Study of plant coumarins
1. Transformations of peucedanin

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The structure of 2-bromooreoselon, which was prepared by bromination of peucedanin or oreoselon with molecular bromine, was established. The compositions and structures of the reaction products of this bromide with amines, such as pyridine, triethylamine, and morpholine, as well as with sodium acetate and potassium hydroxide were studied. The reaction of peucedanin with *m*-chloroperoxybenzoic acid affords peuruthenicin isobutyrate.

Key words: coumarins, furocoumarins, peucedanin, oreoselon, peuruthenicin, *m*-chloroperoxybenzoic acid, bromination, quaternization.

Coumarins produced by higher plants and fungi and those prepared by synthetic methods can serve as biologically active compounds of medical interest and, concequently, have attracted considerable attention.[1—3] Furocoumarin-containing drugs, which exert the photosensitizing and photoprotective action, such as psoralen, isopsoralen, 8-methoxypsoralen, bergapten, and isopimpinellin, are used in therapy of skin diseases.[4] 4-Hydroxycoumarin derivatives are used as anticoagulants.[4] Some plant coumarins hold considerable promise as antiviral (anti-HIV)[5—8] and antitumor agents.[9—12]

Siberian flora is endowed with plants valuable as sources of coumarins.[13] Among these plants is, undoubtedly, Peucedanum (*Peucedanum morisonii* Bess., the *Apiaceae* or *Umbelliferae* family), which is widespread in Western Siberia.[14] Thirteen coumarin derivatives were identified in roots of this plant.[15] Furocoumarin peucedanin (**1**) can easily be isolated in a yield of 4% of the weight of the dry material. It is known that peucedanin sensitizes photohemolysis[16] and exhibits antitumor activity.[17] The pronounced biological activity and availability of peucedanin have stimulated our interest in studying its chemical properties.

The aim of the present study was to synthesize peucedanin derivatives by modifications of the furan ring.

Results and Discussion

Bromination of peucedanin (**1**) with an equimolar amount of bromine has been reported[18] to afford monobromide identical to that prepared by bromination of oreoselon (**2**) (the hydrolysis product of peucedanin) under the same conditions (Scheme 1). However, the yields and the structure of this monobromide have not documented. We established the structure of the monobromide by comparing the ^{1}H NMR spectra of this compound and oreoselon. The fact that the spin-spin coupling of the signal for the H atom bound to the tertiary C atom of the isopropyl group in the bromide is simpler (septet, J = 6.8 Hz) compared to the signal for the corresponding H atom in oreoselon (septet of doublets, J = 6.8 Hz, J = 4.0 Hz) indicates that the H(2) atom in the latter compound is replaced by Br. Therefore, the monobromide under study is 2-bromooreoselon (2-bromo-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (**3**)). It was demonstrated that the yields of bromide **3** prepared by bromination of peucedanin and oreoselon with an equimolar amount of molecular bromine were 92 and 98%, respectively.

We studied the behavior of bromide **3** in reactions with amines. Refluxing of **3** with pyridine in 95% ethanol afforded a quaternization product, *viz.*, *N*-{2-(1-methylethyl)-3,7-dioxo-7*H*-furo[3,2-*g*][1]benzopyran-2-yl}pyridinium bromide (**4**), which was isolated as monohydrate. The reaction was accompanied by the formation of the already known 2-(1-methylethylidene)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (**5**)[19] as a result of elimination of HBr from the starting bromide **3**. In addition, we isolated 2-ethoxyoreoselon (2-ethoxy-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (**6**)). Compounds **4**, **5**, and **6** were obtained in 67, 22, and 7% yields, respectively. Refluxing in chloroform under analogous conditions afforded compounds **4** and **5** in 62 and 17% yields, respectively. Under analogous conditions, refluxing of bromide **3** with more basic triethylamine in chloroform gave compound **5** in 47% yield. Storage of bromide **3** with morpholine in chloroform at 25 °C for 24 h led to the nucleophilic substitution of

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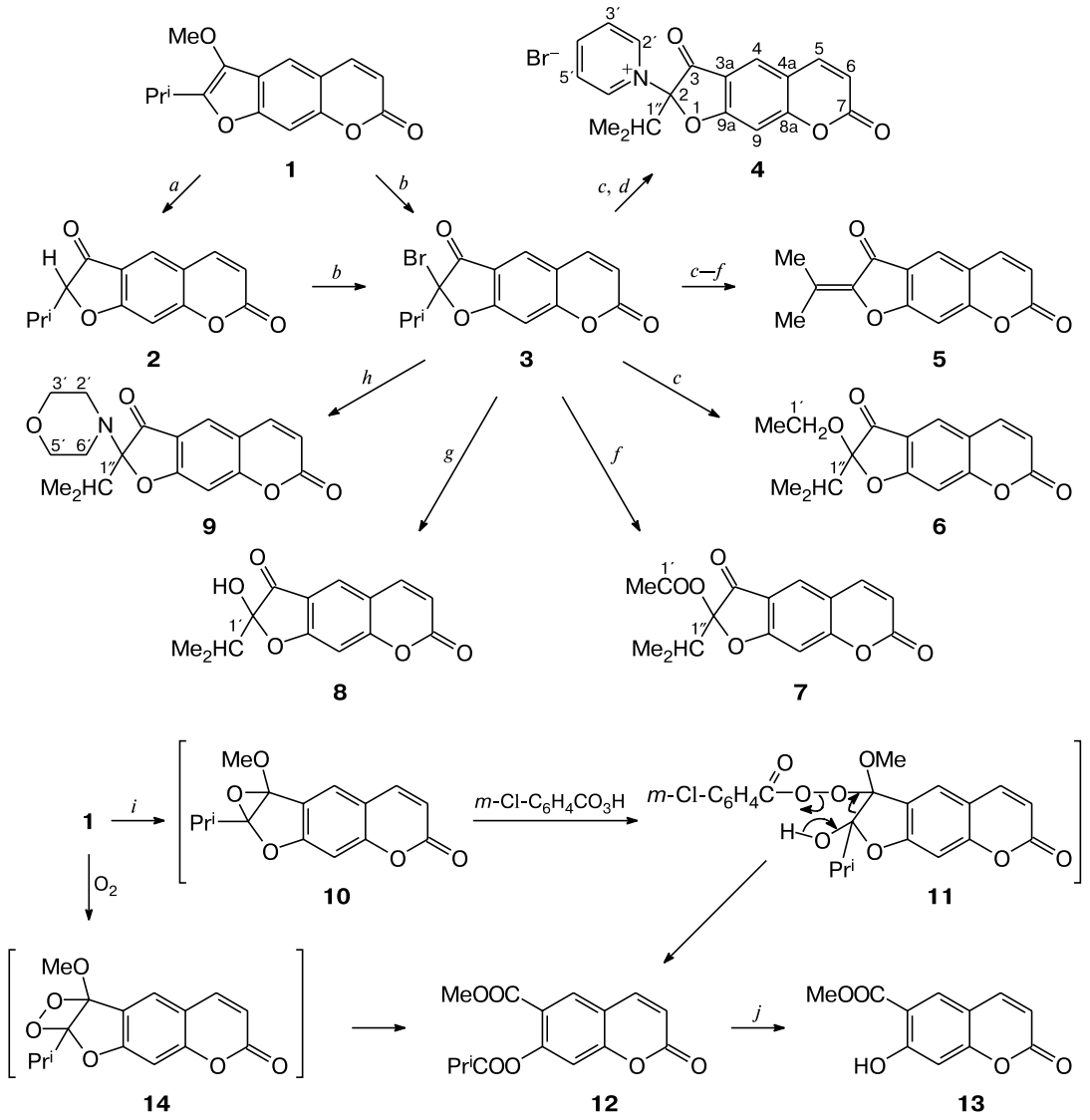
Scheme 1



Reagents and conditions: *a*. Concentrated HCl, MeOH, 60 °C. *b*. Br_2, $CHCl_3$, 25 °C. *c*. C_5H_5N, EtOH, 78 °C. *d*. C_5H_5N, $CHCl_3$, 63 °C. *e*. Et_3N, $CHCl_3$, 63 °C. *f*. AcONa, AcOH, 118 °C. *g*. 10% KOH solution, 100 °C, and then H_2SO_4. *h*. Morpholine, $CHCl_3$, 25 °C. *i*. MCPBA. *j*. NaOH, MeOH, 25 °C, and then H_2SO_4.

the bromine atom giving rise to 2-(1-methylethyl)-2-morpholino-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (**9**) in 72% yield.

Upon refluxing of compound **3** in glacial acetic acid in the presence of anhydrous AcONa, the bromine atom underwent nucleophilic substitution resulting in the formation of 2-acetoxyoreoselon, *viz.*, 2-acetoxy-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (**7**), in 27% yield. This reaction produced unsaturated ketone **5** as the major product (the yield was 44%). Dissolution of bromide **3** in a 10% KOH solution at high temperature followed by neutralization of the solution gave 2-hydroxyoreoselon, *viz.*, 2-hydroxy-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (**8**), in 83% yield.

Peucedanin (**1**) underwent an unexpected transformation upon oxidation with *m*-chloroperoxybenzoic acid (MCPBA). The reaction of **1** with two equivalents of the peroxy acid gave the known peuruthenicin isobutyrate (**12**), which has been synthesized earlier[20] and extracted from the plant.[15] The possible reaction mechanism presented in Scheme 1 involves the following steps: 1) formation of intermediate peucedanin 2,3-epoxide (**10**); 2) cleavage of the epoxy ring by the addition of the second MCPBA molecule giving rise to peroxy ester **11**; 3) subsequent elimination of *m*-chlorobenzoic acid to form di-

rectly compound **12**. The mechanism of cleavage of bicyclic tetrasubstituted olefins with MCPBA has been discussed earlier.[21] It was demonstrated[22] that 2-methyl-4,5,6,7-tetrahydrobenzofuran undergoes analogous cleavage with peroxy acids. An alternative mechanism involves the transformation of peroxy ester **11** into 1,2-dioxetane derivative **14** followed by is decomposition to give isobutyrate **12**. In the plant, oxidation of peucedanin (**1**) most likely starts with the addition of singlet oxygen giving rise to dioxetane **14** and completed with decomposition of the latter to form compound **12**. Data on the synthesis of 1,2-dioxetanes from enol ethers and their decomposition were summarized in the publication.[23] It should be noted that, under the above-described conditions, oreoselon (**2**) remains unconsumed.

Alkaline hydrolysis of isobutyrate **12** under mild conditions affords a compound (in 94% yield) identical to natural peuruthenicin (**13**).[15,20]

To summarize, simple chemical transformations of peucedanin provide a route to the synthesis of promising coumarin derivatives.

Experimental

The syntheses were performed with the use of freshly distilled solvents and reagents of high-purity grade. The melting points were determined on a Kofler apparatus. The IR spectra were recorded on a Vector 22 spectrometer in KBr pellets. The UV spectra were measured on a Specord UV—Vis spectrophotometer in ethanol ($C = 10^{-4}$ mol L^{-1}). The molecular weights and elemental compositions were determined on a high-resolution Finnigan MAT 8200 mass spectrometer. The NMR spectra were recorded on a Bruker AC 200 spectrometer (200.13 MHz for ^1H and 50.32 MHz for ^{13}C) for 10% solutions in $CDCl_3$, unless otherwise indicated, at 25 °C with resonance stabilization based on the signal for the deuterium atom of the solvent. The chemical shifts were measured relative to the signal of $CHCl_3$ as the internal standard (δ_H 7.24 and δ_C 76.90). The multiplicities of the signals in the ^{13}C NMR spectra were determined according to standard procedures using JMOD experiments and off-resonance proton irradiation. The assignment of the signals in the ^1H and ^{13}C NMR spectra of compounds **3—9** was made using the data for the model compound, *viz.*, oreoselon.[15]

Peucedanin (1) was extracted from air-dry roots of *Peucedanum morisonii* by refluxing in *tert*-butylmethyl ether, m.p. 85—87 °C (*cf.* lit. data[24]: m.p. 85—87 °C (from Et_2O)). ^1H NMR, δ: 1.28 (d, 6 H, Me_2C, J = 6.8 Hz); 3.18 (sept, 1 H, H(1′), J = 6.8 Hz); 3.88 (s, 3 H, OMe); 6.28 (d, 1 H, H(6), J = 9.6 Hz); 7.22 (s, 1 H, H(9)); 7.51 (s, 1 H, H(4)); 7.72 (d, 1 H, H(5), J = 9.6 Hz) (*cf.* lit. data[15]). IR, ν/cm^{-1}: 823, 877, 1039, 1120, 1142, 1214, 1284, 1364, 1390, 1444, 1461, 1577, 1634, 1725 (C=O), 2933, 2972.

Oreoselon (2) was prepared by hydrolysis of peucedanin (**1**) according to a known procedure.[24] A mixture of peucedanin (30.4 g) and MeOH (152 mL) was heated to 55 °C on a water bath until complete dissolution was achieved. Concentrated HCl (60 mL) was added dropwise with stirring to the hot solution, an exothermic reaction being observed. Hydrochloric acid was added at a rate such that the temperature of the reaction mixture was no higher than 60 °C. After cooling, the product was filtered off and dried at 100 °C. The dry product was recrystallized from refluxing 95% ethanol (620 mL). Oreoselon (**2**) was obtained in a yield of 24.2 g, m.p. 177—178 °C (*cf.* lit. data[25]: m.p. 177—178 °C (from EtOH)). The mother liquor was concentrated to ~20 mL to give the second crop (1.7 g) of oreoselon. The total yield was 25.9 g (90%). ^1H NMR, δ: 0.81 and 1.10 (both d, 3 H each, Me_2C, J = 6.8 Hz); 2.31 (sept.d, 1 H, H(1′), J = 6.8 Hz, J = 4.0 Hz); 4.48 (d, 1 H, H(2), J = 4.0 Hz); 6.27 (d, 1 H, H(6), J = 9.6 Hz); 6.93 (s, 1 H, H(9)); 7.67 (d, 1 H, H(5), J = 9.6 Hz); 7.73 (s, 1 H, H(4)). IR, ν/cm^{-1}: 496, 745, 814, 830, 936, 979, 1046, 1105, 1144, 1156, 1356, 1394, 1469, 1485, 1576, 1629, 1711, 1726 (C=O), 2931, 2964.

2-Bromooreoselon (2-bromo-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione) (3). A solution of bromine (2.13 g, 13.3 mmol) in $CHCl_3$ (13.3 mL) was added dropwise with stirring to a solution of peucedanin (**1**) (3.44 g, 13.3 mmol) in $CHCl_3$ (26.6 mL), each drop of the bromine solution becoming colorless. After removal of the solvent *in vacuo* (the bath temperature was 60 °C), the amorphous precipitate was dried at 10 Torr and triturated with diethyl ether (5 mL). Crystals of compound **3** were filtered off. The yield was 3.97 g (92%), m.p. 140—141 °C (*cf.* lit. data[18]: m.p. 140—141 °C). Found, *m/z*: 321.98409 $[M]^+$. $C_{14}H_{11}BrO_4$. Calculated: M = 321.98412. ^1H NMR, δ: 0.95 and 1.33 (both d, 3 H each, Me_2C, J = 6.8 Hz); 2.51 (sept, 1 H, H(1′), J = 6.8 Hz); 6.37 (d, 1 H, H(6), J = 9.6 Hz); 7.01 (s, 1 H, H(9)); 7.73 (d, 1 H, H(5), J = 9.6 Hz); 7.91 (s, 1 H, H(4)). ^{13}C NMR, δ: 16.6 and 17.4 (both q, $(\underline{C}H_3)_2C$); 36.4 (d, C(1′)); 98.9 (s, C(2)); 101.4 (d, C(9)); 115.2 (d, C(6)); 115.5 (s, C(3a)); 115.8 (s, C(4a)); 126.0 (d, C(4)); 143.2 (d, C(5)); 158.7 (s, C(9a)); 161.1 (s, C(8a)); 169.4 (s, C(7)); 192.5 (s, C(3)). IR, ν/cm^{-1}: 489, 724, 800, 837, 860, 918, 934, 1018, 1101, 1117, 1146, 1355, 1393, 1481, 1581, 1631, 1726, 1744 (C=O), 2980, 3081.

Reaction of 2-bromooreoselon with pyridine. *A*. A mixture of 2-bromooreoselon (**3**) (4.78 g, 14.8 mmol), dry pyridine (1.17 g, 14.8 mmol), and 95% ethanol (28 mL) was refluxed for 1.5 h. After cooling, a precipitate of **2-(1-methylethylidene)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (5)** was filtered off in a yield of 0.78 g (22%), m.p. 283—285 °C (*cf.* lit. data[19]: m.p. 283—285 °C (from AcOH)). Found, *m/z*: 242.05822 $[M]^+$. $C_{14}H_{10}O_4$. Calculated: M = 242.05790. ^1H NMR (10% solution in a CF_3CO_2D—$CDCl_3$ mixture, 2 : 1, v/v, $CHCl_3$ as the internal standard), δ: 2.30 and 2.48 (both s, 3 H each, Me_2C); 6.60 (d, 1 H, H(6), J = 9.6 Hz); 7.29 (s, 1 H, H(9)); 8.07 (d, 1 H, H(5), J = 9.6 Hz); 8.15 (s, 1 H, H(4)). IR, ν/cm^{-1}: 513, 670, 751, 765, 845, 866, 1130, 1146, 1181, 1223, 1256, 1352, 1395, 1442, 1482, 1573, 1621, 1655, 1701, 1730 (C=O), 3047.

Ethanol was removed from the mother liquor *in vacuo* (the bath temperature was 60—70 °C), and diethyl ether (10 mL) was added to the cooled residue. The precipitate that formed was thoroughly ground and filtered off. ***N*-{2-(1-Methylethyl)-3,7-dioxo-7*H*-furo[3,2-*g*][1]benzopyran-2-yl}pyridinium bromide monohydrate (4)** was obtained as a powder in a yield of 4.15 g (67%). Cooling of the hot solution in 95% ethanol afforded colorless crystals of the product. After heating above 150 °C, the latter was decomposed and turned yellowish. At a temperature higher than 170 °C, colorless needle-like crystals sublimed. Found (%): C, 54.45; H, 4.29; Br, 18.83; N, 3.10. $C_{19}H_{16}BrNO_4 \cdot H_2O$ ($C_{19}H_{18}BrNO_5$). Calculated (%): C, 54.30;

H, 4.32; Br, 19.01; N, 3.33. ^{1}H NMR (10% solution in CD_3OD), δ: 1.14 and 1.27 (both d, 3 H each, Me_2C, J = 6.8 Hz); 3.34 (sept, 1 H, H(1″), J = 6.8 Hz); 6.62 (d, 1 H, H(6), J = 9.6 Hz); 7.78 (s, 1 H, H(9)); 8.26 (d, 1 H, H(5), J = 9.6 Hz); 8.39 (s, 1 H, H(4)); 8.55 (br.t, 2 H, H(3′), H(5′), J = 7.5 Hz); 9.02 (tt, 1 H, H(4′), J = 8.0 Hz, J = 1.0 Hz); 9.76 (br.d, 2 H, H(2′), H(6′), J = 7.5 Hz). ^{1}H NMR (5% solution in D_2O, H_2O as the internal standard (δ 4.80)), δ: 0.88 and 1.01 (both d, 3 H each, Me_2C, J = 6.8 Hz); 3.03 (sept, 1 H, $Me_2C\underline{H}$, J = 6.8 Hz); 6.43 (d, 1 H, H(6), J = 9.6 Hz); 7.48 (s, 1 H, H(9)); 7.99 (d, 1 H, H(5), J = 9.6 Hz); 8.11 (s, 1 H, H(4)); 8.23 (br.t, 2 H, H(3′), H(5′), J = 7.5 Hz); 8.70 (tt, 1 H, H(4′), J = 8.0 Hz, J = 1.0 Hz); 9.42 (br.d, 2 H, H(2′), H(6′), J = 7.5 Hz). IR, ν/cm^{-1}: 512, 678, 700, 741, 755, 780, 827, 866, 937, 970, 1096, 1123, 1355, 1388, 1472, 1529, 1583, 1628, 1745 (C=O), 2935, 2972, 3043. UV (EtOH), λ_{max}/nm (logε): 258 (4.46), 347 (3.97).

Storage of the oily residue, which was obtained after removal of diethyl ether from the ethereal filtrate, for one day afforded crystals of **2-ethoxyoreoselon (2-ethoxy-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione) (6)**. The yield was 0.30 g (7%), m.p. 124—125 °C (from diethyl ether). Found, *m/z*: 288.10002 $[M]^+$. $C_{16}H_{16}O_5$. Calculated: M = 288.09976. ^{1}H NMR, δ: 0.81 and 0.99 (both d, 3 H each, Me_2C, J = 6.8 Hz); 1.11 (t, 3 H, $C\underline{H}_3CH_2$, J = 6.8 Hz); 2.17 (sept, 1 H, H(1″), J = 6.8 Hz); 3.33 and 3.42 (both m, 1 H each, $CH_3C\underline{H}_2$); 6.28 (d, 1 H, H(6), J = 9.6 Hz); 6.90 (s, 1 H, H(9)); 7.67 (d, 1 H, H(5), J = 9.6 Hz); 7.74 (s, 1 H, H(4)). ^{13}C NMR, δ: 14.9, 15.4, and 15.7 (all q, Me); 34.1 (d, C(1″)); 60.5 (t, C(1′)); 100.3 (d, C(9)); 112.4 (s, C(2)); 114.2 (s, C(3a)); 114.5 (d, C(6)); 118.5 (s, C(4a)); 124.3 (d, C(4)); 143.3 (d, C(5)); 159.2 (s, C(9a)); 161.5 (s, C(8a)); 172.1 (s, C(7)); 198.0 (s, C(3)). IR, ν/cm^{-1}: 828, 896, 913, 1001, 1040, 1190, 1290, 1350, 1394, 1483, 1572, 1625, 1733 (C=O), 2977. UV, λ_{max}/nm (logε): 223 (4.26), 254 (4.54), 297 (4.16), 350 (4.23), 409 (3.50).

B. Dry pyridine (1.17 g, 14.8 mmol) was added to a solution of 2-bromooreoselon (**3**) (4.78 g, 14.8 mmol) in $CHCl_3$ (28 mL). The reaction solution was refluxed for 1.5 h, which was accompanied by the formation of a solid residue. The mixture was concentrated *in vacuo* (the bath temperature was 60 °C) to ~10 mL. The precipitate was filtered off from the hot solution, washed with hot $CHCl_3$ (2×3 mL), and dried. The product (4.43 g) was triturated with hot (70 °C) water (2×44.3 mL). The combined aqueous filtrates were concentrated *in vacuo* (the bath temperature was 60 °C) and the residue was dried (10 Torr). Monohydrate of salt **4** was obtained in a yield of 3.83 g (62%). The residue, which remained undissolved after trituration with hot water, was dried on a filter at 10 Torr (the bath temperature was 60 °C). Compound **5** was obtained in a yield of 0.60 g (17%). Compounds **4** and **5** were identified by comparing their IR spectra with the spectra of the authentic samples.

Reaction of 2-bromooreoselon with triethylamine. 2-Bromooreoselon (**3**) (14.4 g, 44.6 mmol) was added with stirring to a solution of triethylamine (4.80 g, 47.5 mmol) in $CHCl_3$ (84 mL). The resulting solution was refluxed using a reflux condenser equipped with a calcium chloride tube on a water bath for 1.5 h. Water (30 mL) was added to the warm solution and the mixture was vigorously stirred. The precipitate that formed was filtered off and washed with a minimum amount of chloroform and water and then dried in a drying oven at 130 °C. Compound **5** was obtained in a yield of 5.06 g (47%), m.p. 283—285 °C, and identified by comparing its IR spectrum with the spectrum of the authentic sample.

2-Acetoxyoreoselon (2-acetoxy-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione) (7). A mixture of 2-bromooreoselon (**3**) (6.64 g, 20.6 mmol), anhydrous powdered AcONa (3.46 g, 42.2 mmol), and glacial acetic acid (26 mL) was refluxed for 1 h. After cooling, the precipitate was filtered off, washed with diethyl ether (3×10 mL), and dried. The residue was thoroughly washed with water (3×10 mL) to remove an impurity of sodium acetate and dried at 130 °C. Compound **5** was obtained in a yield of 2.20 g (44%), m.p. 283—285 °C. The product was identified by comparing its IR spectrum with the spectrum of the authentic sample. The acetic acid filtrate was diluted with water (90 mL). The amorphous product that formed was extracted with diethyl ether (4×20 mL), the extract was washed with water (2×20 mL), the solvent was removed, and the oily residue was triturated with diethyl ether (10 mL). The precipitate that formed was filtered off, recrystallized from AcOEt, and dried. Compound **7** was obtained in a yield of 1.70 g (27%), m.p. 140—141 °C. Found, *m/z*: 302.07928 $[M]^+$. $C_{16}H_{14}O_6$. Calculated: M = 302.07903. ^{1}H NMR, δ: 0.87 and 1.09 (both d, 3 H each, Me_2C, J = 6.8 Hz); 2.07 (s, 3 H, MeCO); 2.24 (sept, 1 H, H(1″), J = 6.8 Hz); 6.30 (d, 1 H, H(6), J = 9.6 Hz); 6.89 (s, 1 H, H(9)); 7.67 (d, 1 H, H(5), J = 9.6 Hz); 7.77 (s, 1 H, H(4)). ^{13}C NMR, δ: 15.0 and 15.1 (both q, $(\underline{C}H_3)_2C$); 19.9 (q, $\underline{C}H_3CO$); 33.4 (d, C(1″)); 100.0 (d, C(9)); 105.5 (s, C(2)); 114.4 (s, C(3a)); 114.4 (d, C(6)); 118.7 (s, C(4a)); 123.9 (d, C(4)); 143.3 (d, C(5)); 159.1 (s, C(9a)); 160.7 (s, C(8a)); 168.3 (s, $CH_3\underline{C}O$); 170.2 (s, C(7)); 194.2 (s, C(3)). IR, ν/cm^{-1}: 825, 889, 939, 962, 983, 1070, 1100, 1129, 1185, 1231, 1286, 1352, 1371, 1389, 1577, 1629, 1743 (C=O), 2940, 2969. UV, λ_{max}/nm (logε): 214 (4.05), 222 (4.06), 254 (4.44), 296 (3.97), 306 (3.96), 348 (4.04).

2-Hydroxyoreoselon (2-hydroxy-2-(1-methylethyl)-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione) (8). A mixture of 2-bromooreoselon (**3**) (516 mg, 1.60 mmol) and a 10% KOH solution (4.50 g, 8.02 mmol) was refluxed with stirring for 15 min. The resulting dark-colored solution was cooled to 20 °C, and a 10% H_2SO_4 solution was added with stirring to pH 4. The oil that formed was extracted with diethyl ether (3×5 mL). The ethereal extract was filtered, and the solvent was removed. The residue was dissolved in ethanol (4 mL) with heating. After cooling, compound **8** was filtered off as yellowish needles. The yield was 345 mg (83%), m.p. 192—193 °C. Found (%): C, 64.30; H, 4.48. $C_{14}H_{12}O_5$. Calculated (%): C, 64.61; H, 4.65. ^{1}H NMR (10% solution in a $CDCl_3$—CD_3OD mixture, 3 : 1, v/v), δ: 0.74 and 0.93 (both d, 3 H each, Me_2C, J = 6.8 Hz); 2.10 (sept, 1 H, H(1′), J = 6.8 Hz); 6.18 (d, 1 H, H(6), J = 9.6 Hz); 6.78 (s, 1 H, H(9)); 7.64 (d, 1 H, H(5), J = 9.6); 7.68 (s, 1 H, H(4)). ^{13}C NMR, δ: 14.9 and 15.5 (both q, $(\underline{C}H_3)_2C$); 33.7 (d, C(1′)); 100.2 (d, C(9)); 108.9 (s, C(2)); 113.7 (d, C(6)); 114.0 (s, C(3a)); 117.5 (s, C(4a)); 124.8 (d, C(4)); 143.8 (d, C(5)); 159.8 (s, C(9a)); 161.2 (s, C(8a)); 171.7 (s, C(7)); 198.7 (s, C(3)). IR, ν/cm^{-1}: 453, 655, 743, 827, 858, 881, 920, 1012, 1196, 1327, 1355, 1394, 1471, 1482, 1570, 1627, 1711, 1732 (C=O), 2958, 3060, 3322 (OH). UV, λ_{max}/nm (log ε): 223 (4.17), 253 (4.45), 299 (4.02), 350 (4.12), 410 (3.40).

2-(1-Methylethyl)-2-morpholino-7*H*-furo[3,2-*g*][1]benzopyran-3,7-dione (9). 2-Bromooreoselon (**3**) (998 mg, 3.09 mmol) was added with stirring to a solution of morpholine (552 mg, 6.34 mmol) in $CHCl_3$ (5.8 mL). The resulting solution was kept at 25 °C for 24 h. Then the reaction mixture containing the

precipitate that formed was mixed with water (4 mL). The aqueous layer was separated. The organic layer was washed with water (2×4 mL) to remove traces of water-soluble products. Chloroform was evaporated *in vacuo*. The residue was triturated with diethyl ether (3×4 mL), dried, and recrystallized from refluxing anhydrous ethanol (28 mL). Compound **9** was obtained as yellowish needles in a yield of 733 mg (72%), m.p. 200 °C (decomp.). Found, *m/z*: 329.12559 $[M]^+$. $C_{18}H_{19}NO_5$. Calculated: M = 329.12631. ^{1}H NMR, δ: 0.66 and 1.04 (both d, 3 H each, Me_2C, J = 6.8 Hz); 2.38—2.78 (m, 5 H, C(2′)H_2, C(6′)H_2, H(1″)); 3.48—3.69 (m, 4 H, C(3′)H_2, C(5′)H_2); 6.22 (d, 1 H, H(6), J = 9.6 Hz); 6.82 (s, 1 H, H(9)); 7.64 (d, 1 H, H(5), J = 9.6 Hz); 7.68 (s, 1 H, H(4)). ^{13}C NMR, δ: 14.8 and 16.2 (both q, Me); 30.9 (d, C(1″)); 46.0 (t, C(2′), C(6′)); 66.3 (t, C(3′), C(5′)); 99.7 (d, C(9)); 109.1 (s, C(2)); 113.7 (s, C(3a)); 114.0 (d, C(6)); 119.5 (s, C(4a)); 124.0 (d, C(4)); 143.3 (d, C(5)); 159.1 (s, C(9a)); 161.4 (s, C(8a)); 172.4 (s, C(7)); 197.3 (s, C(3)). IR, ν/cm^{-1}: 518, 826, 848, 878, 904, 1091, 1121, 1144, 1191, 1288, 1347, 1392, 1484, 1624, 1720, 1747 (C=O), 2855, 2970. UV, λ_{max}/nm (logε): 224 (4.16), 254 (4.44), 299 (4.12), 350 (4.23), 353 (4.06).

Oxidation of peucedanin (1) with *m*-chloroperoxybenzoic acid. A solution of MCPBA (1.94 g, 11.2 mmol) in $CHCl_3$ (11.3 mL) was added dropwise to a solution of peucedanin (**1**) (1.40 g, 5.43 mmol) in $CHCl_3$ (5.4 mL), the mixture being cooled with running water to 20—25 °C. The reaction mixture was kept for 16 h. Then a saturated $NaHCO_3$ solution (10 mL) was carefully added (foaming can occur!) with stirring to the mixture containing the precipitate of 3-chlorobenzoic acid that formed. The organic layer was separated and twice treated with a $NaHCO_3$ solution (the last portion of the washing bicarbonate solution did not give a precipitate of 3-chlorobenzoic acid upon acidification with 10% H_2SO_4). After storage, the transparent organic solution was decanted, the solvent was removed, and the solid residue was recrystallized from MeOH. Peuruthenicin isobutyrate (**12**) was obtained as colorless crystals in a yield of 0.90 g (57%), m.p. 133—134 °C (*cf.* lit. data[20]: m.p. 133—134 °C (MeOH)). The product was identified by comparing its mass spectrum, ^{1}H and ^{13}C NMR spectra, and IR spectrum with the data published in the literature.[15]

Alkaline hydrolysis of peuruthenicin isobutyrate (12). Compound **12** (63 mg, 0.22 mmol) was added to a solution of NaOH (103 mg, 2.58 mmol) in a solution of equal volumes (0.9 mL each) of water and MeOH. After stirring for 2 h, the resulting yellowish solution was acidified with 10% H_2SO_4 to pH 4. The precipitate that formed was dried in air and dissolved in $CHCl_3$. The solution was filtered off and concentrated to dryness. Peuruthenicin **13** was obtained in a yield of 45 mg (94%), m.p. 195—197 °C (*cf.* lit. data[20]: m.p. 195—197 °C (from a benzene—petroleum ether mixture)). The product was identified by comparing its ^{1}H NMR spectrum with the data published in the literature.[15]

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