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7-Acetyl-12-methoxyhorminone from Jamaican *Hyptis verticillata* (Labiatae)

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Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.099
Data-to-parameter ratio = 9.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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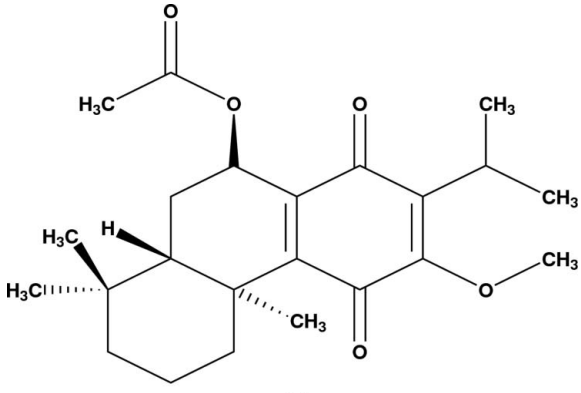
The title compound, a horminone derivative with the systematic name 7-acetyl-12-methoxyabieta-8,12-diene-11,14-dione, $C_{23}H_{32}O_5$, was isolated from *Hyptis verticillata* from St. Mary, Jamaica. In the molecule, there are three fused six-membered rings, namely a substituted quinone ring in a slight boat conformation fused to a central acetyl- and methyl-substituted cyclohexene ring in a half-chair conformation, which is *trans*-fused to a dimethyl-substituted cyclohexane ring in a chair conformation. A single weak intramolecular C—H···O hydrogen bond links molecules into extended chains in the *b* axis direction.

Comment

The *Hyptis* genus has approximately 400 species and is a member of the Labiatae family, which grows mostly in the tropical Americas. A number of these species possess significant biological activities, including teratogenic, antifertility, mycotoxinic and phytotoxinic properties (Delgado *et al.*, 1985). *Hyptis verticillata* (Labiatae), known colloquially as 'John Charles', is widely used in folklore medicine as a treatment for itching, insect stings and rheumatoid arthritis (Porter & Reese, 1998). In Mexico, the plant is known as 'hierda martina' and the whole plant is boiled and rubbed for rheumatism and skin infection (Pereda-Miranda *et al.*, 1993). The acetone and ethanol extracts of the roots of *Hyptis verticillata* have been found to have antimicrobial and cytotoxic activity (Gonzalez *et al.*, 1994). While the aerial parts have been investigated for phytochemicals, the roots have not, to date. From a dichloromethane extract of the roots, the title horminone derivative, (I), which is a new natural product, has been isolated. The synthesis of 7-acetyl-12-methoxyhorminone from 7-acetyl horminone has been reported previously (Ewards *et al.*, 1962).



(I)

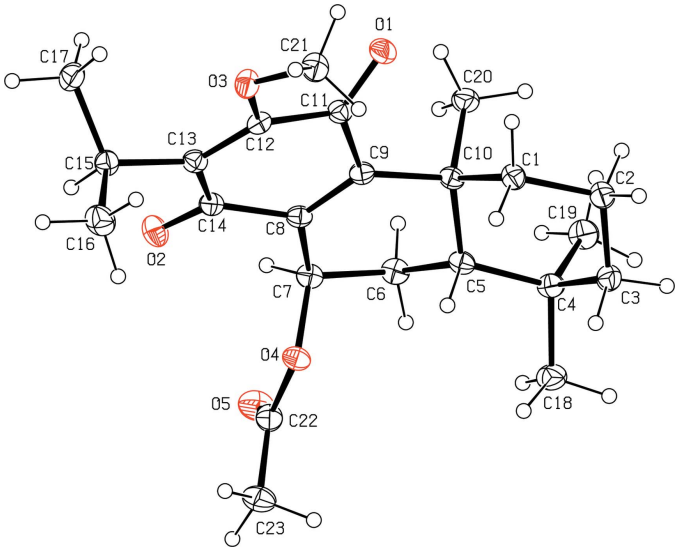


Figure 1
A view of (I), showing displacement ellipsoids drawn at the 30% probability level.

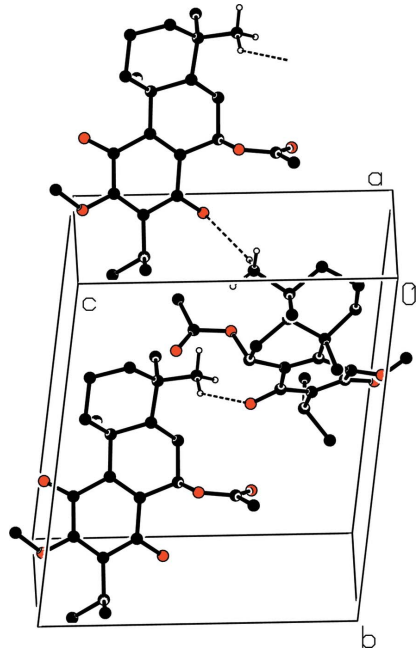


Figure 2
A view of the hydrogen bonds (dashed lines) in the crystal structure of (I). Only the H atoms of the methyl group are shown, as one of these H atoms is involved in the hydrogen bonding.

Compounds with structures closely related to that of (I) have been reported to show significant biological activity as tumour inhibitors (Jonathan *et al.*, 1989) or as antifeedants (Kubo *et al.*, 1984) and to possess antibacterial and antiviral activity (Batista *et al.*, 1995). Although a variety of compounds that contain a horminone core have been isolated and characterized using a variety of spectroscopic methods, X-ray structural reports of these compounds are relatively scarce. A search of the Cambridge Structural Database (Version 5.26 with updates to August 2005; Allen, 2002) revealed only seven structures containing the horminone core (refcodes BANREN, BANRIR, CONCYT, GAMLOV, HACGUN, KEXPUY and QICLIX).

The structure of (I) is shown in Fig. 1. The bond distances and angles are normal and similar to those reported for other compounds that contain the horminone core. The six-membered ring of the *p*-quinone group is in a slight boat conformation, with atoms C8/C9/C12/C13 essentially coplanar (r.m.s. deviation 0.028 Å), while atoms C11 and C14 lie 0.280 (4) and 0.147 (3) Å, respectively, from this plane. In the central cyclohexene ring, atoms C7–C10 are essentially coplanar (r.m.s. deviation 0.002 Å), with atoms C5 and C6 −0.566 (4) and 0.212 (4) Å, respectively, from this plane. Conformational analysis of that ring (Duax *et al.*, 1976) shows that the conformation is a half-chair, with a local pseudo-twofold axis running through the midpoints of the C5—C6 and C8—C9 bonds. The cyclohexene ring is *trans*-fused to this terminal cyclohexane ring, with the methyl group and H atom at the fusion sites being in *trans*-positions. The terminal cyclohexane ring adopts a chair conformation.

In the crystal structure, molecules related by 2_1 screw axes are linked *via* a single weak intermolecular C—H···O hydrogen bond to form one-dimensional chains in the *b* axis direction (Table 2, Fig. 2).

In view of the use of folk medicinal plants as a guide to the development of new pharmaceuticals, studies are currently in progress in our laboratories to explore the structure–activity relationship of natural products isolated from a variety of Jamaican endemic plants.

Experimental

The plant materials were collected in St. Mary, Jamaica, West Indies. A voucher specimen was deposited in the Botany Herbarium, UWI (accession No.35124). The air-dried and milled roots of *Hyptis verticillata* (6.987 kg) were extracted with hexane (2 × 8 l) and then with dichloromethane (2 × 6 l). Both extractions were performed over a 4 d period at room temperature. The dichloromethane extract was then evaporated *in vacuo* to give a dark-yellow residue (23.69 g) which was subjected to column chromatography (silica gel). A crude mixture of 7-acetyl horminone and its methoxy derivative was obtained after elution with (1–5%) ethyl acetate–hexane. The mixture was triturated using cold chloroform to give the residue, 7-acetyl horminone, and the triturant, 7-acetyl-12-methoxy horminone. When 7-acetyl-12-methoxy horminone was allowed to stand in 10% ethyl acetate–hexane solution at room temperature for several days, yellow needles of (I) were formed.

Crystal data

$C_{23}H_{32}O_5$
M_r = 388.49
Monoclinic, $P2_1$
a = 6.0049 (4) Å
b = 14.6876 (5) Å
c = 11.8412 (7) Å
β = 99.190 (2)°
V = 1030.96 (10) Å^3
Z = 2
D_x = 1.251 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5577 reflections
θ = 2.6–27.5°
μ = 0.09 mm^{-1}
T = 150 (1) K
Block cut from needle, yellow
0.26 × 0.20 × 0.16 mm

Data collection

Bruker Nonius KappaCCD area-detector diffractometer
φ scans and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995)
T_{min} = 0.838, T_{max} = 0.988
8813 measured reflections
2444 independent reflections
2018 reflections with $I > 2\sigma(I)$
R_{int} = 0.053
θ_{max} = 27.5°
$h = -7 \rightarrow 7$
$k = -16 \rightarrow 18$
$l = -14 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.099
S = 1.05
2444 reflections
261 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.052P)^2 + 0.083P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXTL/PC* (Sheldrick, 2001)
Extinction coefficient: 0.023 (5)

Table 1
Selected geometric parameters (Å, °).

O1—C11	1.221 (3)	C11—C12	1.498 (3)
O3—C12	1.352 (3)	C12—C13	1.350 (3)
O3—C21	1.442 (3)	C13—C14	1.472 (3)
O2—C14	1.224 (3)	C8—C9	1.345 (3)
O4—C22	1.354 (3)	C8—C7	1.504 (3)
O4—C7	1.470 (3)	C9—C10	1.534 (3)
O5—C22	1.205 (3)		
C12—O3—C21	121.16 (19)	C9—C10—C1	110.94 (19)
O1—C11—C12	119.7 (2)	C9—C10—C5	107.31 (18)
C12—C11—C9	118.0 (2)	C3—C2—C1	111.9 (2)
O2—C14—C13	121.6 (2)	C3—C4—C5	107.83 (19)
C13—C14—C8	119.7 (2)	C6—C5—C4	114.8 (2)
C9—C8—C7	123.7 (2)		
C21—O3—C12—C13	158.7 (2)	C8—C9—C10—C5	−22.9 (3)
C9—C11—C12—C13	−27.7 (3)	C5—C10—C1—C2	53.8 (3)
O3—C12—C13—C14	−179.1 (2)	C10—C1—C2—C3	−56.8 (3)
C11—C12—C13—C14	11.2 (3)	C1—C2—C3—C4	56.1 (3)
C12—C13—C14—C8	10.2 (3)	C2—C3—C4—C5	−51.8 (3)
C13—C14—C8—C9	−16.2 (3)	C3—C4—C5—C10	52.6 (3)
C14—C8—C9—C11	−0.2 (3)	C9—C10—C5—C6	53.6 (2)
C7—C8—C9—C11	175.5 (2)	C9—C10—C5—C4	−173.58 (19)
C14—C8—C9—C10	−175.0 (2)	C1—C10—C5—C4	−54.0 (3)
C7—C8—C9—C10	0.8 (4)	C9—C8—C7—C6	−9.3 (3)
C8—C9—C10—C1	−140.5 (2)	C5—C6—C7—C8	40.8 (3)
C11—C9—C10—C1	44.9 (3)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C18—H18*C*···O2^{i}	0.98	2.56	3.320 (3)	135

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

In the absence of significant anomalous dispersion effects, Friedel pairs were merged. The enantiomer is assigned arbitrarily. All H atoms were included in calculated positions, with C—H distances ranging from 0.98 and 1.00 Å, and were refined in a riding-model approximation, with U_{iso}(H) = 1.2U_{eq}(C), or 1.5U_{eq}(C) for methyl H atoms.

Data collection: *COLLECT* (Nonius, 2002); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXTL/PC* (Sheldrick, 2001); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXTL/PC*.

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