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Constituents of Umbelliferous Plants

IV *. The Coumarins of *Peucedanum palustre* L. The Structure of a New Coumarin

BENT EICHSTEDT NIELSEN and JOHN LEMMICH

The Royal Danish School of Pharmacy, Chemical Laboratory B, Copenhagen, Denmark

A coumarin, $C_{19}H_{20}O_5$, obtained from the root of *Peucedanum palustre* is shown to be (+)-8-(1-angeloyloxy-1-methylethyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one (I). (I) is shown to possess the same configuration at C-8 as athamantin (II) and archangelicin (III).

Furthermore, the root afforded isoimperatorin (IV), (+)-oxypeucedanin (V), ostruthol (VI), and (+)-oxypeucedanin hydrate (VII).

Peucedanum palustre is widely distributed in the Eastern and Middle Europe, but has so far not been investigated chemically. This paper presents the results from an investigation of the coumarin content.

Besides isoimperatorin IV, (+)-oxypeucedanin (V), ostruhol (VI), and (+)-oxypeucedanin hydrate (VII) a blue-fluorescent compound (I), $C_{19}H_{20}O_5$, m.p. 118.5–119°, was isolated.

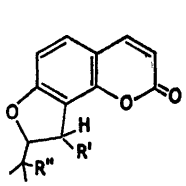
Its coumarin character was strongly indicated by the fluorescence, the absorption bands in the infrared at 1719–1736, 1624, 1584, 1495, and 1459 cm^{-1}, and by its UV-absorption: λ_{max} 218 mμ (4.31) (shoulder), 251 mμ (3.41) 261 mμ (3.46), and 328 mμ (4.20). λ_{min} 245 mμ (3.35), 255 mμ (3.36), and 268 mμ (3.12). The UV-spectrum is similar to that of archangelicin (III) formerly investigated by the present authors.[1]

Treatment of (I) with 85 % phosphoric acid, afforded angelic acid, dihydrooroselone (VIII), and an optical active coumarin (IX) with the empirical formula $C_{14}H_{14}O_4$. The UV-spectrum of (IX) was very similar to that of (I). Saponification of (I) with 1 N sodium hydroxide also afforded (IX). On catalytic hydrogenation of (I) 2 moles of hydrogen were consumed. Subsequent saponification afforded (+)-tetrahydrooroselol (X), a compound earlier prepared on hydrogenation of athamantin (II) by Halpern *et al.*[2] This evidence clearly identifies compound (IX) as (+)-8,9-dihydrooroselol.

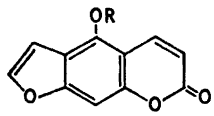
* Part III, *Acta Chem. Scand.* 18 (1964) 932.

Accordingly, the isolated coumarin (I) is 8-(1-angeloyloxy-1-methylethyl) -8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one. These structural assignments are supported by the PMR-spectra.*

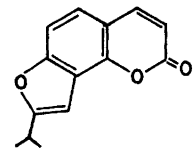
With respect to the stereochemistry it can be stated that (I) has the same configuration at C-8 as athamantin and archangelicin. This conclusion is based partly on the aforementioned degradation of (I) to (+)-tetrahydrooroselol (X) also obtainable from athamantin (II), and partly on a similar degradation of archangelicin (III) to (+)-tetrahydrooroselol (X).



I R' = -H
R" = -O-C(=O)-C(CH3)=CH-CH3



IV R = -CH2-CH=C(CH3)-CH3

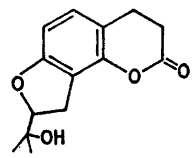


VIII

II R' = R" = O-C(=O)-CH2-CH(CH3)-CH3

V R = -CH2-CH(O-C(=O)-CH(CH3)-CH3)-CH3

III R' = R" = -O-C(=O)-C(CH3)=CH-CH3



IX R' = -H
R" = -OH

VI R = -CH2-CH(O-C(=O)-C(CH3)=CH-CH3)-C(CH3)(OH)-CH3

X

VII R = -CH2-CH(OH)-C(OH)(CH3)-CH3

Further studies on the stereochemistry are in progress.

EXPERIMENTAL

Isolation of the coumarin mixture. The plant material was collected near Copenhagen in October 1963. The dried and ground roots (1 kg) were extracted exhaustively in a Soxhlet extractor with diethyl ether. Upon evaporation of the solvent 80 g of a viscous oil remained. This residue was left in a refrigerator for several days, after which 28.2 g of crystals were filtered off.

Fractionation of the coumarin mixture. The crude mixture was chromatographed on 410 g silica gel (Merck), activated at 120°, and impregnated with 10 % of water. As eluent was used benzene, benzene to which chloroform was added gradually, and finally

* During the preparation of this manuscript the recent work on the structure of columbianadin, a coumarin from *Lomatium columbianum* Mathias & Const., came to the authors' attention. (Wilette, R. E. and Soine, T. O. *J. Pharm. Sci.* **53** (1964) 275).

The results from our work on the structure of the coumarin (I) are in agreement with those published for columbianadin with the exception of the stated $[\alpha]_D$ value for (+)-tetrahydrooroselol. For this compound Wilette and Soine reported $[\alpha]_D^{24} + 300$ (methanol).

chloroform to which methanol was added gradually until a concentration of 30 % of methanol was reached. The following substances were obtained:

(*a*) 16 mg of a compound with a yellow fluorescence, recrystallised from tetrachloromethane-petroleum ether m.p. 108°. The compound gave analytical data concordant with the composition $C_{16}H_{14}O_4$. The IR-data were in close agreement with those published by Perelson [3] for isoimperatorin (IV) (Lit.[4] m.p. 109°).

(*b*) 7.2 g of a compound (I) with a blue fluorescence, recrystallised from ether m.p. 118.5–119.0°, $[\alpha]_D^{26}$ + 227° (*c* 2.8, chloroform). (Found: C 69.43; H 6.05; Calc. for $C_{19}H_{20}O_5$: C 69.50; H 6.14).

(*c*) 2.1 g of a compound with a yellow fluorescence, recrystallised from ether-chloroform m.p. 104.0°, $[\alpha]_D^{27}$ + 17° (*c* 3.0, chloroform). These data, the elementary analysis, and the UV-data were in close agreement with those recently published by Ghoshal *et al.*[5] for the dextro-isomer of oxypeucedanin (V). The IR-spectrum was identical with that of an authentic sample of oxypeucedanin.* Furthermore, the PMR-spectrum verified the structure (V).

Hydrolysis of (V) with boiling oxalic acid solution as described by Späth and Klager [6] afforded (+)-oxypeucedanin hydrate which was recrystallised from chloroform. M.p. 130.5–131°, $[\alpha]_D$ + 13° (*c* 0.9, acetone) (Lit. values [7]; M.p. 131° and $[\alpha]_D^{21}$ +18.9 (acetone)).

(*d*) 1.03 g of a compound with a yellow fluorescence, recrystallised from ether-chloroform m.p. 137.5°, $[\alpha]_D^{23}$ −18° (*c* 1.4, pyridine). The compound gave analytical data concordant with the composition $C_{21}H_{22}O_7$. These data are in close agreement with those published [7] for ostruthol (VI).

Furthermore, by saponification of the compound with methanolic potassium hydroxide and thin layer chromatography of the acidified reaction mixture the compound gave a spot corresponding to oxypeucedanin hydrate (VII).

(*e*) 2.8 g of a compound with a yellow fluorescence, recrystallised from methanol-ether and from chloroform m.p. 131.5–132.0°, $[\alpha]_D^{24}$ +18° (*c* 1.5, acetone). The empirical formula was $C_{16}H_{16}O_6$. The IR-spectrum was identical with that of (+)-oxypeucedanin hydrate (VII) prepared by hydrolysis of the dextro isomer of oxypeucedanin, obtained in fraction *c*.

Treatment of (I) with 85 % phosphoric acid. A solution of 414 mg of (I) in 15 ml 85 % phosphoric acid was heated for one hour on a steam bath. A volatile acid was separated by steam distillation. The acid fraction was neutralized and the *p*-phenylphenacyl ester was prepared and chromatographed on a silicic acid column as earlier described.[1] *p*-Phenylphenacyl angelate, m.p. 87.5–88.5°, was obtained. The identity was established by comparison of the IR-spectrum with that of an authentic sample of *p*-phenylphenacyl angelate (m.p. 90°).

After addition of water, the residue from the steam distillation was extracted with chloroform. The washed and dried chloroform extract was evaporated and chromatographed on 60 g of silica gel (Merck), activated at 120°, and impregnated with 10 % of water. Benzene and benzene to which chloroform was added gradually was used as the eluent. The following substances were obtained:

(*a*) 179 mg of a compound with a yellow fluorescence, m.p. 141.5–142.0°, recrystallised from ether. The elemental composition of the compound was $C_{14}H_{12}O_3$. The compound was identified as dihydrooroselone (VIII) as the IR-spectrum was identical to that of dihydrooroselone synthesized from osthol in the manner described by Späth *et al.*[8] These authors reported the m.p. 142–143°.

(*b*) 13 mg of a compound with a blue fluorescence, recrystallised from ether-chloroform m.p. 162.8–163.3°, $[\alpha]_D^{24}$ +250° (*c* 0.5, methanol). Found: C 68.37; H 5.78. Calc. for $C_{14}H_{14}O_4$: C 68.28; H 5.73).

Bands corresponding to a hydroxyl group appeared in the IR-spectrum. The UV-spectrum was very similar to that of compound (I): λ_{max} 210.5 mμ (4.28), 218 mμ (4.14) (shoulder), 252 mμ (3.33), 262 mμ (3.39), and 328 mμ (4.16). λ_{min} 244 mμ (3.24), 256 mμ (3.30), and 269 mμ (3.13).

The PMR-spectrum of (IX) is shown in Fig. 1. The pair of doublets labelled a and b (δ = 7.6 and 6.2; J = 9 cps) have been assigned to the C-4 and C-3 protons, respectively,

* Kindly placed at our disposal by Professor L. Hörhammer, München.

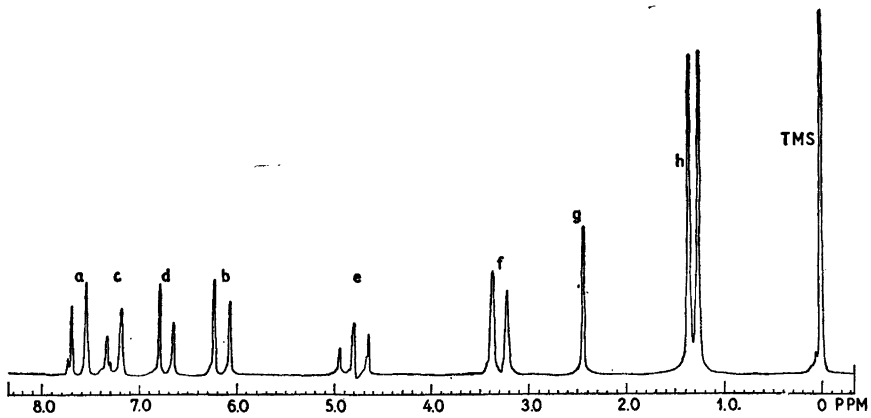


Fig. 1. PMR-spectrum of the compound (IX) (deutero chloroform). Internal standard, tetramethylsilane (TMS).

in the lactone ring. The positions of the other pair of doublets c and d (δ = 7.3 and 6.7; J = 9 cps) are typical of the signals from *ortho* protons in a 1,2,3,4-substituted benzene ring. The lines at e and f form a pattern characteristic of the three protons in the dihydrofuran ring. The signal at g (δ = 2.45) is assigned to the hydroxyl proton. The six proton signal at h is assigned to two methyl groups.

Saponification of (I) with N sodium hydroxide. A solution of 167 mg of (I) in 5 ml of dioxane was added to 50 ml of N sodium hydroxide, and refluxed for one hour. The solution was acidified with diluted sulfuric acid and extracted with diethyl ether. The ether layer was washed with a saturated solution of sodium chloride, dried, and evaporated under reduced pressure. The crystals obtained were recrystallised from ether-chloroform to yield 63 mg of the compound (IX).

Hydrogenation of (I). The compound (I) (331 mg) was dissolved in 30 ml of glacial acetic acid and hydrogenated at 30° using 359 mg of palladium on carbon (10 %) as a catalyst. Within 21 min an amount of hydrogen corresponding to 2 moles was consumed and the reaction was interrupted. The filtered solution was evaporated under reduced pressure, and refluxed with 8.5 ml of 5 % potassium hydroxide for 3¼ h. The acidified solution was extracted with diethyl ether. The dried ether solution was evaporated and the viscous residue was distilled at 0.1 mm Hg and 165° in order to reestablish the lactone ring. The distillate was chromatographed on silica gel (Merck), activated at 120°, and impregnated with 10 % of water. Benzene and benzene-ethyl acetate was used as the eluent. With benzene-ethyl acetate (8:2) 97 mg of a crystalline compound was obtained. Recrystallised from ether-petroleum ether m.p. 113.7—114.5°, $[\alpha]_D^{26}$ +83° (*c* 0.5, methanol). These data, the analytical composition, and the UV-data were in close agreement with those published for (+)-tetrahydrooroselol (X) (Lit. values[2]: m.p. 112—13° and $[\alpha]_D^{19}$ +86.7° (methanol)).

Hydrogenation of archangelicin. Archangelicin (290 mg) was dissolved in glacial acetic acid (30 ml) and hydrogenated at 30° using 287 mg of palladium on carbon (10 %) as a catalyst. Within 4¾ h an amount of hydrogen corresponding to 3.97 moles was consumed and the reaction was interrupted. Further treatment as above afforded 61 mg of (+)-tetrahydrooroselol, m.p. 113—114°, $[\alpha]_D^{28}$ +82° (methanol).

The melting points are corrected and determined in capillary tubes in an electrically heated silicone bath.

The UV-spectra were recorded in ethanol, 96 %, on a Beckman spectrophotometer, Model DK-2.

The IR-spectra were recorded in potassium bromide discs on a Perkin Elmer spectrophotometer, Model 21.

The PMR-spectra were obtained on a Varian V-4 300 NMR spectrophotometer operating at a fixed frequency of 60 Mc/s.

Microanalysis were performed by Dr. A. Bernhardt, Mülheim.

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