Structure of Aristone, a Unique Indole Alkaloid from *Aristotelia chilensis* (Mol.) Stuntz, by *X*-Ray Crystallographic Analysis

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Aristone, aristoteline, aristotelinine, and aristotelone were isolated from *Aristotelia chilensis* and belong to a unique class of alkaloids found only in the genus *Aristotelia*. The structure of aristone was determined by *X*-ray diffraction techniques. Crystals are orthorhombic, space group $P2_12_12_1$, with cell dimensions a = 11.075(3), b = 18.004(4), and c = 7.973(1) Å and Z = 4. The crystal structure was determined by direct methods and atomic positional and thermal parameters were refined by full-matrix least-squares techniques to a R value of 3.8% utilizing 1 717 reflexions. The molecule contains a planar indole moiety with the remainder of the molecule forming a basket-like cavity. There are a number of carbon valence angles less than 105° which indicate internal strain ; however, there are no significant intramolecular interactions.

ARISTOTELIA presents taxonomic problems since some species are polymorphic with true-breeding as well as habit-induced forms. This is complicated further by the abundance of hybrid forms.[1]

The three investigated species of *Aristotelia* contain unique indole alkaloids which are known to incorporate a non-loganin derived monoterpene unit. The distribution of these alkaloids among the other members of the genus and the variations within a species have not been reported. Alkaloids were not detected in *Crinodendron hookerianum*,[2] another species of Chilean Eleocarpaceae: however, other genera and species have not been investigated.

*Aristotelia peduncularis* Hook., collected in Tasmania,

(1) (2)
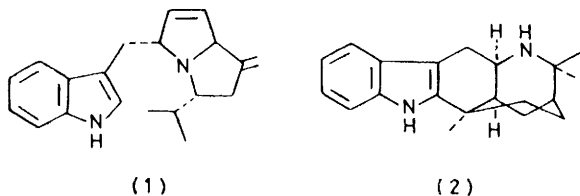
contains the alkaloid peduncularine (1) and three unidentified minor components.[3] The New Zealand species, *Aristotelia serrata*[4] contains the alkaloids peduncularine (1), aristoteline (2), and several unidentified components. *Aristotelia chilensis* has yielded aristoteline

(3) (4) R = H
     (6) R = OH
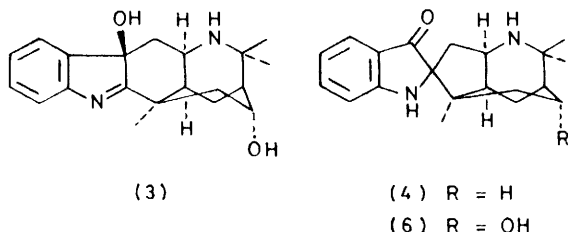
(2),[5] aristotelinine (3),[6] aristotelone (4),[5] and aristone (5).[7] It was postulated that aristone might arise *via* rearrangement of (3) to the ψ-indoxyl species (6) which is related to aristotelone. Models indicated that inter-

action of the aliphatic amine with the benzoyl function is possible to give generation of a carbonium ion species (7); subsequent intramolecular hydrogen migration would lead to the formation of (5).[7] Because of the unusual nature of aristone, we here report details of the structure.

(5) (7)
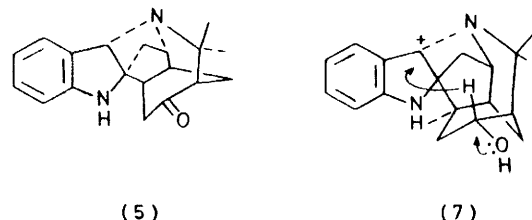
EXPERIMENTAL

Aristotelia chilensis was collected in the summer near Concepcion, Chile. Dried leaves and stems (12 kg) were extracted with warm ethanol, filtered, and the extracts evaporated to dryness. The residue was treated with 2N-HCl, the mixture extracted with $CHCl_3$, and the aqueous layer adjusted to pH 9.5 (aq. NH_3). The solution was re-extracted with $CHCl_3$ which upon evaporation yielded 2.5 g of solid. The solid was chromatographed over alumina, grade II (300 g), yielding 200 mg of aristoteline (2), 10 mg of aristotelone (4), and traces of additional alkaloids. The extraction was repeated with 10 kg of dried leaves, particular attention being paid to the isolation of additional alkaloids. Chromatography yielded 7 mg of aristotelinine (3) and 3 mg of aristone (5). Aristone was recrystallized from benzene–ethyl acetate to yield a white crystalline solid.

Aristone (5), m.p. 240—242 °C (Found: C, 77.85; H, 7.8. $C_{20}H_{24}N_2O$ requires C, 77.89; H, 7.84), $\lambda_{max.}$ (EtOH): 212, 230, and 290 (3.69) nm; $\nu_{max.}$ (Nujol): 3 350, 1 690sh, 1 680, 1 615, 1 285, 1 230, 1 165, 1 150, 1 075, 995, 975, and 760 cm.

A crystal of dimensions $0.3 \times 0.2 \times 0.4$ mm was mounted on a Syntex P2$_1$ diffractometer. Room-temperature lattice parameters were refined by a least-squares procedure utilizing 15 reflections whose angles were measured by a centring routine associated with the Syntex diffractometer.

Crystal Data.—$C_{20}H_{24}N_2O$, M, 308.42. Orthorhombic,

$a = 11.075(3)$, $b = 18.044(4)$, $c = 7.973(1)$ Å, $V = 1 589.9(6)$ Å³, $Z = 4$, $d_c = 1.288$ g cm⁻³, Cu-K_α radiation ($\lambda = 1.541 78$ Å), space group $P2_12_12_1$ (D_2^4, No. 19).

Intensity data were collected by the $\theta : 2\theta$ scanning technique using a variable-scan speed with Cu-K_α radiation and a graphite monochromator. Systematic absences were consistent with the space group $P2_12_12_1$. 1 717 independent

A final difference map showed no peak larger than 0.2 e Å⁻³. All parameter shifts during the final cycle were less than 0.4σ. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1974).[9]

Atomic parameters, with estimated standard deviations, are given in Table 1. Observed and calculated structure factors and thermal parameters are listed in Supplementary Publication No. 22865 (15 pp.).

TABLE 1

Positional parameters for aristone. Non-hydrogen parameters × 10⁴, H × 10³

Atom	x/a	y/b	z/c
C(1)	6 286(2)	9 116(1)	7 203(3)
C(2)	6 084(2)	8 471(1)	6 025(3)
C(3)	6 053(2)	7 695(1)	6 778(2)
C(4)	6 805(2)	7 714(1)	8 377(3)
C(4a)	6 176(2)	8 192(1)	9 658(2)
C(5)	4 896(2)	7 904(1)	10 063(2)
N(6)	4 148(1)	7 827(1)	8 504(2)
C(6a)	3 895(1)	8 606(1)	8 028(2)
C(6b)	2 632(2)	8 917(1)	8 146(2)
C(7)	1 530(2)	8 646(1)	7 631(2)
C(8)	0 505(2)	9 090(1)	7 864(3)
C(9)	0 611(2)	9 784(1)	8 592(3)
C(10)	1 722(2)	10 062(1)	9 087(3)
C(10a)	2 737(2)	9 625(1)	8 865(2)
N(11)	3 937(2)	9 791(1)	9 270(2)
C(11a)	4 559(1)	9 070(1)	9 335(2)
C(11b)	5 937(2)	9 015(1)	9 050(2)
C(12)	4 352(2)	8 584(1)	10 897(2)
C(13)	4 746(2)	7 398(1)	7 167(2)
C(14)	3 958(2)	7 403(1)	5 594(3)
C(15)	4 827(3)	6 582(1)	7 759(4)
C(16)	6 625(2)	9 581(2)	10 107(3)
O(17)	6 024(2)	8 572(1)	4 513(2)
H(1α)	720(4)	928(2)	693(5)
H(1β)	589(3)	957(2)	670(4)
H(3)	633(3)	740(2)	596(5)
H(4β)	749(3)	788(2)	808(4)
H(4α)	691(3)	720(2)	878(5)
H(4a)	662(3)	820(2)	1 066(4)
H(5)	489(2)	743(1)	1 068(3)
H(6a)	417(2)	871(1)	683(3)
H(7)	148(2)	815(1)	716(3)
H(8)	−025(3)	893(1)	749(3)
H(9)	−005(3)	1 006(2)	879(3)
H(10)	181(4)	1 058(2)	960(5)
H(11)	401(3)	1 003(2)	1 017(5)
H(12α)	489(2)	876(1)	1 183(3)
H(12β)	346(2)	855(1)	1 111(3)
H(14α)	389(3)	791(2)	514(4)
H(14β)	321(2)	723(1)	597(3)
H(14γ)	438(3)	714(2)	469(4)
H(15α)	388(3)	641(2)	806(4)
H(15β)	517(4)	629(2)	704(5)
H(15γ)	527(3)	654(2)	879(5)
H(16α)	648(4)	1 021(2)	965(5)
H(16β)	632(3)	956(2)	1 129(5)
H(16γ)	739(4)	955(2)	993(4)

reflections were measured and 1 658 had intensities greater than $2\sigma(I)$. Lorentz and polarization corrections were applied but no absorption corrections were made. A periodically monitored check reflexion indicated no significant changes in intensity during data collection. The direct methods program MULTAN[8] was used to calculate phases for the 400 $|E|$ values greater than 1.2. The phase set with the largest combined figure of merit was selected, and the E map calculated with these phases revealed the positions of all atoms. Alternate least-squares refinements and difference Fourier calculations yielded all hydrogen atoms. Least-squares refinement yielded $R = 0.038$ where $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $R_w = 0.055$. The function minimized in the least-squares refinement was

TABLE 2

Interatomic distances (Å) and angles (°) for aristone

C(1)–C(2)	1.510(3)	C(6b)–C(7)	1.377(3)
C(2)–C(3)	1.521(3)	C(7)–C(8)	1.401(3)
C(3)–C(4)	1.524(3)	C(8)–C(9)	1.383(3)
C(4)–C(4a)	1.506(3)	C(9)–C(10)	1.385(3)
C(4a)–C(11b)	1.581(3)	C(10)–C(10a)	1.384(3)
C(11b)–C(1)	1.533(3)	C(11a)–C(12)	1.539(2)
C(4a)–C(5)	1.543(3)	C(12)–C(5)	1.517(3)
C(5)–N(6)	1.500(2)	C(3)–C(13)	1.575(3)
N(6)–C(6a)	1.479(2)	N(6)–C(13)	1.473(2)
C(6a)–C(11a)	1.525(2)	C(13)–C(14)	1.528(3)
C(11a)–C(11b)	1.546(3)	C(13)–C(15)	1.546(3)
C(6a)–C(6b)	1.510(2)	C(11b)–C(16)	1.526(3)
C(6b)–C(10a)	1.402(2)	C(2)–O(17)	1.221(3)
C(10a)–N(11)	1.401(3)	C(11)–C(11a)	1.471(2)
C(1)–H(1α)	1.08(5)	C(7)–H(7)	0.97(2)
C(1)–H(1β)	1.00(3)	C(8)–H(8)	0.94(3)
C(3)–H(3)	0.89(4)	C(9)–H(9)	0.90(3)
C(4)–H(4β)	0.85(4)	C(10)–H(10)	1.02(4)
C(4)–H(4α)	0.99(4)	N(11)–H(11)	0.84(4)
C(4a)–H(4a)	0.94(3)	C(12)–H(12α)	1.01(3)
C(5)–H(5)	0.99(3)	C(12)–H(12β)	1.01(2)
C(6a)–H(6a)	1.02(2)	C(14)–H(14α)	0.99(3)
C(16)–H(16α)	1.19(4)	C(14)–H(14β)	0.94(2)
C(16)–H(16β)	1.00(4)	C(14)–H(14γ)	0.98(4)
C(16)–H(16γ)	0.86(4)	C(15)–H(15α)	1.12(3)
C(15)–H(15γ)	0.96(4)	C(15)–H(15β)	0.87(4)

C(1)–C(2)–C(3)	117.6(2)	C(1)–C(2)–O(17)	120.5(2)
C(2)–C(3)–C(4)	107.3(2)	C(3)–C(2)–O(17)	121.7(2)
C(3)–C(4)–C(4a)	109.1(2)	C(2)–C(3)–C(13)	114.2(2)
C(4)–C(4a)–C(11b)	113.9(2)	C(4)–C(3)–C(13)	110.2(2)
C(4a)–C(11b)–C(1)	111.4(2)	C(3)–C(13)–C(15)	109.2(2)
C(11b)–C(1)–C(2)	118.0(2)	C(3)–C(13)–C(14)	111.2(2)
C(4a)–C(5)–N(6)	111.4(1)	N(6)–C(13)–C(14)	109.5(2)
C(5)–N(6)–C(6a)	103.3(1)	N(6)–C(13)–C(15)	107.7(2)
N(6)–C(6a)–C(11a)	104.6(1)	C(14)–C(13)–C(15)	106.8(2)
C(6a)–C(11a)–C(11b)	109.9(1)	C(5)–N(6)–C(13)	113.6(1)
C(11a)–C(11b)–C(4a)	100.4(1)	C(6a)–N(6)–C(13)	113.4(1)
C(11a)–C(11b),C(1)	112.5(1)	C(11a)–C(11b)–C(16)	111.6(2)
C(6a)–C(6b)–C(10a)	106.6(1)	C(4a)–C(11b)–C(16)	111.9(2)
C(6b)–C(10a)–N(11)	111.5(2)	C(1)–C(11b)–C(16)	109.0(2)
C(10a)–N(11)–C(11a)	105.3(1)	C(6a)–C(11a)–C(12)	99.7(1)
C(11)–C(11a)–C(6a)	103.5(1)	C(11b)–C(11a)–C(12)	103.2(1)
C(11a)–C(6a)–C(6b)	101.6(1)	C(11a)–C(12)–C(5)	92.6(1)
C(6b)–C(7)–C(8)	118.5(2)	C(4a)–C(5)–C(12)	100.7(1)
C(7)–C(8)–C(9)	120.1(2)	N(6)–C(5)–C(12)	102.6(1)
C(8)–C(9)–C(10)	121.5(2)	N(11)–C(11a)–C(11b)	120.9(1)
C(9)–C(10)–C(10a)	118.6(2)	C(7)–C(6b)–C(6a)	132.1(2)
C(10–C(10a)–C(6b)	120.2(2)	C(6b)–C(6a)–N(6)	120.8(1)
C(10a)–C(6b)–C(7)	121.2(2)	C(5)–C(4a)–C(4)	112.0(2)
N(6)–C(13)–C(3)	112.2(2)	N(11)–C(11a)–C(12)	117.4(1)
C(11b)–C(4a)–C(5)	103.0(1)	C(10)–C(10a)–N(11)	128.3(2)

DISCUSSION

The Figure is an ORTEP drawing[10] of aristone while Tables 2 and 3 contain bond lengths, valence angles, and torsion angles. The molecule contains a planar region composed of the indole moiety and a basket-like cavity composing the remainder of the molecule. Although, the large number of angles smaller than 105°, would

indicate considerable ring strain in the molecule, there are no significant steric interactions. C(11b)–C(4a) = 1.581(3) and C(3)–C(13) = 1.575(3) Å are significantly longer than the value 1.530(9) Å obtained by averaging the remaining $C(sp^3)$–$C(sp^3)$ bond distances. The N(6)–C(13) distance of 1.500(2) Å is significantly longer than the 1.475(4) Å average of the remaining two N–C(sp^3) bonds. These elongations may be associated with relief of ring strain.

The torsion angles of the five-membered heterocyclic ring of the indole moiety indicates a flattened envelope conformation with C(11a) being the flap. The five-membered ring N(6),C(6a),C(11a),C(12),C(5) exhibits a more sharply folded envelope conformation with C(12)

TABLE 3

Torsion angles (°) for aristone

C(6a)–C(6b)–C(10a)–N(11)	−1.8(2)
C(6b)–C(10a)–N(11)–C(11a)	−19.4(2)
C(10a)–N(11)–C(11a)–C(6a)	32.1(2)
N(11)–C(11a)–C(6a)–C(6b)	−32.1(2)
C(11a)–C(6a)–C(6b)–C(10a)	21.2(2)
C(11a)–C(11b)–C(4a)–C(6)	3.8(2)
C(11b)–C(4a)–C(5)–C(12)	−40.4(2)
C(4a)–C(5)–C(12)–C(11a)	59.0(1)
C(5)–C(12)–C(11a)–C(11b)	−57.8(2)
C(12)–C(11a)–C(11b)–C(4a)	33.6(2)
N(6)–C(5)–C(4a)–C(4)	51.3(2)
C(5)–C(4a)–C(4)–C(3)	−54.9(2)
C(4a)–C(4)–C(3)–C(13)	58.5(2)
C(4)–C(3)–C(13)–N(6)	−57.4(2)
C(3)–C(13)–N(6)–C(5)	54.7(2)
C(13)–N(6)–C(5)–C(4)	−51.7(2)
C(5)–N(6)–C(6a)–C(11a)	1.8(2)
N(6)–C(6a)–C(11a)–C(12)	−37.1(2)
C(6a)–C(11a)–C(12)–C(5)	55.5(1)
C(11a)–C(12)–C(5)–N(6)	−56.0(2)
C(12)–C(5)–N(6)–C(6a)	35.1(2)
C(5)–N(6)–C(6a)–C(11a)	1.8(2)
N(6)–C(6a)–C(11a)–C(11b)	70.9(2)
C(6a)–C(11a)–C(11b)–C(4a)	−72.1(2)
C(11a)–C(11b)–C(4a)–C(5)	3.8(2)
C(11b)–C(4a)–C(5)–N(6)	67.8(2)
C(4a)–C(5)–N(6)–C(6a)	−71.9(2)
C(4)–C(4a)–C(11b)–C(1)	6.1(2)
C(4a)–C(11b)–C(1)–C(2)	34.8(2)
C(11b)–C(1)–C(2)–C(3)	−24.6(3)
C(1)–C(2)–C(3)–C(4)	−26.4(2)
C(2)–C(3)–C(4)–C(4a)	67.6(2)
C(3)–C(4)–C(4a)–C(11b)	−57.9(2)

being the flap. The C(5),C(12),C(11a) and C(6a),C(11a),-C(12) valence angles are 92.6(1) and 99.7(1) degrees, respectively. The five-membered ring C(4a),C(5),C(12),-C(11a),C(11b) exhibits a similar sharply folded envelope conformation. Alternatively, the system can be considered to the composed of a six-membered ring N(6),-C(6a),C(11a),C(11b),C(4a),C(5), exhibiting a sharply folded boat conformation with C(12) forming a 1,4 bridge. The six-membered ring composed of N(6),C(13),-C(3),C(4),C(4a),C(5) exhibits a regular chair conformation

while C(1),C(2),C(3),C(4),C(4a),C(11b) exists as a distorted boat. C–H bonds average 0.99(6) with C(16)–H(16α) = 1.19(4) being the maximum and C(4)–H(4a) =0.85(4) being the minimum. The shortest intermolecular contact is 2.44 Å between H(6a) and H(10).
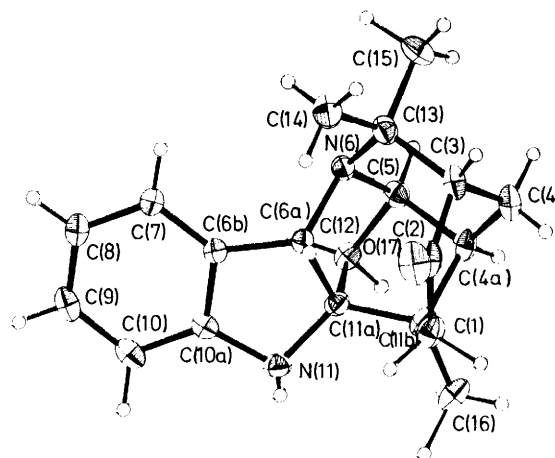

FIGURE ORTEP drawing of aristone. Ellipsoids drawn at 35% probability level while hydrogens are represented by arbitrary size spheres.

Although aristone may be difficult to synthesize, there are no significant steric interactions and ring strain may be the main factor leading to any lowering of stability. The crystals are stable when exposed to the atmosphere at room temperature and no deterioration upon exposure to X-rays was observed.

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