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FARNESOL AND THYMOL DERIVATIVES FROM  
*ASTERISCUS PYGMAEUS*<sup>1</sup>

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**ABSTRACT.**—Investigation of the aerial parts of *Asteriscus pygmaeus* has yielded a new thymol derivative **3** and four new farnesol glucosides **4–7**. The structures of the new compounds were identified by <sup>1</sup>H nmr, <sup>1</sup>H-<sup>13</sup>C correlation, and hrms.

*Asteriscus* (Compositae, tribe Inuleae, subtribe Inulinae) is a small genus with only three species, common in the Mediterranean area. The genus is placed in the *Inula* group close to the genera *Pallenis*, *Bubonium*, and *Rhanterium* (1). While the chemistry of *Asteriscus graveolens* (2) and *Asteriscus sericeus* (3) has been studied, nothing was known of the constituents of *Asteriscus pygmaeus* (DC.) Coss. and Desv.

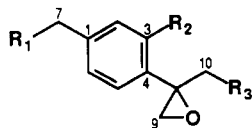
## RESULTS AND DISCUSSION

The aerial parts of *A. pygmaeus* afforded, in addition to known compounds **1** (4) and **2** (5), a new thymol derivative **3**, and four new farnesol glucosides **4–7**.

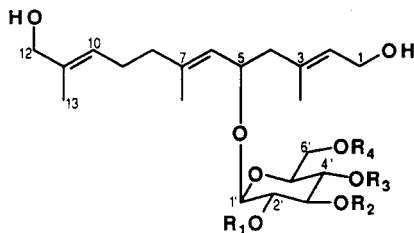
The <sup>1</sup>H-nmr spectrum of **3** was similar to those of **1** and **2**. The presence of the 7-isovalerate was confirmed by the signals observed at  $\delta$  2.24 d, 2.13 m, and 0.95 d. The aromatic protons appeared at  $\delta$  7.47, 7.22, and 7.07 for H-5, H-6, and H-2, respectively, and the

3-isobutyrate signals at  $\delta$  2.86 ddqq and 1.32 d and 10-isobutyrate signals at  $\delta$  2.51 ddqq, 1.11 d, and 1.08 d. Comparison of the chemical shifts of isobutyrate of **3** with those of **1** and **2** indicated that the isovalerate should be at the 7 position.

The <sup>1</sup>H-nmr spectrum of **5** was in part close to those of similar farnesol derivatives. In the <sup>1</sup>H-nmr spectrum of the aglycone skeleton of **5** the presence of two primary oxygen functions was determined from the two methylene signals: one AB system at  $\delta$  3.90 and 3.95, and another at  $\delta$  4.05 (2H). The H-1, CH<sub>2</sub>O-unit, was supported by double doublets at  $\delta$  3.90 and 3.95 that were coupled to an olefinic proton at  $\delta$  5.45. The second oxygen function was placed at C-12, since by nOe difference spectroscopy a clear effect was observed between H-12 (4.5%), H-10 (4%), and H-13. Spin decoupling allowed the assignment of all signals and located the glycosylated hydroxyl group at C-5. Upon irradiation of the H-5 signal at  $\delta$  4.70, correlations were observed at  $\delta$  2.30 and 2.10 (H-4)



- 1** R<sub>1</sub>=H, R<sub>2</sub>=R<sub>3</sub>=OCOCHMe<sub>2</sub>  
**2** R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=OCOCHMe<sub>2</sub>  
**3** R<sub>1</sub>=OCOCH<sub>2</sub>CHMe<sub>2</sub>,  
 R<sub>2</sub>=R<sub>3</sub>=OCOCHMe<sub>2</sub>



- 4** R<sub>1</sub>=R<sub>2</sub>=R<sub>4</sub>=H, R<sub>3</sub>=Ang  
**5** R<sub>1</sub>=R<sub>4</sub>=H, R<sub>2</sub>=Ac, R<sub>3</sub>=Ang  
**6** R<sub>4</sub>=H, R<sub>1</sub>=R<sub>2</sub>=Ac, R<sub>3</sub>=Ang  
**7** R<sub>1</sub>=R<sub>2</sub>=R<sub>4</sub>=Ac, R<sub>3</sub>=Ang

<sup>1</sup>A part of this work was presented at the 39th meeting of the Society for Medicinal Plants Research, 3–7 September, 1991, Saarbrücken, Germany.

and  $\delta$  4.95 (H-6). Signals at a lower field suggested the presence of a sugar moiety, the chemical shifts and coupling constants of which indicated a  $\beta$ -glucopyranoside (Table 1). Also, signals for angelate and acetate groups were observed. The presence of H-3' and H-4' downfield at  $\delta$  5.10 and 4.95 located the two acyl groups at C-3' and C-4' (8). Comparison of the sugar signals of **5** with those of **4** confirmed the acetate at C-3' and the angelate at C-4'. The structure of **5** was confirmed by  $^{13}\text{C}$  nmr (Table 2), and by  $^1\text{H}$ - $^{13}\text{C}$  correlation. The hrms gave a peak at  $m/z$  287.1119 due to  $[\text{sugar} + \text{H}]^+$  (calcd for  $\text{C}_{13}\text{H}_{19}\text{O}_7$ , 287.1130). The farnesol skeleton showed loss of  $\text{H}_2\text{O}$  at  $m/z$  235.1684 (calcd for  $\text{C}_{15}\text{H}_{23}\text{O}_2$ , 235.1698), followed by loss of oxygen at  $m/z$  219.1728 (calcd for  $\text{C}_{15}\text{H}_{23}\text{O}$ , 219.1748) and finally loss of

$\text{H}_2\text{O}$  at  $m/z$  201.1643 (calcd for  $\text{C}_{15}\text{H}_{21}$ , 201.1643).

In the  $^1\text{H}$  nmr of **4**, only one proton of the sugar moiety was observed downfield at  $\delta$  4.79, and angelate signals were present at  $\delta$  6.06, 1.88, and 1.79. Spin decoupling of the sugar moiety placed the angelate group at C-4'. The ms spectrum showed a fragment at  $m/z$  245.1012 (calcd for  $\text{C}_{11}\text{H}_{17}\text{O}_6$ , 245.1025), most likely due to the sugar moiety. The fragmentation pattern of the aglycone skeleton was identical to that of **5** (see Experimental).

$^1\text{H}$ -nmr and hrms analysis of **6** and **7** indicated that the two compounds contained an angelate and two and three acetate groups, respectively. The chemical shifts of the sugar protons placed the acetates at C-2' and C-3' for **6** and C-2', C-3', and C-6' for **7**. Furthermore, the  $^{13}\text{C}$

TABLE 1.  $^1\text{H}$ -nmr Spectral Data of Compounds **4-6**  
(400 MHz,  $\text{CDCl}_3$ , TMS as internal standard).

Proton	Compound			
	4	5	6	7
H-1	4.03 dd (7,13) 3.98 dd (7,13)	3.95 3.90	4.05 4.10	4.15
H-2	5.37 br t (7)	5.45	5.40	5.35
H-4	2.28 dd (7,13) 2.06 dd (6,13)	2.30 2.10	2.23 2.10	2.30 2.15
H-5	4.66 ddd (6,7,9,5)	4.70	4.60	5.65
H-6	4.93 br d (9,5)	4.95	4.61	5.90
H-8	2.04 m	2.05	2.04	2.00
H-9	2.10 m	2.10	2.10	2.15
H-10	5.24 br t (7)	5.30	5.30	5.35
H-12	3.84 br (ABq) (17,1)	4.10	3.95	4.00
H-13	1.53 br s	1.57	1.57	1.63
H-14	1.56 br s	1.60	1.57	1.63
H-15	1.58 br s	1.63	1.57	1.63
H-1'	4.18 d (8)	4.33	4.50	4.50
H-2'	3.26 dd (8,9)	3.45	4.90	4.95
H-3'	3.53 dd (9,9)	5.10	5.28	5.25
H-4'	4.79 dd (9,9)	4.95	5.00	5.15
H-5'	3.23 ddd (3,5,9)	3.35	3.35	3.60
H-6'	3.58 dd (3,13) 3.50 dd (5,13)	3.65 3.55	3.67 3.55	4.10 4.15
OAc		2.00	1.90	2.05, 2.00
OAng	6.06 qq (1.5,7) 1.88 dq (1.5,7) 1.79 dq (1.5,1.5)	6.10 1.90 1.78	6.05 1.88 1.75	6.10 1.90 1.80

TABLE 2.  $^{13}\text{C}$ -nmr Data for Compounds 5 and 7.

Carbon	Compound	
	5	7
C-1	67.47 (t)	67.95
C-2	125.94 (d) <sup>a</sup>	126.68
C-3	140.55 (s) <sup>b</sup>	139.95
C-4	44.78 (t)	44.52
C-5	71.88 (d)	71.28
C-6	124.53 (d) <sup>a</sup>	124.94
C-7	134.83 (s) <sup>b</sup>	135.02
C-8	38.81 (t)	38.34
C-9	24.70 (t)	28.73
C-10	123.88 (d) <sup>a</sup>	123.99
C-11	134.83 (s) <sup>b</sup>	134.98
C-12	58.81 (t)	58.32
C-13	13.59 (q) <sup>c</sup>	13.51
C-14	16.01 (q) <sup>c</sup>	15.93
C-15	16.85 (q) <sup>c</sup>	16.60
C-1'	98.76 (d)	96.83
C-2'	71.99 (d)	71.68
C-3'	74.62 (d)	71.98
C-4'	68.50 (d)	68.09
C-5'	74.30 (d)	72.95
C-6'	60.97 (t)	62.03
Angelate	167.11 (s), 140.11 (d) 126.65 (s), 20.14 (q) 15.63 (q)	165.98 (s), 141.49 (d) 126.12 (s), 24.23 (q) 15.59 (q)
Acetate	170.89 (s), 20.63 (q)	169.09 (s), 176.19 (s) 170.24 (s), 19.99 (q) 20.10 (q), 20.20 (q)

<sup>a,b,c</sup>Signals may be interchanged.

spectrum of 7 (Table 2) was in agreement with the proposed structure.

### EXPERIMENTAL

**PLANT COLLECTION, EXTRACTION AND ISOLATION.**—The air-dried aerial parts (200 g) of *A. pygmaeus* [probably = *A. aquaticus* L. (6)], collected from Marsah-Matrouh, Egypt in March 1991 (voucher specimen deposited in the Department of Botany, El-Minia University) were extracted with MeOH-Et<sub>2</sub>O-petroleum ether (1:1:1), and the extract (5 g) was defatted with MeOH and separated by cc (Si gel) into several fractions. The fraction eluted by Et<sub>2</sub>O-petroleum ether (40–60) (4:6) (30 mg) was separated by hplc [RP 8, flow rate 3 ml/min, MeOH-H<sub>2</sub>O (6:4)] to give 1 (5 mg), 2 (7 mg), and 3 (2 mg). The polar fraction, eluted by Et<sub>2</sub>O-MeOH (20:1) (50 mg), gave by hplc [RP 8, MeOH-H<sub>2</sub>O (1:1)] 4 (5 mg), 5 (15 mg), 6 (4 mg), and 7 (8 mg).

**7-Isovaleryloxy-10-isobutyryloxy-8,9-dihydro-8,9-epoxythymol-isobutyrate [3].**—Colorless oil: ir  $\nu$  (CHCl<sub>3</sub>) cm<sup>-1</sup> 1760, 1740; eims  $m/z$  (rel. int.)

420 (6), [M - isobutyric]<sup>+</sup> 332 (13), [M - isovaleric]<sup>+</sup> 318 (30); <sup>1</sup>H nmr (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.47 (1H, d,  $J$  = 8 Hz, H-5), 7.22 (1H, dd,  $J$  = 8 and 2 Hz, H-6), 7.05 (1H, d,  $J$  = 2 Hz, H-2), 5.10 (2H, s, H-7), 4.60 (1H, d,  $J$  = 12 Hz, H-10), 4.19 (1H, d,  $J$  = 12 Hz, H-10); 3-O-iBu 2.86 ddq, 1.32 d, 7-O-iVal 2.24 d, 2.13 m, 0.95 d, 10-iBu 2.51 ddq, 1.11 d, 1.08 d; [ $\alpha$ ]<sup>24</sup><sub>D</sub> + 6.3 ( $c$  = 0.27, MeOH).

**1,5,12-Trihydroxy-5-O-(4'-O-angeloyl- $\beta$ -D-glucopyranosyl)-farnesol [4].**—Colorless gum: ir  $\nu$  (CHCl<sub>3</sub>) cm<sup>-1</sup> 3580, 3400, 2920, 1720, 1610, 1200; cims  $m/z$  (rel. int.) 245.1012 (calcd for C<sub>11</sub>H<sub>17</sub>O<sub>6</sub>, 245.1025), 235.1684 (calcd for C<sub>15</sub>H<sub>23</sub>O<sub>2</sub>, 235.1698), 219.1728 (calcd for C<sub>15</sub>H<sub>23</sub>O, 219.1748), 201.1643 (calcd for C<sub>15</sub>H<sub>21</sub>, 201.1643); [ $\alpha$ ]<sup>24</sup><sub>D</sub> - 10 ( $c$  = 0.05, MeOH).

**1,5,12-Trihydroxy-5-O-(3'-O-acetyl-4'-O-angeloyl- $\beta$ -D-glucopyranosyl)-farnesol [5].**—Colorless oil: ir  $\nu$  (CHCl<sub>3</sub>) cm<sup>-1</sup> 3560, 3450, 2900, 1700, 1250; cims  $m/z$  (rel. int.) 287.1119 (calcd for

$C_{13}H_{19}O_7$ , 287.1130); [ $\alpha$ ] $^{24}D$  -9.5 ( $r=0.15$ , MeOH).

*1,5,12-Trihydroxy-5-O-(2'-3'-O-diacetyl-4'-O-angeloyl- $\beta$ -D-glucopyranosyl)-farnesol* [6].—Colorless oil: ir  $\nu$  ( $CHCl_3$ )  $cm^{-1}$  3550, 3400, 2950, 1750, 1630, 1250; cims  $m/z$  (rel. int.) 329.1226 (calcd for  $C_{15}H_{21}O_8$ , 329.1236).

*1,5,12-Trihydroxy-5-O-(2',3',6'-triacetyl-4'-O-angeloyl- $\beta$ -D-glucopyranosyl)-farnesol* [7].—Colorless oil: ir  $\nu$  ( $CHCl_3$ )  $cm^{-1}$  3600, 3480, 3000, 1720, 1650, 1280; cims  $m/z$  (rel. int.) 371.1326 (calcd for  $C_{17}H_{23}O_9$ , 371.1342); [ $\alpha$ ] $^{24}D$  -9.0 ( $r=0.44$ , MeOH).

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