N. P. KIR' YALOV, S. D. MOVCHAN

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Abstract

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N. P. KIR' YALOV, S. D. MOVCHAN

ON A NEW GLYCOSIDE–REOSELIN–FROM THE ROOT RESIN OF PARSLEY-LEAVED FERULA–*FERULA PSEUDOREOSELINUM* (RGL ET SCHMALH.) K. POL.

(Presented by Academician M. M. Shemyakin, 20 VIII 1962)

The first information on the constituents of the roots of parsley-leaved ferula belongs to Tsukervanik, Bersutskii, Burtseva, and Aizikovich ([1]). According to the investigations of the authors cited, the roots of parsley-leaved ferula contain about 3.5% essential oil (composition: *dl*-pinene 90%; dβ-phellandrene 5%; cuminaldehyde and a sesquiterpene) and 12.6% resinous substances.

The composition of the resin, however, remained almost unknown. Thus, in the neutral part of the resin only a small amount of a substance of composition $C_{15}H_{26}O_3$ (m.p. 123°) was found, and in the acidic part of the resin, after dry distillation, the authors detected a substance with m.p. 161–162° of composition $C_{14}H_{22}O_3$, assigned to podocarpic acid. In studying the constituents of the resin from the roots of parsley-leaved ferula we noted that the resin, extracted from the roots by means of acetone extraction, does not dissolve completely in ethyl ether. The ether-insoluble part of the resin is a colorless crystalline product which dissolves well in hot water, acetone, and alcohol. After recrystallization from aqueous acetone or other solvents we obtained snow-white plates with m.p. 155–156°, of composition $C_{36}H_{52}O_{15}$. The isolated substance is an optically active compound: $(L)_D - 24.4^\circ$ (C : 10; alcohol), possesses neutral properties, and although on prolonged heating in alkaline medium it dissolves with formation of a salt, on acidification of the solutions this substance separates again unchanged. We regard the substance obtained as newly discovered and propose for it the name reoselin. On heating reoselin with a 2–3% aqueous solution of sulfuric acid, a crystalline product with m.p. 234–235° was obtained, which gave no depression of melting point in a mixed sample with umbelliferone. From the hydrolysate, by steam distillation, a liquid of approximate composition $C_{15}H_{26-24}O$ was obtained (apparently a ketone of the sesquiterpene series, since in the IR spectrum of the liquid an intense absorption maximum at 1709.2 cm^{-1} was found). In the hydrolysate, after separation of umbelliferone and the sesquiterpene ketone, not less than 32% sugar (by Bertrand) was found; according to paper chromatography data, this was a mixture of glucose and fructose, the amount of fructose not exceeding 2–3% (by Kolthoff). On hydrogenation

of reoselin in acetic acid or in alcohol over Pt (from PtO_2), umbelliferone and amorphous substances were obtained. The formation of umbelliferone upon hydrogenation of reoselin confirms its presence in reoselin and proves the stability of the simple ether bond of umbelliferone with the remaining part of the reoselin molecule. An analogous phenomenon was observed earlier, for example, in the study of the properties of umbelliprenin and kocanikin ([2]). Reoselin is readily acetylated and forms a mixture of acetates which, on saponification, give an un-

reoselin. On the basis of the composition and the results of studying the products of acid hydrolysis of reoselin, it could be assumed that reoselin is a simple diester of three substances: umbelliferone $C_9H_6O_3$, ketodiol $C_{15}H_{28}O_3$, and disaccharide $C_{12}H_{22}O_{11}$.

We obtained an idea of the order of linkage of these compounds in reoselin by the action of the gastric juice of the grape snail on reoselin.

Under mild conditions, reoselin was cleaved and a substance with m.p. 61-62°, composition $C_{24}H_{32}O_5$, was obtained, which proved to be a simple ester of umbelliferone and ketodiol $C_{15}H_{28}O_3$, although the latter substance has not yet been isolated in pure form. In addition to the substance with m.p. 61-62°, a large amount of glucose was detected in the hydrolysate and fructose was not found (determinations according to Bertrand and by paper chromatography).

Thus, we come to the conclusion that at the center of the reoselin molecule is the ketodiol $C_{15}H_{28}O_3$, which is linked by one hydroxyl group to umbelliferone and by the other to a disaccharide molecule, i.e., schematically:

$$C_{12}H_{21}O_{11}\text{—}O\text{—}C_{15}H_{26}O\text{—}O$$

$$\begin{array}{c} O \\ | \\ \text{[coumarin ring structure]} \end{array}$$

It is very likely that the disaccharide in reoselin is gentiobiose, but we have not yet succeeded in isolating it, since under the experimental conditions the disaccharide is hydrolyzed to glucose.

The UV spectra of reoselin (λ at 325 mμ) and of its aglycone with m.p. 61-62° (λ at 325 and 253 mμ) confirm the presence of umbelliferone in the initial substances (the maximum at 325 mμ is characteristic of umbelliferone and its derivatives).

The IR spectral data also confirm both the presence of a benzene ring in reoselin (absorption bands at 1555 and 1619 cm^{-1}) and the presence of an unconjugated ketone group (maximum around 1710 cm^{-1}) and a CO-lactone ring (absorption maximum at 1735 cm^{-1}) in reoselin. Glycosides with a general structural plan analogous to reoselin apparently are widely distributed in plants of the genus

Ferula. For example, we have found substances close to reoselin in type of structure in the roots of *F. Samarkandica* Eng. Kor. and *F. Korschinskyi* Eng. Kor.

The microanalyses were carried out by E. A. Sokolova; the UV spectrum (in alcohol) and IR spectra (in Vaseline) were taken by T. V. Sokolova. The roots of *Ferula pseudoreoselinum* were collected in the valley of the Ugam River in the Tashkent region by an expedition under the direction of L. P. Markova.

Experimental Part

Preparation of reoselin. From cut and dried roots the resin was extracted with acetone at room temperature by threefold maceration, each time for several days. The acetone extracts were combined, filtered, and the acetone was distilled off on a water bath. The residue was a dark-brown resin with a terpene odor. Yield 11.4% (based on the air-dry weight of roots).

The resin was dissolved in ether, the insoluble part was filtered off, washed with cold acetone, and recrystallized from aqueous acetone. Snow-white plates, partly gathered into druses, were obtained, m.p. 155–156°. The substance dissolves in hot water, alcohol, acetone, benzene, and chloroform. It is almost insoluble in petroleum ether and ethyl ether. The aqueous solution foams strongly. The substance is bitter to the taste. Upon recrystallization of the substance from aqueous alcohol, chloroform, benzene, or a mixture

petroleum ether and acetone, it retains its crystalline structure and in all cases melts at 155–156°. $(L)_D^{20} - 24.4^\circ$ (C : 10; ethanol).

Found, %: C 59.62; 59.72; 52.45; H 7.13; 7.13; 7.22
$C_{36}H_{52}O_{15}$. Calculated, %: C 59.66; H 7.18

Action of dilute alkalis on reoselin. 0.2 g of reoselin was dissolved in 10 ml of ethanol, 20 ml of alcoholic 0.1 N KOH was added, and the mixture was boiled for 2 hours on a water bath. The alcohol was distilled off, the residue was dissolved in water (it dissolves well), and acidified with dilute sulfuric acid. A precipitate was obtained. It was recrystallized from water. M.p. 155–156°; it gives no depression in a mixture with the original reoselin.

Action of dilute acids on reoselin. 1 g of reoselin was dissolved in 90 ml of hot water, and 10 ml of 20% sulfuric acid was added to the solution; the mixture was boiled for 2 hours with a reflux condenser. At first the solution was clear, but then it gradually became cloudy and light-brown oily droplets appeared. The oil was collected in a Ginsberg apparatus. Yield 0.15 ml. The oil was steam-distilled, dried over ignited Na_2SO_4, and subjected to analysis without additional purification.

Found, %: C 80.70; 80.83; 80.82; H 11.55; 11.29; 11.50
$C_{15}H_{24}O$. Calculated, %: C 81.80; H 10.90

$C_{15}H_{26}O$. Calculated, %: C 81.08; H 11.71

In the IR spectrum of the substance an intense band at 1709.2 cm^{-1} was found. The hydrolysate was cooled and extracted with ether. The ether was distilled off, and the precipitate was recrystallized from hot water. Needle-shaped crystals were obtained. M.p. 234-235°. The substance gives no depression of the melting point in a mixed sample with umbelliferone. The formation of umbelliferone was confirmed by a qualitative reaction (the substance gives blue fluorescence in alkaline solution) and by obtaining the acetyl derivative with m.p. 140-141.5°, which gave no depression of the melting point in a mixed sample with umbelliferone acetate.

The aqueous solution, after isolation of the umbelliferone, was neutralized with soda, evaporated to dryness, and the residue was extracted with alcohol. In the alcoholic solution, 36% sugar (relative to the weight of reoselin) was found by Bertrand' s method. The qualitative composition of the sugars was determined by paper chromatography in a mixture of *n*-butanol, acetic acid, and water, taken in the ratio 4 : 1 : 1. Developer: a mixture of *p*-aminophenol and a concentrated solution of orthophosphoric acid (0.5 : 2). Glucose and fructose were used as standards. Distinct spots of glucose and fructose were found. About 2% fructose was obtained (by Kolthoff' s method).

Hydrogenation of reoselin. 1 g of reoselin was dissolved in 10 ml of ethanol and hydrogenated over Pt (from 0.13 g of PtO_2, prepared by Adams' method). 77 ml of H_2 was absorbed over 5 hours (753 mm; 19°). The solution was filtered, diluted with water, and extracted with ether. The ethereal solution was shaken with soda solution (blue fluorescence). The soda extracts were acidified. The precipitate that separated was recrystallized from hot water. Needles with m.p. 233-235° give no depression of the melting point in a mixture with umbelliferone. No sugar was detected in the aqueous-alcoholic solution (by Bertrand's method). On evaporating the aqueous-alcoholic solution, a glassy amorphous product was obtained, which upon acid hydrolysis gives an oil, glucose, fructose, and a little umbelliferone. On hydrogenation in acetic acid, umbelliferone and amorphous substances were obtained which could not be converted into crystalline form.

Acetylation of reoselin. 0.5 g of reoselin was heated with 5 ml of acetic anhydride and 0.1 g of sodium acetate for one hour on a water bath. Water was added, and the mixture was heated for another 15 min. It was diluted with water, filtered, and the precipitate was recrystallized from water or aqueous alcohol. A non-bitter amorphous substance with softening point 55-56°, n_D^{30} 1.5020, was obtained. Apparently this is a mixture of acetates, since upon saponification it was

reoselin with m.p. 155-156° and acetic acid were obtained. Individual acetates were not obtained.

Cleavage of reoselin by means of the gastric juice of the grape snail. 0.5 g of reoselin was dissolved in 150 ml of warm water, and about 0.5 ml of gastric juice of the grape snail was added to the solution at 36°. The solution

was placed in a thermostat in which the temperature was maintained at 35.5-36° for 72-80 h. The precipitate was filtered off, washed with ether, the ethereal solution was evaporated, and the residue—a yellowish oil—quickly solidified when rubbed with a spatula. The impure product melts in the range 45-55°. The substance was dissolved in chloroform and chromatographed on Al_2O_3 (activity 3-4). After removal of the chloroform, completely colorless, shiny crystals with m.p. 59-60° were obtained; after three recrystallizations from aqueous alcohol they had a constant m.p. 61-62°. The substance crystallizes as needles collected in druses. It is readily soluble in ether, acetone, alcohol, and petroleum ether. It is insoluble in water.

Found, %: C 71.99; 71.88; 72.05; H 8.29; 8.24; 8.18
$C_{24}H_{32}O_5$. Calculated, %: C 72.00; H 8.00
$C_{24}H_{34}O_5$. Calculated, %: C 71.64; H 8.43

In acid solution on heating, the substance is readily cleaved with formation of an oily product and umbelliferone. In the aqueous hydrolysate (after separation of the substance with m.p. 61-62°), glucose was detected (paper chromatography), and fructose was not found.

From the resin of the roots of parsley-like ferula (*Ferula pseudoreoselinum* (Rgl. et Schmalh.) K. Pol.), a new glycoside of composition $C_{36}H_{52}O_{15}$, $(L)D$–24.4°, m.p. 155-156°, was isolated, for which the name reoselin is proposed.

The general plan of the structure of reoselin has been established. At the center of the molecule there is probably a ketodiol of the sesquiterpene series of composition $C_{15}H_{28}O_3$, in which one hydroxyl group is linked to a disaccharide (presumably gentiobiose), and the second to umbelliferone.

Botanical Institute named after V. L. Komarov
Academy of Sciences of the USSR

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CITED LITERATURE

[1] I. P. Tsukervanik, V. P. Bersutskii et al., Bull. Central Asian State Univ., vol. 21, No. 8, 55 (1935). [2] N. P. Kir' yalov, Tr. Bot. Inst., vol. 8 (1961).

Note: Figure translations are in progress. See original paper for figures.