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Crystal Structure of Fukinolidol Di-Bromoacetate

Chuji KATAYAMA,*1 Akio FURUSAKI, Isamu NITTA, Mitsuo HAYASHI*2 and Keizo NAYA

Faculty of Science, Kwansei Gakuin University, Nishinomiya

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Fukinolidol di-bromoacetate, $C_{19}H_{24}O_6Br_2$, is a derivative of the new sesquiterpenoids isolated from the flower stalks of wild butterburs. The crystal of this derivative is monoclinic, with two molecules in a unit cell with dimensions of $a=17.13$, $b=8.21$, $c=7.59$ Å, and $\beta=98.8°$, and with the space group $P2_1$. The structure was elucidated by the heavy-atom method, and the absolute configuration was determined by the application of the anomalous dispersion effect of bromine. The atomic parameters were refined by the least-squares method, using a block-diagonal approximation. The structure thus obtained is the same as that shown by the organic chemical investigation which was carried out parallel with the present X-ray analysis. The molecule has a novel bicyclononane structure with a *cis*-fused system of a five-membered and a six-membered ring; it also has a spiro γ-lactone ring connected to the former ring. The lactone ring is almost planar, and the other five-membered ring takes a typical envelope conformation, while the six-membered ring is of the chair form.

Three new sesquiterpenoids, named fukinolide, fukinanolide, and S-fukinolide, were isolated from the flower stalks of wild butterburs, *Petasites japonicus* Maxim (Japanese name, "Fuki").[1] By alkaline hydrolysis, these substances were then converted to fukinolidol, $C_{15}H_{22}O_4$, mp 177—178°C. In order to elucidate the molecular structure of this compound, including the absolute configuration, an X-ray analysis of its di-bromoacetate derivative was carried out in company with the organic chemical investigation.

Experimental

Fukinolidol di-bromoacetate, $C_{19}H_{24}O_6Br_2$, mp 156—158°C was prepared by the bromoacetylation of fukinolidol with monobromoacetyl bromide under reflux in benzene. This substance is easily soluble in ethyl acetate, but is nearly insoluble in ethanol and in petroleum benzine. Single crystals of a prism shape were obtained from an ethyl acetate - petroleum benzine solution by slow evaporation at room temperature, while those of a crescent shape were obtained from an ethyl acetate - ethanol solution in the same way. A preliminary experiment showed that these two types of crystals gave the same X-ray diffraction pattern. The former crystal elongates along the direction of the b axis, and the latter, along the c axis, as is shown in Fig. 1; all these crystals are monoclinic with the following cell dimensions; $a=17.13\pm0.02$, $b=8.21\pm0.01$, $c=7.59\pm0.01$Å, and $\beta=98.8\pm0.5°$. The space group was uniquely determined to be $P2_1$ from the systematic absence of the reflections. The density observed by the floatation method is 1.61g·cm^{-3}, while that calculated assuming two molecules in the unit cell is 1.607 g·cm^{-3}.

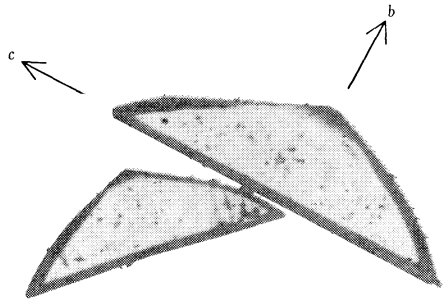


Fig. 1. The crescent shape crystals obtained from an ethyl acetate - ethanol solution.

For the purpose of collecting the intensity data, integrating Weissenberg photographs around the b and c axes were taken with nickel-filtered Cu$K\alpha$ radiation for k values from 0 to 6 and for l values from 0 to 5. The intensities were measured by visual comparison with a standard intensity scale; these values ranged between 1 and 6×10^3. The correction for Lorentz and polarization factor was made in the usual way. The relative values of the observed structure factors of 1678 reflections thus obtained were converted into an absolute scale by Wilson's method.

*1 Present address: Faculty of Science, Nagoya University, Nagoya.

*2 Present address: Research Institute, Toyo Jozo Co., Ltd., Ohito, Tagata, Shizuoka.

1) K. Naya, I. Takagi, M. Hayashi, S. Nakamura, M. Kobayashi and S. Katsumura, *Chem. & Ind.* (London), **1968**, 318.

Structure Determination

The positions of the two bromine atoms were derived from a three-dimensional Patterson function. For the elucidation of the positions of the light atoms, a Fourier synthesis by means of Sim's modified heavy-atom method[2] was carried out. The resulting map revealed that the main frame of the present molecule involves a bicyclic system of a five-membered and a six-membered ring. Besides these twenty-one light atoms, the positions of the remaining four were obtained from the second Fourier map; the R-factor was 0.32. At this stage, as a structure test, the least-squares method was performed assuming the atomic scattering factor of the carbon atom to holds for all the light atoms. After three cycles, the R-factor dropped to 0.25. Since the temperature factors of five atoms converged into values which were smaller than those of the others, these were identified as oxygen atoms. The four atoms which had been formerly regarded as an acetoxy group attached to the six-membered ring turned out to be false peaks, because their temperature factors inclined to diverge. In this way, the positions of five oxygen atoms and sixteen carbon atoms were confirmed, and the reliable positions of the acetoxy group were elucidated from another Fourier synthesis. The structure thus obtained was refined by a block-diagonal least-squares method. After three cycles of refinement using isotropic temperature factors for all the atoms, the R-factor decreased to 0.15. Three more cycles of the final refinement were carried out with anisotropic temperature factors for bromine atoms and isotropic for light atoms. Thus, the final R-factor reached a value of 0.13. The tables of the observed and calculated structure factors are kept by the Chemical Society of Japan.*3

Absolute Configuration

By applying the effect of the anomalous dispersion of bromine, the absolute configuration of the present molecule was determined. The Bijvoet inequalities for twenty pairs of $I(hkl)$ and $I(h\bar{k}\bar{l})$ were observed visually from the Weissenberg photographs around the c axis indexed on the right-handed system. On the other hand, these twenty pairs of structure factors were calculated by including the imaginary part of the anomalous dispersion correction of the scattering factor of bromine for Cu$K\alpha$ radiation ($\Delta f''=1.4$). These observed and calculated inequalities are listed in Table 1. It may be seen that the atomic coordinates correspond to the expression by the left-

Table 1. Bijvoet inequalities

h	k	l	$\lvert F_c(hkl)\rvert$	$\lvert F_c(h\bar{k}\bar{l})\rvert$	$\frac{\lvert F_c(hkl)\rvert^2}{\lvert F_c(h\bar{k}\bar{l})\rvert^2}$	$\frac{I_o(hkl)}{I_o(h\bar{k}\bar{l})}$
7	1	0	23.58	24.91	0.90	>1
13	1	0	2.12	0.79	7.24	<1
−14	1	1	15.23	16.47	0.86	>1
−8	1	1	15.86	15.02	1.11	<1
−8	2	1	16.74	19.14	0.76	>1
6	2	1	5.68	8.50	0.45	>1
7	2	1	22.25	20.67	1.16	<1
9	2	1	20.42	21.90	0.87	>1
12	4	1	6.18	7.25	0.71	>1
15	3	1	6.60	7.27	0.82	>1
17	3	1	1.10	0.44	6.37	>1
−3	2	2	13.94	11.30	1.52	<1
−12	3	2	14.18	12.95	1.20	<1
−20	1	3	5.55	5.28	1.11	<1
−9	2	3	8.35	10.35	0.65	>1
−10	1	4	13.32	11.82	1.27	<1
−5	1	4	19.81	18.16	1.19	<1
−12	2	4	14.94	16.53	0.82	>1
−5	1	5	11.82	11.23	1.11	<1
−14	1	5	8.05	8.60	0.88	>1

2) G. A. Sim, *Acta Cryst.*, **12**, 813 (1959).

*3 The complete data of the F_o–F_c table are kept as Document No. 7003 at the office of the Bulletin of the Chemical Society of Japan. A copy may be secured by citing the document number and by remitting, in advance, ¥ 500 for photoprints. Payment may be made by check or money order payable to: Chemical Society of Japan.

TABLE 2. FINAL ATOMIC PARAMETERS

Atom	x/a	y/b	z/c	B	Atom	x/a	y/b	z/c	B
Br(1)	0.2246	0.9200	0.6701	*	C(7)	0.1951	0.2794	0.1282	3.51
Br(2)	−0.0146	0.5032	0.4401	*	C(8)	0.1473	0.4243	0.0420	3.90
O(1)	0.0734	0.3792	0.0030	4.72	C(9)	0.2259	0.3282	0.3333	3.08
O(2)	0.1703	0.5527	0.0026	4.70	C(10)	0.3040	0.4065	0.3317	3.77
O(3)	0.3170	0.5285	0.6258	4.30	C(11)	0.1376	0.1495	0.1201	4.92
O(4)	0.3807	0.7438	0.5679	7.29	C(12)	0.0569	0.2319	0.0559	6.83
O(5)	0.1704	0.4431	0.3907	3.60	C(13)	0.1497	−0.0096	0.1363	7.19
O(6)	0.1647	0.3035	0.6491	4.35	C(14)	0.4171	0.0185	0.1808	6.07
C(1)	0.3589	0.4268	0.5050	3.98	C(15)	0.4134	0.3852	0.1251	4.78
C(2)	0.3834	0.2725	0.6028	6.82	C(16)	0.3320	0.6697	0.6524	4.79
C(3)	0.4275	0.1552	0.4752	4.28	C(17)	0.2889	0.7586	0.8025	6.03
C(4)	0.3707	0.1335	0.3029	4.84	C(18)	0.1417	0.4074	0.5400	3.72
C(5)	0.3443	0.2885	0.2120	3.61	C(19)	0.0835	0.5444	0.5741	4.58
C(6)	0.2755	0.2584	0.0472	3.89					

* Anisotropic temperature factors in form of $\exp(-B_{11}h^2-B_{22}k^2-B_{33}l^2-B_{12}hk-B_{23}kl-B_{31}lh)$.

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{23}	B_{31}
Br(1)	0.00632	0.02625	0.03708	−0.00481	−0.00790	0.01023
Br(2)	0.00404	0.03287	0.04376	−0.00447	0.01348	−0.00164

TABLE 3. BOND LENGTHS AND ANGLES

Bond lengths (Å)		Bond angles (°)			
C(1) -C(2)	1.49	C(2) -C(1) -C(10)	115	C(5) -C(10)-C(9)	101
-C(10)	1.50	C(2) -C(1) -O(3)	108	C(7) -C(11)-C(12)	105
-O(3)	1.47	C(10)-C(1) -O(3)	107	C(7) -C(11)-C(13)	129
C(2) -C(3)	1.60	C(1) -C(2) -C(3)	110	C(12)-C(11)-C(13)	126
C(3) -C(4)	1.51	C(2) -C(3) -C(4)	107	C(11)-C(12)-O(1)	107
C(4) -C(5)	1.48	C(3) -C(4) -C(5)	114	C(17)-C(16)-O(3)	117
-C(14)	1.59	C(3) -C(4) -C(14)	105	C(17)-C(16)-O(4)	121
C(5) -C(6)	1.59	C(5) -C(4) -C(14)	113	O(3) -C(16)-O(4)	122
-C(10)	1.53	C(4) -C(5) -C(6)	111	C(16)-C(17)-Br(1)	104
-C(15)	1.61	C(4) -C(5) -C(10)	114	C(19)-C(18)-O(5)	107
C(6) -C(7)	1.56	C(4) -C(5) -C(15)	115	C(19)-C(18)-O(6)	124
C(7) -C(8)	1.53	C(6) -C(5) -C(10)	102	O(5) -C(18)-O(6)	128
-C(9)	1.60	C(6) -C(5) -C(15)	105	C(18)-C(19)-Br(2)	109
-C(11)	1.43	C(10)-C(5) -C(15)	109	C(8) -O(1) -C(12)	116
C(8) -O(1)	1.29	C(5) -C(6) -C(7)	105	C(1) -O(3) -C(16)	123
-O(2)	1.17	C(6) -C(7) -C(8)	111	C(9) -O(5) -C(18)	116
C(9) -C(10)	1.46	C(6) -C(7) -C(9)	102		
-O(5)	1.43	C(6) -C(7) -C(11)	121		
C(11)-C(12)	1.54	C(8) -C(7) -C(9)	107		
-C(13)	1.32	C(8) -C(7) -C(11)	104		
C(12)-O(1)	1.31	C(9) -C(7) -C(11)	111		
C(16)-C(17)	1.59	C(7) -C(8) -O(1)	108		
-O(3)	1.19	C(7) -C(8) -O(2)	129		
-O(4)	1.25	O(1) -C(8) -O(2)	123		
C(17)-Br(1)	1.90	C(7) -C(9) -C(10)	106		
C(18)-C(19)	1.53	C(7) -C(9) -O(5)	108		
-O(5)	1.30	C(10)-C(9) -O(5)	110		
-O(6)	1.21	C(1) -C(10)-C(5)	108		
C(19)-Br(2)	1.85	C(1) -C(10)-C(9)	120		

handed system. At the same time, it was established that the positive direction of the *b* axis corresponds to the direction from chord to arc of the crescent-shape crystal, as is shown in Fig. 1. The final atomic parameters, transformed into the right-handed system, are listed in Table 2. Figure 2 shows a composite diagram of the (010) sections, taken as through the atomic centers of the molecule, of the final three-dimensional electron distribution.

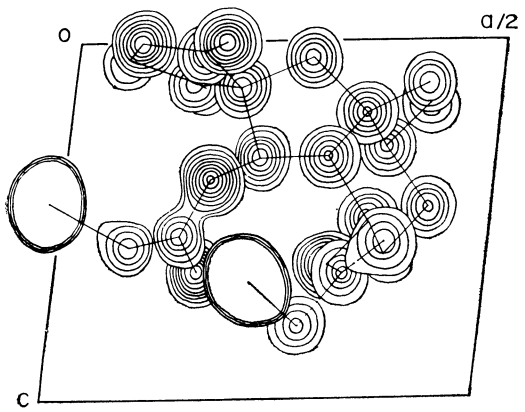


Fig. 2. The final electron distribution. Contours at 1 e.Å^{-3} beginning at 2 e.Å^{-3}.

Result and Discussion

The bond lengths and angles calculated with the final coordinates are listed in Table 3. The average estimated standard deviations of the coordinates are 0.004, 0.018, and 0.028 Å for bromine, oxygen, and carbon atoms respectively.

The molecular framework is shown in Fig. 3; the absolute configuration is taken into consideration. This is the same structure as that concluded by the organic chemical investigation. The molecule has a novel bicyclononane structure, with a

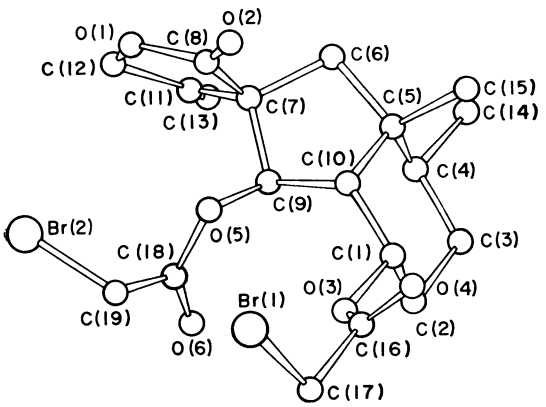
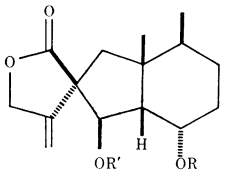


Fig. 3. The molecular framework, taking the absolute configuration into consideration.



R, R' = -C(=O)-CH$_2$·Br

cis-fused system of a five-membered and a six-membered ring; it also has a five-membered γ-lactone ring spiro-fused with the former ring. The lactone ring is almost planar, while the other five-membered ring takes a typical envelope conformation; the C(10) atom is remarkably displaced from the mean plane through the C(5), C(6), C(7), and C(9) atoms. The six-membered ring is a chair form, and the configurations of the C(14) and C(15) atoms are β and O(3) and C(9) atoms α. The O(5), C(8), and C(15) atoms are located on the same side of the five-membered ring. Both acetoxyl groups are almost planar, including C(1) or C(9), but the bromine atoms are considerably out of these planes. The C(16)–O(4) and C(18)–O(6) bonds are orientated nearly in the same direction as the C(1)–H and C(9)–H bonds respectively.

The molecular arrangements projected along the *b* and *c* axes are shown in Figs. 4 and 5 respectively. The intermolecular distances of less than 4.0 Å are all listed in Table 4. The molecules related by a 2_1-screw axis at $x=0$ and $z=1/2$ are linked together along the *b* axis by Br–Br contacts of 3.59 Å. This contact seems to be quite strong, since twice the ordinary Van der Waals radii of bromines are 3.90 Å. Such a short contact

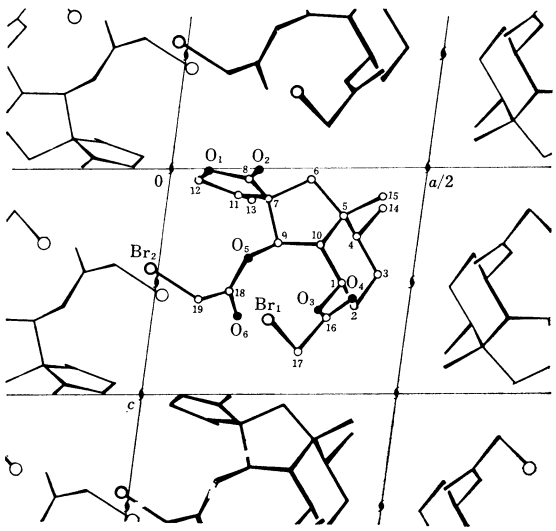


Fig. 4. The molecular arrangements along the *b* axis.

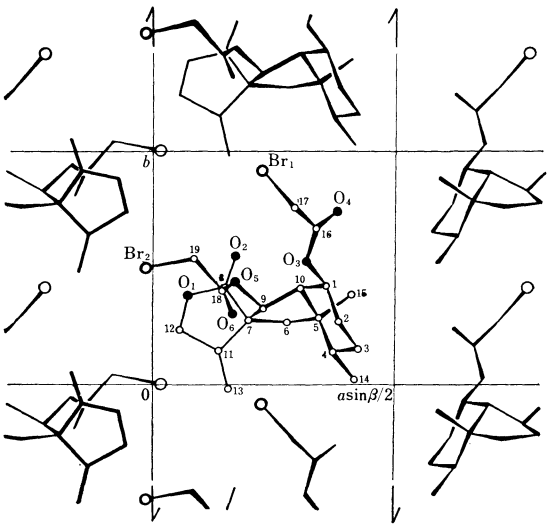


Fig. 5. The molecular arrangements along the *c* axis.

has also been found in the crystal of methyl bromide (3.57 Å).[3] The contacts along the *c* axis are concentrated between the C(8)–O(2) bond of the lactone group and the C(18)–O(6) bond of the acetyl group, related by the translation *c*. This contact seems to be caused by the dipole-dipole interaction between these polar bonds. As a whole, the contacts along the *a* axis are weak compared with those along the *b* and *c* axies.

In the early stages of the present analysis, it was not easy to elucidate the position of the acetyl group attached to the six-membered ring because of the large temperature factor of the group, especially that of the O(4) atom. In the final stages also, the temperature factor of the O(4) atom is about twice as large as those of the other oxygen atoms, and the O(3)–C(16) bond is considerably shorter than the normal bond length even if its estimated standard deviation is taken into consideration. In seeking to explain these facts, it may be considered that this acetyl group has some degree of freedom for the movement, since the group seems to be relatively free from the other part of the molecule and also from the other molecules, considering the interatomic contacts described above.

3) T. Hayafuji and Y. Tomiie, to be published.

TABLE 4. INTERMOLECULAR DISTANCES LESS THAN 4.0 Å

(i)···(ii)			(i)···(iv)		
O(6)	O(1)	3.28	O(4)	C(3)	3.55
	O(2)	3.33		C(4)	3.75
	C(6)	3.32		C(14)	3.77
	C(7)	3.55	O(2)	C(13)	3.75
	C(8)	3.14	Br(1)	O(6)	3.30
	C(11)	3.82			
	C(12)	3.78	(i)···(v)		
O(3)	O(2)	3.98	Br(1)	C(6)	3.96
	C(6)	3.98		C(13)	3.89
C(19)	O(1)	3.50	C(17)	C(14)	3.95
	O(2)	3.34			
	C(8)	3.65	(i)···(vi)		
C(18)	O(1)	3.79	Br(2)	O(6)	3.53
	O(2)	3.62		C(18)	3.96
	C(8)	3.74	Br(1)	Br(2)	3.59
C(2)	C(6)	3.98	C(19)	Br(2)	3.93
	C(15)	3.97			
C(17)	O(2)	3.14	(i)···(vii)		
			O(1)	C(12)	3.62
(i)···(iii)				C(13)	3.87
O(4)	C(3)	3.37			

Key for molecules

i: x, y, z
ii: $x, y, 1+z$
iii: $1-x, 1/2+y, 1-z$
iv: $x, 1+y, z$
v: $x, 1+y, 1+z$
vi: $-x, 1/2+y, 1-z$
vii: $-x, 1/2+y, -z$

All the numerical computations were done on the FACOM 270-20 of the Computing Center of Kwansei Gakuin University and/or the HITAC 5020E of the University of Tokyo.