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A guaianolide-type sesquiterpene lactone

Ying Zhu, Min Yang and Zhong-Jian Jia*

State Key Laboratory of Applied Organic Chemistry, Chemistry and Chemical Engineering College, Lanzhou University, Lanzhou 730000, People's Republic of China

Correspondence e-mail: jiazj@lzu.edu.cn

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The title compound, 3α-hydroxy-11αH-guaia-4(15),10(14)-dien-12,6α-olide, $C_{15}H_{20}O_3$, is a 5,7,5-tricyclic guaianolide. The hydroxy group is equatorial and the methyl group is axial. Three rings, *viz*. a five-membered, a seven-membered and a γ-lactone ring, are *cis*- and *trans*-fused to each other, and adopt half-chair, chair and envelope conformations, respectively. The crystal structure is stabilized by intermolecular O—H$\cdots$O hydrogen bonds between the hydroxy group and the γ-lactone carbonyl O atom along the *b* direction.

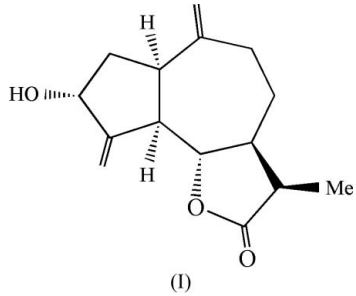
Key indicators

Single-crystal X-ray study
T = 291 K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.085
Data-to-parameter ratio = 10.0

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

Comment

The guaianolides are one of the largest groups of sesquiterpene lactones isolated from higher plants (Roberts & Bryson, 1984; Fraga, 1985, 1986, 1987, 1988, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001) and they are frequently cited as allelopathic agents, especially in plants of the family Compositae. These sesquiterpene lactones have attracted significant interest due to their biological properties, particularly their antitumor and cytotoxic activities (Bruno *et al.*, 2005; Dirsch *et al.*, 2001; Lee *et al.*, 2001; Rodríguez *et al.*, 1976). Some display strong activities against breast, colon, ovarian and lung cancers and are currently under clinical evaluation (Nosse *et al.*, 2003). Therefore, the hemisynthesis (Higuchi *et al.*, 2003; Nosse *et al.*, 2003) and total synthesis (Lange *et al.*, 1998) of these biologically active guaianolides have been reported. The current interest of our group in the phytochemical study of plants from the northwest of China is aimed both at finding new natural compounds with interesting biological activities and also at investigating the occurrence of natural terpenoids which could be used as natural sources of intermediates for the synthesis of high-added-value compounds. In this connection, we have studied guaianolides (Li & Jia, 1989; Jia *et al.*, 1991; Zhu *et al.*, 1991). In this paper, we report the crystal structure and relative stereochemistry of the title guaianolide, (I), isolated from *Saussurea macrota* Franch, which have been rigorously established by X-ray crystallography.



(I)

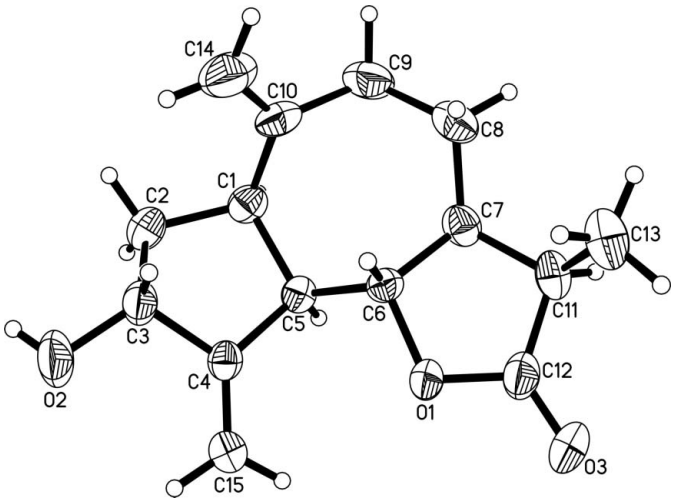


Figure 1
The structure of (I), showing 50% probability displacement ellipsoids

Colourless needle crystals of (I) were obtained by recrystallization from EtOAc. The IR spectrum shows the presence of hydroxyl (3457 cm^{-1}), γ-lactone (1751 cm^{-1}) and double-bond (1637 cm^{-1}) functionalities. As shown in Fig. 1, compound (I) is proposed to be a guaianolide having a C_{15} skeleton.

The present X-ray diffraction analysis of (I) reveals the stereochemistry of the O2 hydroxy group at C3 as the α-orientation and that of the methyl atom C13 as the β-orientation. The Csp^3-O distances are O2—C3 = 1.410 (3) Å (associated with the hydroxy group), and O1—C12 = 1.343 (3) and O1—C6 = 1.458 (2) Å in the γ-lactone. The Csp^2-O distance, in the γ-lactone is O3═C12 = 1.203 (3) Å. The bond distances of the two terminal double bonds are C4═C15 = 1.306 (3) Å and C10═C14 = 1.314 (4) Å, and the bond length of C11—C13 is 1.534 (4) Å. These bond lengths are consistent with reported values (Acosta *et al.*, 1992; Rychlewska & Serkerov, 1991; Rychlewska & Kisiel, 1991).

The ring junctions in this tricyclic molecule are *cis*-fused at C1—C5 and *trans*-fused at C6—C7, which are similar to the observations in the literature (Rychlewska & Kisiel, 1991). Torsion angles of these three rings are listed in Table 1. The seven-membered ring in most guaianolide-type sesquiterpenoids most closely approximates the twist-chair conformation. However, the seven-membered ring of (I) has a conformation that approximates more closely to a chair conformation than to a twist-chair form. An approximate mirror plane passes through atom C8 and the mid-point of the C1—C5 bond, and the asymmetry parameter ΔC_s is 1.7° (Duax *et al.*, 1974, 1976; Gómez C. *et al.*, 1987). The five-membered carbocyclic ring adopts a half-chair conformation, which has an approximate twofold axis passing through atom C5 and the midpoint of the C2—C3 bond, and the asymmetry parameter ΔC_2 is 1.5° (Duax *et al.*, 1974, 1976; Zhu *et al.*, 1991; Watson *et al.*, 1987). The γ-lactone ring can be described as having a flattened envelope conformation, with an approximate mirror plane passing through atom C7 and the midpoint of the O1—C12 bond, and the asymmetry parameter ΔC_s is 0.67° (Gómez C. *et al.*, 1987; Watson *et al.*, 1987; Watson & Zabel, 1982; Vaszquez *et al.*, 1992).

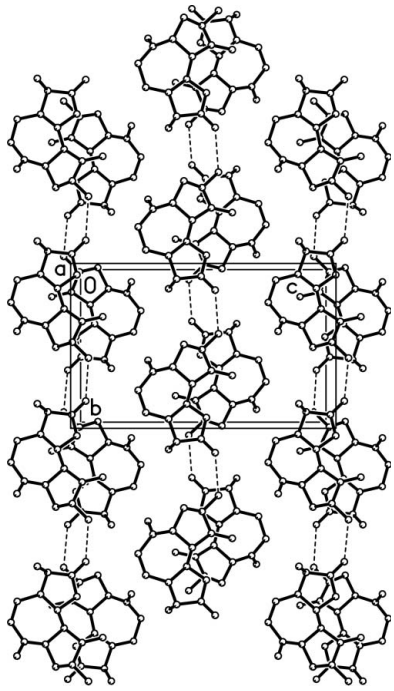


Figure 2
The molecular packing of (I). Dashed lines indicate hydrogen bonds. H atoms have been omitted.

The molecules of (I) are linked in the crystal structure by an O—H···O hydrogen bond. The hydroxy group of atom O2 as donor forms an intermolecular hydrogen bond with lactone carbonyl oxygen O3 as acceptor at (x, 1 + y, z) along the b direction (Table 2).

Experimental

Powdered whole plants of *Saussurea macrota* (6 kg) were extracted three times with methanol (15 l) at room temperature and the extract was concentrated under reduced pressure. The residue was dissolved in water (1 l) and then extracted successively with petroleum ether (330–350 K) (1 l), EtOAc (1 l) and *n*-butanol (1 l). The EtOAc-soluble fraction was separated to give compound (I) (25 mg) by repeated silica-gel (200–300 mesh) column chromatography with petroleum ether–EtOAc (3:1) [m.p. 396 K (EtOAc)]. Optical rotation: $[\alpha]_D^{25}$ +31.0° (*c* 2.5, $CHCl_3$). Crystals suitable for X-ray studies were recrystallized by slow evaporation of a solution of (I) in EtOAc at room temperature.

Crystal data

$C_{15}H_{20}O_3$
M_r = 248.31
Orthorhombic, $P2_12_12_1$
a = 8.346 (1) Å
b = 9.951 (1) Å
c = 15.934 (2) Å
V = 1323.3 (3) Å^3
Z = 4
D_x = 1.246 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 26 reflections
θ = 3.5–13.2°
μ = 0.09 mm^{-1}
T = 291 (2) K
Block, colourless
0.56 × 0.50 × 0.44 mm

Data collection

Siemens *P*4 diffractometer	$\theta_{max} = 26.9°$
ω scans	$h = 0 \rightarrow 10$
Absorption correction: none	$k = 0 \rightarrow 12$
1828 measured reflections	$l = -1 \rightarrow 20$
1661 independent reflections	3 standard reflections
1152 reflections with $I > 2\sigma(I)$	every 97 reflections
$R_{int} = 0.007$	intensity decay: 3.1%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0413P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.085$	$\Delta\rho_{max} = 0.15$ e Å^{-3}
$S = 0.98$	$\Delta\rho_{min} = -0.11$ e Å^{-3}
1661 reflections	Extinction correction: *SHELXL97* (Sheldrick, 1997)
166 parameters	Extinction coefficient: 0.032 (2)
H-atom parameters constrained	

Table 1
Selected torsion angles (°).

C5—C1—C2—C3	32.1 (2)	O1—C6—C7—C11	−26.4 (2)
C1—C2—C3—C4	−41.7 (2)	C6—C7—C8—C9	−64.7 (3)
C2—C3—C4—C5	35.7 (2)	C7—C8—C9—C10	61.3 (3)
C3—C4—C5—C1	−15.8 (2)	C5—C1—C10—C9	74.8 (3)
C10—C1—C5—C6	−8.1 (3)	C8—C9—C10—C1	−86.6 (3)
C2—C1—C5—C4	−10.2 (2)	C6—C7—C11—C12	26.5 (3)
C12—O1—C6—C7	16.4 (3)	C6—O1—C12—C11	1.2 (3)
C1—C5—C6—C7	−62.6 (3)	C7—C11—C12—O1	−18.1 (3)
C5—C6—C7—C8	88.4 (3)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2*O*···O3^{i}	0.82	1.98	2.748 (2)	157

Symmetry codes: (i) $x, y + 1, z$.

All H atoms were refined as riding on their parent atoms, with C—H = 0.93–0.98 Å and O—H = 0.82 Å, and with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(O)$. In the absence of significant anomalous dispersion effects, Friedel pairs were averaged.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1994); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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