

Communications to the editor

VERRUCARIN L, A NEW MACROCYCLIC
TRICHOHECENE

Sir:

We wish to report the isolation of the new macrocyclic trichothecenes, verrucarín L (**1a**) and its acetate (**1b**), from the fermentation of *Myrothecium verrucaria* (ATCC #24571). These are the first macrocyclic trichothecenes¹⁾ isolated from a fermentation which are substituted on the C-8 position of the central ring. Virtually all of the heretofore reported roridins and verrucarins are macrocyclic esters of verrucaro^{1,2)} with the exception of the baccharinoids which were isolated from a higher plant³⁾ and the recently reported 7,8-epoxyroridins.⁴⁾ The baccharinoids possess either a β -epoxy group at C-9, C-10 (baccharins) or an 8β -hydroxyl group (baccharinols). However, there is reason to suspect that the true origin of the oxygen functionality in the A-ring of the baccharinoids is through a plant mediated transformation of microbially produced macrocyclic trichothecenes.³⁾ The C-8 hydroxyl and acetoxy groups in **1a** and **1b**, respectively, are in the α position, a stereochemistry normally encountered in the simple trichothecenes²⁾ but of opposite stereochemistry to that observed in the baccharinoids.³⁾

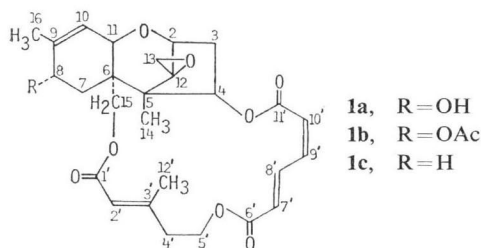
A large scale fermentation of *M. verrucaria* has yielded most of the previously characterized roridins and verrucarins in addition to several new derivatives.⁵⁾ Purification of the chromatography fractions most closely associated with roridin A and verrucarín A yielded two minor constituents, verrucarín L (**1a**) [mp 230~235°C, $[\alpha]_D^{27} + 15.0^\circ$ (*c* 0.92, CHCl₃), and λ_{max} (EtOH) 262 nm (log $\epsilon = 4.42$)] and verrucarín L acetate (**1b**) [mp 132~135°C, $[\alpha]_D^{27} + 29.7^\circ$ (*c* 0.52, CHCl₃)

Table 1. ¹³C and ¹H NMR data for verrucarín L (**1a**) and verrucarín L acetate (**1b**)^a.

Position	Verrucarín L	Verrucarín L acetate
2	79.0d	79.0d (3.86d) [4.6]
3	35.3t	34.9t
4	75.1d	74.0d
5	48.8	49.0
6	42.5	42.2
7	30.1t	26.5t
8	66.8d	68.8d
9	139.7	136.5
10	120.9d (5.58d) [5]	123.9d (5.64d) [5]
11	67.2d	67.0d (3.76d) [5]
12	65.5	65.3
13	48.1t (2.99AB) [4]	47.9t (2.97AB) [4]
14	6.9q (0.86)	7.0q (0.86)
15	65.0t	64.5t
16	20.6q (1.87)	21.0q (1.75)
1'	165.7	165.6
2'	118.2d (5.85)	117.8d (5.86)
3'	156.6	156.9
4'	40.3t	40.2t
5'	60.5t	60.4t
6'	165.5 ^b	165.4
7'	127.2d ^b (6.00d) [16]	127.8d ^b (5.96d) [15]
8'	139.3d (8.10dd) [11, 16]	138.8d (8.01) [11, 16]
9'	139.7d (6.65dd) [11, 11]	136.5d (6.61dd) [11, 11]
10'	125.6d ^b (6.12d) [11]	125.2d ^b (6.07d) [11]
11'	165.7	165.8
12'	17.3q (2.26d) [1.2]	17.1q (2.27d) [1.0]
	MeCO	170.9
	MeCO	20.4q (1.94)

^a In CDCl₃, parts per million from TMS (0.0 ppm). ¹³C NMR spectra were determined on Varian CFT-20 and FT-80A spectrometers operating at 20 MHz. ¹³C NMR signals were assigned using SFORD techniques and by comparison with literature values (see W. BREITENSTEIN & CH. TAMM, Helv. Chim. Acta 61: 1975, 1978). ¹H NMR spectra were determined on a Varian XL-100 FT-spectrometer.

^b Assignments may be reversed.



and λ_{\max} (EtOH) 261 nm ($\log \epsilon = 4.28$). Verrucarin L has an Rf value (silica gel, 30% EtOAc in hexane) slightly higher than the Rf value for roridin A, and the Rf value of acetate **1b** is slightly higher than the Rf value for verrucarin A. The proton spectrum of **1a** was very similar to the proton spectrum of verrucarin J (**1c**). In addition, acetylation of **1a** gave a monoacetate (**1b**) indicating the presence of one hydroxyl group. The position of the hydroxyl group was established by hydrolysis of **1a** to give 4 β ,8 α ,15-trihydroxy-12,13-epoxytrichothec-9-ene, a compound previously characterized in our laboratories.⁶⁾ The C-13 and proton NMR data for **1a** and **1b** are given in Table 1.

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