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Calycanthine monohydrate

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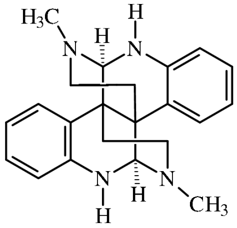
The title compound [systematic name: 21,24-dimethyl-3,12,21,24-tetraazahexacyclo[9.7.3.3^{2,10}.0^{1,10}.0^{4,9}.0^{13,18}]tetracosa-4,6,8,13(18),14,16-hexaene monohydrate], $C_{22}H_{28}N_4 \cdot H_2O$, crystallizes in space group $P2_12_12_1$ with $Z = 4$ and exhibits approximate C_2 symmetry. Intermolecular hydrogen bonds [O—H···N = 2.872 (3)° and N—H···O = 3.062 (4) Å] form chains along the direction [010].

Comment

The genus *Palicourea Aubl.* is a member of the family *Rubiaceae* and consists of approximately 200 species which are mostly distributed from Mexico to Argentina. Previous studies of this genus have yielded triterpenes (Valverde *et al.*, 1999), alkaloids (Stuart & Woo-Ming, 1975*a*), a fluoroacetate (Stuart & Woo-Ming, 1975*b*) and a cyclic polypeptide (Bokesch *et al.*, 2001), many of them possessing interesting biological properties such as anti-HIV-1 and anticancer activities. *Palicourea coriacea*, called 'douradinha', is well known in Brazilian Cerrado medicine and its leaves are used to treat kidney stones. As part of our continued interest in plants from Brazilian Cerrado we have investigated the crude extract of *P. coriacea* against gram-positive bacteria. The antibacterial activity-guided fractionation by bioautography indicated that the activity was mainly associated with the less polar alkaloid. This compound was isolated by silica-gel chromatography and the structure of the title compound, (I), has been elucidated based on spectroscopic data and confirmed by X-ray crystallographic analysis.



(I)

A search of the November 2003 release of the Cambridge Structural Database (Allen, 2002) showed that (I) has been reported as salts, with cell parameters but no atomic coordinates; calycanthine dihydrobromide dihydrate (Hamor & Robertson, 1962) was studied using film techniques. The general aspects of the calycanthine $C_{22}H_{28}N_4^{2+}$ dication have been discussed by Hamor & Robertson (1962).

Fig. 1 shows the molecule of (I) with the atomic numbering scheme. As can be seen in Table 1, the mean length of the Csp^2—N bonds of 1.413 Å is close to the accepted value of 1.40 Å. Also, the mean length of the Csp^3—N bonds of

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.065
wR factor = 0.150
Data-to-parameter ratio = 8.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

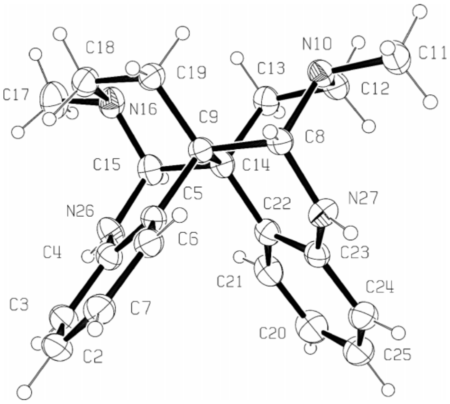


Figure 1
View of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitray radii.

1.463 Å is close to the accepted value of 1.47 Å. The rings N26→C4→···→C15 and N27→C8→···→C23 show envelope conformations, with Cremer & Pople (1975) parameters Q (Å) of 0.565 (3) and 0.551 (2), θ (°) of 52 (3) and 52 (3), and φ (°) of 243.2 (3) and 242.1 (3), respectively.

The solvent water molecule plays an important role as a bridge between calycanthine molecules, forming molecular chains running along the [010] direction, as can be seen in Fig. 2. The intermolecular N—H···O and O—H···N hydrogen-bond parameters are given in Table 2.

Experimental

The aerial parts of *Palicourea coriacea* were collected in Goiânia, State of Goiás, Brazil, and air-dried. The ethanolic extract of the leaves was submitted to acid–base treatment and fractions corresponding to different pH ranges were purified by repeated chromatographic separation and preparative thin-layer chromatography, leading to the isolation of the major alkaloid calycanthine as a brown powder. The spectroscopic data (NMR and IR) and the melting point of the calycanthine were in complete accordance with those reported in the literature (Adjibade *et al.*, 1992). Crystals of (I) suitable for single-crystal X-ray diffraction studies were obtained as brown blocks by recrystallization from chloroform and methanol (m.p. 518–523 K); ^{1}H NMR (CDCl$_3$, 300 MHz): δ 2.40 (6H, *s*), 2.26 (2H, *ddd*, J = 13.2, 11.7, 3.9 Hz), 2.60 (2H, *ddd*, J = 12.9, 6.6, 1.2 Hz), 1.30 (2H, *ddd*, J' = 13.2, 3.9, 1.5 Hz), 3.12 (2H, *td*, J = 13.2, 5.7 Hz), 6.99 (2H, *td*, J' = 7.8, 1.2 Hz), 6.53 (2H, *td*, J = 7.8; J'' = 1.2 Hz), 6.81 (2H, *td*, J = 7.8, 1.2 Hz), 6.26 (2H, *dd*, J = 7.8, 1.2 Hz); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 42.52, 46.49, 31.65, 35.89, 124.38, 124.99, 116.30, 126.50, 111.97, 145.32, 70.97; IR (KBr) $\nu_{\max}$/cm^{-1}: 3433, 3412, 2933, 2809, 1603 and 1578.

Crystal data

$C_{22}H_{26}N_4\cdot H_2O$
M_r = 364.48
Orthorhombic, $P2_12_12_1$
a = 10.419 (6) Å
b = 12.996 (2) Å
c = 13.841 (2) Å
V = 1874.1 (11) Å^3
Z = 4
D_x = 1.292 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 21.2–40.1°
μ = 0.64 mm^{-1}
T = 293 (2) K
Irregular, brown
0.35 × 0.32 × 0.20 mm

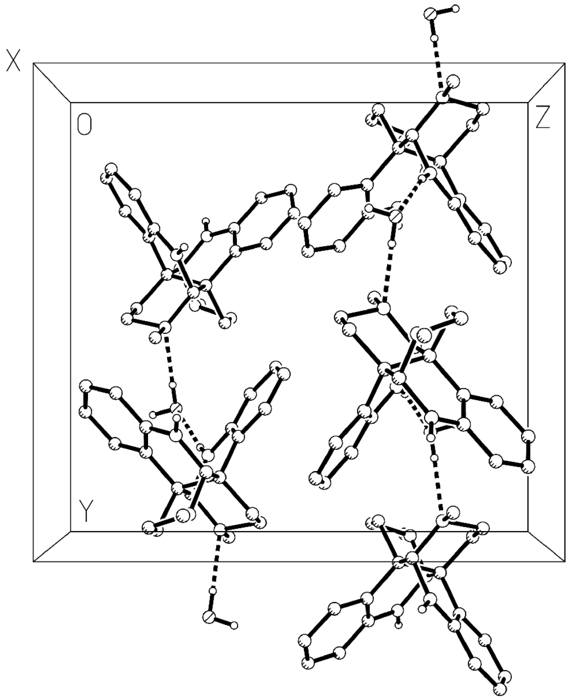


Figure 2
Packing diagram, viewed down the *a* axis. Intermolecular O—H···N and N—H···O hydrogen bonds are shown as dashed lines. Only the H atoms involved in hydrogen bonds are shown.

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: none
2102 measured reflections
2051 independent reflections
2018 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.015
$\theta_{\max}$ = 74.9°
$h = 0 \rightarrow 13$
$k = 0 \rightarrow 16$
$l = -1 \rightarrow 17$
2 standard reflections
frequency: 120 min
intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.065$
$wR(F^2) = 0.150$
S = 1.16
2051 reflections
254 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1114P)^2 + 0.1995P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.023$
$\Delta\rho_{\max}$ = 0.47 e Å^{-3}
$\Delta\rho_{\min}$ = −0.38 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.141 (8)

Table 1
Selected geometric parameters (Å, °).

C4—N26	1.376 (4)	C15—N26	1.457 (3)
C8—N27	1.442 (3)	C15—N16	1.467 (4)
C8—N10	1.481 (3)	N16—C17	1.457 (4)
N10—C11	1.453 (4)	N16—C18	1.466 (4)
N10—C12	1.476 (3)	C23—N27	1.378 (3)
C11—N10—C12	109.8 (2)	C4—N26—C15	121.6 (2)
C11—N10—C8	110.5 (2)	C4—N26—H26	119.2
C12—N10—C8	111.48 (18)	C15—N26—H26	119.2
C17—N16—C18	110.5 (3)	C23—N27—C8	122.2 (2)
C17—N16—C15	113.4 (3)	C23—N27—H27	118 (2)
C18—N16—C15	112.3 (2)	C8—N27—H27	119 (2)

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

$D-\mathrm{H}\cdots A$	$D-\mathrm{H}$	$\mathrm{H}\cdots A$	$D\cdots A$	$D-\mathrm{H}\cdots A$
O1—H1$W\cdots$N10	0.911 (17)	1.961 (18)	2.872 (3)	179 (3)
N27—H27$\cdots$O1$^{\rm i}$	0.88 (4)	2.21 (4)	3.062 (4)	165 (3)

Symmetry code: (i) $-x, \frac{1}{2}+y, \frac{3}{2}-z$.

All H atoms, except H1W, H2W and H27, were positioned geometrically and allowed to ride on their parent atoms, with C—H distances in the range 0.93–0.97 Å, and with $U_{\rm iso}$(H) = 1.5$U_{\rm eq}$(C) for methyl H atoms and 1.2$U_{\rm eq}$(C) for other H atoms. The H atoms of the water molecule were located in a difference Fourier map and were refined with O—H distances restrained to 0.88 (2) Å and with H$\cdots$H distances restrained to 1.44 (1) Å, and were refined with $U_{\rm iso}$(H) = 1.2$U_{\rm eq}$(O). These restraints ensure a reasonable geometry for the water molecule, since atom H2W is not involved in hydrogen bonding. Atom H27 was found in a difference map and refined freely. Atom H26 was positioned geometrically and its coordinates were not refined, because no hydrogen bond was observed involving N26. Due to the absence of any significant anomalous scatterers in the compound, the absolute configuration could not be determined and the 51 sets of Friedel equivalents were merged before the final refinement.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *Software*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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