Phytochemistry, 1980, Vol. 19, pp. 2781–2782. © Pergamon Press Ltd. Printed in England. 0031 9422/80/1201 2781 $02.00/0

p-HYDROXYACETOPHENONE DERIVATIVES FROM *ARTEMISIA CAMPESTRIS* SSP. *GLUTINOSA*

J. DE PASCUAL-T., I. S. BELLIDO, M. S. GONZÁLEZ, M. R. MURIEL and J. M. HERNÁNDEZ
Department of Organic Chemistry, Salamanca University, Spain

(*Received* 11 *February* 1980)

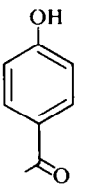
Key Word Index—*Artemisia campestris*: Compositae; *p*-hydroxyacetophenone derivatives.

Abstract—The weakly acidic fraction from *Artemisia campestris* ssp. *glutinosa* contains five *p*-hydroxyacetophenone derivatives, which are structurally and biogenetically related.

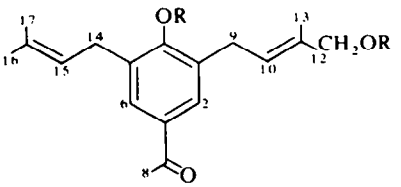
The weakly acidic fraction of the hexane extract from *Artemisia campestris* L. ssp. *glutinosa* (Gay ex Besser) Batt.*, consists of 20% of the hexane extract, previously steam-distilled, and by chromatography on silica gel, affords *p*-hydroxyacetophenone (**1**) (0.152 g, 0.6%) and its derivatives **2** (3.00 g, 12%), **3** (0.150 g, 0.6%), **4** (0.167 g, 1.1%) and **5** (1.90 g, 7.7%). **2**–**5** have not so far been reported as natural products.

2 was isolated as a solid, mp 109–110° (C_6H_6), M^+ = 288 ($C_{18}H_{24}O_3$) and UV: λ_{max}^{EtOH} at 226 (ε = 17 262) and 282 (ε = 14 821) nm. IR ($CHCl_3$): 3600, 3310 (OH), 1690 (C=O), 1650 (C=C), 1600, 1500 (aromatic), 1380, 1320, 1290, 1200, 1100, 1000, 850 cm^{-1}. This functionality was confirmed by the ^1H NMR spectrum, indicative of a tetrasubstituted aromatic ring, the substituents of which were identified as –COMe, –OH, isopentenyl and 4-hydroxyisopentenyl (Table 1). MS, *m/e* (%): 288 (M^+, 8), 270 ($M^+ - H_2O$, 47), 255 (270 – Me, 90), 227 (255 – CO, 100), 213 (26), 199 (45), 185 (29), 171 (81), 143 (21), 133 (19), 128 (27), 119 (29), 115 (20), 105 (12), 91 (16), 69 (21), 43 (5). All above data, and those of its diacetate **2a** [IR: 1770, 1750 (C=O of acetate groups), 1695 (C=O), 1650 (C=C), 1610 (aromatic), 1380, 1250 (Ac-O), 1220, 1170, 1100, 1050, 940, 820 cm^{-1}], agree with the proposed structure: 4-hydroxy-5-2-isopentenyl)-3-(4-hydroxy-2-isopentenyl)-acetophenone.

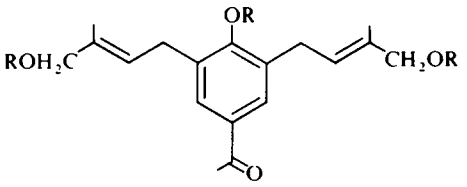
3 is a solid, mp 120° ($CHCl_3$), M^+ = 304 ($C_{18}H_{24}O_4$), UV: λ_{max}^{EtOH} at 227 (ε = 22 186) and 283 (ε = 16 046). The ^1H NMR spectrum shows signals which agree with a tetrasubstituted aromatic ring, the substituents being



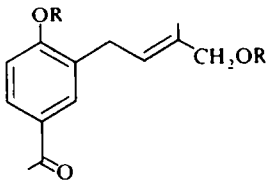
1



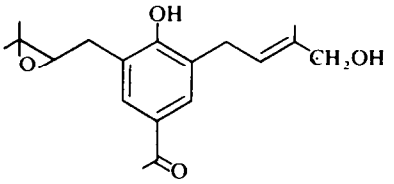
2 R = H
2a R = Ac



3 R = H
3a R = Ac



4 R = H
4a R = Ac



5

* The plant was identified by Prof. Dr. B. Casaseca Mena from the Department of Botany of Salamanca University, where a specimen is held (Herbarium No. 7362).

Table 1. ^{1}H NMR data for the *p*-hydroxyacetophenones of *Artemisia* (60 MHz, TMS)

	2*	2a*	3†	3a*	4†	4a*
H-2	7.70 *s*	7.75 *s*	7.64 *s*	7.70 *s*	7.80 *d*(2)	7.90 *d*(2)
H-6					7.70 *dd*(8, 2)	7.85 *dd*(8, 2)
H-5	—	—	—	—	7.16 *d*(8)	7.16 *d*(8)
H-8	2.52 *s*	2.58 *s*	2.46 *s*	2.57 *s*	2.48 *s*	2.57 *s*
H-9	3.48 *d*(8)	3.38 *d*(8)	3.47 *d*(7)	3.36 *d*(7)	3.44 *d*(8)	3.36 *d*(8)
H-14	3.32 *d*(7)	3.25 *d*(7)			—	—
H-10	5.35 *t*(8)	5.53 *t*(8)	5.38 *t*(7)	5.50 *t*(7)	5.62 *t*(8)	5.60 *t*(8)
H-15	5.30 *t*(7)	5.30 *t*(7)			—	—
H-12	4.40 *br. s*	4.72 *br. s*	4.24 *s*	4.70 *s*	4.00 *br. s*	4.52 *s*
H-17	1.75–1.78 *br. s*	1.75, 1.80 *s*	1.78 *s*	1.80 *s*	—	
H-13					1.75 *br. s*	1.76 *br. s*
H-18					—	—
Ph-OH	8.00 *br. s*	—	—	—	—	—
Ph-OAc	—	2.38 *s*		2.35 *s*	—	2.34 *s*
R-OAc	—	2.10 *s*	—	2.08 *s*		2.08 *s*

*$CDCl_3$.
†$(CD_3)_2CO$.

identified as –COMe, –OH and two 4-hydroxyisopentenyl groups (Table 1). MS, *m/e* (%): 304 (M^+, 3), 286 ($M^+ - H_2O$, 11), 271 (286 – Me, 7), 268 (286 – H_2O, 8), 253 (268 – Me, 39), 225 (34), 202 (100), 187 (94), 183 (32), 159 (54), 144 (22), 141 (23), 131 (32), 107 (14), 91 (18), 77 (11), 43 (9). Acetylation of **3** yields the triacetate **3a**. IR (film): 1770, 1745 (CO of acetate groups), 1690 (C=O), 1650 (C=C), 1605, 1500 (aromatic), 1380, 1250 (Ac-O), 1215, 1170, 1040, 830 cm^{-1}. All above data agree with the proposed structure for **3**: 4-hydroxy-3,5-di(4-hydroxy-2-isopentenyl)-acetophenone.

4 was isolated as a very pale yellow solid, slightly soluble in $CHCl_3$, mp 84–85°; M^+ = 220 ($C_{13}H_{16}O_3$); UV: λ_{max}^{EtOH} at 229 (ε = 14 200) and 285 (ε = 9850) nm; IR (KBr): 3580, 3440 (OH), 1660 (C=O), 1600, 1510 (aromatic), 1380, 1300, 1280, 1140, 1030, 1020, 840 cm^{-1}. The ^{1}H NMR spectrum suggests a 1,3,4-trisubstituted aromatic ring, the substituents being –COMe, –OH and 4-hydroxyisopentenyl (see Table 1). MS, *m/e* (%): 220 (M^+, 3), 202 ($M^+ - H_2O$, 88), 187 (202 – Me, 100), 169 (187 – H_2O, 7), 159 (187 – CO, 48), 147 (19), 144 (17), 141 (17), 131 (22), 107 (13), 91 (11), 77 (7), 43 (4). Acetylation of **4** yields the diacetate **4a**. Allylic oxidation of **4** (MnO_2–C_6H_6) [1], yields an oily conjugated aldehyde, whose spectral data are identical with those reported for artemispermal, isolated by Bohlmann *et al.* [2, 3] from *Artemisia monosperma* and *Doronicum pardalianches* (Compositae).

5 is a solid, mp 62° ($CHCl_3$), UV: λ_{max}^{EtOH} at 232 (ε = 16 600) and 285 (ε = 13 800) nm. IR (film): 3400 (OH), 1665 (C=O), 1600 (aromatic), 1440, 1360, 1320, 1290, 1190, 1140, 1095, 1010, 950, 865 cm^{-1}. ^{1}H NMR (δ, ppm): 7.60 (2H, *br. s*, H-2, H-6), 5.40 (1H, *t*, *J* = 8 Hz, H-10), 4.24 (2H, *br. s*, H-12), 3.84 (1H, *t*, *J* = 6 Hz, H-15), 3.46 (2H, *d*, *J* = 8 Hz, H-9), 2.94 (2H, *app.t*, *J* = 6 Hz, H-14), 2.50 (3H, *s*, H-8), 1.80 (3H, *s*, H-13), 1.33 (6H, *s*, H-17, H-18). MS, *m/e* (%): 304 (M^+, 9), 286 ($M^+ - H_2O$, 42), 271 (286 – Me, 68), 253 (271 – Me, 18), 243 (271 – CO, 18), 225 (23), 201 (47), 185 (49), 171 (100), 159 (51), 149 (23), 133 (33), 128 (42), 119 (33), 115 (29), 105 (18), 91 (24), 77 (18), 43 (15), 28 (7).

All above data agree with the proposed structure, and this was confirmed by partial synthesis from **2**. Epoxidation of **2**, with *m*-CPB–CH_2Cl_2 [4], yields a substance identical in all respects with **5**. The isolation of **5** as a natural product is quite interesting from the biogenetical point of view, because this type of epoxide has been proposed as the precursor of some *p*-hydroxyacetophenone derivatives [5].

REFERENCES

1. Goldman, I. M. (1969) *J. Org. Chem.* **34**, 1979.
2. Bohlmann, F. and Ehlers, D. (1977) *Phytochemistry* **16**, 1450.
3. Bohlmann, F. and Abraham, W. R. (1979) *Phytochemistry* **18**, 668.
4. Fieser, L. F. and Fieser, M. (1967) *Reagents for Organic Synthesis*, p. 135. J. Wiley, New York.
5. Bohlmann, F. and Grenz, M. (1970) *Ber.* **103**, 90.