

Neridienone A, a pregnane from the roots of *Nerium oleander*Rishi Kumar,^a Ram Sagar,^b
Arun K. Shaw^b and Prakas R.
Maulik^{a*}^aMolecular and Structural Biology Division,
Central Drug Research Institute, Lucknow 226
001, India, and ^bMedicinal and Process
Chemistry Division, Central Drug Research
Institute, Lucknow 226 001, IndiaCorrespondence e-mail:
maulik_prakas@yahoo.com

Key indicators

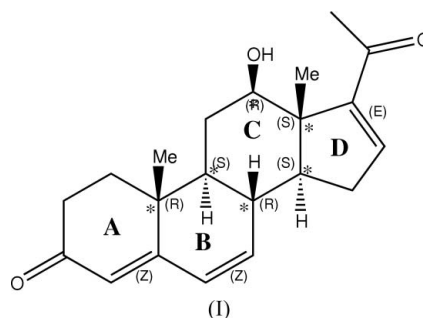
Single-crystal X-ray study
 $T = 293\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.005\text{ \AA}$
 R factor = 0.043
 wR factor = 0.097
Data-to-parameter ratio = 7.7For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

In the title compound, 12 β -hydroxypregna-4,6,16-triene-3,20-dienone, $\text{C}_{21}\text{H}_{26}\text{O}_3$, rings *A* and *B* are in almost half-chair conformations, ring *C* is in a chair conformation and ring *D* is in a 14 α -envelope conformation. The *A/B* ring junction is quasi-*trans*, whereas the *B/C* and *C/D* ring junctions both approach *trans* character. The molecule as a whole is slightly convex towards the β side. Intra- and intermolecular hydrogen bonding, together with van der Waals interactions, plays a major role in the crystal structure.

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Comment

Neridienone A is a pregnane compound and was initially isolated from the root bark of *Nerium odorum* (Yamauchi *et al.*, 1974; Abe & Yamauchi, 1976). Later, it was also isolated from the roots of *Nerium oleander* (Huq *et al.* 1999). This class of compounds has been found to possess various biological activities. 12 β -Hydroxypregn-4-ene-3,20-dienone, the dihydro derivative of neridienone A, and several other C_{21} steroids, have been found to possess effects against fish as the defence mechanism of water beetles (Chada *et al.* 1970). Neridienone A appeared to have a similar toxic effect towards goldfish as that reported for the cortexone and cybisterone derivatives (Abe & Yamauchi, 1976). This prompted us to undertake the present X-ray crystallographic study of neridienone A, (I). In the scheme, the asymmetric C atoms are indicated by asterisks.



The conformation of compound (I) and the atom-numbering scheme are shown in Fig. 1. The molecule consists of a fused four-ring system (*A*, *B*, *C* and *D*), to which an acetyl group is attached at the C17 position, two β -oriented methyl groups are attached at C13 and C10, respectively, and a β -oriented hydroxy group is attached at C12. In the molecule, rings *A* and *B* have almost half-chair conformations: the deviations of atoms C1 and C2 are -0.44 (7) and 0.23 (7) \AA , respectively, from the least-squares plane through atoms C3, C4, C5 and C10 for ring *A*, while the deviations of atoms C9 and C10 are -0.43 (6) and 0.31 (6) \AA , respectively, from the

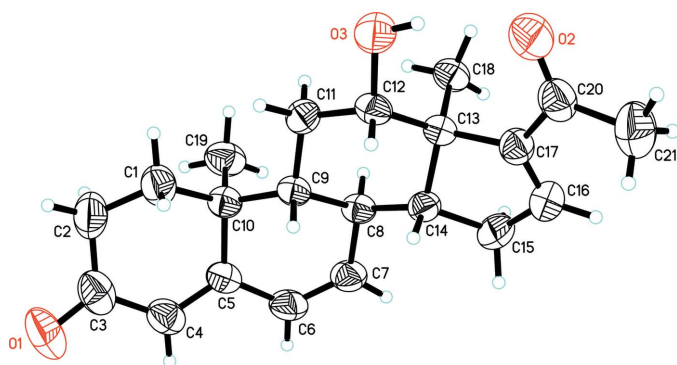


Figure 1
The molecular structure of (I), with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

least-squares plane through atoms C5, C6, C7 and C8 for ring *B*. Ring *C* has a chair conformation, with a β -equatorial hydroxyl group at C12; the deviations of atoms C9 and C13 are -0.69 (4) and 0.73 (4) Å, respectively, from the least-squares plane through atoms C11, C12, C14 and C8. Ring *D* has a 14α -envelope conformation; the deviation of atom C14 is 0.61 (5) Å from the mean plane through atoms C16, C17, C13 and C15.

The *B/C* and *C/D* ring junctions approach *trans* character, whereas the *A/B* ring junction is quasi-*trans* (Bucourt, 1974). This quasi-*trans* character is due to the existence of the trigonal atom C5. A list of the endocyclic torsion angles about the three ring junctions, which support the above mentioned ring-junction characteristics, is given in Table 2.

The molecule as a whole is slightly convex towards the β side. A list of the functional groups with their orientations and deviations from the C5–C17 mean plane (determined by all the atoms of rings *B*, *C* and *D*) is given in Table 3.

The molecular packing of (I) reveals that the hydroxy group at C12 is involved in intramolecular O–H...O hydrogen bonds. In addition to van der Waals interactions, a weak intermolecular C–H...O interaction also occurs (Fig. 2, Table 1).

Experimental

The chloroform fraction of *Nerium oleander* was subjected to repeated column chromatography over silica gel using acetone–hexane as an eluant of increasing polarity, to yield Neridienone A as a crystalline solid (m.p. 477 K; literature value 483 K). Spectroscopic analysis: ^1H NMR (200 MHz, CDCl_3 , δ , p.p.m.): 7.0 (1H, *dd*, $J = 3.0$ and 1.8 Hz, H16), 6.18 (1H, *brd*, $J = 11.4$ Hz, H7), 6.11 (1H, *d*, $J = 10.2$ Hz, H6), 5.82 (1H, *brs*, OH, disappeared on D_2O shake), 5.70 (1H, *s*, H4), 3.72 (1H, *dd*, $J = 9.5$ and 4.6 Hz, H12), 2.63 (1H, *m*, H15A), 2.59 (1H, *dd*, $J = 7.0$ and 3.2 Hz, H2A), 2.39 (3H, *s*, H21), 2.35 (1H, *m*, H15B), 2.32 (1H, *m*, H2B), 2.31 (1H, *m*, H8), 2.07 (1H, *m*, H1A), 1.98 (1H, *m*, H11A), 1.79 (1H, *m*, H1B), 1.61 (1H, *m*, H14), 1.55 (1H, *m*, H11B), 1.38 (1H, *dd*, $J = 9.8$ and 3.5 Hz, H9), 1.14 (3H, *s*, H19), 0.96 (3H, *s*, H18); FAB MS, calculated for $\text{C}_{21}\text{H}_{26}\text{O}_3$: m/z 326; found: 327 $[\text{M}+1]^+$, 309, 289, 154, 136. Diffraction quality crystals of (I) were grown by slow evaporation of a solution in acetone–hexane mixture (1.2 v/v) at room temperature.

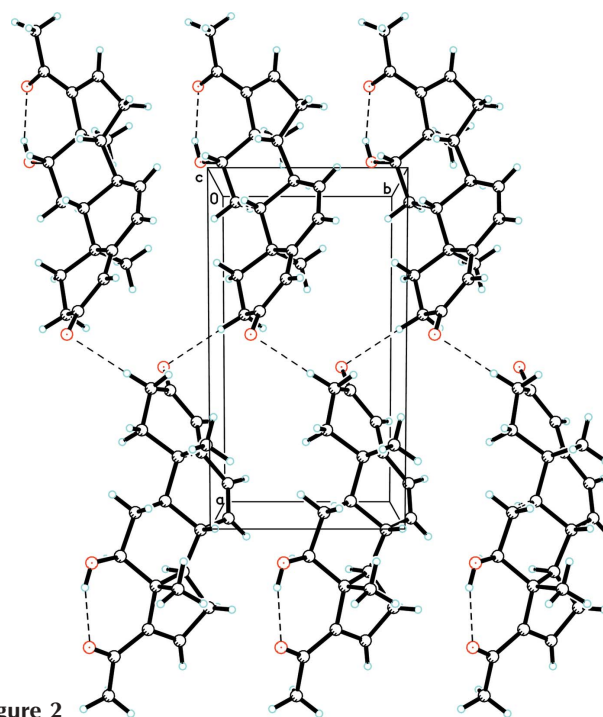


Figure 2
A molecular packing diagram for (I), showing intramolecular O–H...O hydrogen bonds and a weak intermolecular C–H...O hydrogen bond (dashed lines).

Crystal data

$\text{C}_{21}\text{H}_{26}\text{O}_3$	$D_x = 1.235 \text{ Mg m}^{-3}$
$M_r = 326.42$	Mo $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 44 reflections
$a = 11.585$ (2) Å	$\theta = 4.8$ – 12.5°
$b = 6.242$ (1) Å	$\mu = 0.08 \text{ mm}^{-1}$
$c = 12.313$ (2) Å	$T = 293$ (2) K
$\beta = 99.73$ (1) $^\circ$	Block, colourless
$V = 877.6$ (3) Å 3	$0.33 \times 0.25 \times 0.23 \text{ mm}$
$Z = 2$	

Data collection

Bruker <i>P4</i> diffractometer	$h = -13 \rightarrow 13$
$\omega/2\theta$ scans	$k = 0 \rightarrow 7$
Absorption correction: none	$l = 0 \rightarrow 14$
1704 measured reflections	3 standard reflections
1704 independent reflections	every 97 reflections
1302 reflections with $I > 2\sigma(I)$	intensity decay: none
$\theta_{\text{max}} = 25.0^\circ$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0456P)^2 + 0.0311P]$
$R[F^2 > 2\sigma(F^2)] = 0.044$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.097$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.08$	$\Delta\rho_{\text{max}} = 0.14 \text{ e } \text{Å}^{-3}$
1704 reflections	$\Delta\rho_{\text{min}} = -0.19 \text{ e } \text{Å}^{-3}$
221 parameters	
H-atom parameters constrained	

Table 1
Hydrogen-bond geometry (Å, $^\circ$).

$D\text{—}H\cdots A$	$D\text{—}H$	$H\cdots A$	$D\cdots A$	$D\text{—}H\cdots A$
C2—H2A...O1 ⁱ	0.97	2.42	3.391 (5)	174
O3—H3...O2	0.82	1.98	2.756 (3)	157

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

Table 2Endocyclic torsion angles ($^{\circ}$) about the ring junctions in (I).

Junction	Atoms	Angle	Character
A/B	C4–C5–C10–C1	18.2 (4)	Quasi- <i>trans</i>
	C6–C5–C10–C9	–40.9 (3)	Quasi- <i>trans</i>
B/C	C7–C8–C9–C10	–47.9 (3)	<i>trans</i>
	C14–C8–C9–C11	57.1 (3)	<i>trans</i>
C/D	C12–C13–C14–C8	–62.2 (3)	<i>trans</i>
	C17–C13–C14–C15	39.2 (3)	<i>trans</i>

Table 3Functional groups of (I), with their orientations and distances (\AA) from the C5–C17 mean plane.

Functional group	Orientation	Distance
C18	β -axial	1.86 (3)
C19	β -axial	1.69 (4)
O1	α -axial	–2.11 (4)
O3	β -equatorial	0.07 (4)
C20	α -axial	–0.60 (4)
C21	α	–1.32 (5)

All H atoms were placed in geometrically idealized positions and allowed to ride on their parent atoms, with C–H = 0.93–0.98 \AA and O–H = 0.82 \AA , and with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C}, \text{O})$. In the absence of significant anomalous scattering effects, Friedel pairs were merged.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL-NT* (Bruker, 1997); program(s) used to refine structure: *SHELXTL-NT*; molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXTL-NT*.

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References

- Abe, F. & Yamauchi, T. (1976). *Phytochemistry*, **15**, 1745–1748.
- Bruker (1997). *SHELXTL-NT*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
- Bucourt, R. (1974). *The Torsion Angle Concept in Conformational Analysis*, in *Topics in Stereochemistry*, edited by E. L. Eliel & N. L. Allinger, Vol. 8, p. 159. New York: Interscience.
- Chada, M. S., Joshi, N. K., Mamdapur, V. R. & Sipahimalani, A. T. (1970). *Tetrahedron*, **26**, 2061–2064.
- Huq, M. M., Jabbar, A., Rashid, M. A., Hasan, C. M., Ito, C. & Furukawa, H. (1999). *J. Nat. Prod.* **62**, 1065–1067.
- Siemens (1996). *XSCANS*. Version 2.21. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
- Yamauchi, T., Abe, F., Ogata, Y. & Takahashi, M. (1974). *Chem. Pharm. Bull.* **22**, 1680–1681.