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A LABDANE DITERPENE FROM *CALCEOLARIA CORYMBOSA*<sup>1</sup>

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ABSTRACT.—A labdane-type diterpene, *ent*-9-*epi*-labda-8(17), 12Z, 14-trien-19-yl malonate (**1**), was isolated from the aerial parts of *Calceolaria corymbosa*. The structure of the new compound was deduced on the basis of spectral data.

In our search for diterpenoids occurring in the *Calceolaria* genus (1,2), we have examined the aerial parts of *Calceolaria corymbosa* R. and Pav. (Scrophulariaceae), a species that grows in the coastal hills of central Chile (3). From this source, we have isolated and elucidated the structure of a labdatriene diterpene as the methyl ester of compound **1**. This is the second report of a labdane-type diterpene isolated from this genus (2).

## RESULTS AND DISCUSSION

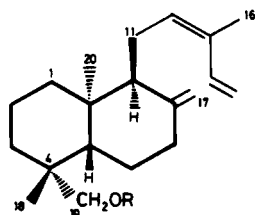
The aerial parts of *C. corymbosa* were extracted with petroleum ether and CH<sub>2</sub>Cl<sub>2</sub>. The CH<sub>2</sub>Cl<sub>2</sub> extract was subjected to cc on Si gel, using increasing proportions of EtOAc in petroleum ether as solvent, affording fractions that contained a diterpenic acid. These frac-

tions were methylated and, after successive cc purifications, yielded the methyl ester of **1**, with the molecular formula C<sub>24</sub>H<sub>36</sub>O<sub>4</sub> ([M]<sup>+</sup> at *m/z* 388). It was an oil, and its spectral data showed characteristic signals of a bicyclic labdatriene skeleton, closely related to diterpenoids previously isolated from *Calceolaria densifolia* (2).

The <sup>1</sup>H-nmr spectrum showed signals of two conjugated double bonds at δ 5.25 (1H, t, H-12), 6.72 (1H, dd, H-14), 5.15 (1H, dd, H-15 trans), 5.05 (1H, dd, H-15 cis). These values and those observed in the <sup>13</sup>C-nmr spectrum at δ 133.90, 132.50, 130.30, and 113.30 for C-12, C-13, C-14, and C-15, respectively, indicated a *Z*-type conjugated diene system in the side chain (4–6).

By comparing these <sup>13</sup>C-nmr data with those of related labdanes (5), a shielding effect was observed on C-1 (δ 36.37) and C-5 (δ 46.75) and a deshielding effect on C-20 (δ 23.07). These shifts are characteristic of the 9-epimeric diterpenes which are usually present in the *Calceolaria* genus (2,7,8).

The presence of a methylmalonic ester was deduced from the signal at δ 3.35 (3H, H-22) corresponding to the methylene group of a malonate moiety. The <sup>13</sup>C-nmr spectrum confirmed this assignment with the presence of signals at δ 167.00, 41.45, and 166.54, which correspond to the malonate carbons.



<b>1</b>	R=COCH <sub>2</sub> COOH
<b>1</b> methyl ester	R=COCH <sub>2</sub> COOMe
<b>2</b>	R=H
<b>2</b> acetate	R=Ac

<sup>1</sup>Part 12 in the series "Diterpenoids from *Calceolaria* Species." For Part 11 see Chamy *et al.* (1).

The remaining  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr absorptions are consistent with the structural features of an *ent-9-epi-8(17), 12Z, 14-labdatriene* skeleton with the primary ester group axially oriented. This is confirmed by the signals at  $\delta$  3.90 (1H, d,  $\text{H}_a$ -19), 4.30 (1H, d,  $\text{H}_b$ -19), and  $\delta$  68.06 (C-19) (9, 10).

On the basis of these data and by comparisons with spectral data of similar diterpenes such as **2** (2,5), and for biogenetic reasons, the methyl ester of **1** was shown to be methyl *ent-9-epi-labda-8(17), 12Z, 14-trien-19-yl malonate*, and the new natural substance **1** corresponds to *ent-9-epi-labda-8(17), 12Z, 14-trien-19-yl malonate*.

The presence of 9-epimeric diterpenes in several species of the *Calceolaria* genus, some of them esterified by malonic acid, could be of chemosystematic value.

## EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**— $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectra were recorded on a 200 MHz spectrometer, using  $\text{CDCl}_3$  solutions, with TMS as internal standard; assignments of  $^{13}\text{C}$ -nmr chemical shifts were made with the aid of DEPT. Mass spectra were recorded at 70 eV. An MeOH solution was used for uv.

**PLANT MATERIAL.**—*C. corymbosa* was collected in the coastal hills of Viña del Mar, V Región, Chile, in September 1989. A voucher specimen (# 0142) is deposited at the Universidad Técnica Federico Santa María.

**EXTRACTION AND ISOLATION.**—The aerial parts of *C. corymbosa* (1.5 kg) were extracted at room temperature with petroleum ether for 72 h, and then with  $\text{CH}_2\text{Cl}_2$  for 72 h. The last extraction afforded 42 g of a syrup. This crude material was chromatographed on a Si gel column and eluted with petroleum ether/EtOAc mixtures of increasing polarity. Fractions of 125 ml were taken and combined based upon tlc and  $^1\text{H}$ -nmr (60 MHz) monitoring. The fractions 70–85 provided a mixture that contained compound **1**. This mixture was treated with ethereal  $\text{CH}_2\text{N}_2$ ; the methylated material was subjected to Si gel cc using petroleum ether-EtOAc (8:1), and fractions of 25 ml were taken. Fractions 9–17 were re-purified by Si gel cc impregnated with  $\text{AgNO}_3$  (10%), using petroleum ether-EtOAc (4:1), affording **1** methyl ester (28.3 mg).

*Methyl ent-9-epi-labda-8(17), 12Z, 14-trien-19-yl malonate (1 methyl ester).*—Viscous yellow oil:  $[\alpha]^{25}_{\text{D}} + 80.0$  ( $\text{CHCl}_3$ ,  $c = 0.7$ ), uv  $\lambda$  max nm ( $\log \epsilon$ ) 227 (3.90);  $^1\text{H}$  nmr (200 MHz)  $\delta$  6.72 (1H, dd,  $J = 17.5, 11.0$  Hz, H-14), 5.25 (1H, t,  $J = 7.0$  Hz, H-12), 5.15 (1H, dd,  $J = 17.5, 1.0$  Hz, H-15 trans), 5.05 (1H, dd,  $J = 11.0, 1.0$  Hz, H-15 cis), 4.65 (1H, d,  $J = 1.0$  Hz, H-17), 4.50 (1H, d,  $J = 1.0$  Hz, H-17'), 4.30 (1H, d,  $J = 11.0$  Hz, H-19), 3.90 (1H, d,  $J = 11.0$  Hz, H-19'), 3.70 (3H, s, H-24), 3.35 (2H, s, H-22), 1.70 (3H, brs, H-16), 0.95, 0.90 (3H each, s, H-18, H-20);  $^{13}\text{C}$  nmr 36.37 (C-1), 18.66 (C-2), 36.37 (C-3), 36.97\* (C-4), 46.75 (C-5), 24.63 (C-6), 31.76 (C-7), 147.90 (C-8), 58.32 (C-9), 37.89\* (C-10), 23.47 (C-11), 133.90 (C-12), 132.50 (C-13), 130.30 (C-14), 113.30 (C-15), 19.77 (C-16), 110.66 (C-17), 27.18 (C-18), 68.06 (C-19), 23.07 (C-20), 167.00 (C-21), 41.45 (C-22), 166.54 (C-23), 52.38 (C-24) (values with an asterisk may be interchanged); ms  $m/z$  (rel. int.)  $[\text{C}_{24}\text{H}_{36}\text{O}_4]^+$  388 (4),  $[\text{M} - \text{Me}]^+$  373 (2),  $[\text{M} - \text{HO}_2\text{CCH}_2\text{CO}_2\text{Me}]^+$  270 (26),  $[\text{M} - \text{CH}_2\text{O}_2\text{CCH}_2\text{CO}_2\text{Me}]^+$  257 (55),  $[\text{270} - \text{Me}]^+$  255 (24),  $[\text{270} - 81]^+$  189 (82),  $[\text{C}_6\text{H}_9]^+$  81 (100), 79 (53), 77 (22), 69 (25), 67 (29).

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