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THE ABSOLUTE CONFIGURATION OF THE ACETYLENIC COMPOUND FALCARINDIOL*

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Key Word Index—*Peucedanum oreoselinum*; Umbelliferae; falcarindiol; (*R*)-heptadecan-8-ol; (*S*)-heptadecan-8-ol; (3*R*,8*S*)-heptadecan-3,8-diol.

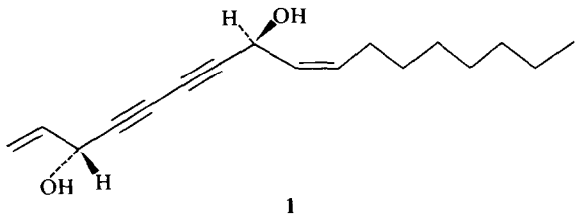
Abstract—The absolute configuration of the acetylenic compound falcarindiol is established as (3*R*,8*S*) and falcarindiol is thus (+)-(3*R*,8*S*)-(*Z*)-heptadeca-1,9-dien-4,6-diyn-3,8-diol. (*R*)-Heptadecan-8-ol and (*S*)-heptadecan-8-ol are synthesized and (3*R*,8*S*)-heptadecan-3,8-diol is characterized.

Falcarindiol is a toxic polyacetylenic compound commonly occurring in umbellifers [1]. It has been shown to possess the structure (*Z*)-heptadeca-1,9-dien-4,6-diyn-3,8-diol, yet without specification of chirality at C-3 and C-8.

Most often, falcarindiol has been isolated in minute quantities only. In this laboratory, however, root material of *Peucedanum oreoselinum* has been shown to be a rich source of (+)-falcarindiol (**1**) [2] and the opportunity of further characterization of this compound has been taken. This communication presents the determination of the absolute configuration of (+)-falcarindiol (**1**).

Compound **1** was subjected to catalytic hydrogenation, during which hydrogenolysis of its allylic oxygen functions took place to some extent. Accordingly four reaction products, heptadecane, (−)-heptadecan-3-ol, a heptadecan-8-ol enantiomer and (−)-heptadecan-3,8-diol were obtained. The absolute configuration at C-3 in falcarinol has previously been established as (*R*) [3]. (−)-Heptadecan-3-ol derived from falcarindiol is identical with the saturated alcohol derived from falcarinol and the configuration at C-3 in falcarindiol is thus (*R*).

Heptadecan-8-ol derived from falcarindiol shows no measurable optical rotation. The mp, however, differs from that of racemic heptadecan-8-ol [4] and as these compounds happen to have very sharp mps, though they are low, the absolute configuration of naturally derived heptadecan-8-ol was established by exploitation of this mp difference.



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*Part 23 in the series "Constituents of Umbelliferous Plants". For Part 22 see Lemmich, E. (1979) *Phytochemistry* **18**, 1195.

(*R*)- and (*S*)-heptadecan-8-ol were synthesized by anodic chain extension of (*R*)-methyl hydrogen 3-acetoxyglutarate. Racemic heptadecan-8-ol was synthesized in the same way from (*R*,*S*)-methyl hydrogen 3-acetoxyglutarate.

Heptadecan-8-ol derived from falcarindiol showed no mp depression after mixing or after co-crystallization with equal amounts of synthesized (*R*)-heptadecan-8-ol. In contrast, mixing with equal parts of synthesized (*S*)-heptadecan-8-ol resulted in a broad depressed mp and after co-crystallization, either from the melt or from solution, in a sharp mp corresponding to that of racemic heptadecan-8-ol. The configuration of heptadecan-8-ol derived from falcarindiol is thus (*R*) corresponding to the (8*S*) configuration of falcarindiol.

EXPERIMENTAL

Hydrogenation of falcarindiol. Falcarindiol (60 mg) in EtOAc (20 ml) was hydrogenated for 8 hr at 0° with Pd/$BaSO_4$ (40 mg) as a catalyst. The reaction products were separated on Si gel with CCl_4–EtOAc (0.25 → 30%) as eluant. The following four compounds were isolated.

Heptadecane (5 mg) was identified by comparison with authentic material (IR, MS).

Heptadecan-8-ol (15 mg), mp 57.2–57.7° (MeOH–H_2O). IR and MS in agreement with the structure. No measurable optical rotation (Et_2O, MeOH or pyridine, *c* 1.4). The mp differed from that of the racemic compound (lit. [4] 52.2–53°).

(−)-*Heptadecan-3-ol* (14 mg), mp 54.0–54.5° (MeOH–H_2O) (lit. [5] 54.0–54.5°). IR and MS in agreement with those of an authentic sample. $[\alpha]_D^{20}$ −5.7° ($CHCl_3$, *c* 1.5) [lit. [3] $[\alpha]_D^{18}$ −5.7° ($CHCl_3$, *c* 1.4)].

(−)-*Heptadecan-3,8-diol* (15 mg), mp 96.3–96.8° (MeOH–H_2O), $[\alpha]_D^{20}$ −5.6° ($CHCl_3$, *c* 1.4). IR and ^{1}H NMR spectrum as expected for the structure. EIMS 70 eV *m/z* (rel. int.): 254 [$M^+ - H_2O$] (0.9), 243 [$M^+ - C_2H_5$] (0.1), 236 [$M^+ - 2\ H_2O$] (0.2), 225 [$M^+ - H_2O - C_2H_5$, *m** 254 → 225] (9), 207 [225 − H_2O, *m** 225 → 207] (6), 157 [cleavage between C-7 and C-8, *m** 272 → 157] (26), 145 [cleavage between C-8 and C-9] (14), 127 [145 − H_2O, *m** 145 → 127] (56), 109 [127 − H_2O, *m** 127 → 109] (100).

Synthesis of (S)-*heptadecan-8-ol.* Chain extension [3, 6] of (*R*)-methyl hydrogen 3-acetoxyglutarate (4 mmol) with nonanoic acid (bp 148°/20 mm Hg, 16 mmol) afforded methyl 3-acetoxydodecanoate (1.4 mmol) isolated by Si gel chromatography. The NMR data were as expected. Deacetylation and demethylation by reported procedures [6] afforded 1.2 mmol (*R*)-3-hydroxydodecanoic acid [mp 62.5–63.0° (C_6H_6–petrol), $[\alpha]_D^{25}$ −16.6° ($CHCl_3$, *c* 1.8) (lit. [8] mp 62.5–63.0°, $[\alpha]_D^{25}$ −15.2° ± 1 ($CHCl_3$, *c* 1.6)]. The IR data correspond to those published [8] and the ^1H NMR spectrum is in agreement with the structure.

(*R*)-3-Hydroxydodecanoic acid was acetylated with Ac_2O (20°, 48 hr), H_2O was added and the mixture left for 24 hr. Evaporation *in vacuo* (20°) left almost pure (*R*)-3-acetoxydodecanoic acid (TLC examination, ^1H NMR spectrum). Without further purification the compound (1 mmol) was submitted to another chain extension by reaction with heptanoic acid (15 mmol, bp 127°/20 mm Hg). From the reaction product 8-acetoxyheptadecan (0.8 mmol) was isolated by chromatography on Si gel. Hydrolysis with 2 N KOH in MeOH (50°, 1 hr) and chromatography on Si gel afforded 0.6 mmol heptadecan-8-ol, mp 57.5–58.0° (MeOH–H_2O), no measurable optical rotation ($CHCl_3$, *c* 7.6). Mp and IR data correspond to those of heptadecan-8-ol derived from falcarindiol. Mmp between (*S*)-heptadecan-8-ol and naturally derived heptadecan-8-ol (1:1) was 53–5° and after solidifying and repeated determination the mp was 51.0–51.5° corresponding to that of the racemic compound.

(R)-*Heptadecan-8-ol.* From (*R*)-methyl hydrogen 3-acetoxyglutarate (5 mmol) and heptanoic acid (20 mmol, bp 127°/20 mm Hg), (*R*)-3-hydroxydecanoic acid was synthesized in the same way as (*R*)-3-hydroxydodecanoic acid. 1.8 mmol (*R*)-3-hydroxydecanoic acid was isolated [mp 48.3–48.8° (petrol) $[\alpha]_D^{22}$ −19.2° ($CHCl_3$, *c* 2.5) (lit. [9] (+)-3-hydroxydecanoic acid mp 48.4°, $[\alpha]_D^{22}$ +20° ($CHCl_3$, *c* 2.5)].

(R)-3-*Hydroxydecanoic acid* was acetylated as the higher homologue above. Reaction between (*R*)-3-acetoxydecanoic acid (1 mmol) and nonanoic acid (15 mmol, bp 148°/20 mm Hg), hydrolysis and purification afforded 0.8 mmol heptadecan-8-ol [mp 57.5–58.0° (MeOH–H_2O)]. The IR spectrum was identical with that of heptadecan-8-ol derived from falcarindiol and no mp depression was observed for a mixture of these two compounds.

(R,S)-*Heptadecan-8-ol* was synthesized by the same procedures as used for (*S*)-heptadecan-8-ol. Starting material was (*R,S*)-methyl hydrogen 3-acetoxyglutarate [bp 141–4°/0.3–0.4 mm Hg, mp 51–2° (Et_2O–petrol) (lit. [6] bp 145–55°/0.5 mm Hg, mp not reported]. (*R,S*)-Heptadecan-8-ol, mp 51.2–51.5° (MeOH–H_2O) (lit. [4] 52.2–53°).

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