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4,4,14-Trimethyl-3α,20-bis(methylamino)-9,19-cyclo-5α-pregnan-16-ol

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.007 Å
R factor = 0.064
wR factor = 0.192
Data-to-parameter ratio = 8.9

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

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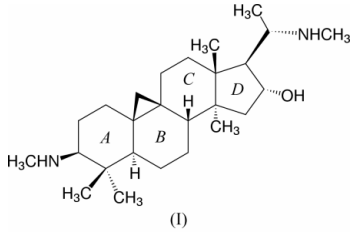
The title compound, $C_{26}H_{46}N_2O$, also known as cyclovirobuxine D, has for the first time been isolated from *Buxus papilosa*. It has a steroid nucleus in *trans*/*cis*/*trans* configuration. Two of the three cyclohexane rings adopt half-chair conformations and the third ring, with an equatorially attached methylamino substituent, is in a chair conformation. The cyclopentane ring has a half-chair conformation and the *N*-methylaminoethane group is equatorially attached to it. N—H···O and C—H···N interactions are observed in the molecular structure and the crystal structure is stabilized by van der Waals interactions.

Comment

Buxus papilosa is a shrub which grows gregariously on limestone. It is widely distributed in northern parts of Pakistan (Ikram *et al.*, 1968). Extracts of *Buxus papilosa* have been used as a febrifuge, for rheumatism and for many other ailments (Schlittler *et al.*, 1949). Plants of the genus *Buxus* are rich sources of steroidal alkaloids, and quite a large number of triterpenoidal alkaloids have been reported from different species (Shamma *et al.*, 1973). These alkaloids possess interesting anticholinesterase activities (Choudhary *et al.*, 2003).



(I)

The title compound, (I), also known as cyclovirobuxine D, has strong coronary effects on pig heart (Grossini *et al.*, 1999) and Arkopharma has identified cyclovirobuxine D as the most active agent against HIV and AIDS (Durant *et al.*, 1998). We have isolated (I) for the first time from *Buxus papilosa*. It was previously isolated from the same genus but from different species, *viz*. *B. wallichiana*, *B. sempervirens* and *B. microphylla* (*Buxaceae*).

The structure of (I) contains the fused four-ring steroid system, *A*/*B*/*C*/*D*. The steroid nucleus has a *trans*/*cis*/*trans* configuration for ring junctions *A*/*B*, *B*/*C*, *C*/*D*. Of the cyclohexane rings, ring *A* adopts a chair conformation and rings *B* and *C* adopt half-chair conformations. The cyclopentane ring *D* has a half-chair conformation. The methylamino substituent is attached equatorially to ring *A* [C1—C2—C3—N1 = −176.1 (4)°] and the C23—N1—C3—C2 torsion angle of 83.5 (7)° indicates a (+)-synclinal conformation. The *N*-

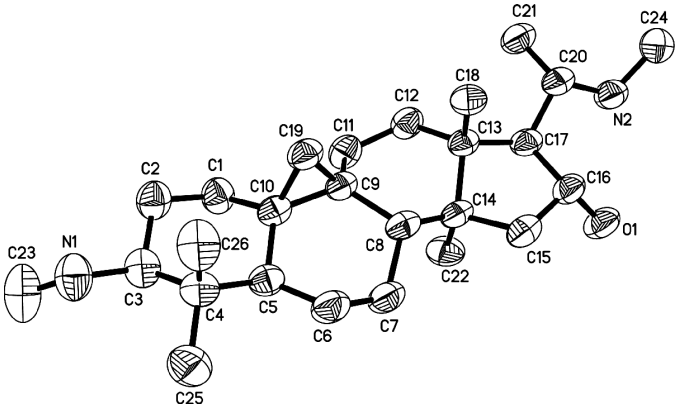


Figure 1
The structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. For clarity, H atoms have been omitted.

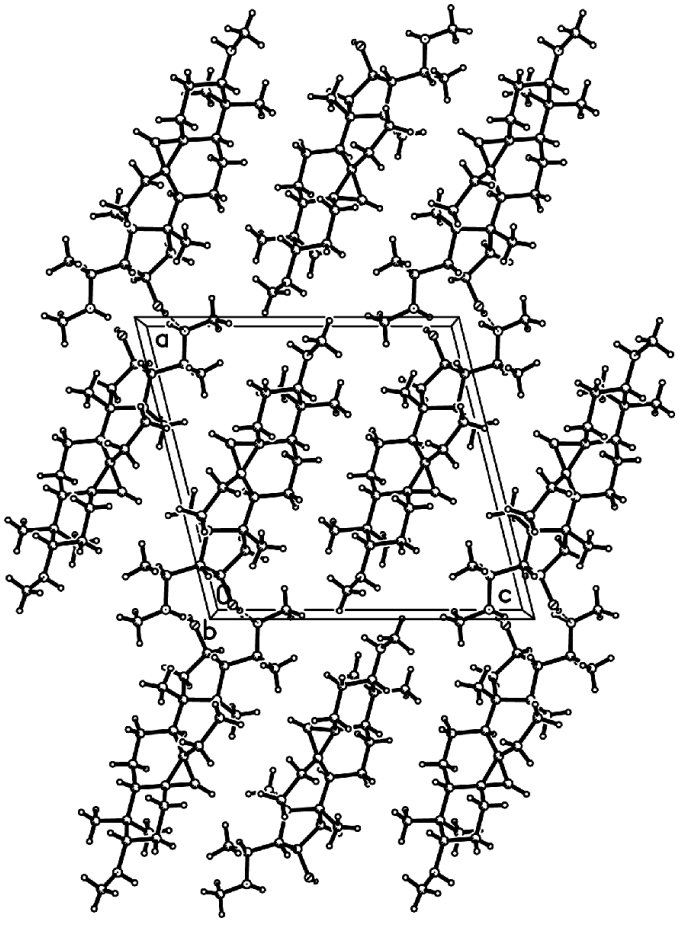


Figure 2
A view of the molecular packing in (I), viewed down the *b* axis.

methylaminoethane substituent is also attached equatorially, to ring *D* [C14—C13—C17—C20 = −165.0 (5)° and C13—C17—C20—N2 = −176.5 (4)°]. The sums of the bond angles around N1 (331.1°) and N2 (334.8°) are indicative of sp^3 character.

The bond lengths in (I) show normal values (Allen *et al.*, 1987). Intramolecular N—H···O and C—H···N interactions are observed (Table 2), but no classical intermolecular hydrogen bonds. Neither the hydroxyl group nor amino atom N2 is involved in hydrogen bonding.

Experimental

The air-dried ground roots of *B. papilosa* were soaked in methanol for a period of 7 d at room temperature. The mixture was then filtered and concentrated under reduced pressure. The concentrated aqueous methanol extract was dissolved in distilled water and defatted with petroleum ether. The aqueous layer was then acidified up to pH 3 and extracted with chloroform. The aqueous fraction was then rendered basic with liquid ammonia (pH 7–10) and extracted with chloroform to obtain the basic fraction. Comparative thin-layer chromatography of both acidic and basic extracts showed similar compounds. Therefore, both were mixed together and subjected to a repeated routine column chromatographic procedure, firstly with column silica (E. Merck, type 60) and finally using flash silica gel (E. Merck, 234–300 mesh) to afford cyclovirobuxine D, (I), after elution with petroleum ether–acetone–diethylamine (30:69:1) in 2.31 × 10^{-3}% yield (R_F = 0.79, 20% acetone: hexane and a few drops of diethylamine). Compound (I) was recrystallized from petroleum ether–chloroform–acetone (1:1:1). The melting point is 478–483 K, similar to that reported in the literature (Voticky, 1975).

Crystal data

$C_{26}H_{46}N_2O$
M_r = 402.65
Monoclinic, $P2_1$
a = 13.410 (3) Å
b = 6.7225 (13) Å
c = 13.946 (3) Å
β = 104.032 (4)°
V = 1219.6 (4) Å^3
Z = 2
D_x = 1.096 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 8359 reflections
θ = 1.5–25.0°
μ = 0.07 mm^{-1}
T = 293 (2) K
Plate, colourless
0.58 × 0.27 × 0.19 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.963, T_{max} = 0.988
6796 measured reflections
4093 independent reflections
2925 reflections with $I > 2\sigma(I)$
R_{int} = 0.026
θ_{max} = 25.0°
$h = -14 \rightarrow 15$
$k = -7 \rightarrow 7$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.064
$wR(F^2)$ = 0.192
S = 1.03
2333 reflections
263 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + 0.1417P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C23	1.425 (9)	N2—C20	1.478 (5)
N1—C3	1.468 (6)	O1—C16	1.419 (5)
N2—C24	1.457 (7)		
C23—N1—C3	115.4 (5)	C10—C19—C9	60.9 (3)
C24—N2—C20	113.4 (4)		
C23—N1—C3—C2	83.5 (7)	C13—C17—C20—N2	−176.5 (4)
C23—N1—C3—C4	−148.8 (6)	C16—C17—C20—C21	180.0 (4)
C18—C13—C14—C22	173.7 (4)	C13—C17—C20—C21	−57.9 (6)
C16—C17—C20—N2	61.4 (6)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2N···O1	0.91	2.24	2.982 (6)	139
C25—H25A···N1	0.96	2.52	2.905 (9)	104
C26—H26A···N1	0.96	2.55	2.945 (8)	105

H atoms attached to C and O atoms were placed in calculated positions (O—H = 0.82 Å and C—H = 0.96–0.98 Å), with U_{iso} values constrained to be $1.5U_{eq}$ of the carrier atom for the methyl H atoms and $1.2U_{eq}$ for the others. Atoms H1N and H2N were located in a difference map and allowed to ride on the attached atoms with $U_{iso}(H) = 1.2U_{eq}(N)$. The Friedel reflections were merged before the final refinement because of the absence of significant anomalous scattering effects. Owing to a large fraction of weak data at higher angles, the 2θ maximum was limited to 50°.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*, *PARST* (Nardelli, 1995) and *PLATON* (Spek, 1990).

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