(−)-SESAMIN AND (−)-SAVININ FROM ACANTHOPANAX SESSILIFLORUM AND THEIR NMR SPECTRA

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Of the glycosides previously isolated from the roots of Acanthopanax, two are mono- and diglucosides of the lignan (−)-syringaresinol [1]. In the present paper we describe the isolation from Acanthopanax of two free lignans: (−)-sesamin and (−)-savinin. A spatial structure of (−)-savinin is proposed on the basis of an analysis of the NMR spectrum.

(−)-Sesamin (I) was isolated from an ethereal extract of the roots of Acanthopanax. The IR and NMR spectra (taken on a JNM-C-60 spectrophotometer in $CDCl_3$) of our sample of sesamin agreed with those given in the literature [2, 3]. The assignment of the signals in the NMR spectra of sesamin is given in the table.

Chemical shift, ppm	Nature of signals	No. of protons	Assignment of the signals
			NMR spectrum of sesamin
3.04	multiplet	2	Protons at C_1 and C_5
3.83	quartet	2	Axial protons at C_4 and C_8
4.23	quartet	2	Equatorial protons at C_4 and C_8
4.72	doublet	2	Axial protons at C_2 and C_6
5.84	singlet	4	Protons of the methylenedioxy groups
6.69—6.38	doublet	6	Protons of the benzene ring
			NMR spectrum of savinin
2.3—3.1	multiplet	2	Protons at C_4
3.5—3.9	quartet	1	Protons at C_3
4.2		2	CH_2 protons of a lactone ring
5.85	quartet	2	$O-CH_2-O$ of ring A
5.95	doublet	2	$O-CH_2-O$ of ring B
6.58—7.05	singlet	6	Aromatic protons
7.4	doublet	1	Protons at C_1

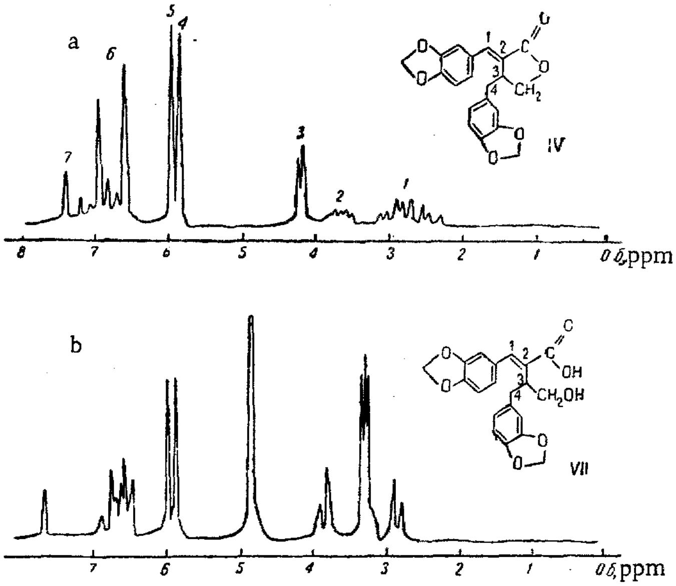
When an ethereal extract of the roots of Acanthopanax was allowed to stand for a long time, (−)-savinin crystallized out. It can also be isolated by chromatographic separation of a methanolic extract.

The melting point, specific rotation, UV and IR spectra of the substance agree with data in [4]. In order to convince ourselves of the complete identity of our sample with savinin isolated previously [4–6], we prepared some of its derivatives, including savinic acid and its sodium salt, whose melting points agreed. When savinin was hydrogenated, isohinokinin, identical with that described in [4], was obtained.

The structure of hinokhinin (II) and of isohinokinin (III) was proposed by Schrecker and Hartwell [4]. According to these authors, the two substances are, respectively, cis- and trans-isomers at C_2 with the configuration at C_3 present in savinin unchanged. In order to determine the configuration of savinin relative to the double bond, we have analyzed the NMR spectra of savinin (figure, a); the assignment of the signals of this substance is given in the table.

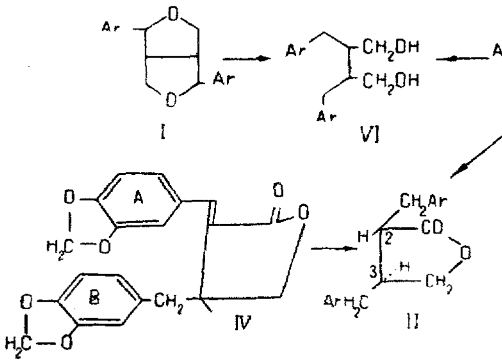
In contrast to the spectrum of sesamin, the signals of the 4th and 5th protons of the methylenedioxy groups were split. This may possibly be due to the fact that the protons of the methylenedioxy group of ring A come into the field of ring B and their signal is displaced in the direction of stronger magnetic fields. (An analogous but larger displacement is observed in the NMR spectra of otobain [7]). Consequently, the benzene rings of savinin are adjacent in space, which is possible only with a cis-configuration relative to the double bond. On this basis, the spatial structure (IV) is proposed for savinin. Apparently the synthetic isohibalactone [8] (isosavinin) is the trans-isomer.

In the region of strong fields (2.3–3.1 ppm) the NMR spectrum contains the typical AB part of an ABX spectrum, which can be given in the savinin molecule only by the protons at C_4 (AB part) and at C_3 (X part). An analysis of the AB spectrum leads to the followin spin-spin interaction constants: J_{AB} = 14 cps; J_{AX} = 3.5 cps, and J_{BX} = 7 cps. The X part of the spectrum appears at 3.5–3.9 ppm as an unresolved multiplet, since the proton at C_3 interacts further with the protons of the methylene group of the lactone ring. The latter give a doublet (4.2 ppm) with J = 4.5 cps, the resolution being due to interaction with the proton at C_3. It is interesting that the protons at C_4 proved to be nonequivalent, although ring B is not rigidly fixed. It is possible that this is due to the influence of the lactone ring. A confirmation of the fact that the protons at C_4 in savinin are nonequivalent because of the influence of the lactone ring is the NMR spectrum of the hydrolysis product of savinin – savinic acid (VII) (b in figure). The protons at C_4 give a doublet at 2.8 ppm, i.e., they became equivalent. The methylene group, which is now connected to a hydroxyl group, gives a signal displaced to the region of strong fields as compared with savinin (from 4.2 to 3.85 ppm).



NMR spectra. a) (–)-Savinin; b) savinic acid (in deuteromethanol).

Sesamin and savinin have not previously been found in a single plant, although a biogenetic link between them is extremely probable. It is known that sesamin and cubebin (V) give one and the same dihydrocubebin (VI) on hydrogenolysis. The link between cubebin (V) and savinin (IV) is obvious: cubebin (V) on oxidation and savinin (IV) on hydrogenation and further isomerization give the same substance, hinokinin (II). The presence of both substances in one plant confirm the biogenetic similarity of these compounds.



Ar-3,4-methylene-dioxyphenyl

Experimental

Isolation of (–)-sesamin. One hundred grams of an evaporated syrupy ethereal extract was dissolved in 1.2 *l* of chloroform and was shaken with 0.85 *l* of ethylene glycol. The chloroform layer (0.55 *l*) was evaporated to dryness and extracted, with stirring, with a boiling mixture of hexane and heptane (1 : 1) for 2 hr. On cooling, fine yellow spherical bunches of crystals of sesamin were separated out from the extract. Yield 3 g (3% of the ethereal extract), mp 123° C (from ethanol), $[\alpha]^{20}_D$ –60° (c 0.7; $CHCl_3$).

Found, %: C 67.56, 67.62; H 5.25, 5.32. Calculated for $C_{20}H_{18}O_6$, %: C 67.79; H 5.08.

Isolation of (–)-savinin from the ethereal extract. 1.2 kg of the finely-comminuted air-dry roots of *Acanthopanax* was extracted with ether in a Soxhlet apparatus for three days. Yield 1.5% of the weight of the roots. On prolonged standing (20 days and more) the ethereal extract deposited crystals of savinin. Yield 0.5 g (3% of the ethereal extract), mp 146° (from ethanol), $[\alpha]_D^{20}$ −90° (c 0.6; chloroform).

Found, %: C 67.86, 67.99; H 4.75, 4.85. Calculated for $C_{20}H_{16}O_6$, %: C 68.18; H 4.58.

Isolation of (−)-savinin from a methanolic extract. 16 kg of finely-comminuted air-dry roots of *Acanthopanax* was extracted with methanol in an apparatus of the Soxhlet type for 10 days. This gave 900 g of a syrupy extract (5% of the weight of the roots) which was dissolved in the butanol-ethanol-water (5:2:3) system and chromatographed in the same system on a column of Al_2O_3 (neutral, Brockmann activity grade III, 20 × 50 cm), 500-ml fractions being collected. The first three fractions obtained in this separation were enriched in savinin. After evaporation of the fractions, the savinin crystallized in the form of elongated yellow prisms. Yield 7 g (0.75% of the weight of the dry methanolic extract), mp 146° C (from ethanol), $[\alpha]_D^{20}$ −90° (c 0.6; chloroform), $[\alpha]_D^{20}$ −49.4° (c 1.2; acetone).

Found, %: C 67.84, 67.98; H 4.64, 4.57; mol. wt. 366 (by isothermal distillation). Calculated for $C_{20}H_{16}O_6$, %: C 68.18; H 4.58; mol. wt. 354.

Savinic acid (mp 110° C) and its sodium salt (mp 119° C) were obtained by a published method [4].

The hydrogenation of the savinin was carried out in a similar manner to that described in the literature [4], but over Pt/C. The hydrogenation product was separated chromatographically on a column of silica gel (100–200 mesh for preparative chromatography and > 270 mesh for analytical chromatography) in benzene. The fractions were analyzed by chromatography in a thin fixed layer of SiO_2 in the ethyl acetate-chloroform (1:1) system. Isohinokinin, mp 115.5°–116° C, $[\alpha]_D^{20}$ +98.4° (c 0.58; chloroform) was isolated.

The analyses were performed by L. I. Glebko and Zh. I. Ul'kina.

Summary

1. The lignans (−)-sesamin and (−)-savinin have been isolated from *Acanthopanax sessiliflorum*.

2. On the basis of an analysis of the NMR spectrum, the cis-configuration of savinin with respect to the double bond has been proposed.

REFERENCES

1. L. A. Elyakova, A. K. Dzizenko, and G. B. Elyakov, DAN SSSR, 165, no. 3, 562, 1965.
2. K. Freudenberg and G. S. Sidhy, Chem. Ber., 94, 851, 1961.
3. W. A. Jones, M. Beroza, and E. D. Becker, J. Org. Chem., 27, 3232, 1962.
4. A. W. Schrecker and J. L. Hartwell, J. Am. Chem. Soc., 76, 4896, 1954.
5. J. L. Hartwell, J. M. Johnson, D. B. Fitzgerald, and M. Belkin, J. Am. Chem. Soc., 75, 235, 1953.
6. Masumura, J. Chem. Soc., Japan Pure Chem. Sec., 76, 423; 635, 1955; RZhKhim 30838, 1957.
7. T. Gilchrist, R. Hodges, and A. L. Porte, J. Chem. Soc., 5, 1780, 1962.
8. Yamashita Kuohei and Matsui Masano, Bull. Agric. Chem. Soc., Japan, 22, 227, 1958; RZhKhim, 42569, 1959.

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