HETEROCYCLES, Vol. 24, No. 8, 1986

KAZINOL P, A NOVEL ISOPRENYLATED SPIRO-COMPOUND FROM BROUSSONETIA KAZINOKI SIEB.

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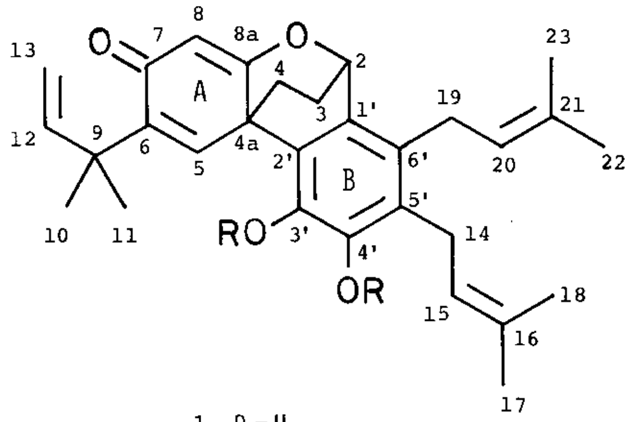
Abstract —— A novel isoprenylated spiro-compound named kazinol P (1) was isolated from a benzene extract of the root bark of Broussonetia kazinoki Sieb. (Japanese name "Himekōzo", Moraceae). The structure was shown to be 1 on the basis of spectral evidence. Kazinol P is regarded biogenetically as a variation of a flavan and/or a 1,3-diphenylpropane derivative, such as kazinol E (2) and kazinol C (6).

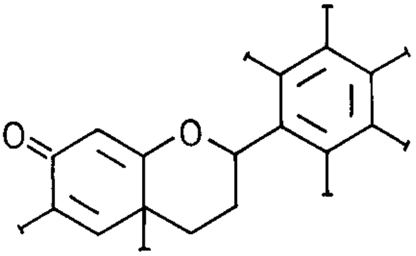
Previously we reported the structure determination of isoprenylated flavans and isoprenylated 1,3-diphenylpropane derivatives obtained from the extract of the root bark, or cortex of Broussonetia kazinoki Sieb. (Japanese name "Himekōzo", Moraceae).[1] In the course of our studies on the components of the same plant, kazinol P was isolated from the root bark. In this paper we report the structure determination of the compound. The benzene extract of the root bark was dissolved in methanol. The methanol extract was fractionated sequentially by the deactivated silica gel column chromatography[2] and preparative tlc, resulting in the isolation of 1 (1.0×10^{-3} % from the root bark).

Kazinol P (1) was obtained as colorless needles, mp 163-168 °C, $[\alpha]_D^{21}$ 0° ($CHCl_3$), M^+=460.2576, $C_{30}H_{36}O_4$, positive to ferric chloride test and sodium molybdate test.[3] The compound 1 showed the following spectra; ir ν_{max}^{KBr} cm^{-1}: 3430 (br), 1650, 1590 (sh), 1575; uv λ_{max}^{EtOH} nm (log ε): 211 (4.61), 228 (infl. 4.29), 240 (infl. 4.17), 282 (3.93). The ir spectrum showed the presence of hydroxyl groups, a conjugated carbonyl group, and a benzene ring. The ^1H nmr spectrum of 1 (400 MHz, $CDCl_3$) was analysed by comparing it with those of isoprenylated flavan derivatives and 1,3-diphenylpropane derivatives.[1,4] The spectrum showed the following proton signals:

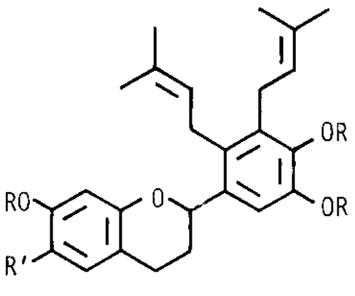


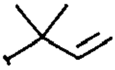
1: R = H

1a: R = CH_3

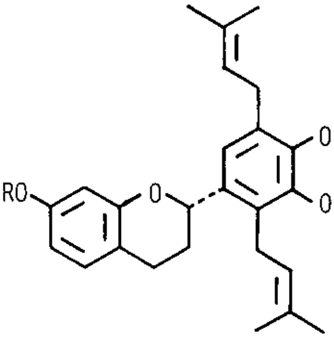


1′



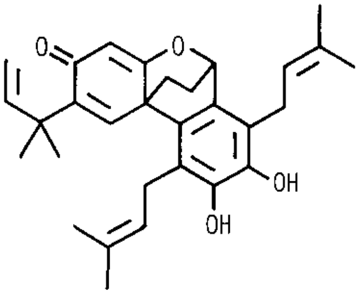
2: R = H, R′ = 

8: R = CH_3 , R′ = H

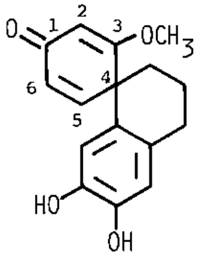


5: R = H

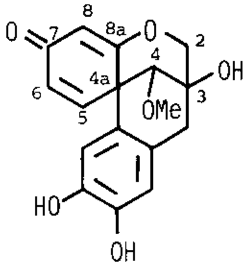
5a: R = CH_3



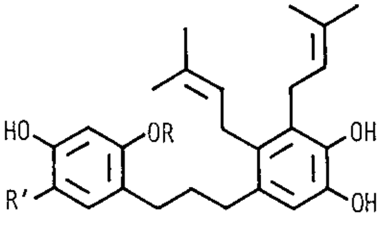
1″

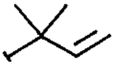


3



4



6: R = H, R′ = 

7: R = CH_3 , R′ = H

Table 1 ^{13}C nmr spectra of 1, 2, 3, and 4

C - No.	1	2	4		3	C - No.	1	2
C - 2	72.4	75.0				C - 1'	124.7	131.0
3	24.4	25.6				2'	119.5	111.3
4	28.6	29.9				3'	142.7^a	142.4
4a	43.2	113.9	52.0	(C-4)	45.9	4'	142.5^a	141.7
5	139.5	127.0	148.0	(C-5)	151.8	5'	126.4^b	130.2
6	137.8	125.1	129.7	(C-6)	122.9	6'	127.2^b	127.0
7	186.0	153.5^a	187.8	(C-1)	186.9	14	27.2^c	27.2^b
8	103.6	105.6	108.6	(C-2)	101.9	15	121.3^d	122.8^c
8a	172.9	155.1^a	174.9	(C-3)	179.9	16	133.7^e	132.4^d
9	40.2	39.8				17	25.5	25.6
10	26.8	27.2				18	17.9	17.9
11	26.9	27.2				19	25.9^c	25.6^b
12	146.9	148.3				20	122.7^d	124.1^c
13	110.1	113.0				21	131.0^e	131.4^d
						22	25.5	25.6
						23	18.0	17.9
solv.	A	A	B		B		A	A

solvent: A; $CDCl_3$ B; dmso-d_6

a — e : Assignments may be interchanged in each column.

Table 2 ^{1}H nmr chemical shifts (ppm)

	C-12-H	C-13-H	
1	6.25	4.97	5.00
2	6.07	5.17	5.21
Δ	+0.18	-0.20	-0.21

measured in $CDCl_3$

Table 3 ^{1}H nmr chemical shifts (ppm) of methoxyl groups

1a	5a	8
3.59	3.73	3.73
3.82	3.80 x 2	3.77
		3.83

measured in $CDCl_3$

1) protons of two 3,3-dimethylallyl groups, δ 1.69, 1.73 (each 3H, d, J=1), 1.76, 1.80 (each 3H, s), 3.37 (4H, m), 4.92 (1H, br t, J=7), 5.10 (1H, br t, J=7), 2) protons of 1,1-dimethylallyl group, δ 1.36 (6H, s), 4.97 (1H, dd, J=1 and 8), 5.00 (1H, dd, J=1 and 15), 6.25 (1H, dd, J=8 and 15), 3) four methylene protons, δ 1.55-1.70 (2H, m), 1.93 (1H, m), 2.18 (1H, m), 4) one methine proton, δ 5.76 (1H, dd, J=1 and 4), and 5) two olefinic protons, δ 5.60 (1H, s), 7.38 (1H, s). The coupling patterns of the methylene and methine protons were similar to those of the relevant protons of *flavan derivatives.*[1a,4] *Treatment of* 1 with dimethyl sulfate and potassium carbonate in acetone gave a dimethyl ether (1a), which is negative to the ferric chloride test. From the above results and the sodium molybdate test, kazinol P seems to be a flavan derivative having a 1,1-dimethylallyl group and two 3,3-dimethylallyl groups, and ortho-dihydroxyl groups in the molecule.

The ^{13}C nmr spectrum was analysed by off-resonance decoupling technique and by comparison with the spectra of the other isoprenylated flavan derivatives, kazinols E (**2**)[1a] and H.[1a] The spectrum showed the following carbon atom signals: 1) carbons in two 3,3-dimethylallyl groups (C-14 ∼ C-23), 2) carbons in a 1,1-dimethylallyl group (C-9 ∼ C-13), 3) one oxygenated methine carbon and two methylene carbons (C-2 ∼ C-4), and 4) carbons in a hexasubstituted benzene ring (C-1' ∼ C-6'). Comparison of ^{13}C nmr spectrum of **1** with those of spirobroussonin B (**3**)[5] and caesalpin J (**4**)[6] indicated that signals at δ 43.2, 172.9 and 186.0 are assignable to spiro-carbon atom, oxygenated olefinic carbon atom, and carbonyl carbon atom, respectively (Table 1). This result suggests that **1** would involve a 3-oxygenated 2,5-cyclohexadienone ring with the spiro-carbon atom in the structure. The above spectral data and the biogenetic analogy to the flavan derivatives,[1a,4] kazinols A (**5**)[4] and E (**2**),[1a] and also to the 1,3-diphenylpropane derivatives,[1] kazinols C (**6**)[1a] and J (**7**),[1b] obtained from the plants of Broussonetia species, led us to the assumption that the carbon skeleton of kazinol P is **1'**.

In the ^{1}H nmr spectrum of **1**, the signal at δ 7.38 is assigned to the proton at C-5 position by comparison of the chemical shift value of the signal with those of the relevant proton signal of **3**[5] and **4**,[6,7] and by consideration of the paramagnetic effect of the B ring. The location of the 1,1-dimethylallyl group at C-6 position was confirmed by the NOE experiment as follows: when the methyl signal at δ 1.36 (6H, s) was irradiated, the NOE was observed in the proton at C-5 (δ 7.38, 15 %). This result was further supported by the comparison of the chemical shift values of the olefinic proton signals of 1,1-dimethylallyl group of **1** with those of the relevant proton signals of **2**, as follows: the olefinic proton signal at C-12 position of **1** shifted downfield from the relevant proton of **2**, while the proton signals at C-13 position shifted upfield by the anisotropic effect of the carbonyl group (Table 2). From above results and the biogenetic analogy to the flavan[1a,4] and 1,3-diphenylpropane derivatives[1] obtained from the plants of Broussonetia species, the structure of kazinol P is possibly represented by **1** or **1"**.

Between them, **1** was preferred based on the following spectral data: In the ^{13}C nmr spectrum of **1**, the chemical shift values of the carbon atoms of B ring, except for the carbon atoms at C-1', 2' and 5' positions which are affected by substituent effect, were similar to those of the relevant carbon atoms of **2** (Table 1). The presence of methoxyl group at C-3' position of **1a** was supported by consideration of the chemical shift values of the proton signals of methoxyl groups of **1a**, kazinol A trimethyl ether (**5a**),[4] and kazinol I trimethyl ether (**8**)[8] (Table 3). In the ^{1}H nmr spectrum of **1a**, one of the methoxyl groups shifted 0.23 ppm upfield from the another one. This result can be explained by the diamagnetic effect of the A ring. Kazinol P is regarded biogenetically as a variation of a flavan and/or a 1,3-diphenylpropane derivative, such as kazinol E (**2**) and kazinol C (**6**).

ACKNOWLEDGEMENT

We are grateful to Prof. S. Sakai, Faculty of Pharmaceutical Sciences, Chiba University, for high-resolution ms measurement.

REFERENCES AND FOOTNOTES

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7. The compounds **3** and **4** showed the relevant proton signals at δ 6.89 and 6.98, respectively.
8. Unpublished data.

Received, 12th May, 1986