NEW O-ACYL DERIVATIVES OF LARICIRESINOL

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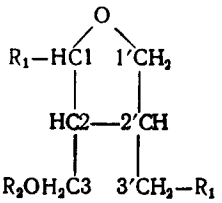
In the light of an investigation of the role of lignans in the vital activity of plants and the pathways of their biogenesis, it appears of interest to study the nature of the interaction of the lignans with other natural compounds. However, at the present time, this question is almost completely exhausted by information on the presence in many plants, with the exception of the conifers, of only one type of derivatives, namely glycosidated lignans [1].

Continuing an investigation of the phenolic components of acetone extracts from the wood of *Abies sibirica* Ledeb. (Siberian fir) and *A. nephrolepis* Maxim. (Khingan fir), in addition to the lignans described previously [2, 3], we have isolated two compounds belonging to previously unknown ester derivatives of the lignans (in our case lariciresinol) and hydroxycinnamic acids (p-coumaric and ferulic acids) (I and II, respectively).



I. R_1 = guaiacyl, R_2 = p-coumaroyl
II. R_1 = guaiacyl, R_2 = feruloyl
III. R_1 = guaiacyl, R_2 = H.

The IR spectra of these compounds contain the absorption bands of ester groups (1705 and 1712 cm^{-1}), and also absorption bands in the 1200-1050-cm^{-1} region which are characteristic for guaiacyl fragments [4]. On alkaline nitrobenzene oxidation, vanillin was formed as the main product.

On alkaline saponification, compounds (I) and (II) were split into equimolecular amounts of lariciresinol (III) and, respectively, p-coumaric and ferulic acids. The lariciresinol isolated from the hydrolyzate coincided in its physicochemical constants and chromatographic properties with the lariciresinol obtained directly from the acetone extract. In supplementation of the systematic study of the spectral properties of lignans begun previously [5], we obtained the PMR spectrum of lariciresinol. A singlet at δ 3.70 ppm is due to the protons of two phenolic methoxy groups, and a multiplet in the weak field (δ 6.58-6.80 ppm) to six aromatic protons. Two singlets in the weak field (δ 7.21 and 7.29 ppm) relate to two hydroxy protons of nonequivalent aromatic rings, and a singlet in the strong field at δ 2.80 ppm to the proton of a primary alcoholic hydroxy group. In the PMR spectrum taken in deuteromethanol, these signals have disappeared as a result of chemical exchange. We assigned a doublet at δ 4.70 ppm to the H-1 proton. The propinquity of this proton to an oxygen atom and an aromatic ring explain the displacement of its signal downfield, and its doublet nature is a consequence of the spin–spin coupling of the H-1 and H-2 protons (J = 5.3 Hz). The assignment of the unresolved multiplets in the δ 2.15-2.45- and 3.95-ppm regions was made, as in the case of the spectra of other lignans [5], by comparing integral intensities. The first multiplet related to the four protons in the 2,2',3' positions.

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In the PMR spectrum of lariciresinol coumarate, the analogous unresolved multiplets were displaced downfield; a multiplet with its center at δ 2.69 ppm relating to the H-2 and H-3' protons, and a multiplet with δ 3.42-4.62 ppm relating to the two H-3 and two H-1' protons. The H-1 proton again resonates in a weaker field. It gives two doublets with similar intensities (δ 4.81 and 4.74 ppm) and approximately the same spin–spin coupling constant ($J_{1,2}$ = 5.5 Hz). When they are superposed, these doublets, the appearance of which is connected with the presence of two isomers, give a distorted triplet.

The protons on the double bond of the coumaroyl residue are resolved in the form of doublets. One of them gives two doublets at δ 6.11 and 5.66 ppm with the splitting constant J of 15.5 and 12.5 Hz. This shows the presence of two isomers. It follows from a comparison of integral intensities that the amount of trans isomer is 72% and of cis isomer 28%. The doublets of the second olefinic proton are superposed on the signals of the aromatic protons, resonating in the δ 6.48-7.01- and 7.21-7.69- ppm regions. Because of superposition, the signals of these protons are not separated. As in lariciresinol, the signal of the protons of the methoxy groups appear in the form of a singlet at δ 3.70 ppm, and the protons of the phenolic hydroxy groups give a broad singlet at δ 6.01 ppm. The signal of the OH groups is displaced upfield on dilution.

The phenolic acids isolated preparatively from the acid fraction of the hydrolyzate were identified by their physicochemical constants and by the GLC analysis of their TMS esters.

On the basis of a comparative analysis of the spectral characteristics of lariciresinol and its coumarate, it may be assumed that O-acylation takes place at the primary alcoholic hydroxyl in the aliphatic chain of lariciresinol. Thus, the IR spectrum of the dimethyl ether of lariciresinol (CCl_4, dilute solution) contains the band of the stretching vibrations of an aliphatic hydroxy group (3638 cm^{-1}), which disappears in the IR spectrum of lariciresinol coumarate. Similarly, in the PMR spectrum of the ester derivative the signal of a proton of an aliphatic hydroxy group is absent.

For a definitive confirmation of the structure, we performed the O-acylation of lariciresinol. Azeotropic esterification yielded lariciresinol coumarate in the form of its trimethyl derivative. This product was completely identical with the trimethyl derivative of compound (I) in its IR and UV spectra and chromatographic properties. The alkaline hydrolysis of the synthetic trimethyl ether of lariciresinol coumarate gave the dimethyl ether of lariciresinol and p-methoxycinnamic acid. The IR spectrum of the dimethyllariciresinol (CCl_4, dilute solution) had the band of the stretching vibrations of a primary alcoholic hydroxy group (3638 cm^{-1}), and the IR spectrum of the methyl ether of p-coumaric acid had a band characteristic for a carboxy group (1700 cm^{-1}).

On the basis of the facts obtained, it has been established that the O-acylation of lariciresinol takes place at the primary alcoholic hydroxyl.

EXPERIMENTAL METHOD

The UV spectra were taken in ethanol on Unicam SP-8000 and SPECORD recording spectrophotometers, the IR spectra (KBr) on an R-20 spectrophotometer, and the PMR spectra in deuterochloroform and deuteromethanol on a Kh-100 radiospectrometer with HMDS as the internal standard, δ scale.

Thin-layer chromatography was performed on polyamide powder and on silica gel impregnated with 2% of sodium metabisulfate in the systems 1) chloroform–acetone and 2) benzene–ethyl acetate (80:20).

Treatment of the Extract. An acetone extract (12 g) of the wood of the Siberian fir or the Khingan fir in the form of a powder was mixed with Celite (1:4 by weight) in acetone, and the mixture was dried and was extracted exhaustively with solvents in the sequence cyclohexane, benzene, ether, chloroform, and acetone.

By preparative chromatography on silica gel in system 1, the chloroform extract (0.9 g) yielded compounds (I) (0.3 g) and (II) (0.1 g). From the acetone extract, chromatography on silica gel in system 1 yielded compound (III).

Lariciresinol p-coumarate (I) formed an amorphous powder with a softening temperature of 85-87°C (benzene). UV spectrum, λ_{max}, nm: 231, 289, 317 (log ε 4.49, 4.27, 4.32). IR spectrum, cm^{-1}: 1702 (C=O), 1610, 1520, 1440 (C_6H_5), 1280, 1240, 1040 (C-O-C), 990, 840, 820 (1,2,4-substitution).

Lariciresinol ferulate (II) formed an amorphous powder with a softening temperature of 97-99°C (mixture of CCl_4 and benzene). UV spectrum, λ_{max}, nm: 232, 287, 330 (log ε 4.40, 3.77, 3.68). IR spectrum $(KBr)_4$: 1280, cm^{-1} 1240, 1040 (C-O-C), 1610, 1510, 1450 (C_6H_5), 990, 840, 810 (1,2,4-substitution).

Lariciresinol (III) formed white crystals with mp 167-168°C (methanol). Its constants have been given previously [6].

Alkaline Saponification of the Esters. A mixture of 0.1 g of (I) or (II) in 3.5 ml of a 5% solution of KOH in methanol was heated at 80°C for 1.5 h.

After the elimination of the methanol, the reaction mixture was diluted with cold water and was extracted repeatedly with water-saturated ethyl acetate. The ethyl acetate extracts were combined, washed with water, and dried over $MgSO_4$. After the solvent had been distilled off, the dry residue was crystallized from methanol, which gave compound (III) with mp 167-168°C. The aqueous layer was acidified with 5% HCl to pH 5.5 and was then extracted with ethyl acetate. After the ethyl acetate extract had been dried over $MgSO_4$, the solvent was driven off and the dry residue was chromatographed on silica gel in system 2.

The saponification of compounds (I) and (II) gave 0.1 g of (III), 0.055 g of p-coumaric acid, and 0.50 g of ferulic acid, respectively. The p-coumaric acid formed white crystals with mp 206-207°C (ethanol). UV spectrum, λ_{max}, nm: 311, 300, 290, 228.5 (log ε 3.94, 3.86, 3.82, 4.05). IR spectrum, cm^{-1}: 1675 (C=O of a carboxy group), 1632, 1603, 1520, 1420 (C_6H_5); 1100, 835 (1,4-substitution).

The ferulic acid formed white crystals with mp 172°C (methanol). UV spectrum, λ_{max}, nm: 318, 295, 228 (log ε 3.94, 3.64).* IR spectrum, cm^{-1}: 1672 (C=O of a carboxy group); 1650, 1604, 1510, 1422 (C_6H_5), 970, 860, 810 (1,2,4-substitution).

Methylation. With cooling, 0.6 ml of dimethyl sulfate was added in a current of helium to 0.1 g of (III), and then the mixture was kept at 45°C in a current of helium and, with vigorous stirring, 0.04 g of KOH in 1.5 ml of ethanol was added. After this, the reaction mixture was heated at 60°C for 2 h. After the end of the reaction, the solvent was driven off, the residue was diluted with cold water, and it was extracted successively with toluene, benzene, and ethyl acetate. The completeness of methylation was checked by TLC on silica gel.

The dimethyl ether of lariciresinol formed colorless crystals with mp 78-79°C (diethyl ether), $[\alpha]_D^{18}$ +22° (c 2.0; acetone). UV spectrum, λ_{max}, nm: 282, 231 (log ε 3.87, 4.25). IR spectrum, cm^{-1}: 3530 (associated OH group), 1465, 1450, 1432, and 1370 (CH_3), 1603, 1510 (C_6H_5).

Azeotropic Esterification of the Dimethyl Ether of Lariciresinol. p-Methoxycinnamic acid was obtained from anisaldehyde [7].

A mixture of methyl p-coumarate (0.05 g), the dimethyl ether of lariciresinol (0.12 g), and toluenesulfonic acid (0.01 g) was carefully stirred in 10 ml of dry CCl_4 in a current of helium. Then the mixture was boiled under reflux until the evolution of water ceased (about 5 h). After this, the mixture was cooled, and the unchanged toluenesulfonic acid was washed out with water. The residue was washed with an aqueous solution of sodium bicarbonate and with water and was dried over $MgSO_4$. After the elimination of the CCl_4, the residue (0.09 g) was chromatographed on silica gel in system 2; 0.04 g of the trimethyl ether of laricyl coumarate was isolated.

SUMMARY

In an investigation of the composition of the extractive substance of the wood of *Abies sibirica* Ledeb. and *A. nephrolepis* Maxim., new O-acylated lignans, previously unknown in nature, have been isolated. The structures of the two new compounds have been established by physicochemical methods and by independent synthesis: they are lariciresinol coumarate and ferulate.

*As in Russian original — Publisher.

The PMR spectra of laricyl coumarate and laricyl ferulate were taken by G. A. Kalabin.

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FUROCOUMARINS OF *Komarovia anisospermum*

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The monotypic genus *Komarovia* Korov. is considered close systematically to the genus *Ferula* L. [1], but this contradicts a number of morphological facts and, in particular, the carpological features of *Komarovia anisospermum* Korov. (heteromericarpia). A study of the chemical composition of the plant may assist in answering the question of the taxonomic propinquity of these two genera.

The thin-layer chromatography of a petroleum ether extract of the roots of *Komarovia anisospermum* showed that the predominating substances in it had R_f 0.64, 0.56, and 0.48. By column chromatography on silica gel we isolated all three substances: R_f 0.64, $C_{16}H_{14}O_4$, mp 106-108°C (I); R_f 0.56, $C_{22}H_{24}O_5$, mp 53-54°C (II); and R_f 0.48, $C_{17}H_{16}O_5$, mp 100-101°C (III).

Substance (I) was identical with isoimperatorin in its melting point, a mixed melting point, and its IR and NMR spectra.

According to its UV and IR spectra, substance (II) is a linear furocoumarin with O-alkyl substituents at C_5 and C_8 [2, 3]. It also follows from the NMR spectrum of substance (II) (Fig. 1) that it is based on the psoralen nucleus substituted in positions 5 and 8: doublets at 7.85 and 5.99 ppm, J = 9.5 Hz, are due to the H_4 and H_3 protons, and doublets at 7.48 and 6.88 ppm, J = 2 Hz, to the H_5' and H_4' protons, respectively. One of the O-alkyl substituents is a methoxy group, which appears in the spectrum in the form of a three-proton singlet at 4.08 ppm, and the other is a geranyloxy group (3,7-dimethylocta-2,6-dienyloxy group): one-proton triplet at 5.46 ppm, J = 7 Hz, and two-proton doublet at 4.69 ppm, J = 7 Hz, due to the methine and methylene protons in the Ar–O–CH_2–CH=C grouping; two-proton singlets at 1.89 and 1.93 ppm, and a broadened one-proton singlet at 4.90 ppm, $W_{1/2}$ = 6 Hz, due to the methylene and methine protons of the =C–CH_2–CH_2–CH=C– fragment; and three three-proton singlets at 1.60, 1.55, and 1.47 ppm due to the protons of the three methyl groups located at C_7 and C_3 of the geranyl residue. The facts given correspond to two variants of the structure of the substance: 8-geranyloxy-5-methoxypsoralen and 5-geranyloxy-8-methoxypsoralen.

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