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The Conductivity of Single Crystals of 1-Methylthymine

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The conductivity of single crystals of 1-methylthymine (2,4-dihydroxy-1,5-dimethylpyrimidine) has been determined using proton-injecting solution electrodes. The conductivities parallel and perpendicular to the H-bonded, (102) planes are $2.4 \times 10^{-10} \pm 1.9 \times 10^{-10}$ and $1.0 \times 10^{-14} \pm 0.4 \times 10^{-14}$/ohm cm, respectively (298°K). The conductivity is ohmic over the range of fields employed for either crystallographic direction. The energy of activation for conduction parallel to the (102) plane is 43 ± 10 kJ/mole.

Introduction

The phenomena of solid-state conduction by protons, instead of by electrons, is of much current interest (*1*) not only because of the interesting theoretical implications of such conduction processes, but because of its possible biological relevance.

The transfer of hydrogens across hydrogen bonds, H-bonds, are necessary for the order–disorder transitions associated with ferroelectric and antiferroelectric behavior in some H-bonded solids (*2*). The transfer of protons can be correlated to acid-base phenomena in the solid state, to such biological processes as the production of mutagenic DNA (*3*), and to the conversion of sunlight to electrical energy (*4*). In addition, solids that exhibit high protonic conductivity are of interest for the development of electrolysis cells and pH meters (*5*).

The sustained conduction of protons in a solid, as originally described by Grotthuss (*6*), requires the presence of an H-bonded network in the solid. Biological compounds are frequently H-bonded in their biological environment as well as the solid state and thus, can be considered as candidates for such conduction. The possibility of intrinsic protonic conduction in biological compounds was suggested by Riehl (*7*) as being the basis for the chemical retrieval of memory in biological systems. As discussed in a previous article (*8*), the electronic conductivities of compounds such as proteins, nucleic acids, amino acids, and the like are very low when measured in the dry crystalline state, falling within the range 10^{-14} to 10^{-17} ohm^{-1} cm^{-1} (298°K). Therefore, electronic conduction is not likely to be important in biological processes. However, the adsorption of a specific amount of water by these same compounds produces protonic conductivities of considerably greater magnitudes than their electronic conductivity, in some cases by as much as 10^8 times (*9*). The role of the water molecules is not understood and appears to vary from one type of compound to another.

Values of protonic conduction in organic compounds have been shown to range from quite high to quite low values (*1*), which lends support to the expectation that protonic conduction may also be of consequence in organic solids. To date, very few biological compounds have been investigated for pro-

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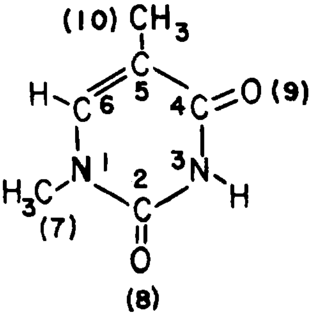
tonic conductivity, so that the possibility of conduction by protons as an important process in biological systems has yet to be determined.

The pyrimidines and purines are classes of compounds that are particularly prominent constituents of biological systems and have the additional advantage of being well characterized in the crystalline state. The conductivity of one such pyrimidine, 1-methylthymine, was determined in this study, with the use of proton-injecting electrodes.

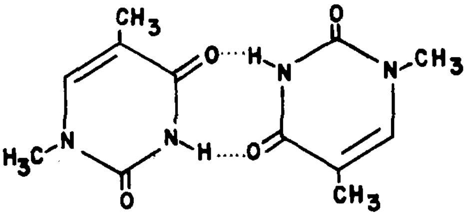
Protonic Conduction Pathways in Crystalline MT

1-Methylthymine, MT (2,4-dihydroxy-1,5-dimethylpyrimidine), closely resembles the nucleoside, thymidine, except that the 2-deoxyribose ring of the latter has been replaced by a methyl group. The chemical structure of MT is given in Scheme 1.



MT is extensively H-bonded in the solid state and in aqueous solutions. It readily forms H-bonded pairs with itself or with other purines and pyrimidines.

The crystal structure of MT has been determined utilizing X-ray diffraction (*10*) and neutron diffraction (*11*) techniques. Its structure is very similar to that of other purines and pyrimidines, such as 9-methyladenine. It consists of sheets of H-bonded MT molecules, spaced 3.38 Å apart, with the sheets lying approximately parallel to the (102) plane. Within the layers, the molecules are primarily H-bonded in pairs as illustrated in Scheme 2.



Analogous H-bonded pairs in which the position of N_1 and C_5 are inverted, on either the left or right side of the dimer, also occur but represent only a 10–12% contribution to the total crystal structure (*11*).

A simplified illustration of the crystal structure of MT projected on the (102) plane (not drawn to scale) is given in Fig. 1. The relative positions of the MT molecules are shown and the H-bonding between the

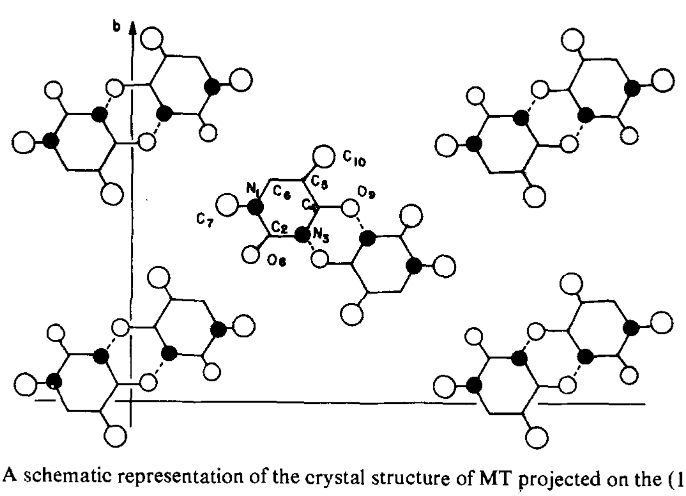


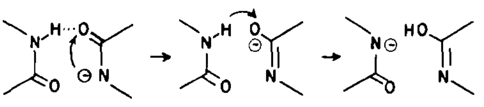
FIG. 1. A schematic representation of the crystal structure of MT projected on the (102) plane.

molecules is indicated by the broken lines. It is clear that one of the carbonyl oxygens, O_8, is not involved in H-bonding with nitrogen. However, O_8 is close, 3.121 Å, to the carbon C_6, on a neighboring molecule. This distance is smaller then the sum of the van der Waals radii of the atoms and is not due to a displacement of the oxygen and the hydrogen attached to C_6 from the molecular plane. It is considered very probable that a weak H-bond occurs between the H and O_8 which accounts for the contraction and adds to the cohesion of the MT pairs in the (102) plane. H-bonds involving C–H hydrogens have been proven to exist in haloforms, acetylenic C–H groups, and HCN (*12*), and also occur frequently in heterocyclic compounds (*13*).

This type of C–H--O H-bond is found in the crystal structures of other biological compounds and is not unique to MT. The same type of close approach of an O to a CH group is found in crystals of uracil (*14*), a nucleotide base found in DNA which is structurally similar to MT, and in adenosyl-3,5′-uridine phosphate (*15*), a crystal exhibiting the same base pairing and helical structure as in DNA, as well as in DNA itself (*16*). It appears that C–H--O interactions of this type function in the stabilization of macromolecular conformations. NMR studies on several purines and pyrimidines in solution confirm that the H involved in the interaction is somewhat acidic and participates in H-bonding (*17*).

The H-bond interaction between the O_8 and C_6–H in the MT crystal may allow protonic conduction parallel to the (102) plane. A possible mechanism is illustrated in Fig. 2. If the H on N_3 were to be transferred to O_8 as a proton, as in II, then an ionic tautomer of MT could be formed, analogous to the formation of an ionic defect in ice. Such charged tautomers are known to exist for pyrimidines, as are the neutral tautomers of the keto-enol form (*18*). Transfer of the proton could then occur through the C–H--O H-bond as in III, which would result in a positive charge residing on C_5. Stabilization of a positive charge on C_5 is likely due to the presence of the electron-donating methyl substituent and the fact that this position is meta to the two nitrogens in the ring (*18*). The subsequent transfer of the proton around the ring to O_8 in a manner analogous to a tautomerism mechanism would allow for the repetition of the previous steps on the neighboring molecules and the conduction of a proton to the electrode.

Stabilization of the accompanying negative charge, generated in step II, can occur through resonance and may be transferred to a neighboring molecule as indicated in Scheme 3.



Sustained protonic conduction by this mechanism would require that the neutral molecule be reformed and I in Fig. 2 be reconstructed. Reestablishment of the original configuration could be accomplished by either the migration of the negative charge or by the injection of a proton from the electrode to neutralize the

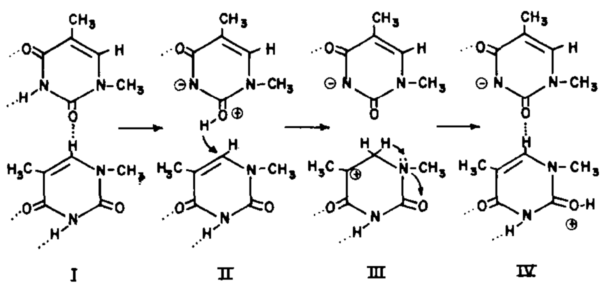


FIG. 2. A possible mechanism for the transport of protons by the MT molecules, parallel to the (102) plane.

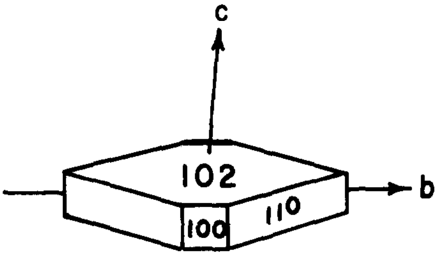


FIG. 3. The typical crystalline habit of MT crystals employed in this investigation.

negative charge. The proposed mechanism implies that protonic conduction could occur in MT parallel to the (102) plane but not perpendicular to the (102) plane, since interplanar H-bonding does not occur. Therefore, if protonic conduction occurs in MT, it would be expected to be anisotropic.

It is experimentally convenient to make conductivity measurements of single crystals where possible perpendicular to the naturally occurring faces of the crystals in order to avoid the possibility of introducing defects or microcracks into the crystal by the cutting and/or polishing process. In the case of the MT crystals, measurements of the conductivity were made parallel and perpendicular to the dominant (and easily identifiable) (102) planes. An illustration of the typical crystalline habit of the MT crystals employed in this study is given in Fig. 3. Measurements parallel to the (102) plane were made by applying the field perpendicular to the natural (110) faces and recording the current density in the same direction. Composite conductivities will be observed in either direction, since neither is parallel to a crystallographic axis.

The conductivity of MT, as for all crystals, is dependent on the direction in which it is measured, and can be represented by a second rank tensor (*19*). Ohm's law (1) describes the relationship between the current density, $\bar{J}$, and the applied field,

$$\bar{J} = \sigma \bar{E}, \qquad (1)$$

$\bar{E}$, for most solids, at low fields where $\bar{J}$ and $\bar{E}$ are vector quantities. In three-dimensional systems, $\bar{J}$ and $\bar{E}$ can be represented by the vectors (j_1, j_2, j_3) and (E_1, E_2, E_3), where the subscripts 1, 2, and 3 denote the crystallographic *a*-, *b*-, and *c*-axis, respectively. If the conducting properties of the solid are anisotropic, then $\bar{J}$ may not be parallel to $\bar{E}$ and components of σ occur along several axes. Thus, Eq. (1) must be replaced by three linear equations of the form

$$j_i = \sigma_{i1} E_1 + \sigma_{i2} E_2 + \sigma_{i3} E_3. \qquad (2)$$

The resulting array of coefficients of σ are the components of the conductivity tensor. This can be simplified by the transformations imposed on it by the crystalline symmetry. The symmetry of MT is of the monoclinic class (with the *b*-axis taken as the diad axis) and has the conductivity tensor shown in Eq. (3) (*19*):

$$\begin{bmatrix} \sigma_{11} & 0 & \sigma_{31} \\ 0 & \sigma_{22} & 0 \\ \sigma_{31} & 0 & \sigma_{33} \end{bmatrix}. \qquad (3)$$

The components of the observed conductivity can be resolved from this array by using the proper multiplication of the matrix by the vectors of the field and current density utilized in the experiment. For instance, if the field is applied parallel to the *b*-axis and $\bar{J}$ is measured in the same direction, the conductivity measured will have only one component, σ_{22}, but if the field is applied parallel to the *a*-axis and $\bar{J}$ is measured along the *c*-axis, σ_{31} will be observed. If the field is not applied along a crystallographic axis, but at a specific angle to it, and the current density is measured in the same direction, $\bar{J}$ will not necessarily be parallel to $\bar{E}$ and only the component of $\bar{J}$ parallel to $\bar{E}$, J_{11}, will be measured. The components of this field, $\bar{E}'$, can be referenced to the principal axes by the direction cosines, where the cosine is of the angle between the specific crystallographic axis and $\bar{E}'$. The component of $\bar{J}$ parallel to $\bar{E}'$ is the sum of the components of $\bar{J}$ resolved along $\bar{E}'$. For example, if the field is applied perpendicular to the (110) face of a monoclinic crystal, as it was for MT, $\bar{E}'$ will be directed at an angle of 45° to either the *a*- or *b*-axis. The matrix representation of the vector $\bar{E}'$ is then, $\bar{E}' = (\cos\theta_1 E_1, \cos\theta_2 E_2, 0)$, $\theta_1 = \theta_2 = 45°$ and

$$\bar{J} = (\cos\theta_1 \sigma_{11} E_1, \cos\theta_2 \sigma_{22} E_2, 0),$$

so that the component of $\bar{J}$ parallel to $\bar{E}'$ becomes

$$J_{\parallel} = \cos^2\theta_1 \sigma_{11} E + \cos^2\theta_2 \sigma_{22} E. \quad (4)$$

The conductivity is then given by the following equation:

$$\begin{aligned}\sigma &= \cos^2\theta_1 \sigma_{11} + \cos^2\theta_2 \sigma_{22} \\ &= 0.5\sigma_{11} + 0.5\sigma_{22},\end{aligned}$$

which can be rewritten as:

$$\sigma_{\parallel(102)} = 0.5\sigma_a + 0.5\sigma_b. \quad (5)$$

Therefore, the conductivity measured parallel to (102) in MT will be composed of one-half the magnitude of both the *a*- and *b*-components of conductivity. If either σ_a or σ_b dominates the conductivity, the value of the composite conductivity will be determined principally by the dominant term.

If the field is applied perpendicular to the (102) face, then the observed conductivity will also be a composite. Using the same procedure as outlined above, the conductivity obtained in this direction is

$$\sigma_{\perp(102)} = 0.25\sigma_a + 0.5\sigma_{ac} + 0.25\sigma_c. \quad (6)$$

Thus, the conductivity measured perpendicular to the (102) face will have three components and the separation of these components cannot be achieved unless additional measurements are made.

It can be seen from the crystal structure of MT given in Fig. 1 that the conduction of protons by the mechanism proposed will be in a direction roughly parallel to the *b*-axis. Protonic conduction parallel to the *a*- or *c*-axis would correspond to a transport of protons between the layers of MT molecules, so that neither direction would be favored. If, however, $\sigma_{\perp(102)}$ is small in comparison to $\sigma_{\parallel(102)}$, the contribution of σ_a to $\sigma_{\parallel(102)}$ is also small, and $\sigma_{\parallel(102)}$ can be assumed to be approximately equal to $0.5\sigma_b$.

Experimental

Single crystals of MT were grown by slow evaporation of a saturated solution of MT in distilled and deionized water at 331°K. The MT used was of very high purity and was obtained from the Cyclo Chemical Company.

The major form of MT crystals obtained were transparent, colorless platelets (Fig. 3) with the (102) face predominant, and much less frequently, prisms with the forms {102}, {110}, and {100} developed were obtained. The MT crystals exhibited perfect cleavage parallel to the (102) plane. MT belongs to the $P2_1/c$ space group of the monoclinic class of crystals and has the unit cell dimensions: $a = 7.351$, $b = 12.091$, and $c = 7.602$ Å with $\beta = 89° 58'$ (*10*).

Crystals of suitable size for conductivity measurements were obtained with difficulty. Typical sizes of the MT platelets were 2.5 × 2.5 × 0.2 mm and 1.0 × 0.5 × 0.3 mm for prisms. The crystals were examined microscopically to ensure that only those free of visible defects were used for the conductivity measurements.

Measurements of the conductivities were made with the same cell and electrical apparatus as described previously (*8*), except that saturated aqueous solutions of MT were used as the proton-injecting electrodes. The crystal and apparatus were kept in a dessicated chamber for 12–24 hr prior to measurement to avoid contributions from adsorbed water. The measurements themselves were made in the dessicated chamber if the atmospheric humidity was greater than ~15%. The dessicant employed was $CaCl_2$ which will reduce the relative humidity to ~7%.

Crystals of MT with sufficient development of the {110} planes were not easily grown. Consequently, some of the measurements of the conductivity of MT parallel to the (102) plane were made with a crystal cut from a larger platelet crystal. The cut crystal was too small and fragile to be polished, but the cut faces were smooth enough to be used directly.

Results and Discussion

MT exhibited ohmic conductivity over the range of fields measured, up to ~20 kV/cm. The conductivity of MT was measured both parallel to the (102) plane, ∥(102), and perpendicular to it, ⊥(102). A typical current density-applied field characteristic for the conductivity of MT both ∥(102) and ⊥(102) is given in Fig. 4. The ohmic conductivity measured parallel to (102) was found to be equal to $2.4 \times 10^{-10} \pm 1.9 \times 10^{-10}$ $\text{ohm}^{-1}\,\text{cm}^{-1}$ (298°K), which is an average of trials conducted on two different crystals. This is somewhat larger than that found for 9-methyladenine (*8*) (see Table I) and is comparable to the conductivity of ice at 263°K (*20*). Although one of the crystals used was cut from a larger crystal, its conductivity was only slightly greater than the conductance measured across the natural crystalline faces in this direction. Therefore, it does not seem likely that the higher value can be attributed to defects generated during the cutting process.

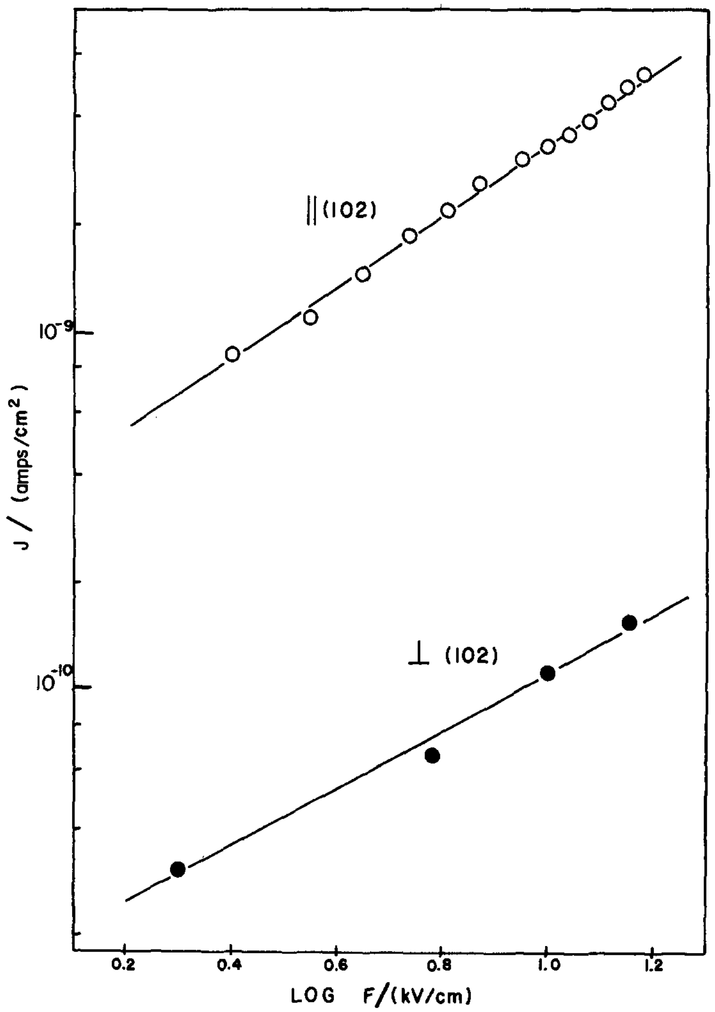


FIG. 4. A typical current density-applied field characteristic for MT measured parallel (○) and perpendicular (●) to the (102) plane at 298°K, with proton-injecting solution electrodes.

TABLE I

CONDUCTIVITIES OF SEVERAL PURINES AND PYRIMIDINES SINGLE CRYSTALS (298°K)

Compound	Direction of measurement	Grown from	Conductivity (ohm^{-1} cm^{-1})	σ_0 (ohm^{-1} cm^{-1})	E_a (kJ mole^{-1})	Reference
Thymine	∥*b*-axis	Vapor phase	$<2.6 \times 10^{-14}$	—	—	*22*
	∥*b*-axis	Methanol solution	$<2.6 \times 10^{-15}$	—	—	*22*
Thymidine	∥*c*-axis	Methanol solution	$<2.3 \times 10^{-13}$	—	—	*22*
9-Methyladenine[a]	∥(100)	Aqueous solution	2.5×10^{-13}	10^{-5}	51.5 ± 13.4	*8*
	⊥(100)	Aqueous solution	7.0×10^{-15}	10^{-2}	75.4 ± 19.0	*8*
Isocytosine[a]	∥*b*- and *c*-axes	Aqueous solution	$\sim 10^{-20}$	10^{-3}	85 ± 17	*23*

[a] Measurements made with proton-injecting electrodes.

The conductivities of the crystals were measured without guard electrodes due to their small size.

After the field was applied to the MT crystal, the current rapidly dropped from an initially high value and leveled-off to a stable, lower value. The stable value was achieved approximately 20 min after the application of the field and was taken as the conductivity. This type of polarization is often observed with ionic conduction, e.g., protonic conduction, and is taken as evidence for ionic conduction (*1*). This polarization has been attributed to space charges resulting from the accumulation of charged particles near the electrodes (*21*) or alternatively to dielectric displacement currents (*1*). When the applied potential is removed from MT, but the crystal electrodes are connected through the electrometer, a negative current is observed which decays in the same manner as the positive current and approximately the same or shorter times were required to reach a steady value, dependent upon whether the residual current was equal to or greater than the highest positive current measured. A similar response to the electric field was observed for the conduction of 9-methyladenine (*8*). Since the electrodes appear to be ohmic (see below) with no evidence for space-charge limited currents, it seems most reasonable to attribute the polarization to dielectric displacement phenomena.

The conductivity ⊥(102) was strictly ohmic over the same fields as those used in the parallel direction, as illustrated in Fig. 4, with a value of $1.0 \times 10^{-14} \pm 0.4 \times 10^{-14}$ ohm^{-1} cm^{-1} at 298°K. Measurements of the conductivity in this direction were made on three different crystals and the value of σ given represents the mean value of these measurements.

The magnitude of $\sigma_{\perp(102)}$ is comparable to the conductivity of 9-methyladenine observed perpendicular to the H-bonded plane (Table I) and is $\sim 10^4$ times lower than that obtained parallel to the (102) plane. The difference in magnitude of the conductivities indicates that the conduction of MT is anisotropic.

The ohmic conductivity of MT, either parallel or perpendicular to the (102) plane, was not markedly affected by an increase of surrounding water vapor pressure in the range from 10 to 50% humidity. However, humidities higher than 50% generally resulted in nonohmic behavior being observed at higher fields as well as an increase in the ohmic conductivity by a factor on the order of 10. The response to the applied field by the crystal was also affected, in that the current did not show as sharp a decay and instead of stabilizing at a particular value, reached a low value and then began to rise continuously with time. The appearance of nonohmic currents due to adsorbed water has been reported for other solids (*23*, *24*). If surface conduction due to adsorbed water were a major contributing factor to the observed conductivities, an increase of the ambient water vapor pressure should have resulted in much higher values of the conductivity than those actually observed. This absence of an increased conductivity (10 to 50% humidity) supports the conclusion that the reported conductivities are true bulk conductivities, and not surface conductivities. The observed anisotropy further substantiates this, since the presence of adsorbed water would have resulted in more isotropic values of the conductivity.

The temperature dependence of the conductivity was measured ‖(102) plane over the temperature range 292–341°K. The energy of activation ‖(102) was found to be 43 ± 10 kJ mole^{-1} (based on the measurements of one crystal). The Arrhenius plot depicting the temperature dependence of the conductivity of MT is given in Fig. 5. The energy of activation obtained is lower than that for the conduction in the analogous direction in 9-methyladenine (Table I) and may represent a difference in the conduction mechanism. The value measured is very similar to that obtained for protonic conductors and is very much smaller than that observed for electronic conduction in similar compounds (*8*).

Measurements of the temperature dependence of the conductivity ⊥(102) were unsuccessful and reproducible values could not be obtained. It is expected that the energy of activation for conduction ⊥(102) would be greater than that observed in the parallel direction because of the differences in room-temperature conductivities.

The magnitude of $\sigma_{\parallel(102)}$ is very much greater than $\sigma_{\perp(102)}$ and implies that the contribution of σ_a to the former must be quite small and can be neglected. Therefore, σ_b must

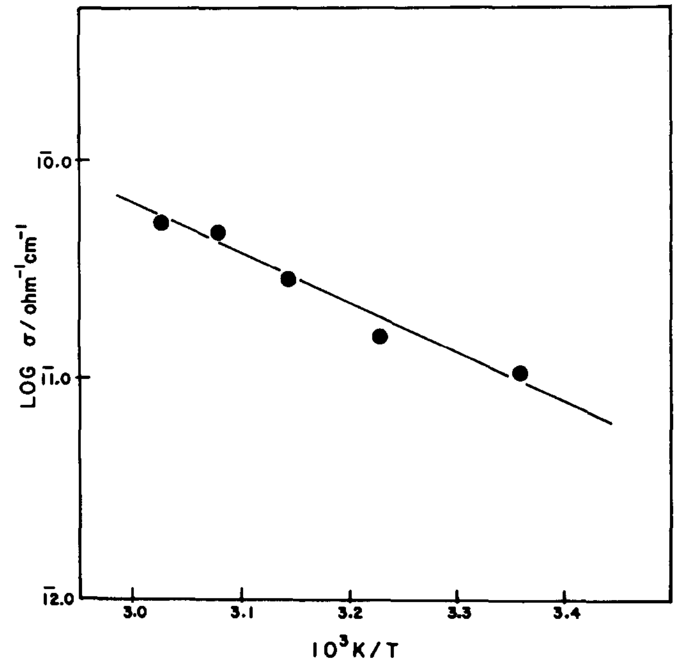


FIG. 5. The Arrhenius plot of the conductivity of MT measured parallel to the (102) plane with aqueous solution electrodes.

have a value of ~5 × 10^{-10} ohm^{-1} cm^{-1} and appears to be the major axis of conduction. Dehydration of several MT crystals showed the presence of traces of water in the crystals probably incorporated during the crystallization process, which may provide a mechanism for a protonic contribution to $\sigma_{\perp(102)}$.

Samples of MT crystals, when heated in an oven at 403°K for several days, showed an approximate 2% weight loss. This represents the presence of approximately three impurity water molecules for every 100 MT molecules or a concentration of 1 × 10^{21} molecules cm^{-3}.

It is very likely that the position of the water molecules, if incorporated within the crystal, are between the layers of MT molecules as they are in the hydrate of thymine, thymine monohydrate (*25*). The water molecules could then H-bond between O_8 and a lone pair situated on a N atom in an adjacent layer. The X-ray and neutron diffraction analysis would not have been sensitive enough to reveal the presence of impurity water molecules in the concentration indicated by the dehydration experiments.

Incorporation of water molecules into the MT crystalline lattice by processes other than those occurring during the crystallization, such as incorporation by diffusion of water from the aqueous electrodes, is not a strong possibility. Significant diffusion of water molecules into the crystalline lattice would require a larger planar separation between the MT molecules, since the planar separation of the thymine molecules in thymine monohydrate is 3.89 Å (*25*), as compared to 3.38 Å in MT. The larger separation in thymine monohydrate is wholly due to the hydrate water molecules, the separation returns to the normal van der Waals distance when the water molecules are removed. Thymine monohydrate dehydrates rapidly at room temperature indicating that the hydrate crystal structure is not a particularly stable one. Therefore, it does not seem likely that diffusion of water molecules into the MT crystalline lattice would occur to any extent during conduction measurements.

The σ_0 values for MT ∥ and ⊥(102) are 10^{-4} and 10^{-6} ohm^{-1} cm^{-1}, respectively. These values are analogous to those obtained for 9-methyladenine and isocytosine (Table I), which were measured uncut. Both values are lower than 10^{3} ohm^{-1} cm^{-1}, a value indicative of purely intrinsic protonic conduction, according to the criteria proposed by Schmidt (*26*), so that the conduction may arise from extrinsic sources, such as impurity water molecules as well as from intrinsic sources. A compressed powder sample of isocytosine exhibited a conductivity comparable to that of MT, i.e., 10^{-11} ohm^{-1} cm^{-1} (303°K), but its value of σ_0 was 10^{6} ohm^{-1} cm^{-1} (*23*). High values of σ_0 are associated with samples which are defective, i.e., cracked or polycrystalline (*26*). Therefore, the low value of σ_0 indicates the conduction is not due to defects such as microcracks in the crystal.

The ohmic conductivity of MT ∥(102) plane is greater than that obtained for single crystals of the structurally similar compounds, thymine and thymidine, as given in Table I. The conductivity measurements of thymine and thymidine were made using silver-paint electrodes and displayed conductivities that were ohmic over the voltage range employed, i.e., up to 1.25 kV cm^{-1}. The energy of activation of the conduction process was not determined so that it is not possible to compare it to the value obtained for MT.

The conductivities of thymine and thymidine measured as compressed powders are very similar to the values reported for the single crystals (*27*), 1.1 × 10^{-15} and 10^{-11}–10^{-13} ohm^{-1} cm^{-1}, respectively, which are considered to be electronic. The conductivities of adenine and adenosine measured as compressed powders are 5.9 × 10^{-17} (*28*) and 10^{-15} ohm^{-1} cm^{-1} (*27*), respectively. Based on these data, the conductivities of thymine compounds appear to be about 10^{2}–10^{3} times greater than that of the adenine compounds. This correlates to the difference found between the conductivities of 9-methyladenine and MT single crystals measured parallel to the H-bonded planes.

The difference in the conductivities of adenine and thymine compounds can be related to the differences in the structure of the two compounds and, possibly, to the types of H-bonding involved. It is also of interest to consider if their conductivity difference can be related to functional differences of the two types of compounds in a biological system. Riehl proposed that protonic conduction in macromolecules comprised of nucleotide bases could function in the human memory system in the same manner as "memory switches" in a computer (*7*). If such were to be the case, differences in the nucleotide molecular ratios in a DNA or RNA macromolecule, resulting in different magnitudes of conductivity, could serve as a means of differentiation between the separate bits of information. Riehl's hypothesis correlates with earlier theories of the chemical process of memory that proposed that permanent changes in the ratios of the nucleotide bases in RNA molecules in brain cells occurred upon the storage of long term memory (*29–31*). Evidence has been accumulated that RNA changes in the brain nerve cells accompany learning and these changes are unique to the learning task. This has led to the development of a more detailed hypothesis of the chemical changes involved in the memory and learning process (*32–34*). In part, this hypothesis proposes the activation or modification of a DNA molecule in some way so as to produce new types of RNA molecules, which go on to participate further in the memory process; these new types of RNA molecules have a specific and unique nucleotide base ratio. The modification of DNA, which determines the synthesis of the RNA molecules, must therefore be unique to the bit of information to be encoded. It may be possible that structural differences of the purines and pyrimidines that make up the nucleotide bases, reflected in properties such as the conductivity or the ability to transport protons, may play an important role in such a process. The actual function of DNA and RNA macromolecules in the memory storage and retrieval process is still, however, largely unknown.

In summary, it would appear likely that MT is capable of protonic conduction. The observed anisotropy of the conductivities and the observed energy of activation parallel to (102) is consistent with protonic conduction and the mechanism proposed. Furthermore, the energy of activation is of the magnitude expected for protonic conductors, and is lower than that expected for electronic conduction. The lack of nonohmic behavior in the conductivity of MT suggests that proton-injection may not be as important as thermally produced protons. It is possible that the impurity water molecules in MT could serve as sources of protons for the conduction process and thereby increase the magnitude of the conduction. Such proton sources would not have been available in the thymine single crystals since they were not grown from aqueous solutions (Table I). The concentration of the impurity waters has been shown to be small, so that the conductivity would still be governed by the H-bonded structure of MT and could not be due to H-bonded chains of water molecules. Since water is an ever present constituent of living systems, extrinsic sources of protons should always be available in a biological system so that the biological relevance of the protonic conductivity of compounds such as MT may be enhanced if such extrinsic sources partially contributed to the conductivity.

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