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PHENOLIC AND ACETYLENIC METABOLITES FROM *ARTEMISIA ASSOANA*

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Key Word Index—*Artemisia assoana*; Compositae; Anthemideae; structure elucidation; phenolic compounds; flavonoids; coumarins; acetylenes; chemotaxonomy; ^{1}H NMR; ^{13}C NMR.

Abstract—Nine flavones, three coumarins, two flavone glycosides, *p*-hydroxyacetophenone and methyl caffeate have been isolated from the aerial parts of *Artemisia assoana*. Six diacetylenic spiroketal enol-ethers, a mixture of *n*-alkyl *p*-coumarates and a new phenylpropanoid metabolite, sinapyl alcohol diisovalerate, have been isolated from root extracts of the same plant. ^{1}H and ^{13}C NMR spectra of some of these compounds are given and taxonomic aspects are discussed.

INTRODUCTION

Artemisia assoana Willk. is a small shrub with short, herbaceous stems and hairy, whitish leaves, which is dispersely scattered in arid, mountain regions in South Europe [1]. The classical work of de Candolle [2] did not include this species but placed the probably synonymous *A. lanata* in the sect. *Absinthium* on the basis of its morphological features. On the other hand, Willkomm and Lange [3] included *A. assoana* and its synonymous species in the sect. *Euartemisia*, made up of the older sect. *Absinthium* DC., *Abrotanum* Bess. and *Dracunculus* Bess. In a more recent treatment [1], *A. assoana* has been placed in the subgenus *Artemisia*, which includes sect. *Absinthium* DC., *Abrotanum* Bess. and the European species of sect. *Seriphidium* Bess. Furthermore, it is considered to be synonymous with *A. pedemontana* Balb., *A. caucasica* Willd., *A. lanata* Willd. and perhaps *A. alpina* Pallas ex Willd.

Although no previous chemical research on *A. assoana* has been published, two related or synonymous species have been investigated. Bohlmann *et al.* [4] isolated acetylenes (*E*)- and (*Z*)-**7**, (*E*)-**8**, (*E*)-**9**, (*E*)-**10** and (*Z*)-**10** from *A. pedemontana*. More recently, two Spanish groups have isolated several guaianolides [5, 6] and flavone **4** [5] from the aerial parts of *A. lanata*.

In the present paper, we wish to report the results of our studies on both aerial parts and roots of *A. assoana*, which between them yielded the following products: salvigenin (**1**), jaceosidin (**2**), cirsilineol (**3**), 5-hydroxy-6,7,3′,4′-tetramethoxyflavone (**4**), 6-methoxytricin (**5**), artemetin (**6**), apigenin, luteolin, chrysoeriol, luteolin-7-glucoside, apigenin-7-rutinoside, umbelliferone, scopoletin, isofraxidin, *p*-hydroxyacetophenone, methyl caffeate (aerial parts), (*E*)- and (*Z*)-**7**, (*E*)-**8**, (*E*)- and (*Z*)-**9**, (*E*)-**10**, a mixture of long-chain *n*-alkyl *p*-coumarates (**11**) and sinapyl alcohol diisovalerate (**12**) (roots), the latter compound being reported for the first time in nature.

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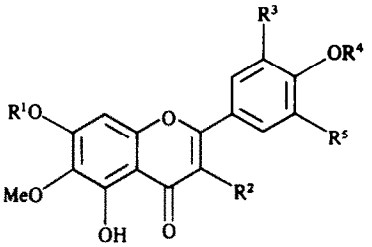
RESULTS AND DISCUSSION

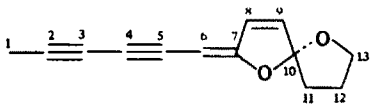
All known compounds were identified by their spectral properties (IR, UV, MS, ^{1}H and ^{13}C NMR) and, where appropriate, by their melting points and/or optical rotations. In several cases (all unnumbered compounds), identification was confirmed by direct comparison with authentic samples.

Compound **11** was a semi-solid product, which gave a single spot on TLC plates, and was shown to be a mixture of straightchain *n*-alkyl *p*-coumarates by NMR and mass spectroscopy (see Experimental). The *p*-coumaric esters of the *n*-alkanols C_{20}, C_{22} and C_{24} were the main components of the mixture. Free *n*-alkanols were also detected in minor amounts in the roots, but were not further characterized. Similar mixtures of *n*-alkanols and *n*-alkyl *p*-coumarates have been reported in *A. campestris* [7].

Compound **12** had two equivalent methoxyl groups (δ3.90, *s*, 6H), two ester groups (^{13}C NMR: δ170.70 and 172.90; IR: 1760 and 1732 cm^{-1}), two equivalent aromatic hydrogen atoms (δ6.61, *s*, 2H) and a symmetrically tetrasubstituted benzene ring (four aromatic signals in the ^{13}C NMR spectrum). Furthermore, characteristic signals of a *trans*-Ar-CH=CH-CH_2OCOR fragment were visible as two double triplets (1H each) at δ6.22 (J = 16 and 6.4 Hz) and 6.50 (J = 16 and 0.9 Hz), and a double doublet at δ4.71 (J = 6.4 and 0.9 Hz). Finally, two non-equivalent isovaleroyl residues gave rise to two doublets (6H each) at δ0.97 and 1.06 (J = 6.5 Hz), two doublets (2H each) at δ2.23 and 2.45 (J = 7.5 Hz) and a complex multiplet (2H) centred at δ2.20. The ^{13}C NMR spectrum was consistent with this structural assignment as it showed two carbonyl signals, six signals in the aromatic/olefinic region, one signal from an oxygen-bonded aliphatic carbon atom, one methoxyl signal and three pairs of signals (methyl, methylene and methine) from the isovaleroyl residues (see Experimental). The positions of the carbon signals matched well the chemical shift values expected for structure **12** [8]. In the mass spectrum, a weak molecular ion at m/z 378 ($C_{21}H_{30}O_6$) was visible. Two intense signals at m/z 294 ([M − 84]$^+$ base peak) and



1 $R^1 = R^4 = Me$, $R^2 = R^3 = R^5 = H$
2 $R^1 = R^2 = R^4 = R^5 = H$, $R^3 = OMe$
3 $R^1 = Me$, $R^2 = R^4 = R^5 = H$, $R^3 = OMe$
4 $R^1 = R^4 = Me$, $R^2 = R^5 = H$, $R^3 = OMe$
5 $R^1 = R^2 = R^4 = H$, $R^3 = R^5 = OMe$
6 $R^1 = R^4 = Me$, $R^2 = R^3 = OMe$, $R^5 = H$



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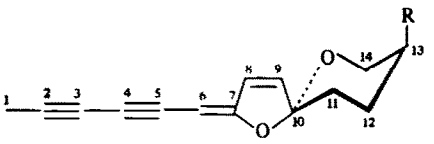
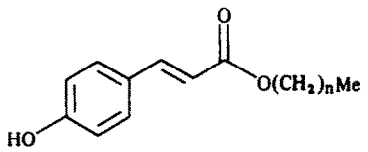
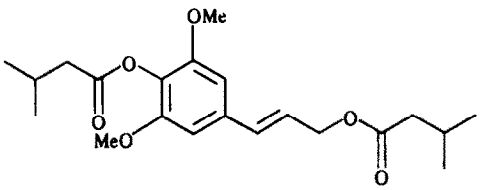


8 R = H
9 R = OAc
10 R = OCO*i*Bu



11



12

210 ($[M - 2 \times 84]^+$) could be explained by successive loss of the isovaleroyl residues as isopropylketene (C_5H_8O) fragments. The UV spectrum of **12** did not show any change on addition of base, thus demonstrating the absence of a free phenolic hydroxyl group. Structurally similar compounds have been found in some Compositae [9, 10].

With the exception of salvigenin and apigenin-7-rutinoside, all the above mentioned known compounds are precedented in the genus *Artemisia*, though not with the same frequency. Jaceosidin (**2**) has been found in nine *Artemisia* spp. [11–13] belonging to the sect. *Absinthium* DC. and *Abrotanum* Bess., while cirsilineol (**3**) and artemetin (**6**) have been reported in eight and nine *Artemisia* spp., respectively, belonging to all sections. Flavones **4** and **5**, however, are much less frequent and have been described only in three *Artemisia* spp. of the sect. *Absinthium* and *Abrotanum* [11–13]. Luteolin, apigenin and chrysoeriol are almost ubiquitous metabolites and their appearance is thus of little taxonomic value. Luteolin-7-glucoside is also common in *Artemisia* spp. [14, 15] but apigenin-7-rutinoside, as far as we know, has not been reported in this genus.

The coumarins umbelliferone, scopoletin and isofraxidin are very common in Compositae, especially in the genus *Artemisia* [16–18]. Methyl caffeate, *p*-hydroxyacetophenone and its derivatives, although much less frequent, are also precedented in this genus [19–22].

Metabolites from the roots of Compositae have very often been investigated because of their great chemical, pharmacological and taxonomic interest [16, 17]. Acetylenes [23] are commonly found in most Compositae tribes. The Anthemideae tribe is especially rich in many types of acetylenic metabolites [24], with spiroketal enolethers such as **7–10** [in both stereoisomeric (*E*/*Z*) forms] being characteristic chemical markers of this tribe. Polyacetylenes may fulfill various ecological roles (nematicidal, antibiotic, insect repellent, etc.) [17, 25]. (*E*)-**7** has been reported to exhibit spasmolytic and antiphlogistic properties [26].

Polymethylated flavonoids, sesquiterpene lactones and caffeic acid esters are present in aerial parts of practically all tribes of Compositae. Coumarins and acetylenes are also common constituents of the species of most tribes [16, 17]. Within Anthemideae, 6- and/or 8-oxygenation and extensive methylation of flavonoids are usual chemical characters [27]. In the case of *A. assoana*, the predominance of flavones over flavonols, the high degree of methylation and the absence of 8-oxygenation may point to an advanced character of this species [27, 28]. Moreover, *Artemisia* spp. belonging to the sect. *Absinthium* DC. usually yield very predominantly flavones and few classes of flavonols, whereas members of the sect. *Abrotanum* Bess. form a rich variety of both flavones and flavonols with various degrees of methylation [13, 29]. The above mentioned results could be taken as further support for the inclusion of *A. assoana* in the sect. *Absinthium*. The flavonoid contents is also important from the pharmacological point of view, since flavonoids are attributed a host of interesting clinical properties [30–32].

Polyacetylenic compounds are not only important chemical markers within Anthemideae [33], they are even useful for infrageneric subdivisions in the genus *Artemisia* [34–36]. As in other members of the *Absinthium* group, appreciable amounts of the C_{13}- and C_{14}-spiroketals **7–10** were present in the roots of *A. assoana*. In this species, the stereoisomeric *E*-forms (*cis*) were markedly predominant, as observed in *A. pedemontana* [4]. We did not detect, however, sesamin-type lignanes nor thiophene derivatives [36]. *p*-Coumaric acid esters like **11** may be widely distributed in the *Absinthium* group [34].

The ^{1}H NMR spectra of compounds **1–10** and the ^{13}C NMR spectra of compounds **2** and **4–10**, some of them in two solvents ($CDCl_3$ and DMSO-d_6), are given in Tables 1–4. The ^{13}C NMR spectra of flavones **5** in DMSO-d_6 [37] and **6** in $CDCl_3$ [38] have been reported previously. The assignments of C-7/C-9 in **5** and of C-2/C-9 in **6** have been interchanged for a better consistency with the spectra of related compounds [29, 39]. ^{13}C NMR spectra of (*E*)- and (*Z*)-7 and other polyacetylenes [40–44] have also been published. As can be seen in Table 4, the peak assignment for C-8/C-9 is the inverse of the published one [40]. This signal attribution has been made in

Table 1. ^{1}H NMR spectral data for compounds **1–6** (200 MHz, DMSO-d_6, room temp.)

Compound	H-3	H-8	H-2′	H-3′	H-5′	H-6′	OMe	5-OH
1	6.91‡ *s*	6.94‡ *s*	8.06 *d* (9.0)*	7.11 *d* (9.0)	7.11 *d* (9.0)	8.06 *d* (9.0)	3.92 *s* 3.85 *s* 3.73 *s*	12.80 *s*
1†	6.57‡ *s*	6.52‡ *s*	7.83 *d* (8.8)	7.00 *d* (8.8)	7.00 *d* (8.8)	7.83 *d* (8.8)	3.95 *s* 3.90 *s* 3.87 *s*	12.80 *s*
2	6.86 *s*	6.60 *s*	7.60–7.50 *m* AB part of an ABX system		6.92 *d* (9.0)	7.60–7.50 *m* AB part of an ABX system	3.88 *s* 3.75 *s*	13.00 *s*
3	6.92‡ *s*	6.93‡ *s*	7.65–7.55 *m* AB part of an ABX system		6.93 *d* (9.0)	7.65–7.55 *m* AB part of an ABX system	3.91 *s* 3.89 *s* 3.72 *s*	13.00 *s*
4	7.02 *s*	6.96 *s*	7.59 *d* (2.2)		7.13 *d* (8.6)	7.71 *dd* (8.6; 2.2)	3.93 *s* 3.88 *s* 3.85 *s* 3.73 *s*	12.90 *s*
4†	6.55‡ *s*	6.51‡ *s*	7.29 *d* (2.1)		6.94 *d* (8.5)	7.48 *dd* (8.5; 2.1)	3.95 *s* 3.94 *s* 3.93 *s* 3.90 *s*	12.30 *s*
5	6.94 *s*	6.64 *s*	7.30 *s*			7.30 *s*	3.87 *s* (× 2) 3.74 *s*	13.00 *s*
6		6.83 *s*	7.63 *d* (2.1)		7.11 *d* (8.5)	7.68 *dd* (8.5; 2.1)	3.91 s 3.85 s (× 2) 3.81 *s* 3.73 *s*	12.50 s
6†		6.47 *s*	7.65 *d* (2.1)		6.96 *d* (8.5)	7.69 *dd* (8.5; 2.1)	3.97 *s* (× 2) 3.95 *s* 3.91 *s* 3.86 *s*	12.5 *s*

*Coupling constants in Hz.

†In $CDCl_3$.

‡Assignments bearing the same superscript may be interchanged within the corresponding spectrum.

Table 2. ^{1}H NMR spectral data for compounds 7–10 (200 MHz, $CDCl_3$, room temp.)

H	(*E*)-7	(*Z*)-7	(*E*)-8	(*E*)-9	(*Z*)-9	(*E*)-10
1	1.97 *d* (1.0)*	1.98 *d* (1.0)	1.97 *d* (1.0)	1.97 *d* (1.0)	1.99 *d* (1.0)	1.97 *d* (1.0)
6	4.89 *br s*	4.58 *br s*	4.94 *br s*	4.97 *br s*	4.63 *br s*	4.97 *br s*
8	6.67 *d* (5.7)	AB system 6.22 *d* (5.6)	6.63 *d* (5.7)	6.68 *d* (5.8)	AB system 6.24 *d* (5.7)	6.68 *d* (5.8)
9	6.21 *dd* (5.7; 1.8)	6.13 *d* (5.6)	6.22 *dd* (5.7; 1.8)	6.25 *dd* (5.8; 1.7)	6.20 *d* (5.7)	6.25 *dd* (5.8; 1.7)
11/12	2.30–2.00 *m* (4H)	2.40–2.00 *m* (4H)	2.10–1.50 *m* (6H)	2.40–1.90 *m* (3H) 1.80–1.60 *m* (1H)	2.40–1.90 *m* (3H) 1.80–1.60 *m* (1H)	2.30–1.90 *m* (3H) 1.80–1.60 *m* (1H)
13	4.20–3.90 *m* (2H)	4.30–3.90 *m* (2H)		4.95 *m* (1H)	4.92 *m* (1H)	4.92 *m* (1H)
14β			4.00–3.80 *m* (2H)	3.89 *br d* ($\simeq$ 12.9)	3.89 *br d* ($\simeq$ 12.9)	3.88 *br d* ($\simeq$ 12.9)
14α				4.11 *dd* (12.9; 1.7)	4.25 *dd* (12.9; 1.7)	4.12 *dd* (12.9; 1.6)
AcO				2.11 *s* (3H)	2.11 *s* (3H)	
*i*BuCO$_2$						0.98 *d* (6H) (6.5) 2.25 *d* (2H) (7.5) 2.30–2.10 *m* (1H)

*Coupling constants in Hz.

Table 3. ^{13}C NMR spectral data of compounds 2, 4–6 (50 MHz, DMSO-d_6, room temp.)

	2	4	4*	5	6	6*
2	163.68	163.58	163.85	163.59	155.27	155.88
3	102.71	103.61	104.21	103.09	137.97	138.85
4	182.12	182.26	182.46	182.06	178.11	178.90
5	152.71[a]	152.64[a]	153.07[a]	152.64[a]	151.61[a]	152.33[a]
6	131.30	131.88	132.55	131.43	131.66	132.35
7	157.20	158.64	158.66	157.76	158.58	158.82
8	94.26	91.63	90.54	94.51	91.27	90.39
9	152.37[a]	152.23[a]	152.90[a]	152.47[a]	151.53[a]	152.80[a]
10	104.05	105.12	105.98	103.87	105.56	106.60
1'	121.54	122.76	123.58	120.44	122.09[b]	122.95
2'	110.19	109.41	108.71	104.33	111.60[c]	110.92
3'	147.99	149.02	149.25	148.17	148.49	148.85
4'	150.69	152.02[a]	152.26[a]	139.83	151.36[a]	151.48
5'	115.73	111.65	111.11	148.17	111.64[c]	111.37
6'	120.30	120.08	119.98	104.33	121.94[b]	122.20
OMe (3)					59.58[d]	60.15[b]
(6)	59.90	59.99	60.72	59.88	59.87[d]	60.84[b]
	55.93	56.44	56.25	56.34(×2)	56.32	56.33
		55.88	56.04(×2)		55.70	56.10
		55.73			55.59	56.00

*In $CDCl_3$.

[a, b, ...] Assignments bearing the same superscript may be interchanged within the corresponding spectrum.

the case of (*E*)-10 by two-dimensional heteronuclear shift correlation and extrapolated to the other acetylenic spiroketals.

We are presently investigating the presence of sesquiterpene lactones in aerial parts and roots of *A. assoana*.

EXPERIMENTAL

IR: films; UV: MeOH; NMR: instrument as described elsewhere [29]. For all flavonoids, NMR measurements were performed in DMSO-d_6 at room temp. (27°), with the solvent signals as reference [29]. Compounds 1, 4 and 6 were also measured in $CDCl_3$ with TMS as int. standard. Compounds 7–12 were all measured in $CDCl_3$.

Plant material. Aerial parts and roots of *A. assoana* were collected in Dec. 1984 at Puebla de Valverde (Teruel, Spain) and authenticated by Prof. J. Mansanet, Botany Department, Faculty of Biology, Valencia. A voucher specimen is deposited in the herbarium of the above mentioned Department.

Extraction and chromatography. Aerial parts of the plant (3 kg)

Table 4. ^{13}C NMR spectral data of compounds 7–10 (50 MHz, $CDCl_3$, room temp.)

	(*E*)-7	(*Z*)-7	(*E*)-8	(*E*)-9	(*Z*)-9	(*E*)-10
1	4.60	4.74	4.59	4.58	4.78	4.62
2	79.67	80.58	79.54	79.78	80.79	79.75
3	65.06	65.40	65.11	64.92	65.14	65.01
4	76.40	79.94	76.32	76.55	79.06	76.60
5	71.53	70.77	71.60	71.18	70.46	71.24
6	79.73	78.83	79.73	80.51	79.57	80.52
7	168.93	167.16	169.83	169.39	167.58	169.44
8	125.81	127.45	125.00	125.51	127.08	125.50
9	136.04	135.25	138.54	137.56	137.12	137.68
10	120.94	121.06	112.78	112.02	112.20	112.09
11	35.54	35.61	32.51	27.17	27.28	27.29
12	24.53	24.48	19.28	23.22	23.21	23.37
13	69.69	69.66	24.44	66.09	66.31	65.76
14			64.25	65.55	65.55	65.62
AcO				170.61	170.61	
				21.30	21.30	
*i*BuCO$_2$						172.56 *s*
						43.59 *t*
						25.85 *d*
						22.38 *q*

were air-dried, finely ground and extracted at room temp. with 80% aq. MeOH (25 l, 7 days) and then with 50% aq. MeOH (10 l, 13 days). Both extracts were combined, concd *in vacuo* to remove most of the MeOH and successively extracted with hexane, Et_2O and EtOAc (6 l each). The remaining aq. extract did not contain significant amounts of flavonoids (TLC) and was discarded. After taking to dryness, the weights of the hexane, Et_2O and EtOAc extracts were, respectively, 14, 23 and 5 g.

The hexane extract was chromatographed on a silica gel column and eluted with hexane–Et_2O mixtures containing increasing amounts of Et_2O. Flavones **6** (70 mg) and **4** (70 mg) were successively eluted as the only flavonoid compounds, the other components of this extract being waxes and essential oils.

The Et_2O extract was chromatographed on a Polyamide column (Macherey-Nagel SC6) and eluted with toluene–MeOH mixtures containing increasing amounts of MeOH. Six main fractions (I–VI) were collected after inspection by TLC. Fraction I was re-chromatographed on silica gel (elution with $CHCl_3$–EtOAc mixtures), yielding successively **1** (8 mg), **6** (50 mg), **4** (68 mg) and **3** (20 mg). Fraction II yielded by CC on silica gel (elution with hexane–EtOAc mixtures) *p*-hydroxyacetophenone (90 mg), umbelliferone (50 mg), scopoletin (35 mg) and isofraxidin (30 mg). Fraction III was re-chromatographed on silica gel and eluted with hexane–Et_2O mixtures, yielding methyl caffeate (125 mg), **2** (48 mg) and **5** (8 mg). Fraction IV was re-chromatographed on Polyamide and eluted with toluene–MeOH mixtures, yielding chrysoeriol (20 mg). Fractions V and VI were also re-chromatographed on Polyamide (elution with toluene–MeOH–MeCOEt 7:1:1) yielding, respectively, apigenin (40 mg) and luteolin (50 mg).

The EtOAc extract was chromatographed on a Polyamide column and eluted with H_2O–MeOH mixtures containing increasing amounts of MeOH. Three main fractions (A–C) were collected. Fraction A was re-chromatographed on silica gel (elution with Et_2O), yielding more isofraxidin (20 mg). Fraction B was submitted successively to CC on Polyamide (elution with toluene–MeOH–MeCOEt 5:1:1), PC (elution with TBA) and CC on Sephadex LH-20 (elution with MeOH). This yielded apigenin-7-rutinoside (4 mg). Fraction C was rechromatographed successively on Polyamide (toluene–MeOH–MeCOEt 3:1:1) and Sephadex LH-20 (MeOH), yielding luteolin-7-glucoside (12 mg).

Roots of the plant (350 g) were air-dried, finely ground and extracted at room temp. with hexane–Et_2O (2:1) (3 l, 5 days) and Et_2O (3 l, 5 days) [45]. The combined extracts were concd *in vacuo* (7.2 g) and chromatographed on a silica gel column. Elution with hexane–Et_2O mixtures containing increasing amounts of Et_2O yielded successively (*E*)-**8** (660 mg), (*E*)-**10** (370 mg), (*E*)-**7** (440 mg) and a complex mixture of compounds. This mixture was resolved by repeated prep. TLC on silica gel (toluene–Et_2O mixtures), yielding (*Z*)-**7** (8 mg), (*Z*)-**9** (10 mg), (*E*)-**9** (10 mg), **11** (15 mg) and **12** (20 mg).

Compound **11** was a waxy, semisolid product. IR ν_{max} cm^{-1}: 3250, 1710, 1630, 1605, 1169, 1120, 832, 720; UV λ_{max}: 312 nm; (+ NaOMe): 359 nm. ^1H NMR ($CDCl_3$), δppm: 7.61 (*d*, 1H, J = 16 Hz, Ar–C<u>H</u>=), 7.41 (*d*, 2H, J = 8.6 Hz, arom. H *meta* to OH), 6.83 (*d*, 2H, J = 8.6 Hz, arom. H *ortho* to OH), 6.29 (*d*, 1H, J = 16 Hz, =C<u>H</u>–CO_2R), 4.18 (*t*, 2H, J = 6.7 Hz, CO_2CH_2), 1.70 (*m*, *ca* 2H, $CO_2CH_2C\underline{H}_2$), 1.50–1.10 (*m*, *ca* 40H, methylene chain), 0.87 (*t*, *ca* 3H, J = 6.7 Hz, terminal CH_3); ^{13}C NMR ($CDCl_3$), δppm: 167.71 (s, CO), 157.75 (*s*), 129.96 (*d*), 127.33 (*d*), 115.90 (*d*) (arom. C), 144.37 (*d*), 115.75 (*d*) (olefinic C), 64.75 (*t*, <u>C</u>H_2OCO) 31.95 (*t*), 29.72 (*t*, very intense and broad), 28.78 (*t*), 26.01 (*t*), 22.71 (*t*), 14.12 (*q*) (aliphatic chain). MS *m/z* (rel. int.): 556 (0.3), 528 (0.3), 500 (1.9), 472 (7.8), 444 (7.8), 166 (85), 165 (32), 164 (100), 147 (65), 119 (28). From the intensities of the molecular peaks *m/z* 556–444, it was estimated that the product was a mixture of the *p*-coumarates of the *n*-alkanols C_{20} (43%), C_{22} (43%), C_{24} (10%), C_{26} (2%) and C_{28} (2%).

Compound **12** was a colourless oil. IR ν_{max} cm^{-1}: 1760, 1732, 1596, 1135; UV λ_{max}: 220, 265 nm, not changed by addition of base; ^1H NMR ($CDCl_3$), δ ppm: 6.61 (*s*, 2H, arom. H), 6.50 (*dt*, 1H, J = 16 and 0.9 Hz, Ar–C<u>H</u>=), 6.22 (*dt*, 1H, J = 16 and 6.4 Hz, =C<u>H</u>–CH_2), 4.71 (*dd*, 2H, J = 6.4 and 0.9 Hz), C<u>H_2</u>OCOR), 3.90 (*s*, 6H, 2× OMe), 2.45 (*d*, 2H, J = 7.5 Hz, C<u>H_2</u>CO_2Ar), 2.23 (*d*, 2H, J = 7.5 Hz, CH_2CO_2R), 2.20–2.10 (*m*,

2H, C<u>H</u>–CH_2CO_2), 1.06, (*d*, 6H, J = 6.5 Hz <u>Me_2</u>$CHCO_2Ar$), 0.97, (*d*, 6H, J = 6.5 Hz, <u>Me_2</u>$CHCO_2R$); ^{13}C NMR ($CDCl_3$), δ ppm: 172.90 (*s*, CO_2R), 170.70 (*s*, CO_2Ar), 152.31 (*s*), 134.61 (*s*), 128.82 (*s*), 103.41 (*d*) (arom. C), 134.00 (*d*), 123.72 (*d*) (olefinic C), 64.59 (*t*, <u>CH_2</u>OCOR), 56.10 (*q*, 2 × OMe), 43.43 (*t*), 43.02 (*t*, 2 × <u>CH_2</u>CO), 26.04 (*d*), 25.74 (*d*, 2 × <u>CH</u>–CH_2CO), 22.44 (*q*), 22.34 (*q*, 2 × <u>Me_2</u>CH). MS *m/z* (rel. int): 378 $[M]^+$ (3), 294 $[M - C_5H_8O]^+$ (100), 277 (2), 210 $[M - 2C_5H_8O]^+$ (44), 193 (25).

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