

Crystal Structure of 2,4-Diselenouracil

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The crystal structure of 2,4-diselenouracil has been determined to provide some quantitative molecular information about the nature of hydrogen bonding exhibited by this compound in solution. The crystal is monoclinic, with space group $P 2_1/c$, with $a = 4.41 \text{ \AA}$, $b = 14.90 \text{ \AA}$, $c = 10.69 \text{ \AA}$, and $\beta = 108.4^\circ$. The observed density is $2.42 \text{ Gm. cm.}^{-3}$ and that calculated for four molecules in the unit cell is $2.33 \text{ Gm. cm.}^{-3}$. The structure was determined by the heavy atom technique and refined by block diagonal least squares to an R value of 0.136. The compound was found to exist primarily in a zwitterionic amidic configuration rather than the keto form. The seleniums formed relatively strong hydrogen bonds of the form $N(H) \cdots Se$ with distances of 3.47 and 3.75 \AA .

VARIOUS EXPERIMENTAL observations (1, 2) have indicated that selenium analogs of pyrimidine and purine bases are able to form relatively strong hydrogen bonds in solution. Many of these seleno-bases have also been shown to be pharmacologically active antineoplastic agents (3, 4). It has been implied (5) that this activity may be attributable to the "formation of unusually strong hydrogen bonds when incorporated into deoxynucleic acids." The present X-ray investigation of one of these seleno-derivatives, 2,4-diselenouracil, was primarily undertaken to obtain structural information about the nature of the intermolecular hydrogen bonding.

EXPERIMENTAL

Diselenouracil crystallizes from ethanol-water solutions as yellow dichroic prisms, which exhibited twinning along the (100) plane. Many batches of recrystallized material were examined for the presence of a "single" crystal, but all crystals appeared to be twinned. It was found necessary to use a crystal from which the twin had been dissected for the collection of intensity data. The fragment used showed excellent extinction under the polarizing microscope, but photographs indicated that a small amount of the twin remained; this was estimated to be less than 10% from oscillation photographs.

Oscillation and Weissenberg photographs taken about the a and b axes using Cu radiation ($\lambda = 1.5418 \text{ \AA}$) showed the crystal to be monoclinic, with unit cell dimensions of $a = 4.41 \text{ \AA}$, $b = 14.90 \text{ \AA}$, $c = 10.69 \text{ \AA}$, and $\beta = 108.4^\circ$ (with estimated standard deviations of 0.5%). The space group, as determined from Weissenberg photographs and confirmed by the determination and refinement of the structure, is $P 2_1/c$. The density measured by flotation in a mixture of tetrabromoethane and chloroform was found to be 2.42 Gm./cm.^3 , and that calculated for a unit cell containing four molecules of diselenouracil was 2.33 Gm./cm.^3 .

The intensity data were recorded on equi-inclination Weissenberg photographs using multiple film packs. The dissected crystal (dimensions

0.14 mm. along a , 0.04 mm. along b , and 0.02 mm. along c) was first mounted about the a axis for collection of layers $h = 0, 1$, and 2, and it was then cut in half perpendicular to a and remounted about b to obtain the layers $k = 0$ and 1. The intensities were estimated visually and corrected for Lorentz polarization effects. The structure factors for the data about the two axes were put on the same scale by comparing common reflections. There were 649 unique reflections that gave measurable values; this represents approximately 55% of all unique reflections in the Cu sphere.

Determination and Refinement of Structure.—

The positions of the two selenium atoms were easily located from an unsharpened Patterson synthesis, and the atoms comprising the pyrimidine ring were then found in a Fourier synthesis phased on the seleniums. The atomic identity of the six ring atoms was obtained by electron density calculations at the atomic sites. The refinement of the positional and isotropic thermal parameters of the molecule was carried out by block diagonal least squares, using a program described by Mills and Rollett (6). The weighing scheme used in the refinement was similar to that of Hughes (7). During the final cycles of refinement it was necessary to give zero weight to 36 weak reflections, as they appeared to be significantly influenced by the presence of the twin. The refinement was considered to be complete when the parameter shifts were less than one-third of their estimated standard deviations, which were calculated from the diagonal elements of the normal matrix. The positional and thermal parameters obtained are listed in Table I. The final R value

TABLE I.—POSITIONAL AND ISOTROPIC THERMAL PARAMETERS FOR 2,4-DISELENOURACIL

Atom	x/a	y/b	z/c	B_{150}
N(1)	-0.296	0.088	0.380	3.5
C(2)	-0.248	0.020	0.302	3.1
Se(2)	-0.3976	-0.0951	0.3275	4.1
N(3)	-0.118	0.038	0.199	3.5
C(4)	0.013	0.118	0.173	3.4
Se(4)	0.2002	0.1359	0.0249	3.5
C(5)	-0.056	0.193	0.257	3.9
C(6)	-0.204	0.175	0.361	4.3

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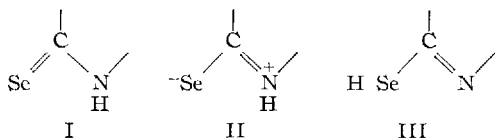
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(equals $\Sigma |F_0| - |F_c|/\Sigma |F_0|$) was 0.136 for all 649 reflections. A list of the observed and calculated structure factors can be obtained from the authors. The atom form factors used in the above calculations for carbon and nitrogen were those of

Berghuis *et al.* (8), and for selenium those of Thomas and Umeda (9) were used after being corrected for anomalous scattering. All computations were done on a Ferranti mercury electronic computer, using many of the programs described by Mills and Rollett (6).

RESULTS AND DISCUSSION

From X-ray studies on uracil (10) and various uracil containing compounds (11-14) it has been shown that in the solid state it exists primarily in the diketo form rather than the enol configuration. The C(2)-Se(2) and C(4)-Se(4) bond lengths of 1.89 and 1.99 Å. (E.S.D. 0.05 Å.), respectively, suggests that the electronic structure around the selenium would be predominantly a zwitterionic amidic configuration (II) rather than I.



The enol form (III) was eliminated as a possible configuration, as this structure was found to be isomorphous with the crystal structure of dithiouracil (17), for which hydrogen atoms were found attached to the nitrogens. The presence of the amidic configuration rather than the enolic one is also consistent with the dipole moment, ultraviolet spectra, and ionization measurements (2, 18) made on 2-pyridylselenone and its *N*-methyl derivative. The sum of the covalent bond radii for Se and C is 1.94 Å. for the single bond and 1.74 Å. for the double bond (15). These results are not surprising in the light of the studies of Mautner (1), which showed that Se has a greater ability than S and O to withdraw electrons from N in pyridine and pyrimidine derivatives.

The E.S.D.'s given above for the Se bonds is twice that calculated from the diagonal elements of the normal matrix, as it is felt that this is a more reasonable approximation to the errors. Relatively large standard deviations for the pyrimidine ring bonds (0.1 Å.) makes it impossible to assess their bond orders and, therefore, precludes any discussion of this part of the molecule.

Though selenium compounds are not usually thought of as hydrogen bond participants, in diselenouracil the seleniums appear to form such interactions. The short Se...N distances of 3.47 and 3.75 Å. and the angles around the nitrogen atoms indicate that the seleniums are forming relatively strong hydrogen bonds (Fig. 1). These hydrogen interactions are attributable to the electronic configuration and seem to be a function of the amount of polarization in the C-Se bonds. In the structure of *N*-phenyl-*N'*-benzoylselenourea (16) a Se...N hydrogen bond of 3.83 Å. was found, and it could

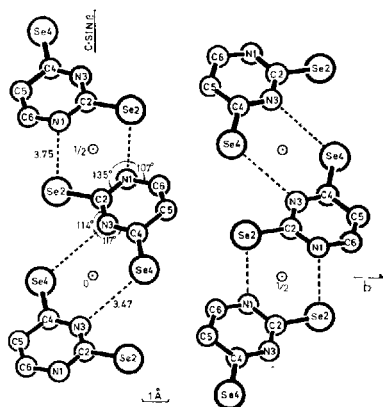


Fig. 1.—Packing diagram of 2,4-diselenouracil as viewed down the *a* axis. Probable hydrogen bonds are indicated by broken lines.

also be attributed to the electron-withdrawing property of the selenium. The importance of such bonding is best realized in connection with the postulate (5) that the antineoplastic activity of selenium derivatives of purine and pyrimidine bases may be related to their ability to form strong hydrogen bonds with their complement base within the helical deoxyribonucleic acid (DNA).

The least squares plane through the eight atoms, indicated they are coplanar; *i.e.*, the deviation of any atom from this plane is less than an E.S.D. of its positional parameter along the normal to the plane. This observation is consistent with the results on uracil and thymine.

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