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A new norkaurane-γ-lactone from *Parinari sprucei*

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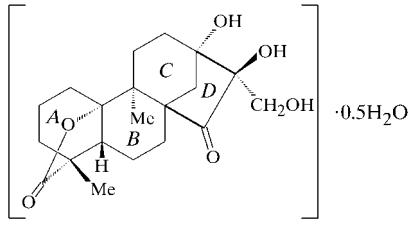
The title tetracyclic diterpenoid, 10,13,16,17-tetrahydroxy-9-methyl-15-oxo-20-norkaurane-18,10-carbolactone hemihydrate, $C_{20}H_{28}O_6{\cdot}0.5H_2O$, is a plant metabolite from *Parinari sprucei*, part of the Venezuelan Amazon flora. The asymmetric unit consists of two nearly identical molecules of the diterpenoid and one molecule of water. Some of the geometric parameters reflect steric strain in the molecule. The extended structure is characterized by hydrogen bonds and weaker hydrogen-mediated interactions, which involve all of the hydroxy groups and propagate in sheets that coincide with the (002) family of planes. The water molecule acts as a double hydrogen-bond donor and single acceptor and thus plays a critical role in the pattern of intermolecular interactions.

Comment

Tetracyclic diterpenoids with hydrocarbon skeletons derived from a rearranged norkaurane-type structure are widespread among the plant metabolites (Bruno *et al.*, 2002; Niu *et al.*, 2002; Hanson, 2003, and references therein). Many of these substances exhibit biological activities that are well known from ancient times and are used by traditional healers in the treatment of various diseases. Such substances are usually employed in Chinese medicine and agricultural practices. Owing to their possible utilization in pharmacology and farming, this class of substances has been widely investigated, and several studies concerning both the development of new synthetic strategies (King *et al.*, 1997; Zhang *et al.*, 2001; Vieira *et al.*, 2002) and structural and biological characterizations have been reported recently (Hedden & Phillips, 2000; Duan *et al.*, 2001; Rundle *et al.*, 2001; Yang *et al.*, 2002). However, while there have been many spectroscopic studies on kaurane derivatives, only a limited number of crystallographic analyses are present in the literature (*e.g.* Karle, 1972; Zabel *et al.*, 1980; Reynolds *et al.*, 1991; Hokelek *et al.*, 2001; Sun *et al.*, 2002).

The title compound, (I), was isolated from the leaves of *Parinari sprucei*, a tree of the Chrysobalanaceae family growing in the Amazon forest, as part of research on the medicinal and food plants native to Latin America (Braca *et al.*, 1999, 2000). A few other species of the *Parinari* genus have been studied in depth, leading to the identification of nor- and *ent*-kaurene diterpenes (Lee *et al.*, 1996; Garo *et al.*, 1997) strictly correlated to (I). The crystallographic study of (I) reported here was carried out in order to obtain structural information that could help find a correlation between the stereochemistry of the functional groups and the biological effects of these substances (Puliti & Mattia, 1999, 2000; Puliti *et al.*, 2001; Ciasullo *et al.*, 2002).



(I)

The asymmetric unit is formed by two diterpenoid units and one water molecule. The two independent organic molecules display geometric and conformational similarities, and are related by a pseudo-twofold axis almost parallel to the *c* direction, coupled with a translation of 2.2 Å. Upon best-fit superposition, the r.m.s. deviation of corresponding atoms, excluding the disordered hydroxymethyl group on atom C16 (see below), is only 0.027 Å, the largest difference (0.069 Å) being associated with the carbonyl O6 atom. Both of the molecules exhibit partial disorder limited to the exocyclic hydroxymethyl group on atom C16, which is disordered over two orientations in one molecule and three orientations in the other. A similar disorder, involving the axial hydroxymethyl substituent on atom C4, was found in psiadian, a related kaurane diterpene (Mossa *et al.*, 1992). In (I), the lactone ring lies on the same side (α-oriented) as the axial C20 methyl group, which is shifted from atom C10 of the normal kaurane skeleton to the C9-atom position. These structural features are also present in tetrachyrin (Zabel *et al.*, 1980) and in other tetracyclic *friedo*-kauranoids, analogues of rosane lactone, such as eupatalbin and eupatoralbin (Herz *et al.*, 1979), as well as in kaurene lactones from Zimbabwean plants belonging to the *Parinari* genus (Garo *et al.*, 1997). In addition to the tertiary hydroxy group on atom C13, which is equatorially oriented, a second tertiary hydroxy group is present on atom C16, where the hydroxymethyl substituent affected by positional disorder is also located.

Fig. 1 shows a perspective view of the two independent molecules of (I), together with the atom-labelling scheme. (The atom numbers of the second molecule are 20 greater than those of the equivalent atom in the first, while the

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numbering in the latter molecule reflects the chemical numbering scheme.) The enantiomer was chosen according to the absolute stereochemistry of an eupatalbin derivative, deduced by CD (circular dichroism) analysis (Herz *et al.*, 1979), and that of a kaurene-γ-lactone Br derivative determined using anomalous dispersion (Garo *et al.*, 1997; note that the stereochemistry at atom C9 is incorrectly reported by these authors as *R*). On this basis, the configurations at the chiral centres of (I) are fixed as 4*R*,5*R*,8*R*,9*S*,10*S*,13*S*,16*R*.

On average, bond lengths and angles (Table 1) are in the expected ranges (Herz *et al.*, 1979; Zabel *et al.*, 1980; Garo *et al.*, 1997; Hokelek *et al.*, 1999, 2001; Sun *et al.*, 2002). Some deviations from normal bond length and angle values can be attributed to intramolecular steric strain. In particular, the bond lengthening along the atomic sequence C10—C9—C8—C15—C16, as well as some deviations from the ideal Csp^3 and Csp^2 angles, help alleviate the short intramolecular O1···C20, O3···C5 and O4···C11 contacts.

The *A*/*B* and *B*/*C* ring junctions are *trans*. Rings *A* and *C* are in chair conformations, slightly distorted toward half-boats, while ring *B* adopts a twist-boat conformation. The γ-lactone group and ring *D* are both in envelope forms, with apices at atoms C5 and C14, respectively; the displacements of these atoms from the best planes through the remaining ring atoms are 0.633 (2) Å for atom C5 and 0.683 (3) Å for atom C14 [0.624 (2) Å for atom C25 and 0.711 (2) Å for atom C34].

The packing pattern is governed chiefly by hydrogen-bond interactions, which extend along the *a* and *b* directions, at $c = 0$ and $\frac{1}{2}$ (Fig. 2). Each water molecule is engaged in three hydrogen bonds, serving as a double donor to the lactone carbonyl groups of the two independent diterpene units and as a single acceptor from the tertiary hydroxy group (O2) attached to atom C13 of a screw-related molecule. Furthermore, weaker hydrogen-mediated contacts connect the organic moieties, yielding a complex array of interactions. The geometry of the hydrogen-bonding interactions and other contacts is given in Table 2. Excluding the disordered groups, the intermolecular van der Waals distances are greater than 3.40 Å for C···O interactions and greater than 3.72 Å for C···C interactions.

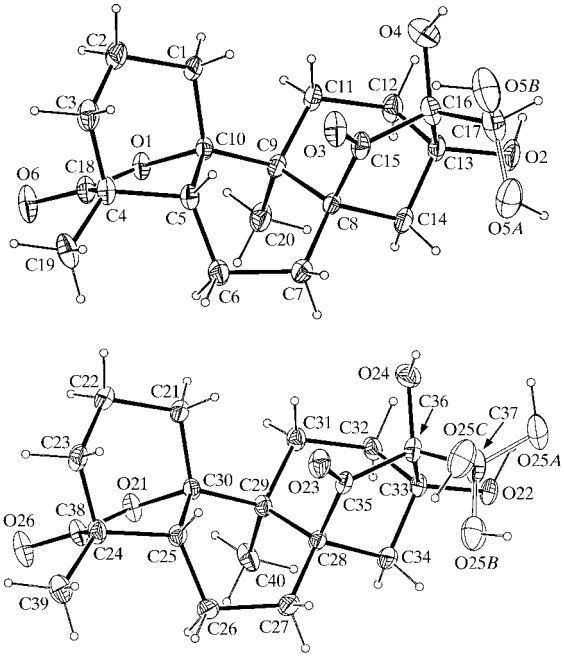

Figure 1
A perspective view of the two independent molecules of (I), showing the atom labelling for non-H atoms. Displacement ellipsoids are drawn at the 30% probability level.

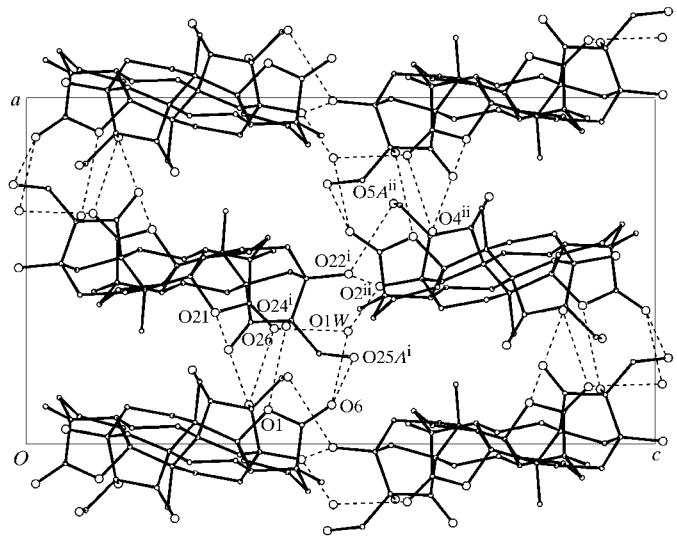

Figure 2
The crystal packing projected on to the *ac* plane. H atoms have been omitted for clarity and dashed lines indicate hydrogen bonds. [Symmetry codes: (i) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$; (ii) $\frac{1}{2}-x, 1-y, \frac{1}{2}+z$.]

Experimental

Compound (I) was isolated from a chloroform extract of air-dried leaves of *Parinari sprucei* collected in the Amazon forest of Venezuela. Single crystals were obtained by slow evaporation from chloroform at room temperature.

Crystal data

$C_{20}H_{28}O_6 \cdot 0.5H_2O$
$M_r = 746.86$
Orthorhombic, $P2_12_12_1$
$a = 11.627\ (3)$ Å
$b = 14.7157\ (19)$ Å
$c = 21.081\ (3)$ Å
$V = 3607.0\ (11)$ Å^3
$Z = 8$
$D_x = 1.375$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 27.0$–$29.5°$
$\mu = 0.84$ mm^{-1}
$T = 291.0\ (5)$ K
Rectangular prism, colourless
$0.48 \times 0.17 \times 0.09$ mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
4152 measured reflections
4152 independent reflections
3553 reflections with $I > 2\sigma(I)$
$\theta_{max} = 74.8°$
$h = 0 \rightarrow 14$
$k = 0 \rightarrow 18$
$l = 0 \rightarrow 26$
3 standard reflections
frequency: 200 min
intensity decay: none

Refinement

Refinement on F^2	$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$R[F^2 > 2\sigma(F^2)]$ = 0.032	$\Delta\rho_{min}$ = −0.23 e Å^{-3}
$wR(F^2)$ = 0.098	The absolute configuration was chosen according to that of the known bromine derivative of norkauren-γ-lactone (Garo *et al.*, 1997); this known configuration gives rise to the Flack (1983) value shown below
S = 1.04	
4152 reflections	
512 parameters	
H-atom parameters constrained	Flack parameter: 0.04 (18)
$w = 1/[\sigma^2(F_o^2) + (0.0557P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	
$(\Delta/\sigma)_{max}$ = 0.001	

Table 1
Selected geometric parameters (Å, °).

O1—C10	1.494 (2)	O21—C30	1.482 (2)
O1—C18	1.339 (3)	O21—C38	1.348 (3)
O2—C13	1.434 (3)	O22—C33	1.433 (2)
O3—C15	1.206 (3)	O23—C35	1.194 (3)
O4—C16	1.443 (3)	O24—C36	1.412 (3)
O6—C18	1.215 (3)	O26—C38	1.212 (3)
C8—C9	1.582 (3)	C28—C29	1.584 (3)
C8—C15	1.546 (3)	C28—C35	1.524 (3)
C9—C10	1.585 (3)	C29—C30	1.592 (3)
C15—C16	1.554 (3)	C35—C36	1.552 (3)
C16—C17*A*	1.514 (4)	C36—C37*A*	1.527 (3)
C17*A*—O5*A*	1.434 (4)	C37*A*—O25*A*	1.393 (3)
C10—O1—C18	109.61 (17)	C30—O21—C38	109.46 (17)
C5—C4—C18	100.49 (19)	C25—C24—C38	100.68 (18)
C5—C4—C19	116.6 (2)	C25—C24—C39	117.0 (2)
C7—C8—C9	114.06 (19)	C27—C28—C29	113.46 (18)
C7—C8—C15	114.2 (2)	C27—C28—C35	113.36 (19)
C14—C8—C15	97.68 (17)	C34—C28—C35	99.58 (16)
C1—C10—C9	115.79 (18)	O21—C30—C29	107.60 (17)
C5—C10—C9	114.78 (17)	C25—C30—C29	115.07 (17)
C14—C13—C16	102.9 (2)	C34—C33—C36	101.76 (18)
O3—C15—C8	127.0 (2)	O23—C35—C28	128.3 (2)
O3—C15—C16	122.8 (2)	O23—C35—C36	121.8 (2)
C13—C16—C15	101.5 (2)	C33—C36—C35	102.06 (17)
O1—C18—O6	120.9 (2)	O26—C38—O21	119.9 (2)
O6—C18—C4	128.3 (2)	O26—C38—C24	129.5 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H1O···O1*W*^{i}	0.95	1.79	2.720 (3)	167
O4—H2O···O21^{ii}	0.95	2.77	3.503 (3)	135
O4—H2O···O26^{ii}	0.95	2.51	3.370 (3)	150
O5A—H3O···O2	0.95	2.69	3.102 (4)	107
O5*A*—H3O···O22^{iii}	0.95	2.18	3.053 (4)	152
O5*B*—H4O···O3	0.95	2.18	2.937 (10)	135
O5*B*—H4O···O21^{ii}	0.95	2.88	3.420 (12)	117
O22—H21O···O2^{iv}	0.95	1.86	2.775 (3)	161
O22—H21O···O25*A*	0.95	2.47	2.851 (4)	104
O24—H22O···O1^{v}	0.95	2.08	3.015 (2)	168
O24—H22O···O6^{v}	0.95	2.73	3.423 (3)	130
O25*A*—H23O···O6^{v}	0.95	2.32	3.230 (5)	160
O25*B*—H24O···O22^{iv}	0.95	2.13	3.020 (7)	155
O25*C*—H25O···O5*A*^{vi}	0.95	2.21	3.029 (15)	145
O25*C*—H25O···O23	0.95	2.48	2.780 (8)	98
O1*W*—H1*W*···O6	0.95	1.91	2.842 (3)	168
O1*W*—H2*W*···O26	0.95	1.96	2.898 (3)	169

Symmetry codes: (i) $\frac{1}{2}-x, 1-y, z-\frac{1}{2}$; (ii) $-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iii) $x-\frac{1}{2}, \frac{3}{2}-y, -z$; (iv) $\frac{1}{2}+x, \frac{3}{2}-y, -z$; (v) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (vi) $1+x, y, z$.

All H atoms were found in difference Fourier maps and were included in the final refinements with idealized geometry and U_{iso}(H) values of $1.5U_{eq}$(parent atom). H atoms attached to C and O atoms were constrained to lie 1.00 and 0.95 Å, respectively, from their parent atoms. Hydroxy H atoms were refined as members of rigid groups, allowing rotation about the adjacent C—O bonds. The H atoms of disordered hydroxymethyl groups were fixed in the final cycles of refinement. The water molecule was refined as a rigid group.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *Structure Determination Package* (Enraf–Nonius, 1985); structure solution: *SIR*92 (Altomare *et al.*, 1993); structure refinement: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA1027). Services for accessing these data are described at the back of the journal.

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