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ALKALOIDS FROM DENDROBATID POISON FROGS: TRANS-DECAHYDROQUINOLINES AND INDOLIZIDINES

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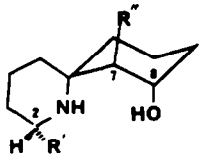
Abstract - Skin extracts from one population of the Colombian poison-frog Dendrobates histrionicus contain a variety of histrionicotoxins (2,7-disubstituted 1-azaspiro[5.5]-undecan-8-ols) and other alkaloids. Two of the major alkaloids are trans-decahydroquinolines whose gross structures based on mass and nuclear magnetic resonance spectral analysis are 2,5-diallyl-trans-decahydroquinoline **219A** and 2-allyl-5-pent-2-en-4-ynyl-trans-decahydroquinoline **243A**. A minor isomer, **243A'**, is also present. X-ray crystallographic analysis of **219A**·HCl reveals the absolute configuration as [2S,4aS,5S,8aS]2,5-diallyl-trans-decahydroquinoline. A dihydroxydihydro-**219A** was also isolated and shown by nuclear magnetic resonance spectral analysis to be 2-allyl-5-(2,3-dihydroxypropyl)-trans-decahydroquinoline (**253D**). Four of the alkaloids from Dendrobates histrionicus are indolizidines namely (5E,9E)-3-n-butyl-5-n-propylndolizidine **223AB**, its two ω-hydroxy congeners **239AB** (hydroxypropyl) and **239CD** (hydroxybutyl), and (5E,9E)-3-n-butyl-5-methylindolizidine **195B**. Structures are based on nuclear magnetic resonance spectral analysis.

Poison-frogs of the dendrobatid species Dendrobates histrionicus have been the source of a variety of unique alkaloids including histrionicotoxins (1-4), gephyrotoxins (3) and, indolizidines, pyrrolidines, piperidines and (allo)pumiliotoxins (5). The structures of some dendro alkaloids from D. histrionicus are shown in Figure 1. In view of the large number of alkaloids found in skin extracts of dendrobatid frogs, a code system of nomenclature was introduced in 1978 (6). Alkaloids were designated by molecular weight in bold face type with an added letter (or letters) to identify alkaloids of the same nominal molecular weight. Skin extracts from twelve different populations of Dendrobates histrionicus have been analyzed by combined gas chromatography-mass spectrometry and found to contain a total of about sixty different alkaloids, including over a dozen histrionicotoxins (7). The simple decahydroquinoline **195A** (pumiliotoxin C, 2-n-propyl-5-methyl-cis-decahydroquinoline) isolated originally as a major alkaloid from Dendrobates pumilio (8) was absent from all populations of Dendrobates histrionicus. Certain alkaloids from Dendrobates histrionicus were proposed to be decahydroquinolines in an earlier study (3). But definitive proof of either the occurrence of decahydroquinolines in Dendrobates histrionicus or the occurrence of decahydroquinolines other than **195A** in dendrobatid frogs at all has been lacking. Indeed, introduction of chemical ionization with deuteroammonia to detect exchangeable NH or OH during combined gas chromatographic-mass spectral analysis of alkaloid fractions (5) revealed that many compounds considered to be possibly decahydroquinolines were instead bicyclic tertiary amines; in many cases these appear to be indolizidines (7). Two alkaloids, namely **219A** and **243A** have now been isolated as major constituents from one population of Dendrobates histrionicus (Santa Cecilia, Río San Juan, Depto. Risaralda, Colombia) and shown to be 2,5-disubstituted-trans-decahydroquinolines by nuclear magnetic resonance spectral analysis. The configuration of **219A** was 2S,4aS,5S,8aS as shown by x-ray analysis of a crystal of the hydrochloride. An isomer of **243A**, namely **243A'** and a dihydroxy analog of dihydro **219A**

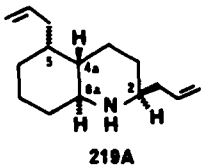
were also isolated. ,5-Disubstituted indolizidines were major alkaloids in this population of frogs. The structures of the alkaloids isolated from the Santa Cecilia population of Dendrobates histrionicus are shown in Figure 1, while the amounts isolated are documented in Table 1. A gas chromatographic profile for the alkaloids are shown in Figure 2.

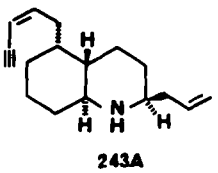
Histrionicotoxins.

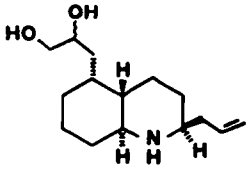
This population of Dendrobates histrionicus contains nine histrionicotoxins; alkaloids whose mass spectra are characterized by a dominant ion at m/z 96 ($C_6H_{10}N^{\oplus}$) (6). The major histrionicotoxins are histrionicotoxin (283A), isodihydrohistrionicotoxin (285A) and allodihydrohistrionicotoxin (285C) (Table 1). The chemical and spectral properties of the various histrionicotoxins have been reported (1-4).



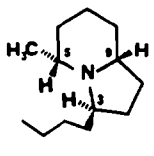
	R'	R"
283A	cis $-CH_2CH=CHC\equiv CH$	cis $-CH=CHC\equiv CH$
285A	$-CH_2CH_2CH=C=CH_2$	cis $-CH=CHC\equiv CH$
285C	$-CH_2CH_2CH_2C\equiv CH$	cis $-CH=CHC\equiv CH$

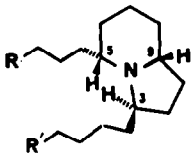

219A


243A

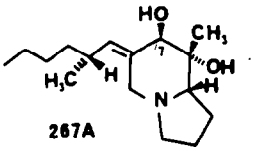


253D


195B



223AB	R,R' = H	
239AB	R = OH	R' = H
239CD	R = H	R' = OH



267A

Figure 1. Alkaloids from a population of Dendrobates histrionicus: Histrionicotoxins (283A, 285A, 285C), trans-decahydroquinolines (219A, 243A, 253D), indolizidines (195B, 223AB, 239AB, 239CD) and an allopumiliotoxin (267A). An isomer of 243A, designated 243A' also is present in extracts from this population.

Table 1. Isolation of alkaloids from skin extracts of a population of Dendrobates histrionicus.

Alkaloid		Amount (mg)
Histrionicotoxins	283A	42
	285A + 285C	74
Allopumiliotoxins	267A	<1
Decahydroquinolines	219A	107
	243A	20
	243A'	10
	253D	10
Indolizidines	195B	12
	223AB	39
	239AB	58
	239CD	10

Extracts were prepared from 640 skins of frogs collected at Santa Cecilia, Depto. Risaralda, Colombia and fractionated as described in EXPERIMENTAL.

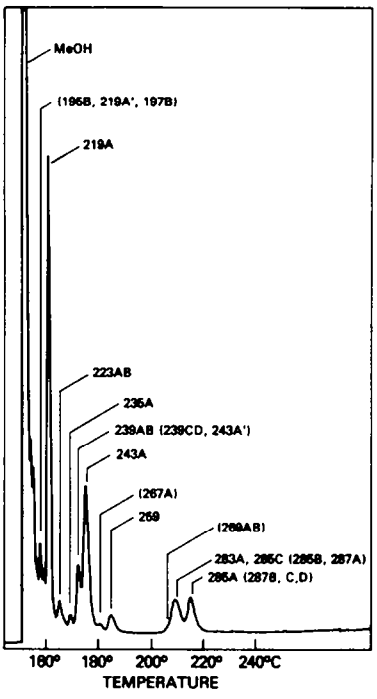


Figure 2. Gas chromatographic profile for alkaloids from a population of Dendrobates histrionicus (Sta Cecilia, Río San Juan, Depto. Risaralda, Colombia, February, 1983). Extract from 3 skins, which were obtained at the same time as the 640 skin sample (Table 1), was partitioned to obtain alkaloids as described (5). A sample of 2 µl of methanolic alkaloids equivalent in amount to 2 mg wet skin was injected at 150°C onto a 1.5% OV-1 column. After the maximum for the solvent peak was passed, the column was programmed at 10°C per min from the initial 150°C to 280°C at a flow rate of helium of 30 ml/min. Emergent temperatures differ somewhat with different batches of column packing. A flame ionization detector was used. Alkaloids identified and characterized by combined gas chromatography-mass spectrometry are designated by their molecular weights and where necessary with an added code letter. Trace constituents are in parentheses (see ref. 5,6 for further details and gas chromatographic profiles of alkaloids from other populations of D. histrionicus). Alkaloid **253D** was not detected in this sample from 3 skins, but was isolated from the 640 skin sample.

Decahydroquinolines.

Two of the major alkaloids (**219A**, **243A**) from this population were isolated and appeared by nuclear magnetic resonance spectral analysis to have the structures shown in Figure 1. Like the parent decahydroquinoline **195A** ("pumiliotoxin C") their mass spectra are dominated by a single fragment ion resulting from cleavage of the 2-substituent (see EXPERIMENTAL). The proton magnetic resonance spectra of **219A**, **243A**, **243A'** and **253D** are shown in Figure 3. The carbon 13-nuclear magnetic resonance spectral assignments are reported in Table 2. Assignments for **195A** (2-n-propyl-5-methyl-cis-decahydroquinoline) are reported for comparison. Both **219A** and **243A** are accompanied by an isomer that emerges slightly earlier on gas chromatographic analysis (Figure 2). These will be referred to as **219A'** and **243A'**. The configuration of these isomers is as yet not fully resolved. Of these two isomers only **243A'** was isolated after preparative chromatographies. Further properties of the decahydroquinolines **219A**, **243A**, **243A'** and **253D** are presented in EXPERIMENTAL.

X-ray diffraction analysis of the HCl salt of alkaloid **219A**, $C_{15}H_{26}N^{+}\cdot Cl^{-}$, confirmed the molecular formula and established the relative and absolute configuration and conformation. The substance crystallizes in space group $P2_12_12_1$ with cell parameters a = 7.340(3)Å, b = 8.400(3)Å, c = 25.096(8)Å, Z = 4, V = 1547.5Å^3, mol wt (with HCl) 255.84, and calculated density of 1.098 gm/cm^3. Intensity data were collected with CuK_α radiation from a platelet (.48 x .09 x .03 mm) on an automated four-circle diffractometer for both hkl data and the Friedel pairs $\bar{h}\bar{k}\bar{l}$ to a maximum scattering angle 2θ = 115° using a 2.0° scan and variable scan speed depending upon the intensity of the reflection. The structure was solved by direct phase determination (9) and refined by least-squares refinement using both the hkl and $\bar{h}\bar{k}\bar{l}$ data

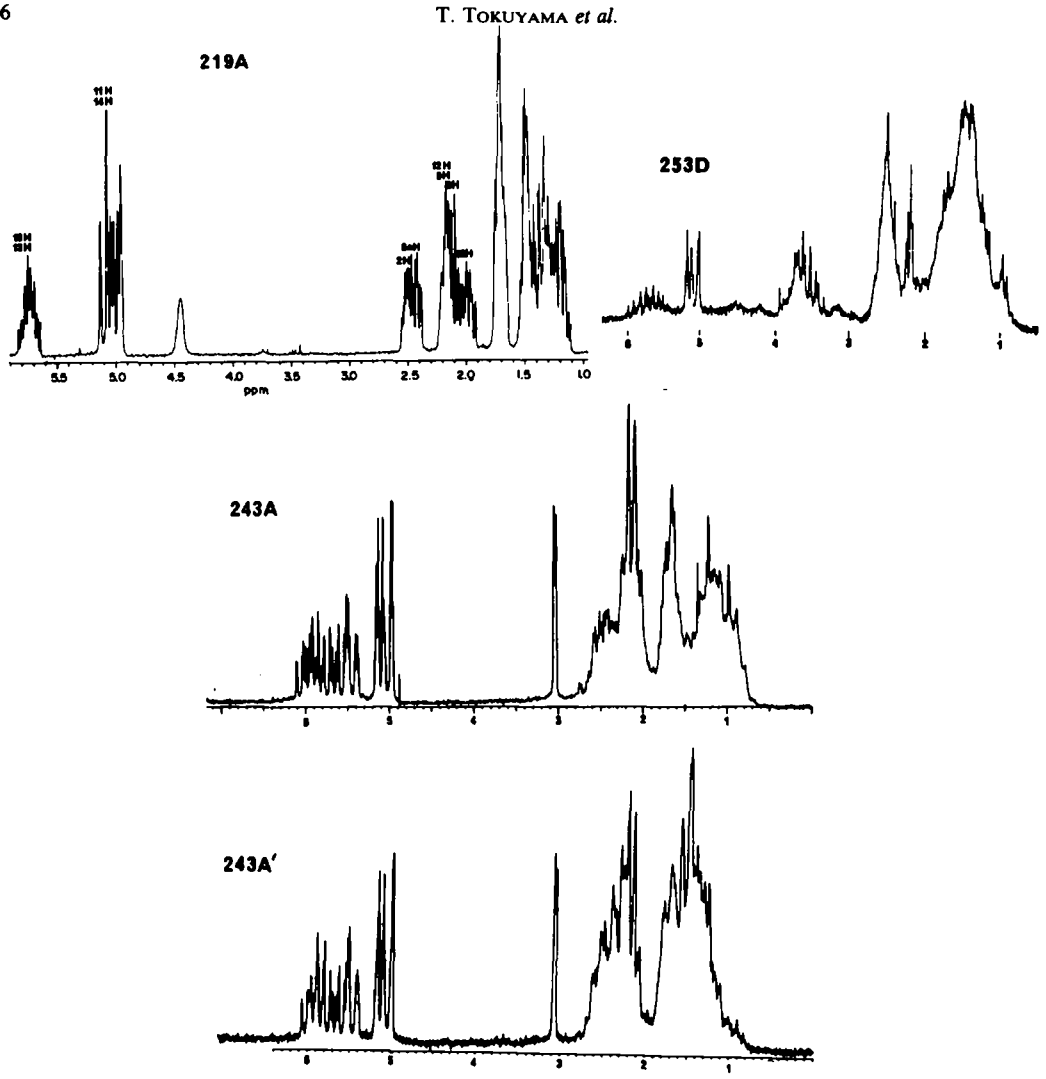


Figure 3. Proton magnetic resonance spectra ($CDCl_3$) of decahydroquinolines **219A**, **243A**, **243A'** and **253D**. The spectrum for **219A** was at 300 MHz, the others at 100 MHz. Chemical shifts are in δ.

Table 2. Carbon 13-magnetic resonance assignments for trans-decahydroquinolines **219A**, **243A**, **243A'**, and **253D** from Dendrobates histrionicus and for the perhydro derivative of **219A** (perhydro **219A**) and for pumiliotoxin C (**195A**), a cis-decahydroquinoline from D. pumilio .

Carbon Number	219A	243A	243A'	253D	Perhydro 219A	195A
2	55.6	56.0	56.0	56.0	56.5	57.8
3	28.6	28.8	28.9	29.3	28.9	27.3
4	28.6	31.9	29.6	28.7	28.6	27.1
4a	44.9	45.9	45.1	45.2	46.1	42.7
5	37.2	41.0	37.8	33.4	37.7	27.4
6	33.7[a]	33.6	33.8[a]	34.0	34.4	36.0
7	18.8	24.5	19.6	19.5	19.6	21.3
8	32.7[a]	32.7	32.8[a]	32.8	33.4	33.5
8a	55.1	61.5	55.5	55.4	56.5	56.1
9	41.2	41.4	41.3	41.3	39.5	39.7
10	135.2	135.5	135.5	135.4	19.2	19.1
11	116.8	117.2	117.4	117.3	14.4	14.2
12	30.8	33.3	27.8	29.5	29.5	19.9
13	136.7	144.2	146.1	70.1	21.5	--
14	114.7	109.0	108.6	67.3	14.3	--
15	--	80.6	80.7	--	--	--
16	--	81.3	81.3	--	--	--

[a]Assignments are tentative and values may be interchanged with the column.

to determine the absolute configuration. The absolute configuration is based on the anomalous scattering of the Cl^- ion by CuK_α radiation (10). The value of the agreement factor $R = \sum||F_o|-|F_c||/\sum|F_o|$, where $|F_o|$ are 1867 experimentallly observed values greater than $3\sigma(F_o)$ and $|F_c|$ are the calculated structure factors, is 5.60% for the configuration shown in this paper and 6.85% for the other antipode. The large difference in R factors overwhelmingly gives a preference to the configuration with the smaller R factor with a confidence level of 99.99% (11). Weighted R factors (R_w = 5.71% and 7.17% for the two hands, respectively) yield the same result.

The stereodiagram in Figure 4 shows the absolute configuration as well as the configuration at the various asymmetric centers. The decahydroquinoline moiety has a trans junction, contrary to the occurrence of a cis-decahydroquinoline moiety in pumiliotoxin C (2,8) and gephyrotoxin (2). The allyl side chain ortho to the N is equatorial whereas the second allyl side chain is axial to the cyclohexane moiety. Remarkably, the configuration at the 2 position (S) of **219A** is opposite to that of the cis-decahydroquinoline pumiliotoxin C, but is the same as in the histrionicotoxins with which **219A** (and **243A**) almost always occur in dendrobatid skin extracts.

Fractional coordinates for the non-hydrogen atoms are listed in Table 3. Bond lengths, bond angles, and torsional angles for the ring system are all within expected values. An un-

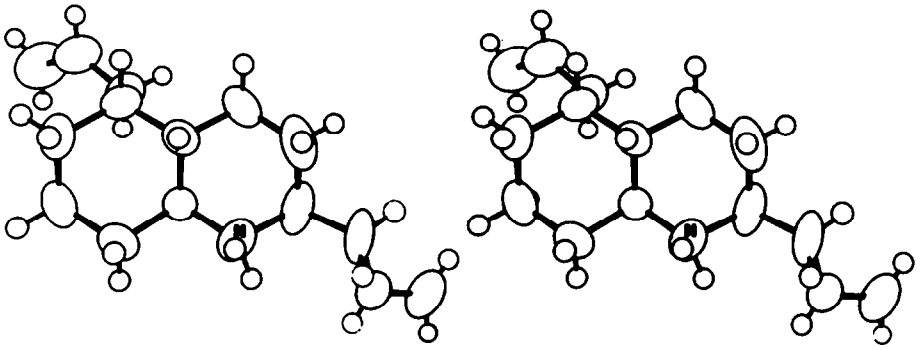


Figure 4. Stereodiagram of the absolute configuration of dendrobatid alkaloid **219A**, drawn from experimentally determined coordinates by x-ray diffraction.

Table 3. Fractional coordinates (x 10^4) and thermal factors ($Å^2$ x 10^3) for the hydrochloride (see Figure 5 for numbering of carbons).

Atom	x	y	z	U_{eq}*
Cl	9667(1)	6160(1)	524(1)	68(1)
N(1)	3931(4)	6410(5)	399(1)	62(1)
C(2)	4661(6)	4774(6)	271(2)	77(2)
C(3)	4486(7)	3752(60	771(2)	88(2)
C(4)	5373(7)	4506(5)	1259(2)	74(2)
C(5)	4499(5)	6131(4)	1365(2)	55(1)
C(6)	5192(6)	6957(5)	1873(2)	66(2)
C(7)	4180(6)	8519(5)	1945(2)	73(2)
C(8)	4422(7)	9603(5)	1466(2)	82(2)
C(9)	3768(6)	8797(5)	957(2)	69(2)
C(10)	4701(6)	7197(4)	882(2)	50(1)
C(11b)	3684(22)	4621(15)	-278(5)	91(7)
C(11a)	3573(17)	3792(15)	-145(3)	79(5)
C(12a)	4056(13)	4311(11)	-690(3)	70(4)
C(12b)	4189(13)	3117(14)	-560(4)	67(6)
C(13)	4590(8)	3263(7)	-1062(2)	97(2)
C(14)	7253(7)	7140(7)	1894(2)	81(2)
C(15)	7903(8)	7714(7)	2421(2)	96(2)
C(16)	8802(10)	8952(9)	2529(3)	125(3)

*$U_{eq} = 1/3\sum_i\sum_j U_{ij}a_i^*a_j^*\cdot a_i a_j$
+Atoms C(11) and C(12) disordered among two positions each with 56% occupancy for a and 44% occupancy for b.

expected feature is positional disorder in the allyl chain ortho to the N atom, particularly for the penultimate atom shown in positions 12A and 12B in the packing diagram in Figure 5. The occupancy of the A positions is 56% and 44% for the B positions as determined by the least-squares squares refinement when the sum of the two positions was constrained to be 1.0 and the occupancy of atoms 11A and 12A was linked, as well as the occupancy of 11B and 12B. It appears that the disorder is random from cell to cell since there are no approaches closer than the sum of van der Waals' radii between atoms in either conformation and atoms in neighboring molecules. To test whether the postional disorder occurred in other crystals, x-ray data collected from a sample crystallized at a different time yielded identical results. Coordinates for atoms C11A and C11B are not particularly precise, since it is always difficult to refine positions of atoms in close proximity to each other. The two different conformations for the disordered allyl chain are reminiscent of the conformation for analogous side-chains ortho to N in pumiliotoxin C (10) and in dihydrohistrionicotoxin (12).

Packing in the cell is dominated by $N^+H\cdots Cl^-$ bonds that wind about a two-fold screw axis perpendicular to the view in Figure 5. The vertical NH···Cl bond has an $N^+\cdots Cl^-$ distance of 3.153(6)Å, while the lateral $NH\cdots Cl^-$ bond has an $N^+\cdots Cl^-$ distance of 3.134(6)Å. This mode of packing is a common arrangement and is entirely analogous to that found in pumiliotoxin C (see Figures 2 and 4 in ref. 8). Closest approaches betwen C atoms in neighboring molecules are C(15)···C(16) = 3.98Å, C(13)···C(4) = 3.90Å, and C(13)···C(9) = 3.95Å.

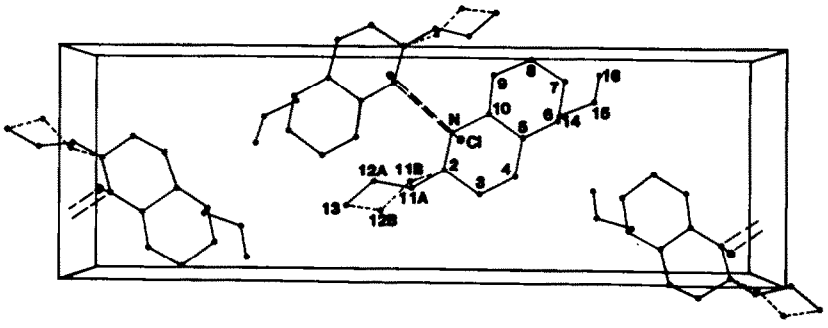


Figure 5. Stereodiagram of the packing in the crystal of the hydrochloride salt. The NH···Cl hydrogen bonds are indicated by dashed lines. The axial directions are a→, c↑ and b directed into the plane of the page. The two positions of the side chain are designated by 11A-12A-13 (solid line) and 11B--12B--13 (dashed line). Note the numbering in this Figure and in Table 3 and in supplementary material are arbitrary and do not conform with IUPAC numbering used elsewhere in the paper.

Indolizidines.

The gross structure of indolizidine **223AB** (formerly referred to as "gephyrotoxin" **223AB**) was proposed in 1978 (6) and subsequently defined as (5R,9R)-3-n-butyl-5-n-propylindolizidine by comparison to the four possible synthetic diastereomers (13). Comparison of the PMR and carbon 13-magnetic resonance spectra of natural **223AB**, **239AB** and **239CD** revealed the structures of the latter two compounds (ref. 5 and Table 4). All three of these indolizidines are levo-rotatory. Recently, the 3R,5R,9R enantiomer of indolizidine **223AB** has been synthesized and shown to be levorotatory (14) indicating that the natural indolizidines **223AB**, **239AB** and **239CD** also have the 3R,5R,9R configuration.

Another alkaloid **195B** was isolated from this population of Dendrobates histrionicus and its structure revealed as (5R,9R)-3-n-butyl-5-methylindolizidine by comparison of its proton and carbon 13-magnetic resonance spectra to those reported by Sonnet et al. (16) for synthetic material (Table 4). Indolizidine **195B**, unlike its congeners **223AB**, **239AB** and **239CD**, is dextrorotatory (see EXPERIMENTAL), which is remarkable since it suggests that this alkaloid has the opposite, namely 3S,5S,9S configuration, than the other 3,5-disubstituted indolizidines. Further properties of the indolizidines are in EXPERIMENTAL.

Table 4. Carbon 13-magnetic resonance assignments for indolizidines **195B**, **223AB**, **239AB** and **239CD** (solvent $CDCl_3$).

Carbon Number	195B	223AB	239AB	239CD
1	32.4 (33.0)[b]	30.9	31.6(30.7)[c]	30.8
2	26.3 (26.8)	26.3	26.1(25.8)	26.3
3	59.0 (56.6)	58.5	58.6(58.7)	58.5
5	52.0 (51.8)	56.6	55.0(55.9)	56.7
6	34.5 (35.3)	32.4	29.8(29.2)	33.0
7	24.7 (24.9)	24.6	24.5(24.0)	24.6
8	30.0 (30.6)	30.0	30.9(29.9)	29.9
9	58.8 (58.9)	59.0	59.1(59.8)	59.1
10	24.9 (25.2)	24.9	25.0(25.3)	25.3
11	29.2 (29.6)	29.1	29.0(28.6)	23.1
12	23.0 (23.3)	22.9	23.0(22.7)	32.1
13	14.2 (14.3)	14.1	14.2(13.7)	62.7
14	20.5 (20.9)	35.9	29.3(28.8)	35.8
15	--	18.9	27.9(27.9)	18.9
16	--	14.5	63.3(62.5)	14.5

[a]Assignments of 1-C and 2-C on indolizidine rings were confirmed through observations of their larger $^1J_{CH}$-values for which DANTE-pulse sequence (15) were applied. Assignments of the side-chain carbons were determined primarily by their T1 values.
[b]The reported values for synthetic (5**E**,9**E**)-3-n-butyl-5-methylindolizidine (16) are in parentheses. The only value that does not agree with present values for **195B** is for carbon 3.
[c]Values of **239AB** reported for a sample isolated from another population of D. histrionicus (Altos de Busy, Choco, Colombia, ref. 5) are in parentheses.

EXPERIMENTAL

High-resolution mass spectral data were obtained on JEOL D-300 mass spectrometer electron impact (70eV). Combined gas chromatography-mass spectrometry was on a 1.5% OV-1 Chromasorb G AW-DMCS column programmed from 150-280°C at 10°/min with a Finnegan 1015 mass spectrometer. NMR were obtained on a JEOL FX-100 or a Varian XL-300 MHz spectrometer. PMR determined at 99.60 MHz were with the use of a 16**K** Fourier transform and 1 KHz spectra range for a digital resolution of 0.12 Hz. Typically, free induction decays from a 45° pulse were collected at 6 sec intervals. ^{13}C NMR spectra were determined at 25.05 MHz using a 16K or 8K Fourier transform and 5 KHz spectra range for a digital resolution of 0.61 or 1.22 Hz. Typically, 2000 free induction decays from a 45° pulse were collected at 1.5 sec intervals to obtain a completely decoupled spectra.

Isolation of Alkaloids from Dendrobates histrionicus

Methanolic extracts from 640 skins of Dendrobates histrionicus (Sta. Cecilia, Depto. Risaralda, Colombia) were prepared and partitioned between aqueous methanol/chloroform (see ref. 6 for general procedure). Alkaloids were then extracted from chloroform phase into 0.1 N HCl. After adjusting pH to 10 with aqueous ammonia, the aqueous layer was extracted first with hexane and then chloroform. The hexane and chloroform layer were evaporated in vacuo to dryness to afford 0.50 g and 0.20 g of alkaloids respectively.

Preparative chromatography of the hexane extract on a DIOL column (Merck, prepacked Lobar column, size B) with a mixed solvent of n-hexane, chloroform and triethylamine (85:15:1) yielded eight main fractions (H-1 to H-8) as monitored by refractive index. Fraction H-1 and H-2 were rechromatographed on the DIOL column separately with n-hexane containing triethylamine (0.5%) to afford indolizidines **195B** and **223AB** (12 mg and 39 mg respectively). Fraction H-3 (14 mg) consisted of a complex mixture. Fraction H-4 consisted of almost pure decahydroquinoline **219A** (107 mg). Fraction H-5 was re-chromatographed on the DIOL column with n-hexane, dioxane, tetrahydrofuran and triethylamine (95:2.5:2.5:1) to afford decahydroquinolines **243A** and **243A'** (20 mg and 10 mg). Fraction H-6 (74 mg) consisted of a mixture of dihydrohistrionicotoxins (**285A**, **285C**). Fraction H-7 and H-8 afforded pure histrionicotoxin (**283A**) (42 mg) and indolizine alkaloid **239AB** (47 mg) respectively.

The chloroform extract was chromatographed on a reversed phase silica gel column (Merck, prepacked Lobar column, RP-8, size B) with a mixed solvent of acetonitrile and 0.7 M phosphate buffer pH 4.6 (35:65) to yield three main fractions (C-1 and C-3). Decahydroquinoline **253D** (10 mg) eluted in fraction C-1. Fraction C-2 and C-3 afforded indolizidines **239CD** (10 mg) and **239AB** (11 mg) respectively.

Reduction of Alkaloid 219A and Formation of HBr Addition Products

Alkaloid **219A**·HBr was reduced with hydrogen gas (45 psi) and 10% Pd-C in methanol for 2 hrs. The resulting perhydro-derivative was found to be contaminated with a saturated HBr addition product. After isolation by preparative chromatography, mass spectral and nmr spectral analysis indicated that addition had occurred preferentially to the double bond of the 5-allylic moiety. Addition of both HCl and HBr to the 5-allylic moiety of **219A** was found to occur under non-reducing conditions in methanol. The mass spectra of alkaloid **219A**, the perhydro derivative and the HBr addition product were as follows (the intensities relative to a base peak set equal to 100 are in parentheses):

219A; m/z 219(0.5), 218(0.8), 179(15), 178(100).

Perhydro-**219A**; m/z 223(1.5), 222(1.7), 194(1.2), 193(1.3), 181(15), 180(100).

HBr addition product of **219A**; m/z 301(<0.5), 300(<0.5), 299(<0.5), 298(<0.5), 260(85), 258(85), 179(14), 178(100).

Phenylboronide Formation from Alkaloid **253D**

Treatment of alkaloid **253D** with phenylboronic acid in chloroform at room temperature afforded a monoboronide. The mass spectra of **253D** and its phenylboronide are as follows:

253D; m/z 253(0.5), 252(0.8), 222(6), 213(16), 212.1658(100, $C_{12}H_{22}NO_2$).

253D (phenylboronide); m/z 339(0.3), 338(1), 298(100), 147(12).

Optical Rotations

The following rotations were obtained. The temperature at which the $[\alpha]_D$ was measured is reported.

Trans-decahydroquinolines

219A +9.7° (c 2.0 CH_3OH) 24°

243A -15.2° (c 1.37 CH_3OH) 16°
-30.7° (c 1.37 $CHCl_3$) 16°

243A' -0.96° (c 0.73 CH_3OH) 16°
-18.6° (c 0.73 $CHCl_3$) 16°

Indolizidines

195B +65° (c 0.41 CH_3OH) 16°
·HCl +36° (c 0.52 CH_3OH) 24°

223AB -35° (c 0.49 CH_3OH) 16°C
-44° (c 1.0 n-hexane) 27°C

Synthetic **223AB** (3R,5R,8aR) -69.2 (c 0.55 CH_3OH) 20° (from ref. 14)

239AB -38° (c 1.0 CH_3OH) 16°C

239CD -52° (c 0.19 CH_3OH) 16°C

Supplementary Material Available: Listing of observed and calculated structure factors as well as tables of bond lengths, bond angles, anisotropic thermal parameters for the nonhydrogen atoms and coordinates for hydrogen atoms has been provided for deposition at the Cambridge Crystallographic Data Centre.

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