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A Structure Analysis of a Bromo Derivative of Parasiticolide A by the X-Ray Diffraction Method

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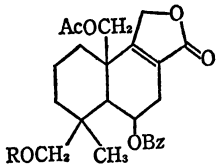
Synopsis. The structure of a bromo-derivative of parasiticolide A, $C_{26}H_{29}O_8Br$, has been determined by single-crystal X-ray analysis. The compound crystallized in the space group $P2_12_12_1$, with $a=14.658$, $b=15.323$, and $c=11.181$ Å. The absolute configuration of the molecule was determined using the anomalous dispersion effect of the bromine atom for Cu$K\alpha$ radiation.

Parasiticolide A (I) was isolated as a new metabolite from a strain of *Aspergillus parasiticus* Speare IFO 4082, which produces a small amount of carcinogenic aflatoxins.[1] Although the structural formula of parasiticolide A had been determined by means of chemical and spectroscopic methods,[1] the three-dimensional structure and the absolute configuration of this compound remained unsolved. Therefore, a bromo-derivative of parasiticolide A (II) has been studied by the X-ray diffraction method in a series of works on the structures of the metabolites of the genus *Aspergillus*.[2-4]



(I) R: CH_3CO-
(II) R: $BrCH_2CO$-

The bromo-derivative of parasiticolide A was prepared by the acylation of a partial hydrolysis product of parasiticolide A and bromoacetylbromide. The compound crystallized from acetone solution in the form of colorless prisms elongated along the b-axis. The cell dimensions were obtained by the least-squares fits of the Bragg angles of forty-nine reflections measured by a Toshiba four-circle diffractometer. The crystal data were as follows: $C_{26}H_{29}O_8Br$, $M=549.4$, mp 206—208 °C, orthorhombic, space group $P2_12_12_1$, $a=14.658(6)$, $b=15.323(6)$, $c=11.181(5)$ Å, $V=2511.4$ Å^3, $Z=4$, $D_o=1.45$ g/cm^3, $D_x=1.45$ g/cm^3. The intensities were measured from a specimen with dimensions of *ca.* $0.36\times0.16\times0.14$ mm on a diffractometer with a scintillation counter equipped with a pulse-height analyzer. The stationary-crystal stationary-counter method was used, with a counting time of 30 seconds. The intensities of 1782 independent reflections were measured up to $\sin\theta/\lambda=0.53$ with Ni-filtered Cu $K\alpha$ radiation. The background for each reflection was taken from plots of the background as a function of 2θ. The intensities were corrected only for the Lorentz and polarization factors.

The structure was solved by the heavy-atom method and refined by a block-diagonal least-squares method. In the early stage of the refinement, all the lighter atoms were assumed to be carbon atoms. Eight oxygen atoms were assigned on the bases of the temperature factors and of the chemical sense. The refinement with anisotropic temperature factors reduced the R value to 0.079. The absolute configuration of the molecule was determined using the anomalous dispersion effect of the bromine atom ($\Delta f'=-0.9$ and

TABLE 1. THE COMPARISON OF CALCULATED AND OBSERVED INTENSITIES ($\times5$) OF FRIEDEL-PAIR REFLECTIONS

h k l	$F_c(hkl)$	$F_c(\bar{h}\bar{k}\bar{l})$	$I_o(hkl)$	$I_o(\bar{h}\bar{k}\bar{l})$
1 1 1	364	341	>	
1 6 1	286	264	>	
3 1 1	509	539	<	
4 3 1	435	418	>	
2 5 2	217	203	>	
3 2 2	171	156	>	
3 6 2	267	293	<	
5 2 2	144	167	<	
1 5 3	269	255	>	
2 3 5	193	217	<	

The right-handed coordinate system is adopted.

TABLE 2. FINAL ATOMIC PARAMETERS AND THEIR ESTIMATED STANDARD DEVIATIONS ($\times10^4$) FOR NON-HYDROGEN ATOMS

The anisotropic temperature factors are of the form;
$\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+\beta_{12}hk+\beta_{13}hl+\beta_{23}kl)]$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	-2633(1)	-2323(1)	-1003(1)	92(1)	49(1)	124(1)	-3(1)	-20(1)	-3(1)
C(1)	-1891(5)	3154(5)	655(7)	47(4)	51(4)	79(7)	-4(7)	5(9)	-18(9)
C(2)	-2610(5)	2463(6)	685(8)	49(4)	64(5)	102(8)	20(7)	23(9)	-14(10)
C(3)	-2877(5)	2152(6)	-563(8)	43(4)	58(4)	105(8)	-2(7)	10(9)	9(10)
C(4)	-2063(5)	1813(5)	-1287(6)	37(3)	48(4)	65(6)	0(6)	-18(7)	3(8)
C(5)	-1303(5)	2521(5)	-1275(7)	41(3)	46(4)	71(6)	3(6)	4(8)	0(8)
C(6)	-494(5)	2395(5)	-2143(7)	41(3)	40(3)	77(6)	8(6)	-7(7)	16(8)
C(7)	59(6)	3210(5)	-2346(7)	54(4)	50(4)	83(7)	-5(7)	13(9)	25(9)
C(8)	81(6)	3750(6)	-1233(8)	49(4)	50(4)	106(8)	-17(7)	-24(10)	25(10)
C(9)	-394(5)	3636(5)	-215(7)	45(4)	43(3)	85(7)	1(6)	-15(9)	23(9)
C(10)	-1010(5)	2865(5)	10(6)	41(3)	48(4)	72(6)	0(6)	-11(8)	-3(9)
C(11)	-186(7)	4357(6)	625(8)	73(5)	54(4)	106(8)	-30(9)	-8(12)	-3(10)
C(12)	625(7)	4560(6)	-1088(9)	79(6)	57(5)	122(10)	-30(9)	-32(14)	-10(12)
C(13)	-1736(5)	922(5)	-838(7)	44(4)	40(3)	96(7)	2(6)	-2(10)	-4(9)
C(14)	-2400(6)	1694(6)	-2596(8)	54(4)	56(4)	98(7)	-14(8)	-23(10)	-15(9)
C(15)	-469(5)	2202(5)	749(6)	47(4)	48(4)	72(6)	3(7)	-21(8)	10(9)
C(16)	160(6)	2115(6)	2688(7)	53(4)	63(5)	88(7)	-15(8)	-12(10)	42(10)
C(17)	298(7)	2598(8)	3838(8)	73(5)	96(7)	91(8)	14(11)	-23(11)	16(13)
C(18)	-2219(6)	-529(5)	-739(7)	59(4)	46(4)	86(7)	-7(7)	-8(10)	14(9)
C(19)	-2982(7)	-1140(6)	-1155(12)	69(5)	48(4)	194(14)	-18(8)	-63(16)	-12(14)
C(20)	612(5)	1258(5)	-2490(7)	34(3)	51(4)	98(8)	-1(6)	-2(9)	-16(9)
C(21)	1167(5)	566(5)	-1969(8)	45(4)	39(3)	102(8)	-10(6)	-7(10)	-27(9)
C(22)	1016(6)	256(6)	-811(8)	51(4)	51(4)	103(8)	-6(7)	-8(10)	8(10)
C(23)	1599(6)	-402(6)	-351(9)	63(5)	55(4)	132(10)	16(8)	-26(12)	17(12)
C(24)	2305(7)	-726(7)	-1064(11)	65(5)	54(5)	186(13)	24(8)	-40(16)	7(14)
C(25)	2436(6)	-428(6)	-2187(10)	54(4)	58(4)	150(10)	18(8)	2(13)	-31(12)
C(26)	1865(6)	234(6)	-2686(9)	56(5)	53(4)	128(9)	7(8)	32(12)	-16(11)
O(1)	-2435(3)	288(3)	-1063(5)	45(2)	45(3)	94(5)	-1(4)	1(7)	4(6)
O(2)	-1533(4)	-732(4)	-237(7)	72(4)	54(3)	188(9)	-14(6)	-88(11)	27(9)
O(3)	89(3)	1687(3)	-1681(4)	38(2)	50(2)	73(4)	21(4)	6(5)	8(6)
O(4)	599(4)	1436(4)	-3545(5)	65(3)	74(3)	71(5)	16(6)	22(7)	12(7)
O(5)	1155(6)	4895(5)	-1772(8)	111(6)	76(4)	173(9)	-77(9)	39(12)	55(11)
O(6)	449(4)	4897(4)	-6(7)	64(3)	52(3)	173(8)	-29(5)	-45(9)	0(9)
O(7)	-273(4)	2623(4)	1886(4)	56(3)	62(3)	64(4)	0(5)	-12(6)	4(6)
O(8)	377(6)	1392(5)	2491(7)	119(6)	71(4)	142(8)	40(9)	-112(12)	44(9)

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$\Delta f''=1.5$) for Cu $K\alpha$ radiation. A comparison of the intensities between the Friedel-pair of reflections is given in Table 1. Including hydrogen atoms with fixed parameters and the anomalous dispersion effect of the bromine atom, the final refinement reduced the R value to 0.062 for 1772 reflections. The weighting scheme adopted in the final calculation was $w=0.3$ for $F_o=0$, $w=1.0$ for $0<F_o\leqq 20$, and $w=1.0/(1.0+0.5(F_o-20))$ for $20<F_o$. The final atomic parameters are given in Table 2. The absolute configuration of the molecule is correctly represented by the coordinates in Table 2 if the right-handed coordinate system is adopted. All the atomic scattering factors were taken from the International Tables for X-ray Crystallography.[5] The computations were performed on a TOSBAC-3400 computer at the Tottori University Computing Center, and on a NEAC 2200 N700 computer at the Computation Center of Osaka University.

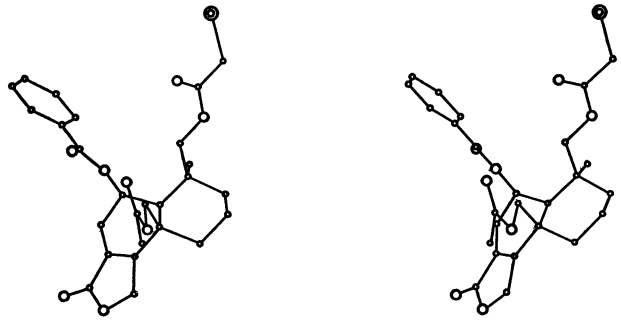

Fig. 1. Stereoscopic view of the molecule.

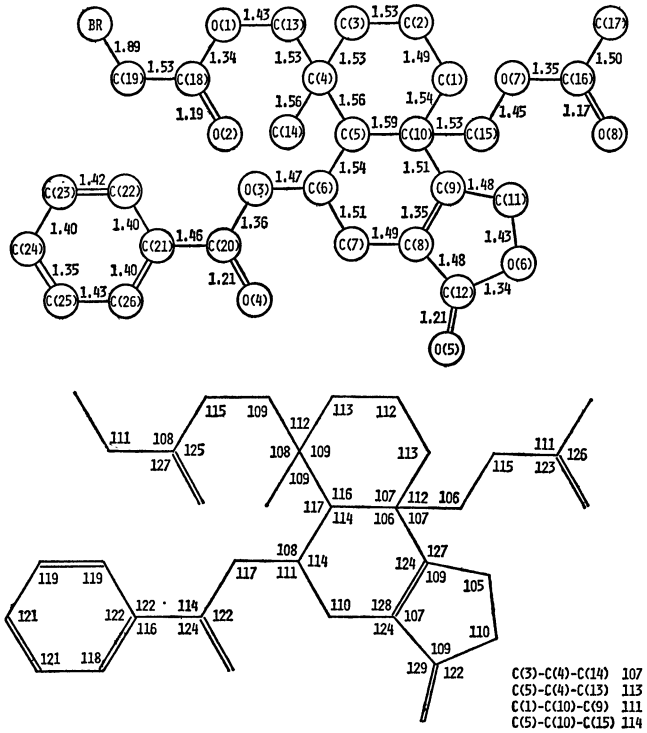

Fig. 2. Bond lengths (l/Å) and angles (φ/°) for non-hydrogen atoms. The mean estimated standard deviation of bond lengths is 0.012 Å, and that of bond angles is 0.7°.

The present analysis has established the three-dimentional structure and the absolute configuration of the bromo-derivative of parasiticolide A. A stereoscopic view of the molecule is shown in Fig. 1, which is drawn with the correct absolute configuration. The bond lengths and angles for non-hydrogen atoms are given in Fig. 2. Two six-membered rings are joined through two equatorial-type bonds. The two acetoxymethyl groups and one benzoyloxy group show a 1,3-diaxial relationship. As a consequence, the bond angles, C(4)–C(5)–C(6), C(4)–C(5)–C(10), C(6)–(5)–C(10), and C(5)–C(10)–C(15), may be widened from the regular tetrahedral angle to release these groups from crowding. The remaining bond lengths and angles seem to be normal for the respective bond types. The details of the stereochemistry of parasiticolide A itself will be published later.

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