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THE ISOLATION OF METHYL CARNOSOATE FROM *SALVIA LANIGERA*

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Key Word Index—*Salvia lanigera*; Lamiaceae; diterpene; methyl carnosoate.

Abstract—In continuation of our studies on the aerial parts of *Salvia lanigera*, the isolation of a new natural methyl ester of carnosic acid is reported. The structure of this ester was elucidated by spectroscopic methods.

INTRODUCTION

In our previous work [1, 2], we reported the isolation and characterization of two diterpenes, isocarnosol (**1**) and 12-hydroxyisocarnosol (**2**) from the petrol extract of *Salvia lanigera*. Further studies on a petrol extract of this plant have led to the isolation of compounds **1**, **2** and **3**. The structure of compound **3** has been elucidated as methyl carnosoate on the basis of spectral studies.

RESULTS AND DISCUSSION

The ^{1}H NMR spectrum of **3** (M^+ at *m/z* 346), showed signals for the protons of two tertiary methyls at δ0.85 and 0.95, in addition to two doublets (J = 6.9 Hz) centred at δ1.18 and 1.2 which represent six protons of the two methyls of an isopropyl group. A single proton septet at δ3.15 (J = 6.9 Hz) was assigned to H-15. The assignment of the latter signal was confirmed by spin decoupling experiments. Also, the ^{1}H NMR spectrum of **3** exhibited an aromatic proton singlet at δ6.65, assignable to H-14.

The IR spectrum of **3** showed bands at 3480 and 1690 cm^{-1} for a hydroxyl group and a carbomethoxy group, respectively; no broad peak was observed in the region 3000–2500 cm^{-1}. Further evidence in favour of the structure **3** is provided by the ^{13}C NMR spectrum which showed 21 signals (Table 1). The unsubstituted aromatic carbon resonates at δ117.8. This low shift for the unsubstituted carbon atom in comparison to C-12 (111.78) in isocarnosol (**1**), or C-11 (110.6) in compound **4** [3], is characteristic of an aromatic carbon remote from an oxygen substituent, as in the case of C-14 in feruginol (**4**). Further confirmation came from the acetylation of **3**, which led to the isolation of a product identical to diacetyl carnosic acid methyl ester (**5**) (mp and ^{1}H NMR) [4].

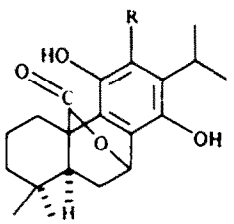
Methyl carnosoate does not appear to have been isolated as a natural product from any genera of Lamiaceae, nor has it been synthesized as yet. However, the diacetyl and dimethyl derivatives are known [5].

It is interesting to point out here that the major diterpene of *S. lanigera* is compound **1**, which has a *p*-dihydroxy grouping. Thus far all the diterpenes which have been isolated from *Salvia* species have the *o*-dihydroxy substituted pattern as in methyl carnosoate.

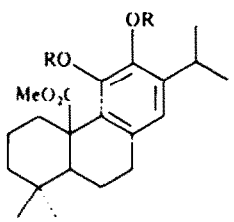
EXPERIMENTAL

All mps: are uncorr.; the NMR spectra were obtained in $CDCl_3$ on a JEOL 100 MHz with TMS as internal reference.

Isolation procedure. Petrol (60–80°) extraction of 2 kg of ground leaves of *Salvia lanigera* (authenticated by the Department of Botany, King Saud University, Riyadh, Saudi Arabia, collected about 200 km north of Riyadh), afforded 150 g of waxy residue. A portion of the extract (50 g) was chromatographed on a column of silica gel using petrol–$CHCl_3$ gradient elution. First, the column was eluted with petrol to afford 12 fractions which could not be induced to crystallize and were not



1 R = H
2 R = OH



3 R = H
5 R = Ac

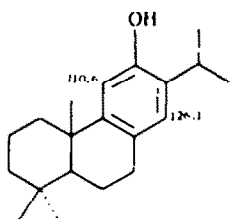


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Table 1. ^{13}C NMR spectrum of compound 3 ($CDCl_3$)

C-1	31.8 (*t*)	C-11	147.7 (*s*)
C-2	19.9 (*t*)	C-12	142.1 (*s*)
C-3	41.4 (*t*)	C-13	139.4 (*s*)
C-4	34.0 (*s*)	C-14	117.9 (*d*)
C-5	54.1 (*d*)	C-15	26.4 (*d*)
C-6	19.9 (*t*)	C-16	23.7 (*q*)
C-7	32.7 (*t*)	C-17	23.4 (*q*)
C-8	134.8 (*s*)	C-18	33.8 (*q*)
C-9	125.3 (*s*)	C-19	18.4 (*q*)
C-10	47.6 (*s*)	C-20	182.0 (*s*)
OMe	61.6 (*q*)		

studied further as they were mostly fats. Next, some fractions were eluted with petrol–$CHCl_3$ (3:1), which showed the same spots on TLC, which were combined and rechromatographed on silica gel (200 g) and elution with petrol–$CHCl_3$ (3:1) yielded 15 fractions from which fractions 13 and 14 gave compound 3. Recrystallization from petrol gave yellowish crystals (340 mg) of 3, mp 175°, $[\alpha]_D^{20} = +46.6°$ ($CHCl_3$; *c* 0.15); UV λ_{max}^{MeOH} nm (ε): 208 (800), 290 (3400), 317 (8120); IR ν_{max}^{KBr} cm^{-1}: 3480, 3450, 3020, 2960, 1690, 1610, 1540, 1500, 1450, 1415, 1385, 1360, 1240, 1205; ^1H NMR ($CDCl_3$); δ 0.85 (*s*, 3H), 0.95 (*s*, 3H), 1.18 (*d*, *J* = 6.9 Hz, 3H), 1.2 (*d*, *J* = 6.9 Hz, 3H), 2.35 (*dd*, *J* = 5.0 and 8.0 Hz, 2H), 2.8 (*br d*, 2H), 3.15 (*septet*, *J* = 7 Hz, H-15), 3.5 (*m*, 2H-7), 3.7 (*s*, 3H, OMe), 6.3 (2H, phenolic OHs), 6.65 (*s*, H-14), 1.4–2.25 (complex signal); ^{13}C NMR: see Table 1.

Subsequent elution of the initial CC, using $CHCl_3$ afforded many fractions. The first two fractions gave compound 1 (300 mg) on evaporation, while the next three fractions were collected and rechromatographed to give 23 mg of compound 2. Compounds 1 and 2 were found to be identical in all respects (mp, IR and ^1H NMR) with authentic samples.

Acylation of compound 3. Compound 3 (40 mg) was dissolved in pyridine (2 ml) and 2 ml of Ac_2O was added and the soln was left overnight at room temp. Usual work-up yielded a residue which was purified on TLC to give 21 mg of diacetyl carnosic acid methyl ester, mp 157–159° (lit. 158–160° [4], 157–158° [5]), its ^1H NMR spectrum was identical with the reported one.

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