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STRUCTURE REVISION OF MYCOTOXIN, VIRIDITOXIN, AND ITS DERIVATIVES

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The structures of viriditoxin, first isolated from Aspergillus viridinutans as mycotoxin, and its derivatives, isolated from Paecilomyces variotii, were revised from 8,8'-binaphtho-α-pyrone to 6,6'-binaphtho-α-pyrone on the basis of spectroscopic investigations. The absolute stereochemistry of the 6,6'-axis was also determined as an R-configuration.

KEYWORDS Aspergillus viridinutans; Paecilomyces variotii; mycotoxin; 6,6'-binaphtho-α-pyrone; 8,8'-binaphtho-α-pyrone; viriditoxin; SC-28763; SC-30532

Viriditoxin was first isolated from a mycelial extract of Aspergillus viridinutans Ducker & Thrower as a compound toxic to mice.1) This compound was also isolated from several fungi, i.e., A. brevipes Smith,2) Paecilomyces variotii Bainier,3) and A. fumigatus Fresenius.4) The structure of viriditoxin was determined as **1** mainly by the analysis of its ^{1}H-NMR spectra and that of its acetate.1) The structures of its analogues, SC-287633) and SC-30532,5) isolated from P. variotii, was determined as **2** and **3**, respectively, by comparing their spectral data with those of viriditoxin.

In our screening of the biologically active fungal metabolites, viriditoxin was isolated from the mycelium of A. viridinutans, strain CBS 127.56.6) Our compound was identical with viriditoxin as shown by comparison of the spectral data including CD curves.1,3) Tetramethyl ether, derived from our compound by methylation with dimethylsulphate and potassium carbonate, was directly identified with viriditoxin tetramethyl ether obtained from Lillehoj. The detailed analyses of the ^{1}H- and ^{13}C-NMR spectra and the ^{1}H-^{13}C shift-correlated 2-dimensional NMR spectrum revealed that viriditoxin had two naphtho-α-pyrone moieties, which connected each other at C-6 and C-6' or at C-8 and C-8'. In the ^{1}H-^{13}C long-range shift-correlated 2-dimensional NMR spectrum of viriditoxin (a coupling constant of 12.5 Hz was employed.), the correlation peaks of two aromatic protons (δ 6.16 and 6.85) appeared with the carbons at δ 109.35 (C-6), 107.67 (C-9a) and 98.84 (C-10a) and with the carbons at δ 109.35 (C-6), 158.94 (C-9) and 107.67 (C-9a), respectively, but there was no correlation between the aromatic carbons bearing the hydrogen (δ 98.09 and 112.91) and the above aromatic protons. These results showed that one of the aromatic protons (δ 6.85) was located at the ortho-position of the methoxy and hydroxy groups, and therefore the two naphtho-α-pyrone moiety was not connected at C-8 and C-8'.

To determine the connectivity of naphtho-α-pyrone in viriditoxin, the difference NOE spectrum of viriditoxin tetramethyl ether (**5**) was studied. When one of the aromatic protons at δ 6.82 was irradiated, the NOE's for the methoxy protons at δ 3.84 and 4.13 appeared, and the NOE of the aromatic proton at δ 6.82 appeared when the methoxy protons at δ 3.84 and/or 4.13 was irradiated. No NOE appeared when the other aromatic proton at δ 6.52 was irradiated. These results showed that the aromatic protons were not located at the peri position each other, but one was located ortho to the two methoxy groups, so the structure of viriditoxin tetramethyl ether was **5**. Therefore the structure of viriditoxin should be revised to 6,6'-binaphtho-α-pyrone as **4**. The assignments of the ^{1}H- and ^{13}C-NMR signals of viriditoxin (**4**) are listed in Table I. It is likely that the structures of SC-28763 and SC-30532 are also to be revised to a 6,6'-dimer (**6** and **7**, respectively) by the comparison of the spectroscopic data, especially ^{1}H- and ^{13}C-NMR spectra,

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Table I. ^1H- and ^{13}C-NMR Chemical Shift Assignments of Viriditoxin (**4**) and Its Tetramethyl Ether (**5**)

	4 in $(CD_3)_2SO$		**5** in $CDCl_3$	
Carbon	δ_C (ppm)	δ_H (ppm)	δ_H (ppm)	$\underline{J}_{H,H}$ (Hz)
1	169.92 (s)			
3	75.69 (Dm)[a)]		4.91 (m)	4.77 (m)
4	31.71 (Tm)	2.85 (m)	2.60 (dd)	15.9, 6.7
			2.88 (dd)	15.9, 6.1
4a	133.05 (m)			
5	112.91 (Dm)	6.16 (s)	6.52 (s)	
5a	138.71 (s)			
6	109.35 (t)			
7	160.16 (m)			
8	98.09 (D)	6.85 (s)	6.82 (s)	
9	158.94 (d)			
9a	107.67 (t)			
10	162.62 (s)			
10a	98.84 (m)			
1'	38.67 (Tm)	2.78 (m)	2.80 (m)	
2'	169.69 (m)			
3'	51.57 (Q)	3.62 (s)	3.67 (s)	
7-OMe	55.86 (Q)	3.70 (s)	3.84 (s)	
9-OMe			4.13 (s)	
9-OH		10.04 (br)		
10-OMe			4.05 (s)	
10-OH		13.35 (br)		

a) Capital letters refer to the coupling $^1J_{C,H}$.

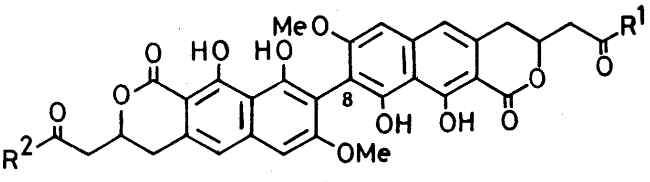
although we did not isolate these compounds.

The CD spectra of viriditoxin (**4**) and its derivatives (**6** and **7**) exhibited strong negative first and positive second Cotton curves[3,5)] as shown in Table II. These are due to the coupling between the ^1B_b transitions of two naphthalene chromophores, and this phenomenon shows that the long axes of naphtho-α-pyrone moieties in **4**, **6**, and **7** are twisted in a counter-clockwise manner as shown by the exciton chirality method.[7)] Thus the chirality of the 6,6'-axis in viriditoxin (**4**), SC-28763 (**6**), and SC-30532 (**7**) was found to be the R-configuration. The stereochemistry at C-3 and C-3' is not yet determined.

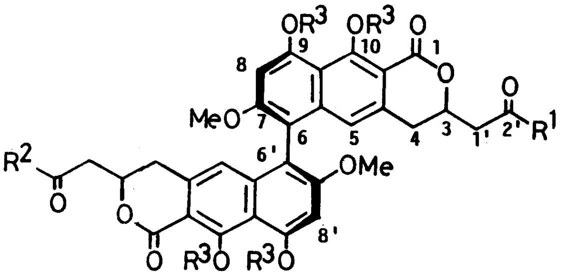
Table II. CD Spectra of Viriditoxin (**4**) and Its Derivatives in $CHCl_3$ [Δε (nm)]

Compound	1st Cotton	2nd Cotton
4	-194.7 (275)	+174.0 (255)
5	-185.2 (269)	+152.4 (248)
6[a)]	-211.5 (273)	+137.3 (252)
7[b)]	-225.8 (276)	+51.2 (257)

a) CD data in reference 3.
b) CD data in reference 5.



1 : $R^1 = R^2 =$ OMe
2 : $R^1 =$ OMe, $R^2 =$ Me
3 : $R^1 = R^2 =$ Me



4 ; $R^1 = R^2 =$ OMe, $R^3 =$ H
5 : $R^1 = R^2 =$ OMe, $R^3 =$ Me
6 : $R^1 =$ OMe, $R^2 =$ Me, $R^3 =$ H
7 : $R^1 = R^2 =$ Me, $R^3 =$ H

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