ORGANIC COMPOUNDS

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Indaconitine 0.5-acetonitrile solvate

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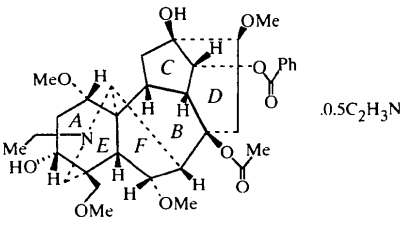
Abstract

The crystal structure of indaconitine hemiacetonitrile solvate, [1α,6α,14α(*E*),16β]-20-ethyl-1,6,16-trimethoxy-4-methoxymethyl-3,13-dihydroxyaconitane-8,14-diyl 8-acetate 14-benzoate hemiacetonitrile solvate, $C_{34}H_{47}NO_{10}\cdot0.5C_2H_3N$, a C_{19} norditerpenoid alkaloid isolated from the roots of *Aconitum chasmanthum* Stapf ex Holmes of Pakistani origin, contains a molecule of the alkaloid and half a molecule of the solvate in an asymmetric unit. The molecular dimensions are as expected. The fused ring system contains one boat, one half-chair, two chair and two envelope conformations. The crystal structure is stabilized by an intermolecular hydrogen bond between indaconitine and acetonitrile, with an O···N distance of 3.036 (6) Å. An hydroxyl group is also involved in an intramolecular interaction with a methoxy group, with an O···O separation of 2.643 (5) Å.

Comment

Aconitum chasmanthum Stapf ex Holmes, a plant indigenous to the western Himalayas, is abundant in alpine and subalpine zones, between altitudes of 2200 and 4000 m, from Chitral to Hazara and Kashmir. It contains a large number of diterpenoid alkaloids, *e.g.* chasmaconitine and chasmanthinine (Achmatowicz & Marion, 1964), homochasmanine (Achmatowicz & Marion, 1965), indaconitine (Miana *et al.*, 1971), and chasmanine (Pelletier *et al.*, 1984). Benn (1993) has published a comprehensive review on the distribution, biosynthesis, pharmacology, commercial aspects and chemistry of diterpenoid alkaloids. In this article we report the crystal structure of indaconitine, (1), as its hemiacetonitrile solvate, which has been determined unequivocally by the X-ray crystallographic method.



(1)

The crystal structure of the title compound contains a molecule of indaconitine (Fig. 1) and half a molecule of disordered acetonitrile solvate in an asymmetric unit. The absolute structure could not be established reliably. However, the absolute structure reported in this article is the same as that known for chasmanine 14-α-benzoate hydrochloride (De Camp & Pelletier, 1977). The molecular dimensions in (1) are normal and lie within expected values for the corresponding bond distances and angles, with mean bond distances as follows: Csp^3—N 1.463 (11), Csp^3—Csp^3 1.54 (2), Csp^3—O 1.42 (3), Csp^2—O 1.346 (4), and C=O 1.193 (1) Å, while the Csp^3—Csp^2 and Csp^2—Csp^2 distances are 1.488 (6) and 1.473 (4) Å, respectively.

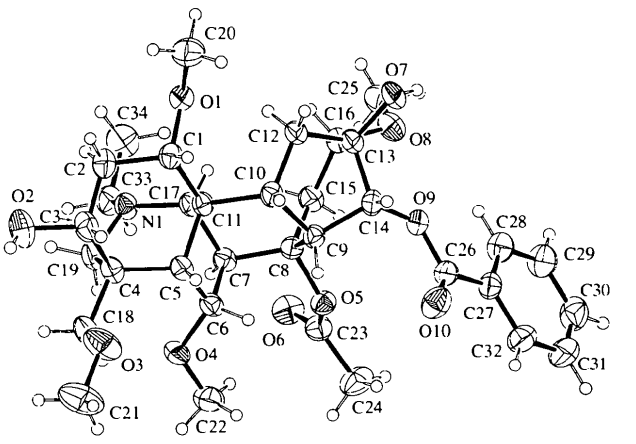


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of (1) with the atomic numbering scheme. Displacement ellipsoids are plotted at the 30% probability level for non-H atoms and H atoms are assigned as circles of an arbitrary radius. One of the disordered methyl sites, C22*A*, has been ignored.

The fused rings in the main frame of the molecule in (1) adopt conformations identical to the corresponding rings reported in chasmanthinine (Parvez *et al.*, 1998*a*), chasmaconitine (Parvez *et al.*, 1998), and 3α-bikhaconine (Parvez *et al.*, 1998*b*). The six-membered rings *A* (C1–C5 and C11) and *E* (C4, C5, C11, C17, N1 and C19) adopt chair conformations. The six-membered ring *D* (C8, C9 and C13–C16) has

a half-chair conformation, with C14 0.889 (4) Å out of the plane of the remaining ring atoms. The seven-membered ring *B* (C5–C11) adopts a boat conformation. The five-membered rings *C* (C9, C10, C12, C13 and C14) and *F* (C5–C7, C11 and C17) display C14- and C17-envelope conformations, respectively. Atom C14 is 0.705 (5) Å out of the plane of the remaining four atoms of ring *C*, which is essentially planar [maximum deviation 0.030 (2) Å]. C17 is 0.737 (4) Å out of the plane formed by the rest of the atoms of ring *F*. The phenyl ring of the benzoate moiety attached to C14 was constrained to be planar, and O9 and O10 are 0.082 (5) and 0.039 (5) Å, respectively, out of the plane of the phenyl ring.

The crystal structure is stabilized by inter- and intramolecular hydrogen bonds. There is a strong hydrogen bond between the solvate and a hydroxyl group of the alkaloid, with an O···N distance of 3.036 (6) Å. A hydroxyl group is also involved in an intramolecular interaction with a methoxy group, with an O···O separation of 2.643 (5) Å; details of these interactions are given in Table 2.

Experimental

Indaconitine was isolated from the roots of *Aconitum chasmanthum*, collected from the Rescuta Top area in Kashmir. The alkaloid was re-crystallized from a mixture of acetone:acetonitrile (1:1) at room temperature by slow evaporation.

Crystal data

$C_{34}H_{47}NO_{10}\cdot 0.5C_2H_3N$
M_r = 650.25
Monoclinic
*C*2
a = 32.802 (3) Å
b = 9.267 (2) Å
c = 11.756 (2) Å
β = 108.93 (1)°
V = 3380.3 (10) Å^3
Z = 4
D_x = 1.278 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 25 reflections
θ = 20–30°
μ = 0.767 mm^{-1}
T = 293 (1) K
Prismatic
0.5 × 0.3 × 0.2 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
5691 measured reflections
5647 independent reflections
5016 reflections with $I > 2\sigma(I)$
R_{int} = 0.015
θ_{max} = 65°
$h = 0 \rightarrow 38$
$k = -10 \rightarrow 10$
$l = -13 \rightarrow 13$
3 standard reflections every 200 reflections
intensity decay: 2.9%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.067
$wR(F^2)$ = 0.188
S = 1.038
5647 reflections
404 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.131P)^2 + 1.608P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.008
$\Delta\rho_{max}$ = 0.638 e Å^{-3}
$\Delta\rho_{min}$ = −0.260 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.1 (3) (3051 Friedel pairs)

Table 1. *Selected geometric parameters (Å, °)*

O1—C20	1.425 (5)	O7—C13	1.429 (4)
O1—C1	1.435 (4)	O8—C25	1.390 (6)
O2—C3	1.431 (5)	O8—C16	1.431 (4)
O3—C18	1.398 (5)	O9—C26	1.342 (5)
O3—C21	1.398 (6)	O9—C14	1.432 (4)
O4—C22	1.410 (10)	O10—C26	1.192 (5)
O4—C6	1.416 (4)	N1—C33	1.448 (5)
O5—C23	1.349 (4)	N1—C17	1.468 (4)
O5—C8	1.478 (4)	N1—C19	1.473 (4)
O6—C23	1.194 (5)		
C20—O1—C1	114.1 (3)	C26—O9—C14	119.0 (3)
C18—O3—C21	112.6 (4)	C33—N1—C17	114.3 (3)
C22—O4—C6	115.9 (4)	C33—N1—C19	109.6 (3)
C23—O5—C8	121.4 (3)	C17—N1—C19	116.4 (3)
C25—O8—C16	113.6 (4)		

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···N2^i	0.82	2.26	3.036 (6)	157
O7—H7···O8	0.82	2.16	2.643 (5)	117

Symmetry code: (i) $x, y, 1 + z$.

Based on the systematic absences, packing considerations, a statistical analysis of intensity distribution and the successful solution and refinement of the structure, the space group was determined to be *C*2 (No. 5). Friedel pairs (3051) were collected and were not merged. The methoxymethyl group attached to C6 was disordered and its atoms were allowed to refine at two sites, C22 and C22*A*, with non-equivalent site-occupancy factors of 0.533 (8) and 0.467 (8), respectively. The phenyl ring was allowed in the refinement as a regular hexagon. The H atoms were included at geometrically idealized positions, with C—H and O—H 0.95 and 0.82 Å, respectively. A disordered molecule of acetonitrile solvate was located on a twofold axis. The non-H atoms of (1) were allowed anisotropic displacement parameters, while the solvate C and N atoms were allowed isotropic thermal vibrations.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1994). Program(s) used to solve structure: *SAPI91* (Fan, 1991). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997). Molecular graphics: *TEXSAN*. Software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1503). Services for accessing these data are described at the back of the journal.

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Pseudaconitine

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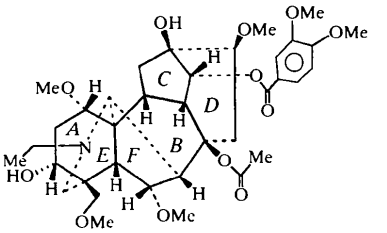
Abstract

The crystal structure of pseudaconitine, [1α,6α,14α(*E*),-16β]-20-ethyl-1,6,16-trimethoxy-4-methoxymethyl-3,13-dihydroxyaconitane-8,14-diyl 8-acetate 14-(3,4-dimethoxybenzoate), $C_{36}H_{51}NO_{12}$, a C_{19} norditerpenoid alkaloid, contains discrete molecules separated by normal van der Waals distances. The molecular dimensions are as expected. The fused ring system contains two chair, one half-chair, one boat and two envelope conformations. There are inter- and intramolecular hydrogen bonds, with O···O separations in the range 2.671 (4)–2.865 (3) Å.

Comment

Continuing our crystallographic studies of C_{19} norditerpenoid alkaloids (Parvez *et al.*, 1998, 1998*a*,*b*,*c*), we now report the crystal structure of pseudaconitine, (1), a diterpenoid base. This has been isolated from the roots of *Aconitum falconeri*, which is found extensively in the northern areas of Pakistan.



(1)

The crystal structure contains pseudaconitine molecules (Fig. 1) separated by normal van der Waals distances. The absolute structure could not be established in this analysis; however, the absolute structure reported in this article is the same as that known for chasmanine 14-α-benzoate hydrochloride (De Camp & Pelletier, 1977). The molecular dimensions in (1) are normal and lie within expected values for the corresponding bond distances and angles, with mean bond distances as follows: Csp^3—N 1.449 (13), Csp^3—Csp^3 1.53 (3), Csp^3—O 1.41 (3), C—$C_{aromatic}$ 1.385 (17), Csp^2—O 1.350 (13) and C=O 1.19 (3) Å.

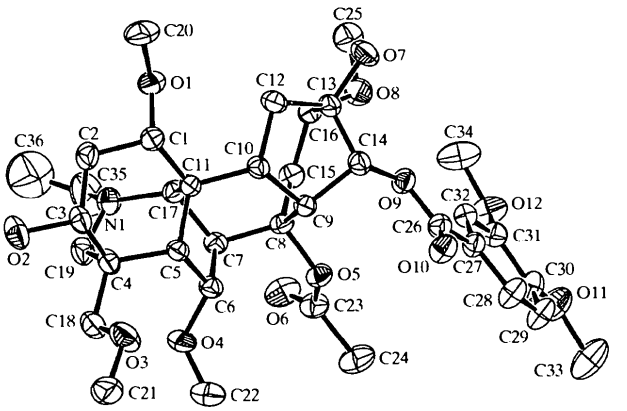


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of (1), with the atomic numbering scheme. Displacement ellipsoids are plotted at the 30% probability level. The minor fractions of C25 and C36 have been excluded.

The six-membered rings *A* (C1–C5 and C11) and *E* (C4, C5, C11, C17, N1 and C19) adopt chair conformations. These rings are slightly flattened, as observed in