Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

3α-Hydroxytirucalla-7,24-dien-21-oic acid: a triterpene from *Protium crenatum* Sandwith

Asiloé J. Mora,[a]* Gerzon Delgado,[a] Graciela Díaz de Delgado,[a] Alfredo Usubillaga,[b] Nancy Khouri[b] and Ali Bahsas[c]

[a]Laboratorio de Cristalografía, Facultad de Ciencias, Departamento de Química, Universidad de Los Andes, Mérida 5101, Venezuela, [b]Instituto de Investigación, Facultad de Farmacia, Universidad de Los Andes, Mérida 5101, Venezuela, and [c]Laboratorio de Resonancia Magnética Nuclear, Facultad de Ciencias, Departamento de Química, Universidad de Los Andes, Mérida 5101, Venezuela
Correspondence e-mail: asiloe@ciens.ula.ve

Received 12 September 2000
Accepted 16 February 2001

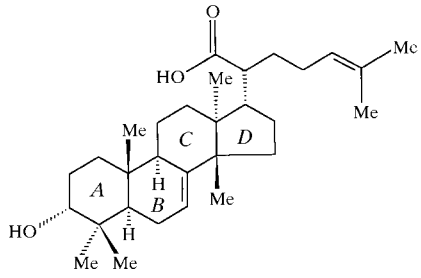
The crystal structure of the title compound, $C_{30}H_{48}O_3$, a triterpene extracted from the resin of *Protium crenatum* Sandwith, is reported. The aliphatic acidic side chain is attached to the tirucallene four-ring system on its α-face and is extended by 7.248 (5) Å in the 'left-hand' orientation.

Comment

The title compound, (I), was isolated from the resin of *Protium crenatum* Sandwith (Burseraceae), a tree about 35 m tall that grows in lowland, lower mountain and riparian forests in northern Brazil, Colombia, Guyana and Venezuela (Daly, 1997). The resin is used by the indigenous peoples as an anti-inflamatory agent. Similar tirucallane compounds have previously been isolated from elemi resin (Arigoni *et al.*, 1995; Coterrell *et al.*, 1970; Argay *et al.*, 1997), which is produced by a Burseraceae tree from the Philippine Islands. It has also been reported as a constituent of the oleoresin of *Aucoumea klaideana*, a large tree from equatorial Africa (Tessier *et al.*, 1982; Guang-Yi *et al.*, 1989). New tirucallane triterpenes have recently been reported as constituents of the bark of *Dysoxylum macranthum*, a Meliaceae tree from New Caledonia (Mohamad *et al.*, 1999).

The structure of (I) was initially inferred from ^{13}C and ^{1}H NMR data and HMBC (heteronuclear multiple bond correlation), and solved by single-crystal X-ray diffraction, which established its true composition and relative stereochemistry. However, the absolute structure was not established in this study. The configuration adopted was that occurring in all tirucallene structures found in the Cambridge Structural Database (Allen & Kennard, 1993), which implied refining the structure in the enantiomorphous space group $P3_121$.

The molecular structure of (I) (Fig. 1) shows that the *A*, *B*, *C* and *D* rings adopt chair [$\Delta C_2(2–3)_{min}$ = 1.8 (6), $\Delta C_2(3–4)_{max}$ = 9.4 (6), $\Delta C_s(2)_{min}$ = 4.2 (4), $\Delta C_s(1)_{max}$ = 8.9 (5)], half-chair [$\Delta C_2(7–8)$ = 6.5 (6)], half-chair [$\Delta C_2(9–11)$ = 6.5 (6)] and half-chair [$\Delta C_2(13–14)$ = 8.4 (5)] conformations, respectively (Griffin *et al.*, 1984).



(I)

The hydroxyl group at position 3, the methyl group at position 13 and the aliphatic chain at position 17 are substituents of the α-face of the triterpene ring system, while the methyl groups at positions 10 and 14 project out of the β-face. A similar arrangement is found in other tirucallene compounds, such as schinol, a triterpene found in the pink peppercorn (*Schinus terebinthifolius*; Jain *et al.*, 1995), and in cuachalalic acid, a triterpene from *Amphyterygium adstringens* (Watson *et al.*, 1987; Soriano-García *et al.*, 1987). This conformation seems to persist in solution, as shown by the ^{1}H NMR signal from the β hydrogen on C3 at δ = 3.50 p.p.m. (singlet). The C7═C8 bond length of 1.353 (5) Å is slightly longer than the average distance of 1.32 (1) Å observed for 15 tirucallene fragments found in the Cambridge Structural Database (Allen & Kennard, 1993).

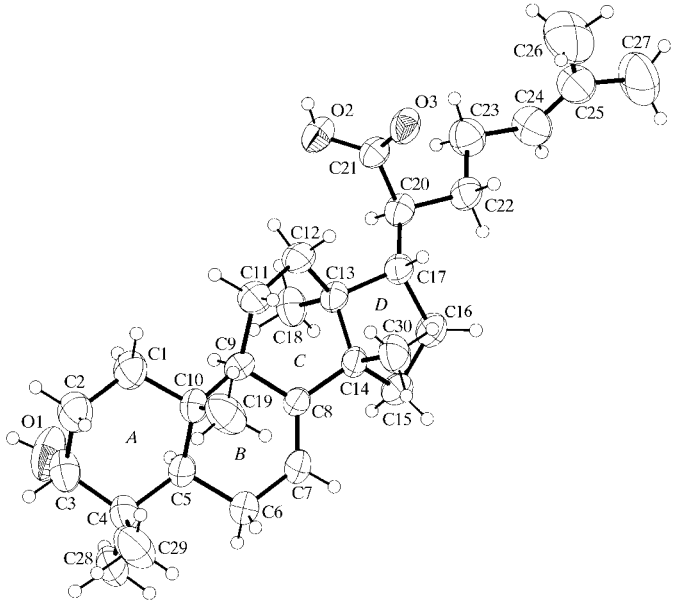


Figure 1
The molecular view of (I) showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radii.

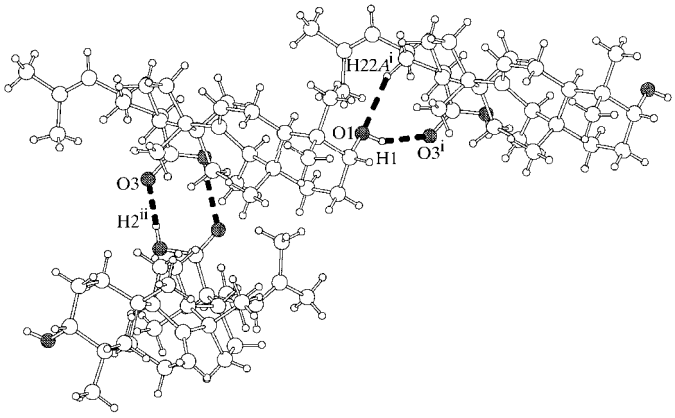


Figure 2
The hydrogen-bonding scheme for (I) [symmetry codes: (i) $1 + x, 1 + y, z$; (ii) $-x, -x + y, \frac{1}{3} - z$].

The side-chain conformation plays an important role in inhibitory activity in cell membranes (see, for example, Jain *et al.*, 1995). In compound (I), the aliphatic acidic side chain adopts a fully extended configuration in the 'left-hand' orientation [C22 *anti* to C13; C13—C17—C20—C22 −172.2 (3)°], extending by 7.248 (5) Å out of the tetracyclic nucleus. This orientation is in contrast with that found in the closely related triterpene 3-oxo-5α,13α,14β,17α-lanosta-7,24-dien-20-oic acid methyl ester from elemi resin (Argay *et al.*, 1997), in which the side chain extends towards the'right-hand' side.

The geometrical data for the principal intermolecular contacts of (I) are reported in Table 1 and these interactions are shown in Fig. 2. Chains of molecules related by a unit-cell translation along the *a* and *b* axes are linked by O—H···O═C hydrogen bonds and additional weak van der Waals C22—H22*A*···O1^{iii} contacts of 3.404 (6) Å [symmetry code: (iii) $x - 1, y - 1, z$]. A second hydrogen bond, of the type C—O—H···O═C, involving the carboxylic acid groups of molecules related by the 3_1 screw axes, results in an extended ribbon of molecules running in the [110] direction. The borders of each ribbon consist of hydrophobic methyl groups which do not form any inter-ribbon contacts.

Experimental

The resin from *Protium crenatum* Sandwith was obtained by making incisions in the bark of trees found at the Forest Reserve of Ticoporo, Barinas State, Venezuela, at an altitude of about 200 m. The resin was dissolved in diethyl ether and filtered to remove solid impurities. It was then fractionated over silica gel, eluting with hexane and hexane–diethyl ether mixtures. Fractions eluted with 8% Et_2O were subjected to preparative thin-layer chromatography, yielding 310 mg of pure 3α-hydroxytirucalla-7,24-dien-21-oic acid, (I), suitable for X-ray analysis (m.p. 473–475 K). Spectroscopic data: IR (KBr, ν_{max}, cm^{-1}): 3470, 1688; EIMS: M^+, 456 ($C_{30}H_{48}O_3$, 11°). Assignment of ^{1}H NMR and ^{13}C NMR signals was made by use of standard two-dimensional NMR techniques. ^{1}H NMR (400 MHz, $CDCl_3$, δ, p.p.m.): 5.24 (1H, *br s*, H7), 5.09 (1H, *t*, *J* = 7.2 Hz, H24), 3.50 (1H, *br s*, H3), 2.32 (1H, *m*, H9), 2.30 (1H, *dt*, *J* = 9.8 and 4.1 Hz, H20), 2.05 (1H, *d*, *J* = 8.3 Hz, H6α), 1.99 (1H, *m*, H17), 1.96 (1H, *m*, H22*A*), 1.94 (1H, *m*, H23*A*), 1.90 (1H, *m*, H2α), 1.85 (1H, *m*, H22*B*), 1.77 (1H, *m*, H6β), 1.72 (1H, *dd*, *J* = 11.8 and 5.6 Hz, H5), 1.70 (1H, *m*, H15α), 1.67 (3H, *s*, H27), 1.62 (1H, *m*, H23*B*), 1.60 (1H, *dd*, *J* = 3.2 and 7.9 Hz), 1.57 (3H, *s*, H26), 1.52 (1H, *m*, H1α), 1.51 (1H, *m*, H15β), 1.45 (1H, *m*, H16α), 1.42 (1H, *m*, H12α), 1.40 (1H, *m*, H12β), 1.32 (1H, *d*, *J* = 3.2 Hz, H1β), 1.26 (1H, *m*, H11α), 0.95 (3H, *s*, H30), 0.94 (3H, *s*, H29), 0.92 (3H, *s*, H18), 0.84 (1H, *m*, H11β), 0.80 (3H, *s*, H28), 0.72 (3H, *s*, H19); ^{13}C NMR (400 MHz, $CDCl_3$, δ, p.p.m.): 181.8 (C21), 145.3 (C8), 132.1 (C25), 123.7 (C24), 118.2 (C7), 76.5 (C3), 51.0 (C14), 49.7 (C17), 48.2 (C9), 47.8 (C20), 44.5 (C5), 43.3 (C13), 37.3 (C4), 34.8 (C10), 33.4 (C12), 32.4 (C22), 31.2 (C1), 30.2 (C15), 27.7 (C28), 27.3 (C30), 27.0 (C11), 25.7 (C27), 25.3 (C2), 23.9 (C6), 21.8 (C18), 21.7 (C29), 17.6 (C26), 17.5 (C16), 12.9 (C19).

Crystal data

$C_{30}H_{48}O_3$
M_r = 456.68
Trigonal, $P3_121$
a = 11.3717 (6) Å
c = 36.739 (3) Å
V = 4114.4 (4) Å^3
Z = 6
D_x = 1.106 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 3464 reflections
θ = 3.0–50.7°
μ = 0.07 mm^{-1}
T = 293 (2) K
Plate, colourless
0.4 × 0.3 × 0.3 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
22 258 measured reflections
2915 independent reflections
1621 reflections with $I > 2\sigma(I)$
R_{int} = 0.088
θ_{max} = 25.4°
h = −11 → 13
k = −13 → 13
l = −44 → 44

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.140
S = 0.90
2915 reflections
295 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0844P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O3^{i}	0.82	2.08	2.825 (4)	151
O2—H2···O3^{ii}	0.82	1.91	2.666 (3)	153

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

All H atoms were placed in geometrically calculated positions and their isotropic displacement parameters were set to 1.2 times (1.5 times for CH_3 groups) the equivalent displacement parameter of their parent atoms.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *DIAMOND* (Brandenburg, 1998); software used to prepare material for publication: *PLATON for Windows* (Spek, 2000) and *SHELXL*97.

We thank the CDCHT–ULA (grant No. SA-128-93), CONICIT–Venezuela (grant No. LAB-97000821) and CeCalcULA. We also thank the University of California,

Santa Barbara, for allowing the use of their facilities to collect diffraction data from the title compound during the sabbatical of GDD. The MRL facilities are funded by the MRSEC Program of the National Science Foundation under award No. DMR96-32716.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1159). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 1, 31–37.
Argay, G., Kalman, A., Vladimirov, S., Zivanov-Stakic, D. & Ribar, B. (1997). *Z. Kristallogr. New Cryst. Struct.* **212**, 61–62.
Arigoni, D., Jeger, O. & Ruzicka, L. (1995). *Helv. Chim. Acta*, **26**, 222–230.
Brandenburg, K. (1998). *DIAMOND*. Version 2.0. Crystal Impact GbR, Bonn, Germany.
Coterrell, G. P., Halsall, T. G. & Wriglesworth, M. J. (1970). *J. Chem. Soc. C*, pp. 739–743.
Daly, D. C. (1997). *Flora of the Venezualan Guayana*, Vol. 3, edited by J. Steyermark, P. E. Berry & B. K. Holst, pp. 688–728. St Louis: Missouri Botanical Garden Scientific Publications.
Griffin, J. F., Duax, W. L. & Weeks, C. M. (1984). Editors. *Atlas of Steriod Structures*, Vol. 2, pp. 7–10. New York: Plenum.
Guang-Yi, L., Gray, A. I., Patalinghug, W. C., Skelton, B. W., Waterman, P. G. & White, A. H. (1989). *Aust. J. Chem.* **42**, 1169–1170.
Jain, M. K., Yu, B.-Z., Rogers, J. M., Smith, A. E., Boger, E. T. A., Ostrander, R. L. & Rheingold, A. L. (1995). *Phytochemistry*, **39**, 537–547.
Mohamad, K., Martin, M.-T., Litaudon, M., Gaspard, C., Sévenet, T. & Païis, M. (1999). *Phytochemistry*, **52**, 1461–1468.
Sheldrick, G. M. (1997). *SHELXL*97 and *SHELXS*97. University of Göttingen, Germany.
Siemens (1996). *SMART* and *SAINT*. Versions 4.0. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Soriano-García, M., Toscano, R. A., Ortíz, B., Navarrete, A., Sanchez-Obregon, R., Barrios, H. & Yuste, F. (1987). *Acta Cryst.* C**43**, 990–991.
Spek, A. L. (2000). *PLATON for Windows*. University of Utrecht, The Netherlands.
Tessier, A. M., Delaveau, P. & Piffault, N. (1982). *Planta Med.* **44**, 215–217.
Watson, W. H., Domínguez, X. A., Vázquez, G. & García, S. (1987). *Rev. Latinoam. Quim.* **18**, 89–90.