Journal of Natural Products
Vol. 51, No. 6, pp. 1140-1147, Nov-Dec 1988

HUMULENES AND OTHER CONSTITUENTS OF *FERULA LATIPINNA*

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ABSTRACT.—Chemical analysis of *Ferula latipinna* yielded five new sesquiterpenes, carotanes **1** and **6** and the humulenes **12**, **13**, and **16** as well as three new phenylpropanes **20**, **22**, and **24**, a phenolic derivative **25**, scopoletin, isoscopoletin, diosmetin, veratric, and *p*-methoxybenzoic acids, and a new trimethoxyphenanthrene **27**. The structures of the new compounds were elucidated by spectroscopic methods and chemical reactions.

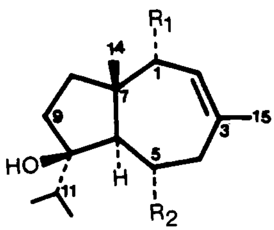
Some 130 species of *Ferula* L. (Umbelliferae) are to be found in the Old World (1), from the Mediterranean area to Central Asia and also in Macronesia. In the Canary Islands three species have been reported to date: *Ferula linkii* Webb, *Ferula lancerottensis* Parl, and *Ferula latipinna* Santos (2). The latter species is endemic to La Palma though it may also occur in La Gomera. It is clearly differentiated from the other two species, most distinctively by its broad pinnules. It grows on steep mountain sides and in clearings in the evergreen forest zone on the north side of the island where it is prized by the local goatherds for its galactophorous properties.

Ferula species are rich in sesquiterpenes (3), including α-humulenes from *Ferula juniperina* Eug. Kor. (4–6), *Ferula xeromorpha* Eug. Kor. (7,8), and *Ferula tschatcalensis* M. Pimen. (9), γ-humulenes from *Ferula ceratophylla* Regl. ex Schmalh. (10), apiene esters from *Ferula haussknechtii* Wolff ex Rech. (11), and himachalenes from *F. xeromorpha* (12). Similar substances have now been isolated from *F. latipinna*.

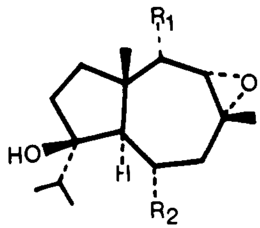
RESULTS AND DISCUSSION

Stilbenes and phenylpropanes from *F. latipinna* were reported earlier (13). The current study of the EtOH extract of the roots and aerial part of this plant species afforded sesquiterpenes **1**–**11**, eight of which had previously been found in other *Ferula* species: 10β-hydroxy-5α-*p*-hydroxybenzoyloxy-1α-angeloyloxydauc-2-ene [**3**], 10β-hydroxy-5α-*p*-anisoyloxy-1α-angeloyloxydauc-2-ene [**4**] (14), lapidin [**5**] (15), lapiferin [**7**], lapiferol [**8**] (16), felikiol 3-angelate [**9**], and webiol 3-angelate [**11**] (17). Felikiol [**10**] was found for the first time as a natural product. Compounds **1** and **6** have not hitherto been reported. Three new humulenes **12**, **13**, and **16**, himachalol [**17**] (18), five phenylpropanes including myristicin [**18**], crocatone [**19**], and compounds **20**, **22**, and **24**, a new phenolic derivative **25**, a new trimethoxyphenanthrene **27**, and the coumarins scopoletin and isoscopoletin, the flavonoid diosmetin, and veratric and *p*-methoxybenzoic acids were also obtained. These are the first coumarins and flavonoids to be found in the Canary Islands *Ferula* species. The known substances were identified by comparison with authentic samples.

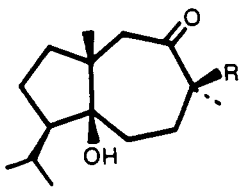
Compound **1**, mp 77–78°. Ms did not directly establish the molecular formula; however, the fragment at *m/z* 275 $[M - C_3H_7 - C_5H_8O_2]^+$ corresponds to the formula $C_{25}H_{38}O_5$, with the loss of an isopropyl radical and angelic acid. The ease with which the isopropyl radical was lost indicates that compound **1** must be a carotane-skeleton sesquiterpene with the hydroxy at C-10. The ir clearly shows the presence of hydroxy groups (3580, 3460 cm^{-1}), esters (1700, 1260, 1230 cm^{-1}), and double bonds (1640, 840 cm^{-1}). The ^{1}H nmr is similar to that of tingitanol (19), differing in that **1** does not have a signal for a geminal hydroxy proton at C-8.



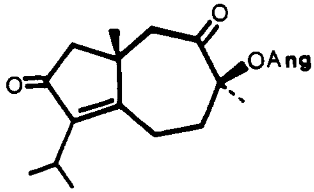
1 $R_1=R_2=$OAng
3 $R_1=$OAng, $R_2=$*O*-*p*-hydroxybenzoate
4 $R_1=$OAng, $R_2=$*p*-anisate
5 $R_1=$O, $R_2=$OAng
6 $R_1=$O, $R_2=$*O*-vanillate



7 $R_1=$OAc, $R_2=$OAng
8 $R_1=R_2=$OH



9 R=OAng
10 R=OH



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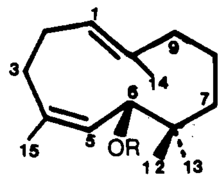
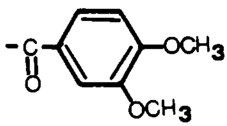
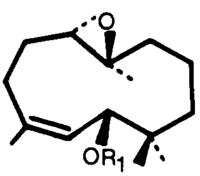
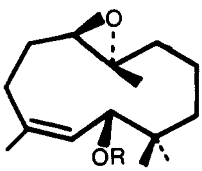


12 R=veratrate

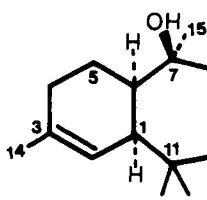
veratrate =




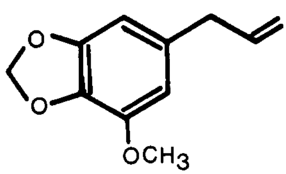
13 $R_1=$veratrate
14 $R_1=$H
15 $R_1=$*p*-Br-C_6H_4-CO



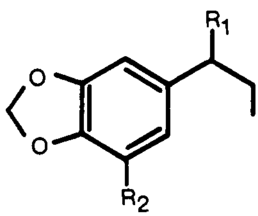
16 R=veratrate



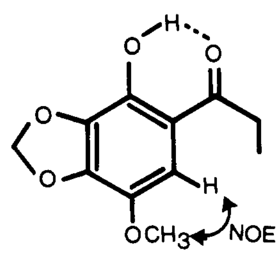
17



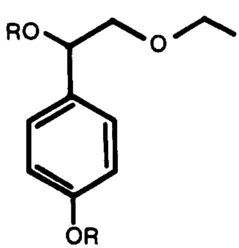
18



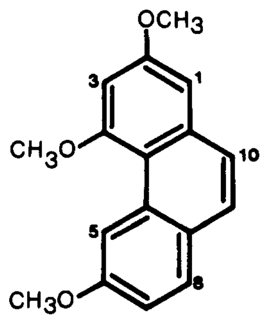
19 $R_1=$O, $R_2=$OMe
20 $R_1=R_2=$OH
21 $R_1=R_2=$OAc
22 $R_1=$OH, $R_2=$OMe
23 $R_1=$OAc, $R_2=$OMe



24

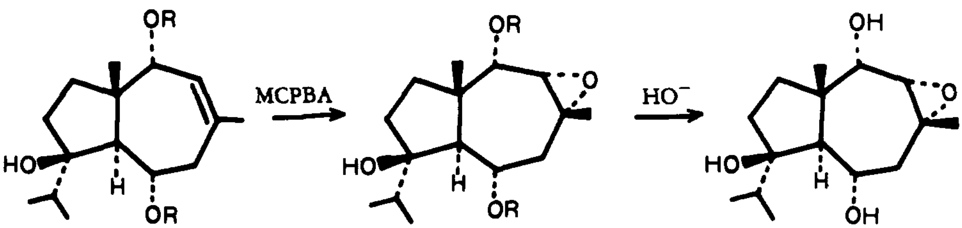


25 R=H
26 R=Ac



27

The ester group positions were ascertained by the following reactions (Scheme 1). Treatment of **1** with MCPBA yielded the epoxyderivative **2**. The ^{1}H-nmr spectrum showed signals for an angular methyl at δ 1.26 (3H, s, H-14), two tertiary methyls at δ 0.88 (3H, s, H-12) and 0.91 (3H, s, H-13), an oxirane methyl at δ 1.43 (3H, s, H-15) with the corresponding proton at δ 3.00 (1H, d, J = 5.4 Hz, H-2), and signals for the epoxyangeloyloxy moiety. Alkaline hydrolysis of **2** gave a triol with physical and spectral data (ir, ^{1}H nmr) identical to those of lapiferol [**8**] (16). Compound **1** was given the name 8-desoxytingitanol.



1 R=Ang **2** R=epoxyangeloyl **8**

SCHEME 1.

Compound **6** is a lapidol derivative. Aromatic acyl group absorptions were observed in its ir spectrum, and ^{1}H, ^{13}C nmr, and ms confirmed the presence of a vanillate group. Alkaline hydrolysis of **6** gave lapidol (15) and vanillic acid.

Sesquiterpene **12** was isolated as a colorless oil, composition $C_{24}H_{34}O_4$; ir showed absorptions (1690, 1600, 1590, 1510 cm^{-1}) for an aromatic acyl group which was identified as a veratrate from its ^{1}H-, ^{13}C-nmr, and ms data. The ^{1}H nmr of **12** showed two vinyl protons and vinyl methyls indicating the presence of two double bonds. Its composition, the two double bonds, and the nature of the methyl groups suggest that this product probably has a monocyclic humulene skeleton (20–22). The position of the aromatic acyl group at C-6 was confirmed by the ^{1}H-nmr spectrum where the doublet at δ 5.50 (1H) was coupled with the signal of H-5 at δ 5.40. NOe experiments on **12** showed that the $\Delta^{1,10}$ and Δ^4 double bonds have E and Z configurations, respectively, and that the stereochemistry of the acyl group at C-6 is β (11). NOe interactions were observed for H-1 and H-6, H-7α and H-3α, for H-5 and H-12 and H-15, for H-6 and H-3α, H-7α and H-13, for H-14 and H-2β, and for H-15 and H-5.

Compounds **13** and **16** have ^{1}H- and ^{13}C-nmr spectra analogous to those of **12** (see Table 1), differing in that the former have a 1(10)-oxirane ring. The disposition of this ring was determined by spectroscopic analysis. Alkaline hydrolysis of **13** gave veratric acid and a monodesacyl derivative **14** with the empirical formula $C_{15}H_{26}O_2$, analogous to that described first by Itokawa and co-workers (23,24) and later by Miski *et al.* (11). Treatment of **13** with Cl-*p*-bromobenzoyl gave *p*-bromobenzoyl ester **15** identical to that described by the above authors.

Compound **16** proved to be analogous to **13**, the only difference being the epoxide stereochemistry. The structure was confirmed by ^{13}C nmr [62.4 (C-1) and 62.9 (C-10) compared with 60.8 for both carbons in compound **13**], and comparison with known compounds (24).

The phenylpropanoids **20** and **22** were purified as acetyl derivatives. Compound **20** gave a diacetate **21**, molecular formula $C_{14}H_{16}O_6$ (*m/z* 280 $[M]^+$). In the ^{1}H-nmr spectrum signals for two acetyl groups were observed at δ 2.03 (3H) and 2.27 (3H). Compound **22** gave a monoacetate **23**, molecular formula $C_{13}H_{16}O_5$ (*m/z* 252 $[M]^+$). The ^{1}H nmr exhibited signals for an acetyl and a methoxy group at δ 2.06 (3H) and 3.89 (3H), respectively. Hydrolysis of **21** followed by treatment with CH_2N_2 gave **22** while hydrolysis of **23** gave an alcohol identical (ir, ^{1}H nmr, ms) to that obtained by $NaBH_4$ reduction of **19**, earlier isolated from *Ferula ugamica* G. Kor. (25).

Phenylpropanoid **24** was a crystalline substance, mp 95–96°, $C_{11}H_{12}O_5$ (*m/z* 224 $[M]^+$), which turned dark blue when treated with $FeCl_3$. Absorption bands for carbonyl and aromatic groups were visible in the ir spectrum (1650, 1605, 1504 cm^{-1}), and ^{1}H nmr clearly showed the presence of a methylenedioxy group and a methoxy group on an aromatic ring [δ 6.10 (2H), 3.88 (3H)]. The structure of **24** was confirmed by nOe difference spectroscopy.

The phenolic compound **25** was a colorless oil with molecular formula $C_{10}H_{14}O_3$ (*m/z* 182 $[M]^+$). In the ^{1}H-nmr spectrum, two doublets appeared in the aromatic region at δ 7.15 (2H, $J=8$ Hz) and 6.79 (2H, $J=8$ Hz) corresponding to protons in the ortho position on a substituted aromatic ring. A quartet at δ 3.42 (2H, $J=7$ Hz) and a triplet at δ 1.84 (3H, $J=7$ Hz) were assigned to an ethoxy group. Compound **25** was treated with Ac_2O/pyridine to give the diacetate **26** as an oil: $C_{14}H_{18}O_5$; no $[M]^+$, *m/z* 221 $[M-C_2H_5O]^+$. The ^{1}H-nmr spectrum showed two singlets at δ 1.97 (3H) and 2.20 (3H), attributed to the protons of aliphatic and aromatic acetyls, respectively, a triplet at δ 4.44 (1H, $J=6$ Hz), an acetate group geminal proton, and a doublet at δ 4.06 (2H, $J=6$ Hz) assignable to a -CH_2O-. The proposed structure was confirmed by ^{13}C-nmr analysis. Compound **25** is probably an artifact of the extraction process.

The new substituted phenanthrene **27** had the molecular formula $C_{17}H_{16}O_3$ (*m/z* 268 $[M]^+$). In the ^{1}H-nmr spectrum there were signals for methoxy groups at δ 3.95, 3.99, and 4.10 (each 3H, s) and for seven aromatic protons at δ 6.75 and 6.89 (each 1H, d, $J=2.5$ Hz, H-1 and H-3 or vice versa), 7.20 and 7.50 (each 1H, d, $J=8.7$ Hz, H-9 and H-10 or vice versa), 7.17 (1H, dd, $J=8.7$, 2.5 Hz, H-7), 7.75 (1H, d, $J=8.7$ Hz, H-8), and 9.07 (1H, d, $J=2.5$ Hz, H-5). The methoxy groups had to be positioned at C-2, C-4, and C-6, by comparison of the ^{1}H-nmr spectrum of **27** with those of 2,7-dihydroxy-4,6-dimethoxyphenanthrene (26).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected. Ir spectra were taken in $CHCl_3$ and ^{1}H nmr in $CDCl_3$ at 200 MHz. ^{13}C nmr were measured in $CDCl_3$ at 22.6 MHz and ms were obtained using a direct inlet system at 70 eV.

PLANT MATERIAL.—The roots and aerial part of *F. latipinna* were collected in the Gallego area, La Palma, in April 1986. A voucher specimen is deposited in the Herbarium of the Faculty of Pharmacy, Universidad de La Laguna.

ISOLATION OF COMPOUNDS.—The dried and powdered roots and aerial part of the plant (10 kg) were extracted with EtOH in a Soxhlet. The EtOH extract was concentrated in vacuo, yielding 50 g crude viscous oil. This oil was chromatographed on a Si gel column packed in C_6H_6, then eluted with C_6H_6/EtOAc mixtures of increasing polarity. The fractions obtained with an 8:2 mixture gave **1** (1.5 g), **3** (1.2

g), **4** (10 mg), **5** (800 mg), **7** (920 mg), **9** (100 mg), **11** (50 mg), **12** (960 mg), **13** (70 mg), **16** (30 mg), **17** (950 mg), **18** (10 mg), **19** (1.2 g), **20** (isolated as diacetate, 12 mg), **22** (isolated as acetate, 15 mg), **24** (22 mg), and **27** (11 mg); a 3:2 mixture gave **6** (200 mg), **8** (20 mg), **10** (25 mg), **25** (9 mg), scopoletin (20 mg), isoscopoletin (8 mg), diosmetin (1.5 g), veratric acid (2 g), and *p*-methoxybenzoic acid (920 mg). Sephadex LH-20 columns packed in hexane-$CHCl_3$-MeOH (2:1:1) and/or preparative tlc (Si gel in thicknesses ranging from 1 to 5 mm) developed with hexane-EtOAc (4:1, 7:3, and 3:2) were used in the further purification of the compounds.

Compound **1**.—Crystallized with di-isopropyl ether as plates; mp 77–78°; ir ν max 3580, 3460, 1700, 1640, 1450, 1380, 1155, 1100, 1080, 1035, 975, 950, 910, 880, 840 cm^{-1}; ^1H nmr δ 6.03 (2H, m, angelic acid), 5.70 (1H, d, J = 7.4 Hz, H-2), 5.23 (1H, td, J = 3, 11 Hz, H-5), 4.85 (1H, d, J = 7.4 Hz, H-1), 2.62 (1H, d, J = 11 Hz, H-6), 1.98–1.79 (4 × Me, m, angelic acid), 1.75 (3H, s, H-15), 1.13 (3H, s, H-14), 0.84 (6H, d, J = 6.7 Hz, H-12 and H-13); ms *m/z* (rel. int.) $[M - C_3H_7 - \text{angelic acid}]^+$ 275 (3), 235 (4), 218 (5), 203 (4), 175 (72), 157 (14).

Epoxidation of **1**.—Compound **1** (200 mg) in $CHCl_3$ (3 ml) was added to a solution of MCPBA (300 mg) in $CHCl_3$ (4 ml). The mixture was left at room temperature for 2 days and worked up in the usual way, giving the epoxyderivative **2** (150 mg): ^1H nmr, δ 5.17 (1H, t, J = 11 Hz, H-5), 4.97 (1H, d, J = 5.4 Hz, H-1), 3.00 (1H, d, J = 5.4 Hz, H-2), 1.56–1.28 (4 × Me, m, epoxyangelic acid), 1.43 (3H, s, H-15), 1.23 (3H, s, H-14), 0.90 (6H, d, J = 7 Hz, H-12 and H-13).

Hydrolysis of **2**.—Compound **2** (90 mg) was treated with 3% NaOH in MeOH (10 ml) at room temperature, and after 4 h the mixture was worked up in the usual way, giving **8** (20 mg) (16).

Compound **6**.—Mp 176–178° (hexane/EtOAc); $[M - C_3H_7]^+$ at 359.1510, $C_{20}H_{23}O_6$ requires 359.1494; ir ν max 3510, 3000, 2955, 1685, 1640, 1600, 1590, 1512, 1460, 1420, 1355, 1275, 1100, 1030, 930 cm^{-1}; ^1H nmr δ 7.58 (1H, dd, J = 1.8, 8.2 Hz, H′-7), 7.52 (1H, d, J = 1.8 Hz, H′-3), 6.95 (1H, d, J = 8.2 Hz, H′-6), 6.01 (1H, br s, H-2), 5.83 (1H, m, H-5), 3.02 (1H, dd, J = 5, 16 Hz, H-4α), 2.57 (1H, d, J = 9.6 Hz, H-6), 2.46 (1H, dd, J = 2.5, 16 Hz, H-4β), 2.00 (3H, br s, H-15), 1.39 (3H, s, H-14), 0.86 (6H, d, J = 6.7 Hz, H-12 and H-13); ^{13}C nmr δ 208.3 (C-1), 166.3 (C′-1), 150.8 (C-3)[1], 150.5 (C′-4)[1], 146.6 (C′-5), 128.6 (C-2), 124.2 (C′-7), 121.8 (C′-2), 114.5 (C′-3), 112.0 (C′-6), 84.7 (C-10), 70.8 (C-5), 56.1 (OMe), 55.3 (C-7), 50.3 (C-6), 38.3 (C-4), 36.9 (C-9), 36.4 (C-11), 31.2 (C-8), 28.3 (C-15), 18.4 (C-14), 18.2 (C-12), 17.4 (C-13). The number of protons directly attached to each carbon was verified with the DEPT pulse sequence. Ms *m/z* (rel. int.) $[M - C_3H_7]^+$ 359 (7), 235 (26), 217 (9), 191 (23), 168 (36), 163 (10).

Hydrolysis of **6**.—Compound **6** (100 mg), dissolved in MeOH (2 ml), was treated with a 3% solution of KOH in MeOH (3 ml), at room temperature for 10 h. Usual workup afforded lapidol (6 mg) and vanillic acid (12 mg).

Compound **12**.—$[M]^+$ at *m/z* 386.2434, $C_{24}H_{34}O_4$ requires 386.2435; ir ν max 3080, 3015, 2965, 2930, 1690, 1650, 1600, 1585, 1510, 1460, 1410, 1380, 1360, 1175, 1140, 1130, 1105, 1025, 930 cm^{-1}; ^1H nmr δ 7.61 (1H, dd, J = 1.95, 8.5 Hz, H′-7), 7.51 (1H, d, J = 1.95 Hz, H′-3), 6.82 (1H, d, J = 8.5 Hz, H′-6), 5.47 (1H, d, J = 10.4 Hz, H-6), 5.37 (1H, br d, J = 10.4 Hz, H-5), 5.22 (1H, br t, J = 8 Hz, H-1), 3.87 (6H, s, 2-OMe), 2.80 (1H, m, H-3), 2.17 (2H, m, H-2), 1.86 (1H, dt, J = 3.2, 13.2 Hz, H-3), 1.73 (3H, br s, H-15), 1.64 (3H, br s, H-14), 1.06 (3H, s, H-12), 0.84 (3H, s, H-13); ms *m/z* (rel. int.) $[M]^+$ 386 (3), 290 (1), 206 (2), 204 (37), 189 (20), 182 (100), 167 (23); ^{13}C nmr see Table 1.

Compound **13**.—Mp 147–148° (hexane); $[M]^+$ at *m/z* 402.2397, $C_{24}H_{34}O_5$ requires 402.2404; ir ν max 3200, 2965, 2938, 1700, 1600, 1590, 1510, 1460, 1380, 1360, 1265, 1175, 1130, 1105, 1020, 950 cm^{-1}; ^1H nmr δ 7.66 (1H, dd, J = 1.5, 8.3 Hz, H′-7), 7.55 (1H, d, J = 1.5 Hz, H′-3), 6.88 (1H, d, J = 8.3 Hz, H′-6), 5.73 (1H, d, J = 10.5 Hz, H-6), 5.39 (1H, br d, J = 10.5 Hz, H-5), 3.92 (6H, s, 2-OMe), 2.84 (2H, m, H-1 and H-3), 1.82 (3H, br s, H-15), 1.39 (3H, s, H-14), 1.06 (3H, s, H-12), 0.96 (1H, s, H-13); ms *m/z* (rel. int.) $[M]^+$ 402 (0.86), $[M - C_9H_{10}O_4]^+$ 220 (3), 205 (2), 202 (1), 187 (2), 183 (10), 182 (100), 165 (82); ^{13}C nmr see Table 1.

Hydrolysis of **13**.—Compound **13** (60 mg) dissolved in MeOH (3 ml) was treated with a 3% solution of KOH in MeOH (4 ml) at room temperature for 24 h. Usual workup and subsequent purification by cc on Si gel column using C_6H_6-MeCN (9:1) as eluent yielded alcohol **14** (20 mg): ^1H nmr, δ 5.37 (1H, br d, J = 10.2 Hz, H-5), 4.28 (1H, d, J = 10.2 Hz, H-6), 2.84 (1H, dd, J = 3.4, 10.7 Hz, H-1), 1.82 (3H, br s, H-15), 1.30 (3H, s, H-14), 0.96 (3H, s, H-12), 0.86 (3H, s, H-13).

[1]Assignments interchangeable.

TABLE 1. ^{13}C-nmr Data for Compounds **12**, **13**, and **16**.

Carbon[a]	Compound		
	12	**13**	**16**
1	124.6	60.8	62.4
2	25.1	29.3	28.7
3	32.8	25.1	25.1
4	142.3	141.4	141.8
5	122.2	122.6	122.7
6	74.5	74.0	75.2
7	36.6	37.5	37.3
8	23.6	19.8	22.2
9	35.8	38.7	37.3
10	136.0	60.8	62.9
11	37.7	37.6	37.3
12	24.6	24.5	24.2
13	24.0	23.0	23.1
14	18.8	16.7	21.8
15	23.0	23.5	23.2

[a]Veratrate: 166.0 (C′-1), 123.5 (C′-2), 111.2 (C′-3), 148.7 (C′-4), 152.9 (C′-5), 110.4 (C′-6), 123.4 (C′-7), 55.9 (OMe), 60.0 (OMe).

p-Bromobenzoate **15** *from* **14**.—Compound **14** (15 mg) was acylated with *p*-bromobenzoyl chloride and dry pyridine at room temperature overnight, then extracted with $CHCl_3$ and purified by preparative tlc using C_6H_6-MeCN (9:1) as eluent to give the bromobenzoate **15** (16 mg): mp 173–175° [lit. (23) 175–179°]; ^{1}H nmr δ 7.87 (2H, d, J = 8.5 Hz, H′-4 and H′-6), 7.56 (2H, d, J = 8.5 Hz, H′-3 and H′-7), 5.73 (1H, d, J = 10.5 Hz, H-6), 5.38 (1H, br d, J = 10.5 Hz, H-5), 2.92 (2H, m, H-1 and H-3), 1.82 (1H, br s, H-15), 1.39 (3H, s, H-14), 1.08 (3H, s, H-12), 0.91 (3H, s, H-13).

Compound **16**.—Colorless oil: $[M]^+$ at m/z 402.2415, $C_{24}H_{34}O_5$ requires 402.2406; ir ν max 3015, 3000, 2960, 2920, 2860, 1690, 1590, 1505, 1455, 1410, 1280, 1260, 1170, 1015, 940, 930 cm^{-1}; ^{1}H nmr δ 7.68 (1H, dd, J = 1.9, 8.4 Hz, H′-7), 6.90 (1H, d, J = 8.4 Hz, H′-6), 5.70 (1H, d, J = 10.5 Hz, H-6), 5.56 (1H, d, J = 1.8 Hz, H′-3), 5.44 (1H, br d, J = 10.5 Hz, H-5), 3.94 (6H, s, 2-OMe), 3.14 (1H, t, J = 13 Hz, H-3), 2.98 (1H, dd, J = 3.1, 11 Hz, H-1), 1.77 (3H, br s, H-15), 1.32 (3H, s, H-14), 1.14 (3H, s, H-12), 0.94 (3H, s, H-13); ms at m/z (rel. int.) $[M]^+$ 402 (3), 359 (1), 290 (1), 237 (2), 220 (14), 205 (6), 192 (4), 182 (100); ^{13}C nmr see Table 1.

Himachalol [**17**].—Mp 63–65° [lit. (18) 67–68°]; $[M]^+$ at m/z 222.2003, $C_{15}H_{26}O_1$ requires 222.2003; ir ν max 3590, 3440, 3000, 2920, 2815, 1530, 1510, 1500, 1465, 1435, 1430, 1385, 1375, 1365, 1235, 1060, 1025, 908, 860 cm^{-1}; ^{1}H nmr δ 5.48 (1H, d, J = 5.8 Hz, H-2), 1.58 (3H, br s, H-3), 1.15 (3H, s, H-15), 0.89 (3H, s, H-12), 0.76 (3H, s, H-13); ^{13}C nmr δ 133.3 (s), 125.7 (d), 76.1 (s), 51.9 (d), 43.6 (d), 41.3 (t), 38.4 (s), 36.4 (t), 33.5 (q), 32.6 (q), 31.7 (t), 26.8 (q), 23.7 (q), 22.3 (t), 19.9 (t); ms m/z (rel. int.) $[M]^+$ 222 (1), $[M-Me]^+$ 207 (4), $[M-H_2O]^+$ 204 (36), 189 (12).

Compounds **21** *and* **23**.—A mixture of alcohols **20** and **22** (40 mg) was treated overnight with Ac_2O/pyridine at room temperature, and after workup, the reaction mixture was purified by cc on Si gel using C_6H_6-MeCN (19:1) as eluent to give a diacetate **21**: $[M]^+$ at m/z 280.0952, $C_{14}H_{16}O_6$ requires 280.0952; ^{1}H nmr δ 6.69 (1H, d, J = 1.5 Hz, H-Ar), 6.58 (1H, d, J = 1.5 Hz, H-Ar), 5.96 (2H, s, OCH_2O), 5.51 (1H, t, J = 6.8 Hz, H-COAc), 2.27 (3H, s, ArOAc), 2.03 (3H, s, OAc), 1.76 (2H, m, $-CH_2-$), 0.84 (3H, t, J = 7.4 Hz, Me); ms m/z (rel. int.) $[M]^+$ 280 (34), $[M-C_2H_2O]^+$ 238 (46), 221 (17), 209 (19), 196 (60), 179 (28); and a monoacetate **23**: ^{1}H nmr δ 6.52 (1H, s, H-Ar), 6.49 (1H, s, H-Ar), 5.94 (2H, s, OCH_2O), 5.53 (1H, t, J = 7 Hz, H-COAc), 3.89 (3H, s, OMe), 2.06 (3H, s, OAc), 1.96 (2H, m, $-CH_2-$), 0.86 (3H, t, J = 7.5 Hz, Me); ms m/z (rel. int.) $[M]^+$ 252 (42), 223 (6), 210 (46), 195 (4), 193 (37), 181 (100).

Hydrolysis of **23**.—Compound **23** (15 mg) dissolved in MeOH (1.5 ml) was treated with a 3% solution of KOH in MeOH (2 ml) for 8 h. After usual extraction, tlc purification with C_6H_6-EtOAc (4:2) gave alcohol **22** (4 mg).

Reduction of **19**.—Compound **19** (400 mg) in MeOH (10 ml) was treated with $NaBH_4$ (100 mg) at 0° for 2 h. Usual workup afforded the alcohol **22** (300 mg).

Compound **24**.—Mp 95–97° (hexane/Me_2CO); $[M]^+$ at *m/z* 224.0687, $C_{11}H_{12}O_5$ requires 224.0684; ir ν max 1650, 1605, 1504, 1420, 1330, 1280, 1150, 1060, 1010 cm^{-1}; ^1H nmr δ 12.50 (1H, s, HOAr), 6.90 (1H, s, H-Ar), 6.10 (2H, s, OCH_2O), 3.88 (3H, s, OMe), 2.95 (2H, q, $J=7.5$ Hz, -CH_2-), 1.22 (3H, t, $J=7.5$ Hz, Me); ms *m/z* (rel. int.) $[M]^+$ 224 (43), $[M-Me]^+$ 209 (1), $[M-H_2O]^+$ 206 (1), 195 (100), 180 (3), 167 (6).

Compound **25**.—Colorless oil (9 mg); ^1H nmr (80 MHz, $CDCl_3$) δ 7.15 (2H, d, $J=8$ Hz, H-Ar), 6.79 (2H, d, $J=8$ Hz, H-Ar), 4.40 (1H, t, $J=5.5$ Hz, O-CH-Ar), 3.60 (2H, d, $J=5$ Hz, -CH_2-O), 3.42 (2H, q, $J=7$ Hz, O-CH_2-), 1.84 (3H, t, $J=7$ Hz, Me).

Acetylation of **25**.—Compound **25** (9 mg) dissolved in pyridine (1 ml) was treated with Ac_2O (0.5 ml) at room temperature for 12 h. Extraction as usual gave the acetate **26** (8 mg): ^1H nmr, δ 7.27 (2H, d, $J=8.5$ Hz, H-Ar), 6.99 (2H, d, $J=8.5$ Hz, H-Ar), 4.44 (1H, t, $J=6$ Hz, OAc-*CH*-Ar), 4.06 (2H, d, $J=6$ Hz, -CH_2-O), 3.34 (2H, q, $J=7$ Hz, O-CH_2-), 2.20 (3H, s, ArOAc), 1.97 (3H, s, OAc), 1.10 (3H, t, $J=7$ Hz, Me); ^{13}C nmr δ 170.9 (s), 169.4 (s), 150.5 (s), 136.4 (s), 127.9 × 2 (d), 121.7 × 2 (d), 79.1 (d), 67.9 (t), 64.7 (t), 21.1 (q), 20.9 (q), 15.2 (q); ms *m/z* (rel. int.) $[M-CH_2Me]^+$ 235 (1), $[M-OCH_2Me]^+$ 221 (1), 193 (44), 179 (2), 175 (4), 152 (10), 151 (100).

Compound **27**.—Mp 105–107° (hexane); $[M]^+$ at *m/z* 268.1096, $C_{17}H_{16}O_3$ requires 268.1099; ir ν max 1620, 1600, 1450, 1430, 1350, 1295, 1270, 1235, 1160, 1090, 1060, 820 cm^{-1}; ms *m/z* (rel. int.) $[M]^+$ 268 (100), $[M-Me]^+$ 253 (30), $[M-2Me]^+$ 238 (10), 225 (57), 210 (69), 195 (20), 165 (42), 139 (52).

ACKNOWLEDGMENTS

This work was partly financed by a grant from the CAICYT (PR 84-0191-C03-01). J.G.D. is indebted to the AIETI Foundation for a fellowship.

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Received 22 March 1988