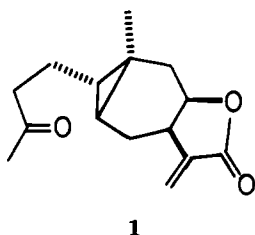


SESQUITERPENE LACTONES FROM A POPULATION OF
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Previous publications (1-7) have described some of our work on the chemical constituents of several *Helenium* species (Compositae), a genus of ca. 50 members (8) located mainly on the American continent. The biological and agricultural importance of this group of plants is well known inasmuch as several species are highly toxic and, when eaten by dairy cattle, impart a bitter taste to their milk (9). Helenanolides are the main constituents of this genus, although its classification by flavonoid chemistry has been proposed (10, 11).

Here we report that the sesquiterpene lactones carabrone [**1**] (12) and linifolin A [**2**] (13, 14) were isolated from the extracts of aerial parts of a population of *Helenium integrifolium* (H.B.K.) Benth. & Hook. [*Dougaldia integrifolia* (H.B.K.) Cass.].

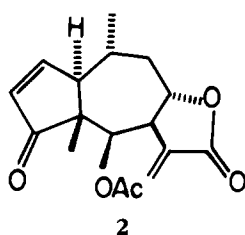


Because of the various stereochemical arrangements and conformational distortions of the cycloheptane ring, and X-ray analysis of linifolin A [**2**] was undertaken. Crystal data for **2** are listed in the Experimental Section. Figure 1 shows the computer generated drawings of two crystallographically independent molecules (A and B) existing in the solid state

and differing only slightly in the conformation of the seven-membered ring.

Table 1 lists atomic coordinates of the conformer A, and tables listing atomic coordinates, bond lengths, bond angles, hydrogen coordinates, and structure factors of both conformers (A and B) are available on request to the senior author.

The conformation of the cycloheptane ring of **2** approximates to a half-distorted chair, similar to the conformations found in stramonin B (15) and bromohelenalin (16), but different from the conformations found in florigrandin (17), rudmollin (18), and hymenolane (19), where the cycloheptane ring is a boat. Figure 1 also indicates that the observed values for $J_{6,7}$ and $J_{7,8}$ (4.7 and 9.2 Hz) (13) accord with structure **2** where the dihedral angles involving H(6)-H(7) and H(7)-H(8) are 32 and



163°, respectively. The cyclopentane ring is an envelope with C(5) as the flap.

EXPERIMENTAL

PLANT MATERIAL.—Aerial parts of *H. integrifolium* were collected near Nevado de Toluca volcano, State of Mexico, in September 1983. Reference specimens are deposited in the National Herbarium, Instituto de Biología de la Universidad Nacional Autónoma de México (voucher GD 1153).

EXTRACTION AND ISOLATION.—Air-dried aerial parts (2.58 kg) were twice extracted with

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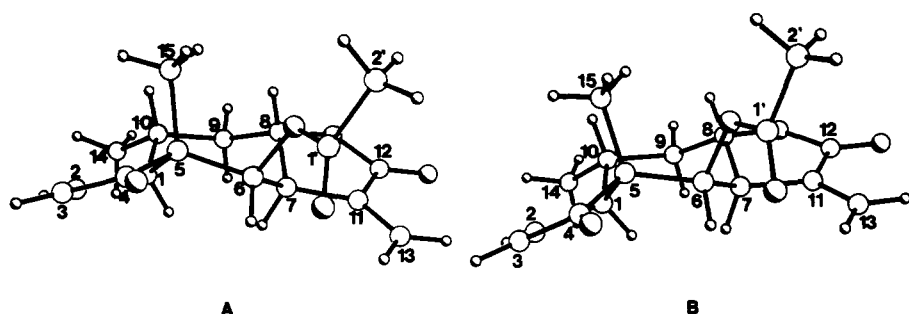


FIGURE 1. Computer-generated drawings of two crystallographically independent molecules (A and B) of linifolin A [2].

hexane to afford 37.1 g residue, and then with $\text{Me}_2\text{CO}-\text{CH}_2\text{Cl}_2$ (1:1, twice) affording 49.1 g syrup. The hexane extract was charged on a silica gel column eluted with hexane-EtOAc gradient beginning with 100% hexane. Carabrone [1] [mp 86-88°, lit. 90-91° (12)] was obtained from fractions eluted with hexane-EtOAc (4:1). The $\text{Me}_2\text{CO}-\text{CH}_2\text{Cl}_2$ extract was also chromatographed on a silica gel column using a hexane- Me_2CO gradient elution system. Compound 1 was also isolated from the less polar fractions of this chromatography, and linifolin A [2] was crystallized from the fractions eluted with hexane- Me_2CO (7:3) (mp and mmp 188-190°). The total yield of 1 was 0.15% and of 2, 0.07% (dry wt). The compounds were identified by comparison of spectral data (ir, uv, ^1H and ^{13}C nmr) and by direct comparison with authentic samples.

CRYSTALLOGRAPHIC ANALYSIS OF 2.—X-Ray structure analysis.—Linifolin A [2] was crystallized by slow evaporation from hexane/ Me_2CO solution. Crystal data: $\text{C}_{34}\text{H}_{40}\text{O}_{10}$, $M_w=608.7$, orthorhombic, space group $\text{P}2_12_12_1$, $a=6.463(5)$, $b=12.872(4)$, $c=37.911(13)\text{\AA}$, $V=3154(1)\text{\AA}^3$, $D_c=1.28\text{ g cm}^{-3}$, $F(000)=1296$, $T=293\text{ K}$, $Z=8$, $\mu(\text{MoK}\alpha)=0.88\text{ cm}^{-1}$. Using a crystal $0.32\times0.35\times0.48\text{ mm}$, lattice parameters were obtained from 25 machine-centered reflections with $4.3<2\theta<21.5^\circ$. Reflections in one octant of reciprocal space were measured with an index range of $h\ 0\rightarrow6$, $\ell\ 0\rightarrow13$, $\ell\ 0\rightarrow40$, using the ω -scanning mode with graphite-monochromatized $\text{MoK}\alpha$ radiation on a Nicolet R3m four-circle diffractometer, variable scan speed, scan width $1.0\ (^\circ)$, and two standard reflections ($0\ 2\ \bar{9}; 0\ 4\ \bar{1}$) monitored every 50 measure-

TABLE 1. Positional Parameters ($\times 10^4$) and Equivalent Isotropic Temperature Factors (\AA^2) for conformer A of linifolin A [2]

$$U_{\text{eq}}=(U_{11}\times U_{22}\times U_{33})^{1/3}$$

Atom	x	y	z	U_{eq}
O(1a)	12402(7)	9877(3)	2575(1)	67(1)
O(2a)	9047(6)	9167(3)	1948(1)	48(1)
O(3a)	4678(6)	6963(3)	2008(1)	53(1)
O(4a)	5218(8)	6152(2)	1493(1)	82(2)
O(5a)	12307(8)	9118(4)	1735(1)	94(2)
C(1a)	8479(8)	8134(4)	2875(1)	39(2)
C(2a)	9694(11)	8505(5)	3196(1)	56(2)
C(3a)	11178(11)	9167(5)	3115(1)	61(2)
C(4a)	11152(9)	9382(4)	2737(1)	49(2)
C(5a)	9147(9)	8911(3)	2588(1)	39(2)
C(6a)	9483(8)	8417(3)	2218(1)	34(1)
C(7a)	8098(8)	7471(4)	2156(1)	39(2)
C(8a)	5800(9)	7629(4)	2245(1)	41(2)
C(9a)	5234(9)	7312(4)	2619(1)	46(2)
C(10a)	6129(10)	7945(4)	2921(1)	44(2)
C(11a)	8035(10)	7045(4)	1792(1)	50(2)
C(12a)	5877(11)	6664(4)	1734(1)	57(2)
C(13a)	9481(12)	6946(5)	1548(2)	73(3)
C(14a)	5643(12)	7396(5)	3266(2)	70(2)
C(15a)	7673(10)	9879(4)	2576(2)	53(2)
C(16a)	10585(12)	9437(5)	1720(2)	68(2)
C(17a)	9752(16)	10188(6)	1454(2)	107(4)

ments. The intensities were corrected for Lorentz and polarization effects, but no absorption corrections were applied. Of the 2389 reflections within the 2θ range of 3° – 45° collected, 2132 had values of $|F_o|^2$ that were greater than three times their estimated standard deviations, and these were used in the final refinement of structural parameters. The structure was solved by direct methods (20) with some difficulties, which are inherent to the space group. The correct structure was found using 200 phases with $|E| > 1.4$ and ten reflections in the starting set, and refined by cascade matrix least-squares techniques with anisotropic temperature factors for the nonhydrogen atoms. The H atoms of the tertiary CH, secondary CH₂, and primary CH₃ groups were assigned coordinates based on the expected bonding geometry. All H atom coordinates were refined and had a fixed isotropic temperature factor, $U = 0.06 \text{ \AA}^2$. The function minimized was $\Sigma \omega(\Delta F)^2$ with a statistical weight of the form $\omega = \sigma^2(F_o) + 0.003(F_o)^2$, where σ is the standard deviation of the observed amplitudes based on counting statistics. The final conventional R factor was 0.053 and $\omega R = 0.076$ ($\omega R = [\Sigma \omega(|F_o| - |F_c|)^2 / \Sigma |F_o|^2]^{1/2}$); scattering factors for O, C, and H atoms were from International Tables for X-ray Crystallography (21), and the isotropic extinction parameter $X = 0.0004$. A final difference Fourier synthesis revealed no peaks higher than those assigned earlier to hydrogen atoms, and the weighting appeared reasonable.

The final atomic coordinates for the nonhydrogen atoms of the conformer A are listed in Table 1, and pertinent data of the crystallographic analysis are available on request to the senior author.²

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²Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK.