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The Crystal and Molecular Structure of Echinosporin

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Echinosporin, 6-carbamoyl-1-hydroxy-3,5-dioxatricyclo[6.3.0.0^{4,9}]undeca-6,10-dien-2-one, is a novel antibiotic. The space group is $P2_12_12_1$ with $a=9.716(1)$, $b=13.823(1)$, $c=7.202(1)$ Å, and $Z=4$. The structure was solved by the direct method and refined to the R value of 0.049 by the block-diagonal least-squares method using 1239 reflexions. The molecule has a fused tricylo structure which consists of two six-membered rings and one five-membered ring.

Echinosporin is a novel antibiotic produced from a strain of *Streptomyces echinosporous*.[1] Although the structure has been assigned by the chemical and spectroscopic techniques,[2] the X-ray analysis has been undertaken to confirm the structure.

Experimental and Structure Determination

Prismatic crystals of the title compound were obtained from an ethyl acetate solution. A crystal with dimension of $0.5\times0.4\times0.3$ mm^3 was used for the data collection on a Rigaku four-circle automated diffractometer with Mo $K\alpha$ radiation ($\lambda=0.71069$ Å). The space group was determined from systematic absences ($h00$ for odd h, $0k0$ for odd k, $00l$ for odd l) on the photographs. The accurate cell dimensions were determined by least-squares with 2θ values of 16 high-angle reflexions measured on the diffractometer. Crystal data are as follows: $C_{10}H_9NO_5$; $M.W.=223.18$; $P2_12_12_1$; $Z=4$; $a=9.716(1)$, $b=13.823(1)$, $c=7.202(1)$ Å; $D_x=1.533$ g cm^{-3}; μ(Mo $K\alpha$)$=1.386$ cm^{-1}. All independent reflexions within the range of $2\theta\leqq55°$ were collected by the use of the ω-2θ scan mode with a scanning rate $4°(2\theta)$ min^{-1}. Stationary background counts were accumulated for 10 s before and after each scan. Periodic checks of the intensity values of three standard reflexions showed no significant X-ray damage or crystal decay. Corrections for absorption and extinction were not applied. A total of 1300 independent reflexions were obtained, of which 1242 ($|F_o|>3.0\sigma(|F_o|)$) were considered as observed.

The phases of 274 refiexions with $|E_o|\geqq1.2$ were assigned with MULTAN.[3] The best set of phases was used to calculate an E map, which gave 16 significant peaks. The structural parameters were refined by the block-diagonal least-squares method with a modified HBLS program. At the stage $R=0.081$, all hydrogen atoms were found on the difference map. The reflexions, 0 1 4, 2 1 0, and 0 2 1, were excluded from refinement because they seemed to suffer from secondary extinction. The final R value was 0.049 for 1239 reflexions. The weighting system used in the final stage was $w=0.3$ for $|F_o|<1.8$ and $|F_o|>18.2$ and $w=(0.00115|F_o|^2-0.12675|F_o|+4.48559)^{-1}$ for $1.8\leqq|F_o|\leqq18.2$. Atomic scattering factors were taken from "International Tables for X-Ray Crystallography."[4] The final positional and thermal parameters are given in Table 1.**

** The tables of observed and calculated structure factors, anisotropic thermal parameters of non-hydrogen atoms and torsion angles in the molecule are kept as Document No. 8309 at the Chemical Society of Japan.

TABLE 1. FRACTIONAL ATOMIC COORDINATES WITH THEIR ESTIMATED STANDARD DEVIATIONS AND TEMPERATURE FACTORS

Atom	x	y	z	B_{eq} or B/Å^2
C(1)	0.3804(3)	0.0956(2)	0.3364(5)	2.66
C(2)	0.4282(3)	0.1851(2)	0.3223(5)	2.59
C(3)	0.5788(3)	0.2060(2)	0.3360(5)	2.69
C(4)	0.6622(4)	0.1199(3)	0.4123(5)	3.13
C(5)	0.6036(3)	0.0321(2)	0.3103(5)	3.07
C(6)	0.2306(3)	0.0703(2)	0.3246(5)	2.83
C(7)	0.6096(3)	0.1306(2)	0.0275(5)	2.63
C(8)	0.6517(3)	0.2169(2)	0.1472(4)	2.48
C(9)	0.8008(3)	0.1989(3)	0.1979(5)	3.27
C(10)	0.8057(3)	0.1433(3)	0.3455(6)	3.52
O(1)	0.4647(2)	0.0155(2)	0.3608(4)	3.39
O(2)	0.1452(2)	0.1348(2)	0.3055(4)	3.69
O(3)	0.6072(2)	0.0427(2)	0.1114(3)	2.85
O(4)	0.5851(3)	0.1354(2)	−0.1351(4)	4.08
O(5)	0.6190(3)	0.3050(2)	0.0622(4)	3.49
N	0.2009(3)	−0.0232(2)	0.3361(5)	3.67
HC(2)	0.365(3)	0.233(2)	0.316(5)	2.9
HC(3)	0.598(4)	0.276(2)	0.402(4)	2.7
HC(4)	0.656(4)	0.109(3)	0.528(5)	3.6
HC(5)	0.666(5)	−0.037(3)	0.364(7)	6.4
HC(9)	0.870(3)	0.219(2)	0.130(5)	2.7
HC(10)	0.876(4)	0.124(3)	0.382(5)	3.7
HO(5)	0.622(5)	0.303(3)	−0.087(7)	6.5
HAN	0.250(4)	−0.063(3)	0.354(6)	4.3
HBN	0.084(5)	−0.046(3)	0.250(7)	7.5

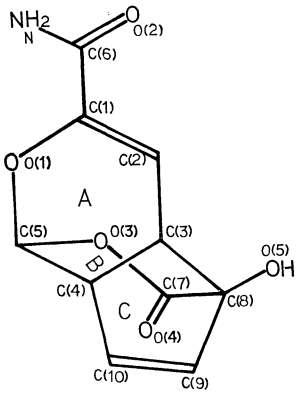

Fig. 1. The numbering system.

TABLE 2. BOND LENGTHS AND ANGLES

Bond length	l/Å	Bond angle	θ/°
C(1)-C(2)	1.325(5)	C(2)-C(3)-C(8)	114.2(3)
C(1)-C(6)	1.499(5)	C(4)-C(3)-C(8)	98.6(3)
C(1)-O(1)	1.389(4)	C(3)-C(4)-C(5)	104.3(3)
C(2)-C(3)	1.495(5)	C(3)-C(4)-C(10)	101.9(3)
C(3)-C(4)	1.540(5)	C(5)-C(4)-C(10)	111.1(3)
C(3)-C(8)	1.540(5)	C(4)-C(5)-O(1)	111.1(3)
C(4)-C(5)	1.529(5)	C(4)-C(5)-O(3)	112.9(3)
C(4)-C(10)	1.510(5)	O(1)-C(5)-O(3)	107.1(3)
C(5)-O(1)	1.417(5)	C(1)-C(6)-O(2)	119.6(3)
C(5)-O(3)	1.441(5)	C(1)-C(6)-N	115.7(3)
C(6)-O(2)	1.225(5)	O(2)-C(6)-N	124.7(4)
C(6)-N	1.327(5)	C(8)-C(7)-O(3)	116.9(3)
C(7)-C(8)	1.527(5)	C(8)-C(7)-O(4)	124.3(3)
C(7)-O(3)	1.358(4)	O(3)-C(7)-O(4)	118.8(3)
C(7)-O(4)	1.197(4)	C(3)-C(8)-C(7)	107.4(3)
C(8)-C(9)	1.514(5)	C(3)-C(8)-C(9)	102.2(3)
C(8)-O(5)	1.400(4)	C(3)-C(8)-O(5)	111.5(3)
C(9)-C(10)	1.313(6)	C(7)-C(8)-C(9)	105.4(3)
Bond angle	θ/°	C(7)-C(8)-O(5)	111.8(3)
C(2)-C(1)-C(6)	123.6(3)	C(9)-C(8)-O(5)	117.7(3)
C(2)-C(1)-O(1)	123.2(3)	C(8)-C(9)-C(10)	109.0(3)
C(6)-C(1)-O(1)	113.2(3)	C(4)-C(10)-C(9)	110.5(4)
C(1)-C(2)-C(3)	121.2(3)	C(1)-O(1)-C(5)	113.6(3)
C(2)-C(3)-C(4)	112.9(3)	C(5)-O(3)-C(7)	122.3(3)

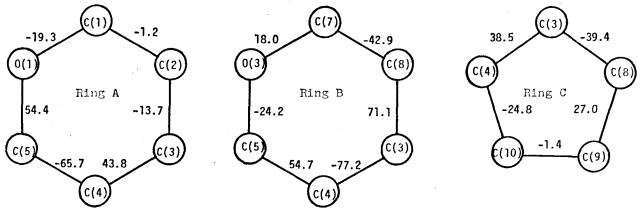

Fig. 2. The torsional angles in the rings A, B, and C

Results and Discussion

The present X-ray analysis has established the structure of echinosporin that has a novel system as shown in Fig. 1. The bond lengths and bond angles are listed in Table 2. The bond lengths are within the range of the expected values. The C(4)–C(3)–C(8), C(10)–C(4)–C(3), and C(9)–C(8)–C(3) bond angles in the five-membered ring are appreciably smaller than those values of 1,2-diphenyl-1-pentene.[5] The O(1)–C(1)–C(2), C(6)–C(1)–C(2), C(7)–O(3)–C(5), and O(4)–C(7)–C(8) bond angles are, on the other hand, rather large. These results suggest that the bond angles, rather than the bond lengths, are distorted by the strain accumulated in the molecule. Although the O(4)···O(5) distance is 2.762 Å, the O(4)···H–O(5) angle of 99.6° and the O(4)···H distance of 2.37 Å may exclude a possibility of the O(4)···H–O(5) intramolecular hydrogen bond.

In Fig. 2, the torsion angles in the two six-membered rings and the five-membered ring are shown. The ring B takes a distorted chair conformation, the O(3) part being flattened and the C(3) part being puckered. The ring A is quite distorted and takes an envelope conformation. The C(1), C(2), C(3), C(5), and O(1) atoms are coplanar within ±0.1 Å, only the C(4) atom deviating by 0.694 Å from the mean plane. The ring C takes an envelope conformation, the C(3) atom being puckered. The dihedral angle between the plane consisting of the C(3), C(4), and C(8) atoms and the least-squares plane of the C(4), C(8), C(9), and C(10) atoms is 40.8°. The amide part is planar within 0.003

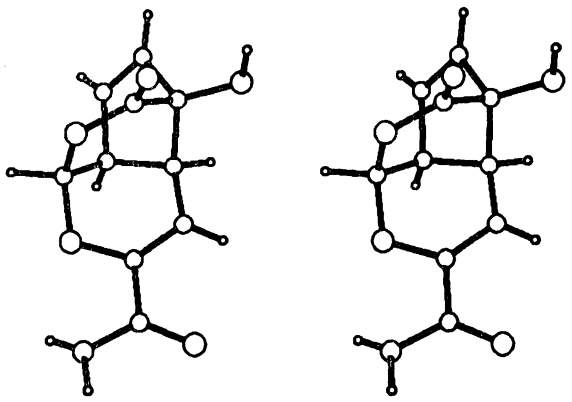

Fig. 3. Stereoscopic view of the molecule, drawn by a program for a NOVA 3, TSD:XTAL.[6]

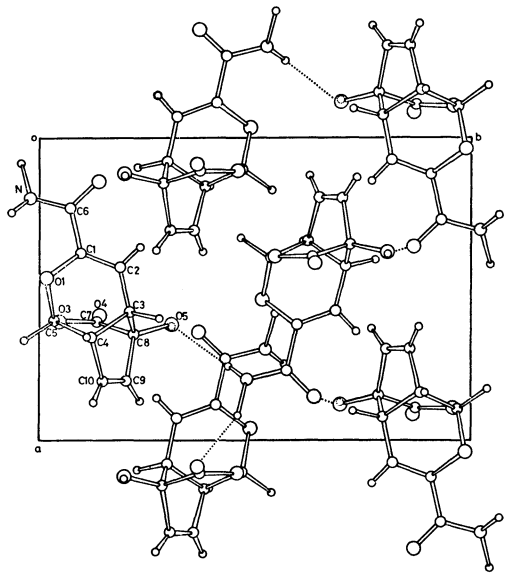

Fig. 4. The crystal structure viewed along the c axis.

TABLE 3. HYDROGEN BOND DISTANCES AND ANGLES

A-H···B	l(A···B)/Å	∠A-H···B/°
N-HB(N)^{I}···O(4)^{II}	3.189(5)	126.1
O(5)-H^{I}···O(2)^{III}	2.787(4)	149.6
N-HA(N)^{I}···O(5)^{IV}	3.039(4)	173.2

I: (x y z)
II: (0.5−x −y 0.5+z)
III: (0.5+x 0.5−y −z)
IV: (1.0−x −0.5+y 0.5−z)

Å. The stereoscopic drawing of the molecule is shown in Fig. 3.

The crystal structure viewed along the c axis is shown in Fig. 4. There are three intermolecular hydrogen bonds as listed in Table 3. The dotted lines in the Fig. 4 indicate the hydrogen bond.

References

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