deacetylaspidospermine (II): M.p. 107—109°C; $[\alpha]_D^{20}$ +8° (methanol). UV spectrum: 246 (3·88) and 289 nm (3·41). IR spectrum: 3350, 1660, 1460, 1395 and 800 cm^{-1}. ^{1}H-NMR spectrum, 0·60 t, 1·75 m, 2·20 q. 3·75 s and 6·65 m ppm. Mass spectrum (*m/z*): 312 (M^+, $C_{20}H_{28}N_2O$): 284, 174, 160, 152 and 124 (100%, $C_8H_{14}N$).

Vincadifformine (III): M.p. 93—95°C; $[\alpha]_D^{20}$ +500° (methanol). UV spectrum: 288 (3·99), 300 (4·00) and 326 nm (4·19). IR spectrum: 3380, 1660, 1610, 1550, 1480, 1470 and 750 cm^{-1}. Mass spectrum (*m/z*): 338 (M^+, $C_{21}H_{26}N_2O_2$), 214, 167, 154 and 124 (100%, $C_8H_{14}N$).

Aspidosine (IV): M.p. 250—253°C; $[\alpha]_D^{20}$ —12° (ethanol). UV spectrum: 246 (3·91) and 289 nm (3·42). IR spectrum: 3350, 3100, 1600, 1450, 1180, 1140 and 800 cm^{-1}. ^{1}H-NMR spectrum: 0·8 t, 4·50 s, 6·75 m and 7·00 s ppm. Mass spectrum (*m/z*): 298 (M^+, $C_{19}H_{26}N_2O$), 270, 172, 160, 152, 146 and 124 (100%, $C_8H_{14}N$).

Vallesine (V): M.p. 154—156°C; $[\alpha]_D^{20}$ —90° ($CHCl_3$). UV spectrum: 214 (4·47) and 255 nm (3·94). IR spectrum: 2810, 1680, and 1600 cm^{-1}. ^{1}H-NMR spectrum: 0·70 t, 3·90 s, 4·35 m, 6·80 m and 9·15 s ppm. Mass spectrum (*m/z*): 340 (M^+, $C_{21}H_{28}N_2O_2$), 339, 312, 160, 152 and 124 (100%, $C_8H_{14}N$).

Demetylaspidospermine (VI): M.p. 112—114°C; $[\alpha]_D^{20}$ +114° ($CHCl_3$); UV spectrum: 225 (4·40), 260 (3·53) and 291 nm (3·21). IR spectrum: 3470, 1650, 1595, 1570 and 1280 cm^{-1}.

^{1}H-NMR spectrum: 0·75 t, 2·30 s, 2·35 s, 4·05 m and 6·80 m ppm. Mass spectrum (*m/z*): 340 (M^+, $C_{21}H_{28}N_2O_2$), 339, 312, 297, 160, 146 and 124 (100%, $C_8H_{14}N$).

Appariciné (VII): M.p. 188—190°C; $[\alpha]_D^{20}$ —166° ($CHCl_3$); UV spectrum: 304 nm (3·70); IR spectrum: 3150, 2930, 1600, 1450, 1320 and 750 cm^{-1}; ^{1}H-NMR spectrum: 1·45 dd, 4·3 d, 5·25 q, 7·5 m and 7·95 s ppm; Mass spectrum (*m/z*): 264 (M^+, $C_{18}H_{20}N_2$), 249, 235, 222, 208, 194 and 180.

Eburnamonine (VIII): M.p. 178—181°C; $[\alpha]_D^{20}$ +100° ($CHCl_3$); UV spectrum: 242 (4·13), 266 (4·07), 293 (3·68) and 302 nm (3·68); IR spectrum: 1705, 1690, 1630 and 750 cm^{-1}; Mass spectrum (*m/z*): 294 (M^+, $C_{19}H_{22}N_2O$, 100%), 293, 265, 237, 224, 180, 168, 167 and 147 (M^{++}).

Tubotaiwine (IX): Not crystallizable as base; $[\alpha]_D^{20}$ +550° ($CHCl_3$); UV spectrum: 218 (4·10), 292 (3·98) and 325 nm (4·00); IR spectrum; 3380, 1680, 1610 and 1490 cm^{-1}; Mass spectrum (*m/z*): 324 (M^+, $C_{20}H_{24}N_2O_2$), 295, 293, 267, 229, 182, 181, 180, 167, 95 and 71 (100%).

Condylocarpine (X): M.p. 158—161°C; $[\alpha]_D^{20}$ +900° ($CHCl_3$); UV spectrum: 230 (4·03), 288 (4·00) and 328 nm (4·16); IR spectrum: 3380, 3010, 1670, 1605 and 1480 cm^{-1}; ^{1}H-NMR spectrum: 1·58 d, 3·85 s, 4·15 s, 5·30 q and 6·70 m ppm; Mass spectrum (*m/z*): 322 (M^+, $C_{20}H_{22}N_2O_2$), 264, 158, 121 (100%), 107, 106, 92 and 79.

Preparation of Aspidosine[13] (*IV*)

Aspidospermine (1·0 g) and 48% HBr (20 ml) were refluxed for 2 h. The mixture was evaporated under reduced pressure, treated with hot water and percolated. The aqueous solution was alkalized with ammonia and the free bases extracted with chloroform. The chloroform extract was washed with water, dried over anhydrous sodium sulphate and evaporated under reduced pressure. The product obtained was chromatographed on a silica gel column using chloroform and methanol for elution. Aspidosine (560 mg) crystallized from ethanol with a m.p. of 250—253°C.

Preparation of Vallesine[14] (*V*)

Deacetylaspidospermine (500 mg) was refluxed with 10 ml of formic acid and 25 ml of benzene for 4 h. The solution was cooled and extracted with 5% H_2SO_4. The acidic solution was treated with ammonia and extracted with diethyl ether. The extract was washed with water, dried over anhydrous calcium chloride and evaporated under reduced pressure. Yield 480 mg of vallessine, m.p. 153—155°C.

Preparation of Demethylaspidospermine[13] (*VI*)

Aspidospermine (1·0 g) and aluminum chloride (5 g) were dissolved in xylene (40 ml) and refluxed for 45 min at 120°C. The excess of aluminum chloride was destroyed with cold water and ice. The solution was mixed with 50 ml of 1M-HCl and the organic phase was removed and extracted three times with 10 ml of 1M-HCl. The acid solution was adjusted with ammonia to pH 10—11 and extracted with chloroform. The extract was dried over sodium sulphate and filtered. The filtrate was evaporated under reduced pressure to yield 780 mg of needles of m.p. 110—113°C.

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