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A New Lignan from Norway Spruce

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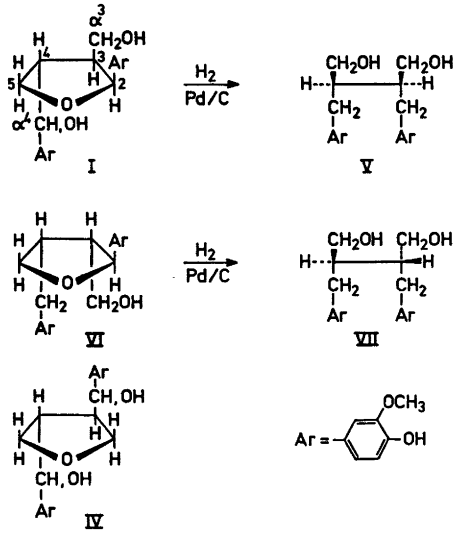
A new lignan tetrahydro-α^4, *r*-2-bis(4-hydroxy-3-methoxyphenyl)-*c*-3, *t*-4-furandimethanol (I), has been isolated from sound root sapwood as well as from the reaction zone induced by attack of *Fomes annosus*. The identification is based on NMR, MS, and hydrogenation studies. Two other nonidentified lignans were isolated and characterized by MS. HPLC and TLC data are given for a series of lignans.

In connexion with studies on changes in root sapwood from Norway spruce [*Picea abies* (L.) Karst.] attacked by *Fomes annosus* (Fr.) Cke, small amounts of a crystalline, apparently new lignan (I) (m.p. 148 – 152 °C: $[\alpha]_D$ – 10.4°) were isolated, together with crude fractions containing two other nonidentified compounds (II and III). The colour reactions and mobilities of the three compounds in thin layer chromatography (TLC) were similar to those of the lignan liovil (IV) (Table 1). Using high-pressure liquid chromatography (HPLC), small amounts of II and III have now been obtained in a pure state. The mass spectra of compounds I – III showed very similar fragmentation patterns (the more important peaks are given in Table 2) and the same molecular ion (*m/e* 376) as found for liovil (IV). The available amounts of compounds II and III, apparently also lignans, were too small for further identification, but the crystalline compound I was identified as described below.



I V VI VII IV

The elemental analysis and the mass spectrum of I were in agreement with the formula $C_{20}H_{24}O_7$. Catalytic hydrogenation yielded a product (V), chromatographically indistinguishable from (–)-*seco*-isolariciresinol (VII), the known hydrogenation product from (+)-lariciresinol (VI).[2] The available amount of compound V did not permit an accurate optical rotation determination. The mass spectra of V and VII were very similar (see EXPERIMENTAL), but NMR revealed slight but significant differences between the two com-

Table 1. Chromatographic properties of compounds I – VII.

Compound	LC retention time (min)	TLC: R_F value relative to VI		Colour with spray
		Solvent *a*	Solvent *b*	
I	10.0	0.45	0.72	red orange
II	8.0	0.35	0.86	red orange
III	19.2	0.52	0.67	red orange
IV	4.8	0.45	1.00	red orange
V	5.4	0.45	0.72	green
VI	6.2	1.00	1.00	brown
VII	5.4	0.45	0.72	green

Table 2. Mass spectra of compounds I – IV.

m/e	Intensities, % I	II	III	IV
65	17	15	20	10
69	44	26	17	27
77	9	7	12	7
81	10	7	13	9
91	7	5	12	5
93	22	20	23	9
94	12	8	11	8
122	14	9	11	8
124	9	5	12	6
131	10	5	13	6
137	100	100	100	100
138	65	42	26	29
151	17	11	22	6
153	88	53	53	32
175	26	7	24	13
180	10	7	10	5
206	27	11	16	12
340	5	2	3	8
358	25	7	11	11
376, M^+	24	11	11	3

pounds (Table 3). Most important, only compound VII showed separate doublets for the primary methylene protons H_A, H_B and a doublet for the methylene protons H_C,H_D. This indicated that compound V was the diastereomer of compound VII, since the latter compound is optically active, V must be the *meso*-isomer.

The NMR spectrum of I was very similar to those of lignans containing a 2,3,4-substituted tetrahydrofuran ring, [3–10] and the fact that the compound yielded *meso-seco*-isolariciresinol (V) on hydrogenation indicated a lariciresinol structure with an extra benzylic hydroxyl and with *trans*-oriented 3- and 4-protons.

The structure determination of I is supported by successive spin decoupling of the H-3 and H-4 protons in the NMR spectrum of I and its tetraacetate, respectively. The sharp doublets at δ 4.47 and 4.50 in the NMR spectrum of I must arise from two single benzylic hydrogens, the doublet at δ 4.47 being due to the hydrogen in the α^4-position.

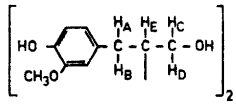
The upfield shift (δ 4.50) and the large coupling constant (J 8.4 Hz) for proton H-2 in the spectrum of I compared with (+)-lariciresinol, VI, (δ 4.75, J 6.5 Hz) indicates *cis*-oriented 2- and 3- protons. The *trans*-orientation of the corresponding protons in (+)-lariciresinol (VI) is based on its formation by hydrogenation of (+)-pinoresinol,[11] the absolute configuration of which is well established.[12–14] NMR spectra of the related tetrahydrofuro[3,4-*c*]furan lignans (*e.g.* pinoresinol) seems to offer the closest parallel to those of compounds I and VI. In their spectra the benzylic hydrogen is reported at δ 4.40 – 4.45 (J 6.0 – 7.0 Hz) and 4.80 – 4.85 (J 4.0 – 5.5 Hz) for *cis*- and *trans*-oriented 2- and 3-protons, respectively.[3,4,9,10]

These results verify the suggested structure of compound I or its enantiomer.

EXPERIMENTAL

TCL was performed on Silica Gel HF_{254} (Merk) plates with (*a*) 1:1 dichloromethane-acetonitrile and (b) 7:3 hexane-ethanol as solvents. The plates were sprayed with diazotized sulfanilic acid in 10 % aqueous sodium carbonate, followed by light spraying with 50 % sulfuric acid.

Table 3. NMR data of compounds V and VII.



	2-H	5-H	6-H	H_A	H_B	H_C	H_D	H_E	OMe
V	6.55 – 6.70 m			2.60 d		3.45 – 3.80 m		1.85 – 2.15 m	3.80 s
				$J_{AE}=J_{BE}=7.5$ Hz					
VII	6.59 d	6.66 d	6.53 q	2.60 d	2.62 d	3.59 d		1.75 – 2.10 m	3.73 s
$J_{26}=1.6$ Hz $J_{56}=7.8$ Hz $J_{AE}=6.8$ Hz $J_{BE}=7.4$ Hz $J_{CE}=J_{DE}=5.0$ Hz									

High-pressure liquid chromatography (HPLC) was performed on a Waters ALC-202 instrument with a 180 cm × 3 mm column containing Silica Gel (Corasil II, Waters) and 9:1 petroleum ether (b.p. 40 – 60 °C) – ethanol as solvent. The flow rate was 5 ml/min, and the detector a UV-monitor operating at 280 nm.

The NMR spectra were recorded on a Varian HA-100D instrument, in methanol-d_4 (if not otherwise stated) using tetramethylsilane as an internal standard. The singlet, doublet, quartet and multiplet patterns are designed s, d, q, and m, respectively. The mass spectra were recorded on a Varian CH-7 instrument.

A previous paper [1] described the isolation of compound I (20 mg) in the crystalline state from the mother liquor after crystallization of liovil. This was obtained from a subfraction after chromatography on silicic acid of the 2-butanone extract of the reaction zone from roots of Norway spruce attacked by *Fomes annosus* (fraction 8 in experiment C in that report). The mother liquor thus obtained, combined with the next subfraction (fraction 9), was fractionated in the present investigation on a silicic acid column (90 × 2 cm) using solvent *a*. From a subfraction containing compounds II, III, liovil and some I, small amounts of the unidentified compounds II and III (*ca.* 1 mg of each) were obtained in a chromatographically pure state by repeated HPLC. The retention times, using the conditions given above, and the mobilities and colour reaction in TLC are given in Table 1, together with similar information for compounds IV – VII for comparison.

In a similar way, using a combination of chromatography on Sephadex LH-20, silicic acid and HPLC, compounds I – III were also detected in a 2-butanone extract of sound sapwood from the previous investigation. Compound I was thereby also isolated in sufficient amount to yield an NMR spectrum, identical with that of compound I isolated from the reaction zone.

Compound I. Crystallized from ethanol, m.p. 148 – 152 °C, $[\alpha]_D^{20}$ −10.4° (*c* 1.8, methanol). (Found: C 63.8; H 6.4 $C_{20}H_{24}O_7$ requires C 63.8; H 6.4.) IR; ν_{max} (KBr): strong bands at 1035, 1060, 1130, 1160, 1275, 1435, 1520, 1600, and 1610 cm^{-1}. The MS data are given in Table 2. NMR: δ 2.26 (m, 1 H, H-3), 2.62 (m, 1 H, H-4), 3.66 (m, 4 H, H-5, H-5′, H-α^3, H-$\alpha^{3'}$), 3,84 (s, 3 H, OMe), 3.86 (s, 3 H, OMe), 4.47 (d, 1 H, *J* 9.2 Hz, H-α^4), 4.50 (d, 1 H, *J* 8.4 Hz, H-2), 6.7 – 7.0 (m, 6 H).

I-tetraacetate (Ac_2O/pyridine) amorphous. NMR ($CDCl_3$): δ 1.96 (s, 3 H, aliphatic acetyl), 2.05 (s, 3 H, aliphatic acetyl), 2.30 (s, 6 H, 2 aromatic acetyls), 2.32 (m, 1 H, H-3), 2.67 (m, 1 H, H-4), 3.78 (m, 2 H, H-5 and H-5′), 3.85 (s, 6 H, 2 methoxyls), 4.11 (q, 1 H, *J* 6.6 and 11.7 Hz, H-α^3), 4.37 (q, 1 H, *J* 5.0 and 11.7 Hz, H-$\alpha^{3'}$), 4.57 (d, 1 H, *J* 7.6 Hz, H-2), 5.79 (d, 1 H, *J* 9.6 Hz, H-α^4), 6.8 – 7.1 (m, 6 H).

Compound I (*ca.* 5 mg), in dry tetrahydrofuran (10 ml), was hydrogenated in the presence of 5 % palladium on carbon for 3 h under ambient conditions, and the catalyst was then filtered off and carefully washed with methanol. The product obtained (compound V) after evaporation, was purified from small amounts of impurities by TLC, using solvent *b*. MS: *m/e* 77 (6 % of base peak), 91(4), 94(8), 122(10), 137(*100*), 138(21), 163(4), 189(5), 194(4), 362(12, M+). Compare the MS of (−)-*seco*-isolariciresinol (VII) run under similar conditions (direct inlet, 140 °C): *m/e* 77 (9 % of base peak), 91(6), 94(12), 122(16), 137(*100*), 138 (38), 163(7), 189(10), 194(6), 362(22), M+).

The NMR data of compounds V and VII are given in Table 3.

Compounds II and III. The MS data are given in Table 2 and the chromatographic data in Table 1. The red-orange colour developed on spraying is notable, indicating an α-hydroxyvanillyl structure.

(+)-*Lariciresinol* (VI). NMR: δ 2.2 – 3.0 (m, 4 H), 3.81 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.5 – 4.1 (m, 4 H, $-CH_2-$), 4.75 (d, 1 H, *J* 6.5 Hz, H-2), 6.45 – 6.95 (m, 6 H).

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