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

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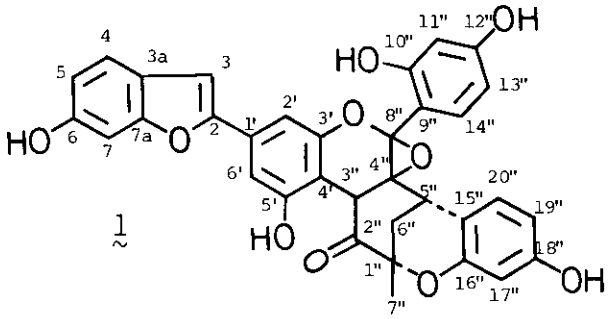
Abstract —— A novel 2-arylbenzofuran derivative, mulberrofuran Q, was isolated from the reddish violet powder (lenticel) of the surface of the root bark of cultivated mulberry tree (Ichinose, a cultivated variety of Morus alba L.). Its structure was shown to be 1 on the basis of spectral and chemical evidence. Mulberrofuran Q 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 several 2-arylbenzofuran and stilbene derivatives from the reddish violet powder (lenticel) obtained from the surface of the Morus root bark.[1-4] In this paper, we report the structure determination of a novel 2-arylbenzofuran derivative, mulberrofuran Q isolated from the powder.

The acetone extract of the reddish violet powder (lenticel) obtained from the surface of the Morus root bark (Ichinose, a cultivated variety of Morus alba L.[5]) was fractionated sequentially by the silica-gel column chromatography and preparative tlc, resulting in the isolation of 1 (0.14 % yield from the powder).

Mulberrofuran Q (1), amorphous powder, $[\alpha]_D^{21}$ +82.4° (c=0.278, EtOH), $FeCl_3$ test (brown),[6] gave the FD-MS which showed the molecular ion peak at m/z 592, and ^{13}C nmr spectrum which indicated the presence of thirty-four carbon atoms [nine aliphatic carbons, twenty-four aromatic carbons, and one carbonyl carbon] (Table I). These results indicated the composition of mulberrofuran Q to be $C_{34}H_{24}O_{10}$. The compound 1 showed the following spectra: ir ν_{max}^{KBr} cm^{-1}: 3360 (br), 1690, 1610; uv λ_{max}^{EtOH} nm (log ε): 222 (sh 4.43), 280 (4.16), 284 (sh 4.15), 321 (4.45), 335 (sh 4.32). The ir spectrum showed the presence of a carbonyl group and the uv spectrum was similar to those of the 4'-substituted 6,3',5'-trioxygenated 2-arylbenzofuran



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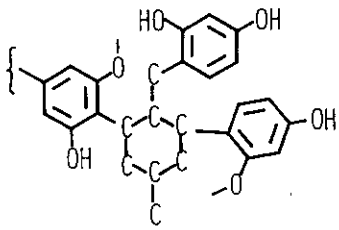

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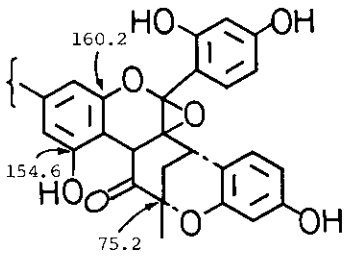

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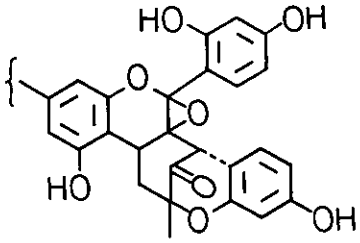

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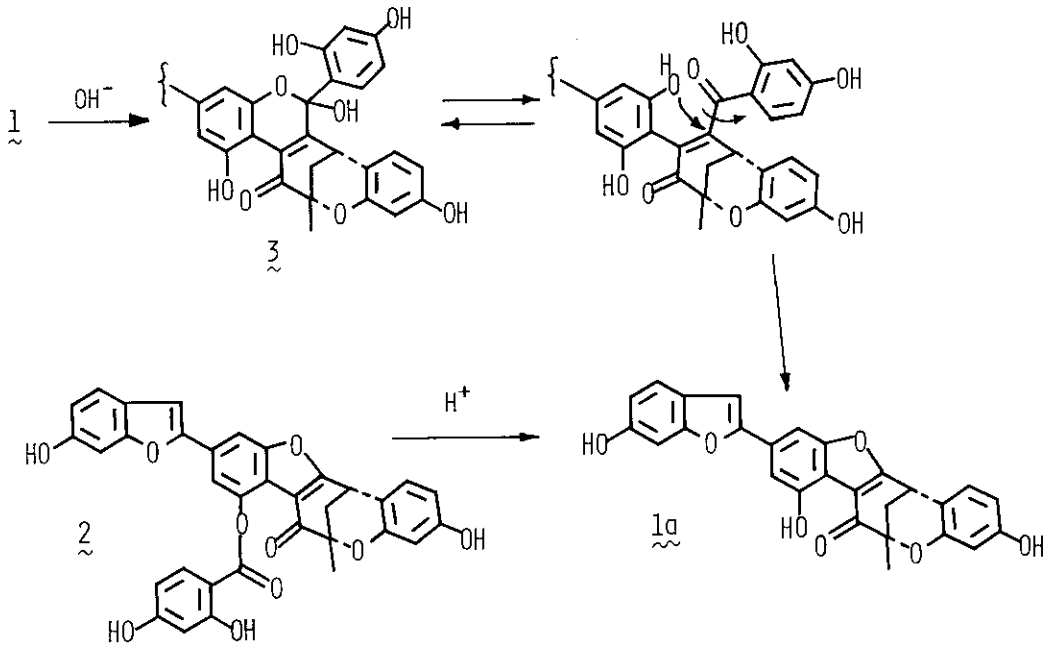
Fig. 1



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1a

Chart 1

Table I ^{13}C nmr spectra of 1, 1b and 1c (ppm)

	1*	1b**	1c**		1*	1b**	1c**
C-2	158.1	159.3	159.6	C-9"	114.3	111.9	111.7
C-3	101.7	100.8	100.8	C-10"	166.2	161.3	158.9
C-3a	122.0	121.9	121.9	C-11"	97.9	98.3	99.1
C-4	121.3	120.5	120.4	C-12"	172.2	162.4	159.2
C-5	112.7	111.6	111.5	C-13"	102.8	104.0	103.6
C-6	154.7	154.0	154.5	C-14"	133.7	132.0	131.2
C-7	98.5	95.4	95.5	C-15"	112.8	121.1	120.4
C-7a	155.9	154.3	155.1	C-16"	155.1	155.1	156.8
C-1'	132.1	132.2	131.3	C-17"	98.2	99.3	99.8
C-2'	104.9	101.6	97.0	C-18"	155.9	155.2	157.4
C-3'	160.2	157.6	192.5	C-19"	111.8	106.3	106.4
C-4'	109.9	112.4	128.2	C-20"	125.9	130.6	128.6
C-5'	154.6	158.4	157.4				
C-6'	107.4	101.5	101.6			54.9	54.9
C-1"	75.2	76.1	75.8			55.2	55.1 x2
C-2"	195.4	200.8	193.9	OCH_3		55.4	55.2
C-3"	49.0	148.3	153.6			55.5	55.5
C-4"	92.2	121.7	114.6			56.0	55.6
C-5"	37.9	34.0	34.2			60.8	
C-6"	31.0	31.5	36.4				
C-7"	22.4	22.9	22.7				
C-8"	109.1	98.9	163.2				

solvent; *: acetone-d_6 **: $CDCl_3$

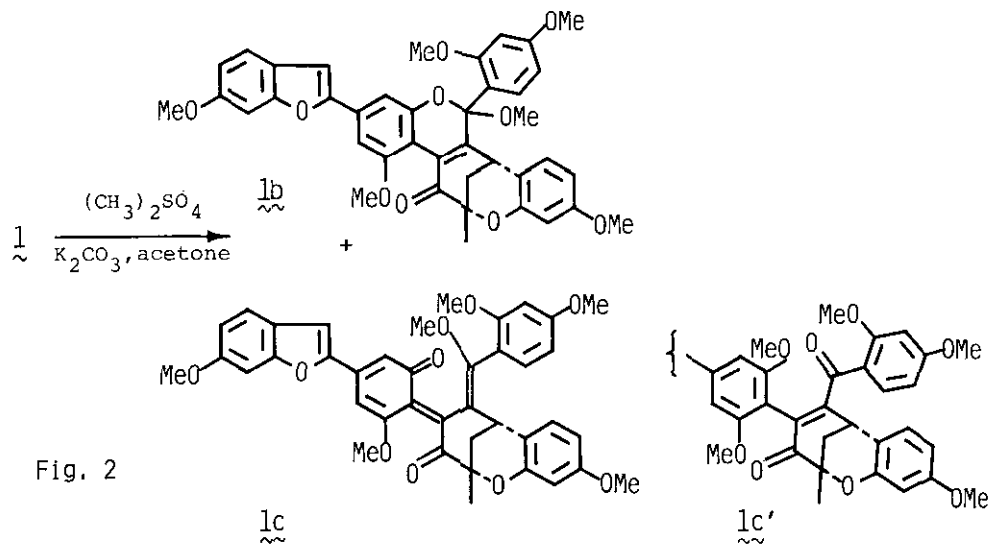

Fig. 2

derivatives.[4,7] The ^1H nmr spectrum of 1 (400 MHz, acetone-d_6) was analysed by a decoupling experiment and by comparison with the spectra of 2-arylbenzofuran derivatives.[4,7] The spectrum showed the following proton signals: 1) protons in a 2-arylbenzofuran moiety, δ6.66 (1H, d, J=2, C-2'-H), 6.81 (1H, dd, J=2 and 8, C-5-H), 6.87 (1H, d, J=2, C-6'-H), 6.94 (1H, br d, J=2, C-7-H), 7.00 (1H, d, J=1, C-3-H), 7.46 (1H, d, J=8, C-4-H), 2) protons in two 2,4-dioxygenated phenyl moieties,

δ 6.37 (1H, dd, J=2 and 9, C-19"-H), 6.38 (1H, d, J=2, C-17"-H), 6.69 (1H, d, J=9, C-20"-H); δ 6.17 (1H, d, J=2, C-11"-H), 6.56 (1H, dd, J=2 and 8, C-13"-H), 7.38 (1H, d, J=8, C-14"-H), and 3) seven aliphatic protons. The ^{13}C nmr spectrum was analysed by off-resonance decoupling technique and by comparison with the spectra of 2-arylbenzofuran derivatives.[4,7] The spectrum showed the following carbon atom signals: 1) carbons in a 2-arylbenzofuran moiety (C-2～C-6'), 2) carbons in two 2,4-dioxygenated phenyl moieties (C-9"～C-20"), and 3) seven aliphatic carbons and one carbonyl carbon (C-1"～C-8") (Table I). Considering that some Diels-Alder type adducts with 4'-dehydroprenyl-2-arylbenzofuran and chalcone were isolated from Morus root bark,[1,3,7] the above spectral data and the biogenetic analogy to these Diels-Alder type adducts led us to the assumption that the carbon skeleton of the $C_8H_7O_2$ moiety is that described as 1'. The structure of this moiety was analysed by the ^{13}C nmr spectrum to contain seven aliphatic carbons and one carbonyl carbon: $-CH_3$, $-CH_2-$, 2 x $-CH<$, 2 x $>C<_{O-}$, $>C<^{O-}_{O-}$, $>C=O$ (Table I). The two singlet signals at δ 92.2 and 109.1 ppm suggest the presence of ketal structure in the moiety.[8] In the ^1H nmr spectrum of 1, the signals of the protons in the moiety were observed at δ 1.75 (3H, s, $-CH_3$), 1.91 (1H, dd, J=4 and 14, $-CH_2-$), 2.76 (1H, dd, J=3 and 14, $-CH_2-$), 2.82 (1H, dd, J=3 and 4, $-CH<$), 3.52 (1H, s, $-CH<$). From the above results, the two possible structures 1" and 1'" were suggested (Fig. 1). Further data to discriminate the structures were obtained by the following long-range selective ^1H decoupling (LSPD) technique.[9] When the methyl proton signal at δ 1.75 (C-1"-CH_3) was weakly irradiated, the signal at δ 75.2 (C-1") varied in its shape and increased in area (ca. 30 %). When the methine proton signal at δ 3.52 (C-3"-H) was weakly irradiated, the signals at δ 154.6 (C-5') and 160.2 (C-3') varied in their shape. From these results, the structure 1" seems to be more favorable than 1'". To clarify the structure of the $C_8H_7O_2$ moiety further data were obtained as follows. Treatment of 1 with potassium carbonate in acetone gave the compound 1a and the starting material.[10] The compound 1a was identified with the hydrolysis product of mulberrofuran M (2),[4] which seems to be derived from the hemiketal intermediate (3) through the intramolecular Michael addition described in Chart 1. Further data supporting the presence of epoxide ring in the moiety was obtained by the examination of the hexamethyl ethers (1b, c) obtained by treatment of 1 with dimethyl sulfate and potassium carbonate in acetone[11] (Fig. 2). The compound 1b, EI-MS m/z 676 (M^+), showed the following ^1H nmr spectrum (acetone-d_6): 1) protons in a 2-arylbenzofuran moiety, δ 6.71 (1H, d, J=2, C-2'-H), 6.86 (1H, dd, J=2 and 8, C-5-H),

6.98 (1H, d, J=2, C-6'-H), 7.12 (1H, br d, J=2, C-7-H), 7.17 (1H, d, J=1, C-3-H), 7.45 (1H, d, J=8, C-4-H), 2) protons in two 2,4-dioxygenated phenyl moieties, δ 6.33 (1H, d, J=2, C-11"-H), 6.45 (1H, dd, J=2 and 8, C-13"-H), 7.21 (1H, d, J=8, C-14"-H); δ 6.47 (1H, dd, J=2 and 8, C-19"-H), 6.49 (1H, d, J=2, C-17"-H), 7.25 (1H, d, J=8, C-20"-H), 3) six aliphatic protons, δ 1.67 (3H, s, C-1"-CH_3), 1.95 (1H, dd, J=4 and 14, C-6"-H), 2.56 (1H, dd, J=2 and 14, C-6"-H), 3.89 (1H, dd, J=2 and 4, C-5"-H), and 4) protons of methoxyl groups, δ 3.46, 3.68, 3.83, 3.86, 3.92, 4.03 (each 3H, s). The ^{13}C nmr spectrum was analysed by comparing with that of 1, and showed the signals of hemiketal carbon atom at δ 98.9 (C-8"), olefinic carbon atoms at δ 121.7 (C-4") and 148.3 (C-3"), and one methine carbon atom at δ 34.0 (C-5") (Table I). From these spectral data, the structure 1b was suggested for the hexamethyl ether. The compound 1c, EI-MS m/z 676 (M^+), showed the following ^1H nmr spectrum (acetone-d_6): 1) protons in a 2-arylbenzofuran moiety, δ 6.78 (1H, d, J=2, C-2'-H), 6.80 (1H, d, J=2, C-6'-H), 6.87 (1H, dd, J=2 and 8, C-5-H), 7.13 (1H, br d, J=2, C-7-H), 7.14 (1H, d, J=1, C-3-H), 7.46 (1H, d, J=8, C-4-H), 2) protons in two 2,4-dioxygenated phenyl moieties, δ 6.27 (1H, dd, J=2 and 8, C-13"-H), 6.35 (1H, d, J=2, C-11"-H), 7.04 (1H, d, J=8, C-14"-H); δ 6.46 (1H, dd, J=2 and 8, C-19"-H), 6.47 (1H, d, J=2, C-17"-H), 7.11 (1H, d, J=8, C-20"-H), 3) six aliphatic protons, δ 1.63 (3H, s, C-1"-CH_3), 2.30 (1H, dd, J=3 and 13, C-6"-H), 2.77 (1H, dd, J=3 and 13, C-6"-H), 4.00 (1H, t, J=3, C-5"-H), and 4) protons of methoxyl groups, δ 3.50, 3.64, 3.68, 3.75, 3.78, 3.87 (each 3H, s). In the ^{13}C nmr spectrum, the signals of two carbonyl carbon atoms were observed at δ 192.5 and 193.9, while the hemiketal carbon atom signal could not be observed (Table I). From these spectral data, the two possible structures (1c, c') were suggested (Fig. 2). As chemical shift values of the carbon atoms (and protons) at C-2' and -6' positions appeared nonequivalent,[7] it is suggested that the structure 1c is considered to be more favorable than the structure 1c'. From above results, we propose the formula (1) for mulberrofuran Q. Biogenetically mulberrofuran Q seems to be derived from the Diels-Alder type adducts, such as mulberrofurans C (4)[7b] and J (5),[7c] through the hemiketal intermediate (6) and mulberrofuran I (7),[1] and also to be an intermediate to mulberrofuran M (2).[4] Accordingly, a biogenetic pathway of mulberrofurans[1,3,7] can be postulated as described in Chart 2.

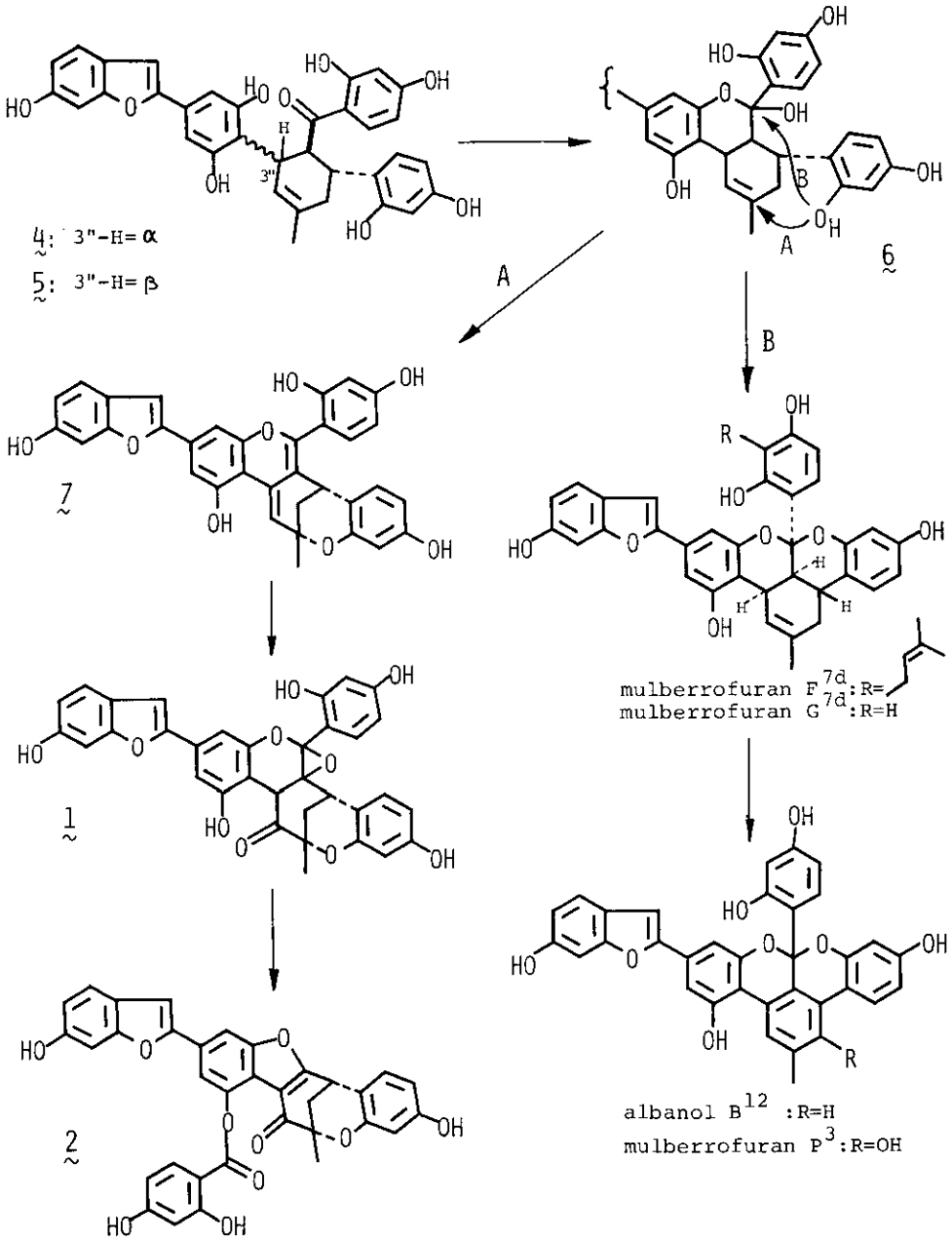
4: 3"-H= α
5: 3"-H= β
A
B
6
7
1
2
mulberrofuran F [7d]: R=
mulberrofuran G [7d]: R=H
albanol B [12] : R=H
mulberrofuran P [3]: R=OH

Chart 2

ACKNOWLEDGEMENT

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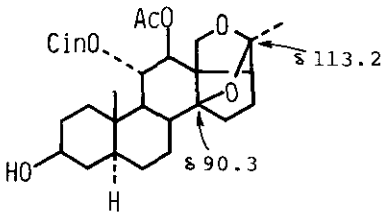

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10. A mixture of 1 (38 mg) and K_2CO_3 (5 g) in acetone (30 ml) was refluxed for 2 h to give 1a (3 mg) and the starting material (30 mg).
11. A mixture of 1 (40 mg), $(CH_3)_2SO_4$ (0.2 ml), K_2CO_3 (5 g) in acetone (30 ml) was refluxed for 2 h to give 1b (20 mg) and 1c (20 mg).
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