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MORACIN C AND D, NEW PHYTOALEXINS FROM DISEASED MULBERRY[1)]

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Two antifungal compounds, moracin C and D, have been isolated from fungus-infected cortex and phloem tissues of mulberry shoots and their structures have been determined to be formulas 3 and 5 on the basis of the spectral and chemical evidence, respectively.

We recently reported the structures of moracin A and B (1 and 2), which were isolated from acetone extracts of cortex and phloem tissues of decorticated mulberry shoots (Morus alba Linné) infected with Fusarium solani f. sp. mori.[2)] Further systematic fractionation of the extracts, guided by assay against Cochliobolus miyabeanus, led to isolation of two new antifungal compounds, moracin C and D, in 0.02 and 0.01% yield, respectively, which were not detected in the corresponding extracts of healthy tissues. We now wish to report the structure and antifungal activity of the compounds.

Moracin C (3), $C_{19}H_{18}O_4$, mp 198-199 °C, m/e 310 (M^+, base), gave the triacetate (3a), mp 156-157 °C, and the trimethyl ether (3b), mp 121-122 °C. The IR spectrum indicated the absence of carbonyl functions and the UV spectrum suggested the presence of a 2-phenylbenzofuran skeleton[2)] [λ_{max}^{EtOH} 219 nm (ε 31900), 287 (sh, 15800), 296 (sh, 18400), 319 (40900), and 333 (34600)], which was supported by the NMR spectrum (CD_3COCD_3) of 3: δ 7.43 (1H, d, J = 8, 4-H), 6.85 (1H, do d, J = 8 and 2, 5-H), 7.01 (1H, do d, J = 2 and 0.8,[3)] 7-H), 6.95 (1H, d, J = 0.8,[3)] 3-H), and 6.97 (2H, s, 2'- and 6'-H). The spectrum also revealed the presence of three hydroxyl [δ 8.51 (1H, br s) and 8.35 (2H, br s)] and 3-methyl-2-butenyl (prenyl) groups [δ 1.67 and 1.80 (each 3H, s), 3.45 (2H, br d, J = 7), and 5.38 (1H, br t, J = 7)]. Disposition of the two hydroxyl and prenyl groups was deduced from the two-proton singlet (δ 6.97) and a characteristic fragmentation peak[4)] [m/e 255, 93% ($M^+ - C_4H_7$)]. All these spectral data were completely consistent with structure 3. Ozonolysis of 3b resulted in cleavage of the benzofuran skeleton to yield an ester (4), $C_{19}H_{18}O_7$, m/e 358.1085, with two formyl groups [δ ($CDCl_3$) 9.67 (1H, t, J = 2) and 10.06 (1H, s)], supporting the assigned structure (3).

Moracin D (5), $C_{19}H_{16}O_4$, mp 130-131 °C, m/e 308 (M^+), gave the diacetate (5a), mp 125-126 °C, and the dimethyl ether (5b), gum, and showed no absorption due to carbonyl functions in the IR spectrum. The UV [λ_{max}^{EtOH} 219 nm (ε 25700), 329 (30000), 342 (41700), and 360 (35200)] and NMR spectra indicated the presence of a 2-substituted 6-hydroxybenzofuran system [δ 7.42 (1H, d, J = 8, 4-H), 6.84 (1H, do

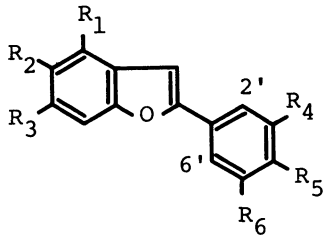
d, J = 8 and 2, 5-H), 7.01 (1H, br d, J = 2, 7-H), 7.07 (1H, d, J = 0.8, 3-H), and 8.63 (2H, br s, 6-OH, overlapped over 5'-OH)]. The NMR spectra also revealed the presence of a chromene system with a hydroxyl group (δ 8.63, overlapped over 6-OH), at peri position (C-5') to the 4'-chromene proton [5, δ 6.96 (1H, d, J = 1.6, 6'-H) 6.82 (1H, do d, J = 1.6 and 0.8,[5] 8'-H), 6.73 (1H, do d, J = 10 and 0.8,[5] 4'-H), 5.69 (1H, d, J = 10, 3'-H), and 1.42 (6H, s, $2CH_3$ at C-2'): 5a,[5] δ 6.47 (1H, br d, J = 10, 4'-H), 5.85 (1H, d, J = 10, 3'-H), and 1.45 (6H, s, $2CH_3$ at C-2')]. The difference in chemical shift of 4'- and 3'-protons of the chromene ring between 5 and 5a and the long-range coupling between the 4'- and 8'-chromene protons can be explained well by structure 5.[5] Treatment of 3 with 2,3-dichloro-5,6-dicyanobenzoquinone (1.2 equiv) in benzene (room temp, 5 h) effected cyclodehydrogenation to give a mixture, from which 5 could be isolated in 12% yield. The result establishes the structures (5 and 3) for moracin D and C.

Moracin C and D (3 and 5) showed antifungal activity against pathogenic and non-pathogenic fungi (Table 1).

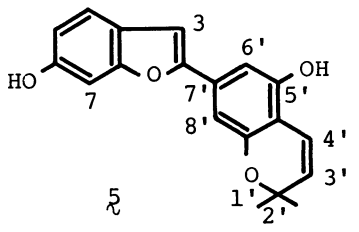
Table 1 Antifungal activity of 3 and 5

Fungus	3[a]	5[a]
Fusarium roseum	3.5-7	7-14
F. lateritium f. sp. mori	7-14	28-56
F. solani f. sp. mori	224	112
Diaporthe nomurai	14-28	7-14
Stigmina mori	112-224	56-112
Rosellinia necatrix	<3.5	<3.5
Cochliobolus miyabeanus[b]	28-56	14-28

a) Minimum concentration (μg/ml) required for complete inhibition of fungal growth.
b) A non-pathogen against the mulberry.



1 $R_1=R_3=OCH_3, R_2=R_5=H, R_4=R_6=OH$
2 $R_3=R_6=OCH_3, R_1=R_5=H, R_2=R_4=OH$
3 $R_1=R_2=H, R_3=R_4=R_6=OH$
$R_5=CH_2CH=C(CH_3)_2$



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REFERENCES and NOTES

1) Part 2 of "Studies on Phytoalexins of the Moraceae." Reference 2 can be considered as Part 1 of this series.
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