

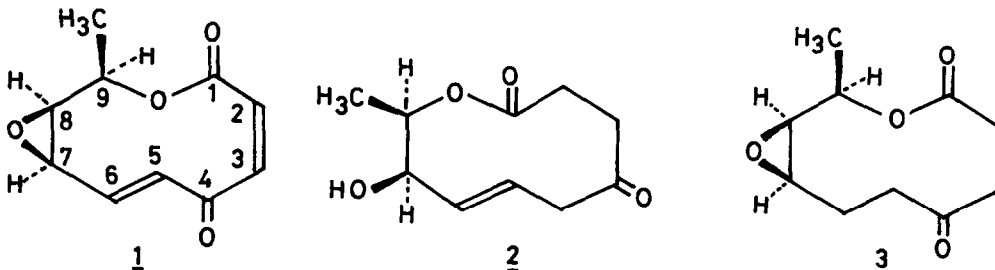
A NEW FUNGAL MORPHOGENIC SUBSTANCE, PYRENOLIDE A FROM PYRENOPHORA TERES

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Summary A new ten-membered lactone, pyrenolide A, was identified as a new fungal morphogenic substance and its structure including absolute stereochemistry was elucidated.

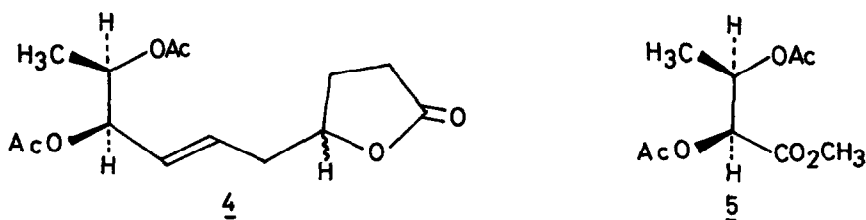
In our search for biologically active substances among fungal metabolites, we have found that Pyrenophora teres IFO 7508 produced a morphogenic substance. When it was applied to the fungal hyphae of several species (1-10 µg/disc), many irregularly swollen hyphae were formed. It was obtained from the culture filtrate as colorless needles, mp 93°C, $(\alpha)_D^{20}$ -262° (c 0.68, CHCl₃), and designated as pyrenolide A. In this paper, we wish to describe the structural elucidation of a new ten-membered lactone, pyrenolide A (1).

Pyrenolide A has C₁₀H₁₀O₄ (EI-MS, m/e 194.0580 (2%, M⁺); CI-MS (reagent gas, ammonia), m/e 212 (100%, M+18⁺); λ(MeOH) 222 nm (ε 6700), 245 (7200); ν(CHCl₃) 1735, 1665, 1615 cm⁻¹. The ¹H-NMR spectrum (CDCl₃) shows the presence of a secondary methyl group (H₃C-CH-O-CO-: δ 1.50, 3H, d, J=7 Hz; 5.55, 1H, dq, J=7, 2 Hz), a cis-disubstituted epoxide (3.78, 1H, ddd, J=6, 4.5, 1 Hz; 3.20, 1H, dd, J=4.5, 2 Hz), and Z- and E-disubstituted olefins both conjugated with carbonyl groups (-CO-CH=CH-CO-: 6.62 and 6.08, ABq, J=12 Hz) and (-CO-CH=CH-CH-: 6.75, 1H, dd, H=17, 6 Hz; 6.12, 1H, dd, J=17, 1 Hz), respectively. These partial structures have been confirmed by double resonance experiments and the ¹³C-NMR spectrometry using selective proton decoupling technique (δ 192.8(C-4), 166.5(C-1), 145.7(C-6), 133.4(C-5), 134.5 and 128.6(C-2, C-3), 66.1(C-9), 60.8 (C-8), 54.6(C-7) and 16.8(C-10).



Reduction of 1 with Zn in acetic acid gave quantitatively an allyl alcohol (2) as a single product: mp 115-6°C; $(\alpha)_D^{20} + 61^\circ$ (c 1.0, CHCl₃); $\nu(\text{CHCl}_3)$ 3400, 1720, 1705, 990 cm⁻¹. And catalytic hydrogenation of 1 with Pd-C gave a tetrahydro derivative (3): mp 128-131°C; $(\alpha)_D^{23} - 31^\circ$ (c 0.31, CHCl₃); $\nu(\text{CHCl}_3)$ 1735, 1705 cm⁻¹. These results show the presence of the cross-conjugated γ -oxo- and γ, δ -epoxy- α, β -unsaturated ketone in 1. Therefore 1 is tentatively assigned as (Z,E)-7,8(cis)-epoxy-4-oxodeca-2,5-dien-9-olide. In order to confirm the carbon skeleton of 1, 1 was transformed to decan-9-olide¹. The epoxide (3) was converted to 4-oxodec-7-en-9-olide (cis, trans mixture) by the method of Cornforth, et al.² The latter was hydrogenated with Pd-C to give 4-oxodecan-9-olide: $(\alpha)_D^{22} - 79^\circ$ (c 1.0, CHCl₃); $\nu(\text{CCl}_4)$ 1735, 1710 cm⁻¹. Thioketalization and desulfurization (Ra-Ni) of the ketone afforded (-)-decan-9-olide: $(\alpha)_D^{22} - 33^\circ$ (c 0.5, CHCl₃). For direct comparison, the authentic one, was prepared from 3-oxodecan-9-olide³, and the both compounds were identified by tlc and GC-mass spectrometry.

The absolute stereochemistry of 1 was determined as follows. When the allyl alcohol (2), which retained the asymmetric carbons of C-8 and C-9 in 1, was successively subjected to NaBH₄ reduction, alkaline hydrolysis and acetylation, afforded the epimeric γ -lactones (4): $\nu(\text{CCl}_4)$ 1782, 1735 cm⁻¹. Treatment of 4 with ozone and successively with Jones reagent and diazomethane gave methyl (+)-2,3-diacetoxybutyrate (5): $(\alpha)_D^{22} + 23.6^\circ$ (c 0.5, CHCl₃). 5 was directly compared with both its threo⁴ and erythro⁵ isomers prepared by the reported methods, and found to be identical in all respects (tlc, IR, ¹H-NMR, GC-mass, and optical rotation) with (+)-threo isomer derived from L-threonine. Therefore 2 has (8R,9R) configuration and 1 has (7R,8R,9R).



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