X-RAY CRYSTALLOGRAPHIC STRUCTURAL STUDY ON A CINNAMOLIDE-CLASS SESQUITERPENE LACTONE FROM DRIMYS WINTERI FORST. VAR. CHILENSIS

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ABSTRACT

In order to ascertain the structure and secure the assignment of the stereochemistry of the title compound an X-ray analysis was performed, the absolute configuration was not determined by this analysis.

Keywords: X-ray diffraction, cinnamolide - class sesquiterpene.

INTRODUCTION

Drimys winteri J.R. Forst is a plant used in folk medicine of the many Latinoamerican countries. In Chile, *Drimys winteri* (canelo) is used by the indigenous Mapuche in the treatment of several stomachal diseases, ulcers and hemorrhages¹. Chemical studies have shown the presence of a variety of sesquiterpenes with drimane skeleton² and flavonoids. Some of these structures have shown significant antibacterial, antifungi, antitumor and insecticide properties^{3,4}. The extract of *Drimys winteri* leaves afforded Cinnamolide and Drimenin two lactones with drimane skeleton. Cinnamolide have not been previously reported for these species. Recently it has been reported that the title compound was also isolated of *Cinnamosma macrocarpa*⁵. In order to ascertain the structure and secure the assignment of the stereochemistry of the title compound an X-ray analysis was performed, the absolute configuration was not determined by this analysis. The X-ray crystallographic analysis confirms the previously proposed molecular structure, including the molecular conformation. The molecular structure is shown in Fig. 1 and selected geometric parameters are given in Table I. The structure consists of a drimane skeleton.

The methyl group at C9a is seen to be β -oriented. The cyclohexene ring A and cyclohexane ring B exist in a half-chair and a chair conformation, respectively [$Q_1 = 0.538(3)^\circ$, $\varphi_2 = 227.4(4)^\circ$, $q_2 = 0.428(3)^\circ$ for ring A; $Q_1 = 0.556(4)^\circ$, $\varphi_2 = 21(4)^\circ$, $q_2 = 0.060(4)^\circ$ for ring B], and the lactone ring an envelope on C3a conformation⁶. The A and B rings are trans-fused. Bond lengths are within expected ranges⁷. There are no unusually short contacts between the molecules and the crystal packing is controlled by weak van der Waals interactions.

Source of material

Drimys winteri was collected from the Estuary of Reloncaví, Xth Región, Chile in November 2005. 2 kg of bark was extracted in dichloromethane and concentrated under vacuum, to yield 180 g. 30 grams of crude extract was subjected to flash chromatography on silicagel G, 70-200 mesh with hexane-ethyl acetate mixtures of increasing polarity as elution solvents. Pure components were obtained by further chromatography on silicagel of the fraction 10% hexane-ethyl acetate (11 g) and recrystallization from methanol, at room temperature afforded colorless crystals of Drimenin (0.02g) suitable for X-ray diffraction analysis.

Table I. Structure determination summary for Drimenin (C₁₅H₂₂O₂).

Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
Unit cell dimensions	a = 7.6271(11)Å
	b = 12.0631(9)Å
	c = 14.5232(13)Å
Crystal	Colorless, prism, 0.13 x 0.10 x 0.08 mm
Volume, Z	1336.2(2) Å ³ , 4
Absorption coefficient	0.075 mm ⁻¹
Diffraction, scan mode	Nonius KappaCCD area-detector diffractometer, $\omega/2\theta$
N(hkl)measured, N(hkl)unique	4398, 1692
Reflections observed, I>2 σ (I)	1444
Final R indices	R ₁ = 0.0601 wR ₂ = 0.1380
R indices (all data)	R ₁ = 0.0749 wR ₂ = 0.1503
Largest diff. peak and hole	0.202 and -0.149 e.Å ⁻³
Computing structure solution	SIR97 ⁸
Computing structure refinement	SHELXL-97 ⁹
Refine ls. hydrogen treatment	Treated by a mixture of independent and constrained refinement

Table II. Atomic coordinates ($\text{\AA} \times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$). $U(\text{eq}) = (1/3) \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$ founded for ($\text{C}_{15}\text{H}_{22}\text{O}_2$).

Atom	x	y	z	U(eq)
O(1)	6371(4)	2125(3)	8176(2)	87(1)
O(2)	5174(4)	1983(2)	9565(2)	66(1)
C(1)	3742(5)	1387(3)	10002(2)	60(1)
C(3)	5208(5)	1779(3)	8655(3)	56(1)
C(3A)	3667(4)	1098(2)	8409(2)	40(1)
C(4)	3468(4)	506(3)	7662(2)	49(1)
C(5)	1943(4)	-261(3)	7539(2)	52(1)
C(5A)	592(3)	-188(2)	8330(2)	35(1)
C(6)	-866(4)	-1100(3)	8262(3)	51(1)
C(7)	-2127(5)	-952(3)	9076(3)	63(1)
C(8)	-1253(6)	-903(3)	10006(3)	71(1)
C(9)	52(5)	60(3)	10032(2)	58(1)
C(9A)	1483(3)	-55(2)	9285(2)	35(1)
C(9B)	2480(4)	1059(2)	9223(2)	38(1)
C(10)	2759(5)	-1003(3)	9508(3)	59(1)
C(11)	-196(5)	-2307(3)	8245(4)	75(1)
C(12)	-1907(6)	-893(4)	7366(3)	81(1)

Figure 1. A view of the molecular structure of ($\text{C}_{15}\text{H}_{22}\text{O}_2$), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii (ORTEP-3) ¹⁰

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