

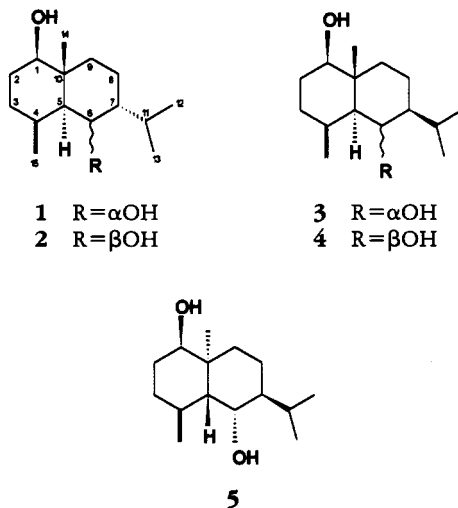
7-EPI-EUDESMANES FROM *TEUCRIUM POLIUM*ALAA KAMEL^{1*}

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ABSTRACT.—Two new sesquiterpene diols, 7-*epi*-eudesm-4(15)-ene-1 β ,6 α -diol [**1**] and 7-*epi*-eudesm-4(15)-ene-1 β ,6 β -diol [**2**], in addition to the known sesquiterpene alcohols, β -eudesmol and α -cadinol, were isolated and identified from *Teucrium polium*. The structures of the new compounds were established by interpretation of their spectroscopic data.

Teucrium polium L. (Lamiaceae) is a plant that grows in the region of the St. Catherine Mountain, Sinai, Egypt. The plant is reputed for its medicinal value in folk medicine. In Egypt, it is used as an appetizer, expectorant, and hypoglycemic (1). It is also used to treat stomachache, and to promote wound healing (2). The volatile oil of *T. polium* has been found to possess antispasmodic activity (3). Previous phytochemical investigations on *T. polium* have revealed the presence of diterpenoids (4–6), iridoids and flavonoids (7), and the individual volatile oil constituents have been identified (3). Gc/ms analysis of the volatile oil showed that sesquiterpenoids comprise the major part of the oil (78.61%) and that certain sesquiterpene alcohols such as β -eudesmol, 10-cadinol, α -cadinol, and the tentatively identified patchouly alcohol, represent 41.21% of the oil (8). The present study deals with the further investigation of the sesquiterpene alcohols of the plant.

Chromatography of the polar fraction of a hexane extract of *T. polium* var. *album* afforded β -eudesmol and α -cadinol, in addition to the new sesquiterpene diols, **1** and **2**. The hreims of **1** showed a $[M]^+$ peak at m/z 238.1930, consistent with a molecular formula of $C_{15}H_{26}O_2$. Other significant fragment ion peaks at m/z 220 ($M^+ - H_2O$) and m/z 202 ($M^+ - 2H_2O$) were also observed. The 1H -nmr spectrum of **1** (Table 1) showed the presence of two olefinic protons of an



exocyclic methylene group (δ 5.01 and δ 4.76), along with three methyl signals at δ 0.77, 0.92, and 1.10, in addition to two downfield carbinol protons at δ 4.12 and 3.42. These data indicate that **1** is a sesquiterpene diol of the β -eudesmane type having both of its hydroxyl groups attached to carbinol carbons (9). The hydroxyl group at C-1 was determined to have a β -configuration in **1** by comparison with the nmr data of the 1 α - and 1 β -hydroxyeudesmanes **3** and **5**, with an observed 1H -nmr signal at δ 3.42 (dd ($J=5$ and 11 Hz)) (Table 1) and a ^{13}C -nmr signal at 79.3 ppm (Table 2) (10–13).

A 1H - 1H COSY nmr experiment on **1** showed clearly that the protons coupled to the resonance at δ 4.12 were on different carbon atoms. One of these neighboring protons (H-7) at δ 1.75 was coupled to H-11 at 2.00 ppm, implying that the second hydroxyl group could only be placed either at position -6 or -8. Were

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TABLE 1. $^1\text{H-Nmr}$ Data for Compounds 1-4.^a

Proton	Compound			
	1 ^b	2 ^b	3 ^c	4 ^d
H-1	3.42 dd $J=5,11$	3.30 dd $J=5,11$	3.42 dd $J=4.5,11$	3.25 dd $J=5,11$
H-3	2.31 ddd $J=1.5,4.5,12$			
H-5	2.10 m			
H-6 α		4.32 br s		4.25 m $W_{1/2}=7$
H-6 β	4.12 dd $J=5,11$		3.71 t $J=10$	
H-7	1.75 m			
H-11	2.0 m			
H-12	0.92 d $J=7.5$	0.93 br s	0.87 d $J=7$	0.95 d $J=6$
H-13	1.10 d $J=7.5$	0.96 br s	0.95 d $J=7$	0.95 d $J=6$
H-14	0.77 s	0.91 s	0.70 s	0.90 s
H-15 α	5.0 d $J=1.5$	5.01 d $J=1.5$	5.01 d $J=1$	5.0 br s
H-15 β	4.76 d $J=1.5$	4.90 d $J=1.5$	4.74 d $J=1$	4.86 br s

^aValues in ppm, J in Hz.^bMeasured in CDCl_3 at 400.16 MHz.^cData from González *et al.* (14).^dData from García-Granados *et al.* (15).

the second hydroxyl group to occur at C-8, the coupling pattern of the C-8 proton would be a doublet of doublet of doublets and not a doublet of doublets as observed. The published data on the known 1,6-dihydroxyeudesmanes **3** and **4** (14-16) match those of ring A of **1** and **2**, but differ in the B-ring where ^{13}C -nmr upfield shifts are observed for C-5, C-7, and C-9, and downfield shifts are seen for C-8 and C-13 (Tables 1 and 2). The proton at δ 4.12 showed a doublet of doublets with two couplings [axial-axial ($J=11$ Hz) and axial-equatorial ($J=5$ Hz)], which is consistent with an axial hydroxyl group on C-6, with the isopropyl group at C-7 being axial as well. The ^{13}C -nmr data of **1** were also consistent with this assignment as one would predict because of the gauche effect, inasmuch as there would be a marked upfield shift for the C-5 and C-9 resonances between **3** (where the isopropyl group is equatorial) and **1** (where the isopropyl group is axial) (17).

A nOe difference nmr experiment on **1** further confirmed the earlier findings, since a nOe was observed for H-6 (δ 4.12) but not for H-1 (δ 3.42) on irradiation of the angular methyl C-14 (δ 0.77) resonance, showing that the 1-hydroxyl group is equatorial and the 6-

hydroxyl group is axial in compound **1**.

Compound **2** differed from **1** in the coupling constant values of the carbinol carbon signal at position -6. In the case of **2**, the couplings of this proton are equatorial-axial and equatorial-equatorial, observed as a broad singlet due to the weak effect of splitting. That this observation is the only difference between **1** and **2** suggests that the hydroxyl group at position -6 in **2** is equatorial, while the rest of the molecule is the same. It was thus concluded that compounds **1** and **3** on one hand, and **2** and **4** on the other, are diastereoisomers, epimeric at C-7. Therefore, the structures and relative configurations of **1** and **2** are 1 β ,6 α -dihydroxy- and 1 β ,6 β -dihydroxy-7-*epi*-eudesman-4(15)-ene, respectively.

The ^{13}C - and ^1H -nmr data of β -eudesmol and α -cadinol, also isolated in this investigation, were identical with published data (18,19).

The existence of 7-*epi*-sesquiterpenoids in plants may be considered unusual. Such compounds are well known as constituents of marine organisms. Thus, the isolation of **1** and **2** from *T. polium* is the first record of 7-*epi*-eudesmanes in plants. However, it has been previously reported that a 7-*epi*-selinane, isointer-

TABLE 2. ¹³C-Nmr Data for Compounds 1-3, and 5.^a

Carbon	Compounds			
	1 ^b	2 ^b	3 ^c	5 ^d
1	79.3	79.9	79.2	84.9
2	32.1	30.8	32.5	—
3	35.3	34.4	35.2	—
4	146.1	146.9	146.4	146.5
5	50.3	52.1	56.2	—
6	69.9	68.6	67.2	69.6
7	44.5	50.0	49.6	—
8	22.3	21.2	18.5	—
9	32.2	29.8	36.5	—
10	41.7	39.8	41.8	—
11	25.2	28.9	26.3	—
12	22.2	20.4	21.1	21.3
13	25.0	20.8	16.4	17.8
14	12.1	13.1	11.7	13.1
15	108.1	108.6	107.9	108.3

^aValues in ppm.^bMeasured in CDCl₃ at 100.61 MHz.^cData from Gutierrez and Herz (16).^dData from Schildknecht *et al.* (13).

medeol, is a consistent of *Cymbopogon flexuosus* and co-existed with several 7β-sesquiterpenoids (20).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—¹H-Nmr spectra were carried out on a Bruker WP 400 instrument at 400.15 MHz and ¹³C-nmr spectra were carried out on the same instrument at 100.61 MHz. The ¹H-¹H COSY and nOe nmr experiments were run on a General Electric QE-300 apparatus at 300.18 MHz. Hreims were run on a Varian VG-70S mass spectrometer. Cc was performed on Lobar Si gel 60 columns (Merck; 440×37 mm). C₁₈ cartridges (Analytichim International) were used for sample clean up. Tlc was performed on Merck Si gel and RP-18 plates and prep. tlc was carried out on a Merck RP-18 plate (20×20 cm; 0.5 mm thickness).

PLANT MATERIAL.—*Teucrium polium* L. var. *album* was collected from near St. Catherine Mountain, Sinai, Egypt, in June 1991. The plant was identified by Dr. M. Gibali, Plant Taxonomy Department, National Research Center, Cairo, Egypt, and a voucher specimen was deposited at the CAIRC (National Research Center Herbarium-Cairo) under No. 1832.

EXTRACTION AND ISOLATION.—A sample (3 kg) of ground air-dried leaves of *T. polium* var.

album was extracted with hexane (5 liters×3). The hexane extract was partitioned between hexane and a mixture of MeOH-H₂O (7:3). The polar aqueous fraction (6.7 g), containing the sesquiterpene alcohols, was passed over a C₁₈ cartridge to retain the sterols and the undesired lipids. Cc of this fraction on Si gel 60 and elution with toluene-Me₂CO (9:1) afforded six fractions, each containing a major sesquiterpene alcohol. All of those fractions were individually subjected to Lobar cc on Si gel using cyclohexane-Me₂CO (92:8) as eluent. After rechromatography on the same material, β-eudesmol (55 mg) and α-cadinol (77 mg) were obtained chromatographically pure, but two other sesquiterpene alcohols were not pure.

Compounds 1 and 2 were separated by prep. tlc on a reversed-phase plate (RP-18) using the solvent system MeOH-H₂O (7:3), which resulted in the isolation of 9 mg of 1 and 4 mg of 2.

β-Eudesmol.—Exhibited ir, ¹H-nmr, ¹³C-nmr, and ms data consistent with literature values (18).

α-Cadinol.—Exhibited ¹H-nmr, ¹³C-nmr, and ms data consistent with literature values (19).

7-epi-Eudesm-4(15)-ene-1β,6α-diol [1].—Obtained as a colorless oil; [α]_D²⁴ +3.12° (c=0.16, CH₂Cl₂); uv λ max (CH₂Cl₂) 228 nm (log ε 3.25); ir ν max (dry film) 3490 (OH), 3377 (CH, aliphatic), 1051, 888 cm⁻¹; ¹H-nmr data, see Table 1; ¹³C-nmr data, see Table 2; eims (30 eV) m/z [M-H₂O]⁺ 220 (21), 202 (11), 187 (13), 177 (24), 149 (11), 134 (23), 125 (20), 121 (70), 120 (30), 109 (52), 107 (82), 95 (37), 81 (71), 69 (48), 55 (100); hreims (70 eV) m/z [M]⁺ 238.193 (10), 220.184 (100), 202.166 (31), 177.135 (38), 159.120 (57), 134.109 (40), 123.079 (64), 121.099 (64), 107.081 (95), 93.065 (36), 81.062 (45), 71.048 (24), 69.070 (23).

7-epi-Eudesm-4(15)-ene-1β,6β-diol [2].—¹H-Nmr data, see Table 1; ¹³C-nmr data, see Table 2.

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