Table V. The ^{31}P Magnetic Shielding Tensor for Some Phosphines and Phosphoryl Compounds

Molecule	$\Delta\sigma$, ppm[a]	σ_{11}, ppm[b]	$\sigma_{\perp}$, ppm[b]	Ref
PF_3	+181 ± 5	357 ± 5	175 ± 5	4
OPF_3	+284 ± 15	594 ± 15	260 ± 15	4
$P(CH_3)_3$	+7.63 ± 0.5	409 ± 5	401 ± 5	This work
$PO(CH_3)_3$	+173.6 ± 0.5	424 ± 5	250 ± 5	This work
$PS(CH_3)_3$	+111.6 ± 0.5	386 ± 5	274 ± 5	This work

[a] Experimentally measured parameter. [b] Absolute shielding scale is based on the PH_3 shielding tensor.[21,22] (See also N. Zumbulyadis, Dissertation, Columbia University, 1974.)

mdyn/Å, respectively) tend to support these findings. The increased bond order in F_3PO is associated with an increase in the cylindrically symmetric charge density around the P–O bond direction. One thus expects σ_{11} in F_3PO to be larger than σ_{11} in $(CH_3)_3PO$, as observed.

The observed difference in σ_{11} between F_3PO and $(CH_3)_3PO$ and the previously reported difference[4] between PF_3 and F_3PO suggest that trends in the individual screening tensor components of nuclei in similar environments bear a more direct correlation to the molecular electronic structure than the more commonly studied trends in the averaged isotropic part of the shielding tensor.

While this manuscript was in preparation Kennedy and McFarlane[20] published similar observations.

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Mass Spectrometer Study of Evaporation of α-Amino Acids

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Abstract: The NH_4^+ proton transfer mass spectra of 19 α-amino acids have been obtained by evaporation of 5–8-nmol samples from a rapidly heated Teflon surface. The protonated amino acid parents are observed in all samples and serve as the base peaks in all spectra but two. Time evolutions of fragment ions are coincident with those of the protonated parent in nearly all cases, indicating that deamination, dehydration, and loss of formic acid occur predominantly in the gas phase. Analyses of the rates of sublimation yield activation energies for sublimation ranging from 12 to 34 kcal/mol. Vapor pressures for the amino acids at the experimentally observed threshold temperatures for sublimation were estimated from the time evolutions of protonated parent ions. Enthalpies of sublimation derived from activation energies for rates of sublimation are used with literature values of heats of solution to calculate heats of aqueous solvation of the α-amino acids.

Mass spectrometric studies of the α-amino acids have been stimulated by a basic interest in their gaseous ion chemistry and the desire to develop a rapid sensitive analytical technique for determination of these biologically important compounds. Electron impact studies were originally carried out by Junk and Svec,[1] chemical ionization mass spectrometry by Milne et al.,[2] Leclerq and Desiderio,[3] Meot-Ner and Field,[4,5] and more recently by Tsang and Harrison.[6] Our interest in these compounds is more in consideration of them as a class of biologically important fragile molecules that present problems in nondestructive evaporation. Both analytical applications of mass spectrometry and basic research on gaseous ion chemistry of amino acids are limited by volatility problems.

We have investigated the evaporation of 19 underivatized α-amino acids from Teflon foil covered probes in a collision chamber of a tandem mass spectrometer. These data have been used to determine parameters of a Langmuir type kinetic vapor

pressure equation.[7] The activation energy for sublimation in the Langmuir kinetic vapor pressure equation is taken as the enthalpy of sublimation and used with available heats of solution of amino acids to calculate heats of solvation of these gaseous molecules. The preexponential term in the rate of sublimation equation is correlated with the entropy of activation of the rate process and provides information on the mechanism of the sublimation process.

The quality of data obtained in sublimation rate studies of amino acids is a sensitive function of sample purity which cannot be maintained if competitive decomposition or condensation processes occur in the course of the sublimation. Earlier studies of Svec and Clyde[8] using a Knudsen cell effusion method gave, in general, lower vapor pressures and higher heats of sublimation than the results obtained in this study. Inspection of mass spectra obtained by Svec and co-workers[1] clearly indicates that chemical reactions such as diketopiperazine formation, etc., provide mechanisms which both deplete the sample and alter the amino acid matrix composition from which the sublimation takes place. Both these factors can introduce error in measurement of vapor pressure equation parameters. For this reason, particular attention was devoted in this work to the use of rapid sample heating and gentle ionization techniques, which were used to demonstrate a much reduced extent of decomposition or condensation reactions competitive with the sublimation process. Errors associated with sample impurity generated in the course of sublimation will be discussed.

Experimental Section

Methods. The proton transfer, rapid heating technique used to generate mass spectra of amino acids has been described previously.[9] NH_4^+ reagent ions were generated in a high-pressure source located in the first stage of a tandem mass spectrometer. Amino acid samples (5 μL) were dispersed from dilute aqueous solutions of known concentrations onto a Teflon foil covered probe and dried in a stream of helium. Samples ranging from 0.3 to 30 nmol were then evaporated from the probe into a Teflon lined collision chamber ($\sim 10^{-6}$ Torr) with the sample probe heated at rates of 10–12 K/s. Ionization of the neutral species occurred by single NH_4^+ collision processes with primary NH_4^+ ion beam intensities of $\sim 10^{-9}$ A. Secondary ion mass spectra ranged in intensity from 10^{-15} to 10^{-18} A with no observable primary beam attenuation. Mass analysis of product ions was obtained with a computer-controlled quadrupole mass spectrometer programmed to scan preselected mass ranges with a minimum dwell time of 2 ms/mass bin. Mass spectra were stored in the computer memory as a function of time and sample probe temperature (measured by a copper–constantan thermocouple). Spectra were initially determined at unit resolution for the purpose of pseudoparent and fragment ion mass identification. Subsequent spectra in the vapor pressure and sublimation temperature coefficient studies were determined at ~3 mass unit resolution to increase sensitivity and reduce quadrupole mass discrimination. Satellite peaks due to the rare stable heavier isotopes of C, O, N, H, etc., are contained in appropriate ion intensities as well as appearing in sums of the normalized ion intensities. The total integrated signal-to-noise ratio in these spectra were 10^2–10^3 for a 5-nmol sample. A Bendix channeltron Model 4028 secondary electron multiplier served as the detector. A characteristic sample sublimation experiment involved ten scans each of approximately 1-s duration. Spectra were measured over a range of ~100 K with temperature intervals of ~10 K.

Chemical ionization (CI) mass spectra of selected amino acids were determined using NH_3 as the reagent gas in a spectrometer which used an Extranuclear Laboratories quadrupole mass analyzer with an off-axis Bendix channeltron detector. The sample probe design was modified to maintain the ~0.2-Torr pressure used in the CI source. The probe was inserted into a Teflon sleeve that provided a gas tight seal to the source housing sufficient to satisfy the differential pumping requirements of the CI source.

Materials. The NH_3 gas employed to generate NH_4^+ was Matheson anhydrous grade. The amino acids were purchased from commercial sources (Gly, Fisher; β-Ala, Sigma; D-Ala, Calif. Found. Biochem. Res.; DL-Val, (+)-L-Arg, DL-Met, Eastman Kodak; L-Tyr, K and K Labs; DL-Ser, Matheson; the remainder were Calbiochem A grade). The purity of the commercial amino acids was at least equivalent to Calbiochem A grade. Aqueous solutions of the respective acids were prepared at concentration levels of 1.0 mg/mL. Amino acid analysis of these samples revealed no cross contamination by other acids in excess of 3% (mol/mol).

Discussion of Errors. Errors in the determination of probe temperatures or errors associated with measurement of mass spectra as a function of pressure were investigated using anthracene. Anthracene, the subject of a number of independent investigations, is a very stable organic molecule not likely to undergo competitive decomposition or polymerization reactions during sublimation. Furthermore, its enthalpy of sublimation is in the same range (~20 kcal/mol) as temperature coefficients of sublimation determined for many of the amino acids. There were unanticipated difficulties with the anthracene calibration, in that it was much more volatile than the amino acids and sublimed over a lower temperature range. In addition the literature reported enthalpy values in two distinct ranges, ~20 and 23.5 kcal/mol, respectively. Our results were ~20 kcal/mol with a scatter in data indicating an error of $\sim \pm 2$ kcal/mol. This result is in excellent agreement with data of Wiedemann[10] measured over the range 250–400 K (20.1 kcal/mol) and with a number of earlier studies.[11,12] However, there are several studies,[13-15] most recently Taylor and Crookes,[15] which give a value of 23.5 ± 0.5 kcal/mol over a slightly higher initial temperature range of vapor pressures. In any event, the anthracene "calibration" shows that errors in the mass spectrometer assay of vapor pressures as a function of temperature are probably <3 kcal/mol.

A more significant potential source of error in determination of sublimation temperature coefficients arises from competitive chemical reactions in the solid sample taking place in the course of the sublimation. These chemical processes which can occur with the amino acids may be surface catalyzed. They deplete the sample and simultaneously alter the substrate molecule's environment in the solid, thus perturbing rates of sublimation.

Earlier work in this laboratory showed a significant variation in sublimation activation energies of the fragile tripeptide PCA-His-Pro-NH_2 (thyrotropin releasing hormone, TRH) when small samples were evaporated from a variety of supporting surfaces.[16] Teflon surfaces gave the lowest activation energies for TRH sublimation. This result was attributed to weaker binding interactions of TRH molecules with the Teflon than with glass, copper, or carbon surfaces. This argument breaks down when larger samples are used in sublimation experiments. Thus if a probe area of 0.01 cm^2 is covered with 10 nmol of sample, the surface could be covered with 10–100 molecular layers of substrate. Insensitivity of activation energies of sublimation to sample size ranging from ~1 to 30 nmol of amino acid suggest that the surface support is not directly correlated with the binding of substrate molecules to the supporting surface. An alternative explanation of the effect of Teflon as a surface support is in its inertness and inability to catalyze competitive reactions.

Examples of matrix effects which can perturb sublimation rates can be shown in the sublimation of tryptophan and methionine, respectively, from a urea lattice. The amino acids were deposited from solutions containing 16/1 and 20/1 mol of urea/tryptophan and urea/methionine, respectively. With methionine the activation energy for sublimation of matrix isolated molecules was 12 ± 3 kcal/mol, compared with 32 ± 2 kcal/mol for the pure compound. A much smaller reduction from 21 ± 2 to 18 ± 2 in the urea matrix was observed in the tryptophan study. In the case of tryptophan it is possible that some aggregation of the amino acid took place in the matrix. This is not likely in the case of methionine in view of the rather large change observed. It is clear that if decomposition or polymerization reactions were to take place to any significant extent in the course of sublimation, products of these reactions could produce matrix effects which could significantly alter rates and temperature coefficients of sublimation.

Efforts to observe such effects were made by varying sample size and rates of sample heating. Volatile products of decomposition might be detected via the time and temperature dependence of their mass spectra, if overall rates of decomposition and sublimation of reaction products differed from the sublimation rates of respective parent amino acid molecules. In general, fragment ions were found to have temperature coefficients of sublimation identical with parent species (results for tryptophan are shown in Figure 1). These results support the hypothesis that such fragments were products of unimolecular

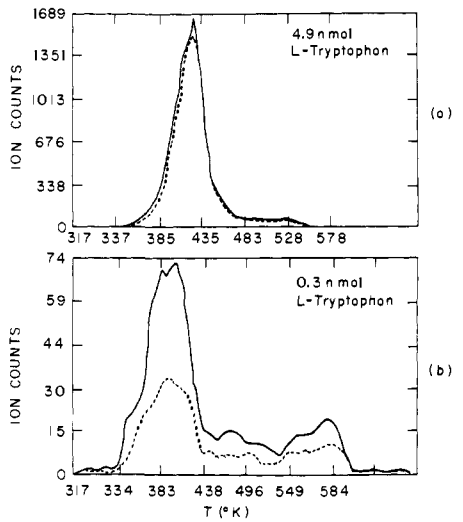

Figure 1. Time-(temperature) dependent evolution of ionic species originating from rapid heating (~10 K/s) of L-tryptophan samples. The solid line corresponds to the ion PH^+ (*m/e* 205) and the dashed line to the ion $PH^+ - NH_3$ (*m/e* 188).

gas-phase decompositions rather than surface reactions. An exception to this generalization was found in the case of L-glutamic acid. Figure 2 shows a displacement of intensity vs. time plots of fragment and parent ions in the L-glutamic acid spectrum. A reduction in heating rate from the usual 12 to 8 K/s shows substantially more evidence of surface dehydration with the probable formation of pyroglutamic acid.

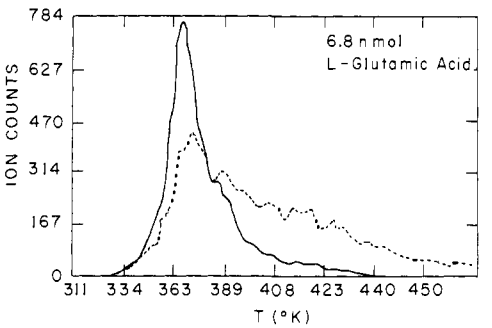

Figure 2. Time-(temperature) dependent evolution of ionic species originating from heating (~8 K/s) of an L-glutamic acid sample. The solid line corresponds to the ion PH^+ (*m/e* 148) and the dashed line to the ion $PH^+ - H_2O$ (*m/e* 130).

In general no other evidence for significant amounts of surface decomposition products that were detectable via temperature resolved mass spectra was obtained. Furthermore, there was no evidence of visible residues on the sample probe of material that could have been formed by polymerization or condensation reactions. Nor was there evidence for diketopiperazine formation or other condensations that would give volatile products detectable by mass spectrometry in these rapid heating experiments.

Results

Mass Spectra and Activation Energies for Sublimation. NH_4^+ ion impact mass spectra of those amino acid samples studied are tabulated in Table I. The relative intensities pre-

Table I. NH_4^+ Proton Transfer Mass Spectra of Amino Acids

Amino acid	%I_i							% ($\Sigma I_i/\Sigma I$)
	PH^+	$PH^+ - NH_3$	$PH^+ - H_2O$	$PH^+ - COOH_2$	$PH^+ - 2H_2O$	$PH^+ - NH_3 - H_2O$	Other species	
				Aliphatic Monoaminomonocarboxylic				
Gly	80.3			*r*			13.6[a]	93.9
β-Ala	71.3		24.8	*r*				96.1
D-Ala	98.0			*r*				98.0
DL-Val	75.4			14.8			9.9[b]	100.0
L-Leu	73.4			22.1			4.4[c]	99.9
				Aromatic				
L-Phe	79.0	1.6		17.9				98.5
L-Tyr	63.4	15.2		12.6		4.2		95.4
L-Trp	50.2	33.5		3.1			2.9;[d] 7.7[e]	94.5
				Hydroxyamino				
DL-Ser	70.0		5.0	18.2	2.3			95.5
DL-Thr	59.0		12.1	16.2	3.2		7.1[f]	98.6
				Dicarboxylic				
L-Asp	39.7	1.1	7.0	15.2			20.0;[g] 11.1[h]	94.1
L-Glu	32.6	2.0	39.1	6.9			16.7[f]	97.3
				Basic				
L-Lys	36.3	24.8	7.0	1.7			17.4;[d] 12.5[i]	99.7
(+)-L-Arg	5.9	20.3	12.3	3.8	6.8	7.6	28.0;[j] 7.3;[k] 1.2[l]	93.2
L-His	63.4	1.1	1.1	22.8			2.2;[f] 2.2;[m] 1.6[n]	94.4
				Sulfur Containing				
DL-Met	56.8	11.2		18.2			4.0;[o] 3.6[p]	94.7
L-Cys	71.0	6.2		9.6		4.3	4.3[q]	95.4
				Secondary				
L-Pro	70.3			26.7				97.0
				Acid Amide				
L-Asn	66.2	4.2	4.8	11.7		9.7		96.6

[a] $PH^+ - 28$. [b] $PH^+ - 38$. [c] $PH^+ - 52$. [d] $PH^+ - HCOOH - NH_3$. [e] $PH^+ - C_2H_5NO_2$. [f] $PH^+ - HCOOH - H_2O$. [g] $PH^+ - 52$. [h] $PH^+ - 60$. [i] $PH^+ - 67$. [j] $PH^+ - N_2H_4CO$. [k] $PH^+ - N_2H_3CO$. [l] $PH^+ - HCOO$. [m] $PH^+ - 65$. [n] $PH^+ - 67$. [o] $PH^+ - HCOOH - CH_3SH$. [p] $PH^+ - CH_3SH$. [q] $PH^+ - H_2S$. [r] Limit of lower mass is 45; thus loss of HCOOH is not observable.

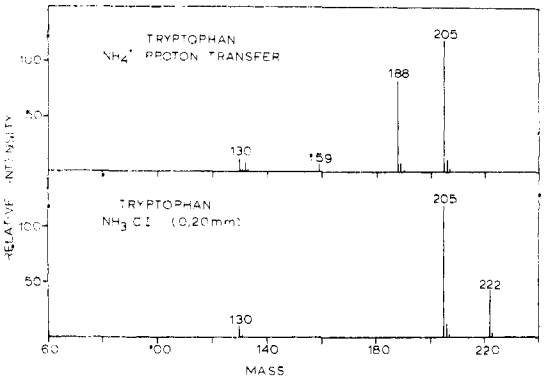

Figure 3. Comparison of NH_4^+ proton transfer (upper) and NH_3 chemical ionization (lower) mass spectra produced by rapid heating of 4.9-nmol samples of L-tryptophan.

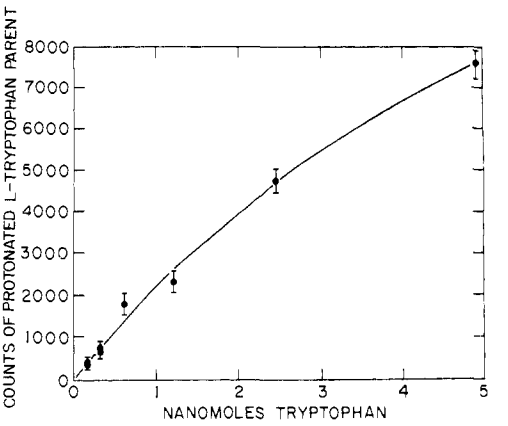

Figure 4. Sample size–ion count response curve obtained with L-tryptophan.

sented are the averages of at least two independent experiments. Agreement between the individual measurements was characteristically within 5%. The fragment species observed are in general agreement with the results of Milne et al.,[2] who have reported CH_4 CI mass spectra of many of the compounds studied herein. Ammonium ion proton transfer generally produces less fragmentation than the corresponding CH_4 CI experiment.

The NH_3 chemical ionization mass spectra of rapidly heated amino acids reveal a lesser degree of fragmentation than the corresponding NH_4^+ proton transfer spectra due to the gas-phase stabilization of the PH^+ species by neutral NH_3 collisions in the CI source. The NH_3 CI spectrum of tryptophan in Figure 3 illustrates this point. Data obtained with tryptophan presented in Figure 4 shows that in the range of 0.3–4.9 nmol the correlation of total PH^+ ion yield and sample size is excellent. If primary beam saturation were a problem, then larger samples would be expected to give integrated ion yields that would be smaller than values extrapolated from a correlation of smaller samples with total ion yield.

Further tests for reproducibility of measurements of the temperature dependence of the rates of sublimation of amino acids were made by varying the rate of heating. Samples of proline and phenylalanine were heated as rapidly as 10 K/s and as slowly as 5 K/min in separate experiments with no significant difference in experimental results. Activation energies for sublimation, evaporation threshold temperatures, and estimated values of the vapor pressures of the respective amino acids at their threshold temperatures are given in Table II.

The activation energies were evaluated from Arrhenius plots with data taken from the onset of sublimation to the maximum relative PH^+ intensity (see Figure 1). The temperature range over which sublimation could be studied before there was evidence of sample exhaustion was ~50 K. A typical plot of log PH^+ vs. $1/T$ for phenylalanine is given in Figure 5. Error limits for sublimation activation energies were derived from the scatter in these plots.

Vapor Pressures. Vapor pressures presented in Table II were estimated from the time required for complete sample sublimation of known sample sizes. The ratio of sample weight to time between the onset of evaporation and sample exhaustion gives an average value of the molecular flux, leaving the sample probe over the sublimation temperature range. This flux divided by the probe area and the mean molecular velocity yields a mean number density from which the average pressure at the probe tip can be computed. Assuming that the relative PH^+ ion intensity in the mass spectrum is directly proportional to

Table II. Amino Acid Kinetic Evaporation Parameters

Amino acid	E_a, kcal/mol	Threshold temp of PH^+ evolution, K	Pressure,[a] atm × 10^{10}	Log $A_{1.5}$[b]
Gly	23 ± 1	325 ± 3	4.6	8.40
β-Ala	25 ± 1	318 ± 5	4.9	10.13
D-Ala	25 ± 2	342 ± 8	4.3	8.81
DL-Val	19 ± 2	320 ± 5	3.1	5.76
L-Leu	20 ± 1	323 ± 4	2.5	6.23
L-Phe	21.5 ± 1.5	342 ± 4	2.8	6.37
L-Tyr	24 ± 2	412 ± 3	1.8	5.10
L-Trp	21 ± 2	340 ± 6	2.8	6.20
DL-Ser	20 ± 1	354 ± 6	2.0	4.85
DL-Thr	23 ± 2	341 ± 6	3.6	7.52
L-Asp	23 ± 1	370 ± 3	7.8	6.68
L-Glu	29 ± 1	353 ± 8	3.3	10.67
L-Lys	21 ± 2	397 ± 2	3.9	4.29
(+)-L-Arg	32 ± 2	441 ± 3	3.8	8.46
L-His	34 ± 2	392 ± 3	2.8	11.49
DL-Met	32 ± 2	363 ± 7	2.8	11.89
L-Cys	23 ± 1	337 ± 3	9.3	8.12
L-Pro	12 ± 2	323 ± 3	2.7	0.75

[a] Pressures are calculated for threshold T of evaporation. [b] Following Langmuir values of A in this equation were calculated using pressures in units of baryes (10^6 baryes = 1 atm).

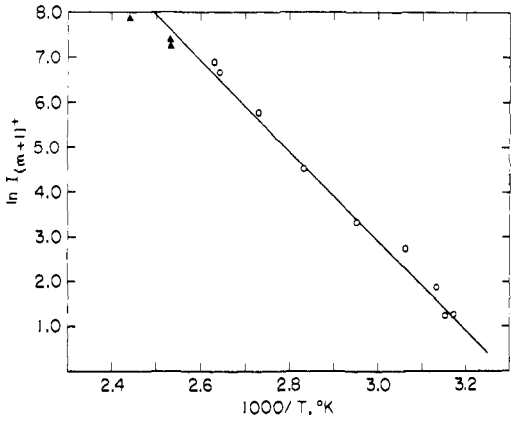

Figure 5. Plot of log $I_{(m+1)^+}$ as a function of reciprocal absolute T K for a 5-nmol sample of phenylalanine. Solid triangle taken near the crest of the sample evolution vs. temperature curve.

the pressure at the probe tip, differential elements of the PH^+ vs. time (temperature) plot can be used to determine the pressure at any temperature from the average value of the flux during the course of the sublimation. The vapor pressure estimate was made near the onset of evaporation, because this condition best satisfies the assumption that the probe surface was completely covered.

The method described above was used to estimate a vapor pressure of anthracene at 309 K of 2×10^{-5} Torr. This can be compared with values of 6.2×10^{-5},[10] 2.6×10^{-5},[13] and 3.0×10^{-5} Torr[15] calculated at 309 K from vapor pressure equations in previous work cited. From this comparison the vapor pressures measured for the amino acids are estimated to be accurate to within an order of magnitude over the experimental temperature range.

Discussion of Results

Determination of Heats of Solvation from Activation Energies. Interest in the energetics of biochemical processes in which amino acids are transferred from polar to nonpolar media (or the reverse) provides an incentive for investigation of amino acid heats of sublimation. The validity of the assumption that sublimation activation energies are equivalent to heats of sublimation in vacuum was recognized by Langmuir.[7] Langmuir established this equality from a kinetic model in which the rate of the reverse condensation process has a zero activation energy below a critical temperature.

The zwitterionic structure of amino acids in aqueous solutions and in the solid state is well established. There is little direct experimental data on gaseous amino acid molecules. Spectroscopic studies on the low-temperature matrix-isolated products of the sublimation of glycine supports the hypothesis that glycine has the classical molecular structure NH_2CH_2COOH in the gas phase.[17,18] Dielectric properties of amino acids in solution support the conclusion that amino acids in nonaqueous media exist as intermolecularly hydrogen-bonded classical species.[19] Junk and Svec[1] observed little or no $(P - CO_2)^+$ ions in the EI mass spectra of amino acids and attributed this to a gas-phase classical structure.

Ab initio calculations of Tse, Newton, Pople, and Vishveshwara[20] on glycine find the gaseous classical structure more stable than the gaseous zwitterion by 29 kcal/mol. This value can be used with the heat of sublimation of glycine and the heat of solution of glycine to calculate a heat of solvation of ~−48 kcal/mol for the gaseous zwitterion. Similarly a value of ~52 kcal/mol is derived for the heat of sublimation of glycine to gaseous zwitterion.

Heats of solvation of gaseous classical amino acids are presented in Table III, calculated from the differences between heats of sublimation (given in Table II) and heats of solution taken from Hutchens' compilation in the CRC Handbook of Biochemistry.[21] Hutchens noted limitations in the heats of solution, problems of questionable purity of materials, errors associated with heats of solution of hydrated amino acids rather than unhydrated crystals, etc. The data compiled by Hutchens show relatively small values for heats of solution at 298 K (~6–7 kcal/mol) and even large percentage errors in these data will not suffice to significantly alter the conclusion that energy of transfer of many of the gaseous amino acids to aqueous solution is ~20 kcal/mol. There are the exceptions of proline with an unusually low heat of sublimation and the more complex amino acids arginine, histidine, and methionine, with transfer energies estimated at ~30 kcal/mol.

Table III. Heats of Solution and Solvation of the Amino Acids: $\Delta H_{solution} - \Delta H_{sublimation} = \Delta H_{solvation}$

Amino acid	$\Delta H_{solution}$,[a] kcal/mol	$\Delta H_{solvation}$,[d] kcal/mol
Gly	3.8	−19.2 ± 1
D-Ala	1.8	−23.2 ± 2
DL-Val	1.4	−17.6 ± 2
L-Leu	1.0	−19.0 ± 1
L-Phe	2.8	−18.7 ± 1.5
L-Tyr	6.0	−18.0 ± 2
L-Trp	1.4	−19.6 ± 2
DL-Ser	5.2	−14.8 ± 1
DL-Thr		
L-Asp	6.0	−17 ± 1
L-Glu	6.5[b]	−22.5 ± 1
L-Lys	−4.0[b]	−25 ± 2
(+)-L-Arg	1.5[b]	−30.5 ± 2
L-His	3.3	−30.7 ± 2
DL-Met	2.8[c]	−29.2 ± 2
L-Cys	5.5	−17.5 ± 1
L-Pro	−0.8	−12.8 ± 2

[a] $\Delta H_{solution}$ (25 °C) values taken from "CRC Handbook of Biochemistry", 2d ed. 1970, p B-68. [b] $\Delta H_{solution}$ values are for D isomer assuming $\Delta H_{solution}$ (D isomer) ≅ $\Delta H_{solution}$ (L isomer). [c] $\Delta H_{solution}$ value for L isomer used assuming $\Delta H_{solution}$ (L isomer) ≅ $\Delta H_{solution}$ (DL isomer). [d] Error limits are based on estimated errors of ΔH_{sub} which have been taken at threshold temperatures of sublimation and not corrected back to 298 K.

Vapor Pressures of Amino Acids. The values of vapor pressures of the amino acid estimated from rates of evaporation of samples of known size are much less accurately determined than the heats of sublimation. Vapor pressures of the amino acids are in general lower than many organic molecular systems in the same range of molecular weights and with similar heats of sublimation. Anthracene, for example, is easily sublimed at room temperature with a heat of sublimation of ~20 kcal, while glycine, leucine, tryptophan, etc., having heats of sublimation in the same range of ~20 kcal/mol, have onset temperatures of sublimation at least 25 K higher. One must conclude that if one uses a kinetic vapor pressure equation of the type[7]

$$P = AT^{\gamma}e^{-b/T}$$

that the preexponential factor AT^{γ} is responsible for relatively lower vapor pressures of amino acids, when compared with anthracene for example. The vapor pressure equation above was used by Langmuir[7] with a value of $\gamma = 1.5$ to predict vapor pressures of the common elements from He to W with $\log A_{1.5} = 6.37 \pm 0.22$. The $A_{1.5}$ notation is used to designate the A factor for the value of γ used in the particular empirical vapor pressure equation. This value of $\log A_{1.5}$ applies to the evaporation of atomic liquids. For solids Langmuir showed that

$$\log A_{1.5_s} = \log A_{1.5_l} + 0.218f$$

where $f = \Delta H_f/T_f$ or the entropy of fusion. Langmuir's equation is an empirical equation and it differs in the value of γ from vapor pressure equations that are derived from equilibrium statistical thermodynamics in which the exponent of the temperature factor in the preexponential term should be $\frac{5}{2}$ rather than $\frac{3}{2}$. For the purpose of our discussion it should be noted that over a relatively narrow temperature range of ~50 K at temperatures of ~350 K, the error made by Langmuir in fitting his results with $\gamma = \frac{3}{2}$ rather than $\frac{5}{2}$ is trivial and is systematic in calculation of the values of the A factor in the vapor pressure equation. The point is that a constant value of log A for various elemental liquids is observed and this observation reflects a uniform value for the entropy of vaporization of these elements predicted by Trouton's or Hildebrand's rule.[22]

If the rate equation for evaporation is presented in terms of absolute reaction rate theory, the relation between the A factor in an Arrhenius type equation and the entropy of activation of the evaporation process becomes clear. The absolute rate equation for evaporation

$$k = (ekT/h)e^{\Delta S^{\ddagger}/R}e^{-E/RT}$$

shows the direct relation between log A and $\Delta S^{\ddagger}$.

Values of log $A_{1.5} = 6.4 \pm 0.2$ can be correlated with a normal or positive entropy of vaporization of atomic species. Langmuir noted that, with molecules with internal degrees of freedom, values of f as large as 122 might be expected. The upper limit of log $A_{1.5}$ depends on the complexity of molecular systems and very large positive entropies of sublimation are possible. Values below 6.0 for log $A_{1.5}$ are clearly anomalous and inconsistent with the increase in entropy expected for vaporization processes.

The data presented in Table II reflect well-behaved sublimation processes for most of the amino acids in terms of log $A_{1.5} > 6$. However, L-Lys, DL-Val, DL-Ser, and particularly L-Pro have log $A_{1.5}$ values that are lower than expected. In the case of L-Pro an error in vapor pressure of greater than five orders of magnitude is required to give log $A_{1.5}$ a value ≥ 6 if the value of the heat of sublimation determined experimentally is accepted. The possibility of experimental error or artifact must always be considered with isolated anomalous results. The proline data have been carefully checked and are reproducible, but analysis of the basis for the low preexponential term in its evaporation rate equation is speculative and will not be presented in this report.

Estimates of vapor pressure and values of enthalpies of sublimation obtained in this work are significantly lower than results reported in a study of Svec and Clyde.[8] Their work was based on weight loss measurements of samples of amino acid heated in a Knudsen cell. Under similar circumstances of temperature and metal supporting surface we have observed higher activation energies for sublimation of fragile molecules, TRH for example. Svec and his co-workers subsequently examined mass spectra of the vapor produced in their Knudsen cells and observed extensive evidence for condensation reactions which can account for errors in vapor pressure and enthalpy of sublimation determination in Knudsen cells.

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