STRUCTURE OF THE COUMARIN GLYCOSIDE REOSELIN FROM THE ROOTS OF *Ferula kirialovii*

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The structure of terpenoid and carbohydrate moieties of the molecule of reoselin have been confirmed by the use of ^{13}C NMR spectra, and the position of the carbohydrate moiety has been corrected. Reoselin is S-(−)-karatavikinol β-sophoroside at the tertiary hydroxy group (S-(−)-karativikinol tertiary-O-β-D-sophoroside) and not at the secondary hydroxy group, as was previously assumed. The absolute configuration of the single asymmetric center, the carbon atom to which the secondary hydroxy group is attached, has been assigned by analogy with S-(−)-epoxysqualene and S-(−)-epoxyfarnesol. S-(−)-Karatavikinol tertiary O-β-D-sophoroside has been isolated from giant fennels, a characteristic feature of which is the biosynthesis via direct antiparallel cyclization of bicyclic sesquiterpenoid derivatives of umbelliferone with the configuration of the ring linkage enantiometric to the linkage of rings A and B of triterpenoids.

It has been shown previously [1, 2] that reoselin (I) is a karatavikinol β-sophoroside [3]. To confirm the structure of the aglycon and of the carbohydrate moiety of (I) and to determine the position of attachment of the latter more accurately, we have studied the ^{13}C NMR spectra of reoselin and of karatavikin — a natural compound [4, a, b, c] that is the keto derivative of karatavikinol. The ^{13}C NMR spectrum of the latter could not be obtained because the amount of substance was insufficient.

Table 1 gives details of the ^{13}C NMR spectra of karatavikin and reoselin that we have obtained and literature figures for the spectra of (2Z,6Z)-3,7,11-trimethyldodeca-2,6,10-triene [7], (2E,6E)-3,7,11-trimethyldodeca-2,6,10-triene [7], farnesol [6], 2,3-dihydroxy-2,3-dihydrosqualene [8], and 5-geranyloxy-7-methoxycoumarin [5]. The names of the compounds are given with the numbering used by the authors of the original publications. In this paper some of the formulas (Fig. 1) of these compounds are assigned a different numbering, common for all the compounds, for convenience of comparing the chemical shifts of the ^{13}C signals.

In the sesquiterpenoid moiety of reoselin (see Table 1), the presence of two trisubstituted double bonds with chemical shifts (ppm) of 118.2 d and 141.8 s, and 123.6 d and 134.9 s has been confirmed. The assignment to the corresponding double bonds was made on the basis of the identity of the first pair of signals with the signals of the analogous part of the molecule in 7-(γ,γ-dimethylallyloxy)coumarin [5] of 118.1 d and 137.9 s and in 5-geranyloxy-7-methoxycoumarin [5] of 118.3 d and 141.8 s; the second pair of signals was identical with the signals of the carbon atoms of the central part of the sesquiterpenoid chain in farnesol [6] — 123.9 d and 134.5 s — and also in squalene, [6, 8] — 124.2 d and 134.4 s — and the polar part of squalene glycol [8] — 124.9 d and 135 s.

The values of the signals of the two methyl groups, C-13 and C-14 (16.5 and 15.9 ppm) are close to those of the analogous methyl groups in (2E,6E)-3,7,11-trimethyldodeca-2,6,10-triene and differ considerably from those for the (2Z-6Z)- isomer (23.39 ppm) [7]. Consequently, there are two trisubstituted trans double bonds in the sesquiterpenoid moiety of reoselin. The value of the signal of the C-13 methyl group coincides with that in the terpenoid part attached to the coumarin residue of 5-geranyloxy-7-methoxycoumarin (16.5 ppm) [5].

In the ^{13}C NMR spectrum of 2,3-dihydroxy-2,3-dihydrosqualene [8], having a grouping analogous to that of the aglycon of reoselin, there are signals at 78.28 and 73.14 ppm corresponding to the C_{10}—OH and C_{11}—OH carbon atoms. In karatavikin [4] the latter signal has a value of 75.7 ppm. There are signals at 78.3 d and 81.2 s in the spectrum of reoselin. The

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TABLE 1. Details of the ^{13}C NMR Spectra of some Terpenoids and Terpenoid Coumarins ($CDCl_3$, δ, 0 — TMS)

Number of the compound	Chemical shifts of the compounds						
	1	2 [7]	3 [7]	4 [6]	5	6 [8]	7 [5]
1	65,2 tr	13 34	13,33	58,2	64,9 tr	28,30	65,5
2	118,2d	118,86	118 17	124,3	118,2d	124,32	118,3
3	141,8s	(135,05)[a]	(134,65)[a]	136,7	141,3s	134,81	141,8
4	39,2tr	(31,87)[b]	39,78	39,4	38,7 tr	39,78	39,2
5	25,7tr	(26,16)[c]	(26,70)[b]	25,2	25,5 tr	26,71	26,0
6	123,6d	124,19	124,23	123,9	123,8d	124,92	
7	134,9s	(135,77)[a]	(135,53)[a]	134,5	133,5s	135,02	
8	36,4tr	(31,92)[b]	39,78	39,3	(33,7tr)[a]	36,89	
9	28,0tr	(26,66)[c]	(26,81)[b]	26,5	(32,7tr)[s]	29,94	26,0
10	78,3d	124 93	124,34	124,6	177,6s	78,28	123,4
11	81,2s	131,30	130,93	130,9	75 7s	73,14	131,6
12	24,9q	25,68	25,67	25,0	25,9q	23,22	25,4
13	16,5q	23,39	15,64	15,5	16 2q	16 00	16,5
14	15,9q	23,39	15 96	13,3	15,5q	16,00	
15	17,6q	17,69	17,64	17,0	15,9q	26,45	17,5

*The values of the signals, the interpretation of which was ambiguous, are given in parentheses.

values of the chemical shifts of the signals of the carbon atoms bearing secondary OH groups in squalene glycol and reoselin coincide. The signal of the carbon atom bearing the tertiary OH group in reoselin is located in a weaker field by 8 ppm than in squalene glycol and in a weaker field by 5.5 ppm than in karatavikin. This suggests that the carbohydrate moiety in reoselin is attached to the C_{11}—OH tertiary alcohol group and not to the C_{10}—OH secondary alcohol group as was previously assumed.

The values of the signals of the methyl groups of the gem-dimethyl grouping in squalene glycol are 23.22 and 26.45 ppm. In reoselin, they become still more nonequivalent (24.9 and 17.6 ppm). In DMSO this difference diminishes (24.2 and 18.6 ppm). The nonequivalence of the chemical shifts of the prochiral methyl groups in reoselin is apparently connected with the steric hindrance arising because of the presence of the cumbersome carbohydrate moiety at the tertiary hydroxyl. In reoselin, as also in squalene glycol, C-9, being present in the β-position with respect to the 10-OH group, is descreened by 2.3 ppm relative to C-5; C-8, in the γ-position with respect to the 10-OH group, is descreened by 2.7 ppm relative to C-4.

The CSs of the signals of the carbohydrate part of the reoselin spectrum (C.1' 94.4; C-2' 83.8; C-3' 76.3; C-4' 69.9; C-5' 76.3; C-6' 61.0; C-1" 105.2; C-2" 75.0; C-3" 76.3; C-4" 69.6; C-5" 76.3; C-6" 61.0) are very close to those of the carbohydrate moiety GLC(2-1)GLC [9] and of methyl O-β-D-glucopyranoside and differ from those in the spectrum of methyl O-α-D-glucopyranoside [10]. A considerable change in the downfield direction is also undergone by the C-2' signal and in the upfield direction by the C-1' signal as compared with the corresponding signals of the unsubstituted β-D-glucopyranoside. This is due to the glycosylation effect of the additional glucose residue at C-2' of the first one, i.e., the carbohydrate moiety of reoselin is that of β-D-sophorose.

The aglycon of reoselin, karatavikinol, has a negative rotation of the plane of polarized light, $[\alpha]_D^{20}$ —9.1° (c 0.7; ethanol) and the same structure of the molecule close to the single asymmetric center as S-(—)-dihydrosqualene glycol [11] and dihydrofarnesol [12, 13] (Fig. 1). The S configuration of this center in karatavikinol follows logically. S-(—)-Epoxysqualene is a biogenetic precursor of the 3-hydroxytriterpenoids and steroids. Reoselin and karatavikinol have been isolated from giant fennels a characteristic feature of which is the biosynthesis of bicyclic sesquiterpenoids umbelliferone derivatives with the enantiomeric configuration of the linkage of rings A and B by direct antiparallel cyclization.

Reoselin is the main glycoside of the resin of the roots of *F. kirialovii* collected by L. P. Markova in the Uzbek SSR (valley of the R. Ugam, July, 1958), by M. G. Pimenov in the Kazak SSR (northern slopes of the Ugam range, R. Sairamsu, August, 1970, and September, 1975), in the Kirghiz SSR (southern slopes of the Chatkal range, R. Kasai-sai, June, 1976), and in the Tadzhik SSR (Mogol-Tau range, May, 1976) and by L. V. Kuz'mina in the Uzbek SSR (Chatkal range, Mount Bolshoi Chimgan, June, 1976). The identity of the glycosides was established from the coincidence of their IR and ^{13}C NMR spectra.

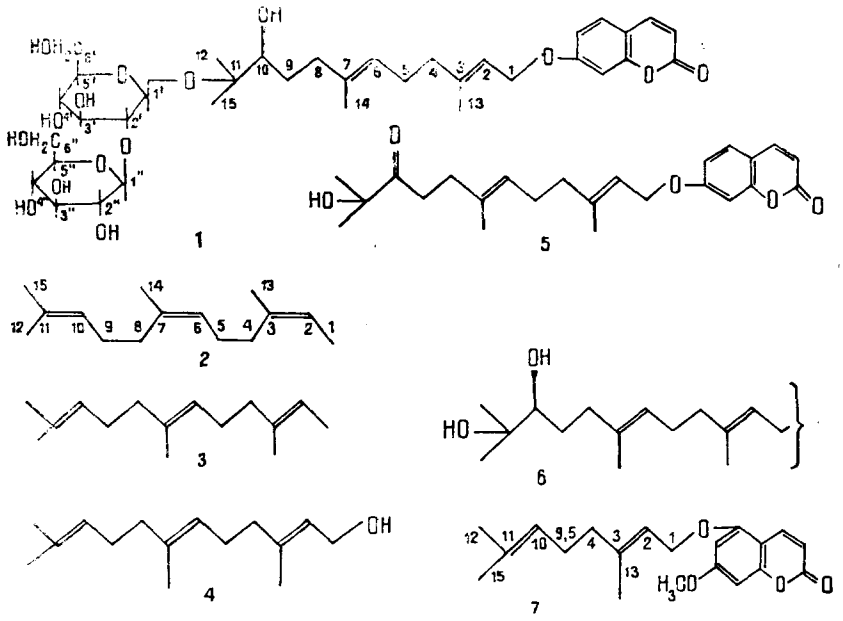

Fig. 1. Formulas of some terpenoids and terpenoid coumarins: 1) reoselin; 2) (2Z,6Z)-3,7,11-trimethyldodeca-2,6,10-triene; 3) (2E,6E)-3,7,11-trimethyldodeca-2,6,10-triene; 4) farnesol; 5) karatavikin; 6) 2,3-dihydroxy-2,3-dihydrosqualene; 7) 5-geranyloxy-7-methoxycoumarin. The names of the compounds are given in the forms used by the authors in the original publications; in this paper the numbering of the carbon atoms has been changed for convenience of comparing their chemical shifts.

EXPERIMENTAL

Angles of rotation were determined on an EPL-AI automatic laboratory polarimeter; the IR spectra of the substances in the form of mulls in paraffin oil were recorded on a UR-10 spectrometer; and ^{13}C NMR spectra were obtained on a Varian CFT-20 instrument using $CDCl_3$ as solvent and TMS as internal standard.

Isolation of Reoselin. The air-dry comminuted roots were covered with acetone and were steeped at room temperature for three days. The extraction was repeated three times. The combined acetone extract was concentrated in vacuum in a hot water bath. The concentrated extract (yield 11% on the air-dry weight) was dissolved in diethyl ether. The precipitate that formed was filtered off and was washed with cold acetone. After repeated crystallization from acetone, colorless crystalline druses were obtained with mp 155-156°C and composition $C_{36}H_{52}O_{15}$, $[\alpha]_D^{20}$ −24.4° (c 1; ethanol). Yield 0.7% on the air-dry weight of the roots. IR spectrum: ν_{max} 3400 s, 1720 s, 1709 s, 1610 s, 1555 w, 1510 w, 1465 s, 1455 s, 1400 sh, 1380 s, 1350 s, 1308 sh, 1283 s, 1235 s, 1203 m, 1180 sh, 1160 s, 1128 s, 1105 sh, 1080 s, 1035 s, 1020 sh, 930 w, 897 w, 950 sh, 840 s.

SUMMARY

Reoselin from the roots of *Ferula kirialovii* M. Pimen (*Ferula pseudooreoselinum* auct.) collected at five points of its area is S-(−)karatavikinol β-D-sophoroside at the tertiary hydroxy group, i.e., S-(−)-karatavikinol tertiary O-β-D-sophoroside.

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FLAVONOIDS OF *Haplophyllum perforatum*.

STRUCTURE AND HYPOAZOTEMIC ACTIVITY OF HAPLOSIDE C

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A new acylated glycoside of limocitrin has been isolated from the epigeal part of *Haplophyllum perforatum* (M.B.) Kar. et Kir. — haploside C — which has the structure of 3,4',5,7-tetrahydroxy-3',8-dimethoxyflavone 7-O-[O-α-L-rhamnopyranosyl-(1 → 2)-(6"-O-acetyl-β-D-glucopyranoside)]. It has been established that haploside C possesses a pronounced hypoazotemic action.

We have reported previously on the isolation of two new limocitrin glycosides from the epigeal part of the *Haplophyllum perforatum* (M. B.) Kar. et Kir. (family Rutaceae) and the determination of their structures [1].

In the present paper we consider the structure and hypoazotemic activity of new flavonol glycoside, haploside C (I). The presence in the UV spectrum of maxima at 260, 275*, 343*, and 385 nm (log ε 4.38, 4.20, 4.05, and 4.26) and qualitative reactions with magnesium in hydrochloric acid and with zirconium oxychloride in citric acid has permitted compound (I) to be assigned to the flavonol derivatives with a free hydroxy group in the C-3 position [2, 3]. A confirmation of this was the formation of limocitrin (3,4',5,7-tetrahydroxy-3',8-dimethoxyflavone (II)) on the acid hydrolysis of haploside C [1]. D-Glucose and L-rhamnose were detected in a hydrolysate of glycoside (I) by thin-layer and paper chromatography. It followed from UV spectra in the presence of diagnostic additives that haploside C had free hydroxy groups in the 3,4',5 positions [2].

Absorption bands in the IR spectrum at 1730 and 1264 cm^{-1} showed that the substance under consideration contained an ester functional group. In the PMR spectrum of the glycoside (I) at 2.02 ppm a singlet signal was observed corresponding to three proton units. The facts given indicated that haploside C contained one acetyl group.

The alkaline hydrolysis of compound (I) led to substance (II), which was found to be identical with haploside E [1] in its physicochemical constants and by a comparison of IR spectra. The acetyl derivative (IV) obtained by the reaction of glycoside (I) with acetic anhydride in pyridine was likewise identical with the peracetyl derivative of haploside E.

In the PMR spectrum of the TMS derivatives of haploside C, the signals of protons geminal to an acetyl group appeared at 4.14-4.45 ppm in the form of a two-proton multiplet with a geminal coupling constant of ~12 Hz. On passing from compound (I) to its de-aceylated analogs

*Inflection.

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