Phytochemistry, Vol. 20, No. 10, pp. 2417–2420, 1981.
Printed in Great Britain.

0031–9422/81/102417–04 $02.00/0
© 1981 Pergamon Press Ltd.

AROMATIC COMPOUNDS FROM *ARTEMISIA CAMPESTRIS* SUBSP. *GLUTINOSA*

J. DE PASCUAL-T., I. S. BELLIDO, M. S. GONZÁLEZ, M. R. MURIEL and J. M. HERNANDEZ

Department of Organic Chemistry, Salamanca University, Spain

(*Received* 13 *February* 1981)

Key Word Index—*Artemisia campestris*; Compositae; aromatics; ^{1}H NMR; stereochemistry.

Abstract—From the weakly acid fraction of the hexane extract from *Artemisia campestris* subsp. *glutinosa*, five new aromatics have been isolated. They have been identified as *o*-hydroxyphenylbutan-2-one, 3-acetyl-4-hydroxyacetophenone, 3-(isopent-2-enyl)-4-hydroxyacetophenone, 3-[4-hydroxyisopent-2(*Z*)-enyl]-4-hydroxyacetophenone, 3-[4-hydroxyisopent-2(*E*)-enyl]-5-(isopent-2-enyl)-4-hydroxyacetophenone and 3-[4-hydroxyisopent-2-(*Z*)-enyl]-5-[4-hydroxyisopent-2(*E*)-enyl]-4-hydroxyacetophenone. The structures have been assigned by spectral data and chemical transformations.

INTRODUCTION

In a previous paper [1], we reported the isolation of *p*-hydroxyacetophenone, **1**, and several derivatives, **5**, **7**, **9** and **10**, from *Artemisia campestris* L. subsp. *glutinosa* (Gay ex Besser) Batt. Now, we have completed the study of the weakly acid fraction of the hexane extract, with the isolation of four new acetophenone derivatives and one aromatic hydroxyketone. The identification of some of these new compounds as stereoisomers of certain of the compounds already isolated has allowed us to assign the correct stereochemistry to the double bonds in the compounds **5**–**11**.

RESULTS AND DISCUSSION

Column chromatography of the weakly acid fraction of the hexane extract of *Artemis campestris* subsp. *glutinosa* afforded *p*-hydroxyacetophenone (**1**) (0.60%), its derivatives **3** (1.00%), **4** (1.10%), **5** (11.20%), **6** (44.80%), **7** (12.00%), **8** (1.80%), **9** (0.77%), **10** (0.60%), **11** (2.00%) and *o*-hydroxyphenylbutan-2-one (**2**) (0.57%).

The IR hydroxyketone **2** showed absorptions due to a phenolic OH group (3360, 1170), aromatic ring (1600, 1500) and a non-conjugated C=O group (1720). The ^{1}H NMR ($CDCl_3$) showed signals at δ (ppm) 2.10 (3 H, *s*, Me—CO), 2.72 (4 H, *br s*, CH_2—CH_2) and 6.83 (4 H, *m*, aromatic-H). These data and the MS, with M^+ 164 ($C_{10}H_{12}O_2$), agree with the proposed structure.

Diketone **3** was identified as a *p*-hydroxyacetophenone derivative by ^{1}H NMR, with signals [δ (ppm)] in good agreement with a 1,2,4-trisubstituted aromatic ring, the substituents being identified as two —COMe groups and one OH group: 2.56 and 2.70 (6 H, 2*s*, 2Me–CO), 6.97 (1 H, *d*, J = 8 Hz), 8.02 (1 H, *dd*, J = 8 and 2 Hz) and 8.35 (1 H, *d*, J = 2 Hz). The MS with M^+ 178, is consistent with the formula $C_{10}H_{12}O_3$.

Compounds **5** and **6** behave very similarly in chromatography and show nearly the same spectral properties: MS, with M^+ 220 ($C_{13}H_{16}O_3$) and ^{1}H NMR, suggesting the presence of a 1,2,4-trisubstituted aromatic ring, with —COMe, —OH and 4-hydroxyisopent-2-enyl groups as substituents (see Table 1). The only significant difference are the signals due to the —CH_2OH groups, which are in both shown as singlets, but at 4.00 ppm in **5**, and 4.28 ppm in **6**. This difference suggests that **5** and **6** may be one pair of (*E*) and (*Z*) stereoisomers.

Different chemical shifts were also observed for the same protons in the diacetates **5a** and **6a** and the methyl ethers **5b** and **6b**. Allylic oxidation of **5b** or **6b** with MnO_2–C_6H_6 [2] gave the corresponding conjugated aldehydes, **5c** or **6c**, whose ^{1}H NMR also showed differences in the chemical shifts of the olefinic proton (H-10) and the formyl-H, which are respectively shown at 6.43 (1 H, *t*, J = 8 Hz) and 9.24 (1 H, *s*) in **5c** and 6.48 (1 H, *t*, J = 8 Hz) and 10.40 (1 H, *s*) in **6c**. Oxidation of **5c** or **6c** with MnO_2–NaCN–MeOH [3] gave **5d** or **6d**. The ^{1}H NMR spectrum of **5d** showed the signal due to the olefinic proton (H-10) at 6.56 ppm, whereas ^{1}H NMR of **6d** showed the same signal at 5.90 ppm (Table 1). These facts, agree with the stereochemistry (*E*) for **5d**, and so on for **5c** and **5**, and the stereochemistry (*Z*) for **6d**, **6c** and **6** [4, 5].

Compounds **7** and **8** are also stereoisomers with M^+ 288 ($C_{18}H_{24}O_3$). Their ^{1}H NMR spectra showed signals due to a 1,2,4,6-tetrasubstituted aromatic ring, with —COMe, —OH, isopent-2-enyl and 4-hydroxyisopent-2-enyl groups as substituents (Table 2) with differences like those in **5** and **6** for the signals due to the —CH_2OH groups: 4.40 for **7** [identified as the (*Z*) isomer] and 4.00 pm for **8** [identified as the (*E*) isomer] (Table 2).

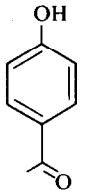
The MS of **10** and **11** showed the same molecular ion at m/z 304, in agreement with the formula $C_{18}H_{24}O_4$. Their ^{1}H NMR agree also with a 1,2,4,6-tetrasubstituted aromatic ring, with —COMe, —OH, and two 4-hydroxyisopent-2-enyl groups (Table 2), but the signal due to the —CH_2OH group at 4.24 (4 H) identifies **10** as the (*Z*,*Z*)stereoisomer, whereas the signals at 4.24 (2 H) and 3.95 (2 H) identify **11** as the (*Z*,*E*) estereoisomer.

For all the reasons above, the stereochemistry of the double bond in **9** (previously reported in this plant, see ref. [1]) must also be (*Z*).

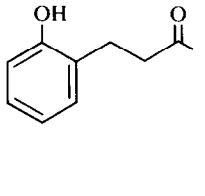
Table 1. ^{1}H NMR spectral data for the *p*-hydroxyacetophenones from *Artemisia* (60 MHz, TMS)

	5*	5c†	5d†	6*	6c*	6d†
H-2	7.80 *d* (2)	7.65 *d* (2)	7.75 *d* (2)	7.75 *d* (2)	7.68 *d* (2)	7.55 *d* (2)
H-5	7.16 *d* (8)	6.80 *d* (8)	6.90 *d* (8)	6.85 *d* (8)	6.80 *d* (8)	7.55 *d* (8)
H-6	7.70 *dd* (8, 2)	7.72 *dd* (8, 2)	7.85 *dd* (8, 2)	7.70 *dd* (8, 2)	7.75 *dd* (8, 2)	7.60 *dd* (8, 2)
H-8	2.48 *s*	2.42 *s*	2.50 *s*	2.50 *s*	2.50 *s*	2.40 *s*
H-9	3.44 *d* (8)	3.60 *d* (8)	3.50 *d* (8)	3.45 *d* (8)	3.82 *d* (8)	3.40 *d* (8)
H-10	5.62 *t* (8)	6.43 *t* (8)	6.56 *t* (8)	5.40 *t* (8)	6.48 *t* (8)	5.90 *t* (8)
H-12	4.00 *br s*	9.24 *s*	—	1.77 *br s*	1.75 *br s*	1.85 *br s*
H-13	1.75 *br s*	1.80 *br s*	1.90 *br s*	4.28 *br s*	10.40 *s*	—
Ph—OMe	—	3.90 *s*	3.90 *s*	—	3.82 *s*	3.82 *s*
—COOMe	—	—	3.70 *s*	—	—	3.70 *s*

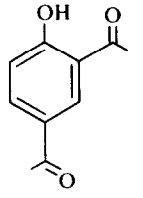
*$CDCl_3$.
†CCl_4,



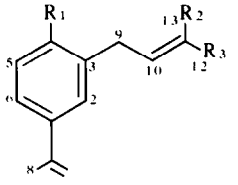
1



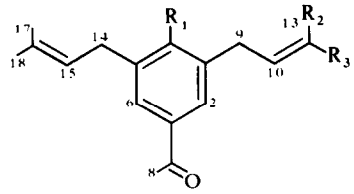
2



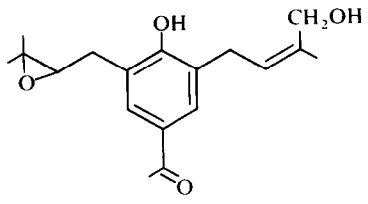
3



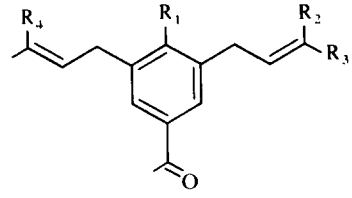
4 $R_1 = OH$, $R_2 = R_3 = Me$
5 $R_1 = OH$, $R_2 = Me$, $R_3 = CH_2OH$
5a $R_1 = OAc$, $R_2 = Me$, $R_3 = CH_2OAc$
5b $R_1 = OMe$, $R_2 = Me$, $R_3 = CH_2OH$
5c $R_1 = OMe$, $R_2 = Me$, $R_3 = CHO$
5d $R_1 = OMe$, $R_2 = Me$, $R_3 = COOMe$
6 $R_1 = OH$, $R_2 = CH_2OH$, $R_3 = Me$
6a $R_1 = OAc$, $R_2 = CH_2OAc$, $R_3 = Me$
6b $R_1 = OMe$, $R_2 = CH_2OH$, $R_3 = Me$
6c $R_1 = OMe$, $R_2 = CHO$, $R_3 = Me$
6d $R_1 = OMe$, $R_2 = COOMe$, $R_3 = Me$



7a $R_1 = OH$, $R_2 = CH_2OH$, $R_3 = Me$
7a $R_1 = OAc$, $R_2 = CH_2OAc$, $R_3 = Me$
8 $R_1 = OH$, $R_2 = Me$, $R_3 = CH_2OH$
8a $R_1 = OAc$, $R_2 = Me$, $R_3 = CH_2OAc$



9



10 $R_1 = OH$, $R_2 = R_4 = CH_2OH$, $R_3 = Me$
10a $R_1 = OAc$, $R_2 = R_4 = CH_2OAc$, $R_3 = Me$
11 $R_1 = OH$, $R_2 = Me$, $R_3 = R_4 = CH_2OH$

Table 2. ^{1}H NMR spectral data for the *p*-hydroxyacetophenones from *Artemisia* (60 MHz, TMS)

	7*	8†	9†	10*	11*
H-2	7.70 *s*	7.60 *s*	7.60 *s*	7.64 *s*	7.60 *s*
H-6					
H-8	2.52 *s*	2.50 *s*	2.50 *s*	2.46 *s*	2.45 *s*
H-9	3.48 *d* (8)	3.35 *d* (8)	3.46 *d* (8)	3.47 *d* (7)	3.38 *d* (7)
H-14	3.32 *d* (7)		2.94 *ap. t* (6)		3.50 *d* (7)
H-10	5.35 *t* (8)	5.65 *t* (8)	5.40 *t* (8)	5.38 *t* (7)	5.45 *m*
H-15	5.30 *t* (7)	5.35 *t* (8)	3.84 *t* (6)		

*$(CD_3)_2CO$.
†$CDCl_3$.

EXPERIMENTAL

Mps are uncorr. UV spectra were recorded in EtOH. ^{1}H NMR spectra were recorded at 60 MHz using TMS as an int. standard. Analytical TLC was performed on Si gel G (Merck), prep. TLC on Si gel $PF_{234-336}$ and CC on Si gel 60.

The plant was identified by Prof. B. Casaseca Mena, from the Department of Botany of Salamanca University, where a specimen is held (Herbarium No. 7362). The aerial parts of the plant (2.640 kg) collected near La Flecha (Salamanca) were finely ground and extracted with hot hexane. The hexane extract, previously steam-distilled, consists of about 65% neutral fraction, 15% acidic fraction and 20% (24.0 g) weak acids. The weakly acid fraction was chromatographed on Si gel and eluted with C_6H_6–ether mixtures and ether, giving: **1** (152 mg), **2** (142 mg), **3** (250 mg), **4** (275 mg), **5** (2.800 g), **6** (11.200 g), **7** (3.00 g), **8** (450 mg), **9** (190 mg), **10** (150 mg) and **11** (142 mg).

o-Hydroxyphenylbutan-2-one (**2**). Colourless oil, IR ν (cm^{-1}): 3360 (OH), 1720 (C=O), 1600, 1500 (aromatic), 1270, 1110, 910, 830; ^{1}H NMR ($CDCl_3$): δ (ppm) 2.10 (3 H, *s*, MeCO), 2.72 (4 H, *br s*), 6.83 (4 H, *m*); ^{1}H NMR (C_6H_6): 1.60 (3 H, *s*), 2.20 (2 H, *dd*, J = 6 and 3 Hz), 2.60 (2 H, *dd*, J = 6 and 2 Hz), 6.80 (4 H, m); M^+ 164 ($C_{10}H_{12}O_2$).

3-Acetyl-4-hydroxyacetophenone (**3**). Mp 64–65° (hex–ether); UV λ_{max} (nm): 234 (ε = 17 276), 277 (ε = 6910), 325 (ε = 3048); IR ν (cm^{-1}): 3300 (OH), 1680, 1650 (2 C=O), 1600, 1500 (aromatic), 1375, 1250, 1130, 900, 840; ^{1}H NMR (see on the text); M^+ 178 ($C_{10}H_{10}O_3$).

3-(Isopent-2-enyl)-4-hydroxyacetophenone (**4**). Mp 90° (hex–ether); UV λ_{max} (nm): 226 (ε = 10 187), 280 (ε = 8445); IR ν (cm^{-1}): 3300 (OH), 1710 (C=O), 1600, 1500 (aromatic), 1370, 1280, 1080, 880, 790; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.75 (6 H, *s*, Me_2C=), 2.52 (3 H, *s*, MeCO), 3.35 (2 H, *d*, J = 7 Hz, Ph–$\underline{CH}_2$), 5.50 (1 H, *t*, J = 7 Hz, HC=), 6.83 (1 H, *d*, J = 8 Hz), 7.67 (1 H, *dd*, J = 8 and 2 Hz), 7.75 (1 H, *d*, J = 2 Hz); M^+ 204 ($C_{13}H_{16}O_2$) [6].

3-[4-Hydroxyisopent-2-(E)-enyl]-4-methoxyacetophenone (**5b**). Treatment of **5** (390 mg) with CH_2N_2–ether gave the methyl derivative **5b** (340 mg), as an oil of IR ν (cm^{-1}): 3400 (OH), 1680 (C=O), 1600, 1500 (aromatic), 1360, 1270, 1080, 1030, 820; ^{1}H NMR (CCl_4): δ 1.55 (3 H, *s*), 2.35 (3 H, *s*), 3.20 (2 H, *d*, J = 8 Hz), 3.75 (3 H, *s*), 3.85 (2 H, *s*), 5.35 (1 H, *t*, J = 8 Hz), 6.58 (1 H, *d*, J = 8 Hz), 7.45 (1 H, *d*, J = 2 Hz), 7.48 (1 H, *dd*, J = 8 and 2 Hz); M^+ 236 ($C_{14}H_{20}O_3$).

Allylic oxidation of **5b**. Treatment of 200 mg of **5b** with MnO_2–C_6H_6 (2) yielded 180 mg of **5c**, mp 46°; IR (cm^{-1}): 2720, 1690, 1650 (C=C–CHO), 1680 (C=O), 1600, 1500 (aromatic), 1360, 1270, 1130, 1030, 820; ^{1}H NMR (see Table 1): M^+ 234 ($C_{14}H_{18}O_3$).

Oxidation of **5c**. Oxidation of 100 mg of **5c** with MnO_2–NaCN–MeOH [3] gave 85 mg of **5d** as a viscid oil, IR (cm^{-1}): 1720 (C=C–COOMe), 1690 (C=O), 1600, 1500 (aromatic), 1340, 1160, 1130, 900, 820; ^{1}H NMR (see Table 1); M^+ 262 ($C_{15}H_{18}O_4$).

3-[4-Hydroxyisopent-2(Z)-enyl]-4-hydroxyacetophenone (**6**). Viscid oil; UV λ_{max} (nm): 227 (ε = 13 687), 279 (ε = 11 568); IR ν (cm^{-1}): 3300 (OH), 1650 (C=O), 1580, 1500 (aromatic), 1350, 1140, 1060, 810; ^{1}H NMR (see Table 1); MS, *m/z* (%): 220 (M^+, 5), 202 ($M^+ - H_2O$, 75), 187 (202 – Me, 100), 169 (187 – H_2O, 12), 159 (187 – CO, 54), 147 (17), 144 (14), 141 (16), 131 (25), 107 (10), 91 (12), 77 (5), 43 (7). Acetylation of **6** (100 mg) give 105 mg of **6a**, oil; IR ν (cm^{-1}): 1750, 1715, 1250, 1215 (2 acetates), 1670 (C=O), 1590, 1500 (aromatic), 1180, 1100, 900, 810; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.82 (3 H, *s*), 2.10 (3 H, *s*), 2.33 (3 H, *s*), 2.57 (3 H, *s*), 3.38 (2 H, *d*, J = 7 Hz), 4.68 (2 H, *s*), 5.47 (1 H, *t*, J = 7 Hz), 7.10 (1 H, *d*, J = 8 Hz), 7.77 (1 H, *dd*, J = 8 and 2 Hz), 7.83 (1 H, *d*, J = 2 Hz); M^+ 304 ($C_{17}H_{20}O_5$).

3-[4-Hydroxyisopent-2(Z)-enyl]-4-methoxyacetophenone (**6b**). From 300 mg of **6**, by treatment with CH_2N_2–ether, 320 mg of **6b** was obtained; mp 95°; IR (cm^{-1}): 3430 (OH), 1665 (C=O), 1590, 1520 (aromatic), 1210, 1190, 1050, 980, 820; ^{1}H NMR (CCl_4): δ (ppm) 1.80 (3 H, *s*), 2.48 (3 H, *s*), 3.32 (2 H, *d*, J = 8 Hz), 3.80 (3 H, *s*), 4.18 (2 H, *s*), 5.30 (1 H, *t*, J = 8 Hz), 6.72 (1 H, *d*, J = 8 Hz), 7.60 (1 H, *d*, J = 2), 7.65 (1 H, *dd*, J = 8 and 2); M^+ 234 ($C_{14}H_{18}O_3$).

Allylic oxidation of **6b**. Oxidation of **6b** (300 mg) with MnO_2–C_6H_6 gave 250 mg of the conjugated aldehyde **6c**, solid, mp 63°; IR ν (cm^{-1}): 2720, 1680, 1650 (C=C–CHO), 1690 (C=O), 1580, 1500 (aromatic), 1360, 1270, 1170, 1120, 1060, 1020, 960, 820; ^{1}H NMR (see Table 1); M^+ 234 ($C_{14}H_{18}O_3$).

Oxidation of **6c**. Oxidation–methylation of **6c** (200 mg) with MnO_2–NaCN and MeOH gave 125 mg of the methyl ester **6d**, oil; IR ν (cm^{-1}): 1720, 1640 (C=C–COOMe), 1690 (C=O), 1600, 1500 (aromatic), 1360, 1260, 1120, 1080, 910, 820; ^{1}H NMR (see Table 1); M^+ 262 ($C_{15}H_{18}O_4$).

3-[Hydroxyisopent-2(E)-enyl]-5-(isopent-2-enyl)-4-hydroxyacetophenone (**8**). Mp 83°; UV λ_{max} (nm): 228 (ε = 23 381), 282 (ε = 16 906); IR ν (cm^{-1}): 3380 (OH), 1690 (C=O), 1650 (C=C), 1610, 1500 (aromatic), 1370, 1290, 1190, 1000, 900, 850; ^{1}H NMR (see Table 2); MS *m/z* (%): 288 (M^+, 6), 207 ($M^+ - H_2O$, 35), 255 (270 – Me, 80), 227 (255 – CO, 81), 213 (40), 199 (25), 185 (31), 171 (100), 143 (16), 133 (15), 128 (46), 119 (36), 115 (19), 105 (10), 91 (22), 69 (26), 43 (14).

Acetylation of **8** (50 mg) gave an oily diacetate, **8a**, IR ν (cm^{-1}): 1760, 1740, 1250, 1220 (two acetates), 1690 (C=O), 1640 (C=C), 1600, 1500 (aromatic), 1380, 1180, 1140, 1080, 910, 820; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.80 (9 H, *br s*), 2.68 (3 H, *s*, AcOR), 2.35 (3 H, *s*, AcOPh), 2.60 (3 H, *s*, MeCO), 3.34 (4 H, *d*, J = 8 Hz, Ph–CH_2), 4.52 (2 H, *s*, CH_2OAc), 5.35 (1 H, *t*, J = 8 Hz, CH=C), 5.62 (1 H, *t*, J = 8 Hz, CH=C), 7.68 (2 H, *s*); ($M^+ - 60$) = 312.

3-[4-Hydroxyisopent-2(Z)-enyl]-5-[4-hydroxyisopent-2-(E)-enyl]-4-hydroxyacetophenone (**11**). Mp 97°; UV λ_{max} (nm): 229 (ε

= 18008), 283 (ε = 13665); IR ν (cm^{-1}): 3350 (OH), 1690 (C=O), 1660 (C=C), 1600, 1510 (aromatic), 1380, 1290, 1180, 1050, 820; ^1H NMR (see Table 2); MS *m/z* (%): 304 (M^+, 4), 286 ($M^+ - H_2O$, 14), 271 (286 − Me, 6), 268 (271 − H_2O, 10), 240 (268–CO, 39), 225 (240 − Me, 35), 202 (100), 187 (85), 183 (25), 159 (46), 131 (30), 107 (16), 91 (22), 43 (10).

REFERENCES

1. De Pascual-T., J., Bellido, I. S., González, M. S., Muriel, M. R. and Hernśhdez, J. M. (1980) *Phytochemistry* **19**, 2781.
2. Goldman, I. M. (1969) *J. Org. Chem.* **34**, 1979.
3. Corey, E. J. and Gilmann, W. M. (1968) *J. Am. Chem. Soc.* **90**, 5616.
4. Jackman, L. M. (1959) *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, p. 122. Pergamon Press, Oxford.
5. Manjarrez, A., Rios, T. and Guzmán, A. (1964) *Tetrahedron* **20**, 333.
6. Bohlmann, F. and Grenz, M. (1970) *Berichte* **103**, 90.