The Crystal and Molecular Structure of Grayanotoxin XVI Hemihydrate

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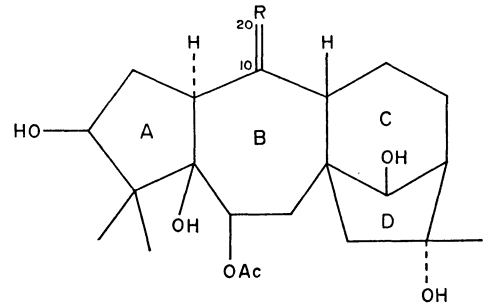
The molecular structure of grayanotoxin XVI, $C_{22}H_{34}O_6$, has been confirmed by means of an X-ray crystal analysis of its hemihydrate. The crystals are orthorhombic, with eight formula units in a unit cell with dimensions of $a=17.503$, $b=37.933$, and $c=6.371$ Å; the space group is $P2_12_12_1$. 4180 unique intensity data were collected on a four-circle diffractometer with LiF-monochromated Cu $K\alpha$ radiation. The structure was solved by the Monte Carlo direct method, using the 30 strongest reflections as the starting set, and was refined by the block-diagonal least-squares method. The final R value was 5.5%. The present analysis has revealed that the crystal used comprises about four parts of grayanotoxin XVI (6-*O*-acetylgrayanotoxin II) and one part of 10,20-dihydrograyanotoxin XVI. The molecules of the major component exist in two different conformations: One has the chair B-ring, and the other the twist-chair B-ring. About two-fifths of the molecules of the latter type are replaced at random by the molecules of the minor component.

Grayanotoxin (hereafter G) XVI is one of the physiologically-active diterpenes isolated from *Leucothoe grayana Max.*[1] On the basis of the chemical evidence, the **1** structure was proposed for this toxic substance. The main purposes of the present study were to confirm **1** and to test the effectiveness of the Monte Carlo direct method, a new phase-determining procedure.[2]



1: R = CH_2 2: R = CH_3, H

Experimental

Single crystals of G XVI hemihydrate were obtained as colorless needles from an ethanol–water solution. A sample with dimensions of about $0.1\times0.3\times0.6$ mm^3 was used for the X-ray measurement. The crystal data are summarized in Table 1. The cell dimensions and reflection intensities were measured on a Rigaku four-circle diffractometer using Cu $K\alpha$ radiation ($\lambda=1.5418$ Å) monochromatized with an LiF crystal. The intensity measurement was made by the θ-2θ continuous-scan technique at a 2θ scan rate of 2° min^{-1}; the background was measured for 30 s at each end of the scan range. The intensities were corrected for the Lorentz and polarization factors, but not for the absorption or extinction effect. In the range of 2θ values up to 140°, 4180 unique structure factor amplitudes above the $\sigma(F)$ level were selected for the structure determination.

Table 1. The crystal data

Formula	$C_{22}H_{34}O_6\cdot0.5\,H_2O$
Formula weight	403.5
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Cell dimensions	$a=17.503(6)$ Å
	$b=37.933(11)$ Å
	$c=6.371(3)$ Å
	$V=4230$ Å^3
Z	8
D_x	1.267 g cm^{-3}
μ (Cu $K\alpha$)	7.14 cm^{-1}

Structure Determination

The present structure containing 57 independent non-hydrogen atoms was solved by means of the Monte Carlo direct method.[2] The 30 strongest reflections were chosen as the starting set. In order to extend the tentative-phase set derived from successively-generated random numbers, 12 cycles of the tangent procedure were performed using 932 $|E|$ values above 1.30; during the first 5 cycles, the phases of the starting reflections were kept constant. Since the 261st phase set showed a low R_K value of 34.4% ($R_K=\Sigma||E_o|-k|E_c||/\Sigma|E_o|$),** 8 additional cycles of the tangent procedure were carried out; the R_K value was reduced to 27.6%. An E-map calculated with 864 phases clearly revealed the locations of all the non-hydrogen atoms except one. The computing time required for the phase determination was about 54 min on a FACOM 230-75 computer. This shows that the Monte Carlo direct method is still effective even for structures composed of more than 50 independent non-hydrogen atoms.

The 56 atomic positions obtained from the E-map were refined by the block-diagonal-matrix least-squares method with isotropic temperature factors. A difference Fourier map revealed that the remaining atom, C(A20), was distributed statistically between two positions in the ratio of about 3 to 2. Since close re-examination of the NMR spectrum demonstrated the presence of the dihydrograyanoid **2**, these two atomic positions, named C(A20a) and C(A20b) respectively, were assigned to the methylene carbon atom in **1** and the methyl carbon atom in **2** respectively. The whole structure thus obtained was refined by the least-squares method with anisotropic temperature factors; 0.6 and 0.4 times the atomic scattering factors of carbon were used for the C(A20a) and C(A20b)

** The second lowest of the R_K values for the 261 sets was 37.3%.

atoms respectively. After all hydrogen atoms, except those attached to the randomly-distributed carbon atom, had been located in a second difference Fourier map, further least-squares refinement was repeated including these hydrogen atoms with isotropic temperature factors. The following weighting scheme was used:

$$W=1/\{\sigma(F)^2 \exp(AX^2+BY^2+CXY+DX+EY)\},$$

where $X=|F_o|$ and $Y=\sin\theta/\lambda$. The A, B, C, D, and E coefficients are constants which were determined from the $(\Delta F)^2$ values. In this manner, the R value reached 5.5%. The atomic parameters are listed in Table 2. The tables of the anisotropic temperature factors and of the observed and calculated structure factors are kept at the Chemical Society of Japan (Document No. 8038).

All the calculations were performed on a FACOM 230-75 computer at the Hokkaido University Computing Center, using our own programs. Random numbers were generated by calling a function RANDOM in the program library of the Computing Center. The atomic scattering factors were taken from the International Tables.[3)]

Results and Discussion

Chemical Structure. The skeletons of the two independent G XVI molecules, A and B, are shown in Fig. 1, where each atom is represented as a thermal ellipsoid enclosing a 50% probability. Table 3 gives the bond distances and angles, and Fig. 2 shows the torsion angles in the tetracyclic systems. The C(A10)–C(A20a) and C(A10)–C(A20b) distances are almost equal, lying nearly midway between the accepted distances for C=C and C–C bonds. However, the projected angle of C(A9)–C(A10)–C(A20a) onto the plane normal to the C(A1)–C(A10) bond is significantly different from that of C(A9)–C(A10)–C(A20b) (see Fig. 3). Although these projected angles, 160 and 137°, deviate from their respective standard values of 180 and 120° by about 20°, they indicate that the C(A10)–C(A20a) and C(A10)–C(A20b) bonds are oriented roughly in the directions of the sp^2 and sp^3 hybrid orbitals on the C(A10) atom respectively, the C(A20b) atom being on the β side of the molecule. Since the apparent thermal motion of the C(A10) atom is greater than that of any other atom in the B-ring, the unusual distances and directions of these

Table 2. The final atomic parameters and estimated standard deviations

(1) The non-hydrogen atoms.

Atom	$x(\times 10^4)$	$y(\times 10^5)$	$z(\times 10^4)$	B_{eq}[a)]/Å^2	Atom	$x(\times 10^4)$	$y(\times 10^5)$	$z(\times 10^4)$	B_{eq}/Å^2
O(A1)	−143(2)	29412(7)	5843(5)	4.91	O(B1)	−819(2)	54556(6)	250(4)	4.65
O(A2)	−491(2)	22523(5)	5107(4)	3.44	O(B2)	−395(2)	49412(5)	3281(3)	3.41
O(A3)	−1786(1)	20713(6)	2542(4)	3.20	O(B3)	−1105(1)	42765(5)	3391(4)	3.00
O(A4)	−2207(2)	19330(8)	−651(5)	5.02	O(B4)	−1342(2)	37691(6)	1713(5)	5.01
O(A5)	−288(1)	16382(5)	−2494(4)	3.31	O(B5)	800(2)	37245(6)	688(5)	4.14
O(A6)	263(2)	9729(6)	−2350(5)	4.39	O(B6)	1890(2)	34799(7)	3265(5)	4.33
C(A1)	179(2)	24642(8)	1922(5)	3.03	C(B1)	266(2)	47926(8)	−48(5)	3.11
C(A2)	309(2)	28657(8)	2318(7)	4.29	C(B2)	−27(3)	50500(9)	−1736(6)	3.87
C(A3)	−347(2)	29887(8)	3661(6)	3.73	C(B3)	−823(2)	51553(8)	−1110(5)	3.69
C(A4)	−1017(2)	27449(7)	3078(5)	2.98	C(B4)	−1136(2)	48359(8)	91(5)	3.24
C(A5)	−597(2)	23795(7)	3005(5)	2.53	C(B5)	−439(2)	47260(7)	1455(5)	2.77
C(A6)	−1004(2)	20946(7)	1741(5)	2.64	C(B6)	−415(2)	43441(7)	2167(5)	2.75
C(A7)	−674(2)	17244(7)	1867(5)	2.81	C(B7)	240(2)	42433(8)	3627(5)	3.00
C(A8)	143(2)	16505(7)	1148(5)	2.65	C(B8)	1066(2)	42540(8)	2827(5)	3.05
C(A9)	768(2)	18245(8)	2545(5)	3.12	C(B9)	1383(2)	46378(9)	2608(6)	3.92
C(A10)	840(2)	22288(10)	2496(8)	4.86	C(B10)	966(2)	49003(9)	1196(6)	3.80
C(A11)	1547(2)	16509(9)	2077(6)	3.96	C(B11)	2243(2)	46234(11)	2163(9)	5.16
C(A12)	1713(2)	16345(10)	−300(7)	4.02	C(B12)	2477(2)	43381(12)	565(8)	5.12
C(A13)	1030(2)	14930(8)	−1558(5)	3.35	C(B13)	2093(2)	39816(10)	978(6)	3.99
C(A14)	340(2)	17331(7)	−1177(5)	2.62	C(B14)	1232(2)	40453(8)	793(5)	3.12
C(A15)	237(2)	12406(8)	1167(5)	3.45	C(B15)	1578(2)	40551(10)	4452(6)	3.82
C(A16)	738(2)	11322(8)	−733(6)	3.56	C(B16)	2173(2)	38412(10)	3234(6)	3.92
C(A17)	1340(3)	8565(9)	−269(7)	4.79	C(B17)	2980(3)	38396(14)	4097(9)	5.74
C(A18)	−1663(2)	27731(10)	4657(7)	4.35	C(B18)	−1856(2)	49235(10)	1336(7)	4.59
C(A19)	−1318(2)	28474(8)	910(6)	3.85	C(B19)	−1335(2)	45493(10)	−1543(6)	4.22
C(A20a)	1569(4)	23878(19)	2310(14)	5.05	C(B20)	1185(3)	52349(11)	1261(10)	5.82
C(A20b)	1303(6)	23275(34)	4211(32)	8.07	C(B21)	−1485(2)	39748(8)	3096(6)	3.38
C(A21)	−2332(2)	19915(9)	1179(7)	3.91	C(B22)	−2098(2)	39270(11)	4662(8)	4.98
C(A22)	−3104(2)	19915(13)	2213(9)	5.39	O(W)	−397(2)	35663(8)	−2030(5)	5.52

a) $B_{eq}=8\pi^2(u_1^2+u_2^2+u_3^2)/3$, where u_i is the root-mean-square deviation in the ith principal axis of the thermal ellipsoid.

TABLE 2. (Continued)

(2) The hydrogen atoms.

The atomic coordinates are multiplied by 10^3.

Atom[a)]	x	y	z	B/Å^2	Atom	x	y	z	B/Å^2
H(A1)	4(2)	243(1)	45(6)	2.9(7)	H(B2b)	26(2)	522(1)	−196(7)	4.0(8)
H(A2a)	27(3)	298(1)	87(8)	5.0(9)	H(B3)	−113(2)	520(1)	−242(7)	3.9(8)
H(A2b)	77(3)	287(1)	329(10)	6.3(11)	H(B6)	−46(3)	420(1)	89(8)	4.8(9)
H(A3)	−50(2)	322(1)	347(6)	3.1(7)	H(B7a)	14(2)	400(1)	419(6)	2.9(6)
H(A6)	−102(2)	218(1)	34(6)	2.7(6)	H(B7b)	18(3)	440(1)	504(9)	5.4(10)
H(A7a)	−99(2)	158(1)	86(6)	2.5(6)	H(B9)	133(2)	473(1)	420(6)	3.3(7)
H(A7b)	−73(2)	163(1)	330(7)	4.4(8)	H(B11a)	242(2)	485(1)	146(7)	4.6(9)
H(A9)	63(2)	173(1)	409(7)	4.2(8)	H(B11b)	253(3)	458(2)	344(10)	6.6(12)
H(A11a)	197(3)	176(1)	282(8)	5.0(9)	H(B12a)	229(3)	445(1)	−63(8)	4.7(9)
H(A11b)	153(2)	141(1)	256(7)	3.8(8)	H(B12b)	306(3)	431(1)	57(8)	5.5(10)
H(A12a)	186(3)	187(1)	−95(8)	4.8(9)	H(B13)	224(2)	382(1)	−7(7)	3.8(8)
H(A12b)	219(3)	149(1)	−71(8)	4.9(9)	H(B14)	110(2)	416(1)	−50(6)	2.6(6)
H(A13)	117(3)	147(1)	−316(8)	5.3(10)	H(B15a)	126(2)	390(1)	537(6)	3.4(7)
H(A14)	46(2)	197(1)	−141(6)	2.9(6)	H(B15b)	185(3)	422(2)	536(10)	6.9(12)
H(A15a)	−24(2)	113(1)	86(7)	4.0(8)	H(B17a)	296(3)	373(1)	559(8)	5.3(10)
H(A15b)	46(2)	116(1)	252(6)	3.1(6)	H(B17b)	316(3)	407(1)	429(8)	5.1(9)
H(A17a)	114(3)	66(1)	11(8)	4.8(9)	H(B17c)	328(4)	363(2)	333(11)	7.9(14)
H(A17b)	166(3)	90(1)	84(8)	5.5(10)	H(B18a)	−210(3)	474(1)	194(9)	6.3(11)
H(A17c)	161(2)	83(1)	−141(7)	4.2(8)	H(B18b)	−226(3)	503(2)	37(11)	7.5(14)
H(A18a)	−206(3)	264(1)	446(8)	5.2(10)	H(B18c)	−173(2)	508(1)	228(6)	3.5(7)
H(A18b)	−180(4)	300(2)	476(12)	8.2(15)	H(B19a)	−170(3)	465(2)	−252(11)	7.3(13)
H(A18c)	−151(4)	269(2)	613(11)	8.1(15)	H(B19b)	−162(3)	436(1)	−90(8)	5.3(10)
H(A19a)	−147(2)	307(1)	103(7)	3.9(8)	H(B19c)	−87(3)	446(1)	−219(8)	4.6(9)
H(A19b)	−174(3)	270(1)	40(8)	4.8(9)	H(B20a)	92(2)	542(1)	57(7)	3.9(8)
H(A19c)	−93(3)	283(1)	−23(8)	4.7(9)	H(B20b)	165(4)	531(2)	213(11)	7.4(13)
H(A22a)	−325(3)	227(2)	241(10)	7.5(13)	H(B22a)	−247(3)	379(2)	427(10)	7.3(13)
H(A22b)	−298(5)	188(2)	346(14)	10.0(19)	H(B22b)	−237(4)	415(2)	499(13)	9.2(17)
H(A22c)	−343(4)	186(2)	140(11)	7.6(14)	H(B22c)	−185(6)	382(3)	590(16)	11.5(23)
H(OA1)	−22(4)	316(2)	643(13)	9.2(17)	H(OB1)	−65(2)	563(1)	−44(7)	4.7(9)
H(OA2)	−43(3)	242(1)	576(8)	5.1(9)	H(OB2)	−47(3)	518(1)	282(8)	5.4(10)
H(OA5)	−41(3)	180(1)	−316(8)	5.1(9)	H(OB5)	105(3)	361(1)	155(8)	4.7(9)
H(OA6)	−8(3)	111(1)	−254(10)	6.5(12)	H(OB6)	220(3)	335(1)	285(10)	6.3(11)
H(B1)	37(2)	456(1)	−80(6)	3.1(7)	H(OWa)	−73(5)	365(2)	−127(15)	10.5(20)
H(B2a)	−3(2)	492(1)	−297(7)	3.9(8)	H(OWb)	0(3)	360(1)	−133(8)	5.0(9)

a) The hydrogen atoms are denoted by the number of the carbon atom to which they are attached, suffixed by a, b, or c where necessary.

two bonds may be due partly to the disordering of the C(A10) atom.

It is thus concluded that, although about three-fifths of the A molecules correspond to compound **1**, the remaining A molecules correspond to compound **2**.*** Since the B molecules having no disordering correspond to **1**, it follows that the present crystal as a whole contains about one-fifth of **2**. This unexpected contaminant is the first 10,20-dihydrograyanoid to be obtained from *Leucothoe grayana Max.*

Molecular Geometry. As Table 3 shows, all the bond distances are normal except for the randomly-distributed C(A20) atom. There is no great difference between the two crystallographically-independent molecules of G XVI.

The five-membered A-rings in both of the molecules take similar envelope forms; the C(4) atom deviates remarkably from the mean plane for the other four atoms onto the α side of the molecule.† Although this conformation makes the O(1)H and O(2)H hydroxyl groups 1,3-diaxial, it is stabilized by the formation of the intramolecular hydrogen bond, O(2)H···O(1) (see Table 4).

The difference between the A and B molecules can be most clearly seen for the conformations of their central seven-membered B-rings; the B-ring of the former has the twist-chair form with an approximate two-fold rotation axis through the C(A10) atom, while that of the latter adopts the chair form with an approximate mirror plane through the C(B6) atom. According to Hendrickson's calculations,[4] cycloheptane prefers the twist-chair conformation. In Hendrickson's

*** Unless otherwise stated, "A molecules" will mean solely molecules of **1** in the description given below.

† The atomic name, C(i), is used when the description is valid for both of the A and B molecules.

Table 3. The bond distances (l/Å) and angles (ϕ/°), with their standard deviations
The standard deviations given in parentheses refer to the last decimal position.

(1) The bond distances.

	Mol. A	Mol. B		Mol. A	Mol. B		Mol. A	Mol. B
C(1)-C(2)	1.560(4)	1.541(5)	C(6)-C(7)	1.521(4)	1.524(4)	C(12)-C(13)	1.536(5)	1.533(6)
C(1)-C(5)	1.557(4)	1.582(5)	C(6)-O(3)	1.463(4)	1.461(4)	C(13)-C(14)	1.533(4)	1.530(5)
C(1)-C(10)	1.507(5)	1.515(5)	C(7)-C(8)	1.526(4)	1.534(5)	C(13)-C(16)	1.553(5)	1.540(6)
C(2)-C(3)	1.506(6)	1.503(6)	C(8)-C(9)	1.558(4)	1.564(5)	C(14)-O(5)	1.428(4)	1.434(4)
C(3)-C(4)	1.539(5)	1.534(5)	C(8)-C(14)	1.552(4)	1.546(5)	C(15)-C(16)	1.551(5)	1.531(5)
C(3)-O(1)	1.447(5)	1.432(4)	C(8)-C(15)	1.564(4)	1.564(5)	C(16)-C(17)	1.513(5)	1.516(6)
C(4)-C(5)	1.570(4)	1.554(5)	C(9)-C(10)	1.539(5)	1.528(5)	C(16)-O(6)	1.456(5)	1.457(4)
C(4)-C(18)	1.517(5)	1.526(6)	C(9)-C(11)	1.543(5)	1.533(6)	C(21)-C(22)	1.503(6)	1.476(6)
C(4)-C(19)	1.529(5)	1.545(5)	C(10)-C(20a)	1.417(8)	1.326(5)	C(21)-O(3)	1.327(4)	1.336(4)
C(5)-C(6)	1.524(4)	1.519(4)	C(10)-C(20b)	1.411(18)		C(21)-O(4)	1.207(5)	1.203(5)
C(5)-O(2)	1.435(4)	1.424(4)	C(11)-C(12)	1.543(6)	1.541(7)			

(2) The bond angles.

	Mol. A	Mol. B		Mol. A	Mol. B
C(2)-C(1)-C(5)	104.9(3)	105.3(3)	C(14)-C(8)-C(15)	100.7(2)	101.5(3)
C(2)-C(1)-C(10)	115.3(3)	117.6(3)	C(8)-C(9)-C(10)	117.9(3)	119.3(3)
C(5)-C(1)-C(10)	116.1(3)	110.9(3)	C(8)-C(9)-C(11)	109.3(3)	109.4(3)
C(1)-C(2)-C(3)	106.5(3)	107.0(3)	C(10)-C(9)-C(11)	110.4(3)	112.6(3)
C(2)-C(3)-C(4)	104.9(3)	104.6(3)	C(1)-C(10)-C(9)	122.2(3)	121.3(3)
C(2)-C(3)-O(1)	108.6(3)	111.6(3)	C(1)-C(10)-C(20a)	114.8(4)	120.5(4)
C(4)-C(3)-O(1)	110.2(3)	109.2(3)	C(1)-C(10)-C(20b)	118.2(6)	
C(3)-C(4)-C(5)	100.4(2)	102.2(3)	C(9)-C(10)-C(20a)	120.0(4)	117.9(4)
C(3)-C(4)-C(18)	111.4(3)	112.4(3)	C(9)-C(10)-C(20b)	107.2(6)	
C(3)-C(4)-C(19)	109.1(3)	107.5(3)	C(9)-C(11)-C(12)	111.9(3)	114.1(3)
C(5)-C(4)-C(18)	115.5(3)	114.6(3)	C(11)-C(12)-C(13)	112.3(3)	112.9(4)
C(5)-C(4)-C(19)	111.1(3)	111.4(3)	C(12)-C(13)-C(14)	108.9(3)	106.2(3)
C(18)-C(4)-C(19)	108.9(3)	108.5(3)	C(12)-C(13)-C(16)	112.8(3)	115.2(3)
C(1)-C(5)-C(4)	103.9(2)	103.3(2)	C(14)-C(13)-C(16)	102.2(3)	102.5(3)
C(1)-C(5)-C(6)	108.6(2)	108.1(2)	C(8)-C(14)-C(13)	101.9(2)	101.6(3)
C(1)-C(5)-O(2)	111.7(2)	111.2(3)	C(8)-C(14)-O(5)	109.8(2)	112.0(3)
C(4)-C(5)-C(6)	115.0(2)	116.4(3)	C(13)-C(14)-O(5)	111.3(2)	112.9(3)
C(4)-C(5)-O(2)	109.3(2)	110.2(2)	C(8)-C(15)-C(16)	108.5(3)	108.1(3)
C(6)-C(5)-O(2)	108.4(2)	107.5(2)	C(13)-C(16)-C(15)	102.5(3)	103.2(3)
C(5)-C(6)-C(7)	116.7(3)	116.3(3)	C(13)-C(16)-C(17)	116.5(3)	115.2(3)
C(5)-C(6)-O(3)	107.2(2)	107.7(2)	C(13)-C(16)-O(6)	108.3(3)	107.9(3)
C(7)-C(6)-O(3)	106.4(2)	104.6(2)	C(15)-C(16)-C(17)	115.1(3)	116.9(4)
C(6)-C(7)-C(8)	120.7(2)	119.9(3)	C(15)-C(16)-O(6)	109.8(3)	105.1(3)
C(7)-C(8)-C(9)	114.1(3)	112.9(3)	C(17)-C(16)-O(6)	104.4(3)	107.9(3)
C(7)-C(8)-C(14)	117.2(3)	116.3(3)	C(22)-C(21)-O(3)	111.2(4)	111.8(3)
C(7)-C(8)-C(15)	106.2(2)	107.9(3)	C(22)-C(21)-O(4)	126.0(4)	124.5(3)
C(9)-C(8)-C(14)	107.7(2)	109.6(3)	O(3)-C(21)-O(4)	122.9(3)	123.7(3)
C(9)-C(8)-C(15)	110.0(3)	107.7(3)	C(6)-O(3)-C(21)	117.4(3)	119.1(2)

computed twist-chair form (hereafter HTC), substituents at the 2a, 2'a, 3a, and 3'a positions sustain strong steric repulsions (see Fig. 4(a)). For the O(A2)H and C(A14)H groups situated at the 3a and 3'a positions, however, no unusually-close contacts are observed: for example, O(A2)···H(A7b), 2.66(4) Å; O(A2)···H(A9), 2.87(4) Å; C(A14)···H(A1), 2.89(3) Å; C(A14)···H(A6), 3.08(3) Å; H(A14)···H(A1), 2.23 (5) Å. This relief of the steric hindrance may be explained from the remarkable flattening of the B-ring, due mainly to the conformational transmission[5] at the *trans* A/B- and *cis* B/C-junctions. The magnitudes of the C(A10)–C(A1)–C(A5)–C(A6) and C(A7)–C(A8)–C(A9)–C(A10) torsion angles, 85.0 and 68.8°, are much smaller than the corresponding value for HTC, 97°; hence, the axial nature of the C(A5)–O(A2) and C(A8)–C(A14) bonds is remarkably decreased.

The occurrence of the chair B-ring should be noted in two respects: (1) The chair cycloheptane is less stable than the twist-chair cycloheptane by 2.16 kcal/mol;[4] (2) the bulky C(B14)H group is placed at a very hindered position on the chair B-ring. In Hendrickson's computed chair form of cycloheptane

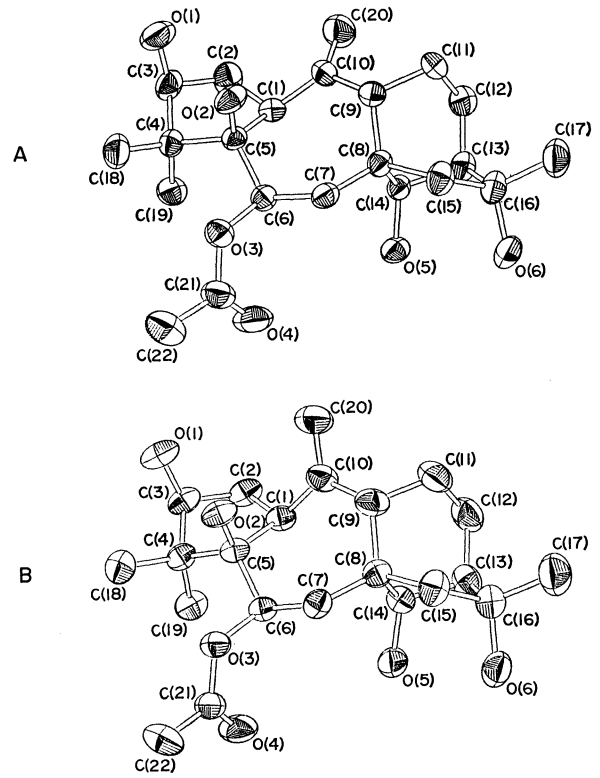


Fig. 1. Perspective views of the A and B molecules. For the sake of clarity, the C(A20b) atom was omitted.

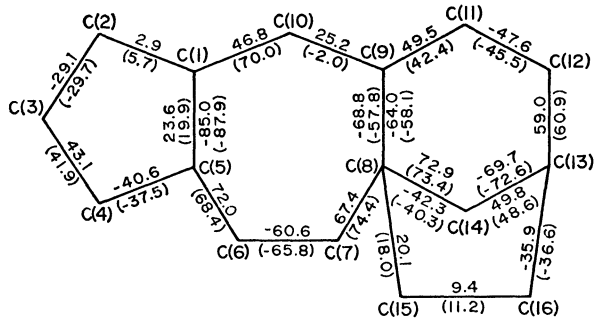


Fig. 2. The torsion angles (ϕ/°) of the A-, B-, C-, and D-rings. Only the torsion angles relevant to atoms which form the same ring are given in the ring. The values for the B molecule are given in parentheses.

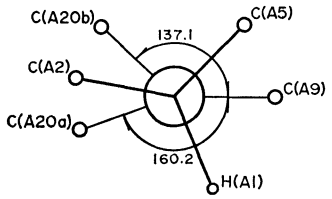


Fig. 3. The projected angles (ϕ/°) onto the plane normal to the C(A1)–C(A10) bond.

(hereafter HC), the 3a-3'a interaction is the severest, and stronger than the 2a-3'a and 2'a-3a interactions in HTC (see Fig. 4(b)). The 3a-3'a repulsion between the C(B14)H group and the H(B1) atom is relieved mainly by the closing of the C(B6)–C(B7)–C(B8)–C(B9) and C(B7)–C(B8)–C(B9)–C(B10) torsion angles. The magnitudes of these torsion angles are

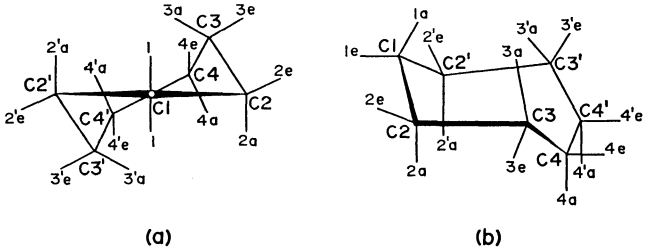


Fig. 4. Hendrickson's (a) twist-chair and (b) chair forms of cycloheptane.

smaller than the corresponding values for HC, 92 and 71°, by about 18 and 13° respectively. Since these torsion angles are opposite in sign, this shows a remarkable decrease in axiality of the C(B8)–C(B14) bond.[6] In spite of such a relief of the 3a-3'a repulsion, the C(B14)H group is still hindered severely: C(B1)···C(B14), 3.344(4) Å; C(B1)···H(B14), 2.82(3) Å; H(B1)···C(B14), 2.66(4) Å; H(B1)···H(B14), 1.98(5) Å.

The exocyclic methylene group in the B molecule, $C(B20)H_2$, sustains great steric repulsions from the two methylene groups, $C(B2)H_2$ and $C(B11)H_2$: H(B20a)···H(B11a), 2.24(7) Å; H(B20b)···H(B2b), 2.12(6) Å. As will be shown by the projected angle of C(B1)–C(B10)–C(B9) onto the plane normal to the C(B10)=C(B20) double bond, 173.1°, these steric repulsions probably push the $C(B20)H_2$ group away from the C(B1)–C(B10)–C(B9) plane to the β side of the molecule. In the G II molecule having the severe H(20a)···H(11a) interaction of 1.92(5) Å,[7] the C(9)–C(10)–C(20) bond angle is greater than the C(1)–C(10)–C(20). In the B molecule, the relation is reversed: C(B9)–C(B10)–C(B20), 117.9°; C(B1)–C(B10)–C(B20), 120.5°. Further, the C(B2)–C(B1)–C(B10) bond angle is expanded from the corresponding angle in G II, 113.3°, to 117.6°, while the C(B5)–C(B1)–C(B10) bond angle is reduced from 119.5° for G II to 110.9°. These changes in bond angle can be explained on the basis of the strong H(B20b)···H(B2b) repulsion.

The six-membered C-rings in both of the A and B molecules take the chair conformation, but are much deformed by three main causes: (1) the three-bond bridge, C(8)–C(15)–C(16)–C(13); (2) the conformational transmission at the *cis* B/C-junction; (3) the steric repulsion between the C(14)H group and the H(1) atom.

In both the A and the B molecules, the form of the five-membered D-ring is intermediate between the envelope form characterized by the mirror plane through the C(14) atom and the half-chair form characterized by the two-fold rotation axis through the C(15) atom. Although the D-ring is forced to take the envelope form by the existence of the chair C-ring, it is probably deformed by the $C(11)H_2$···$C(17)H_3$ repulsion and the O(5)···O(6) hydrogen bonding. In the A molecule, the O(6)H group donates its proton to the O(5)H, while in the B molecule, the latter donates to the former (see Table 4).

Crystal Structure. The crystal structure viewed along the c axis is shown in Fig. 5. There are six kinds of intermolecular hydrogen bonds; the details

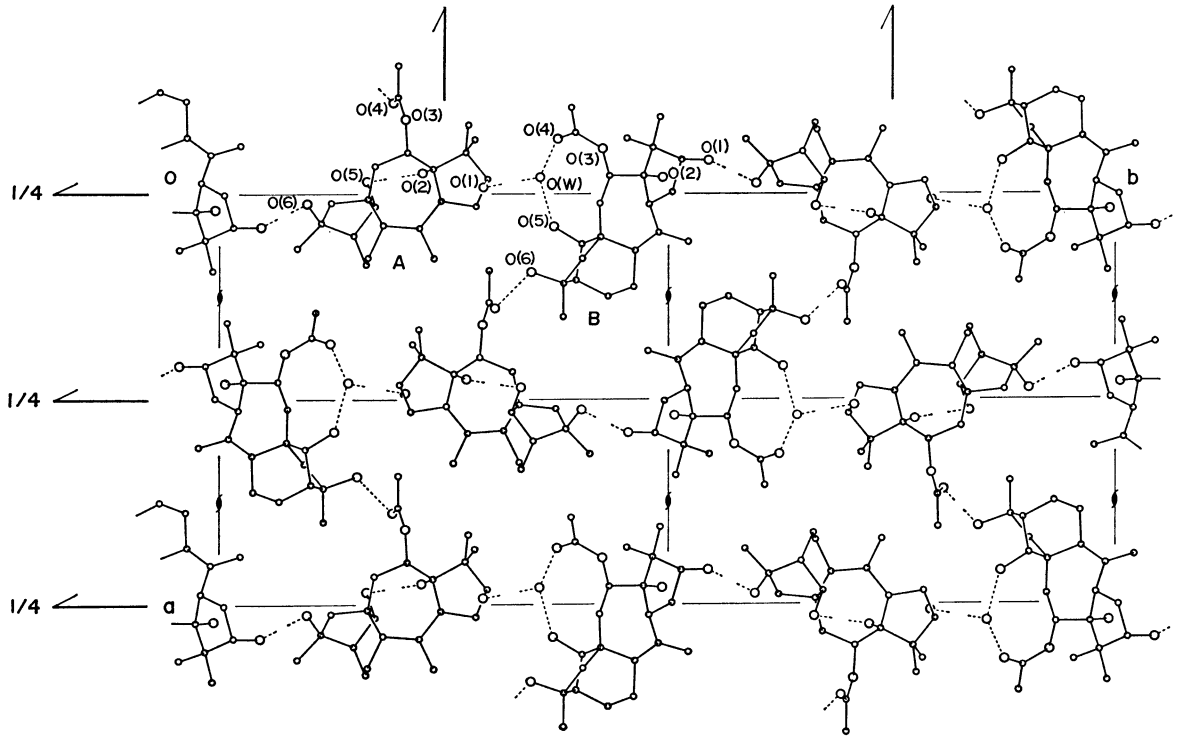


Fig. 5. The crystal structure viewed along the c axis.

Table 4. The hydrogen bonds, X-H···Y

X	Y	X···Y (l/Å)	H···Y (l/Å)	X-H···Y (ϕ/°)
(1) Intramolecular				
O(A2)	O(A1)	2.724(3)	2.04(4)	148(5)
O(A6)	O(A5)	2.703(3)	2.05(5)	139(5)
O(B2)	O(B1)	2.844(3)	2.05(5)	141(4)
O(B5)	O(B6)	2.683(4)	1.89(5)	159(4)
(2) Intermolecular				
O(A1)	O(W)[b]	2.767(4)	1.85(7)	172(7)
O(A5)	O(A2)[c]	2.809(3)	2.04(5)	168(5)
O(B1)	O(A6)[d]	2.866(4)	2.03(5)	166(4)
O(B6)	O(A4)[e]	2.779(4)	2.04(6)	156(6)
O(W)	O(B4)[a]	3.002(5)	2.23(9)	158(8)
O(W)	O(B5)[a]	2.784(4)	1.96(5)	168(5)

The symmetry codes are as follows: a) x, y, z (given in Table 2); b) x, y, $1+z$; c) x, y, $-1+z$; d) $-x$, $1/2+y$, $-1/2-z$; e) $1/2+x$, $1/2-y$, $-z$.

of the hydrogen bonds are given in Table 4. Each water molecule donates its protons to the O(B4) carbonyl and O(B5) hydroxyl oxygen atoms of the same B molecule, and it accepts the proton from the O(A1)H hydroxyl group of the neighboring A molecule. The couples of the A and B molecules connected through such mediation of the water molecule are further held together by the remaining three hydrogen bonds, forming a three-dimensional hydrogen-bonded structure.

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