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^{13}C NMR SPECTRAL ANALYSIS OF EPERUANE DITERPENES

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Key Word Index—^{13}C NMR spectra; eperuane diterpenes; methyl *ent*-labdan-8β-ol-15-oate; *ent*-labdan-8β,15-diol; *ent*-labd-13-en-8β-ol-15-oic acid; eperua-7,13-dien-15-oic acid; methyl eperua-8(9)-en-15-oate.

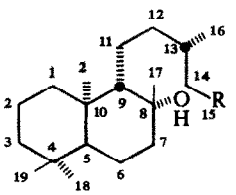
Abstract—The ^{13}C NMR spectra of some eperuane diterpenes have been recorded and the signals assigned. The substituent shielding effects in these compounds, in comparison with those observed in other series of diterpenes, are also presented.

INTRODUCTION

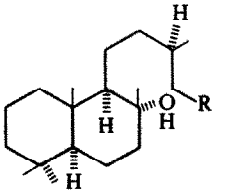
In the last few years considerable interest has been focused on the ^{13}C NMR spectral analysis of labdane diterpenes, [1–3] and its application to the structure elucidation of new compounds of this family of natural products [4, 5]. In this connection, and as part of a project on the isolation of diterpenoids from Brazilian plants [6, 7], it was decided to carry out a ^{13}C NMR spectral analysis of some members of the eperuane diterpene series (also known as *ent*-labdane) and some of their transformation products [8]. This paper describes an analysis of the ^{13}C NMR spectra of the methyl ester of *ent*-labdan-8β-ol-15-oic acid (**1a**), its corresponding reduction and dehydration products **1b** and **5**, respectively; *ent*-labd-13-en-8β-oic acid (**3**), and eperua-7,13-dien-15-oic acid (**4a**) and its methyl ester **4b** [9].

RESULTS AND DISCUSSION

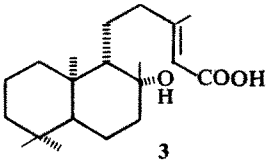
Table 1 lists the carbon shifts of compounds **1a–5**. As expected, the resonances due to the ring A carbons and C-13, C-14, C-15 and C-16 of the sidechain in **1a**, are in good agreement with the reported values for labdanolic acid (**2a**) and related labdane diterpenes [1–3] and were readily assigned. Although the quantitative effects of the hydroxyl substituent are difficult to predict for tertiary alcohols with severe steric interactions [10] it can be observed that C-8, C-7 and C-9, and C-6, which



1a, R = –COOMe
1d, R = –CH_2OH



2a, R = –COOH
2b, R = –CH_2OH



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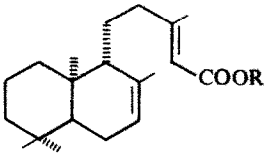
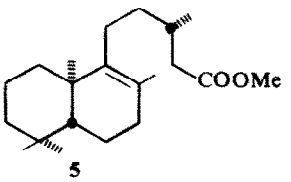


4a, R = H
4b, R = OMe



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*The shift of 18.7 ppm assigned to C-6 of scareol [1] should be reversed with the 20.1 ppm signal, assigned to C-11 (Wenkert, E. personal communication).

Table 1*

	1a	1b	3	4a	4b	5
C-1	39.2†	39.3†	39.3†	39.2	39.2	36.9
C-2	18.2	18.3	18.2	18.8	18.8	19.1†
C-3	42.1‡	42.1	42.0‡	42.3	42.2	41.8
C-4	33.2	33.2	33.2	33.0	32.9	33.3
C-5	55.9	55.9	55.1	50.2	50.1†	51.8
C-6	18.2	18.3	18.2	23.8	23.8	19.4†
C-7	41.3‡	41.2‡	42.2‡	122.7	122.6	33.3
C-8	73.0	73.2	73.2	134.4	134.4	125.4
C-9	59.4	59.4	58.8	54.5	54.4	140.4
C-10	39.0†	39.0†	39.0†	36.9	36.8	37.3
C-11	22.5	22.5	23.5	22.1	22.0	21.8
C-12	42.2	41.5‡	44.8	43.6	43.3	41.5
C-13	31.2	30.5	162.7	163.2	160.2	31.4
C-14	39.2†	39.5†	114.9	115.2	115.1	38.9
C-15	173.3	61.1	171.5	172.2	166.9	173.5
C-16	19.7	19.7	19.2	19.3	18.8	20.1†
C-17	30.5	30.5	30.5	25.3	25.3	25.5
C-18	33.2	33.2	33.5	33.1	32.9	33.6
C-19	21.6	21.6	21.6	21.8	21.8	21.6
C-20	15.1	15.2	15.1	13.6	13.6	19.1
OMe					50.6†	51.3

*The spectra were obtained at 25.2 MHz in the Fourier transform mode in $CDCl_3$ solutions. The δ values are in ppm downfield from TMS.

††The assignments for these signals may be reversed.

are α, β and γ respectively to the HO function, are shielded in **1a** in comparison with the same sites of the labdane diterpenes with an equatorial tertiary alcohol (**2a**, manool, etc).*

The methyl groups of **1a** show shifts in complete agreement with their stereochemical features. The change in the orientation of the OH and Me groups at C-8 does not affect the shift of C-20, according to the general equivalence in steric effects of both groups [11, 12] but induces deshielding of the C-17 methyl group ($\Delta\delta$ for C-17, **1a**–**2a** = 7.4 ppm) showing its equatorial orientation. The methyl shift of *cis*-1-methyl-4-terbutylcyclohexanol, 31.3 ppm [13], confirms the above assignment. C-11 and C-12 of **1a** resonate upfield from comparable sites of **2a**, indicating some effect of the change in the orientation of the substituents at C-8 on the sidechain carbon atoms. The same result was obtained by comparison of all carbon shifts of **1b** with the reported ones for **2b** [3].

The introduction of the Δ^{13} bond causes changes at C-13 and C-14 ($\Delta\delta$ for C-13, **3**–**1a** = 131.5 ppm, $\Delta\delta$ for C-14, **3**–**1a** = 75.7 ppm) but does not affect C-16, as expected [1]. The carbon shifts of the *trans*-decalin system in **3** remains unchanged.

The analysis of the shifts of **4a**, **4b** and **5**, compared with the ones of **1a**, **2a** and **3**, and with related diterpenes, and on the δ values recorded for tricarbocyclic diterpenes [14, 15] show some interesting effects. The Δ^7 bond of **4a** (or **4b**) does not affect C-1, C-2, C-3, C-4 and methyl groups, C-18 and C-19. C-5 and C-10 exhibit the known endocyclic homoallylic effect [16] and resonate upfield in comparison with the same carbons of **1a**, **1b** and **3** ($\Delta\delta$ for C-5, **1a**–**4a** = 5.7 ppm; $\Delta\delta$ for C-10, **1a**–**4a** = 2.8 ppm). C-6 and C-9 show the expected shifts for a substituted cyclohexene system.

The replacement of the sp^3 carbon atom at C-8 of **1a** by one of the triagonal carbons of the Δ^7 bond in **4a**, caused the loss of a δ-*syn*-axial interaction producing an upfield shift of 1.5 ppm on the C-20 methyl group and also a shielding effect of 5.3 ppm on the C-17 methyl group, comparable with the recorded $\Delta\delta$ value (−6.0 ppm) for the methyl groups of 1-methylcyclohexanol and 1-methylcyclohexene [17].

The introduction of the Δ^8 bond in **5** does not produce changes on C-2, C-3, C-4 and its gem-dimethyl groups. In this case, the endocyclic homoallylic effect is observed only on C-5 ($\Delta\delta$ for C-5, **1a**–**5** = 4.1 ppm) using **1a** as reference, due to the γ-effect imposed by the OH group on C-6 of this compound. The C-17 methyl group is unaffected.

Comparison of the shifts of C-1, C-20 and C-11 of **4a** with those of **5**, shows C-1 to be shielded ($\Delta\delta$ = −2.3 ppm), C-20 to be deshielded ($\Delta\delta$ = 5.5 ppm) and C-11 practically unaffected ($\Delta\delta$ = −0.3 ppm) on changing the position of the olefinic linkage from Δ^7 to Δ^8. These effects, which are also observed in the series of pimaradiene diterpenes [14] can be explained by an attenuation of the γ-effect imposed by the pseudoequatorial C-11 on C-20 in **4a**, and an increase of the same effect by C-11 on C-1 in **5**, due to the different orientation of C-11 in both compounds. The same effects for the mentioned carbons is also observed in podocarp-8-ene [15].

EXPERIMENTAL

Compounds **1a**, **3** and **4** were isolated from the bark of *Hymeneae coubaril* [6], **1a** also from the bark of *H. stignocarpa* (unpublished results). The transformation of **1a** into **1b** was carried out by $LiAlH_4$ reduction and the conversion of **1a** into **5** by $SOCl_2$/Py dehydration.

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CAUDICIFOLIN, A NEW DITERPENE FROM *EUPHORBIA CAUDICIFOLIA*

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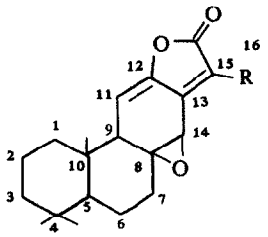
Key Word Index—*Euphorbia caudicifolia*; Euphorbiaceae; diterpenoid; caudicifolin; jolkinolide A.

INTRODUCTION

Euphorbia caudicifolia L. Syn. *Euphorbia neriifolia* non L. (Euphorbiaceae) is found abundantly in the sandy terrain of Sind province in the South East of Pakistan. The latex and root extracts are used in the indigeneous system of medicine and are believed to possess antitumor properties [1]. This prompted us to investigate the alcoholic root bark extract which gave one new diterpenoid Caudicifolin (**1**) and the known diterpenoid [2, 3] Jolkinolide A (**2**) the structures of which are discussed below.



(**1**) R = CH_2OH
(**2**) R = Me
(**3**) R = CH_2OAc

RESULTS

The fresh root bark was extracted with ethanol at room temp. and the extract chromatographed on a Si gel column. Elution with $CHCl_3$–EtOAc (1:2) gave Caudicifolin (**1**) mp 177–182°. $C_{20}H_{26}O_4$: M^+ 330, requires C, 72.72; H, 7.87 found C, 73.16; H, 7.73% $[\alpha]_D^{25}$ = +94.4 (c = 0.7 $CHCl_3$). IR (KBr) cm^{-1}: 1738, (lactone C=O), 1648, 1667 (C=C), 3539 (OH). UV λ_{max}(MeOH) 288 nm (ε = 16 900). Proton NMR ($CDCl_3$ δ): 0.75, 0.88, 0.97 (9H, *s*, methyl 4,4,10), 4.06 (1H, *s*, CH-14), 4.67 (2H, *s*, CH_2-16), 5.59 (1H, *d*, *J* = 6 Hz, CH-11), 2.67 (1H, *d*, *J* = 6 Hz, CH-9). The signal of the hydroxyl proton was masked by CH-9 at 2.67. This was shown by the decrease in intensity of the doublet at 2.67 by addition of CF_3COOH. The IR of this compound also showed the presence of an OH group. This was confirmed when the treatment of this compound with Ac_2O and C_5H_5N gave the acetate (**3**). NMR ($CDCl_3$ δ): 0.72, 0.86, 0.95 (9H, *s*), 2.10 (3H, *s*, OAc), 3.95 (1H, *s*), 4.98 (2H, *s*), 2.69 (1H, *d*, *J* = 6 Hz), 5.62 (1H, *d*, *J* = 6 Hz). IR (film) cm^{-1}: 1648, 1752 (C=O).

Elution of the column with C_6H_6–$CHCl_3$ (1:1) gave a compound mp 220–225°. $C_{20}H_{26}O_3$: M^+ 314. UV λ_{max} MeOH 286 nm (ε 19 685). NMR ($CDCl_3$ δ): 0.73, 0.87, 0.96 (9H, *s*), 2.06 (3H, *s*), 2.63 (1H, *d*, *J* = 6 Hz), 5.46 (1H, *d*, *J* = 6 Hz), 3.72 (1H, *s*). The spectral data of this compound were identical when compared with the literature values of jolkinolide A (**2**).

The close similarity in the NMR spectrum of **1** and **2** clearly showed the presence of a hydroxymethylene group at C-15 in **1** instead of a methyl group as in **2**. That the conjugation pattern in **1** was identical with that in **2** was revealed by the comparison of UV spectra. Thus the OH group in **1** could only be placed at C-16. On the basis of above spectral data of Caudicifolin, its correlation with jolkinolide A from *Euphorbia jolkini* and the isolation of both natural products from the same source we assign structure **1** for Caudicifolin.

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