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19-ACETYLTEUPOLIN IV, A NEO-CLERODANE DITERPENOID FROM *TEUCRIUM POLIUM* SUBSP. *PILOSUM*

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Key Word Index—*Teucrium polium* subsp. *pilosum*; Labiatae; neo-clerodane diterpenoid; 19-acetylteupolin IV.

Abstract—From the aerial parts of *Teucrium polium* subsp. *pilosum* a new neo-clerodane diterpenoid, 19-acetylteupolin IV, has been isolated. Its structure [7β,19-diacetoxy-4α,18; 15,16-diepoxy-6-keto-neo-cleroda-13(16),14-dien-20,12*S*-olide] was established by spectroscopic means and by comparison with closely related compounds.

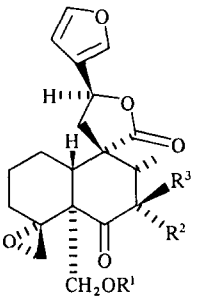
INTRODUCTION

In continuation of our studies on diterpenoid compounds from *Teucrium* species (family Labiatae) [1–4], we have now investigated *T. polium* L. subsp. *pilosum* Decsne (synonym *T. pilosum* Aschers. Schweinf., *T. sinaicum* Boiss.), a plant collected in the State of Qatar (Arabian Gulf). From the aerial parts of this plant we have isolated a new neo-clerodane diterpenoid, 19-acetylteupolin IV (**1**), as the sole diterpenic constituent of this species. The structure of 19-acetylteupolin IV (**1**) was established by spectroscopic (^{1}H NMR and ^{13}C NMR, CD) means and by comparison with closely related compounds such as teupolin IV (**2**) and capitatin (**3**).

RESULTS AND DISCUSSION

19-Acetylteupolin IV (**1**) had a molecular formula $C_{24}H_{28}O_9$ and its IR spectrum showed furanic (3160, 3140, 1505, 878 cm^{-1}), γ-lactone (1750 cm^{-1}), acetate (1740 br, 1250 cm^{-1}) and, probably, ketone (1735 cm^{-1}) absorptions. The ^{1}H NMR spectrum of **1** (Table 1) revealed the existence of a secondary methyl group, a β-substituted furan ring, an α,α-disubstituted oxirane ring, an acetoxymethyl group attached to a quaternary carbon atom and a γ-lactone identical with those found in 19-acetylgnaphalin (**4**), a neo-clerodane diterpenoid isolated from *T. gnaphalodes* [5] and *T. hyrcanicum* [6] whose structure is well known from an X-ray diffraction analysis [7]. In addition, the ^{1}H NMR spectrum of compound **1** showed a one-proton doublet (J = 12.5 Hz) at δ6.30 and an acetoxyl group (δ2.09 or 2.04). These two signals must be attributed to the existence of an acetoxyl group at the C-7β position and this was confirmed as follows. (i) Double resonance experiments showed that the proton at δ6.30 was coupled with a one-proton signal at δ2.36 which appeared as a doublet of quartets (H-8β). Irradiation at δ2.36 transformed the doublet at δ6.30 into a singlet and also the signal of the secondary methyl group (δ1.27, *d*) collapsed into a singlet. (ii) The ^{1}H NMR spectrum of the new diterpenoid (**1**, Table 1) was almost identical with that of teupolin IV (**2**) [8], the only differences being the absence in the latter of an acetyl group and small chemical shift variations caused by the free C-19 hydroxyl group of teupolin IV. (iii) The ^{13}C NMR spectrum of compound **1** (Table 2) showed carbon atom resonances in complete agreement with structure **1** and almost identical with those of teupolin IV (**2**) [8]. The only differences were in the chemical shifts of the C-6 and C-8 carbon atoms (**1**: at δ200.7 *s* and 44.8 *d*, respectively, Table 2; **2**: at δ207.94 *s* and 48.67 *d*, respectively [8]). Whereas the chemical shift difference in the C-6 carbon can be due to the C-19/C-6 interaction (compound **2** possesses a C-19 hydroxyl group which is acetylated in **1**), the rather abnormally high value of the C-8 carbon atom resonance given in **2** could be a misprint, since in capitatin (**3**) it appears at δ40.9 [9].

The new diterpenoid (**1**) is thus the 19-acetyl derivative of teupolin IV. The neo-clerodane absolute configuration of compound **1** was established by its CD curve, which showed a negative Cotton effect ($\Delta\varepsilon_{292}$ −0.88) as 19-acetylgnaphalin (**4**) [5, 7]. The 12*S*-configuration of 19-



	R¹	R²	R³
1	Ac	H	OAc
2	H	H	OAc
3	Ac	OAc	H
4	Ac	H	H

Table 1. ^{1}H NMR spectral data of 19-acetylteupolin IV (**1**) (300 MHz, in pyridine-d_5, TMS as internal standard)*

H-7α	6.30 *d*	H-14	6.63 *dd*	H_B-18‡	3.77 *dd*
H-8β	2.36 *dq*	H-15	7.71 *t*	H_A-19	5.31 *d*
H_A-11	2.66 *dd*	H-16	7.88 *m*	H_B-19	6.12 *d*
H_B-11	2.74 *dd*	Me-17	1.27 *d*	OAc	2.09 *s*
H-12	5.76 *t*	H_A-18†	2.27 *d*	OAc	2.04 *s*

J (Hz): 7α,8β = 12.5; 8β,17 = 6.7; 11A,11B = 14.4; 11A,12 = 11B,12 = 8.6; 14,15 = 15,16 = 1.7; 14,16 = 0.6; 18A,18B = 6.0; 18B,3α = 2.0; 19A,19B = 12.6.

*Spectral parameters were obtained by first order approximation. All these assignments have been confirmed by double resonance experiments.

†*Exo* hydrogen with respect to ring B.

‡*Endo* hydrogen with respect to ring B.

Table 2. ^{13}C NMR chemical shifts (in δ values from TMS) of 19-acetylteupolin IV (**1**)*

C		C		C	
1	23.6 *t*†	9	53.4 *s*‡	17	13.7 *q*
2	24.9 *t*	10	54.4 *d*	18	48.9 *t*
3	32.9 *t*	11	43.4 *t*	19	62.6 *t*
4	61.6 *s*	12	73.0 *d*	20	177.5 *s*
5	54.5 *s*‡	13	125.6 *s*	OAc	170.8 *s*
6	200.7 *s*	14	109.0 *d*		169.6 *s*
7	75.3 *d*	15	145.1 *d*		21.0 *q*
8	44.8 *d*	16	140.9 *d*		20.5 *q*

*In pyridine-d_5 solution.

†SFORD multiplicity.

‡These assignments may be reversed.

acetylteupolin IV (**1**) was established by NOE experiments, since irradiation of the Me-17 protons (δ1.27) caused NOE enhancements in the signals of the H-14 (δ6.63, 4%) and H-16 (δ7.88, 1%) protons and no effect was observed in the signal of the H-12 proton (δ5.76) [10, 11].

EXPERIMENTAL

Mp is uncorr. For general details on methods, see refs [1–5, 7, 10]. Plant materials were collected at Al-Zobarah Farmer, Qatar, in March 1983, and voucher specimens were deposited in the Herbarium of the Qatar University.

Extraction and isolation of 19-*acetylteupolin IV* (**1**). Dried and powdered *Teucrium polium* subsp. *pilosum* aerial parts (250 g) were extracted as described in previous papers. The extract (9 g) was chromatographed over silica gel column (150 g, Merck No. 7734, deactivated with 10% H_2O) eluted with *n*-hexane, *n*-hexane–EtOAc mixtures and pure EtOAc. EtOAc–*n*-hexane (9:1) eluted 19-acetylteupolin IV (**1**, 70 mg) as the sole diterpenic constituent. Mp 230–234° (from EtOAc–*n*-hexane); $[\alpha]_D^{24°}$ + 132.3° (pyridine; *c* 0.161); CD nm (Δε): 340 (0), 292 (−0.88), 250 (−0.09) (MeOH; *c* 0.0318); IR ν_{max}^{KBr} cm^{-1} 3160, 3140, 2990, 2960, 2880, 1750, 1740, 1735, 1505, 1480, 1375, 1250, 1185, 1150, 1045, 1025, 910, 878; ^{1}H NMR (300 MHz, pyridine-d_5): see Table 1; ^{13}C NMR (75.4 MHz, pyridine-d_5): see Table 2; EIMS (direct inlet) 70 eV, *m/z* (rel. int.): 460 $[M]^+$ (0.1), 418 (2.8), 400 (0.7), 387 (5.6), 370 (2.2), 358 (4.5), 327 (43), 189 (13), 161 (9), 95 (31), 94 (19), 91 (17), 81 (26), 79 (13), 69 (10), 55 (10), 43 (100). (Found: C, 62.43; H, 6.09. $C_{24}H_{28}O_9$ requires: C, 62.60; H, 6.13%.)

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REFERENCES

1. Rodriguez, M. C., Barluenga, J., Pascual, C., Rodriguez, B., Savona, G. and Piozzi, F. (1984) *Phytochemistry* **23**, 2960.
2. de la Torre, M. C., Rodriguez, B., Savona, G. and Piozzi, F. (1986) *Phytochemistry* **25**, 171.
3. Hueso-Rodriguez, J. A., Fernandez-Gadea, F., Pascual, C., Rodriguez, B., Savona, G. and Piozzi, F. (1986) *Phytochemistry* **25**, 175.
4. Fernandez, P., Rodriguez, B., Savona, G. and Piozzi, F. (1986) *Phytochemistry* **25**, 181.
5. Savona, G., Paternostro, M., Piozzi, F. and Rodriguez, B. (1979) *Tetrahedron Letters* 374.
6. Gacs-Baitz, E., Radics, L., Oganessian, G. B. and Mnatsakanian, V. A. (1978) *Phytochemistry* **17**, 1967.
7. Martinez-Ripoll, M., Fayos, J., Rodriguez, B., Garcia-Alvarez, M. C., Savona, G., Piozzi, F., Paternostro, M. and Hanson, J. R. (1981) *J. Chem. Soc. Perkin Trans.* 1, 1186.
8. Malakov, P. Y. and Papanov, G. Y. (1983) *Phytochemistry* **22**, 2791.
9. Marquez, C., Rabanal, R. M., Valverde, S., Eguren, L., Perales, A. and Fayos, J. (1980) *Tetrahedron Letters* **21**, 5039.
10. Fayos, J., Fernandez-Gadea, F., Pascual, C., Perales, A., Piozzi, F., Rico, M., Rodriguez, B. and Savona, G. (1984) *J. Org. Chem.* **49**, 1789.
11. Pascual, C., Fernandez, P., Garcia-Alvarez, M. C., Marco, J. L., Fernandez-Gadea, F., de la Torre, M. C., Hueso-Rodriguez, J. A., Rodriguez, B., Bruno, M., Paternostro, M., Piozzi, F. and Savona, G. (1986) *Phytochemistry* **25**, 715.