STUDY OF THE STRUCTURE AND STEREOCHEMISTRY OF FLAVONOID O-RHAMNOSIDES WITH THE AID OF PMR SPECTROSCOPY

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The PMR method has been used in the study of the structure and stereochemistry of a number of flavonoid rhamnosides. The systematic study of the PMR spectra of the native compounds and their TMS ethers and complete acetates has permitted the size of the oxide ring, the conformation of the rhamnose residue, and, in combination with the results of polarimetric analysis, the configuration of the glycosidic bond to be determined. Information on the size of the oxide ring is given by — in addition to, the $J_{2,3}$ proton coupling constant — the signals of the protons at C-5 in the spectra of the full acetates. In the diagnostic region of 3.2–4.0 ppm, only the proton H-5 resonates in the rhamnopyranosides, while for the rhamnofuranosides a different structure of the H-4 signal must be expected. It has been shown that all the compounds studied (more than 20 specimens) are α-L-rhamnopyranosides and have the $^{1}C_{4}$ conformation of the sugar residue. In view of this, the hypothesis has been expressed that the existence of natural flavonoid rhamnosides in the furanoside form is improbable.

The use of proton magnetic resonance for studying a number of flavonoid O-arabinosides and xylosides has permitted us to determine their structures, the conformations of the pentose residues, and the configurations of the glycosidic bonds, and also to put forward a method for determining the size of the oxide rings of the pentose residues [1]. In this connection it was shown that the signals of the protons at C-5 in the spectra of the four acetates are diagnostic.

We have subjected flavonoid rhamnosides to a detailed study with the aim of obtaining information for solving structural and stereochemical problems. For this purpose we have made a systematic study of the PMR spectra of a number of specimens isolated from plant sources by various workers:

kaempferol 3-O-α-L-rhamnoside (afzelin, I), which we isolated from *Pithecellobium dulce* [2] and *Aflatunia ulmifolia* [3];

quercetin 3-O-α-rhamnoside (quercitrin, II), isolated from *Godetia whitneyi* [4], *Hypericum maculatum* [5], *Aflatunia ulmifolia* [6], and *Pithecellobium dulce* [2];

myricetrin 3-O-α-L-rhamnoside (myricitrin, III), isolated from *Sedum selskianum* [7], and also obtained by us from N. F. Komissarenko;

2"-galloylmyricitrin (gallomyricitrin, IV) isolated from *Sedum selskianum* [8];

kaempferol 7-O-α-L-rhamnoside (V), isolated from *Sedum pallescens* [9] and obtained by the partial hydrolysis of kaempferol 3,7-dirhamnoside [9] and of robinin [10] kindly supplied by Dr. Barbara Vermesz (Budapest, Hungary), by Dr. V. I. Glyzin (Moscow, VILR), and by Dr. N. F. Komissarenko (Khar'kov, KhNIKhFI [Khar'kov Scientific-Research Institute of Pharmaceutical Chemistry]);

isorhamnetin 7-O-α-L-rhamnoside (VI), obtained in the partial hydrolysis of brassidin (isorhamnetin 3-O-β-D-glucoside 7-O-α-L-rhamnoside) [11], and provided by N. F. Komissarenko;

herbacetin 6-O-α-L-rhamnoside (VII), isolated from *Rhodiola rosea*;

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TABLE 1. Details of the PMR Spectra of the Rhamnosyl Fragments in Compounds (I–XII) and Their Derivatives

Compound	Solvent	Chemical shifts of the rhamnose protons, δ, ppm						Coupling constants, Hz				
		H-1	H-2	H-3	H-4	H-5	3H-6	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4.5}$	$J_{5,6}$
Afzelin (I)	C_5D_5N.	6,24	5,05	4 52	4,0–4,4		1,37	0	3	10	—	6
Acetate of I	C_6D_6	6,00	6,10	5,70	5 40	3,6	1,00	2	3	10	10	6
Acetate of I	$CDCl_3$	5,60	5,66	5,30	4,93	3,3	0,80	2	3	10	10	6
Quercitrin (II)	C_5D_5N	6,18	5,00	4,60	4,2—4,5		1,40	0	3	10	—	6
TMS ether of II	CCl_4	5,00	4,20	3,56	3,36	2,9	0,70	2	3	9,5	9,5	6
Acetate of II	$CDCl_3$	5,50–5,55		5 14	4,84	3,2	0,83	0	3	10	10	6
Myricitrin (III)	C_5D_5N	6,12	5,00	4,1—4,7			1,43	2	3	—	—	6
TMS ether of III	CCl_4	4,90	4,10	3,50	3,30	3,9	0,75	2	3	9,5	9,5	6
TMS ether of gallomyricitrin (IV)	CCl_4	5,30	5,60	4,93	3,3—3,6		0,90	2	3	—	—	—
Acetate of IV	$CDCl_3$	5 9		5,26	4,92	3,3	0,95	0	3	10	10	6
Kaempferol 7- rhamnoside (V)	C_5D_5N	6,20	4,2–4,7				1,60	0	—	—	—	6
TMS ether of V	CCl_4	5 17	3 4–3,9				1,17	2	—	—	—	6
Acetate of V	C_6D_6	5,27	5,70	5,80	5,50	3,9	1,12	0	3	10	10	6
Acetate of V	$CDCl_3$	5,3–5,6			5,18	3,9	1,20	—	—	10	10	6
Isorhamnetin 7-rhamnoside (VI)	C_5D_5N	6,24	4,20—4 70				1,60	0	—	—	—	6
Acetate of VI	C_6D_6	5,36	5,74	5,80	5,50	3,9	1,13	2	3	10	10	6
Acetate of VI	$CDCl_3$	5,40–5,64			5,20	3,9	1,23	—	—	10	10	6
Herbacetin 7-rhamnoside (VII)	$(CD_3)_2CO$	5,72	1,20	4,00	3,63	3,7	1,30	2	3	9,5	9,5	6
Acetate of VII	C_6D_6	5,10	5,60	5,70	5,50	4,0	1,12	2	3	9,5	9,5	6
Acetate of VII	$CDCl_3$	5,57	5,46	5,38	5,18	3,9	1,18	2	3	9,5	9,5	6
Kaempferol 3,7-dirhamnoside (VIII) 3R*	C_5D_5N	6,24	4 0–5,2				1,40	0	—	—	—	6
7R*		6,20	4,0–5,2				1,60	0	—	—	—	6
TMS ether of VIII 3R	CCl_4	5,00	4,26	~3,8	3,20	3,0	0,77	2	3	9,5	9,5	6
7R		5,17	3,86	3,3–3,8			1,17	2	3	—	—	6
Acetate of VIII 3R	C_6D_6	5 2—6,3				3,7	1,00	—	—	—	10	6
7R		5 2—6,3				3,9	1,14	—	—	—	10	6
Acetate of VIII 3R	$CDCl_3$	5,0—5,7			4,90	3,3	0,80	—	—	10	10	6
7R		5,0–5,7				3,9	1,20	—	—	—	10	6
Acetylpectinolinarin (IX)	C_5D_5N	5,35	4,0–4,7		5,60	—	1,20	0	—	10	10	6
TMS ether of IV	CCl_4	4,35	3,3–3,9		4,76	—	0,78	0	—	9,5	9,5	6
TMS ether of IV	C_6D_6	4,52	—	3,85	5,25	3,7	0,90	2	3,2	9,5	9,5	6
Isopropylidenedatiscin (X)	$(CD_3)_2CO$	4,86	4,05	3,90	3,0–3,6		1,17	0	5	8	—	6
Isopropylidenequercitrin (XI)	$(CD_3)_2CO$	5,90	4 50	4,00	3,40	3,2	0,85	0	5	8	10	6
Acetate of XI	$CDCl_3$	5,83	4,58	4,20	4 76	3,2	0,70	0	5	8	10	6
Phenyl O-α-L-rhamnopyranoside (XII)	$(CD_3)_2CO$	5,50	4,1—4,3			3,6	1,22	2	—	—	10	6
Acetate of XII	C_6D_6	5,33	5,66	5,80	5,45	4,0	1,10	2	3	10	10	6
Acetate of XII	$CDCl_3$	5,4		5,57	5,20	4,0	1,22	—	3	10	10	6
Phenyl O-β-D-rhamnopyranoside (XIII)	$(CD_3)_2CO$	5,25	3.4—4,1				1,30	2	—	—	—	6
Acetate of XIII	C_6D_6	4,74	5 83	5,17	5,42	3,2	1,18	2	3	10	10	6
Acetate of XIII	$CDCl_3$	5,26	5,65	5,0—5,2		3,7	1,34	2	3	—	10	6

*3R — rhamnose residue in position 3; 7R — rhamnose residue in position 7 of kaempferol.

kaempferol 3,7-di-O- α-L-rhamnoside (VIII), isolated from *Sedum pallescens* [9] and provided by V. I. Glyzin;

4‴-acetylpectolinarin (IX), isolated from *Linaria* sp. [12, 13];

2‴, 3‴-isopropylidenedatiscin (X), obtained by the reaction of datiscin with acetone [14]; and

2‴, 3‴-isopropylidenequercitrin (XI), obtained by the reaction of quercitrin (IV) with acetone [14].

As model compounds for comparison we used synthetic samples: phenyl O-α-L-rhamnopyranoside (XII) and phenyl O-β-L-rhamnopyranoside (XIII).

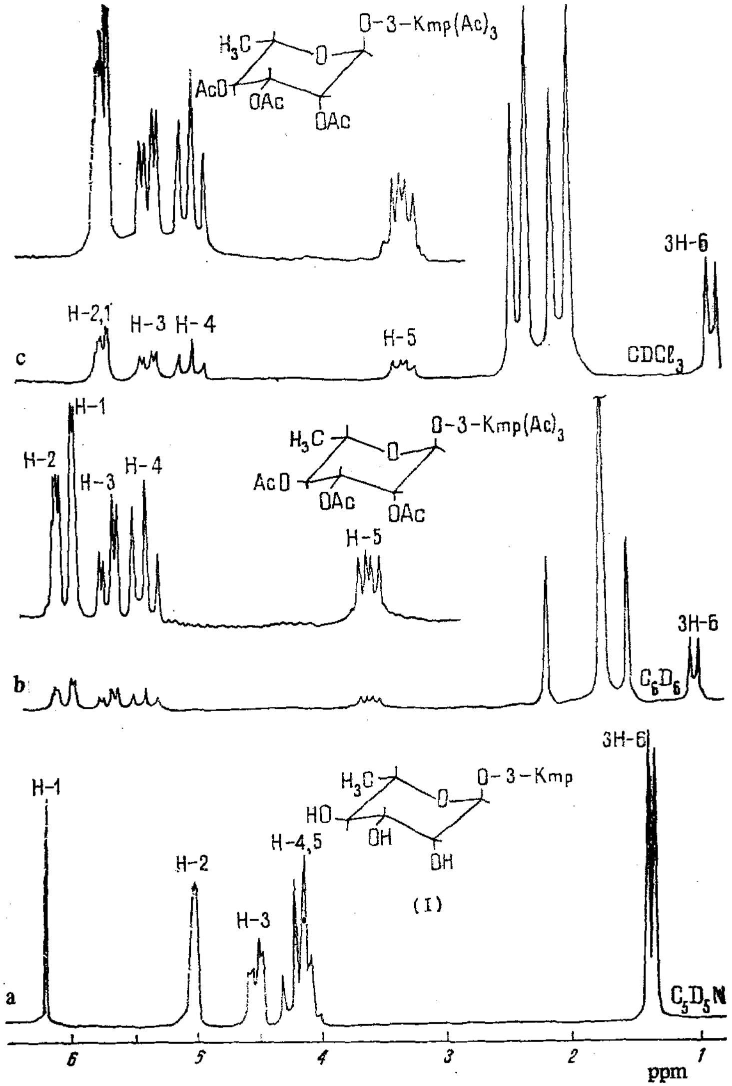


Fig. 1. Fragments of the PMR spectrum of afzelin (I) in [D]-pyridine (a), and of the acetate of (I) in [D]benzene (b), and [D]chloroform (c).

We made a comparative analysis of the PMR spectra of these compounds, of their full acetates, and of their trimethylsilyl ethers (TMS ethers) with the aim of finding a correlation between the vicinal spin—spin coupling constants (SSCCs) of the protons and the structure of the rhamnose residue (size of the oxide ring and its conformation, and the configuration of the glycosidic bond). Samples of one and the same compound obtained from different sources (for example, four samples of quercitrin 3-rhamnoside, six samples of kaempferol 7-rhamnoside, etc.) had identical spectra.

It is known [15] that, in a population of molecules of a given substance, molecules having the most stable conformation corresponding to the minimum free energy predominate. The energy of a conformer in the boat form exceeds that of conformers in the chair form. On the basis of the results of a calculation of the free conformational energy of the chair-form conformers of D-aldohexopyranoses [15, p. 116] it may be expected that the two anomers of L-rhamnopyranose will exist in aqueous solution predominantly in the form of the $^1C_4$ conformers. It has been established by the x-ray and neutron diffraction methods that derivatives of hexopyranoses with the manno configuration exist in the crystalline state as the $^4C_1$ (D) or the $^1C_4$ (L) conformers.

Four chair-type conformational formula are possible for L-rhamnopyranosides (6-deoxy-L-mannosides):

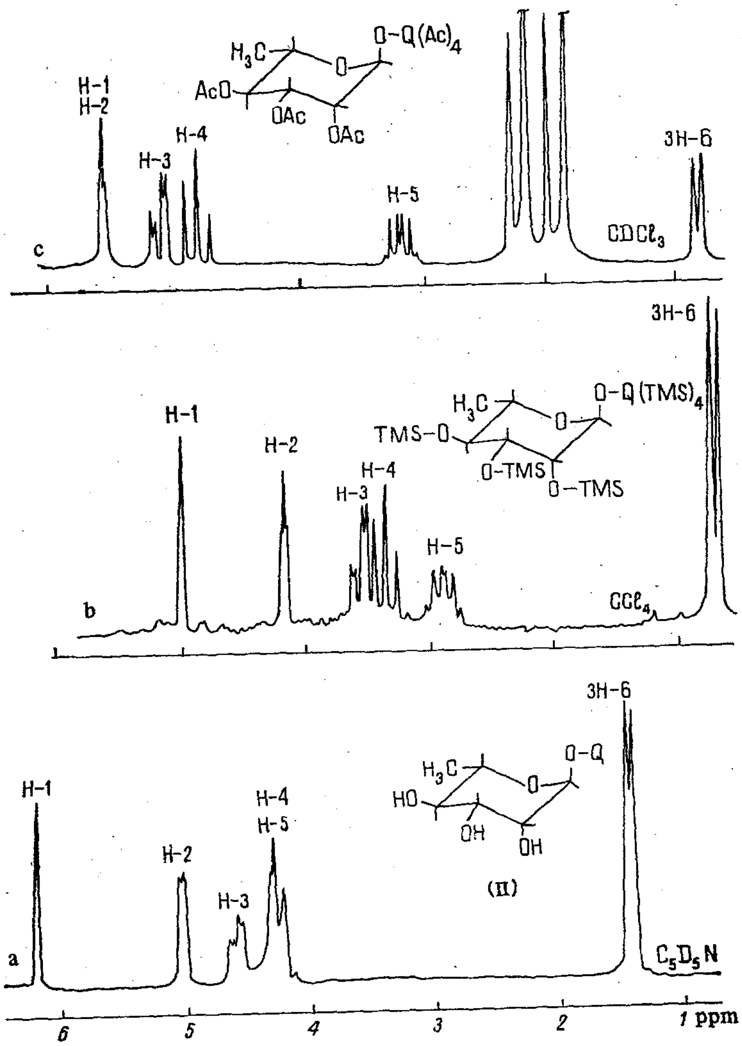
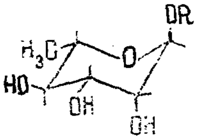
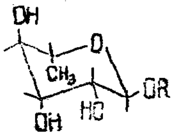


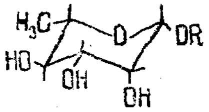
Fig. 2. Fragments of the PMR spectra of quercitrin (II) in [D]pyridine (a), of the TMS ether of (II) in CCl$_4$ (b), and of the acetate of (II) in [D]chloroform (c).



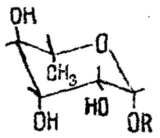
α-L($^1C_4$)



α-L($^4C_1$)



β-L($^1C_4$)



β-L($^4C_1$)

Since it is known that a definite correlation exists between the coupling constants of the vicinal protons and the conformations [16], let us analyze these parameters of the PMR spectra, which are given in Table 1. A comparison shows that, with the exception of compounds (X) and (XI), the SSCCs of the vicinal protons of the rhamnose residues are the same in all cases: $J_{1,2} \approx 2$ Hz, $J_{2,3} \approx 3$ Hz, $J_{3,4} \approx 10$ Hz, $J_{4,5} \approx 10$ Hz.

Evidence of the presence of a rhamnose residue in a flavonoid molecule is the characteristic signal of the methyl group in the form of a doublet with a coupling constant of about 6 Hz at $\delta \approx 0.7$–1.6 ppm (Table 1 and Figs. 1–8).

A strong influence on the chemical shifts of the signals of the protons on the rhamnose residue is exerted by its position: attachment to position 3 or 7 of the flavonoid moiety of the molecule or to another carbohydrate residue [the rutinosides (IX) and (X)]. In all the 3-rhamnosides (I-IV) and their derivatives, the ^{1}H NMR spectra approximate to first-order spectra, and the signals of the rhamnose protons are readily and completely identified (see

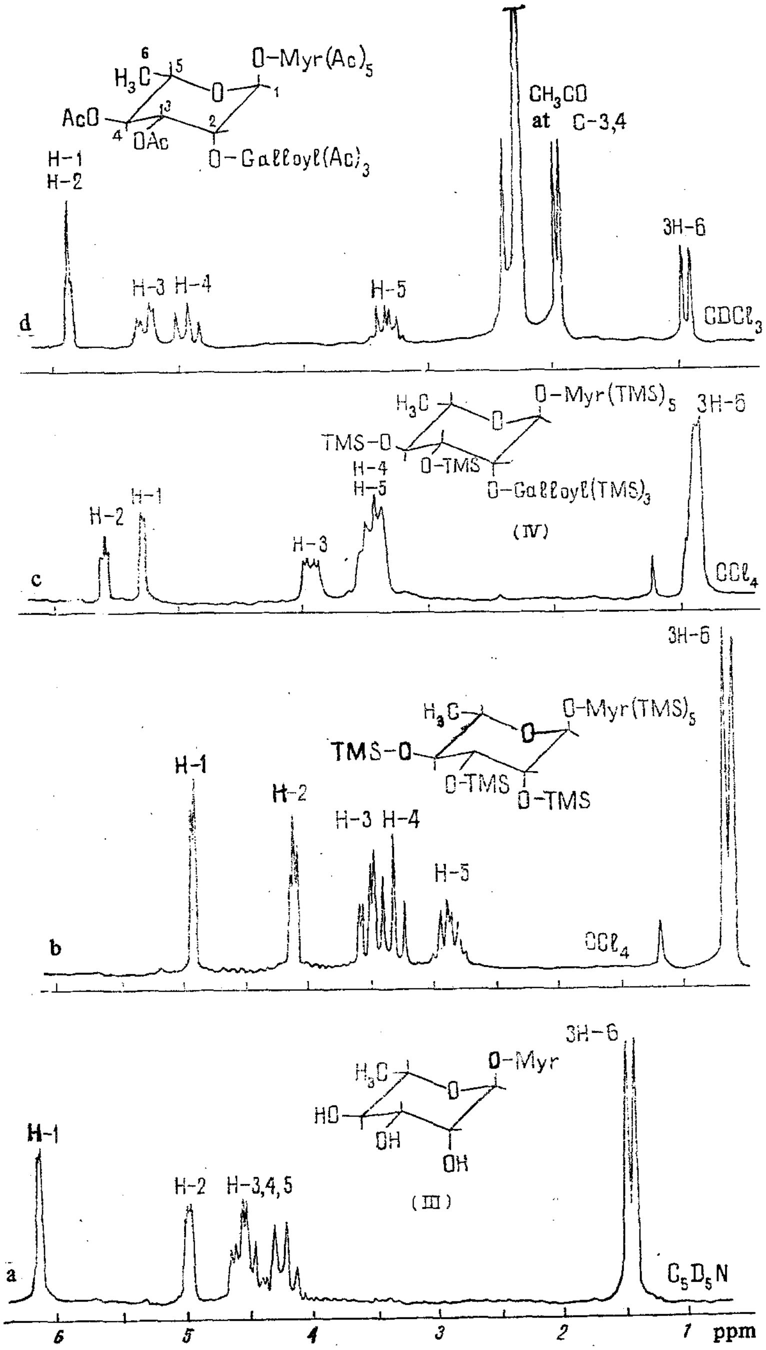


Fig. 3. Fragments of the PMR spectra of myricitrin (III) in [D]pyridine (a), of the TMS ether of (III) in CCl_4 (b), of the TMS ether of gallomyricitrin (IV) in CCl_4 (c); and of the acetate of (IV) in [D]chloroform (d).

Figs. 1-3). In the spectra of the 7-rhamnosides and their derivatives (Table 1 and Figs. 4 and 5), the H-2,3,4,5 protons resonate in a very narrow region and the signals overlap not only in pyridine but also in CCl_4 (TMS ethers), and for this reason the spectra differ considerably from those of the 3-rhamnosides. For the 7-rhamnosides (V—VII), the complete assignment of the signals becomes possible only in the full acetates, although here also, the H-1,2,3,4 protons form a narrower group of signals than in the case of the acetates of the 3-rhamnosides. The observed difference in the PMR spectra of the 3- and 7-rhamnosides is obviously connected with the fact that the free rotation of the rhamnosyl residue in the 3-glycosides is hindered and the anisotropic action of the lateral phenyl group and the carbonyl of the flavone part of the molecule is therefore greatly affected. It must be

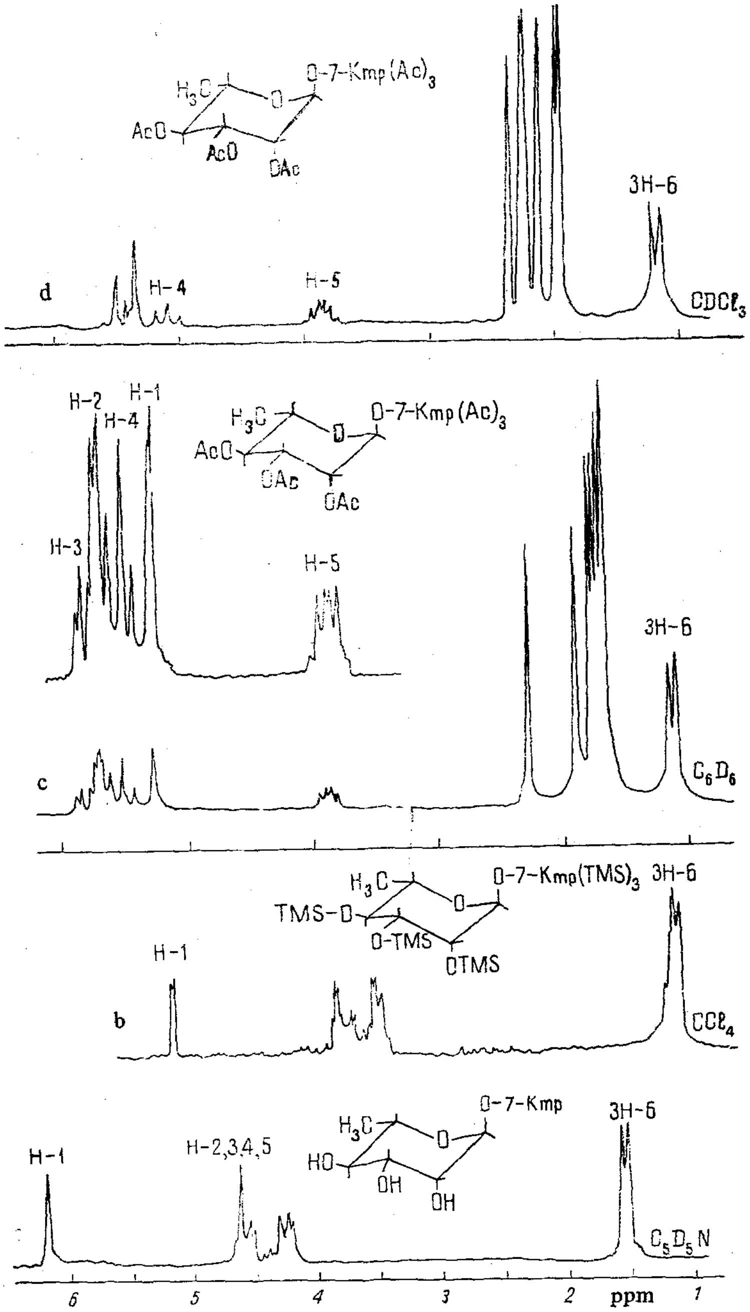


Fig. 4. Fragments of the PMR spectra of kaempferol 7-rhamnoside (V) in [D]pyridine (a), of the TMS ether of (V) in CCl_4 (b), and of the acetate of (V) in [D]benzene (c) and [D]chloroform (d).

noted that steric factors also probably affect the size of the angle of rotation, which is smaller in the 7-rhamnosides than in the 3-rhamnosides:

Compound	$[\alpha]_D^{20}$, deg
Afzelin (I)	–237 (1.0; methanol)
Quercitrin (II)	–182 (1.0; methanol)
Myricitrin (III)	–160 (0.5; methanol)
Gallomyricitrin (IV)*	–40 (0.6; methanol)

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*Gallomyricitrin (IV), which has a small specific rotation, is converted by saponification under mild conditions into myricitrin (III).

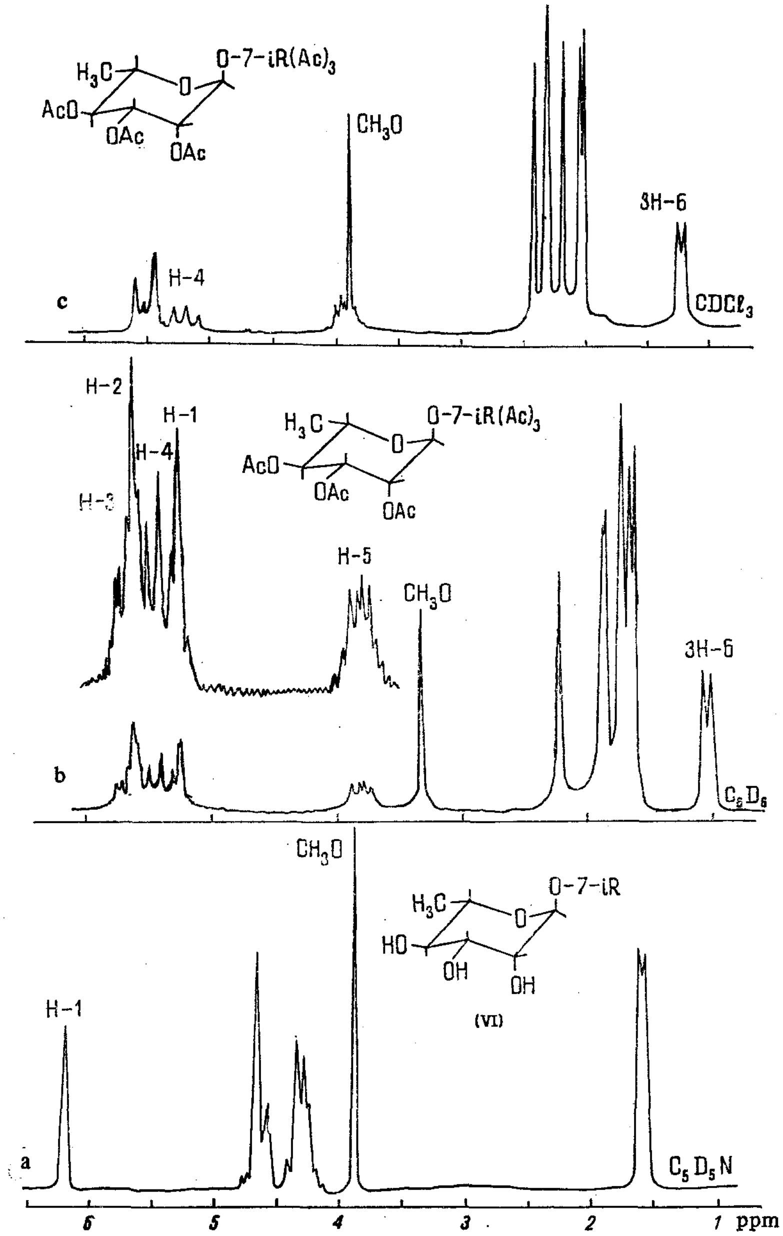


Fig. 5. Fragments of the PMR spectra of isorhamnetin 7-rhamnoside (VI) in [D]pyridine (a), and of the acetate of (VI) in [D]benzene (b) and [D]chloroform (c).

Compounds	$[\alpha]_D^{20}$, deg
Kaempferol 7-rhamnoside (V)	−140 (0.2; methanol)
Isorhamnetin 7-rhamnoside (VI)	−137 (0.2; methanol)
Herbacetin 7-rhamnoside (VII)	−150 (0.2; ethanol)
Kaempferol 3,7-dirhamnoside (VIII)	−224 (0.5; methanol)
Acetylpectolinarin (IX)	−95 (0.4; formamide)
Isopropylidenedatiscin (X)	−66 (0.6; acetone)
Isopropylidenequercitrin (XI)	−76 (0.1; acetone)
Phenyl α-L-rhamnopyranoside (XII)	−92 (0.5; water)
Phenyl β-L-rhamnopyranoside (XIII)	+87 (0.5; water)

In the case of the acetates of the 7-rhamnosides, passage from $CDCl_3$ to C_6D_6 does not affect the chemical shift of the H-5 signal (∼3.9 ppm) (similarly, in (XII) it is 4.0 ppm), but it causes a paramagnetic shift in the case of the 3-rhamnosides (3.3 → 3.6 ppm) and a diamagnetic shift in the case of compound (XIII) (3.7 → 3.2 ppm). Thus, the 3.2-4.0 ppm

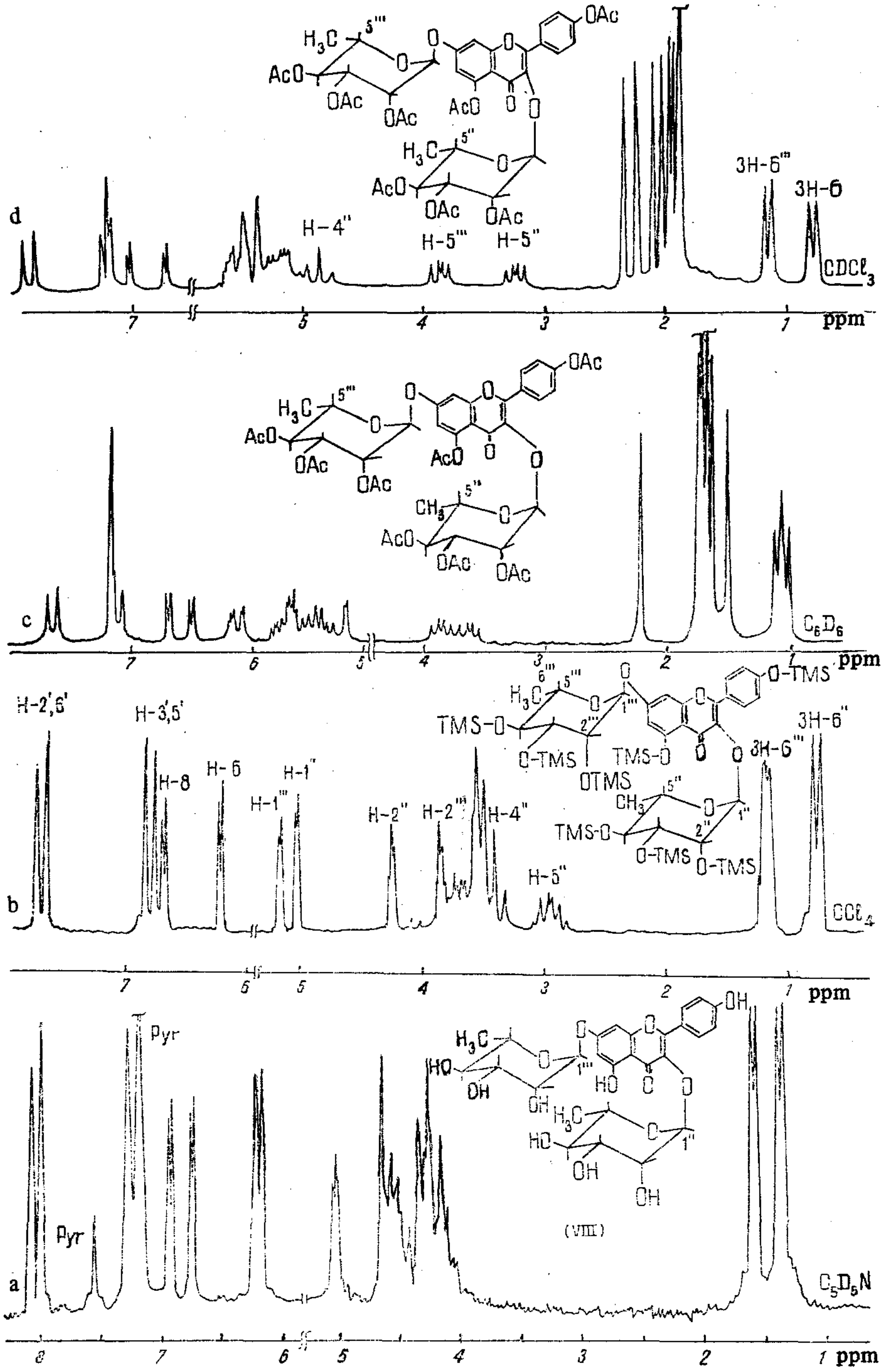


Fig. 6. PMR spectra of kaempferol 3,7-dirhamnoside (VIII) in [D]pyridine (a), of the TMS ether of (VIII) of CCl_4 (b), and of the acetate of (VIII) in [D]benzene (c) and [D] chloroform (d).

region can be recommended as diagnostic in the analysis of acetates of flavonoid rhamnosides.

In the compounds considered (I—VII), as also in the model substances (XII) and (XIII), the observed SSCCs of the vicinal protons characterize them as L-rhamnosides in the predominant $^1C_4$ conformation. In these compounds, the $^4C_1$ conformation is impossible, since if it existed the spectrum would not have the signal in the form of a triplet with two diaxial constants ($J_{3,4} = J_{4,5} = 10$ Hz) that is characteristic for H-4, because in the $^4C_1$ conformation there is no axial proton with two axial neighbors. Furthermore, the α-L($^4C_1$) conformer would have the signal of the anomeric proton in the form of a doublet with a large

SSCC (J_{aa} about 8 Hz). Thus, in all the cases considered the $^1C_4$ conformer of the L-rhamnopyranose residue predominates in the resonance state at room temperature.

On the basis of the model compounds (XII) and (XIII), it can be seen that the determination of the anomeric configuration from the PMR spectra is difficult, since the coupling constant between H-1 and H-2 (about 2 Hz) can be assigned both to the α anomer (ee) and to the β anomer (ae). The dihedral angles between these protons in the $^1C_4$ conformation are identical (60°) and the observed SSCC can be assigned with confidence either to J_{ee} (0.6—3.5 Hz) or to J_{ae} (1.5—5.8 Hz) only if its magnitude lies outside the region of overlapping of the ranges of these constants [16]. Consequently, the choice between the two anomers was made with the aid of polarimetric analysis. The large value and negative sign of the specific rotation in combination with the features of the NMR spectra characterize the substances isolated (I—VII) as α-L-rhamnopyranosides.

It can be seen from a comparison of the spectra (Figs. 1—8) that in deuteropyridine the nature of the spectrum becomes more complicated; the rhamnose signals in it partially overlap and therefore the assignment is not possible for all the protons even though the signal of the anomeric proton is distinguished even in this case. Far more informative are the spectra of the TMS ethers and the acetates, where individual signals of the protons can be seen for almost all the compounds. Nevertheless in order to avoid incorrect conclusions concerning structure, it is desirable to record the spectra of the native glycosides, as well, in acetone or pyridine, particularly in view of our experience of work with guaiaverin (quercetin 3-O-α-L-arabinopyranoside) for the TMS ether of which an inversion of the arabinopyranose ring was detected [1].

The spectra of kaempferol 3,7-dirhamnoside (VIII) and its derivatives in all solvents are the sum of the signals of the carbohydrate protons of kaempferol 3-rhamnoside and 7-rhamnoside (compounds (I) and (V)). The chemical shifts and the multiplicities of the signals, the assignment of which is made in Fig. 6, coincide completely. This permits the conclusion that both rhamnoside residues have the pyranoid form, and compound (VIII) is kaempferol 3,7-di-O-α-L-rhamnopyranoside. This conclusion is confirmed by the fact that kaempferol 7-rhamnoside obtained on the partial hydrolysis of (VIII) is, as has been shown above, the α-L-rhamnopyranoside.

The spectra of rutinosides are far from being first-order spectra and their simplification cannot be achieved by changing the solvent. However, in the two rutinosides under discussion (IX and X), some of the rhamnose signals can be identified, since they undergo a paramagnetic shift thanks to the presence of geminal substituents. In the case of acetylpectinolinarin (IX) such a substituent is the acetyl group, and the gem-acyl proton forms a triplet in the weak field (Fig. 7a, b). To prove the position of the acetyl group we used the INDOR method [13] with the aid of which it was possible to elucidate the structure of the signals of the protons vicinal to the gem-acyl proton. The INDOR spectrum of the TMS ether of (IX) in deuterobenzene was obtained on lines 1 and 3 of the triplet (δ 5.25, $J_1 = J_2 = 9.5$ Hz) and on lines 4 and 5 of the doublet (δ 0.90, J = 6 Hz). It can be seen from the spectrum (Fig. 7c) that one of the signals is a quartet (3.85 ppm), the distance between lines 1 and 2 of which is 3.2 Hz, while the distance between lines 1 and 3 is 9.5 Hz. In glucose, all the protons are in the trans position with respect to one another, and large (more than 8 Hz) values of the coupling constants correspond to them [16]. Thus, the existence of a small constant (3.2 Hz) indicates that the acetyl group is located in the rhamnose residue. Two large constants of vicinal protons in rhamnose are realized only for the C-4 position, i.e., only this position is possible for the acetyl group. The quartet at 3.85 ppm thus relates to the H-3 proton of the rhamnose residue. The second signal (3.6 ppm) obtained in the INDOR spectrum is assigned to the H-5 proton of the rhamnose residue, although it has a different structure: INDOR on the lines of the triplet causes the appearance of a quartet with SSCCs of 6 and 9.5 Hz while on the lines of the doublet — through additional coupling with H-4 — a doublet of quartets shifted by 9.5 Hz relative to one another appears. Thus, INDOR has permitted the elucidation of the structures of all the signals of the rhamnose protons and their SSCCs also indicate the $^1C_4$ conformation of the L-rhamnose residue in the rutinoside (IX).

In the PMR spectrum of the second rutinoside [2''', 3'''-isopropylidenedatiscin (X)] a small paramagnetic shift is observed for the signals of two protons (Fig. 8a), the assignment

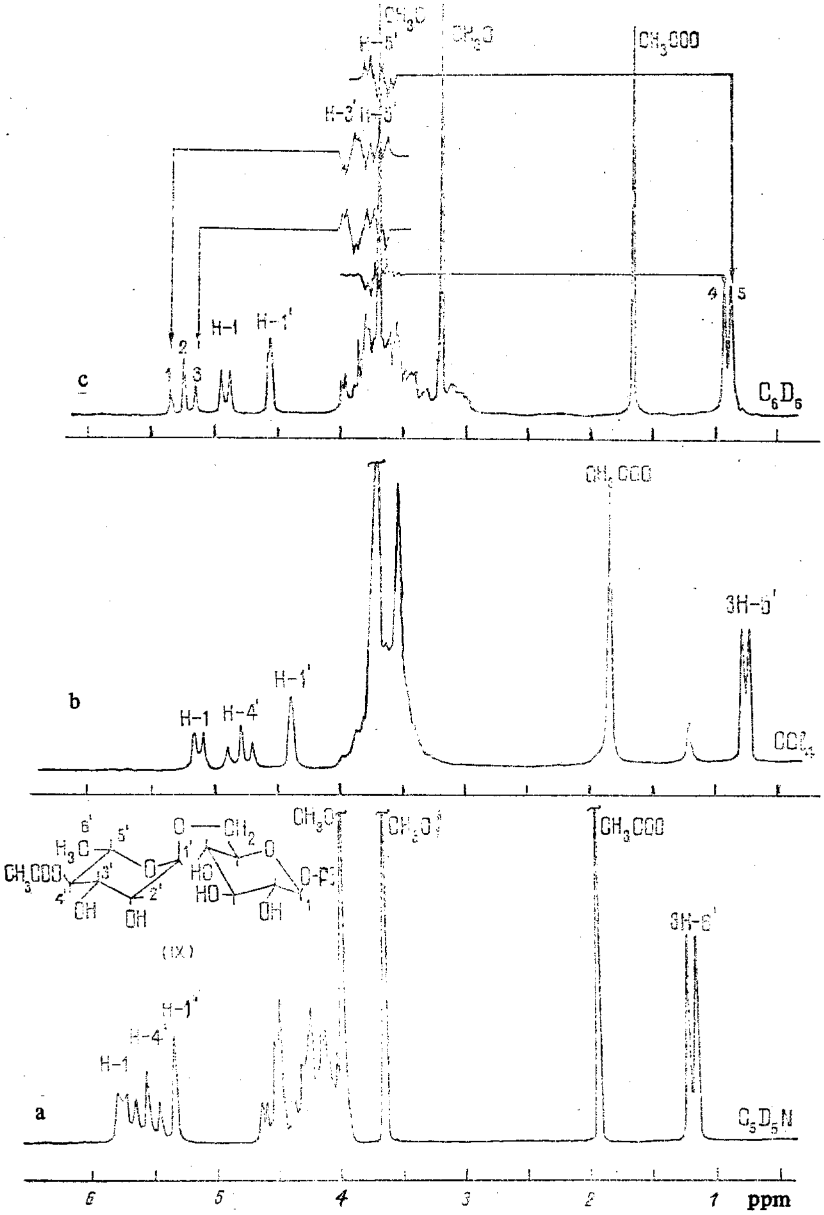
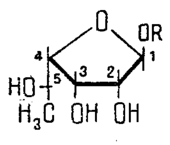


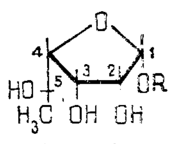
Fig. 7. Fragments of the PMR spectra of acetylpectinolinarin (IX) in [D]pyridine (a), of the TMS ether of (IX) in CCl_4 (b), and in [D]benzene (c) and the INDOR spectrum (c).

of which was made on the basis of the results of a comparison with isopropylidenequercitrin [(XI), Fig. 8b, c]. In compounds (X) and (XI) the signals of the rhamnose protons had different SSCCs (Table 1), and therefore we had recourse to the calculation of the dihedral angles with the aid of the Karplus equation (see the Experimental part). It is obvious on a Dreiding model that the closure of the five-membered dioxolane rings in the formation of the isopropylidene derivatives (X) and (XI) causes a distortion of the $^1C_4$ chair conformation of the α-L-rhamnopyranose residues, and the measured projection angles agree well with those calculated on the basis of the SSCCs. Detailed information has been reported in the literature on the 2,3-isopropylidene derivative of α-D-lyxopyranoside, in which the pyranose ring likewise had a slightly distorted chair conformation [17].

Let us analyze the possibility of assigning the compounds studied to the rhamnofuranosides:



α-L-Rhamnofuranoside



β-L-Rhamnofuranoside

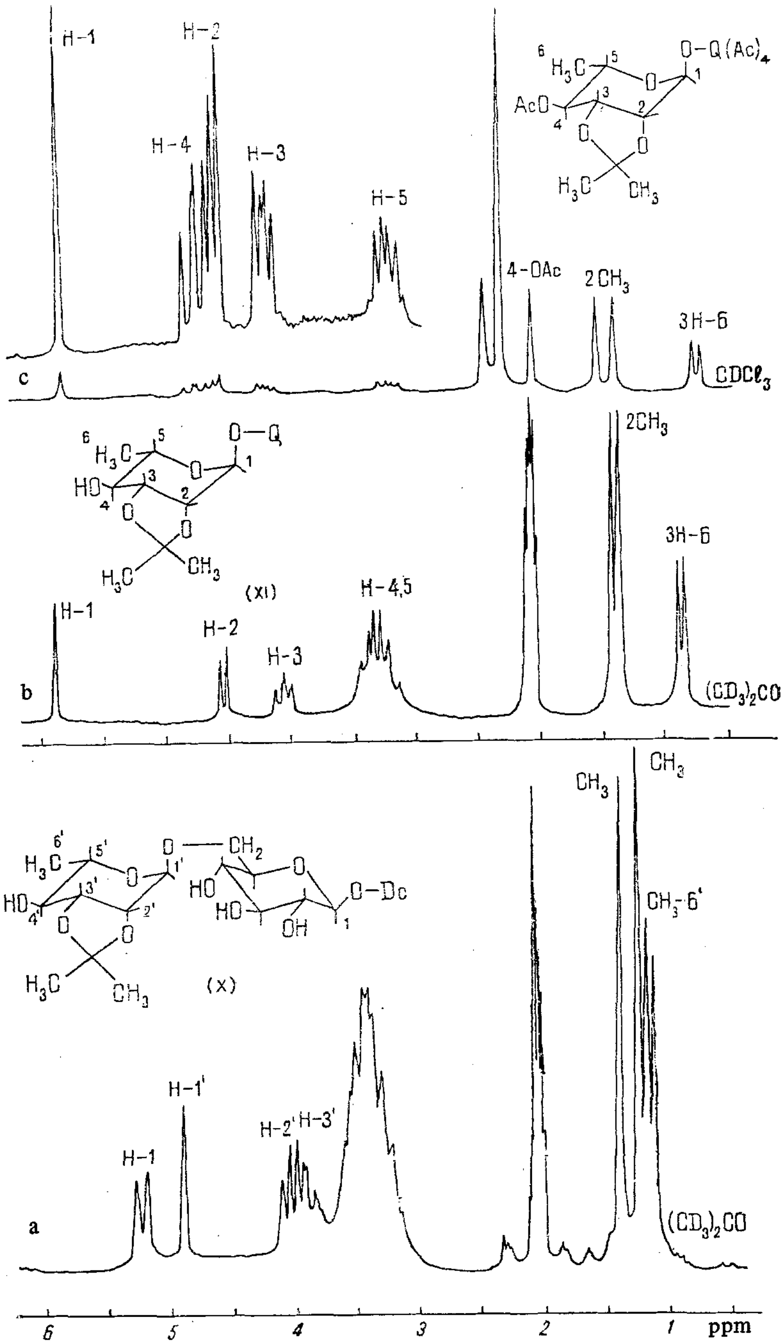


Fig. 8. Fragments of the PMR spectra of isopropylidenedatiscin (X) in [D]acetone (a), of isopropylidenequercitrin (XI) in [D]-acetone (b), and of the acetate of (XI) in [D]chloroform (c).

It has been shown for the O-acylated pentofuranoses [18] and N-β-D-furanosides [19], as examples, that the SSCCs for the vicinal cis hydrogens are in the range of 4.3–6.8 Hz, and for trans hydrogens they vary from very small values (<0.5 Hz) to 7.2 Hz. A considerable overlapping between these two ranges of coupling constants makes it difficult to assign cis or trans mutual positions for neighboring hydrogens in a five-membered ring if the SSCC between these hydrogens is more than 4 Hz. However, if the SSCC is less than 4 Hz it can be reliably assigned to neighboring hydrogens with the trans arrangement.

In a β-rhamnofuranoside, all four protons of the ring have the cis configuration, and the constants $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ must be in the range of 4.3–6.8 Hz. In the compounds that we have investigated $J_{1,2}$ has a value of 0 or 2 Hz, and this gives grounds for excluding

TABLE 2

Compound	Vicinal coupling constant, J, Hz	Dihedral angles, degrees	
		calculated from the Karplus equation	measured on a Dreiding model
			$^1C_4$ conformation
I—IX, XII, XIII	$J_{1,2} = 2$	$J_{1,2}$ = 58 and 118	60°
	$J_{2,3} = 3$	$J_{2,3}$ = 51 and 125	60°
	$J_{3,4} = 10$	$J_{3,4}$ = 0 and 180	180°
	$J_{4,5} = 10$	$J_{4,5}$ = 0 and 180	180°
	$J_{5,6} = 6$		
			Distorted $^1C_4$ conformation
X, XI	$J_{1,2} = 0$	$J_{1,2}$ = 78 and 99	78
	$J_{2,3} = 5$	$J_{2,3}$ = 38 and 138	35
	$J_{3,4} = 8$	$J_{3,4}$ = 9 and 158	155
	$J_{4,5} = 10$	$J_{4,5}$ = 0 and 180	180
	$J_{5,6} = 6$		

a rhamnofuranoside with a β-orientated substituent at the glycosidic center. However, the α anomer is also impossible, since the $J_{2,3}$ and $J_{3,4}$ SSCCs in our compounds are, respectively, 3.0—3.2 Hz and 9.5—10 Hz.

Furthermore, as a diagnostic criterion for determining the size of the oxide ring of a rhamnose residue we have recommended the region of the signals of the proton at C-5 in the spectra of the full acetates. For rhamnopyranosides, the H-5 signal consists of a doublet of quartets with $J_{4,5}$ = 10 Hz and $J_{5,6}$ = 6 Hz. This signal is always slightly "diffuse" because of the small components of the quartets and it is easy to identify in the spectra of the acetates, since it is the only one remaining in a comparatively strong field (3.2—4.0 ppm) and the signals of the other rhamnose protons (the anomeric and the gem-acyl methyl protons) undergo a considerable paramagnetic shift and are located in the range of approximately 5—6 ppm.

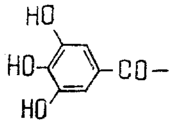
In contrast to the pyranosides, in the furanosides there is not only a proton but also an OH group at C-5, and after acetylation the gem-acyl H-5 proton will be shifted downfield and the signal of the H-4 proton will remain in the strong field and will differ in structure from the H-5 signal of a pyranose (in any case, one must expect considerably smaller values of the $J_{4,5}$ constant). Thus, as was to be expected on the basis of energy factors, all the specimens considered are $^1C_4$ conformers of α-L-rhamnopyranosides. Our results, and also information in the literature [10], force a critical analysis of the cases of the isolation of flavonoid rhamnofuranosides and other glycosides for which the presence of an aldofuranose residue has been shown solely on the basis of IR spectra and molecular rotation values. The possibility of the existence and, all the more, of the wide distribution in plants of flavonoid rhamnosides in the furanoid form appears to us to be unlikely.

EXPERIMENTAL

The physicochemical constants of the glycosides (I—XIII) corresponded to those given in the literature [2—14, 20]. Generally-adopted methods were used to obtain the complete acetates of the glycosides (acetic anhydride, pyridine) and their trimethylsilyl ethers (pyridine, chlorotrimethylsilane, hexamethyldisilazane).

The proton magnetic resonance spectra were obtained on a Varian HA-100D, 100 MHz instrument with tetramethylsilane as internal standard. The figures show fragments of the spectra including the regions of resonance of the carbohydrate protons. The following arbitrary symbols are used in the figures:

Kmp — kaempferol (3,4',5,7-tetrahydroxyflavone);
Q — quercetin (3,3',4',5,7-pentahydroxyflavone);
Myr — myricetin (3,3',4',5,5',7-hexahydroxyflavone);
Pl — pectolinarigenin (5,7-dihydroxy-4',6-dimethyoxyflavone);
Dc — datiscetin (2',3,5,7-tetrahydroxyflavone);
Ac — CH_3CO—;
TMS — $(CH_3)_3Si$—
Galloyl —



With the aid of a transformed Karplus equation [16, p. 396], from the spin—spin coupling constants of the vicinal protons we calculated approximate values of the dihedral angles, which were compared with the dihedral angles measured on Dreiding molecular models for possible boat and chair conformations of L-rhamnopyranose and also the twist and envelope conformations of L-rhamnofuranose. Table 2 gives the conformations that showed satisfactory correlations of the calculated and measured angles.

SUMMARY

A comparative analysis has been made of the PMR spectra of a number of flavonoid O-rhamnosides and rutinosides and their full acetates and TMS ethers which has permitted the determination of the size of the oxide ring in the conformation of the rhamnose residue and, in combination with the results of polarimetric analysis, the configuration of the glycosidic bond.

Information on the size of the oxide ring, together with the H-2 and H-3 signals ($J_{2,3}$) is given by the signals of the proton at C-5 in the spectra of the full acetates. In the case of the rhamnopyranosides, one H-5 proton resonates in the diagnostic region of 3.2-4.0 ppm, while for rhamnofuranoside one must expect a H-4 signal of different structure.

A proof of the presence of a rhamnose residue in a molecule is the characteristic strong-field signal of the methyl group.

All the compounds studied (more than 20 specimens) have been assigned to the α-L-rhamnopyranosides having the $^1C_4$ conformation of the sugar moiety, which is distorted in the case of the 2,3-isopropylidene derivatives. In view of this, the existence of natural flavonoid rhamnosides in the furanoid forms appears unlikely.

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A TRICYCLIC TERPENE HYDROCARBON — CYCLOPINENE

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UDC 547.913.001.2

The reduction of the tosylate of filipendulol (2,7,7-trimethylbicyclo[3.1.1]hept-2-en-6-ol) with lithium tetrahydroaluminate in ether has given a hydrocarbon (I), $C_{10}H_{16}$ (bp 66.5°C/50 mm, n_D^{20} 1.4565, d_{20}^{20} 0.8599, $[\alpha]_D^{19}$ –104.5°. NMR: 0.69 ppm (CH_3); 0.95 ppm (CH_3); 1.17 ppm (CH_3); no signals of olefinic protons. IR: 3054 cm^{-1} (three-membered ring with gem-protons); 1363 and 1387 cm^{-1} (gem-CH_3); absorption bands of multiple bonds absent. Heating (70°C) (I) with a sulfonated cation-exchange resin in hexane gave α-pinene. The hydrogenation of (I) over PtO_2 in acetic acid gave pinane. The most probable structure of (I) is 2,7,7-trimethyltricyclo[$3.1.1.0^{2,4}$]heptane. The substance has been called cyclopinene.

We have reported the isolation from the essential oil of *Achillea filipendulina* Lam. (fernleaf yarrow) of an unknown terpene alcohol, which was called filipendulol [1]. On the basis of a study of the composition, spectral characteristics and chemical transformations, it was assigned the structure of 2,7,7-trimethylbicyclo[3.1.1]hept-2-en-6-ol [2].

When filipendulol tosylate was reduced with lithium tetrahydroaluminate in ether [3], in addition to d-α-pinene a hydrocarbon was obtained with bp 66.5°C/50 mm, n_D^{20} 1.4565, d_{20}^{20} 0.8599, $[\alpha]_D^{19}$ –104.5°. The molecular weight determined mass-spectroscopically was 136.

The NMR spectrum of the hydrocarbon obtained contained three singlets at 0.69 ppm, (3 H), 0.95 ppm (3 H), and 1.17 ppm (3 H), relating to methyl groups, and a methylene hump in the 1.30–2.10 ppm region (7 H). There were signals in the region of resonance of olefinic protons.

The IR spectrum of this compound (Fig. 1) shows no bands in the region of the stretching vibrations of multiple carbon-carbon bonds. The strong band at 3054 cm^{-1} shows the presence in the molecule of a three-membered ring having geminal protons [4, 5]. The spectrum also showed the characteristic splitting of the band at 1380 cm^{-1} due to symmetrical deformation vibrations of methyl groups. It shows that the molecule contains geminal methyl groups [5]. The existence of the latter was confirmed by mass spectrometric characteristics. Thus, in the mass spectrum of the hydrocarbon obtained (Fig. 2) the strongest peak is that of an ion with m/z 93 which is obviously formed as the result of the cleavage of the ring and the subsequent ejection of an isopropyl group.

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*Deceased.

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