

Diffusion, Permeation, and Solubility of Selected Agents In and Through Polyethylene

By M. A. GONZALES, J. NEMATOLLAHI, W. L. GUESS, and J. AUTIAN*

Even though polyethylene containers have and are being used with more frequency to package drug products, diagnostic agents, biological products, and cosmetic preparations, little emphasis apparently has been placed on the possible interactions between solute molecules in the product and the polyethylene. This report presents a study on the diffusion, permeation, and solubility of six compounds (acetophenone, benzaldehyde, benzoic acid, benzyl alcohol, 4-methylacetophenone, and 4-methylbenzaldehyde) in and through polyethylene. Results reveal that benzyl alcohol and benzoic acid had the lowest permeation (P) and diffusion (D) values as compared to the other compounds in the series. This was ascribed to the intermolecular hydrogen bonding potential of benzyl alcohol and benzoic acid; thus the formation of dimer or trimer whose permeation through the polymer is assumed to be restricted. In the case of 4-methylbenzaldehyde and 4-methylacetophenone, the D values obtained were similar to those of the parent compounds (benzaldehyde and acetophenone). Higher P values for the 4-methyl derivatives of benzaldehyde and acetophenone were related to the higher solubility of the molecules in the plastic.

THE PACKAGING of drugs, biological products, diagnostic aids, and cosmetic products in polymeric materials has increased greatly in the past decade. A number of advantages of plastics over the conventional glass, paper, and metals have helped to accelerate the adoption of plastic packaging systems to a host of old and new products entering the medical and para-medical fields. As might be expected with the introduction of new materials for a specific application, certain problems have arisen or may arise which justify research into drug-plastic interactions (1-4).

Presently the most commonly used polymeric material for containers is polyethylene. It has been found to be a good moisture-vapor barrier for aqueous products as well as a good barrier for a number of organic solvents. Pinsky (5) has studied the permeation rates of several classes of organic liquids through polyethylene and has found the rate was lowest with the highly polar substances, increasing in the following order of chemical structures: alcohol, acids, nitro derivatives, aldehydes and ketones, esters, ethers, hydrocarbons, and halogenated hydrocarbons. Salame and Pinsky have been able to develop an arithmetical method for predicting the permeability of liquids through polyethylene (6). They refer to their method as the "Permachor" method. It is interesting to note, however, that only a few reports are available on the barrier properties of

polyethylene in contact with aqueous solutions of specific compounds. It should be apparent that any loss of an ingredient in a drug or similar type of product stored in a polyethylene container would decrease the effectiveness of the drug product leading to possible serious consequences to the patient and the manufacturer of the product.

To develop a body of knowledge on the barrier properties of polyethylene which may be of value to the pharmaceutical or cosmetic scientist, a study was undertaken to determine the diffusion, permeation, and solubility of some commonly found pharmaceutical compounds, namely, benzyl alcohol, benzoic acid, and benzaldehyde. Also included in the study were acetophenone, 4-methylbenzaldehyde, and 4-methylacetophenone which are structurally related to benzoic acid and benzaldehyde. Study of the latter compounds was designed to provide contrasting information on the effect of certain substituents on the rate of diffusion and permeation of the parent compounds.

EXPERIMENTAL

Materials and Supplies—Polyethylene film, 3 mil thickness (Gulf Oil Corp., Chemicals Department, Orange, Tex.); acetophenone, certified reagent grade (Fisher Scientific Co., Fairlawn, N. J.); benzaldehyde, Eastman grade (J. T. Baker Chemical Co., Phillipsburg, N. J.); benzyl alcohol, Eastman grade (Eastman Organic Chemicals, Rochester, N. Y.); 4-methylacetophenone, Eastman grade (Eastman Organic Chemicals, Rochester, N. Y.); 4-methylbenzaldehyde, Eastman grade (Eastman Organic Chemicals, Rochester, N. Y.).

Properties of Polyethylene Film—The density of the film as determined by the use of a density gradient column at 25° was found to be 0.9246 Gm./ml. This value indicates that the film falls in the category of a low density polyethylene. Weight average

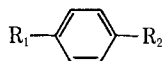
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TABLE I—MOLECULAR STRUCTURES OF COMPOUNDS INVESTIGATED OF THE GENERAL FORMULA



Compd.	R ₁	R ₂	Mol. Wt.	Dipole ^a Moment	Solubilities ^b in Water, % w/v
Benzyl alcohol	—CH ₂ OH	—H	108.13	1.68	4.0
Benzoic acid	$\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---OH} \end{array}$	—H	122.12	1.00	0.34
Benzaldehyde	$\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---H} \end{array}$	—H	106.12	2.77	0.33
Acetophenone	$\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---CH}_3 \end{array}$	—H	120.14	2.77	0.30
4-Methylbenzaldehyde	$\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---H} \end{array}$	—CH ₃	120.14	3.30	0.10
4-Methylacetophenone	$\begin{array}{c} \text{O} \\ \parallel \\ \text{---C---CH}_3 \end{array}$	—CH ₃	134.17	3.20	0.10

^a Values are in Debye units. These values were determined in benzene at 25° as reported in Wesson, L. G., "Tables of Electric Dipole Moments," The Technology Press, Massachusetts Institute of Technology, Cambridge, Mass., 1948. ^b The solubilities in water at approximately 25° are taken from "The Merck Index of Chemicals and Drugs," Merck and Co., Inc., Rahway, N. J., 1960, for benzyl alcohol, benzoic acid, and benzaldehyde. The solubilities for the other compounds were determined experimentally by the authors.

molecular weight was equal to 83,430 while the number average molecular weight was 15,820.¹ The polyethylene had an average of 19.3 methyl groups per 1,000 monomeric units (methylene groups) indicating a high degree of branching and a terminal vinylidene content equal to 0.37 per 1,000 methylene units.¹

Permeation Experiments—The compounds studied in this report with some of their physical constants are listed in Table I. Aqueous solutions of each of these compounds were prepared at a specific original concentration as shown in Table II. Each agent was studied at four different temperatures (40°, 50°, 60°, and 70° ± 0.02°). The permeation experiment was conducted in a cell consisting of two chambers separated by the polyethylene film² secured in place by a clamp (Fig. 1) following the general procedure of Rodell (7). In the left chamber was placed 500 ml. of the solution under study and in the right, 500 ml. of distilled water. The solution and water were heated to a temperature slightly higher than the temperature of the water bath prior to adding them to the permeation cell. The cell was then placed into a constant-temperature water bath adjusted to the desired temperature. At various time periods aliquots from the right chamber were withdrawn and the quantity of the compound was determined spectrophotometrically at the wavelength of maximum absorbance. (See Table II.) From the data a figure was prepared plotting the quantity of the compound passing through the film against time. Each of the compounds was studied in this manner at various temperatures.

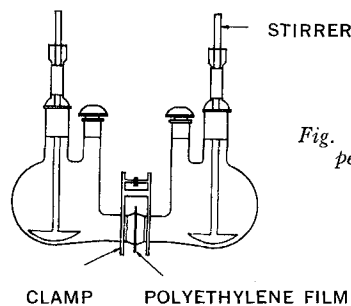


Fig. 1—Diagram of permeation cell.

TABLE II—ORIGINAL CONCENTRATIONS OF SOLUTIONS AND WAVELENGTHS OF MAXIMUM ABSORBANCE

Compd.	% Concn., Wt./Vol.	Wavelength Max. Abs., m μ	Diluting Solvent
Benzyl alcohol	1.0	258	Distilled water
Benzoic acid	0.3	230	0.1 N HCl
Benzaldehyde	0.3	250	Distilled water
Acetophenone	0.3	245	Distilled water
4-Methylbenzaldehyde	0.1	260	Distilled water
4-Methylacetophenone	0.1	257	Distilled water

Representative plots are shown for only two of the compounds (benzyl alcohol and benzaldehyde) in Figs. 2 and 3.

Extrapolation of lines in the various plots to the time axis permitted the calculation of the apparent diffusion coefficient (*D*) using the Barrer relationship (8):

¹ Statistics on molecular weights, branching, and olefinic bonds were generously furnished by Mr. T. O. J. Kresser, Plastics Laboratory, Gulf Oil Corp., Chemicals Department, Orange, Tex.

² Surface area exposed to solution was 22.07 cm.².

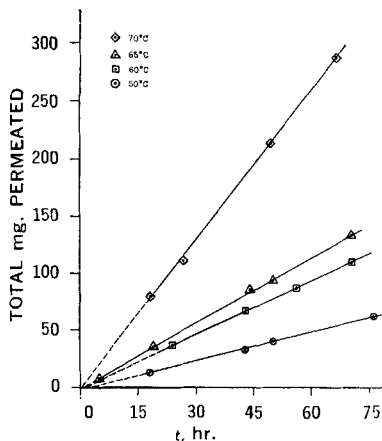


Fig. 2—Permeation plot of benzyl alcohol (1.0%) through polyethylene at several temperatures.

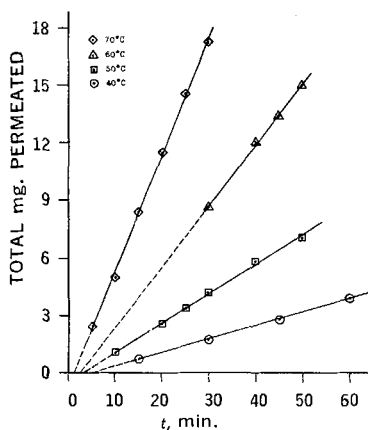


Fig. 3—Permeation plot of benzaldehyde (0.3%) through polyethylene at several temperatures.

$$D = L^2/6\tau \quad (\text{Eq. 1})$$

where L is the thickness of the film and τ is the time lag obtained from the extrapolated line.

The D values for each of the agents at the specific temperature of the experiment are listed in Table III. The same table also includes the activation energy (ΔE_D) of diffusion calculated by the use of the Arrhenius expression:

$$\log D = \log D_0 - \Delta E_D/2.303 RT \quad (\text{Eq. 2})$$

The plots of $\log D$ versus $1/T$ for the solutes under study gave linear relationship, thus permitting the evaluation of ΔE_D from the slopes.

Permeability constants (P) were evaluated for each of the compounds for a given temperature using the expression:

$$P = c/t \cdot LV/CA \quad (\text{Eq. 3})$$

where c/t is the slope of the linear portion of the permeation plot (Figs. 2, 3), L is the thickness of the film, V the total volume of solution, C the original concentration, and A the surface area of the film exposed to the solution. The P values are listed in Table IV, which also includes the activation energies of permeation, evaluated in a manner similar to that described for the activation energy of diffusion.

Solubility coefficients (S) for each of the compounds were calculated by the relation of $P = SD$, and these values are listed in Table V. Heats of solution (ΔH), calculated by the use of the Arrhenius relationship are also included in Table V.

RESULTS AND DISCUSSION

Initial permeation studies were directed to compare the barrier properties of polyethylene toward benzyl alcohol, benzoic acid, and benzaldehyde. As are depicted in Tables III and IV, considerable difference is noted between the aldehyde and either the alcohol or the acid. At 50° benzaldehyde has an apparent diffusion coefficient of 542.0×10^{-10} cm.²/sec., while for benzoic acid and benzyl alcohol the D values are 14.6×10^{-10} cm.²/sec. and 11.6×10^{-10} cm.²/sec., respectively. Comparison of the permeability constants (Table IV) for the three compounds indicates that benzaldehyde possesses a higher permeation rate than benzoic acid or benzyl alcohol and although the difference is not so large as with the diffusion coefficients, it is still significant.

Since the benzaldehyde gave much higher values for D and P than demonstrated for either the benzyl alcohol or benzoic acid, similar studies on three structurally related compounds (acetophenone, 4-methylbenzaldehyde, and 4-methylacetophenone) were undertaken.

Diffusion Coefficients and Activation Energies of Diffusion—As has been indicated above, the diffusion coefficient for benzaldehyde at any temperature was found to be greater than either the benzyl alcohol or the benzoic acid. These latter two compounds have nearly similar D values as may be noted in Table III. The similar apparent diffusion coefficients suggest a similar molecular volume. All other factors being equal, the diffusion coefficient is strongly dependent on the molecular volume of a

TABLE III—DIFFUSION COEFFICIENTS AND ACTIVATION ENERGIES OF SELECTED COMPOUNDS IN POLYETHYLENE

Compd.	$D \times 10^{10}$ cm. ² /sec.				ΔE_D , Kcal./mole
	40°C.	50°C.	60°C.	70°C.	
Benzyl alcohol ^a		11.6	21.3	71.0	12.6
Benzoic acid ^b	5.29	14.6	22.5		15.0
Benzaldehyde	339.0	542.0	737.0	1400.0	8.16
Acetophenone	355.0	592.0	769.0	1210.0	8.05
4-Methylbenzaldehyde	137.0	403.0	557.0	1100.0	6.90
4-Methylacetophenone	179.0	502.0	611.0	1260.0	10.2

^a Experiment at 40° replaced by one at 65°. D at 65° was 27.3. ^b Experiment at 70° discontinued.

TABLE IV—PERMEABILITY CONSTANTS AND ACTIVATION ENERGIES OF SELECTED COMPOUNDS THROUGH POLYETHYLENE

Compd.	$P \times 10^{10}$ ^a				ΔE_p , Kcal./mole
	40°C.	50°C.	60°C.	70°C.	
Benzyl alcohol ^b		0.771	1.49	4.00	11.5
Benzoic acid	0.330	1.00	1.74		17.2
Benzaldehyde	12.7	27.7	56.8	109.0	15.5
Acetophenone	11.2	30.4	60.0	95.9	17.4
4-Methylbenzaldehyde	35.0	55.3	124.0	203.0	17.2
4-Methylacetophenone	22.3	62.3	124.0	203.0	16.5

^a P or the permeability constant is the quantity (in mg.) of agent passing through a film of 1 cm.² surface area and 1 cm. thickness per second when the concentration gradient is 1 mg./ml. P expressed in following units: (mg.)(cm.)/(sec.)(cm.²)(mg./ml.). ^b The permeability constant at 65° was 1.78×10^{-8} .

TABLE V—SOLUBILITY COEFFICIENTS^a AND HEATS OF SOLUTION OF SELECTED COMPOUNDS IN POLYETHYLENE

Compd.	S				ΔH_s , Kcal./mole
	40°C.	50°C.	60°C.	70°C.	
Benzyl alcohol ^b		7.03	6.97	5.63	-1.01
Benzoic acid	6.25	6.86	7.72		2.18
Benzaldehyde	3.74	5.11	7.70	7.87	7.52
Acetophenone	3.16	5.13	7.80	8.50	9.39
4-Methylbenzaldehyde	25.6	13.7	22.2	18.5	10.32
4-Methylacetophenone	12.5	12.4	20.2	16.1	6.25

^a The solubility coefficients are unitless, since they express the ratio of the amount of solute in a volume of plastic over the amount of solute in a volume of solution at equilibrium (mg./ml. per mg./ml.). ^b S at 65° was 6.48.

diffusate molecule, D decreasing with an increase in molecular volume. One may cite as an example the diffusion coefficient of helium at 30° in a low density polyethylene reported in the literature as 81.5×10^{-7} cm.²/sec., while that for oxygen under similar conditions is 6.05×10^{-7} cm.²/sec. (9).

Since the diffusion coefficients for benzyl alcohol and benzoic acid were similar, there is a possibility that the diffusing species of these two compounds had a similar molecular volume. It is known that both benzoic acid and benzyl alcohol are capable of forming dimers by hydrogen and hydrophobic bonding, and it could be that the dimerization gives rise to large diffusate molecules (10-13). The larger diffusion coefficients for benzaldehyde were probably due to smaller diffusing species than those for benzyl alcohol and benzoic acid, since benzaldehyde does not possess a hydrogen capable of hydrogen bonding.

Further support for the existence of larger diffusate molecules with benzyl alcohol and benzoic acid is found in the activation energies for diffusion (Table III). The relatively high activation energies for benzyl alcohol, 12.6 Kcal./mole, and benzoic acid, 15.0 Kcal./mole, as compared to that of benzaldehyde, 8.16 Kcal./mole, may be interpreted as resulting from the high energy required to make a hole in the polymer matrix large enough to allow diffusion of the large dimerized molecules. According to Barrer and other investigators (14, 15) the activation energy for diffusion is strongly influenced by the size of the diffusate molecule and increases with an increase in molecular size. Since benzyl alcohol and benzoic acid require more energy to diffuse in polyethylene than does benzaldehyde, it should follow that benzyl alcohol and benzoic acid possess larger diffusing species than benzaldehyde.

The ability of carboxylic acids to form dimers in aqueous solutions by intermolecular hydrogen bonding and by hydrophobic interactions has been documented in the literature (10-12). Indirect proof

for dimerization of benzyl alcohol has come through several sources. Scheraga *et al.* has shown that alcohols interact with each other through hydrophobic bond formation in model systems (13). Infrared spectra of various concentrations of benzyl alcohol in carbon tetrachloride reveal that the O-H stretching frequency band shifts to lower frequency as a function of concentration. The high boiling point of benzyl alcohol (205.2°), as compared to the lower boiling point of ethylbenzene (136.2°), a molecule having the same molecular weight as benzyl alcohol, is ascribed to the hydrogen bonding capacity of the former.

In the case of acetophenone, 4-methylbenzaldehyde, and 4-methylacetophenone the diffusion coefficients observed were very similar to those of benzaldehyde at 50°. Acetophenone had a D value of 592.0×10^{-10} cm.²/sec., while 4-methylbenzaldehyde and 4-methylacetophenone had values of 403.0×10^{-10} cm.²/sec. and 502.0×10^{-10} cm.²/sec., respectively. Lack of intermolecular hydrogen bonding in this series of compounds would seem to be responsible for the almost identical D values. As with benzaldehyde, these compounds do not form dimers and are very slightly soluble in water (solubilities listed in Table I). The similarity of the diffusion coefficients and activation energies of diffusion of benzaldehyde and its methyl analogs, as listed in Table III, also indicates that the addition of a methyl group does not increase the molecular size enough to alter the diffusivity of these compounds significantly.

Permeability Constants and Activation Energies of Permeability—The permeability constants calculated for benzyl alcohol, benzoic acid, benzaldehyde, and acetophenone were found to have a similar relationship to that existing between the values for the diffusion coefficients of these compounds. The permeability constants for benzyl alcohol and benzoic acid at 50° were 0.771×10^{-8} and $1.00 \times$

10^{-8} , respectively. The values for benzaldehyde and acetophenone were 27.7×10^{-8} and 30.4×10^{-8} . Thus, the trend was generally an increase in the permeation of the compounds in the same order as the diffusion. The permeability constants, however, for the methyl substituted derivative of the latter two compounds were found to be twice as large as those for the parent compounds. The P value at 50° for 4-methylbenzaldehyde was 55.3×10^{-8} while the same constant for 4-methylacetophenone was 62.3×10^{-8} . No such relationship was observed with the diffusion coefficients. The D values for the *p*-methyl analogs were essentially the same as those of the parent compounds.

Except for benzyl alcohol, the values obtained for the activation energies of permeability for all the compounds were in the range of 17 Kcal./mole. Benzyl alcohol had the lowest activation energy, 11.5 Kcal./mole (Table IV). To explore the differences in the permeability, it was necessary to consider the solubility coefficients and the heats of solution of the permeating agents in polyethylene.

Solubility Coefficients and Heats of Solution—In this study the solubility coefficients (S) were found to be approximately the same for benzyl alcohol, benzoic acid, benzaldehyde, and acetophenone (Table V). With benzyl alcohol, however, the S values decreased with an increase in the temperature of the experiment, while the opposite occurred with the other compounds. By definition, the solubility coefficient is a ratio of the concentration of solute in a unit weight or volume of plastic to the concentration of the solute in a unit weight or volume of solution. The solubility coefficient, thus, can be visualized as a distribution ratio, which makes it possible to interpret the solubility data with facility.

Upon increasing the temperature of benzyl alcohol solution, dimerization decreases due to a disruption of intermolecular hydrogen bonding. The relatively high capacity of benzyl alcohol to form hydrogen bonds with water molecules renders it less soluble in polyethylene, thus resulting in a decrease of the S values. An Arrhenius plot of the values of the log of S versus $1/T$ gives a positive slope which yields a negative heat of solution. This may be interpreted as meaning that the exothermic heat resulting from the binding of benzyl alcohol molecules to the polymer chain segments predominates over the endothermic heat of mixing, and the resulting heat of solution is negative (-1.01 Kcal./mole).

All the other compounds studied had positive heats of solution, which would imply that the endothermic heat of mixing was predominant. It could follow that the increase in the solubility coefficients noted for benzoic acid, benzaldehyde, and acetophenone was due primarily to an increase in the mobility of the polymer chains which allowed a faster increase in the solubility of the solute in the polymer than in the solution. In the case of benzoic acid, however, the increase in temperature will result in the cleavage of intermolecular hydrogen bonds, as is true in the case of benzyl alcohol—differing in that benzoic acid molecule possesses two sites for the formation of intermolecular hydrogen bonds. The increase in monomer fraction will result in an increase in the solubility of benzoic acid in water. However, due to the relatively high polar character of benzoic acid molecule the increase in its

solubility coefficient is not so rapid as that for benzaldehyde or acetophenone.

In the case of 4-methylbenzaldehyde and 4-methylacetophenone, the solubility coefficients were found to be twice as high as those of the parent compounds. At 50° 4-methylbenzaldehyde had an S value of 13.72 and 4-methylacetophenone had a similar value of 12.41. The same constants for benzaldehyde and acetophenone were 5.11 and 5.13, respectively. These high solubility coefficients could be ascribed to a decrease in the dielectric constant due to the presence of the methyl substituent.

After reviewing the solubility data, it is possible to explain the apparent anomalous results obtained for the permeability constants and activation energies of permeability. The high solubility coefficients for 4-methylacetophenone accounted for the high permeability constants obtained for these compounds. Since their diffusion coefficients were generally the same as those of their parent compounds, it follows from the relationship $P = DS$ that the permeability constants will vary according to the variation in the solubility coefficients. The solubility coefficients of 4-methylbenzaldehyde and 4-methylacetophenone are twice as large as those of benzaldehyde and acetophenone; thus, the permeability values as well would be expected to rise by twofold.

To propose a rationale for the resultant activation energies of permeability, it is necessary to recall that the activation energy for permeability is a measure of the energy required to allow the net transfer of a mole of solute through the amorphous regions of a plastic. This energy will then be the sum of the activation energy for diffusion and the heat of solution. Since benzyl alcohol had a negative heat of solution, the energy to accomplish the permeation of benzyl alcohol molecules through the polyethylene chains was less than the energy for diffusion. Benzyl alcohol also had the lowest activation energy of permeability.

Although a reasonable hypothesis has been presented in an attempt to explain the data, there are still several complications that should be emphasized. One of these is that the concentrations used in these studies were not always the same and although the constants derived mathematically are concentration independent, the possibility that the differences in concentration may contribute to some unexpected experimental results should not be overlooked. Finally, it should be remembered that with the type of polyethylene used in this experiment the degree of crystallization will decrease with an increase in temperature. In fact, studies above temperatures higher than 70° gave anomalous results which may have been due to the changes in crystallinity. This facet must, however, be investigated more thoroughly before the exact effects of changes of crystallinity on sorption can be presented.

SUMMARY

A series of structurally related aromatic compounds was employed for the evaluation of their permeation through a polyethylene film. Six compounds were used in the study: benzyl alcohol, benzoic acid, benzaldehyde, acetophenone, 4-methylbenzaldehyde, and 4-methylacetophenone.

Results of the experiments revealed that benzyl

alcohol and benzoic acid had the lowest P and D values as compared with the other compounds in the series. This was ascribed to intermolecular hydrogen bonding potential of benzyl alcohol and benzoic acid which produce dimers or trimers whose penetration into the polymer is not favorable.

In the case of 4-methylbenzaldehyde and 4-methylacetophenone, the D values obtained were similar to those of the parent compounds, benzaldehyde and acetophenone. The P and S values, however, were found to be larger. The difference in the P and S values was attributed to the effect of the methyl substituents which gave rise to higher solubility in the plastic.

Quantitative studies as reported here and similar studies with other compounds should be of value to those who may desire to package drugs, cosmetics, or other products in polyethylene.

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Crystal and Molecular Structure of 5-[1-(2'-Deoxy- α -D-ribofuranosyl)uracilyl] Disulfide

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The molecular structure of 5-[1-(2'-deoxy- α -D-ribofuranosyl)uracilyl] disulfide (I) has been determined by X-ray crystallographic analysis. The molecule crystallizes in the orthorhombic space group $P2_12_12_1$, with the following cell dimensions: $a = 9.492 \text{ \AA}$, $b = 14.061 \text{ \AA}$, $c = 16.328 \text{ \AA}$. The valence state about the S-S linkage appears to be markedly different from that observed in other disulfide structures. The torsional angle about this bond is 49° and the S-S bond length was found to be 2.108 \AA . The configurations of both the uracil and the deoxyribofuranosyl residues are different in the two nucleoside units of the molecule. The crystal is bound together by hydrogen bonds.

A STRUCTURAL ANALOG of thymidine, 5-mercapto-2'-deoxyuridine (MUDR), has been recently synthesized (1), and found to be a potent inhibitor in several bacterial systems. This compound and some of its congeners are of potential chemotherapeutic interest because of their ability to inhibit the biosynthesis of DNA (2, 3). Both the α and β anomers of MUDR exhibited rapid autoxidation in aqueous solutions to the corresponding disulfides (4). These disulfides have interesting biochemical and physicochemical properties. They are capable of being reduced nonenzymatically at a virtually instantaneous rate by stoichiometric amounts of thiols (2, 5), and their high

optical activities showed temperature dependence (6).

In an effort to gain further insight into the various properties that could be pertinent as to the mode of action on a molecular level of MUDR and its congeners, X-ray structural studies have been initiated on several of these compounds. This report concerns itself with the crystallographic structure of the first of these compounds to be completed, the disulfide of the α -anomer, 5-[1-(2'-deoxy- α -D-ribofuranosyl)uracilyl] disulfide (I). This compound has additional interest as it appears to be the first α -nucleoside whose crystal structure has been elucidated.

EXPERIMENTAL

The compound crystallizes from water as slightly yellow prisms belonging to space group $P2_12_12_1$, with the following crystallographic data:

$$\begin{aligned}
 a &= 9.492 \pm 0.003 \text{ \AA} \\
 b &= 14.061 \pm 0.002 \text{ \AA} \\
 c &= 16.328 \pm 0.003 \text{ \AA} \\
 \rho(\text{meas.}) &= 1.577 \text{ Gm./cm.}^3 \\
 \rho(\text{calcd.}) &= 1.579 \text{ Gm./cm.}^3 \\
 Z &= 4
 \end{aligned}$$

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