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ENT-NORAMBREINOLIDE FROM *SIDERITIS NUTANS*

Concepción Fernández, Braulio M. Fraga, Antonio G. González, Melchor G. Hernández, James R. Hanson* and Peter B. Hitchcock*

Instituto de Productos Naturales Orgánicos, C.S.I.C. and Departamento de Química Orgánica, Universidad de La Laguna, Tenerife, Canary Islands, Spain; *School of Molecular Sciences, University of Sussex, Brighton BN1 9QJ, U.K.

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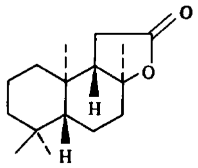
Key Word Index—*Sideritis nutans*; Labiateae; diterpenoid; *ent*-norambreinolide; X-ray analysis.

Abstract—*ent*-Norambreinolide has been isolated from *Sideritis nutans* and its structure determined by X-ray analysis.

Continuing with our work on the phytochemical study of the genus *Sideritis*, endemic to the Canary Islands [1], we describe here the X-ray structure determination of *ent*-norambreinolide (**1**), isolated from *Sideritis nutans* Svent.

This substance, molecular formula $C_{16}H_{26}O_2$, has IR absorptions characteristic of a lactone and two geminal methyl groups. Its ^1H NMR spectrum shows resonances typical of four methyls and of two hydrogens on a carbon allylic to a carbonyl group. In the mass spectrum, the molecular ion (m/z 250) readily loses a methyl group (m/z 235) or carbon dioxide (m/z 206). The loss of both gives a fragment at m/z 191. As only a small quantity of **1** was isolated, an X-ray analysis was carried out. Figure 1 shows its molecular structure. The absolute configuration was determined from the CD curve. *ent*-Norambreinolide in methanol exhibited a negative maximum at 215 nm characteristic of the structure **1**. Its enantiomer has a positive Cotton effect [2].

Compound **1** has not been obtained previously as a natural compound, but its enantiomer has been prepared synthetically by sclareol oxidation [3–5], by ozonization of 12α-hydroxy-13-epimanoyl oxide [6], and by degradation of a manoyloxide derivative [7].



1

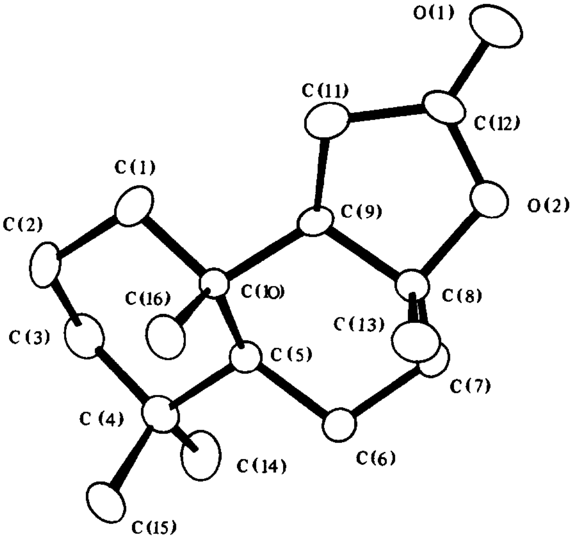


Fig 1. An ORTEP [10] drawing showing the relative molecular structure of *ent*-norambreinolide (**1**).

EXPERIMENTAL

A general description of the procedure to isolate the terpenoid compounds of species of the genus *Sideritis* has been published previously [1].

ent-*Norambreinolide* (**1**). From 700 g of *Sideritis nutans* 15 mg **1** was isolated. Mp 120–122° (from petrol–EtOAc), $[M]^+$ at m/z 250.1931 (calc. for $C_{16}H_{26}O_2$, 250.1933). IR ν_{max} cm^{-1}: 3000, 2950, 2860, 2840, 1760, 1450, 1385, 1380, 1280, 1260, 1190, 1115, 1020, 1010, 950, 925, 910. ^1H NMR (60 MHz, $CDCl_3$): δ0.84, 0.88, 0.92 and 1.33 (each 3H, *s*), 2.27 (2H, *s*). EIMS (rel. int.): 250 $[M]^+$ (1), 235 (18), 207 (11), 206 (9), 191 (7), 150 (9), 149 (6), 137 (19), 136 (14).

Crystal data. $C_{16}H_{26}O_2$, MW = 250 4, monoclinic, $a = 7.583$ (1), $b = 10.850$ (2), $c = 9.504$ (1) Å, $\beta = 110.96$ (2)°, $U = 730.2$ Å, $Z = 2$, $Dc = 1.14$ g/cm^3, F (000) = 276. Monochromated MoKα radiation, $\lambda = 0\,71069$ Å, $\mu = 0.8$ cm^{-1} Space group $P2_1$ from systematic absences of 0*k*0 for *k* odd and successful structure refinement.

Data were measured on an Enraf-Nonius CAD4 diffractometer using a crystal of size *ca* 0.2 × 0.2 × 0.2 mm. Preliminary cell dimensions were found using the SEARCH and INDEX routines of the CAD4 and final values were calculated from the setting angles for 25 reflections with $\theta \simeq 15°$. Intensities for $hk \pm 1$ reflections with $2 < \theta < 25°$ were measured by a $\theta/2\theta$ scan with a scan width of $\Delta\theta = (0\,8 + 0.35 \tan\theta)°$ The scan rate for each reflection was determined by a rapid pre-scan at $10°/\min^1$ in θ, at which point any reflection with $I < \sigma(I)$ was coded as unobserved. The remaining reflections were re-scanned at such a speed as to give a minimum value of $\sigma(I)/I$ of 0 05 subject to a maximum scan time of 60 sec. Two standard reflections monitored every hour showed no significant variation. Data were corrected for *Lp* effects but not for absorption, and after averaging any equivalent reflections 1109 reflections with $|F^2| > \sigma(F^2)$ were used in the structure refinement. The values of $\sigma(F^2)$ were taken as $|\sigma^2(I) + (0.021)^2|^{1/2}/Lp$.

The structure was solved by direct methods using the MULTAN [8] program. Refinement of non-hydrogen atoms with anisotropic temp. factors was by full-matrix least-squares. Hydrogen atoms were placed at calculated positions (C–H 1.08 Å) and held fixed with a common isotropic temp. factor of $B = 6.0$ Å [9]. Refinement converged at $R = 0.053$, $R' = 0.059$, when the maximum shift/error was 0.01 and the weighting scheme was $w = 1/\sigma^2(F)$. A final difference map was completely featureless.

The structure solution and refinement were done on a PDP 11/34 computer using the Enraf-Nonius Structure Determination Package. Scattering factors for neutral atoms were taken from ref. [9].

Final atom coordinates, a list of temperature factors, hydrogen atom positions, and final structure factors have been deposited at the Cambridge Crystallographic Data Centre.

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