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PEUCELINENDIOL, A NEW ACYCLIC DITERPENOID FROM *PEUCEDANUM OREOSELINUM**

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Key Word Index—*Peucedanum oreoselinum*; Umbelliferae; acyclic irregular diterpenoid; polyacetylene; peucelinendiol; falcarindiol.

Abstract—A new diterpenoid has been isolated from roots of *Peucedanum oreoselinum*. Mainly by spectroscopic methods, its structure is shown to be (+)-(*E*)-7-hydroxymethyl-2,6,10,14-tetramethyl-2,9,13-pentadecatrien-6-ol, yet without specification of stereochemistry at C-6 and C-7. Furthermore the roots afforded a high yield of falcarindiol, (+)-(*Z*)-heptadeca-1,9-dien-4,6-diyn-3,8-diol.

INTRODUCTION

During the investigation of the coumarinic constituents of *Peucedanum oreoselinum* [1], two non-coumarinic compounds with almost identical chromatographic properties were observed in the ether extract of the roots. The present communication reports a re-examination of these two constituents which have been found to be readily separable by chromatography on acetylated cellulose. The major compound was identified as falcarindiol, an acetylenic compound previously found in Umbelliferae [2–5], whereas the minor compound appeared to be a new diterpenoid.

RESULTS AND DISCUSSION

Falcarindiol was isolated in considerable quantity and the opportunity was taken for a supplementary characterization of this unstable compound. The results of an investigation of the absolute configuration of falcarindiol will be reported in a separate communication.

The minor constituent (**1**) was obtained as an almost colourless viscous oil, showing optical activity. Bands in the IR spectrum at 3350 and 1660 cm^{-1} and lack of UV absorption above 210 nm were indicative of an unsaturated alcohol with isolated double bonds. The MS of **1** indicated an elemental composition $C_{20}H_{36}O_2$ (M^+ *m/e* 308; $M^+ - H_2O$ *m/e* 290.2609) and the acyclic nature of **1** was established by MS characterization of the single product of catalytic hydrogenation as a hexahydro derivative.

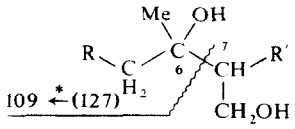
In the ^1H NMR spectrum of **1** in CCl_4, two OH groups gave rise to a two proton peak exchangeable with D_2O. The appearance of these OH signals in DMSO-d_6 solution as a triplet at δ 4.6, and a singlet at δ 4.4, showed that one of the alcohol groups was tertiary and the other one primary. Furthermore, the ^1H NMR spectrum of **1** in CCl_4 solution showed a complex three proton signal at δ 4.95 assigned to three vinylic protons, a methylene signal at 3.55, appearing as a broadened doublet with a 7 Hz splitting assignable to the $-C\underline{H}_2OH$ grouping apparently with a methine neighbour, and a three proton singlet at 1.10 assignable to a methyl group attached to the carbon atom bearing the tertiary hydroxyl group. Five methyl groups gave rise to two broadened, partly resolved singlets at δ 1.58 (*ca* 9H) and 1.63 (*ca* 6H), which is characteristic of vinylic methyls with a *trans* and *cis* relationship respectively to the chain in an acyclic terpenoid [6]. The remaining signals (11H) in the region δ 1.2–2.1 were assigned to methine and methylene groups. By gradual addition of $Eu(DPM)_3$, a one proton signal emerged from this region and was shifted even faster than the methylene protons of the $-CH_2OH$ group. From this observation the presence of a methine group in a neighbouring position to both hydroxyl-bearing carbons was assumed and accordingly a 1,3-relationship of the alcohol groups was indicated. Chemically, this relationship was evidenced by the ready preparation of a cyclic phenylboronate from **1** [7].

No structure based upon a regular diterpenoid skeleton could be written on these grounds. However, when a biosynthetic route involving head to head combination of isoprenoid units was imagined, and the MS fragmentations of **1** and its hexahydro derivative were taken into account, two structural possibilities represented by the formulae **1a** and **1b** existed for **1**. In particular, corresponding structures with interchanged prenyl and geranyl groups were excluded by the abundant occurrence in the MS of **1** of an ion at *m/e* 109, and in the MS of hexahydro **1** of ions at *m/e* 129 and 111. These data were in favour of the formula **1a** for the compound **1** but did not convincingly exclude the possiblity of **1b**.

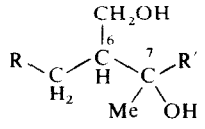
The ^{13}C NMR spectrum of **1** was in full accordance with both of these structural possibilities. In particular, this spectrum very clearly demonstrated the presence of two isopropylidene terminals, in confirmation of **1** being head to head combined. Also, a geranyl rather than a neryl stereochemistry could be concluded more safely from this spectrum than from the proton shift data of the vinylic methyl groups [8].

The definite exclusion of **1b** as a possible structure for compound **1** was achieved by the observation that,

* Part 22 in the series "Constituents of Umbelliferous Plants". For Part 21 see Lemmich, J. and Havelund, S. (1978) *Phytochemistry* **17**, 139.



1a



1b

R = prenyl
R′ = geranyl

not only hexahydro **1**, but also its monomethyl ether, prepared via selective methylation of the primary hydroxyl group in **1**, afforded an abundant MS ion at *m/e* 129. Thus **1** was (+)-(*E*)-7-hydroxymethyl-2,6,10,14-tetramethyl-2,9,13-pentadecatrien-6-ol, the chirality at C-6 and C-7 still being unknown. The trivial name peucelinendiol is suggested for compound **1**. Only a few open chain diterpenoids are known and peucelinendiol (**1**) is the only one in addition to digeranyl [9] which may have arisen by head to head combination of isoprenoid units. As the carbon skeleton of **1** is analogous to that of lavandulol in the monoterpenoid series, its biosynthesis may be assumed to proceed similarly [10].

EXPERIMENTAL

Extraction and purification. The plant material was collected in August at the southern coast of Sweden. The dried (50°) and ground roots (340 g) were extracted with Et_2O which on evapn left 60 g of extract. After dilution with 90% MeOH the extract was defatted with petrol. Gross fractionation of the defatted extract was carried out on Si gel with toluene–EtOAc (5 → 15%) as eluent. Fractions, which on TLC examinations showed two spots, R_f *ca* 0.4 and *ca* 0.5 (Si gel, CH_2Cl_2–MeOH (98:2), visualised with I_2 vapour) were submitted to further fractionation. Chromatography on acetylated cellulose (MN 2100 Ac, *ca* 20%) with MeCOEt–Me_2CO–H_2O (1:3:5) as eluent, alternating with chromatography on Si gel with CH_2Cl_2–CCl_4 (2:1), to which EtOAc (4 → 12%) was added, as eluent, was repeated until the optical rotation of each compound was constant.

(+)-(*Z*)-*Heptadeca*-1,9-*dien*-4,6-*diyn*-3,8-*diol.* Obtained as an almost colourless oil (1.2 g), $[\alpha]_{589}^{20}$ + 284°, $[\alpha]_{436}^{20}$ + 621° (Et_2O, *c* 1). UV $\lambda_{max}^{Et_2O}$nm (log ε): 233 (3.0), 245 (3.0), 259 (2.8). IR and ^{1}H NMR data of the diol together with MS data of the diacetate were consistent with those reported by Bentley *et al.* [4]. A ^{1}H NMR decoupling experiment (270 MHz) showed $J_{9,10}$ = 10 Hz in agreement with the previous assignment of the *Z*-configuration [2, 3].

Peucelinendiol. 0.15 g was obtained as an almost colourless oil, $[\alpha]_{589}^{24}$ + 5.5°, $[\alpha]_{436}^{24}$ + 13.1° (CCl_4, *c* 1.2). No UV absorption above 210 nm (MeOH). IR ν_{max}^{film} cm^{-1}: 3350 (OH), 1660 (C=C). ^{1}H NMR (60 MHz, CCl_4): δ 1.10 (3H, *s*, Me group at C-6), 1.56 (*ca* 9H, *s*, Me groups at C-2, C-10 and C-14), 1.63 (6H, *s*, protons at C-1 and C-15), 1.2–2.1 (*ca* 11H, protons at C-4, C-5, C-7, C-8, C-11 and C-12), 3.55 (2H, *br d*, *J* = 7 Hz, —C<u>H</u>$_2$OH), 4.15 (2H, *s*, —OH, exchangeable with D_2O), 4.95 (3H, *m*, protons at C-3, C-9 and C-13). ^{1}H NMR (60 MHz, DMSO-d_6, partial): δ 3.50 (2H, ill-resolved *t*, *J* = 7 Hz, C<u>H</u>$_2$OH), 4.42 (1H, *s*, tert —OH) and 4.60 (1H, *t*, *J* = 7 Hz, prim —OH). Addition of D_2O changed the pattern at δ 3.50 to an ill-resolved doublet and the signals at δ 4.42 and 4.60 disappeared. ^{13}C NMR (broad band and off-resonance decoupled, $CDCl_3$): δ 136.6 (*s*, C-10), 132.1 and 131.6 (*s*'s, C-2 and C-14), 124.5 and 124.3 (*d*'s, C-3 and C-13), 123.1 (*d*, C-9), 76.8 (*s*, C-6), 63.4 (*t*, —CH_2OH), 47.7 (*d*, C-7), 41.6 (*t*, C-5), 39.9 (*t*, C-11), 26.7 and 25.9 (*t*'s, C-8 and C-12), 25.8 (*q*, C-1 and C-15), 23.4 (*q*, Me at C-6), 22.2 (*t*, C-4), 17.8 (*q*, Me at C-2 and C-14) and 16.3 (*q*, Me at C-10). The deviations from pertinent δ values recorded for geraniol, linalool and lavandulol [8] and otherwise calculated values [11] were < 2 ppm. EI-MS (probe, 70 eV) *m/e* (rel. int.): 308 [M^+] (0.1), 290 [$M^+ - H_2O$] (15), 272 [$M^+ - 2H_2O$, m* 290 → 272] (2), 259 [m* 290 → 259] (13), 247 [m* 290 → 247] (4), 221 [M* 290 → 221] (8), 203 [m* 221 → 203] (9), 109 [cleavage between C-6 and C-7, $-H_2O$, m* 127 → 109] (54), 69 [$C_5H_9^+$] (100). High resolution measurements: 290.2609 and 109.1035.

Hexahydropeucelinendiol. To 1 mg **1** in 1 ml MeOH was added 5 mg Pd/C 5% and a stream of H_2 was passed through the soln for 90 min at 25°. TLC examination showed that only one product was formed. Catalyst and solvent were removed and the reaction product purified on Si gel with CH_2Cl_2–CCl_4–EtOAc (66:33:1 → 60:30:10) as eluent. EI-MS (probe, 70 eV) *m/e* (rel. int.): 299 [M^+ – Me] (4), 296 [$M^+ - H_2O$] (2), 278 [$M^+ - 2H_2O$] (2), 229 [cleavage between C-5 and C-6] (40), 129 [cleavage between C-6 and C-7] (93), 111 [129–H_2O] (32), 69 [$C_5H_9^+$] (100).

Peucelinendiol monomethyl ether. Upon methylation with Me_2SO_4 in Me_2CO [12] only one product was observed. It was purified on Si gel with CH_2Cl_2–CCl_4–EtOAc (66:33:1 → 60:30:10) as eluent. ^{1}H NMR (60 MHz, CCl_4, partial): δ 2.8 (1H, *br* signal, —OH, exchangeable with D_2O), 3.27 (3H, *s*, —OMe), 3.1–3.5 (2H, *m*, —C<u>H</u>$_2$OMe).

Hexahydropeucelinendiol monomethyl ether. Peucelinendiol monomethyl ether (9.3 mg) upon hydrogenation and purification as described above afforded 8.3 mg hydrogenation product. $[\alpha]_{589}^{24}$ – 21.5°, $[\alpha]_{436}^{24}$ – 46.4° (CCl_4; *c* 0.8). FI-MS (probe) *m/e* 328 [M^+]. EI-MS (probe, 70 eV) *m/e* (rel. int.): 328 [M^+] (0.4), 313 [M^+ – Me] (4), 310 [$M^+ - H_2O$] (2), 243 [cleavage between C-5 and C-6] (42), 168 (22), 129 [cleavage between C-6 and C-7] (84), 111 [129 – H_2O, m* 129 → 111] (47), 69 [$C_5H_9^+$] (100).

Peucelinendiol phenylboronate. 10 mg **1**, 10 mg phenylboric acid and 0.3 ml dry Me_2CO was kept at 55° for 4 hr. Purification of the reaction product on Si gel with petrol–EtOAc mixtures as eluents afforded 10 mg non-crystalline phenylboronate. $[\alpha]_{589}^{25}$ + 33.3°, $[\alpha]_{436}^{25}$ + 72.0° (CCl_4, *c* 0.7). ^{1}H NMR (60 MHz, CCl_4, partial): δ 7.1 and 7.6 (totally 5H, *m*'s —C_6<u>H</u>$_5$), OH signals absent. FI-MS (probe) *m/e* 394 [M^+]. EI-MS (probe, 70 eV) *m/e* (rel. int.): 394 [M^+] (23), 379 [M^+ – Me] (1), 351 [m* 394 → 351] (3), 325 [m* 394 → 325] (5), 69 [$C_5H_9^+$] (100).

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REFERENCES

1. Lemmich, E., Lemmich, J. and Nielsen, B. E. (1970) *Acta Chem. Scand.* **24**, 2893.
2. Bohlmann, F., Niedballa, U. and Rode, K.-M. (1966) *Chem. Ber.*, **99**, 3552.
3. Bohlmann, F. and Bornowski, H. (1961) *Chem. Ber.* **94**, 3189.

4. Bentley, R. K., Bhattacharjee, D., Jones, R. E. H. and Thaller, V. (1969) *J. Chem. Soc. C* 685.
5. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*. Academic Press, London.
6. Bates, R. B. and Gale, D. M. (1960) *J. Am. Chem. Soc.* **82**, 5749.
7. Sugihara, J. M. and Bowman, C. M. (1958) *J. Am. Chem. Soc.* **80**, 2443.
8. Bohlmann, F., Zeisberg, R. and Klein, E. (1975) *Org. Magn. Reson.* **7**, 426.
9. Souček, M., Herout, V. and Šorm, F. (1961) *Collect. Czech. Chem. Commun.* **26**, 2551.
10. Banthorpe, D. V., Doonan, S. and Gutowski, J. A. (1977) *Phytochemistry* **16**, 85.
11. Levy, G. C. and Nelson, G. L. (1972) *Carbon-13 Nuclear Magnetic Resonance Spectroscopy for Organic Chemists*. Wiley Interscience, New York.
12. Whistler, R. L. and Wolfrom, M. L. (1963) *Methods in Carbohydrate Chemistry*, Vol. II, p. 147. Academic Press, New York.