

served to vary slightly but to follow a pattern similar to that of normal nonobese mice.

Brain tissue residues of glucose-1-C-14 vary considerably in the gold thioglucose obese and normal nonobese mice, and the observed values support the glucostatic theory of the food intake regulation.

The administration of selected anorectics to normal nonobese mice caused a significant increase in hypothalamic glucose uptake. This effect is possibly involved in the mechanism of food intake inhibition.

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Crystal and Molecular Structure of 1,3-Dihydro-1-hydroxy-3-oxo-1,2-benziodoxole

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The crystal and molecular structure of 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole (I) has been determined by X-ray crystallographic methods. The compound crystallizes as monoclinic needles, in the space group $P2_1/c$ with four molecules in a unit cell of dimensions $a_0 = 12.89$, $b_0 = 4.10$, $c_0 = 14.05$ Å, and $\beta = 96.73^\circ$. The geometry observed around the iodine atom appears to be trigonal bipyramidal. The 11 atoms composing the molecule were found to be coplanar. The C(1)-I, O(3)-I, and O(2)-I bond distances are 2.16 ± 0.05 Å, 2.00 ± 0.05 Å, and 2.30 ± 0.05 Å, respectively, confirming the heterocyclic nature of I. An abnormally short intermolecular I-O distance at 2.90 Å suggests that the iodine may be acting as a Lewis acid.

o-IODOSOBENZOIC ACID (I) has been recognized as an atypical compound ever since it was first synthesized (1). Askenasy and Meyer (2)

suggested that this compound existed as a 5-membered heterocyclic ring, I rather than II. This cyclic configuration was substantiated by the carbonyl shift in the infrared (3). Further evidence favoring the heterocyclic ring structure was offered by Wolf and Hsu (4), who synthesized

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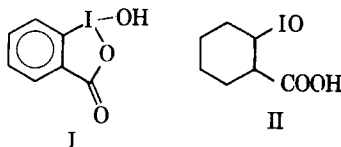
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homologs of I with 6- and 7-membered heterocyclic rings and measured their ionization constants. These pK_a determinations also favored I as the actual structure of this molecule. While there is substantial evidence for I, there is still a lack of information concerning the intramolecular bonding of iodine in these heterocyclic compounds; the present X-ray study of I was undertaken to elucidate this bonding.

EXPERIMENTAL

The compound, obtained by the method of Askenasy (2) as modified by Wolf and Hsu (4), crystallizes from water as fine monoclinic needles, elongated along b . A crystal was mounted about b , and oscillation, Weissenberg, and precession photographs were taken with Ni-filtered $CuK\alpha$ radiation. The unit cell parameters were determined from the zero-layer Weissenberg photograph and an oscillation photograph, the camera radius calibrated with a quartz crystal ($a_0 = 4.9131 \text{ \AA}$, assumed). The cell dimensions are: $a_0 = 12.89 \pm 0.01$, $b_0 = 4.10 \pm 0.01$, $c_0 = 14.05 \pm 0.01 \text{ \AA}$, and $\beta = 96.73 \pm 0.05^\circ$.

The only systematic extinctions noted were those for hOl with l odd, and OkO with k odd, hence requiring the space group to be $P2_1/c$. The density, measured in a mixture of chloroform and bromoform, was found to be $2.3 \pm 0.05 \text{ Gm./cm.}^3$, which is in accord with the value of 2.38 Gm./cm.^3 calculated for four molecules in the unit cell.

Three layers of Weissenberg photographs were used for intensity data. The intensities of 520 independent reflections were measured since it was felt that this amount was sufficient to obtain the essential geometry of the molecule. These data were measured in part with a Baird-Atomic microdensitometer (model CB) and in part visually. Those reflections too weak to be measured on the hOl film were included in the last few cycles of least squares refinement (5) with $F_o = 0.5 \times F_{\text{min}}$. The intensity data were converted to F^2 by applying the usual Lorentz-polarization corrections. Absorption corrections were not made because the crystal was only 0.06 mm. in diameter, and no corrections were made for spot shape. The structure factors were initially scaled together by means of hkO and OkI precession data, and the interlayer scaling was further improved during the final stages of least-squares refinement by comparing the calculated and observed structure factors.

Determination and Refinement of the Structure.—The coordinates of the iodine atom were obtained readily from a three dimensional Patterson synthesis. The position of the 10 light atoms was located from a Fourier synthesis phased on the iodine atom. The refinement of these parameters was carried out isotropically by least squares; the function $\sum w(|F_o| - G|F_c|)^2$ was minimized, where G is the scale factor for the calculated structure factors. The least-squares program of Sparks *et al.* (ACA No. 317) was used for this purpose. The R value ($= \sum (|F_o| - |F_c|)/|F_o|$) was 13.7% after 6 cycles of least-squares refinement. Since the parameters shifts in the last cycle were smaller than their estimated standard deviations (e.s.d.), refinement was completed.

The atomic form factors used for oxygen and carbon in all the calculations are those of McWeeny (6).

TABLE I.—POSITIONAL AND THERMAL PARAMETERS OBTAINED FROM LEAST SQUARES

Atom	x	y	z	B^a
I	0.0890	1.1305	0.1492	1.5
C(1)	0.236	0.894	0.135	0.5
C(2)	0.267	1.010	0.051	2.1
C(3)	0.368	0.838	0.032	2.0
C(4)	0.429	0.750	0.106	3.1
C(5)	0.391	0.634	0.195	4.8
C(6)	0.294	0.760	0.212	2.6
C(7)	0.201	1.145	-0.024	1.8
O(1)	0.235	1.196	-0.108	3.7
O(2)	0.119	1.265	-0.004	2.5
O(3)	0.091	0.926	0.279	2.9

^a Isotropic temperature factors.

The scattering factors used for iodine are those calculated by Thomas and Umeda (7) and these were further corrected for anomalous dispersion (8). All the computations were performed on an IBM 7094 digital computer, made available to us by the U.C.L.A. computing facility.

The positional parameters of the atoms obtained from the least squares are given in Table I. The observed (F_o) and the calculated (F_c) values of the structure factors are given in Table II.

RESULTS AND DISCUSSION

The e.s.d.'s are approximately 0.01 \AA . for the bonds between the light atoms and 8° for the angles between these atoms. The standard deviation for the bonds and angles involving the iodine atom are about half this size. The moderately large deviations for the light atoms are due partly to the presence of the iodine atom, which dominates the scattering of the X-rays, and partly to the incompleteness of the three-dimensional data. (Only 35% of the $CuK\alpha$ sphere was measured.)

Figure 1 shows the intramolecular bond angles and distances for I. The bond angles and distances of the benzoate framework of this compound agree within the 95% confidence level, *i.e.*, twice the e.s.d., with the results found for benzamide (9), salicylic acid (10), benzoic acid (11), and *o*-chlorobenzoic acid (12).

The C(1)-I and O(3)-I bond lengths are in agreement with the sums of their respective covalent radii. These sums are 2.10 \AA . for a C-I single bond and 1.99 \AA . for an I-O single bond (13). The O(2)-I length of 2.30 \AA . is significantly longer than the value predicted from covalent radii. The greater distance observed in this bond possibly may be due to the steric strain in the molecule and/or a greater amount of ionic character in this bond over the normal covalent one.

The configuration of the compounds of the type RIX_2 , where X is a halogen, was predicted (14) to have a trigonal bipyramid arrangement around the iodine atom, *i.e.*, with the halogen atoms at the apices and the three equatorial positions occupied by the R group and the two unshared electron pairs. This arrangement results from the sp^3d hybridization of the iodine orbitals. The structural determination of iodobenzene dichloride (15) had this predicted geometry. This arrangement is also found in the interhalogen compounds ClF_3 (16) and BrF_3 (17). The present structure also appears to have trigonal bipyramid geometry around the iodine, with O(2) and O(3) in the apical positions.

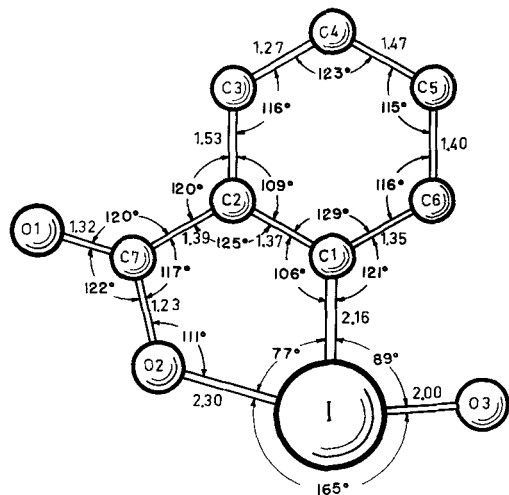


Fig. 1.—Intramolecular distances and angles of I.

The C(1)-I-O(2) and C(1)-I-O(3) angles are 77 and 89°, respectively. These are in accord with those found in the above trivalent halogen compounds, where the corresponding angles were slightly less than 90°. The deviations from 90° observed for these compounds have been explained (18) by the large repulsion between the lone pairs and bonding pairs of electrons. This repulsion may account for the deviation from 90° also observed in the present structure. In addition to this repulsion, the O(2)-I-C(1) angle is further reduced by the strain in the heterocyclic ring of the molecule.

A least-squares plane was calculated through the 11 atoms of the molecule in a manner similar to that described by Schomaker *et al.* (19). The 11 atoms composing the molecule appear to be coplanar since they are within twice the root-mean-square deviation of the L.S. plane (R.S.D. = 0.11 Å.). The equation for the plane is

$$0.365 X + 0.865 Y + 0.345 Z - 4.955 = 0$$

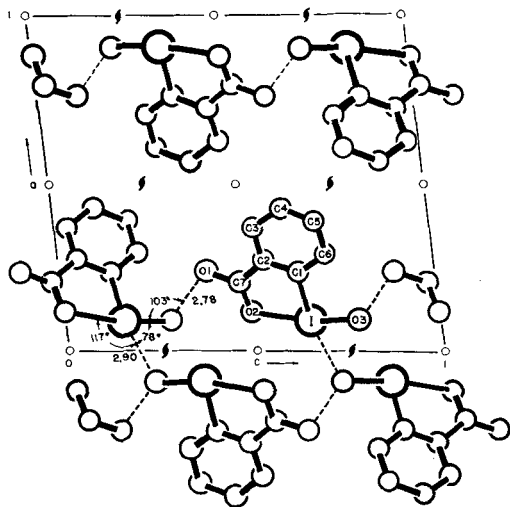


Fig. 2.—Arrangement of the molecules viewed down the *b* axis. The dark lines outline the unit cell.

where *X*, *Y*, and *Z* are in Ångstroms measured along the direct axes. In iodobenzene dichloride, the phenyl ring is perpendicular to the Cl-I-Cl line rather than coplanar with this line.

In a consideration of the angles and distances around the O(3) atom, it appears that it is donating its hydrogen to O(1) of a neighboring molecule. Figure 2 shows this bonding as the dashed line between O(1) and O(3). The hydrogen bond distance of 2.77 Å. is in accord with previously reported O—H...O=C bonds (20).

The intermolecular contact between the iodine of one molecule and O(3) of another molecule related to the first by the screw axis is 2.90 Å. (See Fig. 2.) This distance is significantly less than the sum of the van der Waals radii of the two atoms, which is 3.6 Å. This O(3) atom is 0.6 Å. above the least-squares plane of the first molecule. This type of interaction has been observed in various crystalline iodate structures (21). Trueblood (22) has suggested that this may be another reflection of the tendency of the iodine atom to act as a weak Lewis acid, manifested in many polyiodides and other complexes.

The donation of a normally unshared electron pair at the oxygen appears to give a pseudooctahedral electronic configuration around the iodine in this crystal. The high melting point of the compound (m.p. 240–250°) apparently seems to reflect the strong intermolecular bonding.

Besides the intermolecular contacts discussed above there is one other that is shorter than expected—the iodine atoms related by a translation along *b*. This distance is 0.20 Å. less than the value expected from the van der Waals radius of iodine. In various iodate crystal structures, short I-I contacts also have been observed.

The present results confirm the structure (I) proposed for *o*-iodosobenzoic acid, renamed now as 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole (4), in agreement with IUPAC and "Chemical Abstracts" rules of nomenclature.

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