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Molecular Structure of 5β,6β-Isopropylidenedioxy-15,16,17-trinorgrayan-10(20)-ene-3,14-dione as Revealed by X-Ray Methods

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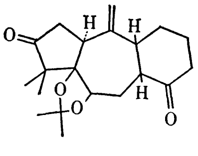
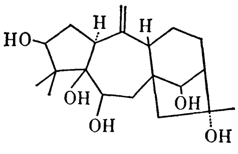
Synopsis. The molecular structure of the title compound has been determined by means of the X-ray method. The A, B, and C rings take half-chair, chair, and chair conformations, respectively, while the heterocyclic ring is of envelope form.

We report herewith on an X-ray study of the molecular structure of 5β,6β-isopropylidenedioxy-15,16,17-trinorgrayan-10(20)-ene-3,14-dione (**1**), obtained from the tetracyclic diterpene grayanotoxin II (**2**). Compound **1** was used as a link in the relay total synthesis of **2**.[1] The present study was undertaken in order to know the exact stereostructure and conformation of **1**.



1



2

Experimental

Single crystals of **1** were obtained as colorless plates or columns from an ethereal solution. A crystal with dimensions of 0.2×0.2×0.4 mm^3 was used for the X-ray measurement. The crystal data are as follows: $C_{20}H_{28}O_4$, mp 208—211 °C; space group $P2_12_12_1$; a=9.500(3), b=21.524(4), c=8.758(3) Å; Z=4, D_c=1.233 g·cm^{-3}. Both the cell dimensions and diffraction intensities were measured on a Rigaku four-circle diffractometer using Cu $K\alpha$ radiation (λ=1.5418 Å) monochromatized with an LiF crystal. The intensities obtained were corrected for the Lorentz and polarization factors, but not for the absorption or the extinction effect. In the range of 2θ-values up to 140°, 1871 unique structure factor magnitudes above $\sigma(F_0)$ were selected for the structural study.

Structure Determination

The structure was determined by means of the Monte Carlo direct method.[2] The starting set was composed of the 10 strongest reflections given in Table 1. Tentative phase values for these reflections were derived from successively generated random numbers. In order to extend this tentative phase set, 10 cycles of the tangent procedure were performed using 380 E-values above 1.30. In this manner, the 40th phase set was extended to 367 phases, showing a low R_k-value of 23.5% ($R_k=\Sigma||E_o|-k|E_c||/\Sigma|E_o|$).[3] An E-map computed with these phases revealed the locations of all 24 non-hydrogen atoms.

It is of interest to compare the 40th random phase set with the correct phases calculated with the final atomic parameters. All the 10 reflections are not assigned phase values close to their correct phases (see Table 1). Great differences of 0.335π, π, and 0.434π can be seen for the (1 2 8), (3 0 7), and (2 19 3) reflections, respectively. It should be noted that, in spite of such great errors, this random phase set could lead to the correct structure. The structure thus obtained was refined by the block-diagonal-matrix least-squares method, first with isotropic temperature factors and then with anisotropic ones. The value $R=\Sigma||F_o|-k|F_c||/\Sigma|F_o|$ was reduced to 9.5%. After 28 hydrogen atoms had been found in a difference Fourier map, the least-squares refinement was repeated including these hydrogen atoms with isotropic temperature factors. For the refinement, the following weighting scheme was used:

Table 1. The 40th phase set and correct phases (in $10^{-3}\pi$)

	h	k	l	$\lvert E\rvert$	Correct	No. 40
1	1	22	0	3.47	500	500
2	3	18	0	3.26	1500	1500
3	2	16	4	3.03	330	500
4	4	3	7	2.98	1384	1500
5	0	18	7	2.84	1000	1000
6	1	2	8	2.84	1915	250
7	3	0	7	2.67	1500	500
8	2	19	3	2.61	66	500
9	0	9	8	2.60	500	500
10	5	13	3	2.58	632	500

$$W = 1/\{\sigma(F_0)^2 \exp(AX^2+BY^2+CXY+DX+EY)\},$$

where $X=|F_o|$ and $Y=\sin\theta/\lambda$. Coefficients A, B, C, D, and E were determined from $(\Delta F)^2$ values in each cycle. In this way, the R value reached 4.5%. The final parameters for the non-hydrogen atoms are given in Table 2.

The calculations for the present study were carried out on a FACOM 230-75 computer at the Computing Center of Hokkaido University, using our own programs. The atomic scattering factors were taken from International Tables for X-Ray Crystallography (1962), Vol. III. The tables of the observed and calculated structure factors are kept at the Chemical Society of Japan (Document No. 7911).

Results and Discussion

The molecular framework of **1** and the torsion angles for the tetracyclic system are shown in Figs. 1 and 2, respectively. Of the two five-membered rings, the A ring takes a somewhat distorted half-

Table 2. Final atomic parameters and estimated standard deviations
The β_{22} values are multiplied by 10^5 and the others by 10^4. The temperature factors are defined as $\exp(-\beta_{11}h^2-\beta_{22}k^2-\beta_{33}l^2-\beta_{12}hk-\beta_{13}hl-\beta_{23}kl)$.

Atom	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	p_{23}
O(1)	1638 (4)	4094 (2)	7025 (3)	209 (4)	401 (7)	151 (3)	−36 (3)	−153 (7)	−6 (3)
O(2)	−1272 (2)	4424 (1)	3950 (2)	110 (2)	175 (3)	106 (2)	16 (2)	−14 (4)	2 (2)
O(3)	−1514 (3)	4342 (1)	1389 (2)	177 (3)	192 (4)	116 (2)	29 (2)	−72 (5)	8 (2)
O(4)	−2260 (3)	2721 (1)	−1629 (2)	155 (3)	355 (6)	107 (3)	−15 (2)	−41 (5)	−4 (2)
C(1)	−454 (3)	3359 (1)	4168 (3)	92 (2)	164 (4)	87 (3)	1 (2)	−5 (5)	8 (2)
C(2)	−192 (3)	3478 (1)	5885 (3)	134 (3)	200 (5)	90 (3)	7 (2)	−23 (6)	7 (2)
C(3)	985 (3)	3947 (1)	5905 (3)	119 (3)	219 (6)	120 (3)	9 (2)	−52 (6)	−10 (3)
C(4)	1215 (3)	4210 (1)	4292 (3)	98 (3)	188 (5)	131 (3)	−5 (2)	−15 (6)	−9 (2)
C(5)	−166 (3)	4015 (1)	3477 (3)	92 (2)	150 (4)	91 (3)	−1 (2)	2 (5)	2 (2)
C(6)	−198 (3)	4055 (1)	1721 (3)	126 (3)	169 (4)	96 (3)	−17 (2)	11 (5)	16 (2)
C(7)	−112 (3)	3447 (1)	816 (3)	102 (3)	197 (5)	88 (3)	−20 (2)	23 (5)	7 (2)
C(8)	−1483 (3)	3061 (1)	825 (3)	81 (2)	195 (5)	93 (3)	0 (2)	−1 (5)	6 (2)
C(9)	−1780 (3)	2669 (1)	2284 (3)	87 (2)	175 (4)	105 (3)	−13 (2)	0 (5)	3 (2)
C(10)	−1815 (3)	3055 (1)	3734 (3)	105 (3)	158 (4)	97 (3)	−11 (2)	12 (5)	15 (2)
C(11)	−790 (3)	2107 (1)	2396 (3)	136 (3)	167 (5)	131 (3)	−7 (2)	−39 (6)	5 (2)
C(12)	−876 (4)	1700 (1)	970 (4)	151 (4)	192 (5)	183 (5)	3 (3)	−26 (8)	−22 (3)
C(13)	−539 (4)	2078 (2)	−459 (4)	123 (3)	288 (7)	147 (4)	−7 (3)	15 (6)	−48 (3)
C(14)	−1483 (3)	2630 (1)	−549 (3)	88 (3)	259 (6)	102 (3)	−27 (2)	19 (5)	−2 (2)
C(15)	2520 (3)	3872 (2)	3622 (5)	91 (3)	339 (8)	187 (5)	−9 (3)	13 (7)	−34 (4)
C(16)	1513 (4)	4906 (1)	4358 (4)	151 (4)	219 (6)	167 (4)	−38 (3)	−25 (8)	−11 (3)
C(17)	−2975 (4)	3098 (2)	4551 (4)	124 (3)	273 (7)	138 (4)	−27 (3)	72 (6)	−16 (3)
C(18)	−1958 (3)	4697 (1)	2661 (4)	144 (4)	189 (5)	132 (4)	20 (2)	−48 (7)	4 (2)
C(19)	−1539 (5)	5374 (1)	2478 (5)	224 (6)	183 (6)	208 (5)	27 (3)	−69 (11)	17 (3)
C(20)	−3538 (4)	4635 (2)	2830 (5)	142 (4)	360 (10)	225 (7)	35 (4)	−96 (10)	−2 (4)

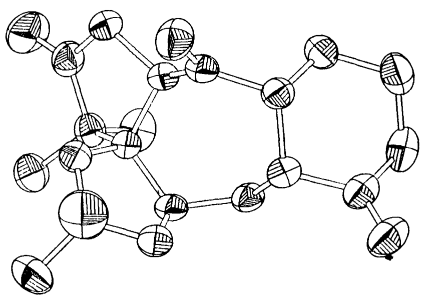


Fig. 1. The molecular framework of **1**.

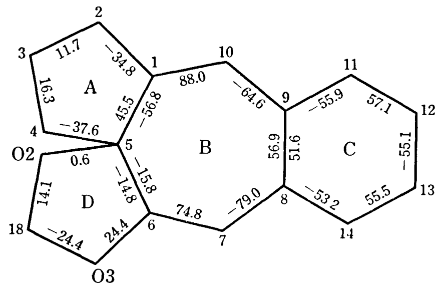


Fig. 2. The torsion angles (°) for the tetracyclic system. For the sake of clarity, only the torsion angles relevant to atoms which form the same ring are given in the ring.

chair form with an approximate two-fold rotation axis through the C(3) atom; the C(16) and O(2) atoms are equatorial and axial, respectively. On the other hand, the D ring takes an almost exact envelope form with an approximate mirror plane through the O(3) atom; the C(19) atom is axial. As a result of such ring conformations, the C(16) and C(19) atoms maintain a distance of 3.482(6) Å from each other. The seven-membered B ring takes a chair-like form and is nearly symmetrical with respect to a plane which runs through the C(9) atom, bisecting the C(5)–C(6) bond nearly perpendicularly. The six-membered C ring has a somewhat flattened chair form in which the axial positions in the C ring of the grayanane skeleton become equatorial and *vice versa*. All the observed bond distances and angles are normal; the average values for C(sp^3)–C(sp^3), C(sp^2)–C(sp^3), C=C, C–O, and C=O bond distances are 1.54, 1.51, 1.32, 1.43, and 1.21 Å, respectively.

References

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2) A. Furusaki, *Acta Crystallogr.*, in press.
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