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An X-Ray Determination of the Structure of Motiol Iodoacetate[*1]

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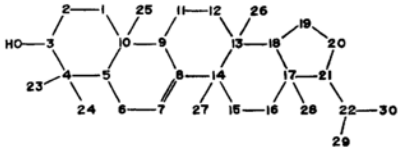
The molecular configuration of motiol has been determined by the X-ray crystal analysis. The crystal of motiol iodoacetate, $C_{32}H_{52}O_2I$, is monoclinic with two molecules in a unit cell of dimensions; $a=17.37$, $b=6.78$, $c=13.04$ Å and $\beta=99.6°$, the space group being $P2_1$. The crystal structure was solved by the heavy atom method. The atomic coordinates and anisotropic temperature factors were refined by block-diagonal matrix least-squares method. The structure determined is, in general, compatible with that derived chemically. The rings A and D are of a chair form, and the rings B and C are of a semi-chair. The molecule bends at the rings B and C to make a bow as a whole. All but one of the methyl groups are in axial junction.

In 1965 Nakamura, Yamada, Wada, Inoue, Goto and Hirata have determined the stuctures of motiol, $C_{30}H_{50}O$, and four related compounds.[1] These triterpene alcohols are obtained from a viscous substance of *Rhododendoron Linearifolium,* from which motiol itself has been isolated by Kariyone, Hashimoto and Tobinaga early in 1952.[2]



Before completing chemical studies, Professors Hirata and Goto of Nagoya University supplied us the crystals of motiol iodoacetate for an X-ray analysis. The present paper describes the three-dimensional structure determination of motiol iodoacetate.

Experimental

The crystals of motiol iodoacetate, $C_{32}H_{52}O_2I$, are colourless and of mica-like form. Cleavage is observed along the (001) plane.

Unit cell dimensions were obtained by the photographic method; the values of a and c were derived from the ($h0l$) Weissenberg photographs on which aluminum powder diffraction lines were superposed for calibration, while that of b was determined from the ($hk0$) and ($0kl$) precession photographs.

Equi-inclination Weissenberg photographs were taken up to the 5th layer along the b axis using multiple-film technique. With Cu$K\alpha$ radiation of 30 kV and 18 exposure time was about 70 hr for each layer. The size of crystal used was about $0.1\times0.3\times1.5$ mm. After X-ray exposure of about 200 hr the crystal was coloured brown and the shape of the diffraction spots became blurred foggy. Therefore, two crystals of about the same size were needed for collection of the complete intensity data.

Intensities of 2511 reflexions were measured by visual comparison with a standard intensity scale, the relative intensity being ranged between 23000 and 1. Some reflexions which were not accessible by the b axis Weissenberg photographs were supplemented from the precession photographs.

Corrections for Lorentz and polarization factors were made in the usual way, while that for absorption was neglected.

Crystallographic Data

Crystallographic and physical data obtained are: Motiol iodoacetate, $C_{32}H_{52}O_2I$. Monoclinic,

$$a=17.37\pm0.04,\ b=6.78\pm0.02,\ c=13.04\pm0.03\ \text{Å},$$

$$\beta=99.6\pm0.5°.$$

Volume of the unit cell, 1514.2 Å.

Systematic absence, ($0k0$) when k is odd. Space group, $P2_1$. Two molecules per unit cell. Density observed (by floatation), 1.32 g·cm^{-3}. Density calculated, 1.30 g·cm^{-3}. Total number of electrons per unit cell, $F(000)=626$. Linear abosrption coefficient for Cu$K\alpha$ radiation, $\mu=93.87$ cm^{-1}.

Structure Determination

Patterson projection on (010) showed clearly a peak corresponding to the iodine-iodine interaction, which gave the coordinates of the iodine as

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1) S. Nakamura, T. Yamada, H. Wada, Y. Inoue, T. Goto and Y. Hirata, *Tetrahedron Letters,* **24**, 2017 (1965).

2) T. Kariyone, Y. Hashimoto and S. Tobinaga, *Pharm. Bull.* (Japan), **5**, 367 (1957).

$x=-0.025$ and $z=0.195$. On the other hand, the y coordinate of the iodine may be assigned arbitrarily as -0.25 in this space group.

A Fourier synthesis was carried out using phases based on the coordinates of the iodine atom. It was very easy to find a general lay-out of the molecule from the resulting electron density distribution; in the section $y=0.25$ where the equivalent iodine atom appeared, there were twelve high peaks which built up major part of the rings A, D and E. The atoms in iodoacetyl group and those in the rings B and C were also recognized as resolved peaks, although there is a pseudo mirror plane at $y=0.25$. Therefore, it was possible to construct two models of the main skeleton; in one model iodoacetyl group and the rings B and C are on the same side of the pseudo mirror plane and in another they are on the opposite. In the former model, the conformation of the cyclohexane ring A is of a boat form, while in the latter it is of a chair.

Since chemical studies supported the latter model, we proceeded at first the refinement of the structure based on it. Even if the general conformation of the molecule had been selected, it was still difficult to decide to which side the y coordinates deviate from the mirror if the deviations are small. For such atoms we gave appropriate y coordinates by inspection. Fourier synthesis was evaluated with phases based on all the atoms. In the resulting electron density distribution, all the peaks corresponding to the light atoms showed very reasonable height and there were found only a few ghost peaks whose heights were not over a half of those of the carbon.

Three cycles of a least-squares refinement were carried out with isotropic temperature factors, initial B being 5.2 Å. The iodine atom was treated as anisotropic (two cycles) and then all the atoms were taken as anisotropic (two cycles). The R factor decreased to 0.177.

In these processes, the y coordinate of C(7) moved from 0.24 to 0.285 across the pseudo mirror plane, and that of C(6) decreased from 0.22 to 0.194 and then increased gradually. Their standard deviations were larger than those of the others. Since it seemed likely that the anomaly should be due to the mislocation of C(6), its y coordinate was changed artificially to be 0.28 across the pseudo mirror. Two cycles of the refinement were conducted so that the R factor dropped from 0.178 to 0.172 and the standard deviations of all the atoms did not differ to much extent.

It is known that the effect of anomalous dispersion of the iodine could not be neglected. Two enantiomorphous structures with the parameters at this stage were examined for 165 sampled reflections. Difference between these enantiomorphs was not quite definite, but one of them seemed to be more favourable. With this model, the least-squares refinement including anomalous dispersion effect was made (one cycle). It gave a slightly lower R factor of 0.169 ($R=0.148$ for non-zero reflexions) and better bond lengths.

Table 1. The final atomic coordinates

Atom	x	y	z
I	−0.0262	−0.2500	0.1848
C(1)	0.3167	0.2839	0.0688
C(2)	0.2219	0.2439	0.0516
C(3)	0.2056	0.1334	0.1368
C(4)	0.2220	0.2120	0.2462
C(5)	0.3172	0.2702	0.2596
C(6)	0.3509	0.3124	0.3700
C(7)	0.4444	0.2918	0.3890
C(8)	0.4740	0.3250	0.2916
C(9)	0.4401	0.3703	0.1978
C(10)	0.3446	0.3777	0.1754
C(11)	0.4744	0.4144	0.1025
C(12)	0.5696	0.4223	0.1239
C(13)	0.5965	0.2782	0.2096
C(14)	0.5697	0.3545	0.3130
C(15)	0.6112	0.2194	0.4063
C(16)	0.7021	0.2588	0.4249
C(17)	0.7342	0.1949	0.3250
C(18)	0.6910	0.3115	0.2348
C(19)	0.7363	0.2630	0.1419
C(20)	0.8252	0.2629	0.2011
C(21)	0.8187	0.2901	0.3203
C(22)	0.8956	0.1840	0.3937
C(23)	0.1784	0.4206	0.2670
C(24)	0.2102	0.0589	0.3250
C(25)	0.3238	0.5978	0.1757
C(26)	0.5748	0.0640	0.1808
C(27)	0.5799	0.5691	0.3320
C(28)	0.7415	−0.0188	0.3189
C(29)	0.8914	0.1950	0.5069
C(30)	0.9667	0.2491	0.3581
C(31)	0.0852	−0.0504	0.0719
C(32)	−0.0034	−0.1083	0.0668
O(1)	0.1154	0.1091	0.1216
O(2)	0.1205	−0.1888	0.0342

The final atomic coordinates and anisotropic temperature factors are listed in Tables 1 and 2 respectively. The composite diagram of the final electron density distribution viewed along the b axis is shown in Fig. 1.

Throughout the refinement process, 2051 reflexions with $\sin\theta/\lambda$ less than 0.550 were used and the atomic scattering factors were taken from the International Tables for X-ray Crystallography. Programme for the least-squares method was written by one of us (T. A.) with block-diagonal matrix approximation. The weights in the least-squares were 1.0 for $F_o>1.0$ and 0.5 for $F_o\leqslant 1.0$, and fudge factors were 0.7 for the scale and positional parameters and 0.5 for the thermal parameters.

TABLE 2. THE FINAL TEMPERATURE FACTORS
in the form of
$\exp\{-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{31}lh+B_{23}kl)\}$

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{31}	B_{23}
I	0.0043	0.0439	0.0128	−0.0019	0.0017	0.0065
C (1)	0.0029	0.0347	0.0085	0.0082	0.0008	0.0070
C (2)	0.0025	0.0490	0.0099	−0.0009	−0.0010	0.0024
C (3)	0.0009	0.0416	0.0107	0.0023	−0.0023	0.0013
C (4)	0.0026	0.0273	0.0079	0.0153	0.0026	0.0076
C (5)	0.0028	0.0284	0.0075	0.0064	0.0017	0.0030
C (6)	0.0029	0.1088	0.0074	−0.0045	−0.0005	−0.0158
C (7)	0.0029	0.0594	0.0065	0.0039	0.0015	0.0122
C (8)	0.0027	0.0266	0.0065	−0.0053	0.0017	−0.0018
C (9)	0.0036	0.0256	0.0062	−0.0018	0.0004	0.0043
C (10)	0.0033	0.0166	0.0071	0.0029	0.0000	0.0034
C (11)	0.0034	0.0435	0.0097	−0.0010	0.0005	0.0113
C (12)	0.0023	0.0400	0.0082	−0.0013	−0.0013	0.0139
C (13)	0.0029	0.0555	0.0076	−0.0211	0.0013	−0.0169
C (14)	0.0029	0.0282	0.0071	−0.0062	0.0017	−0.0091
C (15)	0.0040	0.0330	0.0065	−0.0052	0.0004	0.0125
C (16)	0.0028	0.0546	0.0067	−0.0101	0.0009	−0.0064
C (17)	0.0045	0.0152	0.0086	−0.0048	0.0010	0.0077
C (18)	0.0026	0.0314	0.0059	−0.0072	0.0006	0.0093
C (19)	0.0029	0.0790	0.0088	−0.0197	0.0022	−0.0023
C (20)	0.0028	0.0552	0.0101	0.0015	0.0018	0.0155
C (21)	0.0021	0.0238	0.0096	−0.0005	0.0005	0.0056
C (22)	0.0026	0.0503	0.0097	−0.0032	−0.0010	−0.0020
C (23)	0.0030	0.0328	0.0128	−0.0010	0.0021	−0.0087
C (24)	0.0027	0.0407	0.0114	0.0000	−0.0005	0.0055
C (25)	0.0044	0.0668	0.0170	0.0100	0.0004	0.0019
C (26)	0.0039	0.0389	0.0130	−0.0068	0.0023	−0.0144
C (27)	0.0038	0.0356	0.0149	0.0018	−0.0015	−0.0065
C (28)	0.0030	0.0306	0.0188	0.0025	0.0002	0.0088
C (29)	0.0027	0.0717	0.0114	0.0125	0.0018	0.0123
C (30)	0.0034	0.0648	0.0153	−0.0057	0.0030	−0.0247
C (31)	0.0057	0.0200	0.0067	−0.0034	0.0001	−0.0000
C (32)	0.0015	0.1243	0.0110	0.0337	−0.0022	0.0151
O (1)	0.0038	0.0342	0.0119	0.0090	−0.0008	−0.0037
O (2)	0.0032	0.0411	0.0137	−0.0014	0.0009	−0.0206

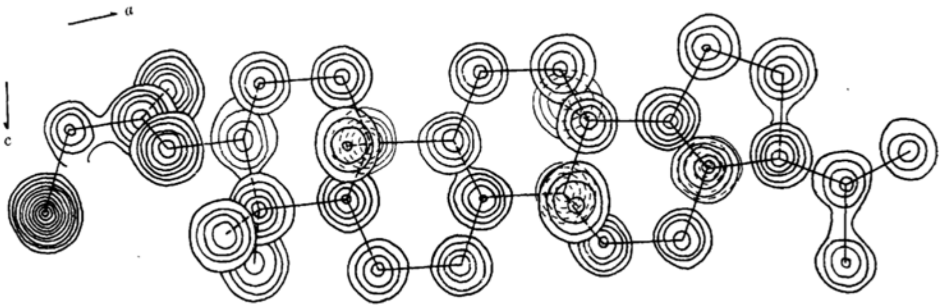

Fig. 1. A composite drawing of the final electron distribution viewed along the *b* axis.
For carbon and oxygen atoms, contours are drawn at intervals of 1 e.Å^{-3}, beginning with 1 e.Å^{-3}.
For iodine atom, contours are drawn at intervals of 5 e.Å^{-3}, beginning with 5 e.Å^{-3}.

Examination of the Alternative Structure

From the crystallographic point of view, the other model in which the ring A has a boat form was also possible as stated in the previous paragraph. This alternative model was subjected to the Fourier and least-squares refinement. Several abnormal figures were obtained in the course of refinement; for example, the bond length C(18)–C(19) became too longe, 1.99 Å, C(19)–C(20)rem arkably short, 1.19 Å and the isotropic temperature factor of C(19) was very large, 16.4 Å². The *R* factor did not go down less than 0.227. Therefore, it was concluded that this structure is not correct.

Some Remarks on Reliability of the Analysis

As mentioned in the previous paragraph, we changed artificially the *y* coordinate of C(6) at a certain stage. It may be of some interest whether this atom moves to the correct position in the other side of the pseudo mirror plane by continuing the least-squares process. We examined this, and found that it needed eight cycles to get the final result from the stage just before the artificial change. One of the reasons why the rate of convergence is so slow is that almost all the atoms in the principal skeleton of the molecule lie near the special plane and that since intensity data were collected from Weissenberg photographs about the *b* axis only the largest *k* reached to about a half of the possible maximum *k* within the copper sphere.

This crystal analysis met another serious difficulty. The crystal sufferred heavy degradation during the X-ray exposure. It was naturally supposed that reflexions on each layer might correspond to different stages of degradation. To examine this possibility the parameters except those related to the *y* direction were refined by the least-squares using several sets of the intensity data which were sampled from the individual layers. Intensity data of (*h*0*l*) and (*h*3*l*) were supposed to be those of rather fresh crystal. Corresponding bond lengths derived from the refinement of each layer are in good agreement, considering the fact that limited number of data makes standard deviations large; mean deviation being 0.054 Å and the maximum 0.17 Å. On the other hand (*h*2*l*) and (*h*5*l*) were taken from the heavily sufferred crystal. Corresponding lengths from these layer data fluctuated to much extent; mean deviation being 0.17 Å and the maximum 0.48 Å. Difference in bond lengths between the new and damaged crystals averages 0.08 Å. Therefore, it may be concluded that the error of the bond lengths due to such a systematic error in intensity data is about 0.1 Å, which is of about the same magnitude as the standard deviation derived formally from the least-squares calculation.

Description of the Structure and Discussion

The structure determined here is compatible, in general, with that derived from chemical studies. The rings A and D have a chair form. Owing to the existence of the double bond, the rings B and C have a half-chair form. All the neighboring rings are trans-fused. The molecule bends at the rings B and C, so that it is bow as a whole. Configurations of O(1) and seven methyl groups (C(22) to C(28)) are also in agreement with chemical argument. Figure 2 shows the perpendicular displacements of the atoms from the mean plane of each ring.

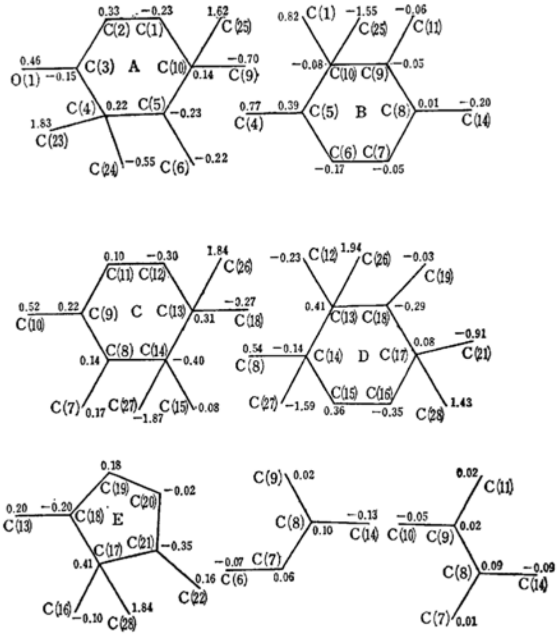

Fig. 2. The deviations of the atoms from the mean plane of each ring.

The bond lengths and angles are given in Fig. 3. Several interesting features are observed in the molecular dimensions, although their physical significance could not be insisted from the view of rather large errors.

(1) While the average bond length of all the C–C is 1.56 Å, the average of C–C bonds which are nearly parallel to the *a* axis is 1.62 Å. As the long axis of the molecule lies in the direction nearly parallel to the *a* axis, this elongation of the C–C may be interpreted as a result of long range intramolecular steric hindrance. The related non-bonded intramolecular distances are listed in Table 3.

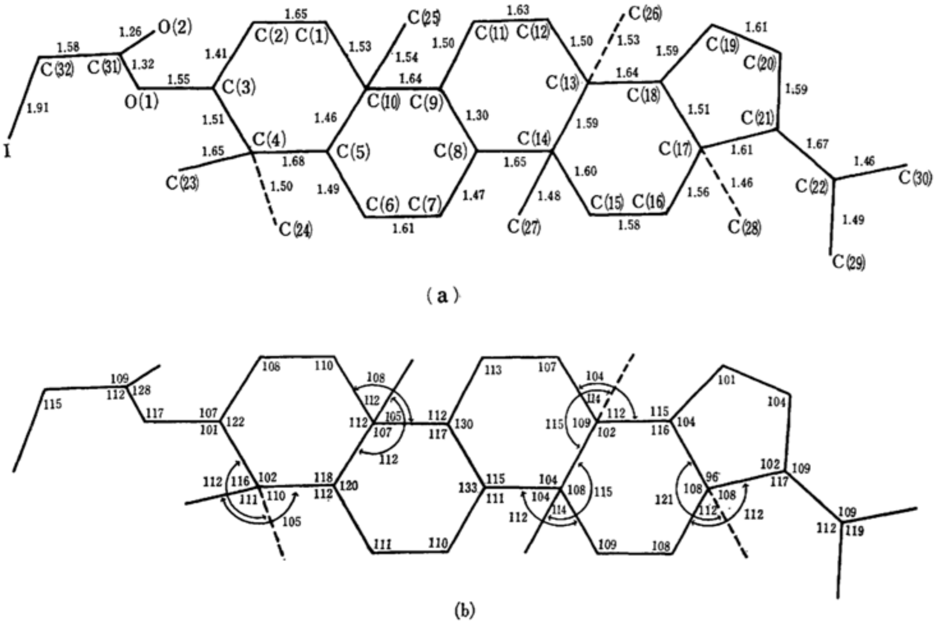

Fig. 3. (a) Bond lengths (Å) and (b) bond angles (°) in the molecule of motiol iodoacetate.

TABLE 3. NON-BONDED DISTANCES IN THE MOLECULE (Å)

C(1) -C(11)	2.84	C(27)-C(12)	2.87
C(23)-C(6)	3.16	C(27)-C(16)	3.09
C(23)-C(25)	3.20	C(27)-C(18)	3.03
C(24)-C(6)	2.97	C(28)-C(15)	3.15
C(25)-C(11)	3.18	C(28)-C(19)	2.99
C(26)-C(8)	3.02	C(28)-C(20)	2.98
C(26)-C(9)	3.16	C(28)-C(22)	3.02
C(26)-C(28)	3.20	C(30)-C(20)	2.93
C(27)-C(7)	3.20		

TABLE 4. INTERMOLECULAR DISTANCES (≤ 4.0Å)

From atom at x, y, z	To atom	In molecule	Distance (Å)
C(6)	C(15)	I	3.99
C(16)	C(24)	I	3.93
C(23)	C(29)	I	3.85
C(29)	C(24)	I	3.91
C(11)	C(26)	II	3.79
C(19)	O(2)	II	3.67
C(20)	O(2)	II	3.37
C(25)	O(2)	III	3.97
C(27)	C(26)	III	3.89
C(27)	C(28)	III	3.99
C(2)	C(32)	IV	3.98
C(31)	C(32)	IV	3.66
C(31)	I	IV	3.91
C(32)	C(32)	IV	3.82
C(32)	C(2)	IV	3.62
O(1)	C(32)	IV	3.45

Molecule	I	$1-x$,	$\frac{1}{2}+y$,	$1-z$
	II	$1-x$,	$\frac{1}{2}+y$,	$-z$
	III	x,	$1+y$,	z
	IV	$-x$,	$\frac{1}{2}+y$,	$-z$

(2) Chemical studies assigned C(7)–C(8) as a double bond. In the present analysis, the average deviation from the mean plane consisting of C(6), C(7), C(8), C(9) and C(14) is 0.079 Å, while that of the mean plane of C(7), C(8), C(9), C(10), C(11) and C(14) is 0.057 Å (Fig. 2). The difference might not be significant, however, C(7)–C(8) is 1.47 Å, while C(8)–C(9) is 1.30 Å. From these figures, it seems likely that the double bond is C(8)–C(9). According to Hirata, there is a possibility of the transfer of the double bond of C(7)–C(8) to C(8)–C(9) at the reaction of iodoacetylation of motiol.[5] If C(8)–C(9) is the double bond, the compound may be called as iso-motiol iodoacetate.

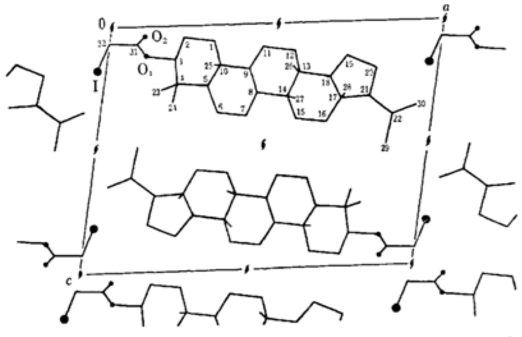

Fig. 4. Arrangement of molecules in the crystal viewed along the b axis.

(3) There are observed very similar aspects of

molecular structures to those in the related compounds such as epilimonol iodoacetate³⁾ and methyl melaleucate iodoacetate.⁴⁾

The arrangement of the molecules in the crystal is shown in Fig. 4. All the intermolecular distances shorter than 4.0 Å are listed in Table 4, which are equal or longer than the normal van der Waals contacts.

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3) S. Arnott, A. W. Davie, J. M. Robertson, G. A. Sim and D. G. Watson, *J. Chem. Soc.*, **1961**, 4183.

4) S. R. Hall and E. N. Maslen, *Acta Cryst.*, **18**, 265 (1965).

5) Y. Hirata, private communication (1967).