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The Molecular Conformation of 6,14-Di-*O*-acetyl-3-*O*-(2-chlorobenzoyl)-grayanotoxin II as Revealed by X-Ray Methods

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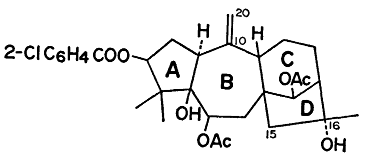
Synopsis. An X-ray crystal analysis has revealed that the six-membered C-ring in the title compound takes a boat conformation, in contrast with that in grayanotoxin II itself.

A series of X-ray crystal analyses[1] revealed that the C-ring conformation of grayanotoxins[2] with the exocyclic double bond, C(10)=C(20), depends largely on the multiplicity of the C(15)–C(16) bond. When this is a single bond, the C-ring prefers a chair conformation. However, the enthalpy difference between the chair and boat conformations of the C-ring is supposed to be small, because the change of the B-ring conformation reduces that energy difference. In this paper, we wish to report an example of grayanoids in which, although the C(15)–C(16) and C(10)–C(20) bonds are single and double bonds respectively, the C-ring adopts a boat conformation.

Experimental

Colorless single crystals of 6,14-di-*O*-acetyl-3-*O*-(2-chlorobenzoyl)grayanotoxin II (**1**) were grown from an acetone-diisopropyl ether solution. The crystal data are as follows: $C_{31}H_{39}O_8Cl$, $M.W.=575.1$, orthorhombic, space group $P2_12_12_1$, $a=12.51(1)$, $b=22.12(2)$, $c=10.39(1)$ Å, $Z=4$, $D_m=1.33\ \mathrm{g\ cm^{-3}}$, $D_c=1.328\ \mathrm{g\ cm^{-3}}$. The intensities were recorded on multiple Weissenberg photographs taken with Cu $K\alpha$ radiation for the 0th—10th layer around the a axis and for the 0th—8th layer around the c axis, and were measured visually with a calibrated intensity scale. The 2811 independent intensity data thus obtained were corrected for the Lorentz and polarization factors, but not for the absorption or the extinction effect.



1

Structure Determination

Various attempts were made to solve the structure by the heavy-atom method or the symbolic-addition procedure,[3] but all such attempts were unsuccessful. Thus, the structure analysis was delayed more than 10 years. Since the Monte Carlo direct method was recently developed,[4] it was applied to the present phase determination. The 50 strongest reflections were chosen as the starting set. In order to extend the tentative-phase set derived from random numbers, 12 cycles of the tangent procedure were performed using 542 $|E|$ values above 1.30. Since the 24th phase set showed a low R_K value of 0.339 ($R_K=\Sigma||E_o|-|E_c||/\Sigma|E_o|$), 6 additional cycles of the tangent procedure were carried out using 658 $|E|$ values above 1.20; the R_K value was reduced to 0.249. An *E*-map based on 641 phases afforded all the 40 non-hydrogen atoms. The structure thus obtained was refined by the block-diagonal-matrix least-squares method with anisotropic temperature factors. The

Table 1. The final atomic parameters and estimated standard deviations

Atom	$x(\times 10^4)$	$y(\times 10^4)$	$z(\times 10^4)$	B_{eq}[a]/Å^2
Cl	11205(3)	2477(2)	1912(4)	5.74
O(1)	7972(5)	2183(3)	1716(7)	2.55
O(2)	6607(5)	2700(3)	4428(7)	2.27
O(3)	6954(5)	3892(3)	5049(7)	2.14
O(4)	4244(5)	4874(3)	4407(7)	2.21
O(5)	1930(6)	4763(3)	5323(7)	2.97
O(6)	9124(7)	2674(4)	411(8)	3.98
O(7)	6902(7)	4880(4)	4476(11)	4.82
O(8)	4276(8)	5509(4)	2688(9)	4.56
C(1)	5539(7)	2946(4)	2553(10)	1.98
C(2)	6114(8)	2432(5)	1837(11)	2.85
C(3)	7208(7)	2698(4)	1598(11)	2.36
C(4)	7410(8)	3203(5)	2601(10)	2.32
C(5)	6382(8)	3166(4)	3488(10)	2.20
C(6)	6080(7)	3748(4)	4178(9)	2.04
C(7)	5062(8)	3698(4)	5011(10)	2.20
C(8)	3992(7)	3793(4)	4320(9)	2.05
C(9)	3640(7)	3265(4)	3370(10)	2.02
C(10)	4479(7)	2770(4)	3138(9)	1.85
C(11)	3258(8)	3503(5)	2071(10)	2.37
C(12)	2422(8)	4011(4)	2171(10)	2.35
C(13)	2659(7)	4417(4)	3325(11)	2.06
C(14)	3877(8)	4387(4)	3555(10)	2.16
C(15)	3093(8)	3870(4)	5340(10)	2.26
C(16)	2193(7)	4217(4)	4639(10)	1.93
C(17)	1137(8)	3838(5)	4561(12)	3.04
C(18)	8468(9)	3120(6)	3376(13)	3.86
C(19)	7465(10)	3813(5)	1872(13)	3.60
C(20)	4202(9)	2189(5)	3385(14)	3.56
C(21)	8894(9)	2253(5)	1093(11)	2.84
C(22)	9590(8)	1709(5)	1279(11)	2.56
C(23)	10664(9)	1777(6)	1614(12)	3.38
C(24)	11375(10)	1276(7)	1681(14)	4.35
C(25)	10949(12)	722(7)	1497(15)	4.97
C(26)	9851(12)	625(6)	1225(17)	5.14
C(27)	9160(10)	1130(5)	1138(13)	3.66
C(28)	7315(9)	4472(5)	5106(12)	2.97
C(29)	8212(9)	4530(6)	6005(13)	3.57
C(30)	4476(9)	5408(5)	3800(12)	2.93
C(31)	4889(11)	5857(5)	4784(14)	4.25

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 *i*th principal axis of the thermal ellipsoid.

final R value was 0.123. The final atomic parameters are listed in Table 1. The table of the anisotropic temperature factors and the F_o-F_c table are kept at the Chemical Society of Japan (Document No. 8148).

All the calculations were performed on a HITAC M-200H computer at the Hokkaido University Computing Center, using our own programs. The atomic scattering factors were taken from the International Tables.[5)]

Results and Discussion

The molecular framework of **1** and the torsion angles for the grayanane skeleton are shown in Figs. 1 and 2 respectively. The A-ring takes an envelope form; the C(2)–C(3)–C(4)–C(5) part is nearly planar. Since this conformation makes the O(1) atom and the $C(18)H_3$ group eclipse each other around the C(3)–C(4) bond, it is probably less stable than the envelope form with a planar C(5)–C(1)–C(2)–C(3) or C(1)–C(2)–C(3)–C(4) part. In fact, the present envelope form has not been observed in grayanotoxins I,[1a)] II,[1b)] XV,[6)] XVI,[1c)] and XIX.[1e)] The B-ring has a chair form with an approximate mirror plane through the C(5) atom, while the C-ring adopts a deformed boat form. Force-field calculations indicate that, in grayanotoxins having the C(15)–C(16) single and C(10)–C(20) double bonds, the molecular conformation with the boat C-ring is less stable than that with the chair C-ring by about 4 kJ mol^{-1}.[7)] If this is true, it follows that the occurrence of the present boat C-ring may be due to the molecular-packing effect. The D-ring takes a conformation intermediate between the envelope form with a mirror plane through the C(14) atom and the half-chair form with a two-fold rotation axis through the C(16) atom.

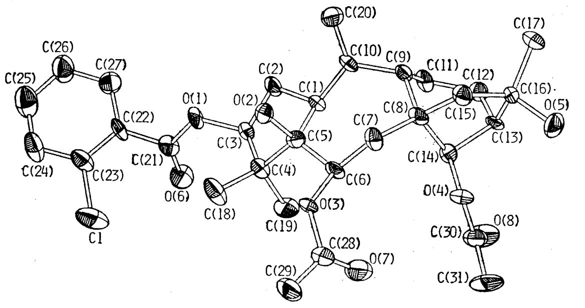


Fig. 1. A perspective view of the molecule of **1**.

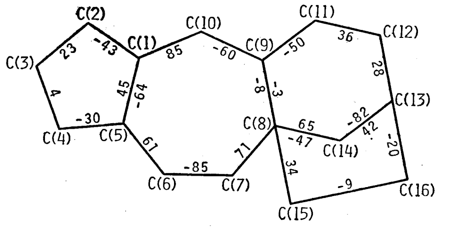


Fig. 2. The torsion angles (ϕ/°) for the grayanane skeleton.
Only the torsion angles relevant to atoms which form the same ring are given in the ring.

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