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EUDESMANE-TYPE SESQUITERPENES FROM *TANACETUM PRAETERITUM* SUBSP. *PRAETERITUM*

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Key Word Index—*Tanacetum praeteritum* subsp. *praeteritum*; Compositae; sesquiterpene lactones; eudesmanolides; sesquiterpene; eudesmane.

Abstract—In a further investigation on *Tanacetum praeteritum* subsp. *praeteritum* a new eudesmanolide and a new sesquiterpene acid ester were isolated. The structures of the compounds were elucidated by spectral methods.

INTRODUCTION

In a previous work with *Tanacetum praeteritum* subsp. *praeteritum*, 15 sesquiterpene lactones have been reported, four of them being new [1]. In a further investigation a new eudesmanolide and a new sesquiterpene acid ester (**1** and **2**) have been isolated from the aerial parts of this plant.

RESULTS AND DISCUSSION

The aerial parts of *Tanacetum praeteritum* subsp. *praeteritum* have afforded a new eudesmanolide (**1**), a new sesquiterpene acid ester (**2**) and a known compound, epoxysantamarin (**3**) [2]. The substances were isolated from the polar fraction of the extract.

The HR-mass spectrum of the compound gave a molecular peak at *m/z* 262.1213, indicating a molecular formula $C_{15}H_{18}O_4$. The ^{1}H NMR spectrum of compound **1** exhibited typical exocyclic methylene protons of the lactone ring at δ 6.14 (H-13, J = 3.5) and 5.47 (H-13′, J = 3.0 Hz), a quaternary methyl singlet at δ 0.94 (H-14), an olefinic methyl doublet at δ 2.17 (H-15, J = 1.5 Hz), a multiplet at δ 5.90 (H-3), a broadened singlet at δ 3.45 (H-1) and a double doublet at δ 3.99 (H-6, J = 10, 10), indicating 6,12-eudesmanolide having a double bond between C-3 and C-4, a hydroxyl group at C-1 and a keto group at C-2. The broadened singlet at δ 3.45 implied the α-position of the hydroxyl group at C-1. The signals were assigned by spin decoupling experiments (Table 1). The singlet at δ 3.45 shifted to δ 4.92 in the ^{1}H NMR spectrum of its acetyl derivative, and the acetyl singlet appeared at δ 2.01. The APT spectrum of the compound confirmed the structure, giving a keto signal at δ 198.1, four olefinic carbon signals at δ 162.4, 138.2, 124.8 and 117.7, two signals at δ 81.6 and 80.3 and the other signals of the skeleton. The carbon signals were assigned by HETCOR experiments. The NOE spectrum of the compound confirmed the α-position of the hydroxyl group at C-1. Irradiation of H-14 gave NOE with H-1 and H-6, irradiation of H-5 caused enhancement of the signal of H-7.

The EI-mass spectrum of **2** gave a peak for a molecular formula $C_{16}H_{20}O_4$ at *m/z* 276.1. The ^{1}H NMR spectrum of **2** was very close to that of arglanine (**4**) [3] (Table 1). The only differences in this spectrum were in the signals of the exocyclic methylene group at C-13, which appeared at δ 6.36 (*s*) and 5.80 (*s*), and a methoxyl signal at δ 3.82 (*s*), while these signals appeared as doublets at δ 6.17 (J = 3.5 Hz) and 5.51 (J = 3.0 Hz) in **4**. These exocyclic methylene singlets, together with the methoxyl signal, indicated an acid ester formed by opening the lactone ring of **4**.

EXPERIMENTAL

General. CC was carried out on Kieselgel 60 (0.063–0.200 mm, Merck) and Sephadex LH-20 (Pharmacia). TLC was performed on precoated silica gel 60 F_{254}, 0.2 mm plates (Merck); spots were detected under UV and spraying acidified ceric sulphate followed by heating. IR spectra were recorded on a Perkin-Elmer 983 instrument. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200L spectrometer with $CDCl_3$, and C_6D_6 as solvents and TMS as int. standard, operating at 200 and 50.32 MHz, respectively. GC-MS spectra were recorded on a VG Zabspec instrument.

Plant material. Tanacetum praeteritum (Horwood) Heywood subsp. *praeteritum* was collected from the southwest part of Turkey (Fethiye). A voucher specimen (ISTE 64370) is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul.

Extraction and isolation. Dried and powdered aerial parts (4.9 kg) were extracted with petrol, $CHCl_3$ and EtOH, respectively. The extracts were combined and

Table. 1. ^{1}H NMR spectra of compounds **1**, **1a**, **2** and **4** (200 MHz)

	1*	1†	1a*	2*	4*
H-1	3.45 *br s*	3.13 *br s*	4.92 *br s*	—	—
H-2	—	—	—	6.60 *d*	6.62 *d*
H-3	5.90 *m*	5.78 *m*	5.95 *br s*	5.86 *d*	5.91 *d*
H-5	3.25 *br d*	2.76 *br d*	3.09 *br d*	2.57 *d*	2.56 *d*
H-6	4.00 *dd*	3.04 *dd*	3.98 *dd*	4.15 *dd*	4.15 *dd*
H-7	2.65 *dddddd*	2.03 *m*	2.61 *m*	2.57 *m*	2.60 *m*
H-8	2.20 *m*	‡	‡	‡	‡
H-8	1.65 *m*	‡	‡	‡	‡
H-9	2.20 *m*	‡	‡	‡	‡
H-9′	1.45 *m*	‡	‡	‡	‡
H-13	6.14 *d*	5.90 *d*	6.15 *d*	6.36 *s*	6.17 *d*
H-13′	5.48 *d*	4.74 *d*	5.48 *d*	5.80 *s*	5.51 *d*
H-14	0.83 *s*	0.34 *s*	0.94 *s*	1.17 *s*	1.20 *s*
H-15	2.18 *s*	1.77 *s*	2.19 *s*	1.58 *s*	1.57 *s*
OAc			2.01 *s*	—	—
OMe				3.82 *s*	—

J (Hz): **1**: 5, 6 = 6, 7 = 10; 7, 13 = 3.5; 7, 13′ = 3.0. **2**, **4**: 1, 2 = 10, 5, 6 = 6, 7 = 11, 13, 13′ = 3.0.

* In $CDCl_3$.

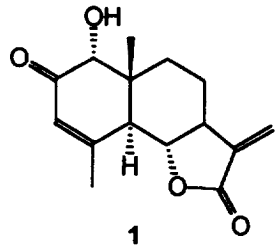
† In C_6D_6.

‡ Obscured.

treated with MeOH. The residue was applied to a silica gel column and eluted with petrol, a gradient of Et_2O being added up to 100% followed by MeOH. The frs from CC were further sepd by prep. TLC and/or Sephadex LH-20. The further eudesmanolides were obtained from the last polar fr. Compound **2** was obtained as a mixt. together with **4**, which was impossible to separate by prep. TLC. Its mass spectrum was determined by GC-MS. Thus, 25 mg **1**, 4 mg **2** and 15 mg **3** were obtained.

Tanapraetenolide (**1**). Amorphous compound. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (OH), 1760 (α,β-unsaturated γ-lactone), 1660 (C=C). UV ($CHCl_3$): 250 nm. ^{1}H NMR: see Table 1. ^{13}C NMR was recorded by APT technique, in which methyl and methine carbons showed negative signals whereas methylene and quaternary carbons showed positive signals. ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 77.6 (−) C-1, 190 (+) C-2, 124.8 (−) C-3, 132.2 (+) C-4, 45.7 (−) C-5, 79.8 (−) C-6, 50.7 (−) C-7, 20.4 (+) C-8, 34.5 (+) C-9, 42.9 (+) C-10, 138.2 (+) C-11, 161.7 (+) C-12, 117.7 (+) C-13, 17.6 (−) C-14, 24.7 (−) C-15. HRMS *m/z* (rel. int.): 262.1213 ($C_{15}H_{18}O_4$) $[M]^+$ (11), 244 $[M-H_2O]^+$ (37), 216 $[244-CO]^+$ (35), 201 $[216-CH_3]^+$ (18), 185 $[201-CH_3]^+$ (21), 173 (26), 161 (25), 149 (35), 135 (48), 111 $[C_6H_7O_2]^+$ (100), 109 (44), 95 (41), 91 (44), 82 (86), 71 (38), 57 (36).

Acetylation of **1**. Compound **1** (6 mg) was treated



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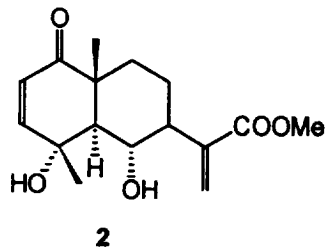

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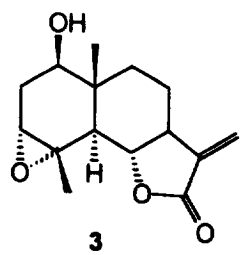

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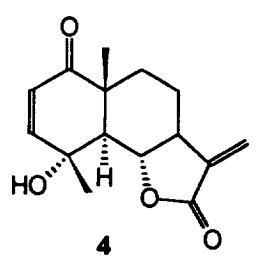

4

with pyridine (1 ml) and Ac_2O (1 ml) overnight. After vacuum evapn it was sepd by prep. TLC, thus **1a** (5 mg) was obtained.

Tanapraetenolide acetate (**1a**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780 (α,β-unsaturated γ-lactone), 1745, 1230 (ester), 1620 (ketone), 1675 (unsaturation). ^1H NMR : see Table 1. HRMS *m/z* (rel. int.): 304 $(C_{17}H_{20}O_5)^+[M]^+$ (16), 262 $[M-42]^+$(31), 244 $[M-CH_3CO_2H]^+$(47), 216 [244 −CO] (38), 201 $[216-CH_3]^+$ (22), 187 (24), 173 (26), 161 (21), 149 (50), 135 (36), 123 (21), 111 (100), 97 (17), 91 (41), 82 (68), 69 (35), 57 (26).

Arglanilic acid methyl ester (**2**). Gum. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440 (OH), 1720 (ester), 1685 (CO-C=C). ^1H NMR: see Table 1. EIMS *m/z* (rel. int.): 276.1 ($C_{16}H_{20}O_4$) $[M]^+$ (39), 261 $[276-CH_3]^+$ (16), 248 $[276-CO]^+$ (63), 247 (63), 233 $[261-CO]^+$ (6), 229 $[247-H_2O]^+$ (66), 215 (63), 201 $[233-CH_3OH]^+$ (46), 187 (44), 173 (37), 163 (26), 159 (49), 149 (64), 135 (100), 123 (83), 107 (36), 95 (38), 91 (61), 81 (43), 69 (26).

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