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ON THE STRUCTURE OF TAIWANIN E

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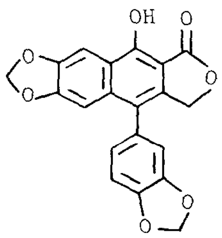
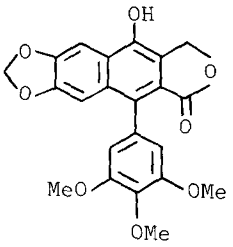
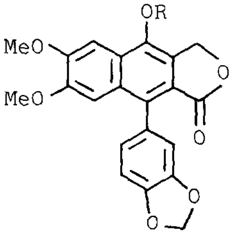
Taiwanin E, a phenolic lignan lactone isolated from Taiwania cryptomerioides Hayata, has been reported by Y.-T. Lin et al. (1) to have the structure (I) on the basis of the spectral evidences, and is the sole example of 1-hydroxy-2,3-naphthalide types (II) among the hitherto known α-hydroxy-2,3-naphthalide lignans. Dehydropodophyllotoxin (III) (2), diphyllin (IV, R=H) (3), and justicidin A (IV, R=Me) (3) have been shown to be of 4-hydroxy-2,3-naphthalide type (V). We now report the nonidentity of taiwanin E with synthetic compound (I) and propose that taiwanin E is also of the type (V) on the basis of NMR spectral evidences.



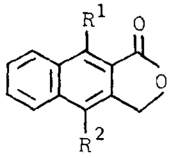
(I)



(III)



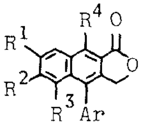
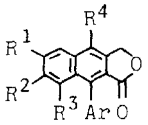
(IV)



(II; R^1=OH, R^2=Ar)
(V; R^1=Ar, R^2=OH)

The lactone methylene protons in the type (II) are expected, in NMR spectrum, to be shielded by the α-aryl nucleus whose orientation is perpendicular to the naphthalene ring. As shown in Table, this shielding effect is evidently observed in the aromatized 2,3-naphthalide lignans of natural or synthetic source. The lactone methylene of taiwanin E is obviously not shielded, whose value, τ 4.66, is closely similar to that of non-shielded taiwanin C, τ 4.62, suggesting that the structure of taiwanin E should be revised to (VI). The compound (I) synthe-

Table. Chemical shift of the lactone methylene in naphthalide lignans

substituent					solvent	type of naphthalide	
R^1	R^2	R^3	R^4	Ar			
MeO	MeO	H	H	3,4-$(MeO)_2C_6H_3$	$CDCl_3$	τ 4.78[a]	τ 4.68[a]
-OCH_2O-		H	H	3,4,5-$(MeO)_3C_6H_2$	"	τ 4.92[a]	τ 4.65[a]
H	H	H	H	3,4-$(MeO)_2C_6H_3$	"		τ 4.57[a]
H	-OCH_2O-		H	3,4-$(OCH_2O)C_6H_3$	——	τ 4.84[b] (helioxanthin)	
-OCH_2O-		H	H	"	$(CD_3)_2SO$		τ 4.62[c] (taiwanin C)
"		H	OH	"	$(CD_3)_2SO$	(τ 4.66[c]) (taiwanin E)	
MeO	MeO	H	OH	"	$CDCl_3$	τ 4.83	τ 4.65[d] (diphyllin)
"	"	"	OMe	"	"	τ 4.92[e]	τ 4.48[f] (justicidin A)
-OCH_2O-		H	OH	3,4-$(MeO)_2C_6H_3$	$(CD_3)_2SO$	τ 4.77	
"		"	OMe	"	$CDCl_3$	τ 4.85	

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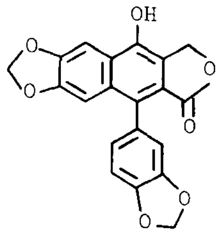
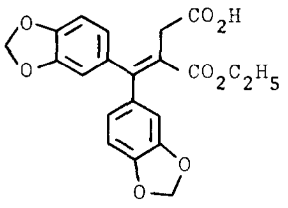
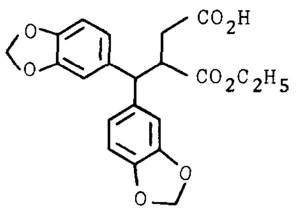
a) See ref. 4.
b) See ref. 5.
c) See ref. 1.
d) Value in $(CD_3)_2SO$.
e) See ref. 3.
f) See ref. 6.



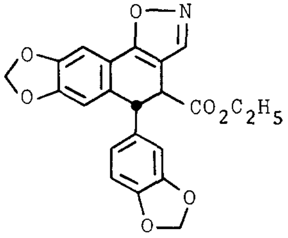
(VI)



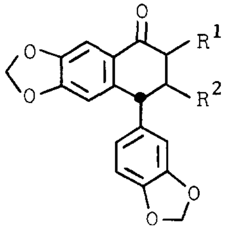
(VII)



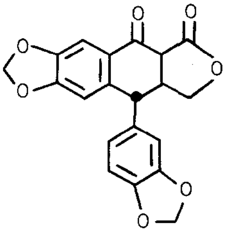
(VIII)



(X)



(IX; R^1=H, R^2=$CO_2C_2H_5$)
(XI; R^1=CN, R^2=CH_2OH)



(XII)

sized showed actually the shielded lactone methylene signal at τ 4.82 in the NMR spectrum and was not identical in its constants (m.p. 251-255°, ν_{max} 3370, 1725) with taiwanin E [reported (1), m.p. 263-267°, ν_{max} 3420, 1745].

Synthesis of compound (I) was achieved by 8-step procedure from ethyl hydrogen benzhydrylidenesuccinate (VII), m.p. 138.5-139.5°, ν_{max}(KBr) 1692(C=O) cm^{-1}. Sodium amalgam reduction of (VII) in bicarbonate buffer solution gave a half ester (VIII), (93%) m.p. 136-137°, which, on heating with acetyl chloride, afforded a tetralone (IX), (59%) m.p. 122-124°, ν_{max}(KBr) 1721, 1671(C=O)cm^{-1}. Formylation of (IX) and subsequent treatment with hydroxylamine hydrochloride gave an isoxazole-ester (X), m.p. 176-177.5°, which was converted, by lithium aluminium hydride reduction and subsequent cleavage with sodium ethoxide, into a cyano-tetralone (XI), dec. p. 256-260°, ν_{max}($CHCl_3$) 2230(C≡N), 1680(C=O)cm^{-1}.

Lactonization of (XI) with hydrogen chloride to (XII), m.p. 231-234°, $\nu_{max}(CHCl_3)$ 1785, 1668(C=O)cm^{-1}, and dehydrogenation with selenium dioxide afforded (I).

Taiwanin E is no longer exceptional and it is noteworthy from the biogenetic point of view that all the natural α-hydroxy-2,3-naphthalide lignans are of 4-hydroxy-2,3-naphthalide types (V).

REFERENCES

1. Y.-T. Lin, T.-B. Lo, K.-T. Wang, and B. Weinstein, Tetrahedron Letters, 849, (1967).
2. W. J. Gensler, F. Johnson, and A. D. B. Sloan, J. Am. Chem. Soc., 82, 6074, (1960).
3. Z. Horii, K. Ohkawa, S. Kim, and T. Momose, Chem. Comm., 653, (1968).
4. L. H. Klemm, K. W. Gopinath, D. Hsu Lee, F. W. Kelly, E. Trod, and T. M. McGuire, Tetrahedron, 22, 1797, (1966).
5. R. S. Burden, L. Crombie, and D. A. Whiting, Tetrahedron Letters, 1035, (1968).
6. K. Munakata, S. Marumo, K. Ohta, and Y.-L. Chen, Tetrahedron Letters, 4167, (1965).