Hydrophobic Interactions and Hydrogen Bonding of ε-Caprolactam in Aqueous Solution

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The forces which are responsible for the secondary structure of biologically important macromolecules are frequently most conveniently examined by studying small model compounds where the number of parameters is limited.[1] Among these forces hydrogen bonding and what has been termed hydrophobic interactions play a dominant role. The latter concept has been recently critically discussed from different viewpoints.[2,3] Lactams have been frequently used as model compounds to investigate the thermodynamics of amide–amide hydrogen bonding[4–7] by methods of infrared spectroscopy. Because infrared methods are based on the absorbance of free or hydrogen-bonded NH groups, they do not necessarily reflect the overall association of lactams which could, especially in aqueous environment, involve stacking of the hydrocarbon rings by nonpolar interactions. This communication describes results obtained through vapor pressure measurements of water–lactam systems. The data reflect in principle all interactions in the system, *i.e.*, hydrogen bonding as well as hydrophobic association. A comparison with results obtained by infrared spectroscopy should thus throw some light on the relative importance of different types of association under various conditions.

Experimental Section

Vapor pressures of ε-caprolactam–water mixtures were measured with a conventional mercury manometer of 15-mm inner diameter. The sample container and manometer constituted a single sealed unit. ε-Caprolactam (Aldrich Chemical Co.)[8] was purified by vacuum distillation. About 20 g of sample was used for each measurement. The sample was entered into the manometer system and frozen by cooling with liquid nitrogen. The system was then evacuated. The sample was repeatedly melted, refrozen, and the system reevacuated to ensure degassing. Subsequently the whole system was sealed under vacuum and placed in a constant-temperature bath, and the height of the mercury columns was read with the help of a cathetometer manufactured by Gaertner Scientific Corp. Four readings were carried out for every measurement. The manometer was shaken between each reading. The precision of the readings was of the order of 0.005 mm. All measurements were corrected for the temperature dependence of the density of mercury. The accuracy of the apparatus was checked by measuring the vapor pressure of pure water at 20–60°. The errors were within ±0.05 mm.

For hydrogen bonding studies near-infrared measurements were performed precisely as previously described for δ-valerolactam.[6] The results for both systems were identical within experimental error.

Results

Table I gives the observed vapor pressures of ε-caprolactam–water mixtures at various temperatures and concentrations. In Figure 1 the observed vapor pressures are plotted against the stoichiometric mole fraction of water at four different temperatures. The upper curves (positive deviation from linearity) are based on the stoichiometric concentration assuming monomeric lactam molecules; the lower curves (negative deviation) are based on the stoichiometric concentration assuming lactam dimers. One qualitative observation is immediately obvious from the lower curves; the solute appears to be essentially dimerized at low lactam con-

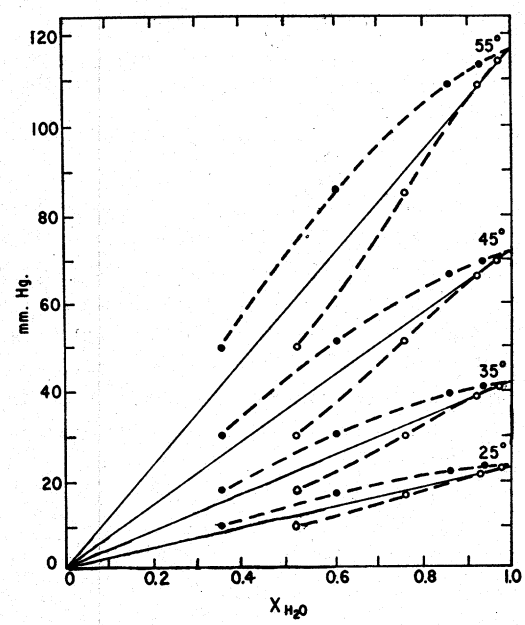

Figure 1. Vapor pressure of ε-caprolactam–water mixtures: upper curves, X_{H_2O} is stoichiometric mole fraction of water based on monomeric lactam; lower curves, X_{H_2O} based on total dimerization.

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(8) Mention of commercial items is for your convenience and does not constitute an endorsement over similar products by the U. S. Department of Agriculture.

Table I: Observed Vapor Pressures for the System ε-Caprolactam–Water (mm)[a]

Temp, °C	X_{H_2O},[b] 0.353	0.611	0.863	0.936
20	7.187	12.458	16.171	17.233
25	9.768	16.912	21.652	23.177
30	13.147	22.751	29.449	31.962
35	17.700	30.250	39.161	41.012
40	23.198	39.446	51.682	53.534
45	30.096	51.451	66.153	69.068
50	39.126	66.885	85.530	89.373
55	50.030	85.285	109.651	114.098
60	64.048	108.297	135.940	...

[a] Average value of four cathetometer readings, corrected for the density of mercury. [b] Stoichiometric mole fraction of water, based on monomeric lactam.

centrations ($X_{H_2O} > 0.9$). At higher lactam concentrations substantial negative deviations from linearity are observed. Although the system is too complex to base detailed conclusions on ideal behavior, apparent average molecular weights can be calculated on the assumption that deviations from linearity are primarily caused by association or dissociation of the lactam. At 25° the following numerical values are obtained: $X_{H_2O} = 0.35$, $\bar{M}/M = 1.28$; $X_{H_2O} = 0.61$, $\bar{M}/M = 1.57$; $X_{H_2O} = 0.86$, $\bar{M}/M = 1.93$; $X_{H_2O} = 0.94$, $\bar{M}/M \approx 2.0$.

Here X_{H_2O} is the stoichiometric mole fraction of water (based on monomeric lactam), $\bar{M}$ is the apparent molecular weight of lactam, and M is the molecular weight of the monomer. (The last value is somewhat uncertain because at high water concentrations the calculations are very sensitive to small changes in P/P_0.) The actual reasons for the negative deviations of the lower curves in Figure 1 at high lactam concentrations are evidently complex. Solute–solvent interactions most probably play an important role. Furthermore, for thermodynamic evaluations fugacities should be employed instead of vapor pressures, although this latter correction would be small. (Data for saturated water vapor are available above 60°;[9] at this temperature the fugacity coefficient is 0.995; at lower temperatures the value should be even closer to unity.)

The temperature variations of P/P_0 at the lowest concentration where evaluation was possible were too small to draw meaningful conclusions. At higher lactam concentrations (*e.g.*, $X_{H_2O} = 0.611$, Table I), P/P_0 increased slightly with temperature.

Discussion

By comparing the results of infrared measurements[6] with vapor pressure data, the following picture emerges: at high amide concentrations substantial amide-to-amide hydrogen bonding occurs even in the presence of water. K_X' has a value of ~0.72 (mole fraction)$^{-1}$ at 25°. This value, as evaluated from infrared data, is apparently independent of concentration; *i.e.*, the fraction of hydrogen-bonded lactam molecules decreases rapidly with decreasing concentration.[6] In dilute solution association through hydrogen bonding is negligible, and the high degree of dimerization, reflected in Figure 1, must take place by another mechanism, most probably through stacking of the hydrocarbon rings which is promoted by water. In Figure 2 a hypothetical vapor pressure curve constructed from infrared data (*i.e.*, based solely on dimerization through H bonding) is compared with measured vapor pressure values. At water concentrations up to *ca.* 0.3 mole fraction (based on monomeric lactam) hydrogen bonding predominates. The lowest measured vapor pressure value is close to the calculated curve. In the region between 0.3 and 0.9 mole fraction of H_2O the situation is complex. Above *ca.* 0.9 mole fraction of H_2O, nonpolar association predominates.

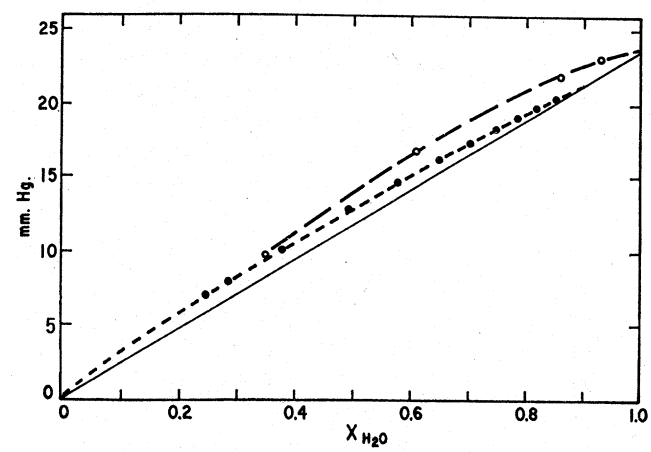

Figure 2. Experimental vapor pressure (open circles) and hypothetical vapor pressure if only H-bonding interactions were present (closed circles) at 25°.

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