Phytochemistry, Vol. 26, No. 4, pp. 1113–1115, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00

ACETOPHENONES AND TERPENOIDS FROM *SENECIO GALLICUS*

JULIO G. URONES, J. DE PASCUAL TERESA, ISIDRO S. MARCOS, ROSALINA FERNÁNDEZ MORO, PILAR BASABE BARCALA and Mª. JOSE SEXMERO CUADRADO

Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad de Salamanca, 37008 Salamanca, Spain

(*Revised received* 25 *July* 1986)

Key Word Index—*Senecio gallicus*; Compositeae; acetophenones; phytol derivatives; eremophilenolide.

Abstract—Six new compounds isolated from the aerial part of *Senecio gallicus* were: 7,11,15-trimethyl-3-methylene hexadecan-1,2-diol diacetate; 7,11,15-trimethyl-3-methylenehexadecan-1,2-diol; 3,5-bis(3-methyl-2-butenyl)-4-acetoxyacetophenone; 3-(2-hydroxy-3-methyl-3-butenyl)-5-(3-methyl-2-butenyl)-4-hydroxacetophenone; 3-(2,3-dihydroxy-3-methyl-butyl)-5-(3-methyl-2-butenyl)-4-hydroxyacetophenone and 1,10-epoxy-8α-hydroxy eremophilenolide.

INTRODUCTION

The pyrrolizidine alkaloids and the sesquiterpenes with a furoeremophilane skeleton are the major components of the genus *Senecio* [1]. There are two previous studies concerning the components of *Senecio gallicus*. One of them refers to flavonoids [2] and the other to alkaloids [3]. In the present study we report the isolation and identification of four *p*-hydroxyacetophenone derivatives; these types of compound have been isolated from other *Senecio* species [4]. Also, two germacrane sesquiterpenes, two phytol-derived diterpenes and one eremophilenolide are described.

RESULTS AND DISCUSSION

Compounds **1**–**7** were isolated by column chromatography of a hexane extract from the aerial part of *Senecio gallicus*. Compound **8** was also isolated from the hexane soluble part of the EtOH extract. We have isolated two compounds identified by physical and spectroscopical properties as germacrane D [5] and 4β-hydroxygermacra-1(10),5-diene [6].

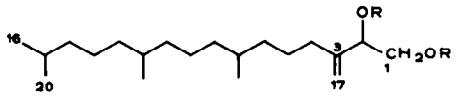
Compound **1** is an unsaturated diol (3400, 890 cm^{-1}); its ^1H NMR shows signals for four $\underline{CH_3}$–CH and one $\underline{CH_2}$=C–CH(OH)–CH_2OH group. The ^{13}C NMR spectrum shows signals for four methyl groups, 11 methylene groups (one CH_2OH and one sp^2 CH_2), four methine groups and one quaternary sp^2 carbon. The structure 7,11,15-trimethyl-3-methylene-hexadecan-1,2-diol was assigned for compound **1**. By acetylation of compound **1** the natural diacetate **2** was obtained. The assignment of the signals in the ^{13}C NMR spectra (see Experimental) of these compounds is based on the data corresponding to phytol [7]. Compounds **3**, **4**, **5** and **6** are *p*-hydroxyacetophenone derivatives with substituents at C-3 and C-5. The major compound is **3** which has two identical chains at these positions and which has been previously reported [8–10]. The acetylation of compound **3** afforded the natural acetate **4**.

In compounds **5** and **6**, one of the chains is the same as in compounds **3** and **4**. The chain at C-3 in compound **5** is CH_2=C(CH_3)–CHOH–CH_2, confirmed by radiation in the ^1H NMR spectrum of the signal centred at 4.41 ppm corresponding to the hydrogen geminal to the hydroxyl group and also by the multiplicity and shielding of the signal in the ^{13}C NMR spectrum (Tables 1 and 2).

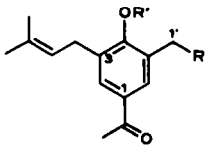
The chain at C-3 in **6** shows two singlet methyl groups corresponding to a structure of $(CH_3)_2$COH–CHOH–CH_2– (Tables 1 and 2).

Compound **7** shows in its ^1H NMR and ^{13}C NMR spectra (see Experimental) signals corresponding to the groups: CH_3–C= (3H, *d*, 1.90, J = 1.4 Hz), CH_3–C (3H, *s*, 0.81), CH_3–CH (3H, *d*, 0.82, J = 6.8 Hz), CH_3O–C (3H, *s*, 3.20),  (1H, *br d*, 2.95, J = 3.5 Hz), four methylene groups and a lactone carbonyl group. It is identified as the epoxy-eremophilenolide by comparison with the spectroscopic data for eremophilenolide described in other *Senecio* species [11].

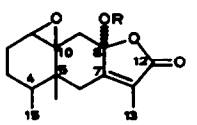
The structure of compound **8** is related to compound **7**



1 R = H **2** R = Ac



	R	R'
3	CH = CMe_2	H
4	CH = CMe_2	Ac
5	CH(OH)C(Me) = CH_2	H
6	CH(OH)C(OH) Me_2	H



7 Me
8 Et
9 H

Table 1. ^{1}H NMR spectra of compounds 3–6

	3	4	5	6
H-2/H-6	7.63 (*s*)	7.67 (*s*)	7.65 (*d*, *J* = 2.1 Hz) 7.55 (*d*, *J* = 2.3 Hz)	7.65 (*br s*) 7.63 (*br s*)
H-1′	3.38 (*br d*, *J* = 7 Hz)	3.24 (*br d*, *J* = 7.2 Hz)	H-1′$_a$ 2.99 *dd* J_1 = 14.7, J_2 = 8.4 H-1′$_b$ 2.82 *dd* J_1 = 14.7, J_2 = 2.4	3.20 *dd*, J_1 = 9.0 Hz, J_2 = 0.9 Hz
H-2′	5.31 (*t*, *J* = 7 Hz	5.22 (*t*, *J* = 7 Hz	4.41 (*br d*, *J* = 8.4 Hz)	4.71 (*t*, *J* = 9.0 Hz
H-4′	1.78 (*d*, *J* = 1 Hz)	1.69 (*d*, *J* = 1 Hz)	4.88 and 5.02 (2 *br s*)	1.21 (*s*)
H-5′	1.78 (*d*, *J* = 1 Hz)	1.75 (*d*, *J* = 1 Hz)	1.81 (*br s*)	1.34 (*s*)
H-1″			3.38 (*br d*, *J* = 7.2 Hz)	3.31 (*m*)
H-2″			5.33 (*t*, *J* = 7.2 Hz)	5.28 (*t*, *J* = 7.3 Hz)
H-4″			1.73 (*d*, *J* = 1.1 Hz)	1.74 (*br s*)
H-5″			1.75 (*d*, *J* = 1.4 Hz)	1.74 (*br s*)
CH_3–CO–	2.54 (*s*)	2.55 (*s*)	2.50 (*s*)	2.53 (*s*)
CH_3–COOAr		2.32 (*s*)		

Table 2. ^{13}C NMR spectra of compounds 3–6

	3	4	5	6
C-1	130.08	133.82*	129.57†	131.18
C-2	128.83	128.07	130.04*	123.29
C-3	127.47	134.48*	125.39	123.05
C-4	157.41	151.31	158.78	161.17
C-5	127.47	134.48*	129.52†	127.22
C-6	128.83	128.07	129.63*	129.92
C-1′	29.63	29.12	38.51	30.38
C-2′	121.47	121.16	77.67	90.19
C-3′	135.02	135.26	146.42	71.91
C-4′	17.92	17.90	111.32	24.22
C-5′	25.79	25.71	18.14	25.69
C-1″			28.96	28.45
C-2″			122.16	121.51
C-3″			133.20	133.17
C-4″			17.84	17.85
C-5″			25.74	25.76
–C(=O)–CH_3	197.30	197.47	197.47	196.68
CH_3–C(=O)–	26.25	26.58	26.14	26.31
–O–C(=O)–		168.51		
CH_3–C(=O)–O		20.52		

*,† Assignments interchangeable.

but in this case the substituent at C-8 is an ethoxy group. This suggests that **7** and **8** are artefacts derived from the natural product **9**.

EXPERIMENTAL

Mps (Kofler hot stage apparatus) uncorr.; ^{1}H NMR: 200 MHz, $CDCl_3$, TMS as internal standard; ^{13}C NMR: 50.3 MHz. Optical rotations were determined with a digital Perkin–Elmer 241 polarimeter.

Extraction and isolation. Senecio gallicus collected in flower in Valparaiso (Zamora, Spain), was dried and extracted with *n*-hexane in a Soxhlet. A voucher specimen of the plant was deposited in the Department of Botany, University of Salamanca. The hexane extract (2.3% with respect to the dried plant) was dewaxed with MeOH. The MeOH-soluble part (44.9% with respect to the hexane extract) was chromatographed on a silica gel column yielding the following compounds.

Germacrane D (21 mg) (hexane and CC on silica gel–$AgNO_3$ 10% hexane–Et_2O, 9:1), **2** (6 mg) (hexane–ether, 9:1; and CC on silica gel–$AgNO_3$ 10% hexane–Et_2O, 8:2), 4β-hydroxygermacra-1(10),5-diene (12 mg) (hexane–Et_2O, 9:1; and CC on silica gel–$AgNO_3$ 10% hexane–Et_2O, 1:1), **3** (16 mg) (hexane–Et_2O, 8:2; and crystallization from hexane), **4** (3.5 mg) [hexane–Et_2O, 8:2; together with **3** and preparative TLC (hexane–AcOEt, 8:2) of the mother liquor from crystallization of **3**], **5** (23 mg) (hexane–Et_2O, 1:1; followed by separation of **3** by crystallization and chromatography of the mother liquor, eluting with hexane–Et_2O, 8:2), **6** (4 mg) (hexane–Et_2O, 1:1; separation of **3** by crystallization and chromatography of the mother liquor, eluting with hexane–Et_2O, 1:1), **7** (18 mg) (hexane–Et_2O, 1:1; and crystallization from *n*-hexane) and **1** (5 mg) (hexane–Et_2O, 1:1 and preparative TLC benzene–Et_2O, 7:3, development 3 ×).

Another part of the plant was extracted at room temp. with EtOH for 3 weeks (5%); the EtOH was evaporated *in vacuo* after which the hexane soluble part (36% with respect to the EtOH-extract) was separated. From this part, besides the above-described compounds, compound **8** (40 mg) was isolated after chromatography on a silica gel column (hexane–Et_2O, 1:1) and preparative TLC with hexane–EtOAc, 8:2, development 3 ×.

7,11,15-*Trimethyl*-3-*methylene-hexadecan*-1,2-*diol diacetate* (**2**). Colourless oil. IR ν_{max}^{film} cm^{-1}: 1740, 1640 and 890; ^{1}H NMR: δ5.3 (3H, *m*, H-17 and H-2), 4.3 (1H, *dd*, *J* = 11.72, 4.39 Hz, H_A-1), 4.15 (1H, *dd*, *J* = 11.72 Hz, 5.86, H_B-1) 2.04 and 2.01 (6H, each *s*, 2 CH_3–C(=O)–O), 0.87 (3H, *d*, *J* = 6.35, H-18), 0.86 (6H, *d*, *J* = 6.59, Me-16 and Me-20), 0.84 (3H, *d*, *J* = 6.35, Me-19).

7,11,15-*Trimethyl*-3-*methylene-hexadecan*-1,2-*diol* (**1**). Colourless oil. $[\alpha]_D$ = −1.2 (*c* = 0.5%, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 1640, and 890 cm^{-1}; ^{1}H NMR: δ5.13 and 4.98 (2H, each *s*, H-17), 4.21 (1H, *dd*, J_1 = 11.23, J_2 = 3.42 Hz, H-2), 3.69 (1H, *dd*, *J* = 11.23, 3.42 Hz, H_A-1), 3.57 (1H, *dd*, *J* = 11.23, 7.32 Hz, H_B-1),

0.86 (6H, *d*, *J* = 6.59 Hz, Me-16 and Me-20), 0.85 (3H, *d*, *J* = 6.35 Hz, Me-18), 0.84 (3H, *d*, *J* = 6.35 Hz, Me-19); ^{13}C NMR: δ65.75 (C-1), 75.12 (C-2), 148.86 (C-3), 33.07 (C-4), 25.64 (C-5), 36.89 (C-6), 32.77 (C-7), 37.50 (C-8), 24.52 (C-9), 37.48 (C-10), 32.86 (C-11), 37.36 (C-12), 24.82 (C-13), 39.45 (C-14), 28.02 (C-15), 22.63 (C-16), 110.61 (C-17), 19.77* (C-18), 19.73* (C-19), 22.72 (C-20).

3,5-*Bis*(3-*methyl*-2-*butenyl*)-4-*hydroxyacetophenone* (**3**). Mp = 90°; UV λ_{max}^{EtOH}: 226, 282 nm (ε = 17262, 14821); IR ν_{max}^{film} cm^{-1}: 3400, 3000, 1650 and 1600.

3,5-*Bis*(3-*methyl*-2-*butenyl*)-4-*acetoxyacetophenone* (**4**). Colourless oil. UV λ_{max}^{EtOH}: 226 and 282 nm. IR ν_{max}^{film} cm^{-1}: 1740, 1690, 1650, 1600 and 850.

3-(2-*hydroxy*-3-*methyl*-3-*butenyl*)-5-(3-*methyl*-2-*butenyl*)-4-*hydroxyacetophenone* (**5**). Colourless oil; $[\alpha]_D$ = 1.36 (*c* = 2.2%, $CHCl_3$); IR ν_{max}^{film} cm^{-1}: 3400, 1670, 1600, 1200 and 900.

1,10-*epoxy*-8α-*methoxyeremophilenolide* (**7**). Mp = 140°; UV λ_{max}^{EtOH}: 220 nm; IR ν_{max}^{KBr} cm^{-1}: 1760, 1695 and 990; ^{1}H NMR: δ3.20 (3H, *s*, H-16), 2.95 (1H, *br d*, *J* = 3.5 Hz, H-1), 2.64 (1H, *br d*, *J* = 13.09 Hz, H_A-6), 2.23 (1H, *br d*, *J* = 13.09 Hz, H_B-6), 2.27 (1H, *br d*, *J* = 14.3 Hz, H_A-9) 1.90 (3H, *d*, *J* = 1.4 Hz, H-13), 0.82 (3H, *d*, *J* = 6.8 Hz, H-15), 0.81 (3H, *s*, H-14); ^{13}C NMR: δ57.80 (C-1), 24.78* (C-2), 21.67* (C-3), 32.98 (C-4), 40.01 (C-5), 33.71 (C-6), 126.20 (C-7), 105.81 (C-8), 40.78 (C-9), 62.82 (C-10), 157.03 (C-11), 171.50 (C-12) 8.23 (C-13), 15.19† (C-14), 14.69† (C-15), 50.59 (C-16).

1,10-*Epoxy*-8α-*ethoxyeremophilenolide* (**8**). Colourless oil: $[\alpha]_D$ = −147.2° (*c* = 0.68%, $CHCl_3$); IR ν_{max}^{film} cm^{-1}: 1760, 1650 and 990; ^{1}H NMR: δ3.49 (1H, *dq*, *J* = 7.08 Hz, H-16), 3.31 (1H, *dq*, *J* = 7.08 Hz, H-16), 2.95 (1H, *br d*, *J* = 3.5 Hz, H-1), 2.64 (1H, *br d*, *J* = 13.09 Hz, H_A-6), 2.24 (1H, *br d*, *J* = 13.09 Hz, H_B-6), 2.28 (1H, *br d*, *J* = 14.37 Hz, H_A-9), 1.95 (1H, *br d*, *J* = 14.37 Hz, H_B-9), 1.88 (3H, *d*, *J* = 1.4 Hz, H-13), 0.83 (3H, *d*, *J* = 6.8 Hz, H-15), 0.81 (3H, *s*, H-14); ^{13}C NMR δ57.72 (C-1), 24.77* (C-2), 21.59* (C-3), 32.98 (C-4), 39.97 (C-5), 33.76 (C-6), 125.84 (C-7), 105.8 (C-8), 40.93 (C-9), 62.9 (C-10), 157.61 (C-11), 171.7 (C-12), 8.26 (C-13), 15.32† (C-14), 15.23† (C-15), 59.08 (C-16), 14.69 (C-17).

*,†Assignments interchangeable.

REFERENCES

1. Bohlmann, F., Knoll, K., Zdero, C., Mahanta, P. K., Grenz, M., Suwita, A., Ehlers, D., Le Van, N., Abraham, W. R. and Natu, A. A. (1977) *Phytochemistry* **16**, 965.
2. Mansour, R. H. A. and Saleh, N. A. M. (1981) *Phytochemistry* **20**, 1180.
3. Risk, A. M., Hammouda, F. M., Ismail, S. I., Ghaleb, H. A., Madkour, M. K., Pohland, A. E. and Wood, G. (1983) *Fitoterapia* **54**, 115.
4. Loyola, L. A., Predreros, S. and Morales, G. (1985) *Phytochemistry* **24**, 1600.
5. Yoshihara, K., Ohta, Y., Sakai, T. and Hirose, Y. (1969) *Tetrahedron Letters* **27**, 2263.
6. Bohlmann, F. and Zdero, C. (1984) *Phytochemistry* **23**, 1798.
7. Breitmaier, E., Voelter, W. (1978) ^{13}C *NMR Spectroscopy*, p. 125. Verlag Chemie, Weinheim.
8. Bohlmann, F., Zdero, C. and Franke, H. (1973) *Chem. Ber.* **106**, 382.
9. Bohlmann, F. and Zdero, C. (1972) *Chem. Ber.* **105**, 2604.
10. Bohlmann, F. and Zdero, C. (1977) *Chem. Ber.* **110**, 295.
11. Zalkow, L. H., Gelbaum, L. T. and Van Derveer D. (1979) *J. Chem. Soc. Perkin I* 1542.