The Isolation and First *X*-Ray Crystal Structures of Two New Germacra-*cis*-1(10),*cis*-4-dien-*trans*-6α,12-olides from *Melampodium*

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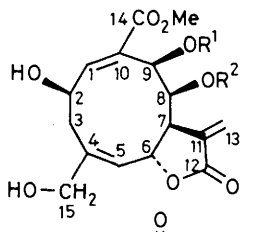
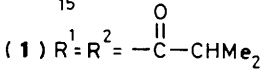
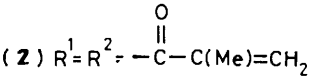
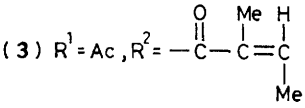
The structures of two new germacra-*cis*-1(10),*cis*-4-dien-*trans*-6α,12-olides, longicornin A from *Melampodium longicorne* and melrosin A from *M. rosei,* have been determined by single crystal *X*-ray analysis; configurational revisions of the structurally related melcanthins A—G are suggested.

Among the various skeletal types of sesquiterpene lactones from higher plants, the germacranolides represent the largest group.[1] Within the four subgroups of the 10-membered rings[2] the germacra-*cis*-1(10),*cis*-4-dienolides are the smallest in number and the only one that has no representative with an established *X*-ray structure. We had previously isolated from *Melampodium* (Compositae, Heliantheae)[3] a number of *cis*, *cis*-germacradienolides (melcanthins A—G)[4,5] but no lactones suitable for *X*-ray analysis could be obtained. Whereas the basic skeletal arrangement of the conformationally flexible melcanthin B[4] and its analogues had been unambiguously assigned by spectral (n.m.r. and m.s.) and chemical studies, its conformation was based on low-temperature ^{1}H n.m.r. data. A tentative [$_1$D$_{14,15}$D$_5$]-conformation[6] of melcanthin B was the basis for the configurational assignments 2α-OH and 9α-OAc. Later biogenetic-type studies,[7] which involved transformations of *cis*,*cis*-germacradienolides into leucantholides (*e.g.* melampodin B[8]) by the action of nucleophilic reagents suggested a conformation [^{1}D^{14},$_{15}$D$_5$] for the *cis*,*cis*-germacradienolide precursors and a C-9β-acyloxy group. These structural uncertainties made it desirable to determine the *X*-ray crystal structure of a *cis*,*cis*-medium ring compound.



(1) $R^1=R^2=$ 

(2) $R^1=R^2=$ 

(3) $R^1=Ac, R^2=$ 

Recently we isolated from *M. rosei* Robins† and *M. longicorne* A Gray† a number of new *cis,cis*-germacradienolides two of which, melrosin A and longicornin A, were crystalline. Longicornin A (**1**),‡ m.p. 145—147 °C and melrosin A (**2**),‡ m.p. 159—161 °C, which exhibited spectral parameters (n.m.r., u.v., m.s.) that were very similar to melcanthin B,[4] were chosen for the *X*-ray diffraction studies.

Crystal Data: Longicornin A, $C_{24}H_{32}O_{10}$, orthorhombic, space group $P2_12_12_1$, a = 12.278(1), b = 13.797(2), c = 14.867(2) Å, Z = 4, D_c = 1.267 g cm^{-3}, R = 0.050 for 2613 data having $F_0 > 3\sigma(F_0)$ and $2°<\theta<75°$, λ = 1.54184 Å for Cu-K_α radiation. Melrosin A, $C_{24}H_{28}O_{10}$, orthorhombic, space group $P2_12_12_1$, a = 11.993(7), b = 13.138(4), c = 15.965(13) Å, Z = 4, D_c = 1.260 g cm^{-3}, R = 0.071, for 442 data having $F_0 > 3\sigma(F_0)$ and $1°<\theta<17°$, λ = 0.71073 Å for Mo-K_α radiation. Intensity data were collected on an Enraf–Nonius CAD4 computer automated diffractometer using the ω-2θ scan technique. The structure of longicornin A was solved using direct methods. Owing to the poor quality of the melrosin A crystals, the data set was of very low resolution, and not sufficient for direct methods. However, since the structures are isomorphous, the ring system of the longicornin A model was used as a starting point for the solution of melrosin A. In both cases refinement was carried out using full-matrix least-squares procedures. Non-hydrogen atoms were refined anisotropically in the longicornin A structure while the melrosin A model is totally isotropic. Hydrogen positions were refined for longicornin A and are in calculated positions for melrosin A.§

The novel germacra-*cis*-1(10),*cis*-4-dienolide skeleton of these molecules is shown in Figure 1, which contains the endocyclic torsion angles for longicornin A. The torsion angle pattern for the cyclodecadiene rings indicates that the conformations of the ring system of the two molecules are experimentally indistinguishable. The conformational agreement is verified by the root-mean-square deviation of the torsion angles, calculated to be 3.4° for the 10-membered rings.

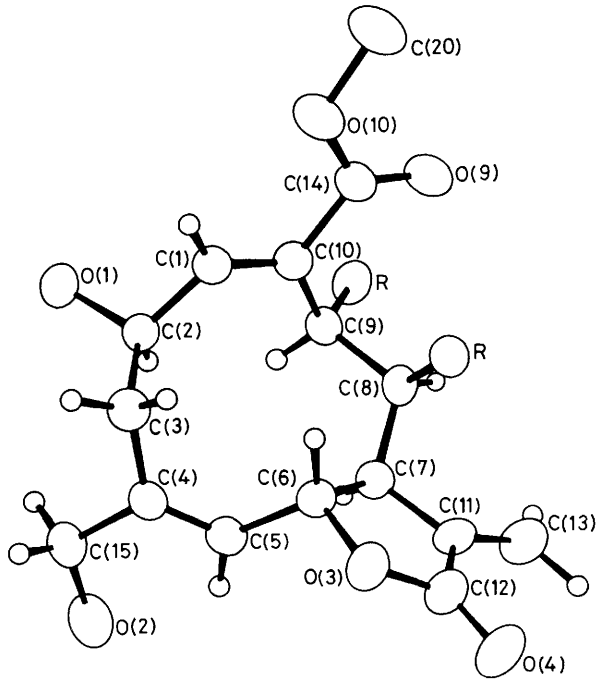


Figure 1. Basic skeletal structure of longicornin A and melrosin A. Substituents at C(8) and C(9), as well as all substituent hydrogen atoms have been omitted for clarity. Endocyclic torsion angles for longicornin A are C(10)–C(1)–C(2)–C(3) 102.1, C(1)–C(2)–C(3)–C(4) −119.0, C(2)–C(3)–C(4)–C(5) 83.0, C(3)–C(4)–C(5)–C(6) 1.8, C(4)–C(5)–C(6)–C(7) −118.7, C(5)–C(6)–C(7)–C(8) 120.6, C(6)–C(7)–C(8)–C(9) −67.4, C(7)–C(8)–C(9)–C(10) 105.6, C(8)–C(9)–C(10)–C(1) −112.8, and C(9)–C(10)–C(1)–C(2) −2.0°. Estimated standard deviations are 0.2—0.3°.

Since the ^{1}H n.m.r. spectral data for the medium ring portion of longicornin A (**1**) and melrosin A (**2**) and their analogues were nearly identical with melcanthin B and its congeners this strongly suggests that the major conformation of the melcanthins is also [$^1D^{14},_{15}D_5$] as in (**1**) and (**2**) (Figure 1). Consequently, the chiral centres C(9) in melcanthin A—G[4,5] and C(2) in melcanthin B and C[4] should be revised to configurational representations as shown for melcanthin B (**3**).

Received, 19th August 1982; Com. 1002

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† *Melampodium rosei* was collected in Sinaloa, Mexico (Hartman & Funk No. 4310) and *M. longicorne* in Pima County, Arizona (Hartman and Funk No. 4385). The plants were identified by Prof. T. F. Stuessy, Ohio State University and vouchers are deposited at the Herbarium of Ohio State University.

‡ Satisfactory elemental analyses were obtained.

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.