reaction. Although a feasible attraction between two dipoles may stabilize the transition state of reaction 1, such a process requires a transfer of Na^+ with the electron and this substantially slows down the reaction,[4,5] particularly if both Na^+ ions have to be dissolvated in the transition state. Such a desolvation, which probably also takes place in disproportionation 2, involves only one Na^+ ion. Finally, reaction 3 is hindered by the repulsion of two negatively charged ions; its rate seems to be by four or five powers of ten slower than the rate of 2. A recent illustration of the importance of the repulsion in electron transfer reactions was provided by Abley and Halpern[6] who found the reaction $BPh_4^- + (IrCl_2)^{2-} \rightarrow BPh_4\cdot + (IrCl_6)^{3-}$ to be substantially slower than the reaction $BPh_4. + (IrCl_6)^{2-} \rightarrow BPh_4^+ + (IrCl_6)^{3-}$, in spite of the fact that the ionization potential of BPh_4^- is much lower than that of the $BPh_4\cdot$ radical.

The reverse reactions (1–3) are exothermic and could be expected to be very fast. Indeed, it is believed that the reverse of reaction 3 is diffusion controlled ($k_{-3} \sim 10^{10}$–10^{11} M^{-1} sec^{-1}). However, the reverse reactions 1 and 2 are relatively slow, $k_{-1} < 4 \times 10^4$ M^{-1} sec^{-1} and $k_{-2} = 3 \times 10^6$ M^{-1} sec^{-1}. It is probable that the change of the geometry of the donor[2a] (T^{2-},Na^+ or $T^{2-},2Na^+$) occurring on its oxidation to the radical anion accounts for the relatively low value of k_{-2} and a further decrease in the rate is expected for the reverse reaction 1 in which the tightly bounded Na^+ ion has to be transferred with the electron.

Finally we wish to report an interesting observation. Typical flash photolysis of T^{2-} in THF led to 20% bleaching of its absorbence. Under the same conditions the bleaching was not observed when dioxane was substituted for THF as a solvent. A similar effect was noted previously in the flash photolysis of sodium pyrenide.[3] Its flash photolysis led to 70–80% of bleaching when THF was used as a solvent, but under the same conditions only 5% of bleaching was observed when the reaction was performed in tetrahydropyran. Sodium pyrenide forms loose pairs in THF but tight pairs in tetrahydropyran, and this difference in the structure was proposed as an explanation of the above phenomenon.[3] Apparently a similar situation is encountered in the present case. The T^{2-} salt has different structure in THF and in dioxane and probably the aggregation is tighter in the latter solvent.

Acknowledgment. The financial support of this study by the Swedish National Science Research Council and the National Science Foundation (U. S. A.) is gratefully acknowledged.

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[5] *E.g.*, N. Hirota, R. Carraway, and W. Schook, *J. Amer. Chem Soc.*, **90**, 3611 (1968); earlier references are given in this paper.

[6] P. Abley and J. Halpern, *Chem. Commun.*, 1238 (1971).

Binding of Hydrogen Donors by Peptide Groups of Lactams. Identity of the Interaction Sites

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Abstract: Binding of hydrogen donors [CH_2Cl_2, CH_3OH, $CHCl_3$, water, and CH_3COOH (glacial)] by poly(1-vinyl-2-pyrrolidinone) and by its monomeric analog 1-ethyl-2-pyrrolidinone was studied by infrared, spin-echo, and viscosity measurements. Water is the most strongly bound, CH_2Cl_2 the weakest. Binding takes place not only at the carbonyl bond of the lactams but also involves the C–N bond which results in an appreciable decrease in the conjugation of the peptide linkage and loss of partial double bond character of the C–N bond. The data on 1-ethyl-2-pyrrolidinone show that a relatively large number of lactam–water species of different composition are formed rather than a well-defined complex as is generally assumed. Hydrogen donor binding by the polymer is weaker than by the monomer, possibly because of the interference of binding sites. The apparent failure of viscosity data to accurately predict the stoichiometry of solution complexes is pointed out.

The interaction between water and peptide groups has significant influence on such phenomena as the conformational behavior of polypeptides and other biological macromolecules,[1–6] the ionic selectivity of cells,[7,8] and the characteristics of membranes for reverse osmosis processes.[9] It is the purpose of this paper to explore certain aspects of the nature and identity of the sites of these interactions; we will propose, for instance, that the C–N bond of N,N-disubstituted amides is also an active binding site and that, consequently, the mesomerism of the peptide linkage[10] is significantly shifted in the presence of hydrogen donors such as water, alcohol, and chloroform (see eq A).

As model substances for our work we have chosen poly(1-vinyl-2-pyrrolidinone), abbreviated PVP (see

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[1] S. Krimm and C. M. Venkatachalam, *Proc. Nat. Acad. Sci. U. S.*, **68**, 2468 (1971).

[2] C. A. Swenson and R. Formanek, *J. Phys. Chem.*, **71**, 4073 (1967).

[3] H. Strassmair, J. Engel, and S. Knof, *Biopolymers*, **10**, 1759 (1971).

[4] M. M. Breuer and M. G. Kennerley, *J. Colloid Interfac. Sci.*, **37**, 124 (1971).

[5] H. Susi, J. S. Ard, and R. J. Carroll, *Biopolymers*, **10**, 1597 (1971).

[6] M. P. Printz, H. P. Williams, and L. C. Craig, *Proc. Nat. Acad. Sci. U. S.*, **69**, 378 (1972).

[7] S. L. Baird, Jr., G. Karreman, H. Mueller, and A. Szent-Györgyi, *ibid.*, **43**, 705 (1957).

[8] R. Damadian, M. Goldsmith, and K. S. Zaner, *Biophys. J.*, **11**, 761 (1971).

[9] D. Vofsi and O. Kedem, Report No. 591, Office of Saline Water, U. S. Department of Interior, Washington, D. C., Dec 1970.

[10] B. Pullman and A. Pullman, "Quantum Biochemistry," Wiley, New York, N. Y., 1963, p 296.

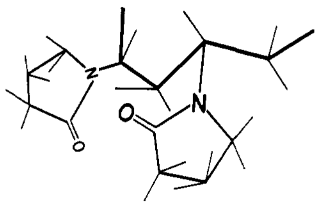
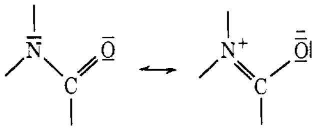


Figure 1. Structure (schematic) of poly(1-vinyl-2-pyrrolidinone).



(A)

Figure 1), a polymer of unusual binding properties[11] and hydrophilicity,[12,13] and its monomeric analog, 1-ethyl-2-pyrrolidinone. Because of the tertiary nitrogen, *direct* inter- and intramolecular hydrogen-bonding effects, which would make a study of peptide group–water interactions much more complicated, are absent. Study of the binding characteristics of the monomeric analog is not only advantageous in cases where the long chain length (and thus high viscosity) of the polymer would be experimentally cumbersome, but also permits us to draw some conclusions on interference effects by adjacent binding sites.

Our experimental techniques involved measurements of translational mobilities by a spin-echo method, infrared spectral analyses of the lactams as well as of the hydrogen donors, and the determination of solution viscosities. From the translational mobilities and the solution viscosities we obtain information on the relative strength of solvent binding and on the complexity of the predominant solution equilibria, whereas the infrared data permit us to identify the actual binding sites and to characterize the most important substrate–ligand interactions.

Experimental Section

Self-Diffusion Measurements. The translational mobilities of CH_2Cl_2, CH_3OH, H_2O, and CH_3COOH (glacial) in PVP as well as of H_2O in 1-ethyl-2-pyrrolidinone and of 1-ethyl-2-pyrrolidinone in D_2O were determined by a spin-echo technique[14] as described in detail previously.[15] (D_2O avoids the difficulties arising in water-poor solutions from separating the signals of the nitrogen-bonded CH_2 group protons of the lactam and of the water protons.) All determinations were performed at 30°.

Infrared Spectral Measurements. The scans were performed with Perkin-Elmer spectrometers, Models 521 and 180, using a Beckman variable-path cell with KRS-5 windows, and a reference beam attenuator. For the experiments displayed in Figures 5 and 6, the cell path was adjusted to give as closely as possible the same peak absorbance. (The strong intensity of the C=O fundamental did not permit much flexibility in the absorption measurements.) The temperature of the cell was about 30°.

Viscosity Determinations. The measurements were performed at 22.8° with the help of calibrated Cannon viscometers.[16]

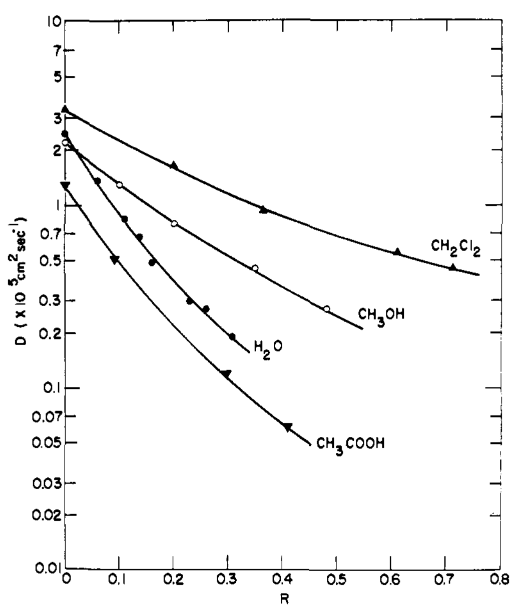


Figure 2. Self-diffusion coefficients of CH_2Cl_2, CH_3OH, H_2O, and CH_3COOH (glacial) in poly(1-vinyl-2-pyrrolidinone) as a function of *R*, the number of monomeric chain units per molecule solvent (temperature 30°).

Materials and Sample Preparations. PVP (K-30), Matheson Coleman and Bell, and 1-ethyl-2-pyrrolidinone, Aldrich Chemicals Co., were used. The PVP was of wide molecular weight distribution (by gel permeation chromatography) with the main peak at $\bar{M}_{\rm rms}$ = 12,000 and a weak side peak near $\bar{M}_{\rm rms}$ = 230,000, $\bar{M}_{\rm w}/\bar{M}_{\rm n}$ = 2.2. It was dried at 60° *in vacuo*. Ethylpyrrolidinone was desiccated by first distilling from it anhydrous EtOH (dried with Mg file turnings) and subsequently distilling the lactam at atmospheric pressure.

Handling, filling, and weighing were done in a drybox. For our purposes, we considered the drying procedures satisfactory if no water absorption was discernible in the fundamental O–H stretching region of the pure samples.

The use of D_2O (99.8%) was indicated since the bending fundamental of H_2O nearly coincides with the carbonyl stretch of the lactams.

Concentrations. Compositions of the polymer solutions is given by *R*, the number of monomeric chain units per molecule solvent.

Results and Discussion

1. Self-Diffusion and Viscosity. The results of the self-diffusion and viscosity measurements are shown in Figures 2–4. Of these, Figure 2 displays the comparison of the concentration dependence of solvent self-diffusion (translational mobility) in the four solvent–PVP systems. Figures 3 and 4 deal with the 1-ethyl-2-pyrrolidinone–water system and display the solution viscosity (Figure 3) and the self-diffusion coefficients of the constituent molecules (Figure 4).

From an inspection of Figure 2 it is evident that water plays a special role in these PVP–solvent systems. Water is by far the smallest molecule of the set (2.6 Å diameter), followed in increasing size by CH_3OH (3.6), CH_3COOH (about 4.2), and CH_2Cl_2 (4.9).[17] Yet, the water molecules are seen to experience motional hindering (decrease of self-diffusion) which is as great as that exhibited by the much larger CH_3COOH molecules.

In order to draw the correct conclusions from these diffusion data, it is necessary to worry first about the

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(11) J. L. Azorlosa and A. J. Martinelly in "Water-Soluble Resins," R. L. Davidson and M. Sittig, Ed., Reinhold, New York, N. Y., 1968, Chapter 7.

(12) H. K. Lonsdale, R. L. Riley, L. D. LaGrange, C. R. Lyons, A. S. Douglas, and U. Merten, Report No. 484, Office of Saline Water, U. S. Department of Interior, Washington, D. C., Dec 1969.

(13) R. L. Riley, C. R. Lyons, and U. Merten, *Desalination*, 8, 177 (1970).

(14) E. O. Stejskal and J. E. Tanner, *J. Chem. Phys.*, 42, 288 (1965).

(15) W. G. Rothschild, *ibid.*, 55, 1402 (1971).

(16) J. R. Van Wazer, J. W. Lyons, K. Y. Kim, and R. E. Colwell, "Viscosity and Flow Measurements," Wiley, New York, N. Y., 1963, Chapter 4.

(17) R. A. Svehla, NASA Technical Report R-132, 1962. The value for CH_3COOH is estimated to be 0.84 of the diameter of CH_3COCH_3; the numerical factor 0.84 represents the ratio of the diameters of CH_3OH and CH_3OCH_3.

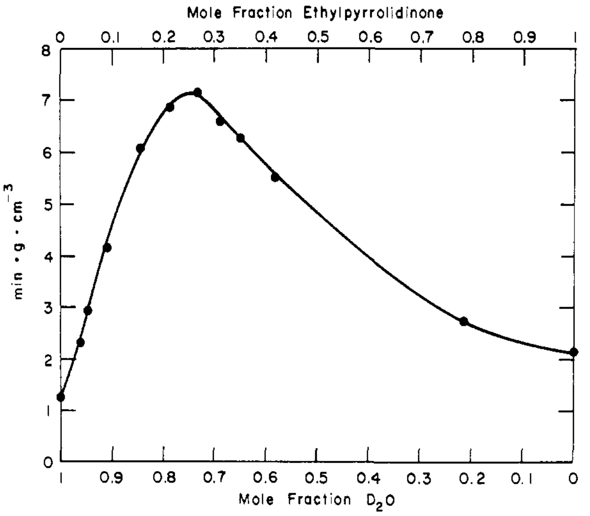

Figure 3. Relative viscosity (effluent time × density) of solutions of 1-ethyl-2-pyrrolidinone and D_2O as a function of composition (temperature 22.8°).

"time of measurements" since this time interval determines the degree of detail with which we can describe the particular dynamical molecular processes.[18] In this respect, it is not difficult to realize that the observed random translational motion of the solvent molecules is an average over the proportions which arise from molecules which are (i) trapped in the cage of the solvated polymer coils,[19] (ii) "bound" specifically by the peptide groups of the coils, and (iii) diffusing in regions between the polymer molecules ("free solvent").[19] In order to see this, we merely relate the measured solvent self-diffusion coefficient D (say, 10^{-5} to 10^{-6} cm^2 sec^{-1}, from Figure 2) with the mean-square displacement $\langle l^2 \rangle$ of the solvent molecule, using the well-known relation

$$D = \langle l^2 \rangle / 6\tau$$

where τ is the corresponding time of observation. Values of τ for our spin-echo measurements are typically of the order of fractions of second;[14] hence, under these conditions (for instance τ = 50 msec), the observed molecule has traveled a (root-mean-square) distance of

$$\langle l^2 \rangle^{1/2} \sim 10^5 \text{ Å}$$

which is larger than the dimension of the solvated polymer coils by about two to three orders of magnitude.[20] Thus, the diffusion data *per se* do not permit a distinction to be made among the different solution environments seen by the diffusants.

On the other hand, viscosity measurements on dilute solutions of these systems (not shown here) indicate that water is the best solvent;[21] therefore, the radius of gyration of the solvated polymer coils should be the largest in the system PVP–water,[20] at least in dilute solutions where this concept has meaning. Consequently, hindering of the translational mobility of solvent which solely arises from molecules trapped within the polymer coils in dilute PVP solutions (environment i above) should be the least for water and the most for CH_2Cl_2 (the poorest solvent).[21] Since Figure 2 shows the opposite behavior, we must conclude that the *specific* interactions between water and the peptide groups of PVP are relatively strong. In fact, comparison of the self-diffusion data shown in Figure 2 with the corresponding measurements in the nonpolymeric system ethylpyrrolidinone–water (open circles in Figure 4) indicates that the decrease of the self-diffusion coefficient of water below a concentration ratio of $R \sim 0.1$ (>0.9 mol fraction of water) is about identical in the polymeric and in the nonpolymeric systems. Notably, within this concentration range, the self-diffusion of water (and thereby its translational mobility) has dropped to less than one-half of the value of pure water; we thus see that the hindering effects on water mobility by physical trapping in the cages of the polymer coils is not observed to be significant in a concentration range $R < 0.1$. Speculatively, this might indicate that the PVP chains prefer a more "linear" conformation in dilute aqueous solutions.

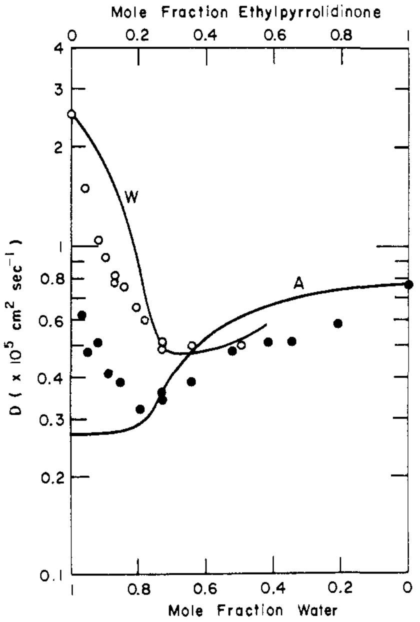

Figure 4. Self-diffusion coefficients of H_2O in 1-ethyl-2-pyrrolidinone (open circles) and of 1-ethyl-2-pyrrolidinone in D_2O (solid circles) as a function of solution composition (temperature 30°). The solid curves are the computed values for the water (W) and the lactam (A) on the basis of a hypothetical equilibrium AW_3 complex (see text).

We now concentrate on the corresponding results in the system 1-ethyl-2-pyrrolidinone–water, which offers greater detail since the manifestations of the specific water–peptide group interactions are not suppressed by a high solution viscosity, particularly in the water-poor concentration range. In this respect, Figure 3 reveals that the solution viscosity in the nonpolymeric system has a pronounced maximum at 0.25 mol fraction of lactam; the viscosity at this maximum is higher by a factor of about 5 than the mean of the component viscosities. As can be seen from Figure 4, the counterparts of this viscosity maximum are (i) a

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[18] W. G. Rothschild, *J. Chem. Phys.*, 57, 991 (1972).

[19] C. Tanford, "Physical Chemistry of Macromolecules," Wiley, New York, N. Y., 1961, p 343-344.

[20] See ref 19, section 10.

[21] B. Vollmert, "Grundlagen der Makromolekularen Chemie," Springer-Verlag, West Berlin, 1962, p 309.

minimum in the self-diffusion coefficient of 1-ethyl-2-pyrrolidinone (solid points) and (ii) the onset of zero-rate decrease (with increasing lactam content) in the self-diffusion coefficient of water (open circles).

It is tempting to ascribe these observations to the formation of a lactam–water 1:3 "complex." Nothing, of course, can be said at this point about the configuration of such adduct, the exact site of bonding, and its lifetime. We assume, however, that the lifetime of a given configuration is much shorter than the time of our measurements (see above). We then write down a simple two-state model of solvent mobility in which the measured self-diffusion coefficient D is the sum of the contributions from "unbound" (D_f) and "bound" (D_b) compound.

$$D^w = x_f^w D_f^w + (1 - x_f^w)\, D_b^w \qquad (1a)$$

$$D^a = x_f^a D_f^a + (1 - x_f^a) D_b^a \qquad (1b)$$

Here, x_f is the fraction of unbound molecules; the superscripts w and a refer to water and lactam, respectively. (It should be noted that the mole fractions x_f and x_b do not refer to the total number of molecules in the solutions but to the total number of water or lactam molecules.) Clearly, $D_b^w = D_b^a = D_b$, where we drop the superscripts from now on.

Numerical evaluation of eq 1 for the analytical solution composition at the hypothetical lactam–water 1:3 complex ($x_f^a = x_f^w$) can be readily obtained by ascribing values to D_f^w and D_f^a. Although both self-diffusion coefficients are surely concentration dependent, we set them equal (out of ignorance) to the respective self-diffusion coefficients of the neat liquids. Then, with (see Figure 4) $D_f^w = 2.5 \times 10^{-5}$ cm^2/sec, $D_f^a = 0.77 \times 10^{-5}$, $D^w = 0.53 \times 10^{-5}$, and $D^a = 0.33 \times 10^{-5}$, we calculate

$$\begin{aligned} x_f^w &= 0.12 \\ D_b &= 0.27 \times 10^{-5}\ \text{cm}^2/\text{sec} \end{aligned} \qquad (2)$$

In other words, at the analytical composition of 3 molecules of water per molecule of 1-ethyl-2-pyrrolidinone, the model predicts that about nine water molecules out of ten are bound by the lactam molecules; the 3:1 water–lactam adduct, itself, has an apparent self-diffusion coefficient of about 0.27×10^{-5} cm^2/sec.

The formation constant of this adduct can now be estimated by insertion of the value of x_f^w into the appropriate expression of the law of mass action

$$3W + A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} AW_3 \qquad k_1/k_{-1} = K$$

$$\frac{[AW_3][W_0 + A_0 - 3AW_3]^3}{[A_0 - AW_3][W_0 - 3AW_3]^3} = K \qquad (3)$$

where the brackets denote the number of molecules and where K is in terms of mole fraction. The zero subscript indicates initial quantities. We find

$$K \sim 395[\text{mf}^{-1}] \qquad (4)$$

The computed self-diffusion coefficients, based on eq 1 and the values of D_b, D_f^w, D_f^a, and K, are entered as the curves designated by W (water) and A (lactam) into Figure 4.

We will now discuss how well the experimental viscosity and self-diffusion coefficient data can be rationalized on the basis of a stoichiometric lactam–water complex and the simple two-state model. We first treat the self-diffusion data (see Figure 4), which show that the water–lactam interactions in this system are much more involved than assumed in our two-state model. For instance, rather small amounts of lactam are observed to affect the mobility of water significantly stronger than predicted by the model; this most likely indicates that the presence of the lactam exerts a rigidifying effect on the water structure. (Additional evidence on this will be presented in the discussion of the spectral data further below.) In other words, the environment in which the water molecules find themselves, is, at least, of a threefold nature: unperturbed regions of water, perturbed regions of water in the neighborhood of lactam molecules, and water layers at or on the active groups of the lactam. (In a water–PVP system we would have, additionally, a distribution of environments of water molecules trapped physically by the coiled polymer chains.)

Furthermore, Figure 4 shows that the diffusion of lactam is faster in water-rich and slower in water-poor regions than predicted. We have infrared evidence (see next section) on considerable self-association of ethylpyrrolidinone; this could conceivably account for the slower diffusion in water-poor regions (the presence of D_2O instead of H_2O should not cause a significant change). Another possibility is that water-bridging takes place between two (or more) lactam molecules; such phenomenon would also explain why diffusion of lactam in water-rich solutions is observed to increase with increasing water content since such bridged adducts should then break up in favor of smaller hydrated individual lactam molecules.

We now turn to the viscometric evidence on formation of a lactam–water 1:3 stoichiometric complex (see Figure 3). In contrast to self-diffusion measurements, the viscosity data mainly reflect the mobility of the largest entities in the solutions; on the basis of this, it appears that the observed viscosity indeed points rather convincingly to a well-defined 1:3 complex. However, Granzhan, *et al.*,[22] find in 1-methyl-2-pyrrolidinone–water a viscosity maximum which corresponds to the 1:2 adduct; since it is difficult to see how replacement of ethyl by methyl should cause such changes in the stoichiometry,[23] this gives a warning that data of this type cannot be readily interpreted in terms of a solution complex of definite composition.

In the next section, we will discuss infrared spectral data on these systems. By this we will, among other information, obtain an indication on the identity of the binding site(s).

2. Infrared Spectral Measurements. (a) Ethylpyrrolidinone–Water System. Carbon–Oxygen Stretch. Only two vibrational fundamental modes of 1-ethyl-2-pyrrolidinone (and of PVP) were observed to be strongly sensitive to the presence of the solvent molecules. One of these two is the C=O stretching mode, which undergoes an apparent shift to longer wavelengths if water is added ("red shift"). As shown in Figure 5 for ethylpyrrolidinone, the magnitude of

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[22] V. A. Granzhan, O. G. Kirillova, L. M. Savenko, and M. I. Kolesnik, *Inform. Soobshch. Gos. Nauch. Issled. Proekt. Inst. Azotn. Prom. Prod. Org. Sin.*, No. 1, 20 (1969).

[23] If anything, one might expect that the methyl derivative binds more water than the ethyl compound because of a smaller degree of hydrophobicity and less steric hindrance as well as increased polarity because of charge stabilization by the CH_3 group; see also P. Assarsson and F. R. Eirich, *J. Phys. Chem.*, 72, 2710 (1968).

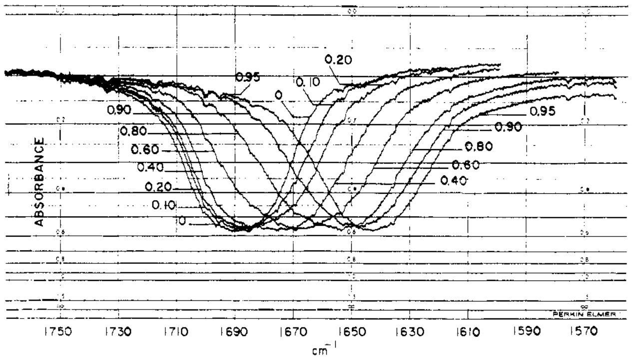

Figure 5. Band contour changes and peak frequency red shifts of the carbon–oxygen stretching fundamental of 1-ethyl-2-pyrrolidinone upon addition of D_2O. The numbers at the contours denote the mole fraction of D_2O. (Photograph of original scans.)

this shift is appreciable, from 1689 cm^{-1} (neat lactam) to 1642 cm^{-1} (5 mol % lactam in D_2O) and 1637 cm^{-1} (1 mol %, not shown here). Closer inspection of Figure 5 indicates that this is not a monotonic band shift *per se*, but concentration-dependent changes in the aspects of the band contour. (i) In the mole fraction range of D_2O of 0 to about 0.40, the high-frequency part of the band contour of the C=O stretch diminishes more slowly than the low-frequency part increases. The contours, approximately, go through a common point near 1683 cm^{-1}. (ii) In the mole fraction range 0.60–0.80, we seem to observe pure band shifts; as much absorption is lost on the high-frequency side as is gained on the low-frequency side. (iii) For a mole fraction of D_2O of 0.80–0.95, the low-frequency part of the C=O band gains now less in intensity than is lost on the high-frequency part. Again, the contours, approximately, cut through a common absorbance near 1648 cm^{-1}.

As a consequence of the above, the (full) band width (at half peak-height) rises from about 34 cm^{-1} (neat liquid) to 45 cm^{-1} (0.20–0.80 mol fraction of D_2O), and thereafter drops back to about 36 cm^{-1} (0.95 mol fraction of D_2O).

It seems difficult to explain these observations by the usual assumption of an active oscillator whose frequency shifts to longer wavelengths with the (concentration-dependent) changes in the medium.[24] Rather, it appears to us that there are several different oscillators, each with its proper frequency, which appear and disappear depending on the conditions of equilibrium between lactam and water; higher-resolution spectra (not shown here), which sharpen some of the features of the band contours (see, for instance, the frequency-invariance of the kinks at 1700 and 1653 cm^{-1} in Figure 5),[25] clearly bear this out. We ascribe these oscillators to C=O motions of lactam–water "species" of different composition; at the lower range of water concentration, the C=O band of pure lactam rapidly diminishes in intensity due to formation of increasingly stable and water-rich lactam species, absorbing at lower frequencies. This process continues until a mole fraction of water of about 0.60 is reached. In the region 0.60–0.80 mol fraction of water, the constancy of the band width (see point ii above) seems to indicate the presence of a few lactam–water species of comparable stability; again, we can safely rule out the existence of a well-defined complex since there is no solvent shift of one and the same band but intensity decreases at higher and compensatory intensity increases at lower frequencies. (See, for instance, in Figure 5 the frequency-invariance of the feature at 1616 cm^{-1}.)[25] Finally, in water-rich solutions, the renewed asymmetry in the changes of the band contour of the C=O stretch —now in an opposite direction to that in water-poor solutions (see point iii above)—makes us believe that further water (however less tightly bound) is added to the hydrated lactam molecules.

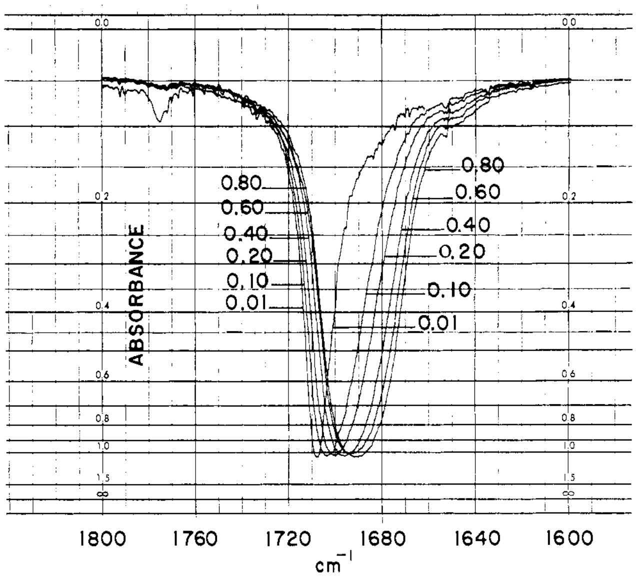

Figure 6. Band contour changes and peak frequency blue shifts of the carbon–oxygen stretching fundamental of 1-ethyl-2-pyrrolidinone upon addition of cyclohexane. The numbers at the contours denote the mole fraction of lactam. The peak at 1775 cm^{-1} is caused by cyclohexane. (Photograph of original scans.)

Conditions in this system are further complicated by strong self-association of the pure lactam. This is evident from the extraordinarily broad band width (34 cm^{-1}) of the C=O stretch, a width much too large[26] for such a heavy molecule, and by the considerable narrowing of this band width upon dilution by inert solvent. For instance, we compute from Figure 6 that the band narrows to 9.5 cm^{-1} for a solution of 1 mol % lactam in cyclohexane. Significantly, this band narrowing is not symmetrical about the band center but skewed; the intensity is lost predominantly in the low-frequency part of the contour. This indicates that associated lactam species, whose C=O stretches are either broadened by strong interactions or absorb at frequencies lower than the unperturbed C=O oscillator of the single lactam molecule, are disappearing upon dilution by inert solvents.[24]

Before we continue with a discussion of the other strongly susceptible vibrational mode of ethylpyrrolidinone, we first describe the changes of the water spectrum in the presence of the lactam.

Oxygen–Deuterium Stretching Region at 2500 cm^{-1}. The O–D stretches of D_2O in solution with 1-ethyl-2-pyrrolidinone are shown in Figure 7. We notice that with increasing amounts of lactam the water band becomes narrower and gradually splits into two distinct

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(24) L. J. Bellamy and R. L. Williams, *Trans. Faraday Soc.*, **55**, 14 (1959).

(25) These kinks are not instrumental nor caused by impurities.

(26) Band widths of larger molecules are mainly determined by their vibrational lifetime (see ref 18). For a rather short lifetime τ of 1 psec, the full band width at half peak-height is $1/\pi c\tau$ = 10 cm^{-1}.

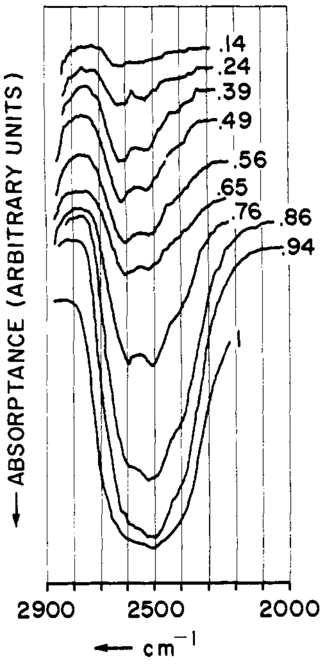

Figure 7. Contour changes of the region of the O–D stretching fundamentals of D_2O in 1-ethyl-2-pyrrolidinone as a function of solution composition. The values at the spectra denote the mole fraction of D_2O. The peak near 2600 cm^{-1} is the asymmetric, the peak near 2500 cm^{-1} is the symmetric O–D stretch. The shoulder near 2400 cm^{-1} represents the overtone of the bending fundamental of D_2O.

peaks[27] which, in turn, reverse their intensities. This change is indicative of an uncoupling of the O–D stretching motions between hydrogen-bonded water molecules.[27] We must therefore conclude that with increasing amounts of ethylpyrrolidinone there is a continual rupture of hydrogen bonds between water molecules in favor of hydrogen-bonding of water to peptide groups. The concomitant shift of the O–D contour to higher frequencies (see Figure 7) shows that the hydrogen bonds between lactam and water are stronger than those between water molecules.[28]

Notably, there is no *abrupt* change in the water band contour with increasing lactam content; this seems to point to a monotonically increasing degree of water binding by lactam rather than to formation of a few well-defined (stoichiometric) lactam–water adducts, in agreement with the gradually shifting equilibria proposed in the previous section.

One further point is worth mentioning, namely that the band contour changes of the O–D stretching region are already observable in a solution of only 6 mol % lactam (see next to lowest trace in Figure 7); in view of the large excess of water molecules it seems reasonable to ascribe this sharpening of the distribution of hydrogen bond energies to "structure ordering" of water molecules[28] (see also Results and Discussion, section 1).

Carbon–Nitrogen Stretch. We return now to the spectrum of the lactam. Besides the C=O fundamental, there is one other band of 1-ethyl-2-pyrrolidinone which, upon addition of water, visibly undergoes profound changes. This is an absorption peak at 1425 cm^{-1}, shown in Figure 8. Its characteristic is that its intensity monotonically drops with increasing water content; in the water-rich solutions, it has nearly disappeared. Notably, its peak frequency stays constant; furthermore, no other band growing in on account of the disappearing peak could be unambiguously identified.[29]

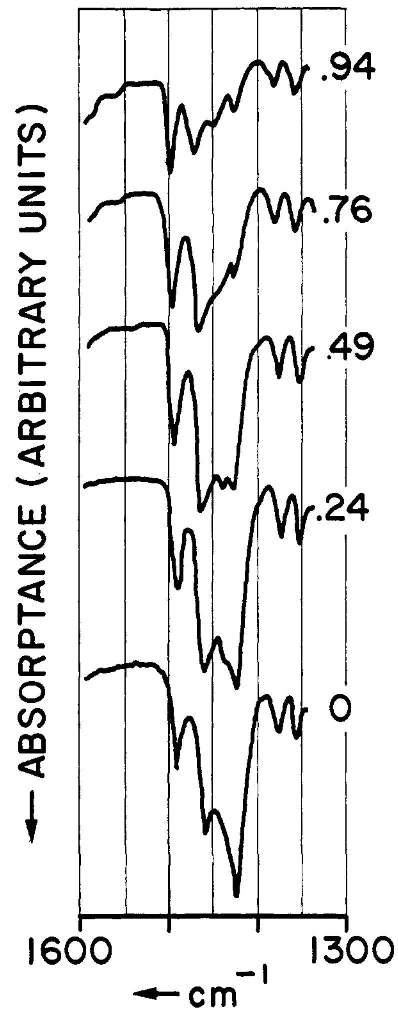

Figure 8. Intensity variation of the conjugated carbon–nitrogen stretch of 1-ethyl-2-pyrrolidinone, at 1425 cm^{-1}, upon addition of D_2O. The values at the tracings denote the mole fraction of D_2O. The other bands in this frequency range belong to CH_2 deformation modes.

We assign this absorption to represent essentially a stretching motion of the C$\overset{\text{---}}{=}$N partial double bond for the following reasons. (i) The strong intensity dependence upon water addition requires an active interaction site; this would seemingly eliminate the CH_2 groups whose deformation modes are in the 1400–1500-cm^{-1} region. (ii) Parsons[30] has assigned a band at 1424 cm^{-1} in 2-pyrrolidinone to the carbon–nitrogen stretch on the basis of convincing arguments. (iii) The same intensity behavior is shown by a band at 1427 cm^{-1} in the (near-identical) spectrum of *N*,*N*-diethylacetamide, the open chain analog of 1-ethyl-2-pyrrol-

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[27] These modes have been assigned to the regions of the asymmetric and symmetric O–D stretches, the asymmetric mode being at the higher frequency. The shoulder to longer wavelengths is the overtone of the D–O–D bending fundamental; it gains intensity from Fermi resonance with the symmetric stretch. See, for instance, D. Eisenberg and W. Kauzmann, "The Structure and Properties of Water," Oxford University Press, London, 1969.

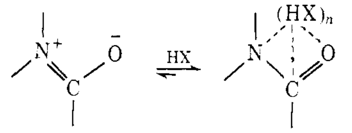
[28] G. Brink and M. Falk, *J. Mol. Struct.*, 5, 27 (1970).

[29] There are slight frequency shifts and intensity variations in nearly all remaining absorption peaks, but none could be detected which change to the same relative degree as the 1425-cm^{-1} band.

[30] A. E. Parsons, *J. Mol. Spectrosc.*, 6, 201 (1961).

idinone, upon addition of water. This means that neither presence of the five-membered ring nor cis–trans conformations about the peptide bond are responsible for the 1425-cm^{-1} band.[10,31] (iv) Dilution by nonreactive solvents, such as cyclohexane and carbon tetrachloride, has no significant effect on the intensity of the 1425-cm^{-1} band. Hence, the band is not caused by self-association of the lactams. (v) Other hydrogen donating compounds, such as CH_3OH and $CHCl_3$, have the same effect as water on the intensity of the 1425-cm^{-1} band, only to a lesser extent. (vi) Electron donors, such as *p*-dioxane, are not effective in decreasing the intensity of the C$\doteq$N mode nor are electron-withdrawing molecules, such as I_2 and ICl, seemingly able to increase it.

Assuming that the assignment of the C$\doteq$N stretch is correct, it is obvious that the presence of hydrogen donors is responsible for the decrease of the intensity of the C$\doteq$N mode. It is less obvious how to rationalize this in the presence of an apparent lack of a frequency change of the band. Possibly, the reason lies in the fact that the electronegativities of C and N are not much different; in other words, the bond moment of the nominal C–N single bond is very small. Therefore, effects which slightly change the electrical anisotropy of these atoms may have profound changes on the bond moment and thus on the infrared intensities, without necessarily appreciably affecting the (strongly covalent) force constant (and thus the frequency).[32] All that would be required from such an effect is a mechanism which favors a decrease in the conjugation of the peptide linkage, as indicated by the longer arrow



This could be achieved, for instance, if strong hydrogen donors "attach" themselves not only at the C=O group but also at the nitrogen atom.[33] Although this explanation is certainly speculative, the important point is to realize that the whole peptide group may be the interaction site and not only the C=O bond.

(b) Poly(vinylpyrrolidinone)–Water. It is now very interesting to see how the peptide group–water interactions discussed above vary when the nonpolymeric 1-ethyl-2-pyrrolidinone is substituted by poly(vinylpyrrolidinone). In general, we have observed the same phenomena in the polymeric as in the nonpolymeric system; addition of water causes an apparent red shift of the C=O fundamental, a gradual decrease of the intensity of the conjugated C—N stretch, and the intensity variation of the deuterium–oxygen stretching fundamentals as described in the Results and Discussion, section 2a. Furthermore, CH_3OH as well as $CHCl_3$ exert the same effect, albeit to a lesser degree, as does water.

However, *quantitatively*, there is a significant difference between the polymeric and nonpolymeric systems. (i) The band width of the C=O stretch of a dry film of PVP amounts to 35 cm^{-1}, as compared to 34 cm^{-1} for 1-ethyl-2-pyrrolidinone. (ii) This band width decreases in a nonreactive solvent (CH_2Cl_2) to only 29 cm^{-1} (1 mol % PVP), which compares to a band width of 9.5 cm^{-1} for a comparable ethylpyrrolidinone solution (see Results and Discussion, section 2a). Furthermore, the small drop from 35 to 29 cm^{-1} in PVP arises again from a decrease at the low-frequency half of the C=O band contour (compare this with Figure 6); the peak frequency (1680 cm^{-1}) of the C=O band of dry PVP film remains practically unaltered upon dissolution in CH_2Cl_2. (iii) Addition of (heavy) water to PVP causes a considerably smaller C=O shift than that observed for ethylpyrrolidinone, for equal amounts of (heavy) water added; going from the pure compounds to a 1 mol % aqueous solution, the shifts are 1680–1648 = 32 cm^{-1} *vs.* 1689–1637 = 52 cm^{-1}, respectively.

Point i is readily explained by the distribution of chain configurations of the polymer, together with the finite chain length and the wide dispersion of the molecular weight.[34] With regard to point ii, the band narrowing from 35 to 29 cm^{-1} reflects most likely the interchain interactions in the solid polymer (interactions which become much less important in the more dilute solutions).

The observations collected under point iii above are the most interesting here; they show that water–peptide group interactions are significantly weaker in the polymeric medium than in the corresponding nonpolymeric solutions. Two reasons can be envisaged to explain this. The first is that the binding sites in PVP interfere with each other;[35] adding ligand to a peptide group makes additions at neighboring peptide groups more difficult. This could simply arise if bridging by water[36] (or other hydrogen donor molecules) between adjacent peptide bonds leads to stabler chain conformations; additional water molecules would then be held in outer solvation layers since they no longer contribute greatly to a lowering of conformational energy.

The second reason for the smaller binding capacity per peptide group in PVP may be simply steric; the accessibility of solvent molecules to the peptide linkage is less in the polymeric than in the nonpolymeric lactam systems on account of the smaller free volume.[37]

Comparison with some directly related previous work is interesting. Glasel[38] concludes, from his deuterium spin-lattice relaxation data of D_2O in PVP, that the carbonyl group of PVP does *not* undergo interactions with water. This apparent discrepancy is, however, resolved if it is realized that (i) his solutions were very dilute in PVP ($R \leq 0.02$, see Figure 2), (ii) he only observed the rotational motion of water, not its translational mobility. There is no reason why a ligand molecule cannot manifest strong binding at a site on the substrate, for instance *via* a much decreased translational

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[31] The assignments by M. Rey-Lafon, M.-T. Forel, and J. Lascombe, *J. Chim. Phys. Physicochim. Biol.*, **64**, 1435 (1967), who believe that 1422 cm^{-1} represents the deformation of the ring CH_2 adjacent to the carbonyl group, are thus unlikely to be correct.

[32] B. H. Thomas and W. J. Orville-Thomas, *J. Mol. Struct.*, **7**, 123 (1971).

[33] There should be a concomitant increase in the "double bond character" of the C=O bond. However, this would not greatly counteract the observed red shifts (see Results and Discussion, section 2a) since dielectric effects on the C=O frequency are small (see ref 24).

[34] R. Zbinden, "Infrared Spectroscopy of High Polymers," Academic Press, New York, N. Y., 1969.

[35] J. Steinhardt and J. A. Reynolds, "Multiple Equilibria in Proteins," Academic Press, London, 1969, p 16.

[36] P. Bacelon and A. De Lozé, *J. Chim. Phys. Physicochim. Biol.*, **69**, 346 (1972).

[37] Similar effects between polymeric and monomeric amide have been found in N,N-disubstituted polyacrylamides; see P. Combelas, F. Cruege, J. Lascombe, C. Quivoron, M. Rey-Lafon, and B. Sebille, *Spectrochim. Acta, Part A*, 26, 1323 (1970).

[38] J. A. Glasel, *J. Amer. Chem Soc.*, 92, 375 (1970).

mobility, but still undergo relatively fast rotational motion about some molecular axis. (In fact, this is the conclusion arrived at by Brüssau and Sillescu[39] from their study of spin-lattice relaxation times of $CDCl_3$ in dilute PVP–chloroform solutions.)

Summary and Conclusions

We consider as a main point of our study to have shown that interactions of peptide groups of lactams with hydrogen donating solvents, particularly with water, are much more complicated than generally assumed. Specifically, our results indicate that the local site of such interactions is not only the carbonyl group but may also involve adjacent "closely coupled" reactive centers, such as the C–N group. One should thus be wary of accepting, without unambiguous proof, certain concepts in the literature which propose specific *atoms* of complicated reactive interaction sites to be the sole center of the dynamic interaction between the site and molecules in the liquid phase.[40] Interaction at the tertiary nitrogen atom of a peptide group had been invoked by Granzhan, *et al.*,[22] for the system water–methylpyrrolidinone. However, this was done in an *ad hoc* fashion; they place one molecule of water each at the C=O group and at the N atom in order to account for their hypothetical 1:2 lactam–water complex.

More generally, our data indicate that water–PVP interactions are relatively strong in comparison with those observed with other hydrogen donating molecules. There are no solution compositions where one could consider the mobility of the water molecules unaffected: in water-rich solutions, the lactams studied here induce structure-promoting effects on water with the subsequent redistribution of hydrogen bonds; in the intermediate concentration range down to water-poor solutions, the water molecules find themselves increasingly at or near the peptide bonds.

Our work also shows that the concept of "degree of binding" is of questionable meaning without reference to the time scales involved and the particular phenomena observed. For instance, the viscosity measurements are particularly sensitive to the interactions involving the largest species in the solutions but rather insensitive to the multiple equilibria present. (Hence, conclusions in the literature on definite compositions[22,41] and solution dynamics[42] of substrate–ligand complexes, derived from viscosity data, must be considered with caution.) The self-diffusion measurements give a more detailed account since they observe different molecular species, but they do not identify the species. The infrared spectral frequency and relative intensity measurements are on the fastest time scale (about 10^{-13} sec); they observe the effect of the interactions on the susceptible local oscillators. Hence, such data identify the interaction sites as well as reflect the complexity of the existing equilibria, but they cannot predict the time scales of the slower individual equilibrium steps nor the stoichiometry of the molecular entities involved in them.

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(39) R. G. Brüssau and H. Sillescu, *Ber. Bunsenges. Phys. Chem.*, **76**, 31 (1972).

(40) See, for instance, P. Combelas, C. Garrigou-Lagrange, and J. Lascombe, *Ann. Chim. (Paris)*, **5**, 315 (1970.

(41) D. D. Macdonald, D. Dunay, G. Hanlon, and J. B. Hyne, *Can. J. Chem. Eng.*, **49**, 420 (1971).

(42) See, for instance, J. Czubryt, E. Tomchuk, and E. Bock, *Ber. Bunsenges. Phys. Chem.*, **75**, 243 (1971).

Optical and Magnetic Properties of Anions of Hexahelicene

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Abstract: The optical rotatory dispersion spectra of the mono-, di-, and trianion of (+)-hexahelicene were determined. The mono- and trianion are paramagnetic. The dianion appears to be diamagnetic.

Hexahelicene has served, since its synthesis and resolution by Newman,[1] as a model substance for observation and calculation of various features of optical activity.[2] Our interest was directed toward it because of its usefulness in the study of dependence of electron-transfer rate on relative optical configuration of reactants.[3] The observation that the rate constants for electron transfer between anion and neutral molecules of hexahelicene are markedly dependent on the relative optical configurations of the reacting pair suggested that knowledge of the optical activity of the anions might be useful in interpreting the data. Accordingly, we have measured the optical rotatory dispersion (ORD) of the anions of hexahelicene. We have as yet not found any illuminating relations between the optical and rate data, but, in view of the intrinsic interest of the optical data and their bearing on the theories of optical activity, we report the results of our optical studies. Included in this report are the electron spin resonance (esr) studies of the anions of hexahelicene.

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(1) M. S. Newman and D. Lednicer, *J. Amer. Chem. Soc.*, **78**, 4765 (1956).

(2) C. W. Deutsche, D. A. Lightner, R. W. Woody, and A. Moscowitz, *Annu. Rev. Phys. Chem.*, 20, 420 (1969).

(3) R. Chang and S. I. Weissman, *J. Amer. Chem. Soc.*, **89**, 5968 (1967).