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NEW GMELINOL-TYPE LIGNAN, LEPTOSTACHYOL ACETATE

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The root of Phryma leptostachya L. subsp. asiatica (Hara) Kitam. (Phrymaceae), a perennial herb, was shown to contain stomach poisons to houseflies[1]. The extraction and fractionation of the root tissues, guided by bioassay in using the insect, had led us to the isolation of leptostachyol acetate (I) as one of the insecticidal principles. The structure elucidation of I is reported herein.

Leptostachyol acetate, m.p. 178~179°, M$^+$ 532.1563, has the molecular formula $C_{26}H_{28}O_{12}$. It showed λ_{max}^{EtOH} 295 and 236 nm(logε 4.0 and 4.2 respectively). The presence of an acetoxy group (1730 and 1240 cm^{-1}: τ8.22, 3H,s), four aromatic methoxy groups (τ6.06, 6H,s and τ6.27, 6H,s), two methylenedioxy functions (2780 and 940 cm^{-1}: τ4.20, 4H,s), and two hydrogens on unsaturated carbon atoms (τ3.79, 1H,s and τ3.81, 1H,s) was indicated by the absorption bands and resonance signals in the IR ($CHCl_3$) and NMR ($CDCl_3$) spectra of I. The presence of carbon-methyl (aside from that of the acetoxy group), aldehyde and hydroxy groups was ruled out from the spectra.

Alkaline hydrolysis of I gave a monohydric alcohol leptostachyol (II), m.p. 134~136°, M$^+$ 490.0148, $C_{24}H_{26}O_{11}$. It did not decolorize potassium permanganate in acetone even when heated for several minutes, therefore aliphatic double bonds are absent in the molecule. In the IR spectrum of II the hydroxy group was infered from the absorption band at ν max 3570 cm^{-1}, while the absorption due to carbonyl group was not shown. The NMR spectrum of II showed the signals of the methoxy groups (τ6.03, 3H,s, τ6.05, 3H,s and τ6.26, 6H,s), the methylenedioxy functions (τ4.15, 2H,s and τ4.17, 2H,s), the hydrogens on aromatic nuclei (τ3.70, 1H,s and τ3.76, 1H,s), and then showed the singlet signal of the hydroxy group (τ5.71, 1H,s).

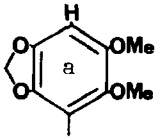
From these data it was deduced that leptostachyol acetate possesses a C_6-C_6O_2-C_6 skeleton, in which the C_6O_2-moiety consists of two saturated cyclic structures with the two ether-oxygen atoms. Biogenetic theory suggested a gmelinol-type structure for leptostachyol.

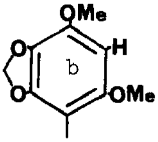
Hydrogenation of II over palladium catalyst afforded a dihydro-glycol (III), amorphous, M^+ 492, $C_{24}H_{28}O_{11}$.

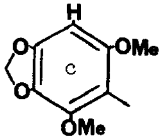
Periodate oxidation of III furnished formaldehyde and a tetrahydrofuran-3-one (IV), m.p. 116~118°, M^+460, $C_{23}H_{24}O_{10}$. In the latter's IR spectrum the five-membered ring ketone was infered from the absorption band at ν_{max} 1752 cm^{-1}.

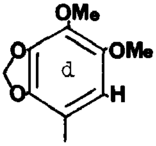
The mass spectra of I and II are in accord with those expected from 1-acetoxy- and 1-hydroxy-perhydrofurofuran lignans[2,3] respectively: subsequently the accurate molecular weight determinations of the important ions fully supported the conclusion. The ion peak at m/e 182.0577 indicated the presence of dimethoxymethylenedioxyphenyl group in the molecules.

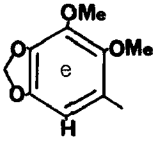
For the six possible structures of dimethoxymethylenedioxyphenyls (a~f), the probable chemical shift positions of aromatic hydrogens were calculated according to Ballantine et al[4]. Applying their figures for deriving the probable position of an aromatic proton, to the closely related lignans such as phrymarolins[5], it was found that corrections of -0.20±0.05 and -0.40±0.10τ had to be always allowed with respect to the meta- and ortho-hydrogens respectively.

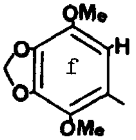












Chemical shift of ArH
(τ -values)

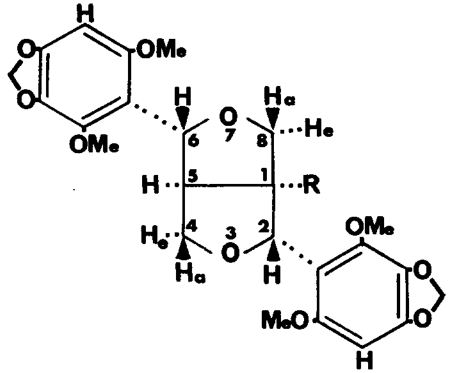
		a	b	c	d	e	f
Theory		3.80	3.90	3.90	3.35	3.35	3.35
Found	(I)	3.79 and 3.81					
	(II)	3.70 and 3.76					

Number of shifted MeO ($CDCl_3 \rightarrow C_6H_6$)		a	b	c	d	e	f
Theory		1	2	1	1	0	1
Found	(II) 2						

The possibilities (b and d~f) were ruled out from the chemical shift positions of the aromatic hydrogens and from the number of shifted signals of methoxyls on changing solvent from $CDCl_3$ to C_6H_6[6]. Structure (a) could also be rejected on biogenetic grounds.

Permanganate oxidation of IV gave an acid, m.p. 154°, as the only recognizable product, identical with 2,6-dimethoxy-3,4-methylenedioxybenzoic acid on the mixed mp.

The remaining signals in the NMR spectra of I and II were capable of being partially resolved as following:



	(I) R=OAc	(II) R=OH
2-H	4.05 (s)	4.37 (s)
4-He	5.73 (q, J=9, J=6)	5.6~6.3
4-Ha	6 ~ 6.3	5.6~6.3
5-H	~ 6.4 (m)	6.76 (m)
6-H	4.74 (d, J=8)	4.54 (d, J=8)
8-He	5.40 (d, J=10)	5.6~6.3
8-Ha	5.80 (d, J=10)	5.6~6.3

The chemical shift values of the axial hydrogens 4-Ha and 8-Ha permit assignment of the stereochemistry of the compound as the diequatorially substituted lignan [7](I and II each).

The fact that the benzylic hydrogen 2-H resonates at an anomalously low field in comparison with the corresponding hydrogens of lignans such as gmelinol can be explained by means of the diamagnetic effect of benzene ring; stereomodels suggest a conformation of II, in which the dihedral angle between the hydrogen and the benzene ring on C-2 is near to 0^{o} due to the steric hinderance of the two ortho-methoxy groups of the substituted phenyl grouping.

Thus 1-acetoxy-2,6-bis(2,6-dimethoxy-3,4-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]octane is proposed as the structure of leptostachyol acetate.

The lignan which incorporates an 1-oxy-function substituted-3,7-dioxabicyclo[3.3.0]octane ring has been rarely known in a series of naturally-occurring lignans[8,9].

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References and Footnote.

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