

Constituents of Umbelliferous Plants

VII.* Coumarins from the Fruits of *Peucedanum palustre* L. The Structure of Two New Coumarins

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From the fruits of *Peucedanum palustre* two new coumarins were isolated. Coumarin (I), $C_{19}H_{20}O_6$, named *columbianadinoxide* is shown to be 8(*S*)-(+)-8-[1-(2(*R*),3(*R*)-2,3-epoxy-2-methylbutyryloxy)-1-methylethyl]-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one.

Coumarin (II), $C_{24}H_{28}O_8$, named *isopeulustrin* is shown to be 8(*S*)-(+)-8-[1-(2(*R*),3(*S*)-3-(3,3-dimethylacryloyloxy)-2-hydroxy-2-methylbutyryloxy)-1-methylethyl]-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one.

Furthermore, the fruits afforded umbelliprenin (III), isoimperatorin (IV), columbianadin (V), (+)-oxypeucedanin (VI), isooxypeucedanin (VII), and peulustrin (VIII).

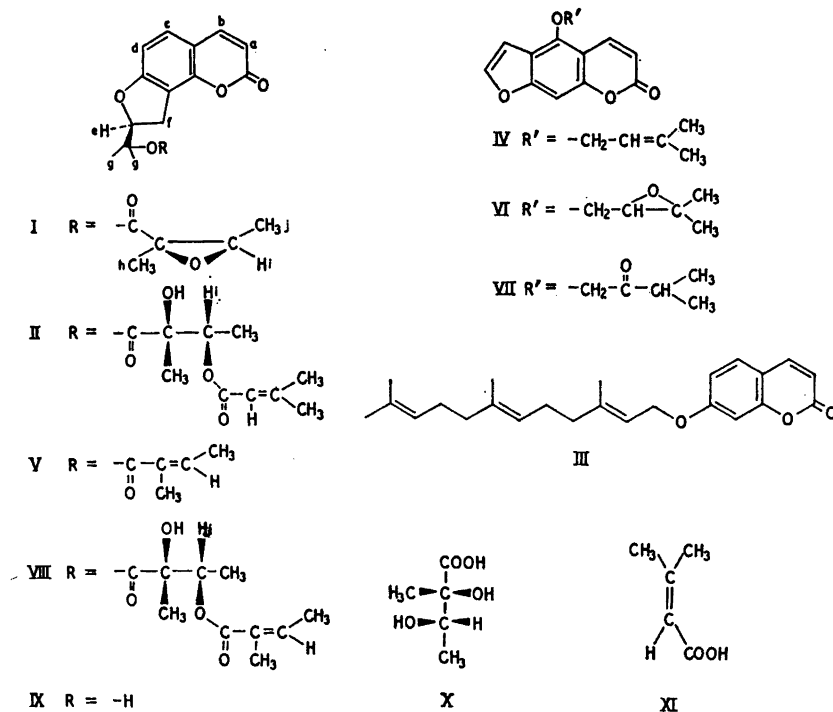
In previous papers^{1,2} the investigations of the coumarins from the root of *Peucedanum palustre* have been reported. This paper presents the results from an investigation of the coumarin content in the fruits.

Besides umbelliprenin (III), isoimperatorin (IV), columbianadin (V), (+)-oxypeucedanin (VI), isooxypeucedanin (VII), and peulustrin¹ (VIII), two blue-fluorescent compounds (I), $C_{19}H_{20}O_6$, and (II), $C_{24}H_{28}O_8$, were obtained.

The compound (I) is named *columbianadinoxide*. The coumarin character of (I) was indicated by the UV-spectrum, which was very similar to that of 8(*S*)-(+)-dihydro-oroselol^{2,3} (IX), and by the absorption bands in the infrared at 1735, 1627, 1582, 1495, and 1462 cm^{-1} .

A treatment of (I) with methanolic sodium hydroxide afforded 8(*S*)-(+)-dihydro-oroselol³ (IX) and 2(*R*),3(*S*)-(+)-2,3-dihydroxy-2-methylbutyric acid (X). These results, the elemental composition and the fact that no bands corresponding to hydroxyl groups appear in the IR-spectrum, indicate the structure (I).

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Further evidence for the structure (I) is derived from the PMR-spectrum (Fig. 1). The doublets at δ 6.1 and 7.6 ($J = 9.5$ cps) are assigned to the protons labelled *a* and *b*. The other pair of doublets at δ 7.25 and 6.75 ($J = 8$ cps) are the signals from the *ortho* protons, *c* and *d*, in the benzene ring.

The triplet at δ 5.1 ($J = 8.5$ cps) corresponding to one proton and the doublet at δ 3.3 ($J = 8.5$ cps) corresponding to two protons are assigned to the CH groups labelled *e* and the CH_2 group labelled *f*, respectively.

The quartet at δ 2.85 ($J = 5$ cps) and the doublet at δ 1.3 ($J = 5$ cps) are the signals from the groups labelled *i* and *j*.

The *gem*-dimethyl protons (*g*) give rise to two singlets at δ 1.59 and δ 1.55.

The singlet at δ 1.38 corresponding to three protons is assigned to the methyl group labelled *h*.

In the aforementioned treatment of (I) with methanolic sodium hydroxide, the nucleophilic attack of hydroxide ions on the epoxide ring can take place only at C-3, the attack at C-2 being sterically hindered.⁴ Since this reaction at C-3 is known to be accompanied by inversion, the formation of 2(*R*),3(*S*)-2,3-dihydroxy-2-methylbutyric acid suggests the glycidic acid moiety of (I) to be 2(*R*),3(*R*)-2,3-epoxy-2-methylbutyric acid. The methyl ester of the same glycidic acid was recently synthesized by Christensen and Kjær.*⁵

* A specimen of this glycidic ester was kindly provided by these authors. On treatment with methanolic sodium hydroxide it also afforded 2(*R*),3(*S*)-(+)-2,3-dihydroxy-2-methylbutyric acid. The procedure used was the same as described for (I).

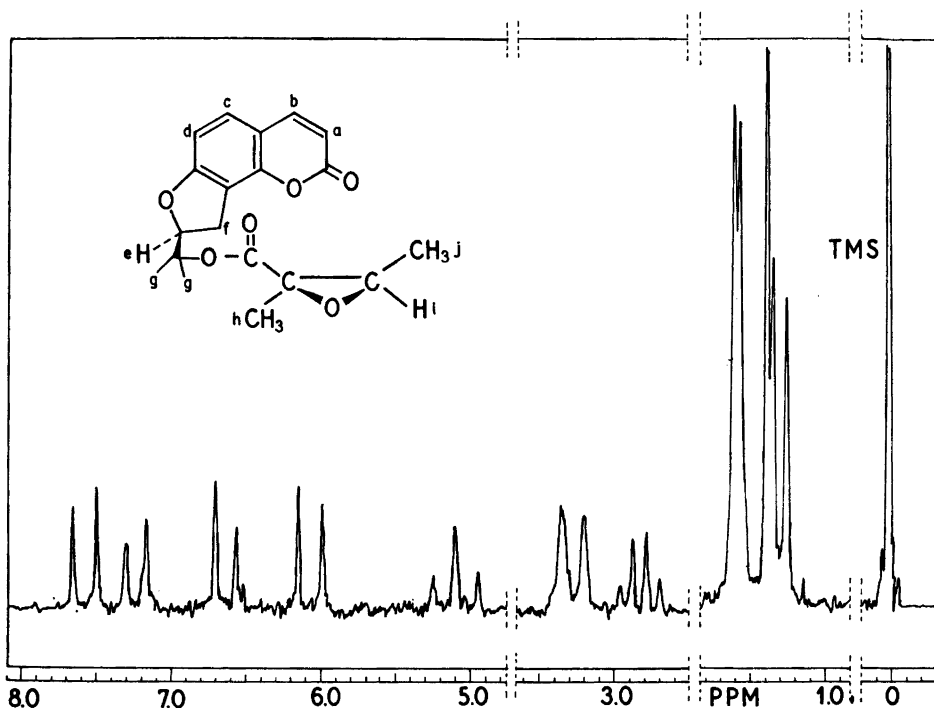


Fig. 1. PMR-spectrum of columbianadinoxide (I) (deuteriochloroform). Internal standard, tetramethylsilane (TMS).

The compound (II) is named *isopeulustrin*. The UV- and IR-spectra are very similar to those of *peulustrin*¹ (VIII).

A treatment of (II) with methanolic sodium hydroxide afforded 8(*S*)-(+)-dihydro-oroselol³ (IX), senecioic acid (XI), and 2(*R*),3(*S*)-(+)-2,3-dihydroxy-2-methylbutyric acid (X).

From the PMR-spectrum, which was similar to that of *peulustrin* (VIII),¹ *isopeulustrin* (II) appeared to be 8(*S*)-(+)-8-[1-(2(*R*),3(*S*)-3-(3,3-dimethylacryloyloxy)-2-hydroxy-2-methylbutyryloxy)-1-methylethyl]-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one (II). Especially the fact that the chemical shifts of the protons labelled *i* in the structures (II) and (VIII) are equal (δ 4.9) indicates that the dihydroxy acid is esterified at the same alcohol group in both coumarins. *Peulustrin* was previously shown to be esterified at the secondary alcohol group.¹

EXPERIMENTAL

Isolation of the coumarins. The plant material was collected near Copenhagen in October 1963. The dried and ground fruits (60 g) were extracted with diethyl ether. Upon evaporation of the solvent 6.2 g of a viscous oil remained. This residue was dissolved

in 90 % methanol, defatted with petroleum ether (b.p. below 50°) and evaporated. The residue (2.9 g) was chromatographed on silica gel (Merck, 100 g) activated at 120° and impregnated with 10 % of water. The eluent was benzene to which increasing amounts of chloroform were added. The following substances were obtained:

(a) 6 mg of a blue-fluorescent compound, recrystallised from ether-petroleum ether, m.p. 61.0–62.5°. The IR-spectrum was identical with that of an authentic sample of umbelliprenin (III). (Ref. 6, m.p. 61–63°).

(b) 9 mg isoimperatorin (IV), recrystallised from benzene m.p. 107–108°. (Ref. 7, m.p. 109°).

(c) 142 mg columbianadin (V), recrystallised from ether, m.p. 118.5–119.0°, $[\alpha]_D^{26} + 227^\circ$ (c 0.6, chloroform).

(d) 46 mg (+)-oxypeucedanin (VI), recrystallised from ether-chloroform, m.p. 103.5–104.0°, $[\alpha]_D^{26} + 16^\circ$ (c 1.8, chloroform).

Isoimperatorin, columbianadin, and (+)-oxypeucedanin were previously obtained from the root of *Peucedanum palustre*.²

Further elution yielded a fraction (850 mg) which was rechromatographed on silica gel (Merck, 70 g) activated at 120° and impregnated with 3 % of water. The eluent was a mixture of methylene chloride-tetrachloromethane (2:1) to which increasing amounts of ethyl acetate were added. The following substances were eluted:

(e) 14 mg of a yellow-fluorescent compound, recrystallised from ether, m.p. 147–148°. The IR-spectrum was identical with that of isooxypeucedanin (VII) prepared from oxypeucedanin as described by Späth and Klager.⁸ (Ref. 8, m.p. 146°).

(f) 125 mg of a blue-fluorescent compound (I). Recrystallised from ether-cyclohexane, m.p. 97.0°, $[\alpha]_D^{26} + 305^\circ$ (c 0.4, methanol). (Found: C 66.44; H 5.92. Calc. for $C_{19}H_{20}O_8$: C 66.27; H 5.85).

(g) 68 mg of a blue-fluorescent compound, recrystallised from ether-chloroform, m.p. 129.5°, $[\alpha]_D^{26} + 278^\circ$ (c 0.5, methanol). The compound was identified as peulustrin (VIII), previously isolated from the root of *Peucedanum palustre*.¹

(h) 144 mg of a blue-fluorescent compound (II), recrystallised from ether, m.p. 137.5–138.0°, $[\alpha]_D^{25} + 273^\circ$ (c 0.4, methanol). (Found: C 65.07; H 6.36. Calc. for $C_{24}H_{28}O_8$: C 64.85; H 6.35).

Treatment of (I) with 0.5 N sodium hydroxide. A solution of 85 mg of (I) in 4 ml 0.5 N methanolic sodium hydroxide was maintained at 50° for 1½ h. Upon addition of 5 ml of water the methanol was partly removed by evaporation under reduced pressure. The reaction mixture was acidified with 4 N sulphuric acid, and after standing over night, adjusted to pH 8 with sodium carbonate and finally extracted with ether.

The extract, after drying and evaporation, yielded 8(S)-(+)-dihydro-oroselol⁹ (IX), which was recrystallised from methanol, m.p. 162.8–163.2°, $[\alpha]_D^{26} + 248^\circ$ (c 0.3, methanol).

The aqueous phase (pH 8) was evaporated and acidified with 4 N sulphuric acid and 10 g of a mixture of diatomaceous earth and anhydrous sodium sulphate (3:1) was added. The almost dry mixture was packed into a column and eluted with diethyl ether (200 ml). The dried ether extract was evaporated and the residue converted to the *p*-phenylphenacyl ester according to the method described by Stodola.⁹ A chloroform extract, containing a mixture of this ester, *p*-phenylphenacyl alcohol and unreacted *p*-phenylphenacyl bromide was evaporated and chromatographed on silica gel (Merck, 10 g), activated at 120° and impregnated with 10 % of water. Benzene with increasing amounts of ethyl acetate was used as the eluent. With a solvent mixture containing 35 % of ethyl acetate a *p*-phenylphenacyl ester, m.p. 165.0°, $[\alpha]_{364}^{25} - 86^\circ$ (c 0.2, chloroform) was obtained. The IR-spectrum was identical with that of an authentic sample of the *p*-phenylphenacyl ester of 2(R),3(S)-(+)-2,3-dihydroxy-2-methylbutyric acid (X), m.p. 164–165°, $[\alpha]_{364}^{25} - 84^\circ$ (c 0.3, chloroform).

Treatment of (II) with 0.5 N sodium hydroxide. A solution of 65 mg (II) in 3.5 ml of 0.5 N methanolic sodium hydroxide was maintained at 50° for 1 h. Upon addition of 5 ml of water the methanol was partly removed by evaporation under reduced pressure. The solution was acidified with 4 N sulphuric acid, and after standing for 15 min, adjusted to pH 8.2 with sodium carbonate and finally extracted with ether.

The extract, after drying and evaporation, yielded 8(S)-(+)-dihydro-oroselol⁹ (IX) which was recrystallised from methanol, m.p. 162.5–163.0°, $[\alpha]_D^{26} + 246^\circ$ (c 0.5, methanol).

The aqueous phase (pH 8.2) was evaporated and acidified with 4 N sulphuric acid, and 10 g of a mixture of diatomaceous earth-anhydrous sodium sulphate (3:1) was added. The almost dry mixture was packed into a column and eluted with diethyl ether (200 ml). The dried ether extract was evaporated and the residue converted to the *p*-phenylphenacyl ester in the usual manner.

The ester mixture was chromatographed on silica gel (Merck, 15 g) activated at 120° and impregnated with 10 % of water. Benzene with increasing amounts of ethyl acetate were used as the eluent. With a solvent mixture containing 2–5 % of ethyl acetate a *p*-phenylphenacyl ester, m.p. 143.5–145.0°, was obtained. This compound was identified as the *p*-phenylphenacyl ester of seneciolic acid (XI), (IR-spectrum). (Ref. 10, m.p. 144.5–146.0°). With a solvent mixture containing 35 % of ethyl acetate a *p*-phenylphenacyl ester, m.p. 165.0°, $[\alpha]_{D}^{25} - 86^{\circ}$ (c 0.05, chloroform) was obtained. These data and the IR-spectrum proved the compound to be the *p*-phenylphenacyl ester of 2(*R*),3(*S*)-(+)-2,3-dihydroxy-2-methylbutyric acid (X).

Melting points, UV-, IR-, and PMR-spectra were determined as described in a previous paper.³ Microanalyses were performed by Dr. A. Bernhardt, Mülheim.

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