Crystal and Molecular Structure of Methyl D-Tetronitroside

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The structure of the novel sugar, methyl D-tetronitroside [methyl 2,3,4,6-tetradeoxy-4-(methoxycarbonylamino)-3-*C*-methyl-3-nitro-D-*xylo*-hexopyranoside], was determined by X-ray analysis. This compound is a structural component of the antitumor antibiotics, tetrocarcins. The space group is $P2_1$ with $a=11.782(3)$, $b=10.271(2)$, $c=11.636(3)$ Å, $\beta=105.12(4)°$, and $Z=4$. The structure was solved by direct methods, and least-squares refinement using 2503 reflexions gave the final R value of 0.079. Both the two independent molecules take a $^4C_1$ chair conformation and they are connected together through two hydrogen bonds. Although the average C-C distance in the rings is 1.527 Å, the C(2)-C(3) distance is significantly long (average 1.546 Å) due to the steric hindrance by the nitro groups.

D-Teronitrose is a structually important component of antitumor antibiotics, tetrocarcins,[1] and is the third naturally occuring nitro sugar discovered in antibiotics. The nitro sugar is so rare in nature that its detailed molecular structure has not yet been reported. Only the structure of the tetronitrose was spectroscopically and chemically elucidated but the molecular configuration was not confirmed because of having the asymmetric carbon atom with the nitro group as a side chain. In this paper we will report the X-ray analysis of methyl D-teronitroside in order to describe the stereochemical features of the nitro sugar. Recently a nitro sugar with the same composition as D-tetronitrose has been isolated from kijanimicins.[2]

Experimental and Structure Determination

The crystals of methyl D-teronitroside prepared by methanolysis of tetrocarcin A[1] were obtained by evaporation from a hexane-dichloromethane solution. A crystal, $0.4\times0.3\times0.3$ mm^3 in size, was used for data collection on a Rigaku four-circle automated diffractometer with graphite monochromated Mo $K\alpha$ radiation ($\lambda=0.71069$ Å). Preliminary unit cell dimensions and space group were obtained from photographs. Accurate cell dimensions were determined by least-squares calculations with the 2θ values of 15 high-angle reflexions measured on the diffractometer. Crystal data are as follows: $C_{10}H_{18}N_2O_6$; $M.W.=262.26$; $P2_1$; $Z=4$; $a=11.782(3)$, $b=10.271(2)$, $c=11.636(3)$ Å, $\beta=105.12(4)°$; $D_x=1.282$ g cm^{-3}; μ(Mo $K\alpha$) $=1.141$ cm^{-1}. All independent reflexions within the range $2\theta\leqq55°$ were collected by use of the ω-2θ scan mode with a scanning rate of $4°(2\theta)$ min^{-1}. Stationary background counts were accumulated for 10 s before and after each scan. Periodic check of the intensities of three standard reflexions showed no significant X-ray damage or decay. Correction for absorption or extinction was not applied. A total of 3308 independent reflexions were obtained, of which 2503 ($|F_o|>3.0\sigma(|F_o|)$) were considered as observed.

The structure was solved by direct methods using MULTAN.[3] The structural parameters were refined by block-diagonal least-squares methods with a modified HBLS program.[4] All the hydrogen atoms were found on a difference Fourier map and included in further refinement with isotropic thermal parameters. The final R value was 0.079 for 2503 observed reflexions. The weighting scheme used in the final stage was $w=(\sigma(F_o)^2+(0.015F_o)^2)^{-1}$. Atomic scattering factors were taken from Ref. 5. The final positional and thermal parameters are given in Table 1.**

Results and Discussion

The stereoscopic drawing of the two independent molecules are shown in Fig. 1, together with the atom numbering system. The absolute configuration of the tetronitrose, D-configuration, has been determined by applying Hudson's rules of isorotation to its α- and

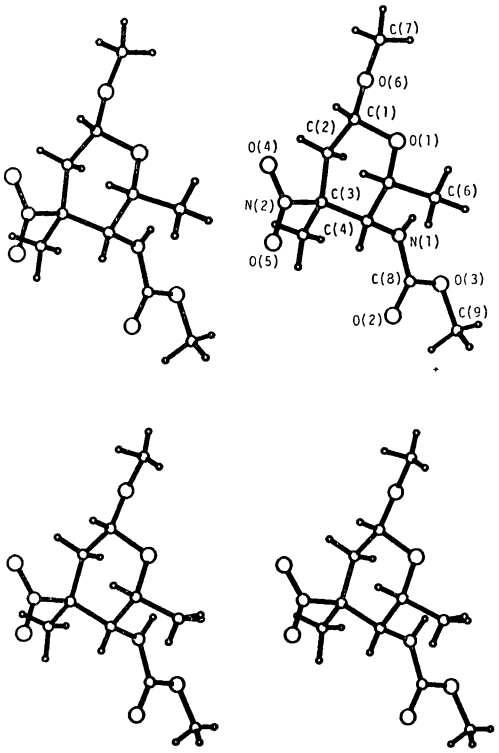

Fig. 1. Stereoscopic drawings of the two independent molecules and the numbering system. a) Molecule A. b) Molecule B.

** The tables of observed and calculated structure factors, and anisotropic thermal parameters are kept as Document No. 8332 at the Chemical Society of Japan.

Table 1-a. Final atomic coordinates with their estimated standard deviations, multiplied by 10^4

Atom	Molecule A				Molecule B			
	x	y	z	B_{eq}/Å^2	x	y	z	B_{eq}/Å^2
O(1)	5793(3)	4154(3)	1761(3)	3.46	8213(3)	6401(3)	3384(3)	3.49
O(2)	5682(3)	4919(4)	5917(3)	4.97	9816(3)	2750(4)	1744(5)	6.38
O(3)	7335(3)	5859(5)	5719(3)	5.18	7898(3)	2275(4)	1412(4)	4.46
O(4)	2490(3)	4451(5)	1329(4)	5.95	10001(4)	8504(5)	1575(5)	7.18
O(5)	2493(4)	4358(6)	3147(4)	7.14	11062(4)	6865(5)	1634(6)	8.98
O(6)	5408(3)	5442(4)	109(3)	4.30	6943(3)	8073(4)	2722(3)	3.75
N(1)	6035(3)	5184(5)	4103(4)	4.12	8474(3)	4299(4)	1812(4)	3.73
N(2)	2931(3)	4721(5)	2352(4)	4.31	10127(4)	7367(5)	1539(4)	4.26
C(1)	4892(4)	4870(5)	937(5)	3.59	8024(4)	7572(5)	2679(4)	3.13
C(2)	4428(4)	5931(5)	1592(4)	3.54	7971(4)	7232(5)	1396(4)	3.14
C(3)	4092(4)	5498(5)	2700(4)	3.50	9035(4)	6461(5)	1269(4)	3.11
C(4)	5003(4)	4537(6)	3438(4)	3.67	9320(4)	5341(5)	2190(5)	3.56
C(5)	5316(4)	3507(6)	2623(5)	3.91	9333(4)	5836(6)	3428(5)	4.16
C(6)	6171(6)	2489(7)	3250(6)	6.12	9549(6)	4801(9)	4361(6)	7.05
C(7)	5579(5)	4555(8)	-766(5)	5.83	6960(5)	8711(7)	3802(5)	5.01
C(8)	6303(4)	5296(6)	5311(5)	3.92	8827(5)	3081(5)	1671(5)	3.96
C(9)	7760(5)	5974(8)	7011(5)	6.00	8170(6)	910(6)	1383(7)	5.90
C(10)	3851(5)	6662(7)	3419(6)	5.44	8888(5)	6000(6)	-2(5)	4.99

Table 1-b. Final atomic coordinates of hydrogen atoms with their estimated standard deviations, multiplied by 10^3

Atom	Molecule A				Molecule B			
	x	y	z	B/Å^2	x	y	z	B/Å^2
HC(1)	425(3)	422(5)	49(4)	3(1)	865(3)	820(4)	300(3)	2(1)
HAC(2)	502(3)	652(4)	185(3)	2(1)	729(3)	672(4)	110(4)	2(1)
HBC(2)	381(3)	628(4)	104(4)	3(1)	790(3)	803(4)	95(3)	2(1)
HC(4)	466(4)	414(5)	395(4)	4(1)	1005(3)	505(4)	224(4)	3(1)
HC(5)	458(4)	317(5)	219(4)	4(1)	991(4)	662(5)	364(4)	6(1)
HAC(6)	581(4)	201(5)	375(4)	4(1)	954(5)	463(7)	497(5)	8(2)
HBC(6)	705(5)	279(6)	379(5)	6(1)	1027(4)	456(5)	442(4)	4(1)
HCC(6)	635(5)	190(7)	266(5)	8(2)	878(7)	421(9)	416((7)	11(2)
HAC(7)	484(4)	421(6)	-118(4)	5(1)	740(4)	836(5)	444(4)	4(1)
HBC(7)	626(4)	415(6)	-53(4)	5(1)	629(4)	913(6)	373(4)	6(1)
HCC(7)	582(6)	494(9)	-149(6)	11(2)	766(5)	942(7)	395(5)	7(2)
HAC(9)	777(4)	508(6)	736(5)	5(1)	893(5)	80(7)	202(5)	8(2)
HBC(9)	855(4)	647(6)	714(5)	6(1)	749(6)	37(8)	122(6)	9(2)
HCC(9)	720(6)	654(8)	733(7)	10(2)	850(4)	87(6)	89(4)	5(1)
HAC(10)	444(4)	705(5)	372(4)	4(1)	810(5)	551(7)	-36(5)	8(2)
HBC(10)	321(4)	707(6)	298(5)	6(1)	887(4)	669(5)	-51(4)	4(1)
HCC(10)	359(6)	630(8)	412(6)	10(2)	955(4)	535(6)	-1(5)	5(1)
HN(1)	653(4)	551(5)	384(4)	4(1)	775(4)	448(5)	189(4)	3(1)

Table 2. Bond lengths and angles

Bond length	l/Å A	l/Å B	Bond angle	θ/° A	θ/° B
C(5)-C(4)	1.527(8)	1.525(8)	C(5)-C(4)-N(1)	110.5(5)	111.7(5)
C(4)-C(3)	1.544(8)	1.548(7)	C(3)-C(4)-N(1)	112.0(5)	109.3(4)
C(3)-C(2)	1.511(8)	1.522(7)	C(4)-N(1)-C(8)	122.4(5)	121.0(5)
C(2)-C(1)	1.512(8)	1.519(7)	N(1)-C(8)-O(3)	110.6(5)	110.0(5)
C(1)-O(1)	1.433(6)	1.440(6)	N(1)-C(8)-O(2)	124.3(6)	125.7(6)
O(1)-C(5)	1.435(7)	1.430(7)	O(3)-C(8)-O(2)	125.1(6)	124.3(6)
C(5)-C(6)	1.503(9)	1.493(11)	C(8)-O(3)-C(9)	116.3(5)	115.6(5)
C(4)-N(1)	1.424(8)	1.450(7)	C(4)-C(3)-N(2)	104.8(4)	106.7(4)
N(1)-C(8)	1.363(8)	1.341(7)	N(2)-C(3)-C(10)	105.7(5)	105.2(4)
C(8)-O(2)	1.205(7)	1.196(8)	C(2)-C(3)-C(10)	111.4(5)	111.6(4)
C(8)-O(3)	1.318(8)	1.343(7)	C(4)-C(3)-C(10)	113.4(5)	113.0(4)
O(3)-C(9)	1.460(9)	1.441(9)	C(2)-C(3)-N(2)	109.9(4)	109.2(4)
C(3)-C(10)	1.527(9)	1.519(8)	C(3)-N(2)-O(4)	120.3(5)	119.7(5)
C(3)-N(2)	1.544(7)	1.552(7)	C(3)-N(2)-O(5)	118.5(5)	117.1(5)
N(2)-O(4)	1.200(7)	1.180(8)	O(4)-N(2)-O(5)	121.2(6)	123.1(6)
N(2)-O(5)	1.229(8)	1.194(9)	C(2)-C(1)-O(6)	108.9(4)	108.6(4)
C(1)-O(6)	1.395(7)	1.387(6)	O(1)-C(1)-O(6)	107.4(4)	107.2(4)
O(6)-C(7)	1.420(9)	1.413(8)	C(1)-O(6)-C(7)	113.2(5)	113.8(4)
O(1)-C(5)-C(4)	108.4(4)	108.6(5)	O(1)-C(5)-C(6)	109.1(5)	107.2(5)
C(5)-C(4)-C(3)	110.0(5)	110.7(5)	C(4)-C(5)-C(6)	114.8(5)	114.1(6)
C(4)-C(3)-C(2)	111.3(5)	110.8(4)	C(5)-C(4)-N(1)	110.6(5)	111.7(5)
C(3)-C(2)-C(1)	115.3(5)	113.1(4)	C(3)-C(4)-N(1)	112.0(5)	109.3(4)
C(2)-C(1)-O(1)	109.5(4)	109.2(4)	C(4)-N(1)-C(8)	122.4(5)	121.0(5)
C(1)-O(1)-C(5)	110.4(4)	111.3(4)	C(5)-O(1)-C(7)	110.4(4)	111.3(4)
O(1)-C(5)-C(6)	109.1(5)	107.2(5)	O(1)-C(5)-C(4)	108.4(4)	108.6(5)
C(4)-C(5)-C(6)	114.8(5)	114.1(6)	C(5)-C(4)-C(3)	110.0(5)	110.7(5)
C(3)-C(2)-C(1)	115.3(5)	113.1(4)	C(4)-C(3)-C(2)	111.3(5)	110.8(4)
C(2)-C(1)-O(1)	109.5(4)	109.2(4)			

β-glycosides; $[M]_{D\alpha}-[M]_{D\beta}=363.5°-66.4°=297.1°$. Very recently α-D-tetronitroside has been synthesized from D-mannose by Yoshii, and its D-absolute configuration was confirmed.[6]

Bond Lengths and Angles. The bond lengths and angles are shown in Table 2. Although most of the corresponding bond lengths in molecules A and B agree within the experimental error, the differences between them by greater than 3σ are observed in the amide bond. The average C–C distance of 1.527 Å in the rings agree with those observed in usual monosaccharides,[7] but the C(2)–C(3) distance (average 1.546 Å) is significantly longer than the other C–C distance in the rings and its reason will be discussed later. The two C–C bonds in the ring are almost equal to the average of 1.435 Å. The average distance of N(2)–C(3) bond (1.548 Å) is in good agreement with the corresponding N–C bond (1.541(3) Å) in *c*-5-methyl-*t*-5-nitro-1,3,2-dioxathian *r*-2-oxide.[8] The C(1)–O(6) bond (average 1.391 Å) is significantly shorter than the O(6)–C(7) bond (average 1.417 Å), which indicates large anomeric effect.

The differences between the corresponding bond angles in the two molecules are rather large compared to those of bond lengths. The average bond angles in the pyranose ring are 110.8 and 110.6° for molecules A and B, respectively, which are in agreement with

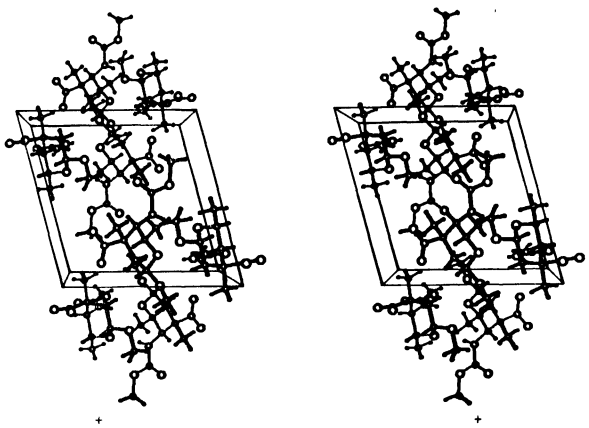

Fig. 2. Stereoscopic drawing of the crystal structure viewed along the b axis. The vertical and the holizontal axes are a and c, respectively. This figure and Fig. 1 were drawn by TSD : XTAL, a program for NOVA 3 computer.[9]

those found in pyranoses.[7]

Conformation. Both of the two independent molecules take a $^4C_1$ chair conformation. Selected torsion angles are tabulated in Table 3. The average torsion angles in the ring, 54.9 and 56.4° in A and B, respectively, are within the range observed for monosaccharides.[7] The *d* values (the deviation of the two atoms from the least-squares plane of the other four atoms forming the seat of a chair)[9] of the ring atoms in two molecules are averaged as follows; O(1) 0.706, C(1) 0.657, C(2) 0.569, C(3) 0.574, C(4) 0.651, C(5) 0.717 Å. The O(1) and C(5) atoms are most puckered, while the C(3) and C(2) atoms are less puckered. The O(4) atom is nearly eclipsed to the C(2) atom (O(4)–N(2)–C(3)–C(2) torsion angle is 6.2° for A and −13.9° for B). Therefore, the O(4) has short contact with C(2); the O(4)···C(2) nonbonded distance is 2.693(8) in A and 2.685(8) Å in B. The less puckering of C(3) and C(2) and the lengthening of C(2)–C(3) bond may cause the relief of steric hindrance, and it eventually causes the large puckering of the O(1) and C(5) atoms.

Table 3. Torsional angles

Torsional angle	ϕ/° A	ϕ/° B
C(1)-O(1)-C(5)-C(4)	68.9	67.9
O(1)-C(5)-C(4)-N(1)	64.7	64.1
O(1)-C(5)-C(4)-C(3)	-59.6	-58.0
C(6)-C(5)-C(4)-N(1)	-57.5	-55.3
HC(1)-C(5)-C(4)-HC(2)	-64.0	-63.8
C(5)-C(4)-C(3)-C(2)	45.9	48.0
C(5)-C(4)-C(3)-N(2)	-72.9	-70.7
N(1)-C(4)-C(3)-C(2)	-77.5	-75.4
HC(4)-C(4)-C(3)-C(10)	-69.8	-69.7
N(1)-C(4)-C(3)-C(10)	49.0	50.8
HC(4)-C(4)-C(3)-N(2)	44.9	45.4
C(4)-C(3)-C(2)-C(1)	-41.9	-46.3
N(2)-C(3)-C(2)-C(1)	73.7	70.9
N(2)-C(3)-C(2)-HBC(2)	-46.3	-50.5
C(10)-C(3)-C(2)-HAC(2)	-51.1	-54.5
C(3)-C(2)-C(1)-O(1)	49.6	53.5
HAC(2)-C(2)-C(1)-O(6)	49.7	50.6
HBC(2)-C(2)-C(1)-O(6)	-69.1	-67.4
HBC(2)-C(2)-C(1)-HC(1)	51.9	54.4
C(3)-C(2)-C(1)-HC(1)	-72.3	-68.1
C(2)-C(1)-O(1)-C(5)	-63.5	-64.6
HC(1)-C(1)-O(1)-C(5)	61.3	57.4
O(4)-N(2)-C(3)-C(2)	-6.2	13.9
O(5)-N(2)-C(3)-C(10)	55.7	70.0
O(5)-N(2)-C(3)-C(4)	-64.4	-50.3
C(7)-O(6)-C(1)-O(1)	-77.8	-76.6
C(7)-O(6)-C(1)-HC(1)	39.6	43.6
C(8)-N(1)-C(4)-C(3)	-109.6	-124.3
C(8)-N(1)-C(4)-HC(4)	8.2	-4.8
HN(1)-N(1)-C(4)-C(3)	72.0	72.7
HN(1)-N(1)-C(4)-C(5)	-51.1	-50.2
C(4)-N(1)-C(8)-O(2)	-3.4	6.0
C(4)-N(1)-C(8)-C(3)	-176.0	175.1
HN(1)-N(1)-C(8)-O(3)	2.8	-13.5
C(9)-O(3)-C(8)-O(2)	-2.7	-8.5
C(9)-O(3)-C(8)-N(1)	176.7	-172.6

Crystal Structure. Crystal structure viewed along the b axis is shown in Fig. 2. The two independent molecules make pairs through the two NH···O hydrogen bonds with following geometry: N(1A)···O(1B) =3.157(6), N(1B)···O(1A)=3.147(6) Å, ∠N(1A)–H···O(1B)=170.1(5), ∠N(1B)–H···O(1A)=157.8(5)°. The paired molecules are packed together with usual van der Waals contacts.

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