Vapor Pressure of Molecular Crystals. XIII. Vapor Pressure of α-Glycine Crystal. The Energy of Proton Transfer

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Glycine is the simplest amino acid, having the zwitterion configuration within the crystal lattice[1]. Three modifications have been reported[2] and the α-form is probably the most stable one at room temperature. The molecular structure of glycine in the vapor phase is not known probably owing to low vapor pressure of the crystal. If glycine sublimes with the molecular configuration (and not the zwitterion configuration), a proton must be transferred from an NH_3^+ group of a zwitterion to a COO^- group of the neighboring zwitterion in the crystalline state. Or, in an alternative way, the proton transfer must occur in the vapor state after the zwitterion has sublimed, and this transfer undoubtedly accompanies greater energy change than it would in the crystalline state[3]. On the other hand, if the sublimation does not accompany the proton transfer, the heat of sublimation would be as great as that of an ionic crystal. The present study aims at the energetics of sublimation, with a hope of obtaining some information about such

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[1] G. Albrecht and R. Corey, *J. Am. Chem. Soc.*, **61**, 1087 (1939); H. Baba, et al., *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **70**, 333 (1949); K. Kuratani, ibid., **70**, 453 (1949).

[2] Y. Iitaka, *Proc. Japan Acad.*, **30**, 109 (1954); J. Bernal, *Z. Krist.*, **78**, 363 (1931).

[3] R. W. Gurney, "Ionic Processes in Solution", McGraw-Hill, N. Y., 1953.

proton transfer. The determination of the relative stability of the modifications of glycine crystals by measurements of vapor pressures presents another interesting problem but will not be considered here.

Experimental

Material.—Glycine (Organic Synthetic Chemicals Co., special grade) was recrystallized from aqueous solution repeatedly and dried over phosphorus pentoxide. The more satisfactory method of drying crystals by vacuum sublimation was not applied because it was found that sublimation gave a mixture of α and γ form of glycine. The modifications were identified by use of the X-ray powder diffraction patterns. Occlusion of water within the crystal lattice may cause a serious error in the measurement of vapor pressure[4] and it is highly probable particularly when we deal with crystals of polar molecules. Pieces of glycine crystals, of the same batch as that used for the pressure measurements, were heated in vacuo to see if the occluded water was present, with the result that no water evolution was detected up to the decomposition temperature, ca. 230°C. The constancy of the vapor pressure at a fixed temperature during a fixed length of time, a few hours, was considered to provide another assurance.

Measurements of Vapor Pressures.—The sublimation pressure was measured between 138 and 153°C with an apparatus, the same as the one reported elsewhere[5], based on the Knudsen effusion method.

Results.—The vapor pressures are listed in Table I. These data well fit the vapor pressure equation

$$\log P(\text{mmHg}) = 13.666 - (6816.8/T)$$

obtained by the method of least squares. The heat, entropy and free energy of sublimation derived from the equation are given in Table II.

TABLE I

VAPOR PRESSURE OF α-GLYCINE

t°C	P(mmHg) $\times 10^3$	t°C	P(mmHg) $\times 10^3$
138.9_8	1.344	145.9_7	2.459
140.6_6	1.557	147.3_3	2.877
142.0_9	1.789	149.2_6	3.289
143.4_9	1.978	150.6_6	3.899
144.7_9	2.360	152.6_8	4.362

TABLE II

HEAT, ENTROPY AND FREE ENERGY OF SUBLIMATION

Heat	Entropy	Free Energy at 298.16°K
31.18±0.49 kcal./mole	49.33±1.17 cal./deg.mole	16.47±0.60 kcal./mole

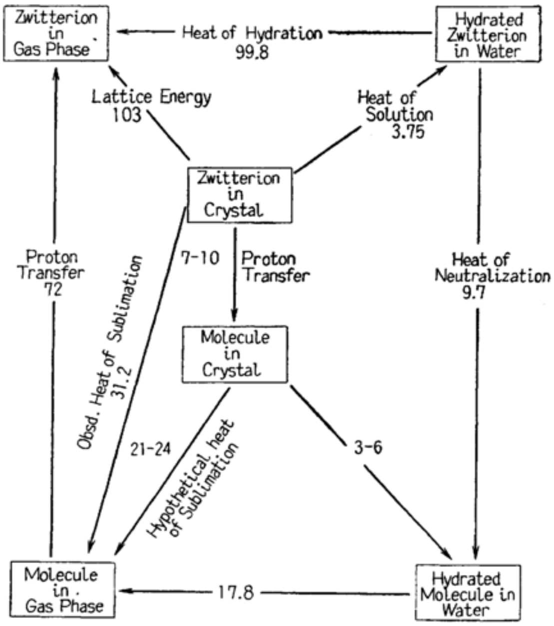

Fig. 1. Energy cycle of glycine (in kcal./mole). Arrows indicate the direction of endothermic changes.

Discussion of the Results

Fig. 1 illustrates an energy-cycle for glycine constructed by use of available thermochemical values. Arrows in Fig. 1 indicate the directions of endothermic changes. This is the final set-up of the energy diagram and we examined other possibilities also, because it was not a priori apparent that the measured heat of sublimation 31.2 kcal./mole corresponds to the change from ‘zwitterion in crystal’ to ‘molecule in gas phase’.

It was first assumed that the observed 31.2 kcal. is the change in heat content in going from the crystal to zwitterions in vapor; in other words this value represents the lattice energy of the crystal if allowance is made for the average kinetic energy of dipolar-ions in vapor. An independent estimate of the lattice energy of glycine has been reported by Shimura from the measured partial molal volume of glycine in aqueous solution by help of Kirkwood's theory on the free energy of hydration[6]. This estimate gives the lattice energy a value as great as 103 kcal./mole. The dipole moment of glycine determined by Buckingham[7] (13.3D) shows

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[4] S. Seki, H. Chihara and K. Suzuki, "Hydrogen Bond", Iwanami Co. (1956), p. 40.

[5] I. Nitta, S. Seki, M. Momotani and K. Sato, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **71**, 378 (1950).

[6] K. Shimura, *J. Agr. Chem. Soc. Japan* (*Nippon Nōgei-Kagaku Kaishi*), **24**, 412 (1951).

[7] A. D. Buckingham, *Australian J. Chem.*, **6**, 323 (1953).

that it is reasonable to assume that unit point charges rest on N and O atoms in a zwitterion so that the electrostatic interaction energy alone in the crystal would amount to about 60 kcal./mole. The total lattice energy including the van der Waals and the hydrogen bond energy will be at least 80 kcal./mole. Therefore our first assumption was wrong and the observed heat of sublimation must correspond not to the lattice energy but to the change in heat content in going from the crystal to molecules in vapor state.

Estimation of the heat of sublimation of a hypothetical crystal composed of glycine molecules, NH_2CH_2COOH.*—The van der Waals energy will contribute about 7.7 kcal. to this hypothetical lattice energy, which is the heat of sublimation[8] of 2-methyl-1-butene, a molecule which is isoelectronic with glycine. The following energy values are assigned to the three hydrogen bonds: 5~6 kcal. for the NH···O 2.76Å long (in diformylhydrazine[9] 2.80Å), 2.5~3.5 kcal. for the bifurcated bonds 2.93 and 3.05Å long (in urea[9] 2.99 and 3.04Å) and 3~4 kcal. for the bond of intermediate length 2.88Å. The sum of all these energy values 20.7~24.7 kcal./mole will be taken as the hypothetical heat of sublimation of molecular crystal of glycine**.

The energies of proton transfer.—By combining the hypothetical heat of sublimation with the observed heat of sublimation 31.2 kcal./mole, we see that the zwitterion crystal is more stable than the molecular crystal by about 7~10 kcal./mole, or in other words a proton transfer in the crystal (a change from $N^+H\cdots O^-$ to $OH\cdots N$) would accompany a heat absorption of 7~10 kcal./mole. If the proton transfer occurred in vapor state, the change

$$NH_2CH_2COOH \rightarrow NH_3^+CH_2COO^-$$

would accompany as much energy absorption as 72 kcal./mole and the "molecular" configuration would be extremely stable in vapor phase in contrast to the situation in the crystalline state. The result that the energy of proton transfer in vapor is about ten times as great as that in a crystal shows that the proton transfer can occur non-adiabatically in the crystal lattice: i.e. as a proton moves along the N···O bond by absorbing the necessary energy, the potential energy curve changes its shape as illustrated schematically in Fig. 2. The strong crystal field may be participating in such a change in the potential energy diagram. Thus the energy of proton transfer in crystal here obtained does not represent the energy for a single proton to move within a fixed "double minimum" potential field, but the energy required for the overall rearrangement of electronic charges in the entire volume of a crystal is included.

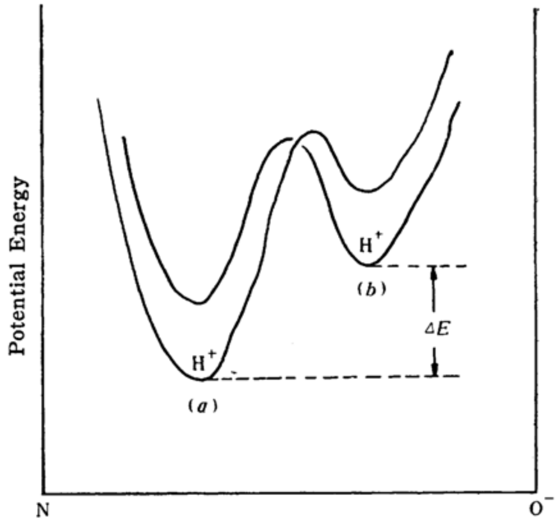

Fig. 2. Change of the potential energy curve in the course of proton transfer. ΔE is the energy of proton transfer (from *a* to *b*) in crystal.

This is a piece of information which we consider to be important in connection with energetics of hydrogen bonding. Participation of hydrogen bonding has often been assumed in various chemical reactions such as in simple hydrogen-deuterium exchange reactions and keto-enol isomerization reactions. Nuclear resonance studies in solution has come to attention of many investigators[10] in relation to the acid-base interaction and they will be one of significant methods of attack against proton transfer in solution.

Glycine is the simplest amino acid constituting complex protein molecules. In

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* By hypothetical it is meant that the crystal structure is the same as that of the zwitterion-crystal except for the position of a hydrogen atom; actually the OH···O bonds would be formed if the molecular crystal were more stable.

[8] S. S. Todd, G. D. Oilver and P. M. Huffman, *J. Am. Chem. Soc.*, **69**, 1519 (1947); D. W. Scott, G. Waddington, J. C. Smith and H. M. Huffman, ibid., **71**, 2767 (1949).

[9] K. Suzuki, S. Onishi, T. Koide and S. Seki, This Bulletin, **29**, 127 (1956).

** The range of uncertainty was taken wide enough in order to cover the limit of validity of discussions.

[10] J. N. Shoolery and B. J. Alder, *J. Chem. Phys.*, **23**, 805 (1955); E. Grunwald, A. Loenstein and S. Meiboom, ibid., **27**, 630, 641 (1957).

view of relatively small amount of energy required for a proton jump in a strong crystalline field, it may be reasonably supposed that such proton jumps can frequently occur in many protein systems with or without bound water molecules. Thus a diminishingly small degree of stimulation, given one end of a fibrous nerve protein coiled in a helical arrangement through NH···O hydrogen bonds, may easily be conveyed to the other end of that nerve protein by synchronous proton transfer. Such a mechanism, in fact, has been proposed by several authors[11] and we believe that we could here present some grounds for such speculative discussions.

The energy of proton transfer in vapor state may be very roughly evaluated by the sequence of changes:

$$NH_2CH_2COOH \xrightarrow[D]{} NH_2CH_2COO + H \xrightarrow[A]{}$$

$$NH_2CH_2COO^- + H \xrightarrow[I]{} NH_2CH_2COO^- + H^+$$

$$\xrightarrow[P]{} NH_3^+CH_2COO^-$$

D, A, I and P may be replaced by the bond dissociation energy of an O—H bond (110.2 kcal./mole), the electron affinity of an O atom (−87.7 kcal./mole), the ionization energy of a hydrogen atom (312.1 kcal./mole) and the proton affinity of an NH_3 molecule (−219 kcal./mole[12]), respectively. The overall change in energy will be 116 kcal./mole in comparison with 72 kcal./mole given in Fig. 1.

Estimation of the heat of self-neutralization in solution and other heats derived therefrom.—The process of self-neutralization in solution may be divided into two steps;

$$H_3N^+CH_2COO^- + H^+ = H_3N^+CH_2COOH - \varDelta H_a$$

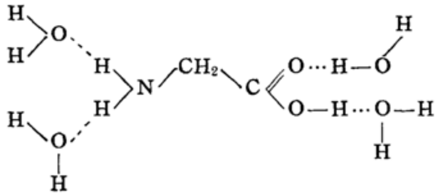
and

$$H_3N^+CH_2COOH = H_2NCH_2COOH + H^+ \quad + \varDelta H_b.$$

$\varDelta H_a$ can be evaluated from the temperature variation of pK_a, giving 1.16 kcal./mole[13]. $\varDelta H_b$ may be approximated by the heat (10.8 kcal./mole) associated with the change

$$H_3N^+CH_2COO^- = H_2NCH_2COO^- + H^+.$$

It is believed that this approximation will not cause a significant error since the reaction takes place in aqueous solution having the static dielectric constant larger than 80. The heat of self-neutralization will then be 9.7 kcal./mole (Fig. 1). This value was used to obtain the heat of solution of hypothetical crystals of molecular glycine 3~6 kcal./mole and the heat of solution of glycine vapor (heat of hydration) 17.8 kcal./mole, both giving a hypothetical solution of molecular glycine*. This is reasonable for a heat of hydration if we assume the hydrogen bond formation scheme like the following one:



The difference 82 kcal./mole between the heat of hydration of zwitterion in vapor and the heat of hydration of molecules in vapor (giving ionic and molecular solutions, respectively) is a rough indication of the effect of ionic charge on N and O atoms when placed in aqueous solution.

Concluding remarks. — The molecular-dipolar ion (zwitterion) relationship now demonstrated for glycine is by no means an exceptional case but may be found in other more familiar systems such as ammonium chloride decomposing into ammonia and hydrogen chloride in the vapor state. Here are apparently the proton jumps occurring in sublimation process, to which a formal analogy of the present treatment may be applicable. It will be interesting to examine the movement of protons or the rôle of hydrogen bonding in more complex amino acids or polypeptides by more-or-less direct means.

Summary

Sublimation pressures of crystalline α-glycine were measured between 138 and 153°C by the effusion method. The pressure equation

$$\log P(\mathrm{mmHg}) = 13.666 - (6816.8/T)$$

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[11] I. Oshida, Y. Oshika and R. Miyasaka, *J. Phys. Soc. Japan*, **10**, 849 (1955); M. L. Huggins, *Am. Scientist*, **31**, 338 (1943); N. Riel, *Naturwissenshaften*, **43**, 145 (1956).

[12] H. Tsubomura, private communication.

[13] E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides as Ions and Dipolar Ions", Reinhold, New York (1943), p. 80.

* This heat of hydration may be compared with the heat of hydration (7.8 kcal.) of propionic acid corrected for the difference in the interaction energy of a methyl group (3.4 kcal.) and that of an amino group (5.6 kcal.) with water, where it has been assumed that three water molecules accommodate to each of methyl and amino groups (cf. J. A. V. Butler, *General Discussion of the Faraday Soc. on the Structure and Molecular Forces in Pure Liquid and Solution*, 229 (1936));

$$7.8 + (3\times5.6) - (3\times3.4) = 14.4 \text{ kcal./mole.}$$

fits well the experimental data. The heat, entropy and free energy (at 25°C) of sublimation were 31.18±0.49 kcal./mole, 49.33 ± 1.17 cal./deg. mole and 16.47 ± 0.60 kcal./mole, respectively. An energy cycle was constructed which correlates zwitterion and molecule in crystal and vapor states, and hydrated zwitterion and molecule in solutions. The observed heat of sublimation corresponds to the change in heat content in going from the zwitterion-crystal to gaseous molecules. The molecular configuration is more stable in vapor state. By using the experimental values of the heat of sublimation, the heat of solution of crystals into water and the temperature dependence of pK_a in solution, with the help of the theoretical values of the lattice energy of the crystal, the following heat values were determined; the heat of proton jump in vapor, $NH_3^+CH_2COO^- \rightarrow NH_2CH_2COOH$, -72 kcal./mole, the heat of proton jump in the crystal 7∼10 kcal./mole, hypothetical heat of sublimation of crystals composed of molecules 21∼24 kcal./mole, the heats of hydration of a zwitterion and a molecule -99.8 and -17.8 kcal./mole, respectively, the heat of solution of the hypothetical crystal to give a solution of molecular glycine 3∼6 kcal./mole, and the heat of self-neutralization in aqueous solution 9.7 kcal./mole. The negative quantities show that the processes are exothermic. It was shown that the proton transfer in a medium of large dielectric constant or in a strong crystalline field requires only a small amount of energy and its significance in chemical reactions and biochemical activities was suggested. Each of the derived heat values was examined by independent checks from different sources, except for the energies of proton transfer.

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