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STRUCTURE OF MULBERROFURAN I, A NOVEL 2-ARYLBENZOFURAN DERIVATIVE FROM THE CULTIVATED MULBERRY TREE (MORUS BOMBYCIS KOIDZ.)[1)]

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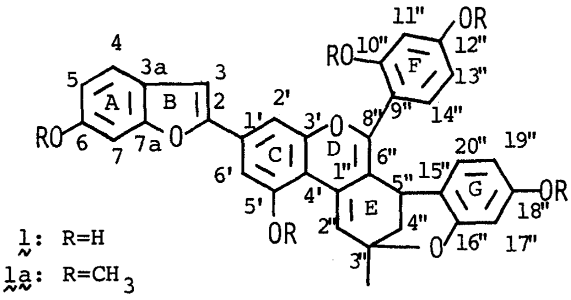
From an acetone extract of the reddish violet powder obtained from the surface of the Morus root bark (Morus bombycis Koidz.), a 2-arylbenzofuran derivative was isolated and named mulberrofuran I. Its structure was shown to be **1** on the basis of spectral evidence. Mulberrofuran I is regarded biogenetically as a variation of a Diels-Alder type adduct of a chalcone derivative and a dehydroprenyl-2-arylbenzofuran derivative.

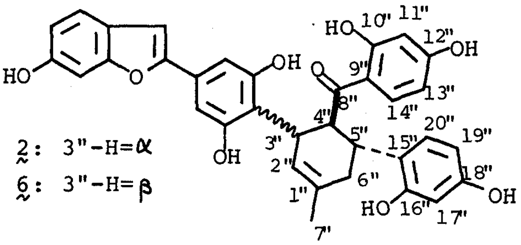
KEYWORDS —— 2-arylbenzofuran; Diels-Alder type adduct; ^{13}C NMR spectra; ^{1}H NMR spectra; selective $^{13}C-\{^{1}H\}$ nuclear Overhauser effect

Previously we reported the structure determination of a series of natural Diels-Alder type adducts isolated from the root bark of the cultivated mulberry tree.[2)] In the course of extended studies of Morus root bark constituents, we isolated a new 2-arylbenzofuran derivative named mulberrofuran I (**1**) from the reddish violet powder obtained from the surface of the Morus root bark (Morus bombycis Koidz.). Preparative thin layer chromatography of the acetone extract of the powder (260 g) on silica gel gave mulberrofuran I (**1**) (240 mg) as a reddish violet amorphous powder.

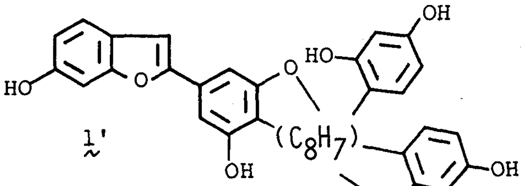
Mulberrofuran I (**1**), $[\alpha]_D^{23}$ +212° (EtOH), showed a molecular ion peak at m/z 560 in its FD-MS. The ^{13}C NMR of **1** indicated the presence of thirty-four carbons (Table 1). Treatment of **1** with dimethyl sulfate gave the pentametyl ether (**1a**) whose mass spectrum showed the fragments at m/z 630.2282 (M^+, $C_{39}H_{34}O_8$), 615.2062 ($C_{38}H_{31}O_8$), 492.1529 ($C_{31}H_{24}O_6$). Work-up of **1** with acetic anhydride in pyridine gave the pentaacetate (**1b**) which showed a molecular ion peak at m/z 770 in its FD-MS. These results revealed the molecular formula of **1** to be $C_{34}H_{24}O_8$. The compound (**1**) showed the following spectra: IR ν_{max}^{KBr} cm^{-1}: 3280 (br), 1665, 1620, 1600 (sh); UV λ_{max}^{EtOH} nm (log ε): 250 (infl. 4.10), 290 (sh 4.10), 330 (sh 4.38), 338 (4.39). The UV spectrum suggested that **1** is a 2-arylbenzofuran derivative.[3)] Acidic solution of **1** showed a red color, which faded when neutralized.[4)] The UV spectrum in the acidic solution showed a bathochromic shift as follows: UV $\lambda_{max}^{EtOH+HCl}$ nm (log ε): 296 (sh 4.09), 330 (sh 4.23), 340 (4.26), 456 (3.79), 548 (4.08). The ^{1}H NMR spectrum of **1** (400 MHz, acetone-d_6) was analysed by a decoupling experiment and by



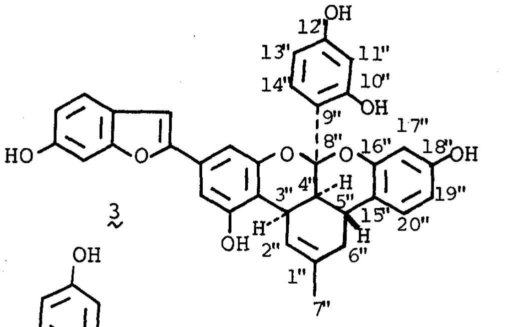
1: R=H
1a: R=CH$_3$
1b: R=COCH$_3$



2: 3''-H=α
6: 3''-H=β



1'



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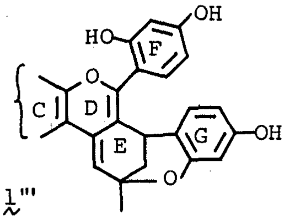
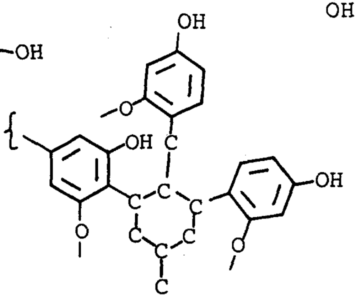
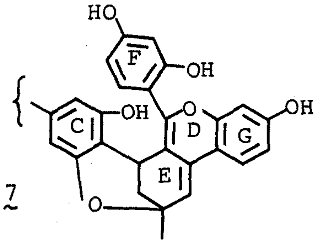


1'''



1''



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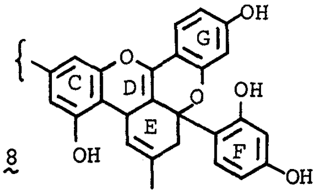

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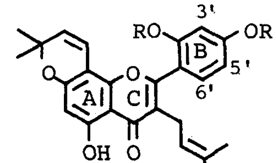
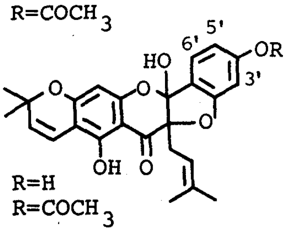
Table 1. ^{13}C NMR Chemical Shifts of Mulberrofurans I (1), C (2) and G (3) in Acetone-d_6

Carbon	1	2	3	Carbon	1	2	3
C-2	155.0*	157.8*	156.7*	C-4"	33.1	47.9	28.5
C-3	102.3	101.9	102.2	C-5"	32.8	33.2	35.1
C-3a	121.3	121.9	122.5	C-6"	116.9	32.4	36.2
C-4	121.2	121.9	122.0	C-7"	28.5	23.8	23.7
C-5	112.5	113.1	113.4	C-8"	142.3	209.5	103.3
C-6	154.0*	155.4*	155.0*	C-9"	112.9	116.4	113.4
C-7	97.4	98.4	98.4	C-10"	156.7*	166.0*	157.9*
C-7a	156.9*	156.5*	157.7*	C-11"	102.9	104.8	103.9
C-1'	130.5	130.9	131.5	C-12"	159.0*	167.0*	159.9*
C-2'	106.0	103.6	105.0	C-13"	107.2	108.8	107.3
C-3'	156.6*	156.5*	156.7*	C-14"	132.2	128.7	130.3
C-4'	119.0	113.6	117.5	C-15"	118.1	122.5	116.8
C-5'	156.0*	156.5*	156.7*	C-16"	153.2*	157.8*	153.3*
C-6'	103.7	103.6	105.4	C-17"	102.9	104.8	104.0
C-1"	126.6	134.1	133.7	C-18"	155.9*	157.8*	154.5*
C-2"	119.9	124.2	122.9	C-19"	107.2	107.5	109.9
C-3"	72.3	36.2	37.2	C-20"	129.4	135.0	127.9

*: Assignments may be interchanged.



4: R=H
4a: R=COCH$_3$



5: R=H
5a: R=COCH$_3$

Table 2. Acetylation Shift of ^{1}H NMR of 1, 4 and 5

Proton	1	1b	Δ	Proton	1	1b	Δ
11"-H	6.61	7.26	-0.65	17"-H	6.21	6.52	-0.31
13"-H	6.59	7.31	-0.72	19"-H	6.16	6.42	-0.26
14"-H	7.29	7.79	-0.50	20"-H	6.55	6.63	-0.08
Solvent	A	A		Solvent	A	A	

Proton	4	4a	Δ	Proton	5	5a	Δ
3'-H	6.55	7.11	-0.56	3'-H	6.40	6.69	-0.29
5'-H	6.59	7.12	-0.53	5'-H	6.46	6.75	-0.29
6'-H	7.23	7.46	-0.23	6'-H	7.30	7.45	-0.15
Solvent	A	B		Solvent	B	B	

A: Acetone-d_6 B: CDCl$_3$

comparison with the spectra of 2-arylbenzofuran derivatives.3) The chemical shifts and coupling constants (Hz) of the 2-arylbenzofuran moiety are as follows: δ 6.82 (1H, dd, J = 2 and 8.5, C-5-H), 6.97 (2H, br s, C-7- and 2'-H), 7.11 (1H, d, J = 1.5, C-6'-H), 7.12 (1H, d, J = 0.9, C-3-H), 7.41 (1H, d, J = 8.5, C-4-H). Comparison of the ^{13}C NMR spectrum of 1 with those of mulberrofurans C (2)5) and G (3)3a) also indicated the substituted pattern on the 2-arylbenzofuran skeleton. The chemical shifts of the carbon atoms on the skeleton, except those of the carbon atoms at C-2, -4' and -6', were similar to those of the relevant carbon atoms of 3 (Table 1). These results suggest that 1 is a 4'-substituted 6,3',5'-trioxygenated 2-arylbenzofuran derivative. As chemical shift values of the protons at the C-2' and -6' positions appeared nonequivalent, it is suggested that one of the hydroxyl groups in the C-ring formed the ether linkage.6)

The presence of two 2,4-dioxygenated phenyl moieties (rings F and G) was suggested by analysing the ^{1}H NMR spectra of 1 and 1b. The chemical shifts and coupling constants (Hz) of the protons on the rings F and G of 1 and 1b are as follows: 1, δ 6.59 (1H, dd, J = 1.8 and 8.2, C-13"-H), 6.61 (1H, d, J = 1.8, C-11"-H), 7.29 (1H, d, J = 8.2, C-14"-H); δ 6.16 (1H, dd, J = 2.5 and 8.5, C-19"-H), 6.21 (1H, d, J = 2.5, C-17"-H), 6.55 (1H, d, J = 8.5, C-20"-H): 1b, δ 7.26 (1H, d, J = 1.8, C-11"-H), 7.31 (1H, dd, J = 1.8 and 8.2, C-13"-H), 7.79 (1H, d, J = 8.2, C-14"-H); δ 6.42 (1H, dd, J = 2.5 and 8.5, C-19"-H), 6.52 (1H, d, J = 2.5, C-17"-H), 6.63 (1H, d, J = 8.5, C-20"-H) Comparison of the ^{1}H NMR spectra of 1 and 1b indicated that the acetylation of the hydroxyl groups on the F-ring caused downfield shifts (-0.50~-0.72 ppm) of the protons on the ring, and that acetylation of the hydroxyl group on the G-ring caused downfield shifts (-0.08~-0.31 ppm). In the case of the B-ring protons of morusin (4)7) and its acetate (4a),7 acetylation of the relevant hydroxyl groups of 4 caused downfield shifts of the protons on the B-ring. On the other hand, the acetylation of the 4'-hydroxyl group of sanggenon A (5)8) caused smaller downfield shifts (Table 2). These results suggest that 1 has a hydroxyl group on the G-ring and two hydroxyl groups on the F-ring, and that the other oxygen atom on the G-ring formed the ether linkage. From the above results, the partial structure (1') was proposed.

Some Diels-Alder type adducts with 4'-dehydroprenyl-2-arylbenzofuran and chalcone were isolated from Morus root bark.2,3,6,10) The biogenetic analogy to these Diels-Alder type adducts led us to the assumption that the carbon skeleton of C_8H_7 moiety is described as 1". The structure of the moiety was analysed by the ^{13}C NMR spectrum to contain eight aliphatic carbons: $-CH_3$, $-CH<$, $-CH_2-$, $>C<^{O-}$, $2\times{>}\underline{C}{=}C<$, ${>}C{=}\underline{C}{<}^{O-}$, ${>}C{=}\underline{C}{<}^{H}$ (Table 1). In the ^{1}H NMR spectrum of 1, the signals of the protons in the moiety were observed at δ 1.57 (3H, s, $-CH_3$), 1.89 (1H, ddd, J = 1.2, 3.7 and 12.5, $-CH_2-$), 2.02 (1H, dd, J = 2.1 and 12.5, $-CH_2-$), 3.77 (1H, br s, $-\overset{|}{C}H-$), 6.78 (1H, d, J = 1.2, $-CH{=}C<$). From the above results, the three possible structures 1''', 7 and 8 were suggested. Further data to discriminate the three possible structures were obtained by the following selective $^{13}C-\{^{1}H\}$ nuclear Overhauser effect (NOE) measurements9) as shown in Fig. 1. When the methyl proton signal at δ 1.57 was irradiated, the NOE was apparently observed between the methyl protons and the oxygenated carbon atom at δ 72.3. The weak NOE between the methylene protons and the carbon atom at δ 72.3 was observed by the irradiation of the signals both at δ 1.89 and 2.02. The NOE was also observed between the methine proton at δ 3.77 and the carbon atom at δ 142.3 by the irradiation of the methine proton signal.

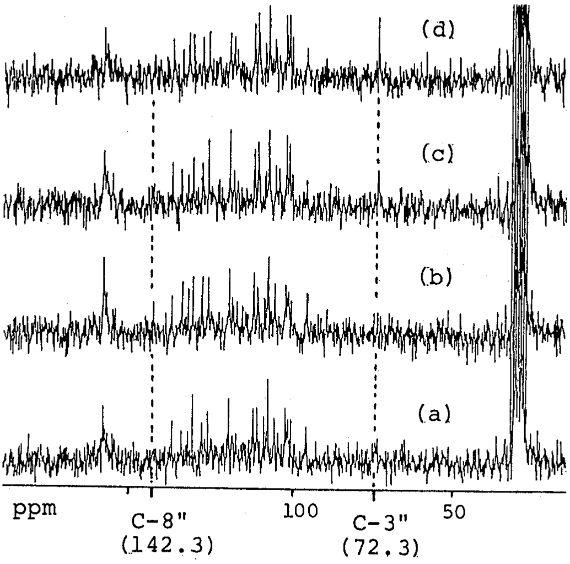


Fig. 1. ^{13}C NMR Spectra of 1
(a) irradiated at −5.44 ppm,
(b) irradiated at the methine proton signal (δ 3.77 ppm),
(c) irradiated at both the methylene proton signals (δ 1.89 and 2.02), and
(d) irradiated at the methyl proton signal (δ 1.57).

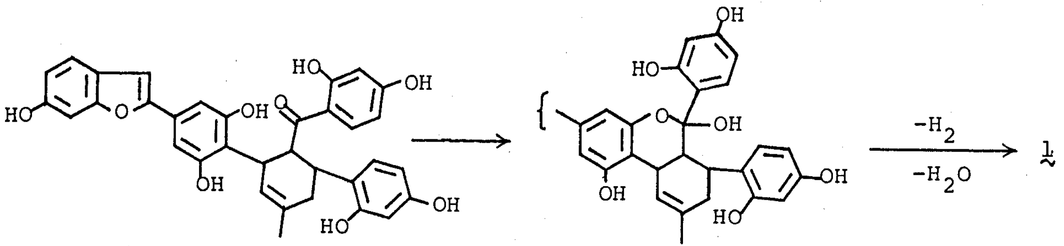


Chart 1

Considering these spectral data and the results of sequential decoupling experiments, the structure of the C_8H_7 moiety is possibly represented by 1''' or 7. The discrimination between 1''' and 7 was carried out on the basis of the ^{1}H NMR spectra of 1 and 1b. The signal of the olefinic proton of 1b at δ 6.32 shifted to a higher applied magnetic field than that of 1 at δ 6.78. The similar acetylation shift was observed in the case of mulberrofuran G (3).[3a] From these results, we propose the formula (1) for the structure of mulberrofuran I.

Biogenetically mulberrofuran I seems to be a derivative induced from the Diels-Alder type adduct, such as mulberrofurans C (2)[5] and J (6)[10] through the hemiketal intermediate described in Chart 1.

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REFERENCES AND NOTES

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