STRUCTURE OF MULBERROFURAN P, A NOVEL 2-ARYLBENZOFURAN DERIVATIVE FROM THE CULTIVATED MULBERRY TREE (MORUS ALBA L.)[1]

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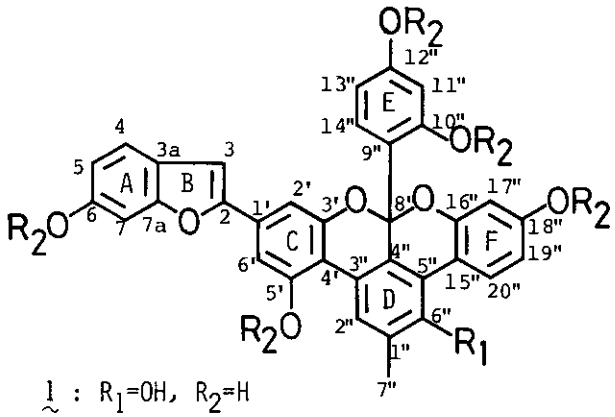
Abstract ——— A novel 2-arylbenzofuran derivative, mulberrofuran P, was isolated from an acetone extract of the reddish violet powder obtained from the surface of the root bark of cultivated mulberry tree (Ichinose, a cultivated variety of Morus alba L.). Its structure was shown to be 1 on the basis of spectral evidence. Mulberrofuran P is regarded biogenetically as a variation of a Diels-Alder type adduct of a chalcone derivative and a dehydroprenyl-2-arylbenzofuran derivative.

Previously we reported the structure determination of a 2-arylbenzofuran derivative named mulberrofuran I (2)[2] and of two stilbene derivatives, kuwanols A (3)[3] and B (4),[3] from the reddish violet powder obtained from the surface of the Morus root bark (Ohshimasō, a cultivated variety of Morus bombycis Koidz.[4]). In the course of extended studies of the reddish violet powder, we isolated a novel 2-arylbenzofuran derivative, mulberrofuran P, from the powder (Ichinose, a cultivated variety of Morus alba L.[4]). *In this paper, the structure determination of the compound is described.*

The acetone extract of the reddish violet powder was fractionated sequentially by silica gel column chromatography, and then by preparative tlc, resulting in the isolation of mulberrofuran P (1).

Mulberrofuran P (1), a blue amorphous powder,[5] $[\alpha]_D^{24}$ +19.5° (ethanol) gave the FD-MS showing a molecular ion peak at m/z 574, and the ^{13}C nmr spectrum indicating the presence of thirty-four carbon atoms [four aliphatic carbons (1 x $-CH_3$, 1 x $>C<^{O}_{O}$, 1 x $-CH=C<_{O}$), thirty aromatic carbons (12 x CH, 9 x C, 9 x C-O)] (Table I).

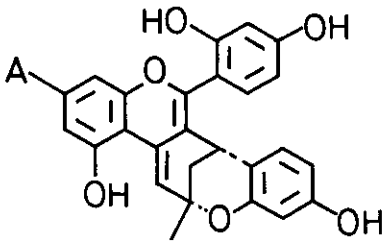
Work-up of 1 with acetic anhydride in pyridine gave the hexaacetate (1a) which showed a molecular ion peak at m/z 826 in its EI-MS. These results indicated the

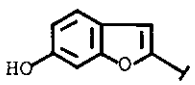


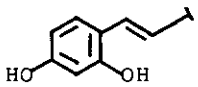
1 : R_1=OH, R_2=H

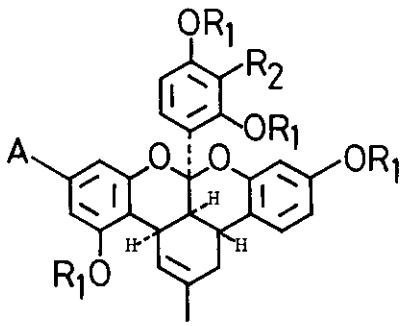
1a : R_1=OAc, R_2=Ac

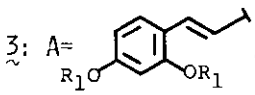
5 : R_1=R_2=H



2: A= 

4: A= 



3: A=  , R_1=R_2=H

3a: A= 〃 , R_1=Ac, R_2=H

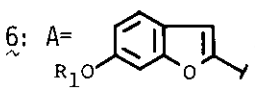
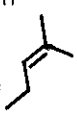
6: A=  , R_1=Ac, R_2= 

Table I ^{13}C nmr spectra of 1 and 5

	1	5		1	5
C-2	157.6	158.2	C-9"	111.6	111.6
C-3	102.2	103.2	C-10"	158.2	160.2
C-3a	121.1	123.0	C-11"	104.4	105.0
C-4	121.5	122.3	C-12"	160.0	160.8
C-5	112.9	113.5	C-13"	106.9	107.6
C-6	154.6	155.0	C-14"	131.1	131.6
C-7	98.1	98.5	C-15"	115.3*	115.7*
C-7a	156.7	157.4	C-16"	152.0	152.7
C-1'	130.9	129.8	C-17"	104.8	105.4
C-2'	105.5	106.1	C-18"	152.0	153.6
C-3'	156.3	157.4	C-19"	110.3	111.6
C-4'	114.9*	116.0*	C-20"	128.2	126.7
C-5'	155.8	157.1			
C-6'	106.0	106.5			
C-1"	127.2	140.8			
C-2"	130.0	125.3			
C-3"	126.1	132.7**			
C-4"	122.5*	122.5*	solvent: CD_3OD		
C-5"	117.7*	130.1**			
C-6"	151.3	121.3			
C-7"	17.5	22.3			
C-8"	106.5	106.7			

*, **: Assignments may be interchangeable.

Table II ^{1}H nmr chemical shifts and acetylation shifts (ppm)

	1[a]	5[a]	1[b]	1a[b]	Δ
3-H	6.93 (br s)	6.97 (d, J=0.5)	7.08 (d, J=1)	7.35 (br s)	-0.27
4-H	7.34 (d, J=8)	7.35 (d, J=9)	7.41 (d, J=8)	7.67 (d, J=8)	-0.26
5-H	6.73 (dd, J=2,8)	6.74 (dd, J=2.5,9)	6.81 (dd, J=2,8)	7.06 (dd, J=2,8)	-0.25
7-H	6.90 (br d, J=2)	6.90 (br d, J=2.5)	6.98 (br d, J=2)	7.41 (br d, J=2)	-0.43
2'-H	6.98 (s)	6.99 (d, J=1.5)	7.08 (d, J=2)	7.47 (d, J=2)	-0.39
6'-H	6.98 (s)	7.01 (d, J=1.5)	7.12 (d, J=2)	7.42 (d, J=2)	-0.30
1"-CH_3	2.65 (s)	2.51 (s)	2.49 (s)	2.40 (s)	+0.09
2"-H	8.35 (s)	8.39 (br s)	8.45 (s)	8.14 (s)	+0.31
6"-H	——	7.52 (br s)	——	——	
11"-H	6.24 (d, J=2)	6.26 (d, J=2.5)	6.29 (d, J=2)	6.94 (d, J=2)	-0.65
13"-H	5.85 (dd, J=2,8)	5.85 (dd, J=2.5,9)	5.92 (dd, J=2,8)	6.72 (br)	-0.80
14"-H	6.20 (d, J=8)	6.13 (d, J=9)	6.24 (d, J=8)	6.72 (br)	-0.48
17"-H	6.47 (d, J=2)	6.47 (d, J=2.5)	6.58 (d, J=2)	6.91 (d, J=2)	-0.33
19"-H	6.46 (dd, J=2,9)	6.52 (dd, J=2.5,9)	6.53 (dd, J=2,8)	6.92 (dd, J=2,8)	-0.39
20"-H	8.38 (d, J=9)	7.61 (d, J=9)	8.43 (d, J=8)	8.13 (br)	+0.30
			$COCH_3$	2.13 2.24 2.29 2.46 2.47 2.56	

solvent a: CD_3OD, b: acetone-d_6 (J in Hz)

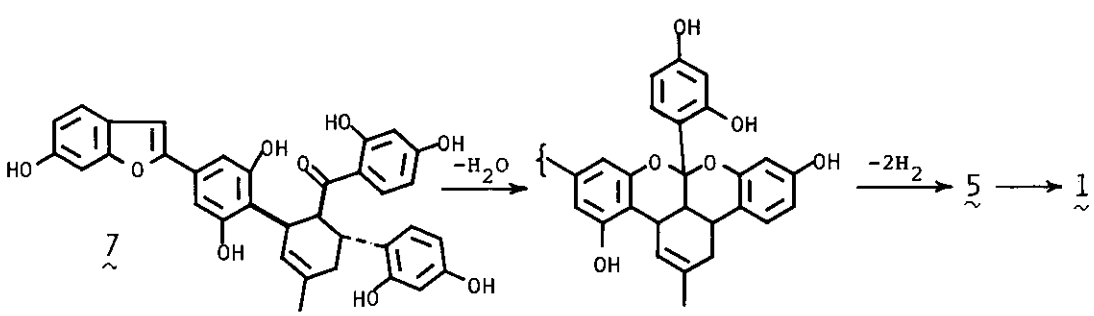


Chart 1

composition of mulberrofuran P to be $C_{34}H_{22}O_9$. Mulberrofuran P was positive to the methanolic ferric chloride test, and its ir spectrum showed absorption bands due to hydroxyl and benzene ring moieties. The uv spectrum of 1 exhibited maxima at 210, 284, 315, 336, 351, and 370 nm, and was similar to that of albanol B (5).[6,7] The ^{1}H nmr spectrum of 1 (CD_3OD) was examined being compared with that of 5, and showed the presence of the following moieties in 1: 1) protons in a 2-arylbenzofuran moiety, δ 6.73 (1H, dd, J=2 and 8, C-5-H), 6.90 (1H, br d, J=2, C-7-H), 6.93 (1H, br s, C-3-H), 6.98 (2H, s, C-2' and C-6'-H),[8] 7.34 (1H, d, J=8, C-4-H), 2) protons in two 2,4-dioxygenated phenyl moieties, δ 5.85 (1H, dd, J=2 and 8, C-13"-H), 6.20 (1H, d, J=8, C-14"-H), 6.24 (1H, d, J=2, C-11"-H); δ 6.46 (1H, dd, J=2 and 9, C-19"-H), 6.47 (1H, d, J=2, C-17"-H), 8.38 (1H, d, J=9, C-20"-H), 3) an aromatic proton, δ 8.35 (1H, s), and 4) protons of a methyl group, δ 2.65 (3H, s). Comparison of the ^{13}C nmr spectra of 1 and 5 indicated that the chemical shifts of the carbon atoms of 1 were similar to those of the relevant carbon atoms of 5, except in the carbon atoms of D-ring skeleton which were affected by additional substituent (Table I). Compared with the ^{1}H nmr spectrum of 1 with that 5, the spectrum of 1 indicated the absence of the proton at the C-6" position, and the C-20" proton signal shifted 0.77 ppm toward downfield from the corresponding proton of 5 (Table II). These results suggest that 1 is a 6"-hydroxy-albanol B. This suggestion was further supported by the following result. Comparison of the ^{1}H nmr spectra of 1 and 1a indicated that the acetylation of the hydroxyl groups at C-5' and C-6" positions caused larger upperfield shifts of the protons at the C-2" and C-20" positions (C-2"-H: +0.31 ppm, C-20"-H: +0.30 ppm) (Table II). The similar shifts were observed in the case of both mulberrofuran F pentaacetate (6)[7] and kuwanol A hexaacetate (3a).[3] From the above results, we propose the formula 1 for the structure of mulberrofuran P. Biogenetically, mulberrofuran P seems to be a derivative of the Diels-Alder type adducts, such as mulberrofuran C (7),[9] and is produced possibly through the steps described in Chart 1.

EXPERIMENTAL

Abbreviations: s=singlet, d=doublet, dd=double doublet, br=broad, sh=shoulder. The general experimental procedures used are described in the previous paper.[7] The following instruments were used: ^{1}H and ^{13}C nmr spectra; JEOL GX-400 FTNMR spectrometer, uv spectrum; Hitachi 340 UV spectrometer, ir spectrum; Hitachi 260-30

IR spectrometer, ms; JEOL JMS 01SG-2 mass spectrometer, optical rotation; JASCO DIP-4.

Isolation of Mulberrofuran P (1)

The reddish violet powder (760 g) obtained from the surface of the root bark of cultivated mulberry tree (Ichinose, a cultivated variety of Morus alba L.) was extracted with acetone. Evaporation of the acetone solution to dryness yielded 69 g of residue. The residue (10 g) was chromatographed on silica gel (200 g) with chloroform-acetone as an eluent, each fraction being monitored by tlc. The fractions eluted with chloroform containing 5 % acetone, which showed on the tlc plate a characteristic blue spot, were evaporated to give the residue (2.2 g). To isolate the colored compound , the residue (2.2 g) was fractionated by preparative tlc (solvent systems, chloroform:acetone=1:1, n-hexane:acetone=1:1, chloroform:methanol=6:1) to give mulberrofuran P (1, 2 mg).

Mulberrofuran P (1)

Compound 1 was obtained as a blue amorphous powder. $[\alpha]_D^{24}$ +19.5° (c=0.0113, ethanol). FD-MS m/z: 574 (M^+), 465. $FeCl_3$ test: positive (blue ⟶ reddish brown). ir ν_{max}^{KBr} cm^{-1}: 3370 (br), 1680 (sh), 1620, 1600 (sh). uv λ_{max}^{EtOH}nm(log ε): 210 (4.72), 284 (4.17), 315 (sh 4.33), 336 (4.53), 351 (4.61), 370 (4.56). ^{13}C and ^1H nmr spectra are described in Table I and II, respectively.

Mulberrofuran P Hexaacetate (1a)

A mixture of mulberrofuran P (1, 3 mg), acetic anhydride (1 ml) and pyridine (0.2 ml) was kept at room temperature for 15 h, and treated as usual. The reaction product was purified by preparative tlc (n-hexane:acetone=3:2) to give hexaacetate (1a, 2 mg). The compound 1a was obtained as colorless powder, $FeCl_3$ test: negative. EI-MS m/z: 826 (M^+), 784, 742, 700. ^1H nmr spectrum is described in Table II.

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