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NEW DAUCANE ESTERS FROM *FERULA TINGITANA*

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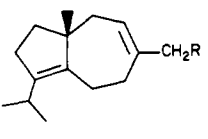
ABSTRACT.—In addition to the three known daucane esters (**2,3,8**) and one phenylpropanoid (**9**), the petroleum ether extract of the roots of *Ferula tingitana* yielded four new daucane esters: 14-*p*-anisoyloxy-dauc-4,8-diene (**1**), acetyltingitanol (**4**), acetyldesoxodehydrolaserpitine (**5**), and 4-β-hydroxy-6-α-*p*-hydroxybenzoyloxy-10-α-angeloyloxydauc-8-ene (**6**). A possible biogenetic pathway for 1,5-*cis*- and 1,5-*trans*-daucanes is presented.

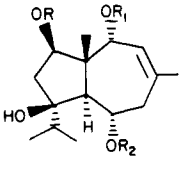
From the C_6H_6 extract of the roots of *Ferula tingitana* L., a medicinal plant from the Mediterranean region (1), we previously isolated the new sesquiterpene ester tingitanol (**2**) (2), as well as the three known sesquiterpene coumarin ethers coladonin, feselol, and isosamarcandin angelate (3). The petroleum ether extract of the same material has now yielded, in addition to tingitanol, three known and four new compounds.

RESULTS AND DISCUSSION

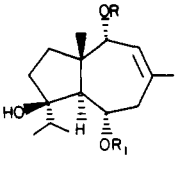
The known compounds from the petroleum ether extract were identified as desoxodehydrolaserpitine (**3**) (2,4), fercomin (**8**) (5), and laserine (**9**) (6,7) by spectral data and direct comparison with authentic samples. The structural analysis of the four new compounds (**1, 4, 5,** and **6**) follows.



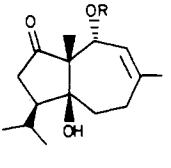
1 R=*p*-anisoyloxy
1a R=H



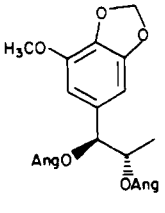
2 R=H, R_1=R_2=Ang
3 R=R_2=Ang, R_1=H
4 R=Ac, R_1=R_2=Ang
5 R=R_2=Ang, R_1=Ac



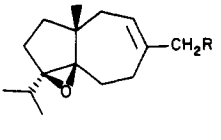
6 R=Ang, R_1=*p*-hydroxybenzoate
7 R=Ang, R_2=*p*-anisate



8 R=*p*-anisate



9



10 R=*p*-anisoyloxy

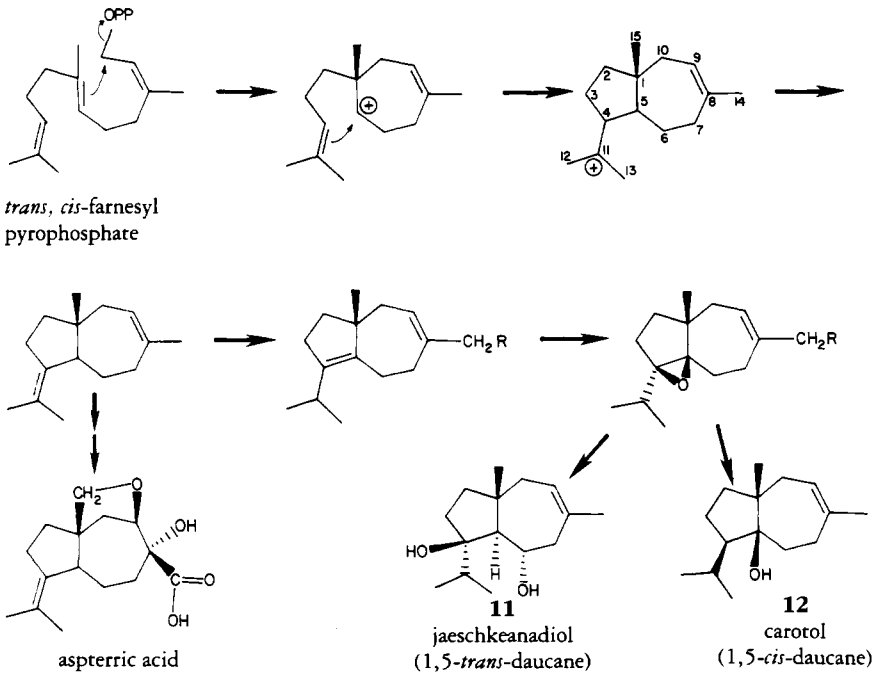
The eims of **1** exhibited a molecular ion at *m/z* 354 in accord with a $C_{23}H_{30}O_3$ molecular formula. The presence of an aromatic acyl group was established by the ir (1710, 1610, 1515, and 1260 cm^{-1}) and uv (260 nm) spectra of **1**. The acyl group in **1** was confirmed as *p*-anisate by the ^{1}H-nmr spectrum which exhibited signals similar to those for 14-*p*-anisoyloxy-4,5-β-epoxydauc-8-ene (**10**), except for the H-11 signal for **1** which appears at δ 2.69. This later feature of the ^{1}H nmr of **1** was in accord with the presence of a double bond at C-4. Furthermore, the absence of vinylic signals other than for H-9 indicated that the double bond must be between C-4 and C-5, similar to that of **1a**. Thus, **1** must be the 14-*p*-anisoyloxy derivative of daucene (**1a**).

Compound **4** was identified as acetyltingitanol by spectral data and direct comparison with the acetylation product of tingitanol (2).

Compound **5**, exhibited a similar ^{1}H-nmr spectrum to the one recorded for **4**, and acetylation of **3** to **5** established that **5** is acetyldesoxodehydrolaserpitine.

Except for side-chain signals the ^{1}H-nmr spectrum of **6** was similar to the one recorded for **7** (8) (the spectrum of **6** exhibited signals for a *p*-hydroxybenzoyl side chain). A molecular ion at *m/z* 456 ($C_{27}H_{36}O_6$) in the eims of **6**, together with a fragmentation pattern similar to that of **7**, also supported this relationship. Conversion of **6** to **7** by methylation with CH_2N_2 confirmed **6** to be 4-β-hydroxy-6-α-*p*-hydroxybenzoyloxy-10-α-angeloyloxydauc-8-ene.

It is of interest that *F. tingitana* as well as *Ferula communis*, *Ferula linkii*, and *Ferula lancerottensis*, members of the subgenus *Euferula* (Boiss.) Korovin, yielded both 1,5-*cis*- and 1,5-*trans*-daucane derivatives (5,8-11), which may be biogenetically related as shown in Scheme 1. These biogenetic considerations require a β-orientation for the oxirane ring of **10**, an orientation that is proposed here on the basis of the correlation of ^{13}C nmr of **10** with those of jaeschkeanadiol (**11**) and carotol (**12**). Nearly identical chemical shifts of the isopropyl methyl groups of **10** (δ 17.5 and 18.5) and **11** (δ17.8 and 18.2, in contrast to those of carotol (**12**) (δ 20.9 and 23.5), indicate the similar shielding effect of the sesquiterpene nucleus and the γ-substituent effect of the C-4



SCHEME 1.

asymmetric center on this part of the molecule; this, in turn, suggests a β stereochemistry for the epoxy group in **10**. In addition, direct comparison of the ^{1}H-nmr spectrum of **10** with that of the synthetic 4,5-β-epoxydauc-8-ene (12) clearly supported this assignment.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Uv spectra were taken in MeOH; ^{1}H nmr and ^{13}C nmr in $CDCl_3$ using TMS as an internal standard at 200 MHz and 22.6 MHz, respectively. Ms were obtained with a direct inlet system at 70 eV.

PLANT MATERIAL.—The roots of *F. tingitana* were collected from the Aegean Coast of Turkey (between Kuşadası and Ephesus) in June 1982. A voucher specimen, identified by Dr. E. Tuzlacı (Istanbul), is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul (ISTE 48938).

ISOLATION AND IDENTIFICATION OF THE COMPOUNDS.—Dried and coarsely powdered roots of *F. tingitana* (2.5 kg) were extracted with petroleum ether in a Soxhlet apparatus. Concentration of the petroleum ether extract provided 146 g of viscous oil. This oil (6 g) was chromatographed on Sephadex LH-20 columns packed in EtOH and cyclohexane-CH_2Cl_2-EtOH (7:4:1). Finally, preparative tlc [1.5-2 mm thickness, silica gel developed with cyclohexane-EtOAc mixtures (4:1 and 7:3)] was used for further purification of the compounds.

14-p-*Anisoyloxydauc-4,8-diene* (**1**).—5 mg; uv λ max nm 260; ir ν max ($CHCl_3$) 2970, 1710, 1610, 1515, 1260, and 770 cm^{-1}; ^{1}H nmr δ 8.01 (2H, d, J=9.1 Hz, H-4′ and 6′), 6.93 (2H, d, J=9.1 Hz, H-3′ and 7′), 5.86 (1H, br t, J=6.5 Hz, H-9), 4.70 (2H, br s, H-14 and 14′), 3.86 (3H, s, H-8′), 2.69 (1H, septet, H-11), 0.98 (3H, d, J=7.2 Hz, H-12), 0.95 (3H, s, H-15), 0.93 (3H, d, J=7.2 Hz, H-13); ms *m/z* (% rel. int.) 354 $[M]^+$ (7.2), 311 $[M-C_3H_7]^+$ (14.3), 218 $[M-C_8H_8O_2]^+$ (21.7), 202 $[M-C_8H_8O_3]^+$ (42), 187 $[M-C_9H_{13}O_3]^+$ (23.8), 175 $[M-C_{11}H_{15}O_2]^+$ (60.3), 159 $(M-C_{11}H_{16}O_3]^+$ (69.8), 135 [p-anisate]$^+$ (100).

Acetyltingitanol (**4**).—18 mg; for ir and ^{1}H-nmr data see Miski *et al.* (2); ms *m/z* (% rel. int.) 476 $[M]^+$ (0.2), 393 $[M-C_5H_7O]^+$ (8), 333 $[M-C_8H_{15}O_2]^+$ (25.3), 317 $[M-C_7H_{11}O_4]^+$ (6.4), 293 $[M-C_{10}H_{15}O_3]^+$ (59.2), 234 $(M-C_{12}H_{18}O_5]^+$ (81.3), 216 (82.4), 191 (63.7), 173 (94.4), 83 [angelate]$^+$ (93.3), 43 [acetate]$^+$ (100).

Acetyldesoxodehydrolaserpitine (**5**).—12 mg; ir ν max (KBr), 3500, 2980, 2960, 1732, 1710, 1695 (sh), 1645, 1260, 1228 cm^{-1}; ^{1}H nmr δ 6.15 (1H, qq, J=1.4 and 7.3 Hz, H-3′), 6.08 (1H, qq, J=1.4 and 7.3 Hz, H-3″), 5.74 (1H, br d, J=7.4 Hz, H-9), 5.36 (1H, dt, J=3.4 and 10.7 Hz, H-6), 4.78 (1H, d, J=7.4 Hz, H-10), 4.76 (1H, dd, J=8.8 and 10.3 Hz, H-2α), 2.72 (1H, bt, J=14.1 Hz, H-7β), 2.70 (1H, d, J=10.7 Hz, H-5), 2.50 (1H, dd, J=8.8 and 14.1 Hz, H-3α), 2.16 (1H, dd, J=3.4 and 14.2 Hz, H-7α), 2.08 (3H, s, O*Ac*), 2.06 (3H, td, J=1.5 and 6.4 Hz, H-4′), 1.99 (3H, td, J=1.5 and 6.4 Hz, H-4″), 1.89 (6H, m, H-5′ and 5″), 1.82 (3H, br d, J=1.2 Hz, H-14), 1.58 (1H, dd, J=10.3 and 14.2 Hz, H-3β), 1.22 (3H, s, H-15), 0.98 (3H, d, J=6.8 Hz, H-12), 0.91 (3H, d, J=6.8 Hz, H-13); ms *m/z* (% rel. int.) 373 $[M-C_5H_{11}O_2]^+$ (21.5), 333 $[M-C_8H_{15}O_2]^+$ (15.7), 290 $[M-C_{10}H_{18}O_3]^+$ (10.6), 273 $[M-C_{10}H_{19}O_4]^+$ (57.4), 233 $[M-C_{13}H_{23}O_4]^+$ (13.9), 216 $[M-C_{12}H_{20}O_6]^+$ (80.6), 198 (36.4), 173 (93.9), 145 (87.5), 83 [angelate]$^+$ (100), 43 [acetate]$^+$ (67.4).

Acetylation of **4**.—Desoxodehydrolaserpitine (**4**) (10 mg) was acetylated with pyridine and Ac_2O for 15 h. The usual work-up gave 12 mg of acetyldesoxodehydrolaserpitine, identical with **5**.

4-β-Hydroxy-6-α-p-*hydroxybenzoyloxy-10*-α-*angeloyloxydauc-8-ene* (**6**).—16 mg; uv λ max nm 308 (sh), 258; ir ν max (KBr) 3380, 2260, 2245, 1710, 1650, 1608, 1590, 1510, 1440, 1270, 850, 770 cm^{-1}; ^{1}H nmr δ 7.95 (2H, d, J=8.4 Hz, H-4′ and 6′), 6.89 (2H, d, J=8.4 Hz, H-3′ and 7′), 6.12 (1H, qq, J=1.2 and 7.3 Hz, H-3″), 5.79 (1H, br d, J=7.1 Hz, H-9), 5.44 (1H, dt, J=2.7 and 10.7 Hz, H-6), 4.94 (1H, d, J= 7.1 Hz, H-10), 2.79 (1H, d, J=10.7 Hz, H-5), 2.78 (1H, br t, J=14.3 Hz, H-7β), 2.23 (1H, dd, J=2.7 and 14.3 Hz, H-7α), 2.06 (3H, td, J=1.2 and 7.2 Hz, H-4″), 1.98 (3H, t, J=1.2 Hz, H-5″), 1.82 (3H, br d, J=1.2 Hz, H-14), 1.23 (3H, s, H-15), 0.98 (3H, d, J=6.5 Hz, H-12), 0.86 (3H, d, J=6.5 Hz, H-13); ms *m/z* (% rel. int.) 456 $[M]^+$ (0.7), 413 $[M-C_3H_7]^+$ (1.2), 356 $[M-C_5H_8O_2]^+$ (1.1), 313 $[M-C_8H_{15}O_2]^+$ (32.4), 275 $[M-C_{10}H_{13}O_3]^+$ (6.4), 235 $[M-C_{12}H_{13}O_4]^+$ (13), 218 $[M-C_{12}H_{14}O_5]^+$ (30.9), 200 (40.2), 175 (95.7), 138 [p-hydroxybenzoic acid]$^+$ (57.6), 121 (p-hydroxybenzoate]$^+$ (100), 83 [angelate]$^+$ (67.3).

Methylation of **6**.—Compound **6** (10 mg) was reacted with CH_2N_2 (in Et_2O) for 16 h. The usual work-up gave 9 mg of **7**, identical with the natural compound (8).

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