Redetermination of the Crystal Structure of XXXX(Times New Roman 11.5pt, Bold)

Eeeee Mmmmm[a] and Nnnnn Hhhhhh[b*](Times New Roman 9pt)

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Received June xx,2010, accepted and available on-line July xx,2010 (Times New Roman 8pt)

Abstract(Times New Roman 9pt, Bold)

C_{22} H_{26} N_2 O_6 S_3,monoclinic, *C*2, *a*=23.99(1), *b*=11.369(5), *c*=22.766(5)Å, *β*=99.12(4)°, *V*=6131(2) Å^3, *Z*=8, *R*gt(*F*)=0.091, *wR*ref(F^2)=0.132,*T*=297K. CCDC no.xxxxxx, antitumor antibiotic. (Times New Roman 9pt)

Introduction(Times New Roman 9pt, Bold)

A novel antibiotic XXX isolated from *Streptimyces xxxx* in Kyowa Hakko Kogyo Co.Ltd.[1] shows a broad antimicrobial activity against Gram-positive and Gram-negative bacteria. The compound is also effective against murine experimental leukemia. In order to disclose the inherent structure of the novel compound we undertook the X-ray analysis. (Times New Roman 9pt)

Experimental(Times New Roman 9pt, Bold)

The single crystals of the compound were grown from a methanol solution. The structure was solved by direct methods and non-H atoms were refined by a full-matrix least squares method with anisotropic temperature factors. Positions of the H-atoms attached to the amide nitrogen atom and the phosphate oxygen atoms were located from difference Fourier synthesis. These H-atoms were refined with isotropic temperature factors. All other H-atoms were geometrically calculated and refined by the riding model. The crystal and experimental data are given in Table 1. (Times New Roman 9pt)

Results and Discussion(Times New Roman 9pt, Bold)

XXXmycin, *N*-[[(S)-3-(3-fluoro-4-morpholinophenyl)-2-oxo-5-oxazolidinyl]methyl] acetamide, is a synthetic antibiotic belonging to a unique class of antimicrobials called the oxazolidinones. Linezolid disrupts bacterial growth by inhibiting the initiation process in protein synthesis.[1] The chemical structure is shown in Fig.1. Linezolid has been approved primarily to fight resistant gram-positive cocci, such as vancomycin-resistant enterococcus, methicillin-resistant *Staphylococcus aureus*, and penicillin-resistant pneumococci. Although Linezolid has been successfully used to treat a number of resistant strains of bacteria, the emergence of linezolid resistance has been already reported. The X-ray analysis of the title compound was undertaken to disclose its inherent three-dimensional structure that is essentially important information in designing the next generation of linezolid to fight resistant bacteria.

There are two crystallographically independent molecules in an asymmetric unit. The two molecules adopt significantly different conformations, as described below. Two piperidine rings adopt chair conformations. It is noteworthy that the nitrogen atoms in both chair conformations are markedly different in the hybridization state. The bond lengths and angles around the nitrogen atoms indicate that the nitrogen atoms in molecules I and II take sp^3 and sp^2 hybridization states, respectively. Both nitrogen atoms are not involved in hydrogen bonds. The chair conformation of molecule I is significantly flattened compared with that of molecule II, as suggested by the torsion angles in the rings. The pyrimidine rings in both molecules are essentially planar. The torsion angles of N101-C104-N105-C105 and N201-C204-N205-C205 being 34.6(9) and 0(1) °, respectively, indicate that the orientations of the piperidine and pyrimidine rings with respect to the C104-N105 and C204-N205 bonds are markedly different. The bond lengths and angles in the molecules are within the expected ranges. The exocyclic bond angles around the C101-N103 and C102-N104 bonds are highly asymmetric. The

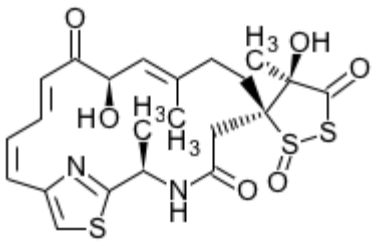

Fig.1 Chemical structure of XXXX(Times New Roman 8.5pt)

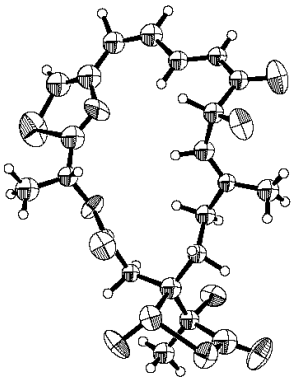

Fig.2 ORTEP structure of XXX, showing 50% probability ellipsoids.

Table 1. Experimental Details (Times New Roman 8.5pt)

Crystal :	yellow plate, 0.30×0.40×0.01
Radiation:	Cu Kα radiation(1.54117Å)
μ(cm^{-1}):	26.32
Diffractometer:	Bruker SMART 1000 CCD
2θmax(°):	54
N(*hkl*)measured:	8907
N(*hkl*)unique:	4201
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs}>2.0\sigma(I_{obs})$,3428
No. parameters refined: 230	
Final residual density: $(\Delta\rho)_{max}$=0.48e/Å^3,$(\Delta\rho)_{min}$=-0.32 e/Å^3	
Goodness-of-fit:	1.03
Programs:	SHELXS-97[*], CrsytalStructure[*], SIR92[*], ORTEPIII[*]

corresponding angles in molecule II are also asymmetrical. The exocyclic bond angles facing the O101 and O201 atoms are significantly smaller than their counterparts. There are six intramolecular and four intermolecular hydrogen bonds. They are listed in Table 4. It is notable that the intramolecular C-H··· N hydrogen bond in each molecule seems to play a key role to determine the relative orientation of the piperidine ring with respect to the pyridine ring. (Times New Roman 9pt)

Table 2. Atomic coordinates and displacement parameters (in Å^2)

Atom	*x*	*y*	*z*	B_{eq}
O(101)	0.9597(5)	0.8849(9)	0.8686(3)	4.2(1)
N(101)	0.8254(6)	0.4892(8)	0.9172(4)	4.1(1)
N(102)	0.8757(6)	0.7525(7)	0.8606(4)	3.5(1)
N(103)	1.0077(7)	0.6384(9)	0.9896(5)	4.7(1)
N(104)	0.7365(7)	0.8877(9)	0.7450(5)	4.6(1)
N(105)	0.6468(7)	0.3394(8)	0.8414(5)	4.8(1)
C(101)	0.9012(7)	0.6214(8)	0.9229(5)	3.7(1)
C(102)	0.7624(7)	0.7517(9)	0.7954(4)	3.9(1)
C(103)	0.6823(8)	0.6126(8)	0.7861(5)	3.9(1)
C(104)	0.7160(7)	0.4811(8)	0.8483(5)	3.8(1)
C(105)	0.6283(9)	0.2412(9)	0.9352(7)	5.2(2)
C(106)	0.502(1)	0.294(1)	0.9940(6)	5.2(2)
C(107)	0.3700(9)	0.289(1)	0.9295(7)	6.1(2)
C(108)	0.3874(9)	0.378(1)	0.8272(8)	6.2(2)
C(109)	0.5186(9)	0.322(1)	0.7734(6)	5.7(2)

Table 3. Selected bond lengths(Å), bond angles(°) and torsion angles(°)

O(101)-N(102)	1.359(9)	O(201)-N(202)	1.363(9)
N(101)-C(101)	1.313(9)	N(201)-C(201)	1.33(1)
N(101)-C(104)	1.361(9)		
C(101)-N(101)-C(104)	119.0(6)		
C(201)-N(201)-C(204)	118.2(6)		
C(104)N(101)C(101)N(103)	178.8(6)		
C(204)N(201)C(201)N(203)	-177.7(7)		
C(101)N(101)C(104)N(105)	176.3(6)		

Acknowledgement. This work was supported by Grants for the Key Technology Research Promotion Program of New Energy and Industrial Technology Development Organization(NEDO) of Japan. (Times New Roman 8.5pt)

References(Times New Roman 9pt, Bold)

1. F.Morady, *Ann.Intern.Med.*, **1982**, 96, 337.
2. CrystalStructure, version 3.5.1, **2000-2003** Crystal Structure Analysis Package, Rigaku and Rigaku/MSC.
3.SIR92: A.Altomare, G.Cascarano, C.Giacovazzo, A.Guagliardi, M.Burla, G.Polidori, and M. Camalli, *J. Appl. Cryst.*, **1994**, 27, 435.
4. ORTEP III, L. J. Farrugia , *J. Appl. Cryst.*, **1997**, 22, 389.
(Times New Roman 9pt)

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