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3,6-Dihydroxy-2-(11-phenylundecanoyl)cyclohex-2-en-1-one from *Virola venosa* bark

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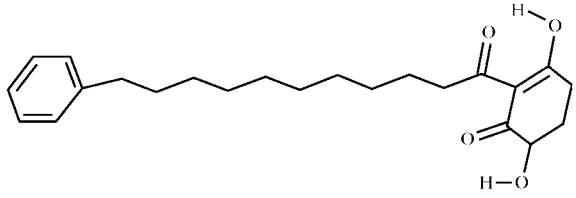
The structure of the title compound, $C_{23}H_{32}O_4$, an arylalkanone isolated from the petroleum ether fraction of the ethanol extract of the bark of *Virola venosa*, has been established by NMR spectroscopy and, for the first time, by X-ray structure analysis. Two independent molecules of the same enantiomer are present in the unit cell. Both molecules exhibit an intramolecular hydrogen bond, which can be correlated with a rare signal observed at 18.28 p.p.m. in the ^{1}H NMR spectrum. The packing, in space group *P*1, is determined by a pseudo-center of symmetry leading to a short intermolecular contact, which is present in one molecule but does not occur in the other. As a consequence, the O—C—C—O torsion angles [−16.9 (3) and −12.7 (3)°] through the ketone and its adjacent hydroxy group are significantly different in the two molecules.

Comment

Ethnobiological studies carried out in Colombia have shown that native tribes use species of *Virola* (Myristicaceae plant family) for the treatment of a wide variety of sicknesses, such as the treatment of mental instability, infected wounds, skin infections, colic and vitiligo (Schultes & Holmstedt, 1971). *Virola venosa* (Benth.) Warb. (Myristicaceae) is a tropical tree endemic at altitudes between 200 and 1300 m above sea level. The plant reaches an average height of 30 m, with a trunk diameter of 35 cm, and has been reported both in the Brazilian Amazon region, where it is known as 'ucuuba-da-mata', and in the Colombian departments Amazonas and Vaupes (Herrera, 1994). Previous publications reveal that blooms, fruits and seeds contain flavanoids, lignanes, arylalkanones and sitosterol. In leaves and roots, alkaloids and stilbenes have been detected (Kato *et al.*, 1992). Studies of the bioactivity of species from the *Virola* plant family showing antimalarial (Lopes, Kato, Andrade *et al.*, 1999), anti-inflammatory (Carvalho *et al.*, 1999), antifungal (Lopes, Kato & Yoshida, 1999; Sartorelli *et al.*, 1998) and antileishmanial activities (Barata *et al.*, 2000) have been reported. The sample of the bark of *Virola venosa* used in the present study was collected in the Amacayacu National Park in Leticia, capital of the Colombian department Amazonas. The isolation and purification of the title compound, (I), was carried out by means of chromatographic techniques. The compound was crystallized from methanol and its structure was elucidated using NMR techniques, mass spectrometry and IR spectroscopy.



(I)

The ^{1}H NMR spectrum of (I) shows a rare signal at 18.28 p.p.m., which was interpreted as an intramolecular hydrogen bond. X-Ray structure analysis shows that the unit cell contains two independent molecules, both with intramolecular hydrogen bonds. The H atoms involved in hydrogen bonding have been located. In fact, peaks for all 64 H atoms of the two molecules of (I) unambiguously emerged from difference Fourier maps. Both independent molecules (labelled *A* and *B*) show sp^2-hybridization-related electron delocalization over atoms O6, C6, C1, C7 and O7, and atoms C1, C2 and O2; this delocalization is manifested in both molecules by an average C—C bond length of 1.435 Å (Table 1). In addition, the C2*A*═O2*A* and C2*B*═O2*B* bond lengths [1.218 (3) and 1.217 (3) Å, respectively] exhibit the properties of regular double bonds, while the C═O bond lengths of the two sp^2 centers at C6 and C7 are significantly elongated in both molecules (see Fig. 1 and Table 1) and have bond orders that are intermediate between double and single bonds. The strong intramolecular hydrogen bonds between

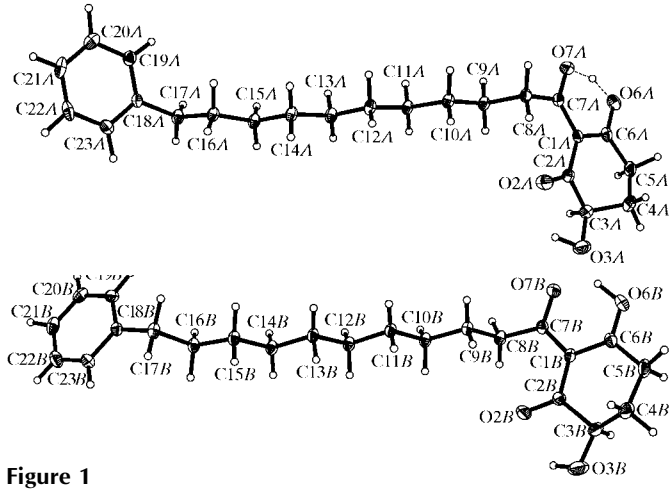


Figure 1
A view of the two molecules of (I) present in the unit cell, showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii. The absolute stereochemistry could not be determined; both molecules are shown with an *R* configuration at C3.

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atoms O6*A* and O7*A*, and atoms O6*B* and O7*B* (Table 2), in which the H atom appears not to be strictly covalently bonded to either O atom, are nearly identical within statistical significance, but in molecule *B*, the H atom appears to be more localized at atom O6 (see Fig. 1 and Table 2). We attribute the signal at 18.28 p.p.m. in the ^{1}H NMR spectrum of (I) to the H atom involved in these strong intramolecular hydrogen bonds. In solution, these differences in intramolecular hydrogen bonding disappear, as only a single resonance is observed in this region of the NMR spectrum. This fact is consistent with the possibility that any differences between molecules *A* and *B* are related to the packing in the crystal structure, as discussed below. The cyclohexane-2,6-dione system of (I) shows an envelope-like conformation, similar to that reported for (5*RS*,6*RS*)-2-acetyl-3,5,6-trihydroxy-5,6-dimethyl-2-cyclohexenone, (II) (Adembri *et al.*, 1988). Like (I), (II) forms a very strong intramolecular hydrogen bond, and these hydrogen bonds are favored by the presence of conjugated systems in both cases. The least-squares planes through these conjugated systems [HO7(6)···O6—C6—C1—C7—O7] for both molecules of (I) show a maximum deviation of 0.034 (2) Å. Each molecule also contains an additional intramolecular hydrogen bond, between hydroxy atom O3 and the neighboring O2 carbonyl group (Table 2), but in this case the hydrogen bonding is more traditional, with atom HO3 in both molecules uniquely bonded to the hydroxy O atom. This bond leads to a lack of protonation at atoms O2*A* and O2*B*, the HO3*A*···O2*A* and HO3*B*···O2*B* distances [1.83 (3) and 1.95 (4) Å] being significantly longer than all other hydrogen bonds present in the two molecules (see Table 2). As a consequence, atoms HO3*A* and HO3*B* belong to normal alcohol functions bonded to sp^3 centers, their signals occurring at 4.04 p.p.m. in the ^{1}H NMR spectrum. The C—O bond lengths at these sp^3 centers [1.416 (3) and 1.403 (4) Å] are typical of single bonds.

The packing in the present structure of (I) features an alternating head-to-tail arrangement (Fig. 2). This is induced by an approximate center of symmetry at the origin. The symmetry breaks down at the chiral atom C3, while the pseudo-center of symmetry extends otherwise throughout the entire packing scheme. A survey of the literature has yielded at least one additional structure where a pseudo-center of symmetry occurs in space group *P*1 (Olovsson *et al.*, 2001). Consistent with the existence of the approximate center of symmetry in the crystal structure, we have observed that the average absolute value of $E^*E - 1$ for (I) is 1.027, clearly consistent with the presence of the pseudo-center.

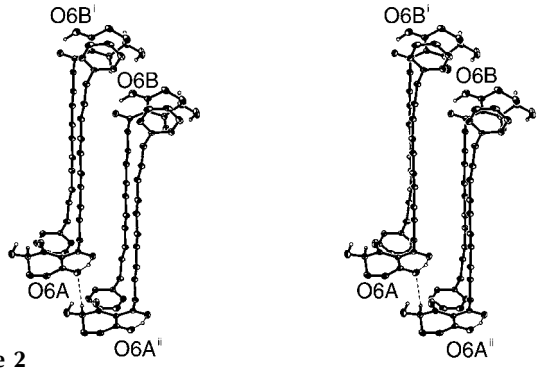

Figure 2
A packing plot, showing the alternating head-to-tail arrangement of (I) and the shortest intermolecular contact approach. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii. [Symmetry codes: (i) $x-1, y, z$; (ii) $x+1, y, z$.]

As anticipated by the presence of approximate symmetry, we have observed that overall the conformations of the two molecules are nearly identical. An exception is the ring O2—C2—C3—O3 torsion angle, which is −16.9 (3)° in molecule *A* and −12.7 (3)° in molecule *B*. This small but significant difference may be related to a close intermolecular contact between molecules *A*, in which atom O6*A* is 2.57 Å from H3*A*, the H atom bonded to C3*A* in a symmetry-related molecule (symmetry code: $x-1, y, z$; Fig. 2). The fact that this close approach occurs uniquely for only one molecule, but not for the other, clearly shows that the pseudo-center of symmetry at (0, 0, 0) is disrupted by the presence of only one enantiomer of (I). Thus, the analogous H atom, *viz*. H3*B* attached to C3*B*, of the second molecule (symmetry code: $x-1, y, z$) points away from atom O6*B* (see Figs. 1 and 2) and no close approach is possible. It seems likely that this packing difference has an influence on the intramolecular hydrogen bonds between atoms O6 and O7 in both molecules. The close contact removes electron density from atom O6*A*, and therefore atom HO7*A* is located closer to atom O7*A* in molecule *A* than atom HO6*B* is to atom O6*B* in molecule *B* (see Figs. 1 and 2).

In summary, (I) belongs to the group of arylalkanones or acylarylrecorcinols that have been found in several species of *Virola* (Myristicaceae plant family), for example, *V. elongata* (Kato *et al.*, 1985), *V. surinamensis* (Blumenthal *et al.*, 1997), *V. sebifera* (Kato *et al.*, 1985) and *V. venosa* (Kato *et al.*, 1992), in the last of which this compound has been detected in the fruits. By contrast, the present article reports, for the first time, the presence of (I) in the bark of the plant.

Experimental

A sample of *Virola venosa* bark was collected in the Amacayacu National Park in the Colombian Amazon region. The botanical determination was realized by Roberto J. Mejia from the Institute of Science, Universidad Nacional de Colombia. A voucher specimen of the plant has been deposited in the National Herbarium of Colombia, No. COL-366258. For the isolation of the compound, the dried and ground bark (1.8 kg) was extracted with ethanol (96%) at ambient temperature. After removal of the solvent, the crude extract (27 g) was treated with petroleum ether (b.p. 233–353 K), yielding, after evaporation of the solvent, a liquid (4.30 g) and a solid phase (6.10 g). The solid phase (5.0 g) was washed with methanol (3 × 2 ml) to afford the dry crude product (380 mg). Flash column chromatography was performed using a mixture of toluene/ethyl acetate (98:2) and silica gel Merck G. The combined fractions containing the compound were evaporated to dryness to yield the pure arylalkanone (184 mg). Crystallization was realized from methanol, yielding colorless geometrically homogeneous needles with a melting point of 325–326 K. The IR, ^{1}H NMR, ^{23}C NMR and EIMS spectroscopic data are more accurate than, but in agreement with, literature data (Kato *et al.*, 1985).

Crystal data

$C_{23}H_{32}O_4$
M_r = 372.49
Triclinic, $P\overline{1}$
a = 6.0335 (1) Å
b = 9.4122 (2) Å
c = 18.7857 (4) Å
α = 81.175 (1)°
β = 89.271 (1)°
γ = 80.703 (2)°
V = 1040.26 (4) Å^3
Z = 2
D_x = 1.189 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 17 747 reflections
θ = 1.0–27.5°
μ = 0.08 mm^{-1}
T = 243 (2) K
Needle, colorless
0.60 × 0.52 × 0.33 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans
7771 measured reflections
4803 independent reflections
4108 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 27.6°
$h = -7 \rightarrow 7$
$k = -12 \rightarrow 12$
$l = -24 \rightarrow 24$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.107
S = 1.03
4604 reflections
499 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0647P)^2 + 0.0674P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.13 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O2*A*—C2*A*	1.218 (3)	O2*B*—C2*B*	1.217 (3)
O3*A*—C3*A*	1.416 (3)	O3*B*—C3*B*	1.403 (4)
O6*A*—C6*A*	1.284 (3)	O6*B*—C6*B*	1.266 (4)
O7*A*—C7*A*	1.265 (3)	O7*B*—C7*B*	1.270 (3)
C1*A*—C6*A*	1.410 (3)	C1*B*—C6*B*	1.420 (3)
C1*A*—C7*A*	1.427 (4)	C1*B*—C7*B*	1.439 (4)
C1*A*—C2*A*	1.459 (3)	C1*B*—C2*B*	1.455 (4)
C6*A*—C1*A*—C7*A*	118.3 (2)	C6*B*—C1*B*—C7*B*	117.9 (2)
C6*A*—C1*A*—C2*A*	118.3 (2)	C6*B*—C1*B*—C2*B*	118.9 (2)
C7*A*—C1*A*—C2*A*	123.5 (2)	C7*B*—C1*B*—C2*B*	123.2 (2)
O2*A*—C2*A*—C1*A*	125.5 (2)	O2*B*—C2*B*—C1*B*	124.7 (2)
O6*A*—C6*A*—C1*A*	120.8 (2)	O6*B*—C6*B*—C1*B*	121.4 (3)
O7*A*—C7*A*—C1*A*	119.5 (3)	O7*B*—C7*B*—C1*B*	119.0 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3*A*—HO3*A*···O2*A*	1.13 (3)	1.83 (3)	2.576 (3)	119 (2)
O3*B*—HO3*B*···O2*B*	0.84 (4)	1.95 (4)	2.582 (3)	131 (3)
O7*A*—HO7*A*···O6*A*	1.10 (4)	1.35 (4)	2.406 (3)	157 (3)
O6*B*—HO6*B*···O7*B*	1.05 (4)	1.49 (4)	2.413 (3)	143 (3)

The absolute configuration could not be determined because of the absence of a strong anomalous scatterer in the crystal. Therefore, for the final refinement, 199 Friedel pairs were merged.

Data collection: *KappaCCD Software* (Nonius, 1997); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1998); software used to prepare material for publication: *SHELXTL-Plus*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1132). Services for accessing these data are described at the back of the journal.

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