Communications to the Editor

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

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From an ethyl acetate extract of the root bark of cultivated mulberry tree (Morus Lhou(ser.) Koidz.), a 2-arylbenzofuran derivative was isolated and named mulberrofuran H. Its structure was shown to be 1 on the basis of spectral evidence. Mulberrofuran H is regarded biogenetically as a variation of a Diels-Alder type adduct of a chalcone derivative and a dehydroprenyl-2-arylbenzofuran derivative.

KEYWORDS ——— Morus Lhou(ser.); mulberry tree; mulberrofuran H; 2-arylbenzofuran; benzofuran; cyclohexene; Diels-Alder type adduct

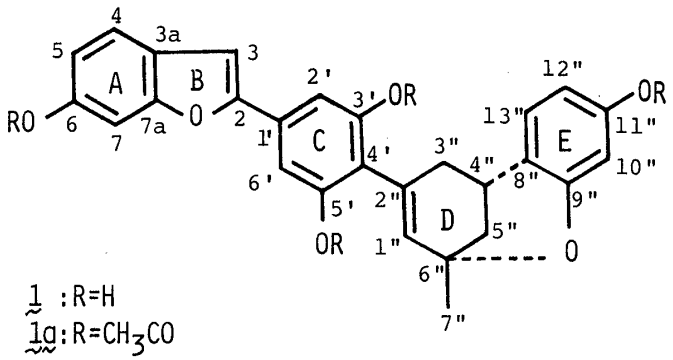
In a previous paper, we reported the structures of two natural hypotensive Diels-Alder type adducts, mulberrofurans F and G, isolated from the root bark of Morus Lhou(ser.) Koidz. (Japanese name "Rosō").[2)] Further extensive fractionation of the ethyl acetate extract of the root bark led to the isolation of a new 2-arylbenzofuran derivative, named mulberrofuran H (1), in 6.6×10^{-4}% yield. We herein describe the structure of the compound.

Mulberrofuran H (1), amorphous powder, $[\alpha]_D^{22}$ +25° (c=0.103, MeOH), negative to $FeCl_3$ test. The molecular formula of 1 was determined to be $C_{27}H_{22}O_6$ by the high-resolution mass spectrum (m/z 442.1415). The ^{13}C NMR spectrum indicated the presence of twenty seven carbons [nine aliphatic carbons (1xCH_3-, 2x-CH_2-, 1x>CH-, 1x>C=C<, 1x-C(-O)-O, 1x>C=C<) and eighteen aromatic carbons (8xCH, 4xC, 6xC-O)] (Table 1). Work up of 1 with acetic anhydride in pyridine gave the tetraacetate (1a) which showed a molecular ion peak at m/z 610 in its MS. The compound (1) showed the following spectra: IR ν_{max}^{KBr} cm^{-1}: 3400, 1620(sh), 1610, 1600(sh); UV λ_{max}^{EtOH} nm(log ε): 220(sh 4.48), 290(sh 4.15), 321(4.52), 333(sh 4.45). The UV spectrum suggested that 1 is a 2-arylbenzofuran derivative.[2-6)] This suggestion was supported through a comparative examination of the ^1H NMR spectrum of 1 (400 MHz, acetone-d_6) with those of 2-arylbenzofuran derivatives.[2-6)] The chemical shifts and coupling constants (Hz) of the 2-arylbenzofuran moiety are as follows: δ 6.81 (1H, dd, J=2 and 9, C-5-H), 6.85 (2H, s, C-2' and 6'-H), 6.97 (1H, d, J=2, C-7-H), 6.99 (1H, br s, C-3-H), 7.39 (1H, d, J=9, C-4-H). Comparison of the ^1H NMR spectra of 1 and 1a indicates that the protons at C-2' and 6' positions seem to be equivalent considering the chemical shift values of the relevant protons, and that the acetylation of the hydroxyl groups on the C-ring caused a downfield shift (0.52 ppm) of the protons in the ring. In the case of the C-ring protons of moracin C (3) and its acetate (3a), acetylation of the relevant

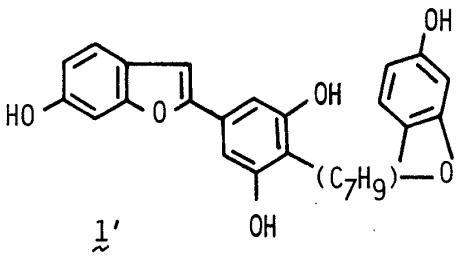
Table 1. ^{13}C NMR Chemical Shifts of Mulberrofurans H (1) and C (2) in Acetone-d_6

Carbon	1	2	Carbon	1	2	Carbon	1	Carbon	1
2	155.7*	156.5*	1'	131.5	130.9	3"	39.8**	11"	156.7*
3	102.2	103.6	2'	103.9	104.8	4"	31.8	12"	108.8
3a	122.4	121.9	3'	157.8*	156.5*	5"	34.6**	13"	132.4
4	121.9	121.9	4'	117.4	113.6	6"	71.8		
5	113.2	113.1	5'	155.2*	156.5*	7"	27.5		
6	155.3*	155.4*	6'	103.9	104.8	8"	119.0		
7	98.4	98.4	1"	130.6		9"	157.1*		
7a	156.7*	157.8*	2"	135.6		10"	103.9		

*: Assignments may be interchanged.
**: Assignments may be reversed.



1 : R=H
1g: R=CH_3CO



1'

Fig. 1

Table 2. Acetylation Shift of ^1H NMR of 1, 3, 4, and 5

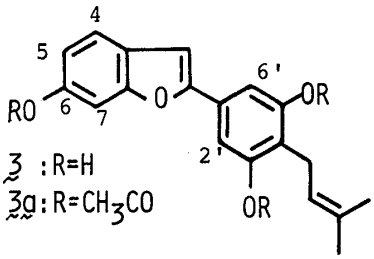
Proton	1	1a	Δ	Proton	1	1a	Δ
2' and 6'	6.85	7.37	-0.52	10"	6.27	6.57	-0.30
				12"	6.37	6.64	-0.27
				13"	6.97	7.14	-0.17
Sol.*	A	B		Sol.	A	B	

Proton	3[7]	3a[8]	Δ	Proton	1	1a	Δ
2' and 6'	6.97	7.41	-0.44	7	6.97	7.25	-0.28
				5	6.81	6.98	-0.17
				4	7.39	7.53	-0.14
Sol.	A	B		Sol.	A	B	

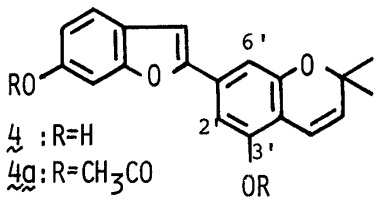
Proton	4[7]	4a[8]	Δ	Proton	3	3a	Δ
2'	6.82	7.12	-0.30	7	7.01	7.24	-0.23
6'	6.96	7.26	-0.30	5	6.85	6.95	-0.10
				4	7.43	7.50	-0.07
Sol.	A	B		Sol.	A	B	

*) Sol.: solvent
A: acetone-d_6
B: $CDCl_3$

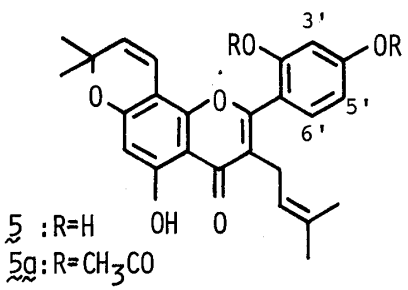
Proton	5[10]	5a	Δ
3'	6.55	7.11	-0.56
5'	6.59	7.12	-0.53
6'	7.23	7.46	-0.23
Sol.	A	B	



3 : R=H
3g: R=CH_3CO



4 : R=H
4g: R=CH_3CO



5 : R=H
5g: R=CH_3CO

hydroxyl group caused a downfield shift (0.44 ppm).[7,8] On the other hand, the acetylation of the 3'-hydroxyl group of moracin D (4) caused a smaller downfield shift (0.30 ppm) of the protons on the C-ring (Table 2).[7,8] These results suggest that the C-ring of 1 is represented by a 4'-substituted-3',5'-dihydroxyphenyl structure. The acetylation of the 6-hydroxyl group of 1 caused downfield shifts of the A-ring protons. Similar shifts were observed in the acetylation of 3 (Table 2).[7,8] In the ^{13}C NMR spectrum of 1, the chemical shifts of the carbon atoms of the 2-arylbenzofuran skeleton, except that of the carbon atoms at C-4', were similar to those of the relevant carbon atoms of mulberrofuran C (2)[4] (Table 1). These results suggest that 1 is a 4'-substituted-6,3',5'-trihydroxy-2-arylbenzofuran derivative.

The presence of a 2,4-dioxygenated phenyl moiety on the structure of 1 was supported by the mass and ^1H NMR spectra of 1 as follows: mass spectrum, m/z 332 (M^+-$C_6H_6O_2$, 100%),[9] 110 ($C_6H_6O_2$, 78%)[9]; δ 6.27 (1H, d, J=2, C-10"-H), 6.37 (1H, dd, J=2 and 8, C-12"-H), 6.97 (1H, d, J=8, C-13"-H). Comparison of the ^1H NMR spectra of 1 and 1a indicates that the acetylation of the hydroxyl group on the 2,4-dioxygenated phenyl moiety caused downfield shifts (0.27-0.30 ppm) of the protons at C-10" and C-12" positions. On the other hand, the acetylation of the 2' and 4' hydroxyl groups of morusin (5) caused larger downfield shifts (0.53-0.56 ppm) of the relevant protons (Table 2).[10] These results suggest that 1 has a hydroxyl group in the 2,4-dioxygenated phenyl moiety, and that the other oxygen atom formed the ether linkage. From the above results, the partial structure (1') was proposed. The remaining part of the C-4' side chain consisted of C_7H_9 was indicated by the ^{13}C NMR spectrum to contain seven aliphatic carbons: $-CH_3$, 2x$-CH_2-$, $>CH-$, $>C<_{O-}$, $H->C=C<$ (Table 1). In order to clarify the complete nature of the C-4' side chain, the ^1H NMR spectrum of 1 was analysed with the aid of sequential decoupling experiments, and the deduced structure of the C-4' side chain, along with the chemical shift values (δ) and the coupling constants (Hz) of the protons of the C_7H_9 moiety, is shown in Fig. 2.

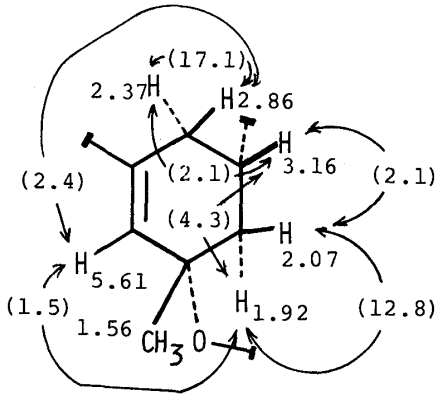


Fig. 2. ^1H NMR Chemical Shifts and coupling Constants (Hz) of D-Ring of 1

Further supporting data for the structure were obtained by the following long-range selective ^1H decoupling (LSPD) technique: when the signal at δ 1.56 (C-6"-CH_3) was weakly irradiated, the signal at δ 71.8 (C-6") increased the area (ca. +70%). The irradiation of the signal at δ 3.16 (C-4"-H) increased the area (ca. +15%) of the C-6" signal, and the irradiation of the signal at δ 5.61 (C-1"-H) also increased the area (ca. +30%) of the same carbon signal. On the other hand, the mass spectrum of 1 showed the characteristic fragment ion at m/z 332, the formation of which seems to be as shown in Chart 1.

From these results, we propose the formula (1) for the structure of mulberrofuran H.

Biogenetically, mulberrofuran H seems to be a derivative induced from the Diels-Alder type adducts, such as chalcomoracin[3] and mulberrofuran C (2),[4] through the mechanism described in Chart 2.

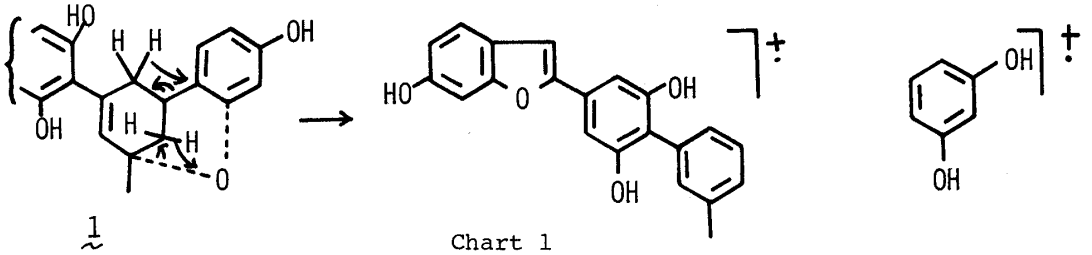


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Chart 1

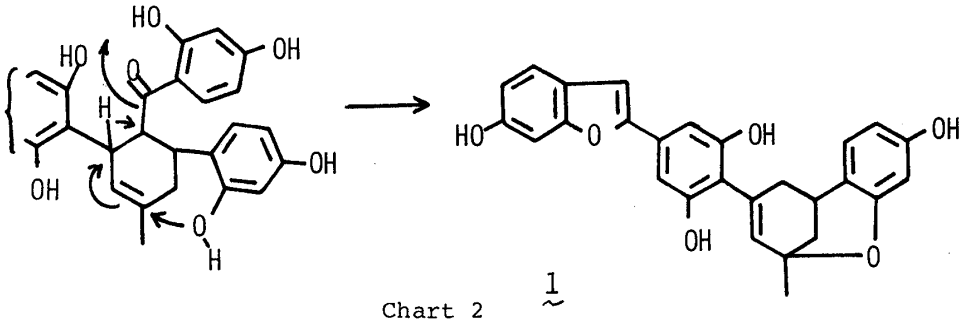

Chart 2 1

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