Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.059$
$wR(F^2) = 0.202$
$S = 1.065$
3462 reflections
432 parameters
H atoms were treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0884P)^2 + 1.5982P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.178$ e Å^{-3}
$\Delta\rho_{min} = -0.210$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0065 (13)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute configuration: assumed rather than determined

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

O1—C2	1.365 (7)	C15—N16	1.484 (7)
C7—C8	1.462 (9)	N16—C17	1.272 (7)
C8—N9	1.271 (8)	C17—C18	1.451 (8)
N9—C10	1.476 (8)	C23—O24	1.361 (7)
O1—C2—C3	120.0 (5)	C17—N16—C15	118.6 (5)
O1—C2—C7	119.4 (6)	N16—C17—C18	123.4 (6)
C6—C7—C8	119.3 (6)	C23—C18—C17	121.9 (5)
C2—C7—C8	121.1 (6)	C19—C18—C17	118.3 (5)
N9—C8—C7	123.8 (6)	O24—C23—C18	119.4 (6)
C8—N9—C10	118.6 (5)	O24—C23—C22	120.1 (5)

Diffraction intensities from the crystals were generally weak and only 56% of the reflections were observed with $I > 2\sigma(I)$. The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985). Methyl H atoms were generated geometrically and refined using the *AFIX* option of *SHELXL*93 (Sheldrick, 1993). The other H atoms were found from a difference Fourier map. The positions of the two hydroxy H atoms were refined with isotropic displacement parameters. The positions of all methyl H atoms and of the other H atoms were refined with displacement parameters 1.3 and 1.15 times the equivalent displacement parameters of the bonded atoms, respectively. It should be noted that the absolute structure was assumed from our purchase rather than determined from the Flack (1983) parameter which gives an unreasonable value in this case, the anomalous dispersion effects being too low.

Data collection: local program (Yoon, Kim & Shin, 1994). Cell refinement: local program (Yoon, Kim & Shin, 1994). Data reduction: local program (Yoon, Kim & Shin, 1994). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1304). Services for accessing these data are described at the back of the journal.

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1-Hydroxybaccatin I, $C_{32}H_{44}O_{14}$, and 2-Deacetoxydecinnamoyltaxinine J, $C_{28}H_{40}O_9$

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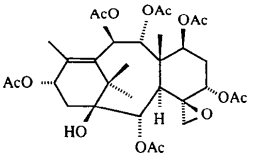
Abstract

The title compounds are diterpenoids isolated from the Himalayan yew (*Taxus wallichiana* Zucc.). The crystal structures allow us to rationalize some peculiar features of the NMR data of the taxane 4(20)-epoxides. Conformational differences between epoxide, olefin-type and oxetane-type compounds like paclitaxel are summarized.

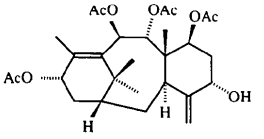
Comment

Over the past decade, considerable attention has been given to taxoids (taxane diterpenoids), a small group of diterpenoids whose archetype is the anticancer drug paclitaxel (Taxol™; Appendino, 1995). There is much heated debate regarding the active conformation of this drug and numerous X-ray investigations have been performed on paclitaxel and other oxetane-type taxoids (Mastropaolo, Camerman, Luo, Brayer & Camerman, 1995, and references therein). The other classes of taxoids have received much less attention and as a result X-ray data are not yet available for taxanes of the 4(20)-epoxide type, the suspected biogenetic precursors of

compounds of the oxetane-type (Della Casa de Marcano & Halsall, 1970). We present here a crystallographic analysis of the taxane epoxide 1-hydroxybaccatin I, (1) (Della Casa de Marcano & Halsall, 1970). The structure of a related compound of the $\Delta^{4(20)}$-type, 2-deacetoxydecinnamoyltaxinine J, (2) (Chattopadhyay & Sharma, 1995), has also been solved and compared.



(1)



(2)

The molecular structure of (1) is shown in Fig. 1. Inspection of the figure allows us to rationalize the two most typical NMR features of natural taxanes of the 4(20)-epoxide type, namely the large (*ca* 1 p.p.m.) chemical shift separation between the geminal oxirane proton, and the upfield chemical shift of H5 (Appendino *et al.*, 1994). In the unnatural α-epoxides, the epoxide protons are almost isochronous (Appendino *et al.*, 1994) and the large chemical shift separation between the oxirane protons of the natural β-epoxides is due to the downfield shift of the proton oriented toward C2 (Appendino *et al.*, 1994). Indeed, Fig. 1 shows that one of the oxirane protons is close to O2 and subjected to its magnetic anisotropy effects. On the other hand, H5 bisects the epoxide ring, thus explaining its upfield NMR resonance, which has sometimes led to an erroneous assignment of the esterification pattern of taxane epoxides (Barboni *et al.*, 1993).

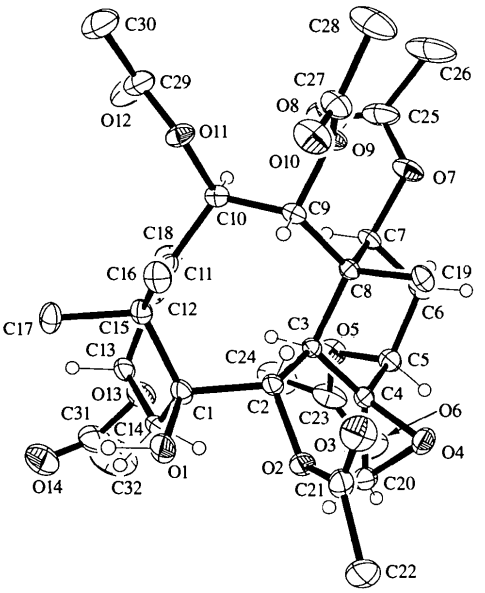


Fig. 1. Drawing of the molecule of compound (1) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

The molecular structure of (2) is shown in Fig. 2. Comparison of the torsion angle sequences in (1) and (2) (Table 1) shows that the geometry of the taxane system is very similar, with ring *A* in a boat, ring *B* in a twist-boat and ring *C* in a chair conformation. The most relevant difference with respect to the conformation of the terpenoid core of paclitaxel is the conformation of ring *C*, which in oxetane-type taxoids adopts a sofa conformation (Mastropaolo, Camerman, Luo, Brayer & Camerman, 1995) (Table 1). This leads to an overall less folded conformation of the terpenoid core in (1) and (2). In both structures, the hydroxyl groups are involved in weak intermolecular hydrogen bonds with the carbonyl O atoms of adjacent acetyl groups: in (1), O1—H···O10($1-x$, $\frac{1}{2}+y$, $1-z$), with O1···O10 3.089 (4) Å, and in (2), O1—H···O9($1-x$, $\frac{1}{2}+y$, $\frac{3}{2}-z$), with O1···O9 2.931 (7) Å.

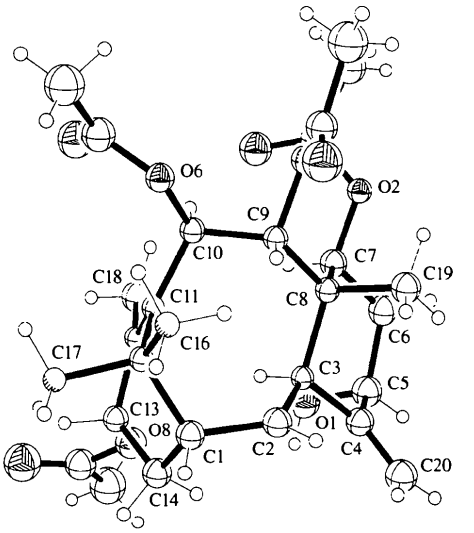


Fig. 2. Drawing of the molecule of compound (2) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

Experimental

Compounds (1) and (2) were isolated from a methanol extract of the stem bark of the Himalayan yew. Crystals were obtained by slow evaporation of acetone solutions.

Compound (1)

Crystal data

$C_{32}H_{44}O_{14}$
M_r = 652.67
Monoclinic
$P2_1$
a = 8.892 (2) Å
b = 11.261 (3) Å
c = 16.681 (5) Å
β = 93.70 (2)°
V = 1666.8 (8) Å^3
Z = 2
D_x = 1.300 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 40 reflections
θ = 14–30°
μ = 0.102 mm^{-1}
T = 293 (2) K
Prism
1.08 × 0.60 × 0.50 mm
Colourless

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction:
empirical *via* ψ scans
(North, Phillips &
Mathews, 1968)
T_{min} = 0.777, T_{max} = 0.900
5398 measured reflections
5029 independent reflections

3490 reflections with
$I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 30°
$h = -12 \rightarrow 12$
$k = 0 \rightarrow 15$
$l = 0 \rightarrow 23$
2 standard reflections
every 50 reflections
intensity decay: none

Refinement

Refinement on F^2
R = 0.058
wR = 0.151
S = 1.067
5027 reflections
414 parameters
H atoms not refined
$w = 1/[\sigma^2(F_o^2) + (0.1007P)^2 + 0.1899P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = -0.011$
$\Delta\rho_{max}$ = 0.395 e Å^{-3}
$\Delta\rho_{min} = -0.211$ e Å^{-3}
Extinction correction: none
Scattering factors from
International Tables for Crystallography (Vol. C)

Compound (2)

Crystal data

$C_{28}H_{40}O_9$
M_r = 520.60
Orthorhombic
$P2_12_12_1$
a = 10.723 (3) Å
b = 14.354 (3) Å
c = 18.592 (4) Å
V = 2861.6 (12) Å^3
Z = 4
D_x = 1.208 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 40
reflections
θ = 20–33°
μ = 0.089 mm^{-1}
T = 293 (2) K
Prism
0.60 × 0.40 × 0.32 mm
Colourless

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction:
empirical *via* ψ scans
(North, Phillips &
Mathews, 1968)
T_{min} = 0.887, T_{max} = 0.889
3073 measured reflections
2828 independent reflections

1821 reflections with
$I > 2\sigma(I)$
R_{int} = 0.011
θ_{max} = 25°
$h = 0 \rightarrow 12$
$k = 0 \rightarrow 17$
$l = 0 \rightarrow 22$
2 standard reflections
every 50 reflections
intensity decay: none

Refinement

Refinement on F^2
R = 0.055
wR = 0.129
S = 1.125
2828 reflections
334 parameters
H atoms not refined
$w = 1/[\sigma^2(F_o^2) + (0.0724P)^2 + 0.7823P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = -0.007$
$\Delta\rho_{max}$ = 0.270 e Å^{-3}
$\Delta\rho_{min} = -0.157$ e Å^{-3}
Extinction correction: none
Scattering factors from
International Tables for Crystallography (Vol. C)

Table 1. *Selected torsion angles of the terpenoid core of (1), (2) and paclitaxel (molecules A and B)*

	(1)	(2)	Paclitaxel *A*	Paclitaxel *B*
C15—C1—C2—C3	−76	−74	−71	−63
C14—C1—C2—C3	48	53	63	63
C1—C2—C3—C8	113	105	100	99
C1—C2—C3—C4	−117	−128	−133	−133
C8—C3—C4—C5	−53	−63	−25	−23
C2—C3—C4—C5	−184	−195	−155	−154
C3—C4—C5—C6	50	57	0	−5
C4—C5—C6—C7	−51	−50	−8	−5
C5—C6—C7—C8	58	53	43	43
C6—C7—C8—C3	−60	−57	−68	−70
C6—C7—C8—C9	178	179	169	168
C7—C8—C3—C4	56	61	56	57
C9—C8—C3—C2	−49	−44	−64	−63
C9—C8—C3—C4	178	185	169	169
C7—C8—C3—C2	−171	−169	−177	−175
C3—C8—C9—C10	−58	−60	−43	−42
C7—C8—C9—C10	61	60	72	73
C8—C9—C10—C11	65	61	59	59
C9—C10—C11—C15	57	60	50	48
C9—C10—C11—C12	−114	−109	−124	−124
C15—C11—C12—C13	−7	−5	−6	−5
C10—C11—C12—C13	163	164	168	167
C11—C12—C13—C14	−37	−37	−39	−41
C12—C13—C14—C1	29	25	33	37
C13—C14—C1—C15	19	24	14	10
C13—C14—C1—C2	−105	−104	−113	−117
C14—C1—C15—C11	−59	−61	−55	−53
C2—C1—C15—C11	66	65	70	72
C1—C15—C11—C12	56	54	55	54

For both compounds, data collection: *P3/PC Diffractometer Program* (Siemens, 1989); cell refinement: *P3/PC Diffractometer Program*; data reduction: *P3/PC Diffractometer Program*; program(s) used to solve structures: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structures: *SHELXTL/PC IRIS* (Sheldrick, 1990) and *SHELXL*93 (Sheldrick, 1993); molecular graphics: *SHELXTL/PC IRIS*; software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1035). Services for accessing these data are described at the back of the journal.

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L-1-Methylproline Monohydrate

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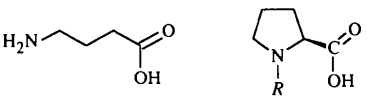
Abstract

The title compound, $C_6H_{11}NO_2.H_2O$, crystallizes in the zwitterionic form with methyl and carboxyl substituents *anti* with respect to each other. The pyrrolidine ring displays an unusual half-chair conformation C_2–C^δ-*endo* (N-*exo*). In the crystal, symmetry-related molecules form zigzag chains extending along the *a* axis. Water molecules connect pairs of these chains by forming two hydrogen bonds.

Comment

Casimiroa edulis is a plant, whose aqueous infusion exhibits potent hypotensive properties, which has been the subject of numerous studies aimed at correlating the sustained hypotension with chemical structures (Lozoya & Enríquez, 1982). Among the secondary metabolites which have been reported in relation to such pharmacological attributes are Nα–Nα-dimethylhistamine, methylhistamine and histamine (Romero, Escobar, Lozoya & Enríquez, 1983). Nevertheless, the search for other constituents continues since a satisfactory understanding of the observed pharmacological properties is still lacking.

During the course of an investigation of the polar constituents of a seed extract, three free amino acids were found in a fraction with very similar chromatographic behaviour. Thus, γ-aminobutyric acid (GABA), (I), L-proline, (II), and L-1-methylproline (hygric acid), (III), were found as the main constituents of a homogeneous fraction exhibiting moderate hypotensive properties on animals. Proline analogues have also been found in other plants (Jones, Naidu, Paleg, Tiekink & Snow, 1987; Solomon, Beer, Waisel, Jones & Paleg, 1994; Jones *et al.*, 1995) and their presence correlated with the environmental stress of the plants.



(I) (II) $R = H$ (III) $R = CH_3$

It can be seen from Fig. 1 that the L-1-methylproline molecule is present in the zwitterionic form with methyl and carboxyl substituents *anti* with respect to each other [C6—N1—C2—C7 torsion angle: −76.3 (4)°]. The pyrrolidine ring adopts a half-chair conformation [Cremer & Pople (1975) parameters: φ = 166 (1)° and Q_T = 0.373 (6) Å], with a pseudo-C_2 axis passing through the C3 atom, and the atoms N1 and C5 displaced by 0.234 (3) and 0.219 (3) Å, respectively, in opposite directions from the mean plane of the five-membered ring. This half-chair conformation differs from the envelope conformation of the pyrrolidine ring observed in L-proline (Kayushina & Vainshtein, 1965), L-hydroxyproline (Donohue & Trueblood, 1952) and 3,4-dihydroxy-L-proline (Karle, 1970). Although half-chair conformations have been found in other methyl proline derivatives (Flippen-Anderson *et al.*, 1983) and the conformation of the pyrrolidine ring in prolyl residues has been found quite flexible (Karle, 1972), the C_2–C^δ-*endo* (N-*exo*) conformation (after Ashida & Kakudo, 1974) observed in this work for the hygric acid is unusual. The dihedral angle χ_1 (N1—C2—C3—C4) of −14.7 (5)° indicates that this amino acid belongs to conformation *B* (Balasubramanian *et al.*, 1971).

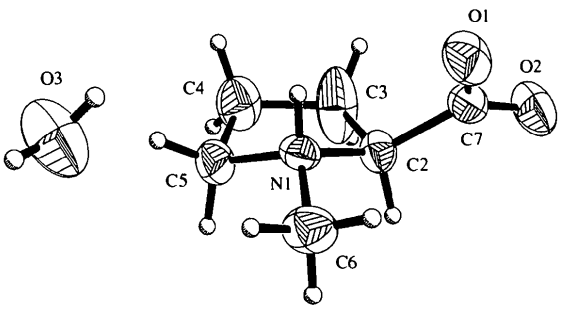


Fig. 1. The title compound showing the labelling of the non-H atoms. Displacement ellipsoids are shown at 50% probability levels.