

Constituents of Umbelliferous Plants

XII.* The Absolute Configuration of Falcarinol, an Acetylenic Compound from the Roots of *Seseli gummiferum* Pall.

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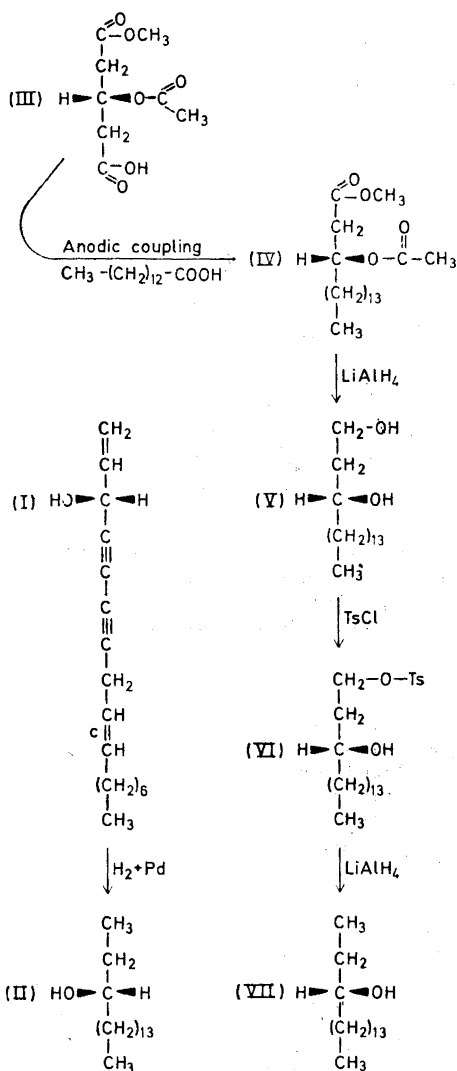
The roots of *Seseli gummiferum* Pall. subsp. *gummiferum*, in addition to a rather complex mixture of coumarins, afforded an unstable acetylenic compound (I). UV-, IR-, and PMR-spectroscopy of (I), supplemented by chemical conversions and investigation of the reaction products by mass spectrometry, showed (I) to be identical with falcarinol (panaxynol), first isolated by Takahashi *et al.* from *Panax ginseng* C. A. Meyer¹ and by Bohlmann *et al.* from *Falcaria vulgaris* Bernh.² Takahashi and Yoshikura³ and Bohlmann *et al.*² independently established the constitution of (I), save for the chirality.

The *cis*-configuration of (I) was earlier shown by synthesis.^{4,2} Now the 3(*R*)-configuration is assigned to falcarinol (I), based on the fact that hydrogenation of (I) yielded (–)-3-hydroxyheptadecane (II). The 3(*R*)-configuration of (II) was established by comparison with the enantiomeric 3(*S*)-3-hydroxyheptadecane (VII), synthesized from (+)-methyl hydrogen 3-acetoxyglutarate (III), previously shown to possess the (*R*)-configuration.⁵

The investigation of the coumarins from *Seseli gummiferum* Pall. subsp. *gummiferum* is in progress.

Experimental. Melting points, determined in capillary tubes, are corrected. The silica gel (Merck, 0.05–0.20 mm) used in column chromatographic separations is activated at 120° overnight prior to use, and then impregnated with 10 % of water. Microanalyses were performed by Dr. Bernhardt, Mühlheim.

* Part XI. *Tetrahedron Letters* 1969 3365.



Isolation and identification of falcarinol (I). The dried and ground roots (900 g) were extracted with ether. Upon evaporation of the solvent 30 g of a viscous oil remained. This residue was dissolved in 90 % methanol, defatted with petroleum ether and evaporated. The residue (8.6 g) was chromatographed on 300 g of silica gel. The eluent was methylene chloride-tetrachloromethane (2:1) to which increasing amounts of ethyl acetate were

added. With a concentration of 2 % of ethyl acetate, 800 mg of an unstable, pale red oil were eluted. The oil was rechromatographed three times on silica gel using methylene chloride-tetrachloromethane (2:1) and methylene chloride as the eluents. Falcarinol (360 mg) was obtained as a colourless oil, $[\alpha]_{578}^{20.0} -10.0^\circ$, $[\alpha]_{436}^{20.0} -24.2^\circ$ (c 1.0, ether); $\lambda_{\max}^{257.5, 244, 232 \text{ nm}}$ ($\epsilon=760, 730, 450$) in heptane. (Ref. 2, $[\alpha]_{578}^{20} -22.5^\circ$, $[\alpha]_{436}^{20} -41.0^\circ$ (c 1.0, ether, Leitz LEP 1); Ref. 6, $\lambda_{\max}^{254, 240, 229 \text{ nm}}$). The IR- and PMR-spectra agreed with those published by Takahashi *et al.*³ for falcarinol.

The ether solution of (I) was, immediately after the measurements of the optical rotation values, analysed by thin-layer chromatography. Only trace amounts of degradation products were detectable. Silica gel GF₂₅₄ (Merck) was used as the adsorbent. The eluent was chloroform-ethyl acetate (19:1) and the spots were visualized under short wave ultraviolet light.

Oxidation of falcarinol (115 mg) with manganese dioxide⁴ yielded 95 mg of the corresponding ketone. The IR- and UV-spectra of the ketone were in agreement with those published by Bohlmann *et al.*⁶ for falcarinone. Hydrogenation of falcarinone⁶ (50 mg) afforded 25 mg of heptadecanone-3, m.p. 46.0–47.0° (methanol-water), (Ref. 6, m.p. 46.0–47.0°; Ref. 7, m.p. 47.6–48.9°). The constitution of heptadecanone-3 was confirmed by mass spectrometry.

(-)-3-Hydroxyheptadecane (II). Falcarinol (I) (98 mg) was dissolved in 30 ml of methanol and hydrogenated (29°, 1 atm) using 64 mg of palladium on barium sulfate (5 %) as a catalyst. Within 20 min an amount of hydrogen corresponding to 6.5 moles was consumed. The extra uptake of hydrogen is due to a partial hydrogenolysis of falcarinol (I). The reaction mixture was filtered, evaporated and chromatographed on silica gel using chloroform-ethyl acetate mixtures as the eluents. In accordance with the consumption of hydrogen, heptadecane (46 mg, identified by GLC and mass spectrometry) and (-)-3-hydroxyheptadecane (II) (28 mg, m.p. 54.0–54.5° (methanol-water), $[\alpha]_{\text{D}}^{18.2} -5.7^\circ$ (c 1.4, CHCl₃)) were eluted. (Ref. 1, m.p. 54.0–54.5°). IR- and mass spectra confirmed the constitution of (II).

(+)-Methyl hydrogen 3-acetoxyglutarate (III). Using dimethyl 3-hydroxyglutarate (112 g) as the starting material, (\pm)-methyl hydrogen 3-acetoxyglutarate (31.7 g, b.p. 142–153°/0.25–0.4 mm Hg; $n_{\text{D}}^{22} 1.4471$) was synthesized.⁵ (Ref. 5, b.p. 145–155°/0.5 mm Hg; $n_{\text{D}}^{22} 1.4470$). Resolution of the racemic

half-ester (25.8 g) through formation of the cinchonidine salts,⁵ followed by five recrystallizations from chloroform-ethyl acetate, afforded 13.5 g of the salt of (+)-methyl hydrogen 3-acetoxyglutarate, m.p. 138.0–139.5°; $[\alpha]_{\text{D}}^{22.1} -62.9^\circ$ (c 5.1, CHCl₃), (Ref. 5, m.p. 89° (Kofler bench); $[\alpha]_{\text{D}}^{22} -62.5^\circ \pm 0.4^\circ$ (c 5, CHCl₃)). The modification of the salt with m.p. 89° (Kofler bench) was obtained by evaporation of an ethyl acetate solution of the cinchonidine salt at room temperature. The above mentioned cinchonidine salt (13.2 g) yielded 3.68 g of (+)-methyl hydrogen 3-acetoxyglutarate (III), b.p. 138–140°/0.2 mm Hg; $n_{\text{D}}^{20} 1.4464$; $[\alpha]_{\text{D}}^{24.9} +6.17^\circ$ (c 20, CHCl₃), (Ref. 5, b.p. 140–150°/0.3 mm Hg; $n_{\text{D}}^{20} 1.4474$; $[\alpha]_{\text{D}}^{25} +6.1^\circ \pm 0.1^\circ$ (c 20, CHCl₃)). IR- and PMR-spectra supported the constitutional assignments.

(+)-Methyl 3-acetoxyheptadecanoate (IV). (+)-Methyl hydrogen 3-acetoxyglutarate (III) (0.0168 mol) and myristic acid (0.0168 mol, m.p. 54.5–55.0°, recrystallized from glacial acetic acid and petroleum ether) were dissolved in methanol (250 ml) containing sodium (90 mg). The solution was electrolysed in a cell containing two cylindrical platinum electrodes, set concentric and with a reciprocal distance of 5 mm. A current of about 1.8 A at 120–145 V was passed until the mixture became neutral (1 h). 300 ml of water were added and the mixture was extracted with five 125 ml portions of petroleum ether. The combined, filtered and dried petroleum ether phases were evaporated and the residue chromatographed on 140 g of silica gel. As the eluent was used benzene, to which ethyl acetate was gradually added (0–3 %). (+)-Methyl 3-acetoxyheptadecanoate (IV) (1.25 g) was obtained, m.p. 26–27°; $[\alpha]_{\text{D}}^{20.1} +2.17^\circ$ (c 9.1, CHCl₃). (Found: C 70.25; H 11.05. Calc. for C₂₀H₃₈O₄: C 70.13; H 11.18). The constitution of (IV) was confirmed by IR- and PMR-spectroscopy.

(+)-1,3-Dihydroxyheptadecane (V). Lithium aluminium hydride (0.020 mol) was stirred with 20 ml of anhydrous ether for 45 min. During 80 min and with stirring a solution of (+)-methyl 3-acetoxyheptadecanoate (0.0032 mol) in 20 ml of anhydrous ether was added to the suspension. The reaction mixture was refluxed for 35 min, cooled in an ice bath, and with vigorous stirring 60 ml of ice-cooled sulfuric acid (1 N) were added drop by drop. After further stirring for 30 min at room temperature the aqueous phase was washed with two times 100 ml of ether. The combined, filtered and dried ether phases were evaporated. Crystallization from chloroform-petroleum ether afforded 672 mg of (+)-1,3-dihydroxyheptadecane (V), m.p. 62.0–62.5°; $[\alpha]_{\text{D}}^{18.9}$

+0.82° (c 6.8, CHCl₃). (Found: C 74.93; H 13.15. Calc. for C₁₇H₃₆O₂: C 74.94; H 13.32). The constitution was confirmed by IR- and PMR-spectroscopy.

(-)-1-*p*-Toluenesulfonyloxy-3-hydroxyheptadecane (VI). (+)-1,3-Dihydroxyheptadecane (V) (0.0013 mol) was tosylated in dry pyridine at ca. -17° using 0.0015 mol of *p*-toluenesulfonyl chloride. The reaction mixture was kept at -17° for 3 1/2 h and then placed in a refrigerator (5°) for 21 h. The reaction was followed by TLC (silica gel GF₂₅₄ (Merck)) with benzene-ethyl acetate (17+3) as the eluent. During 1 h and with stirring the reaction mixture was added to 170 ml of ice-cooled water. Upon addition of 100 ml of hydrochloric acid (4 N) the mixture was extracted with chloroform. The filtered and dried extract was evaporated and the residue chromatographed on 75 g of silica gel using benzene-ethyl acetate mixtures as the eluents. Obtained were 289 mg of (-)-1-*p*-toluenesulfonyloxy-3-hydroxyheptadecane (VI), m.p. 58.0–59.0° (petroleum ether); [α]_D^{20.1} -4.9° (c 2.8, CHCl₃). (Found: C 67.60; H 10.04. Calc. for C₂₄H₄₂O₄S: C 67.54; H 9.92). The IR-spectrum exhibited the absorption bands expected for (VI).

(+)-3-Hydroxyheptadecane (VII). (-)-1-*p*-Toluenesulfonyloxy-3-hydroxyheptadecane (VI) (250 mg) was hydrogenolysed with lithium aluminium hydride (255 mg) according to Zorbach *et al.*⁸ Excess lithium aluminium hydride was destroyed as described above for (+)-1,3-dihydroxyheptadecane. The ether layer, however, was washed with a saturated solution of sodium hydrogen carbonate, dried and evaporated. Crystallization from methanol-water yielded 123 mg of (+)-3-hydroxyheptadecane (VII), m.p. 54.0–55.0°; [α]_D^{18.1} +5.8° (c 1.4, CHCl₃). (Found: C 79.83; H 14.19. Calc. for C₁₇H₃₆O: C 79.61; H 14.15). The IR-spectrum was identical with that of (-)-3-hydroxyheptadecane (II).

Acknowledgement. The authors are grateful to Dr. J. Møller, Physical Laboratory II, University of Copenhagen, for the measurements of the mass spectra as well as for valuable discussions, and to The Botanic Garden, University of Copenhagen, for supplying the plant material.

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Received August 26, 1969.

ESR Evidence for O₂⁻ as a Long-Lived Transient in Irradiated Oxygenated Alkaline Aqueous Solutions

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It is well known that long-lived UV-absorbing transients are formed during irradiation of oxygenated aqueous solutions.¹⁻⁴ Czapski and Dorfman concluded³ that O₂⁻ decays rapidly at all pH values but that unidentified long-lived species are formed at high pH. Among the hypothetical intermediates suggested by these authors³ were the diamagnetic species O₂²⁻, O₃²⁻, and HO₃³⁻ as well as the paramagnetic HO₃²⁻. In establishing the nature of the light absorbing transient formed in alkaline solutions the use of ESR would then seem rational.

Despite its advantages for identification of radicals, ESR has not generally been applied in such work, largely because of its low time resolution. This drawback may be overcome by trapping the radicals at low temperatures. The "rapid-freezing"

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