Crystal Structure of Methyl (8*R*,11*R*,14*S*)-8-[*N*-[(*tert*-Butoxy)carbonyl]amino]-11-(3,5-dichloro-4-hydroxyphenyl)-18,19-dibromo-5-iodo-4-hydroxy-13-methyl-9,12-dioxo-10,13-diaza-2-oxatricyclo[14.2.2.1^{3,7}]heneicosa-3,5,7(21),16,18,19-hexaene-14-carboxylate

Toshitsugu KAI, Naoko KAJIMOTO, Yaeko YAMADA, Yoshihiro HARIGAYA, and Hiroaki TAKAYANAGI

School of Pharmaceutical Sciences, Kitasato University, Shirokane, Minato, Tokyo 108-8641, Japan

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Chloropeptin is a peptide antibiotic isolated from *Streptomyces* sp. WK-3419 as a potent inhibitor against gp 120-CD4 binding.¹ The relative and absolute structures of the compound were estimated by an NMR experiment, chemical degradation and a molecular dynamics calculation.^{2,3}

During the course of our total synthesis of chloropeptin, we succeeded to synthesize the chloropeptin left-hand segment.⁴

The title compound is one of the derivatives of those cyclic left-hand segments. Single crystals of the title compound were obtained from a methanolic solution. Intensity data were

collected on a Rigaku AFC5R diffractometer using Cu K α radiation monochromated with graphite at 23°C. The crystal data are summarized in Table 1. The structure was solved by a direct method (SIR92), expanded by DIRDIF92 and refined by a full-matrix least-squares method with anisotropic thermal parameters for the non-hydrogen atoms. All of the hydrogen atoms indicated in the ORTEP drawing in Fig. 2 were fixed at geometrically reasonable positions and included in an *R*-factor calculation.

Fig. 1 Chemical structure.

Table 1 Crystal and experimental data

Formula: C ₃₂ H ₃₀ O ₉ N ₃ Br ₂ ICl ₂ (CH ₃ OH)	
Formula weight = 990.26	
Crystal size (mm): 0.20 × 0.40 × 0.20	
Crystal system: monoclinic	
Space group: <i>P</i> 2 ₁	<i>Z</i> = 4
<i>a</i> = 19.046(3) Å	
<i>b</i> = 10.503(3) Å	β (°) = 114.54(1)
<i>c</i> = 20.772(3) Å	
<i>V</i> = 3779(1) Å ³	
<i>D</i> _c = 1.645 g/cm ³	
<i>R</i> = 0.085	<i>R</i> _w = 0.206
No. of reflections used = 4218	
($\Delta\rho$) _{max} = 1.11 eÅ ⁻³	
($\Delta\rho$) _{min} = -1.85 eÅ ⁻³	
Measurement: Rigaku AFC5R	
Program system: teXsan	
Structure determination: direct method (SIR92)	
Refinement: full-matrix least-squares

Molecule A

Molecule B

Fig. 2 ORTEP drawing of the molecule, representing heavy atoms as 50% probability ellipsoids and H atoms as spheres of arbitrary radius.

Table 2 Atomic coordinates and equivalent isotropic thermal parameters (B_{eq})

Atom	x	y	z	B_{eq}	Atom	x	y	z	B_{eq}
Cl(1A)	-0.9199(2)	0.049(2)	-2.2513(2)	7.41(9)	I(2B)	-0.59496(6)	0.538(2)	-1.10197(5)	7.22(3)
Cl(2A)	-0.8322(2)	0.536(2)	-2.1910(2)	5.99(7)	Br(3B)	-0.5046(1)	0.144(2)	-1.25759(9)	7.80(4)
I(1A)	-0.59833(6)	0.572(2)	-1.60064(4)	6.69(2)	Br(4B)	-0.73892(9)	-0.155(2)	-1.23176(8)	7.48(4)
Br(1A)	-0.5011(1)	0.154(2)	-1.74067(8)	7.76(4)	O(1B)	-0.6254(5)	0.061(2)	-1.2007(3)	5.3(2)
Br(2A)	-0.74874(8)	-0.124(2)	-1.72658(7)	7.12(4)	O(2B)	-0.7968(5)	-0.318(2)	-1.4961(4)	6.0(2)
O(1A)	-0.6273(5)	0.085(2)	-1.6891(4)	5.5(2)	O(3B)	-0.8286(5)	-0.187(2)	-1.5888(4)	5.3(2)
O(2A)	-0.7945(5)	-0.304(2)	-1.9886(4)	6.1(2)	O(4B)	-0.7856(4)	-0.017(2)	-1.4686(4)	4.6(2)
O(3A)	-0.8204(4)	-0.172(2)	-2.0802(4)	5.4(2)	O(5B)	-0.9229(5)	0.313(2)	-1.7891(4)	6.0(2)
O(4A)	-0.7777(4)	0.000(2)	-1.9594(4)	4.7(2)	O(6B)	-0.7042(4)	0.412(2)	-1.4338(4)	5.0(2)
O(5A)	-0.9130(5)	0.313(2)	-2.2847(4)	5.8(2)	O(7B)	-0.9203(5)	0.494(2)	-1.3710(4)	5.8(2)
O(6A)	-0.6956(5)	0.429(2)	-1.9264(4)	5.8(2)	O(8B)	-0.8822(4)	0.681(2)	-1.4001(4)	5.2(2)
O(7A)	-0.9195(4)	0.497(2)	-1.8713(4)	5.3(2)	O(9B)	-0.5594(4)	0.240(2)	-1.1032(4)	6.2(2)
O(8A)	-0.8842(5)	0.689(2)	-1.8995(4)	5.5(2)	N(1B)	-0.6960(5)	-0.043(2)	-1.5131(4)	4.2(2)
O(9A)	-0.5734(5)	0.266(2)	-1.5893(4)	5.9(2)	N(2B)	-0.7738(5)	0.232(2)	-1.4570(4)	4.0(2)
N(1A)	-0.6870(5)	-0.035(2)	-2.0016(4)	4.4(2)	N(3B)	-0.8088(5)	0.514(2)	-1.3848(4)	4.5(2)
N(2A)	-0.7661(5)	0.245(2)	-1.9514(4)	4.4(2)	C(1B)	-0.5823(7)	-0.061(2)	-1.3471(6)	4.9(3)
N(3A)	-0.8062(5)	0.527(2)	-1.8830(4)	4.5(2)	C(2B)	-0.5777(8)	0.014(2)	-1.2895(6)	5.9(3)
C(1A)	-0.5805(6)	-0.048(2)	-1.8319(6)	5.2(3)	C(3B)	-0.6271(8)	-0.012(2)	-1.2571(5)	5.7(3)
C(2A)	-0.5737(7)	0.032(2)	-1.7740(6)	5.8(3)	C(4B)	-0.6767(7)	-0.112(2)	-1.2793(6)	5.9(3)
C(3A)	-0.6289(7)	0.008(2)	-1.7463(6)	4.9(2)	C(5B)	-0.6823(7)	-0.191(2)	-1.3381(6)	5.2(3)
C(4A)	-0.6823(6)	-0.094(2)	-1.7681(6)	5.2(2)	C(6B)	-0.6354(6)	-0.163(2)	-1.3714(5)	4.8(2)
C(5A)	-0.6863(6)	-0.170(2)	-1.8271(6)	5.2(3)	C(7B)	-0.6407(6)	-0.235(2)	-1.4369(6)	4.9(2)
C(6A)	-0.6345(6)	-0.146(2)	1.8562(5)	4.9(2)	C(8B)	-0.7007(7)	-0.183(2)	-1.5080(6)	5.0(2)
C(7A)	-0.6380(7)	-0.222(2)	-1.9201(5)	5.4(3)	C(9B)	-0.7813(7)	-0.234(2)	-1.5276(6)	5.4(2)
C(8A)	-0.6936(7)	-0.176(2)	-1.9959(6)	4.8(2)	C(10B)	-0.9083(7)	-0.222(2)	-1.6146(8)	6.8(3)
C(9A)	-0.7764(7)	-0.222(2)	-2.0189(6)	5.1(2)	C(11B)	-0.6405(6)	0.004(2)	-1.5376(6)	5.1(3)
C(10A)	-0.9013(7)	-0.207(3)	-2.1103(7)	7.0(3)	C(12B)	-0.7424(6)	0.029(2)	-1.4920(5)	4.3(2)
C(11A)	-0.6353(7)	0.015(2)	-2.0319(7)	5.7(3)	C(13B)	-0.7388(6)	0.174(2)	-1.5022(5)	3.9(2)
C(12A)	-0.7329(6)	0.041(2)	-1.9833(5)	4.3(2)	C(14B)	-0.7885(6)	0.212(2)	-1.5806(5)	4.0(2)
C(13A)	-0.7298(7)	0.186(2)	-1.9948(5)	4.7(2)	C(15B)	-0.8333(6)	0.122(2)	-1.6293(5)	4.4(2)
C(14A)	-0.7782(7)	0.220(2)	-2.0727(5)	4.5(2)	C(16B)	-0.8775(6)	0.161(2)	-1.6989(5)	4.7(2)
C(15A)	-0.8207(7)	0.131(2)	-2.1229(5)	5.5(3)	C(17B)	-0.8782(6)	0.286(2)	-1.7203(5)	4.6(2)
C(16A)	-0.8647(7)	0.164(2)	-2.1918(5)	5.3(2)	C(18B)	-0.8310(7)	0.374(2)	-1.6684(5)	4.9(2)
C(17A)	-0.8695(7)	0.287(2)	-2.2161(5)	4.7(2)	C(19B)	-0.7886(7)	0.336(2)	-1.6005(5)	4.8(2)
C(18A)	-0.8272(6)	0.379(2)	-2.1659(5)	4.1(2)	C(20B)	-0.7510(6)	0.345(2)	-1.4261(5)	4.3(2)
C(19A)	-0.7819(6)	0.344(2)	-2.0958(5)	4.6(2)	C(21B)	-0.7875(6)	0.380(2)	-1.3747(5)	4.4(2)
C(20A)	-0.7439(7)	0.359(2)	-1.9196(5)	4.8(2)	C(22B)	-0.8756(7)	0.559(2)	-1.3859(5)	4.6(2)
C(21A)	-0.7826(6)	0.391(2)	-1.8704(5)	4.6(2)	C(23B)	-0.9530(7)	0.755(2)	-1.4081(6)	5.4(2)
C(22A)	-0.8743(7)	0.562(2)	-1.8843(5)	4.4(2)	C(24B)	-1.0210(8)	0.700(3)	-1.4702(8)	8.2(4)
C(23A)	-0.9569(7)	0.754(2)	-1.9093(7)	6.0(3)	C(25B)	-0.9327(8)	0.890(2)	-1.4229(7)	6.6(3)
C(24A)	-1.0235(9)	0.698(3)	-1.9727(8)	8.8(4)	C(26B)	-0.9605(8)	0.751(2)	-1.3384(7)	6.4(3)
C(25A)	-0.9397(8)	0.892(2)	-1.9234(7)	7.0(3)	C(27B)	-0.7308(6)	0.347(2)	-1.3008(5)	4.0(2)
C(26A)	-0.9684(7)	0.750(2)	-1.8420(7)	6.4(3)	C(28B)	-0.6971(6)	0.439(2)	-1.2473(5)	4.5(2)
C(27A)	-0.7268(6)	0.366(2)	-1.7941(5)	4.5(2)	C(29B)	-0.6393(7)	0.406(2)	-1.1801(5)	5.8(2)
C(28A)	-0.6961(7)	0.458(2)	-1.7440(6)	5.5(3)	C(30B)	-0.6190(7)	0.276(2)	-1.1669(5)	5.5(2)
C(29A)	-0.6433(7)	0.429(2)	-1.6738(6)	5.3(2)	C(31B)	-0.6526(7)	0.187(2)	-1.2193(6)	5.0(2)
C(30A)	-0.6226(7)	0.301(2)	-1.6563(5)	5.3(2)	C(32B)	-0.7087(7)	0.219(2)	-1.2848(6)	5.0(2)
C(31A)	-0.6529(7)	0.209(2)	-1.7087(5)	4.8(2)	O(10)	-0.4650(6)	0.003(2)	-0.0840(6)	9.5(3)
C(32A)	-0.7058(7)	0.242(2)	-1.7769(6)	5.0(2)	O(11)	-0.4208(5)	-0.147(2)	-0.5345(5)	8.1(2)
Cl(3B)	-0.9364(2)	0.051(2)	-1.7586(2)	6.78(8)	C(33)	-0.4861(8)	-0.128(3)	-0.0914(8)	7.5(3)
Cl(4B)	-0.8372(2)	0.531(2)	-1.6925(2)	5.88(7)	C(34)	-0.4846(8)	-0.090(3)	-0.5923(7)	7.5(3)

$$B_{eq} = (8\pi^2/3) \sum_i \sum_j U_{ij} a_i^* a_j^* (\mathbf{a}_i \cdot \mathbf{a}_j).$$

Table 3 Selected torsion angles ($^\circ$)

C11A–N1A–C12A–O4A	178(1)
C11B–N1B–C12B–O4B	-176(1)

The atomic parameters and B_{eq} of non-hydrogen atoms are listed in Table 2. All calculations were performed using the program system (teXsan). An ORTEP drawing of the title compound is shown in Fig. 2.

The X-ray structure determination shows that an asymmetric unit contains two independent molecules (denoted as molecules A and B). Both molecules have nearly the same geometric structure.

The title compound existed as equilibrium mixtures of two stable conformers caused by a rotation of the *N*-methylamide bond in solution.⁴ As shown in Fig. 2, the title compound was found to be a *trans* isomer of the *N*-methylamide bond in the solid state, because the torsion angles of

C11A–N1A–C12A–O4A and C11B–N1B–C12B–O4B were 178° and -176°, respectively.

The absolute configuration of the left-hand segment of chloropeptin proposed by Hirono *et al.*^{2,3} was finally supported by this X-ray analysis through a refinement of the inverted configuration ($R = 0.095$, $R_w = 0.232$).

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