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Helix Destabilization Caused by the Interaction of Unaggregated Sodium Dodecyl Sulfate with Isolated Lysine Residues

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ABSTRACT: The interaction of sodium dodecyl sulfate with random copolymers of L-lysine and (hydroxybutyl)-L-glutamine has been studied by circular dichroism and by the fluorescence of a probe that is sensitive to the presence of detergent micelles. Weight-average molecular weights of the fractionated copolymers gave from 22 000 to 80 000, and the mole fraction of L-lysine is 0.06. The copolymer has little effect on micelle formation by the detergent when the polypeptide concentration is in the range used in the circular dichroism measurements. At higher polypeptide concentrations, the onset of micelle formation by sodium dodecyl sulfate shifts to lower detergent concentration. Circular dichroism reveals the expected thermally induced helix–coil transitions in the copolymers. The detergent has little effect on the helix content at 68 °C, but detergent monomers destabilize the helix at 25 °C. There is no evidence of a change in the helix content of the copolymer after the sodium dodecyl sulfate concentration has risen above the critical micelle concentration. Comparison of the interaction of the detergent with the L-lysine residues in the sparsely charged host–guest copolymers and in highly charged poly(L-lysine) is complicated because the transitions are quite different. The host–guest copolymers undergo the helix–coil transition, but sodium dodecyl sulfate converts fully ionized poly(L-lysine) from a random coil to a β sheet. The conformational change in the host–guest copolymers is not observed until the detergent concentration is more than an order of magnitude larger than that required for the random-coil to β-sheet transition in poly(L-lysine).

By appropriate manipulation of the pH and temperature, poly(L-lysine) in dilute aqueous solution can adopt the conformation of an α helix, β sheet, or statistical coil. Transitions between these conformations can be followed by a variety of spectroscopic techniques, including ultraviolet absorption,[1] optical rotation,[2–4] ultraviolet circular dichroism,[3,5,6] Raman spectroscopy,[7–9] and vibrational circular dichroism.[10,11] The statistical coil is the stable conformation in acidic and neutral solutions because the high charge density on the polymer is incompatible with an ordered structure. At an elevated pH, where the chain is partially deprotonated but still retains sufficient charge so that it is soluble in water, the polymer forms an ordered structure. The ordered structure can be either the α helix or β sheet, with the β sheet being preferred to the α helix at the higher temperatures.[1–11]

Additional conformations become accessible to fully ionized poly(L-lysine) in the presence of selected ionic species of low molecular weight. In some cases, such as the stabilization of the α helix at neutral pH by potassium thiocyanate,[12,13] sodium perchlorate,[13,14] or sodium carbonate,[15] the development of the ordered structure is observed when the concentration of the salt is on the order of 0.1–1.0 M. Conformational transitions are observed at much lower concentrations of the active component when the effective agent is an anionic detergent. Sodium dodecyl sulfate ($NaDodSO_4$) induces the formation of the β structure in fully ionized poly(L-lysine), and the conformational transitions can be observed at detergent concentrations on the order of 10^{-4} M.[16–19] The ordered structure formed is the α helix if the detergent used is sodium octyl sulfate.[18]

Sodium dodecyl sulfate exercises a strong influence on the conformational properties of copolypeptides that contain lysine, and the nature of the order structure formed by a copolypeptide depends on its amino acid sequence.[20,21] Extensive studies by Yang et al. have shown that, in general, the β sheet is favored when the sequence is $(\text{Lys-Xxx})_n$, where Xxx = Ala, Leu, Lys, or Ser. A few other sequences, such as $(\text{Lys-Lys-Lys-Ser})_n$, also favor the β sheet. All of these sequences share the feature that they will produce a β strand in which the side chains on one side are contributed exclusively by Lys. On the other hand, the α helix is the stable structure in the presence of the detergent when the sequence is "random" and either $(\text{Lys}^x, \text{Leu}^{100-x})_n$ or $(\text{Lys}^y, \text{Ala}^{100-y})_n$, where $x < 75$ and $y < 65$. The formation of an α helix induced by $NaDodSO_4$ is likely to be of more biophysical importance than the formation of β sheet because Lys residues in naturally occurring polypeptides usually do not have Lys as a next nearest neighbor. Indeed, interaction with $NaDodSO_4$ of small peptides that contain a few Lys residues often is accompanied by an increase in the helix content.[22,23]

The Zimm–Bragg[24] parameters for helix propagation and helix initiation by isolated Lys residues in a copolypeptide in the presence of $NaDodSO_4$ can be determined by application of the "host–guest" technique,[25] in the manner recently employed for Arg copolymers.[26] The poly[(hydroxyalkyl)-L-glutamines] are particularly suitable for use as hosts because the thermally induced helix–coil transitions of these homopolymers are affected very little by the presence of $NaDodSO_4$.[27,28] If $NaDodSO_4$ affects the helix–coil transition of a copolymer that is composed predominantly of (hydroxyalkyl)-L-glutamine residues, it must be due to an interaction of the detergent with the amino acid residue that is present as the minor component.

Here the "host–guest" technique is applied to copolymers of (hydroxybutyl)-L-glutamine and L-lysine in order to determine σ and s for Lys as a function of temperature at $NaDodSO_4$ concentrations above and below the critical micelle concentration (cmc). The properties of poly(amino acids) in aqueous $NaDodSO_4$ are important because the molecular weight of proteins is frequently determined from the mobility of the complexes that are formed with this detergent. Interaction of the monomeric form of the detergent with an isolated Lys produces a reduction in the helix content of the copolymer. In contrast, the micellar form of the detergent has very little effect on the helix content. The helix-forming tendencies for isolated Lys and Arg residues respond in a similar fashion to the presence of $NaDodSO_4$, and this response is different from that seen in the homopolymers of the cationic amino acids.

Experimental Section

Synthesis. The copolymers were prepared by polymerization of a mixture of the two *N*-carboxy anhydrides, as described by Dygert et al.[29]

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Fractionation. The fractionation of the copolymer of (hydroxybutyl)-L-glutamine and L-lysine was achieved by a repetitive precipitation identical with that used for fractionation of the copolymer of (hydroxybutyl)-L-glutamine and L-arginine.[26]

Composition. Analysis of the amino acid composition was carried out on a PICO-TAG amino acid analyzer (Waters Assoc.) following the same steps used for analysis of the copolymer of (hydroxybutyl)-L-glutamine and L-arginine[26] except that the injection volume was increased from 40 μL to 50 μL.

Ultracentrifuge. The weight-average molecular weight, M_w, for each fraction was determined by the method of low-speed approach to equilibrium. The Spinco model E ultracentrifuge, experimental procedure, and data analysis were the same as those used for the copolymers of (hydroxybutyl)-L-glutamine and L-arginine.[26] The typical uncertainty for the M_w determined for each fraction was about ±8% or less.

Fluorescence. Emission spectra were measured with an SLM 8000C fluorometer equipped with a double monochromator on the excitation side. Excitation was at 388 nm. Slit widths for excitation and emission were 4 and 4 nm, respectively. Magic angle conditions were employed in order to eliminate polarization effects.[30]

Circular Dichroism. Circular dichroism (CD) spectra were measured with a JASCO J-500 A spectropolarimeter by using procedures similar to those employed previously.[26] The fractions were dissolved either in water or in $NaDodSO_4$ solutions with the concentrations of $NaDodSO_4$ being fixed at substantially below (0.0059 M), slightly above (0.011 M), and far above (0.046 M) the critical micelle concentration (cmc) of 0.008 M reported for this detergent species.[31] The fraction with M_w = 31 000 was investigated in more detail, as was a fraction of similar molecular weight (32 000) in which L-arginine is the guest.[26] The range of copolymer concentrations for CD measurements was from 0.01 to 0.03 mg/mL. The temperature range studied was from 5 to 68 °C.

The observed ellipticity at 222 nm, θ_{222}, in millidegrees, was determined from the base-line corrected spectra and converted to the mean residue ellipticity through the equation

$$[\theta]_{222} = \frac{\theta_{222} M_r S}{10 L C} \tag{1}$$

where M_r is the mean residue molecular weight calculated from the amino acid composition and residue molecular weights of (hydroxybutyl)glutamine and lysine, S is the CD scale factor selected for each run, L is the optical path length of the cells in centimeters, and C is the concentration in milligrams per milliliter. The uncertainty in $[\theta]_{222}$ was about 2%. The helix content f_h for each fraction was calculated from $[\theta]_{222}$ through the equation

$$f_h = \frac{[\theta] - [\theta]_c}{[\theta]_h - [\theta]_c} \tag{2}$$

where $[\theta]_c$ and $[\theta]_h$ are the mean residue ellipticities for the completely disordered and completely helical polypeptides, respectively. The value of $[\theta]_c$ at a particular temperature was obtained through the interpolation of a plot of $[\theta]_{222}$ against temperature for poly[(hydroxyethyl)-L-glutamine] in water.[32] A value of −36,000 deg cm^2 dmol^{-1}, which was the measured $[\theta]_{222}$ for poly(L-lysine) at pH 11.5,[6] was chosen for $[\theta]_h$.

Calculations. The Zimm–Bragg theory[24] of the helix–coil transition was employed to analyze the CD data. The method is similar to the one used for the copolymers of (hydroxybutyl)-L-glutamine and L-arginine.[26] The fraction f_h of residues that are in helical states is obtained by standard matrix techniques that rigorously evaluate $N^{-1}\, \partial \ln Z / \partial \ln s$, where Z is the matrix representation of the conformational partition function for a chain of N residues in a specified sequence and s is the statistical weight for helix propagation. The statistical weights for helix initiation and helix propagation by the host were taken from previous work of von Dreele et al.[33] In order to find the best values of σ_g and s_g for the guest it is assumed that σ is a temperature-independent quantity. For an assumed value of σ, the best set of temperature-dependent s is found by minimization of

$$\tau = \sum_T \sum_i [(f_{h,c})_{i,T} - (f_{h,m})_{i,T}]^2 \tag{3}$$

where the subscripts c and m stand for the calculated and measured quantity, respectively. The best s obtained at each temperature was the one that minimizes the contribution to τ from the measurements at that temperature. The minimization was achieved through the use of a grid-searching algorithm described previously.[26]

Table I
Characterization of the Fractionated Copolymers

L-lys content[a]	$M_w \times 10^{-3}$	DP_w
0.056	80	406
0.060	69	353
0.060	68	348
0.053	64	326
0.070	56	288
0.073	45	232
0.069	31	159
0.065	22	113

[a] The lysine content is expressed as the mole fraction.

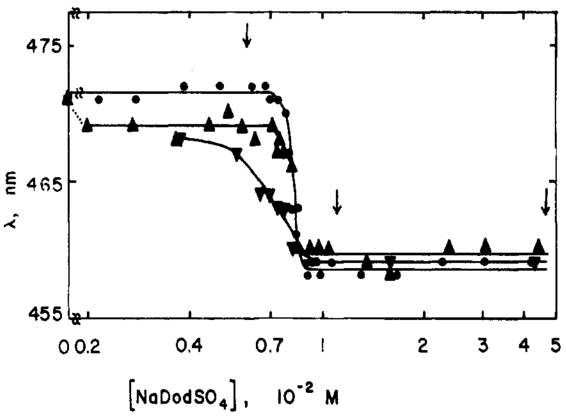

Figure 1. Wavelength of maximal emission from pyrene-1-carboxaldehyde upon excitation at 388 nm at 25 °C. The concentration of the lysine–(hydroxybutyl)glutamine copolymer (M = 56 000) is 0 (●), 0.024 (▲), and 0.052 (▼) mg/mL. The three arrows denote the $NaDodSO_4$ concentrations at which extensive CD spectra were collected for each fraction.

Results and Discussion

Molecular Weight and Composition. The weight-average molecular weight and lysine content measured for the fractions are listed in Table I. The fraction of the residues that are L-lysine is within the range 0.063 ± 0.010. Since the guest residue is the only charged species present and its composition is low, the influence of the polyelectrolyte effect on measured properties may be expected to be weak. Previously Scheraga and co-workers[29] observed no difference between the melting curves obtained in water at neutral pH and those obtained in 0.1 M KCl solutions for a copolymer that had a somewhat higher lysine content than the fractions described in Table I.

Fluorescence. In the recent study of the influence of the interaction of $NaDodSO_4$ with a random copolymer of L-arginine and (hydroxybutyl)-L-glutamine, the three $NaDodSO_4$ concentrations selected were slightly below the cmc, slightly above the cmc, and in excess of a transition in the micelles.[26] The cmc of the detergent, and the concentration at which there is a transition in the micelle, were determined with the aid of a fluorescent probe.[34] The influence of the present copolymer, in which lysine replaces arginine as the guest, on the aggregation of the detergent was assessed by the study of the emission of pyrene-1-carboxaldehyde. Figure 1 depicts the wavelength of maximal emission when the excitation is at 388 nm. In the absence of the host–guest polymer, there is a sharp shift of the emission maximum from 472 ± 1 to 459 ± 1 nm when the $NaDodSO_4$ concentrations passes through

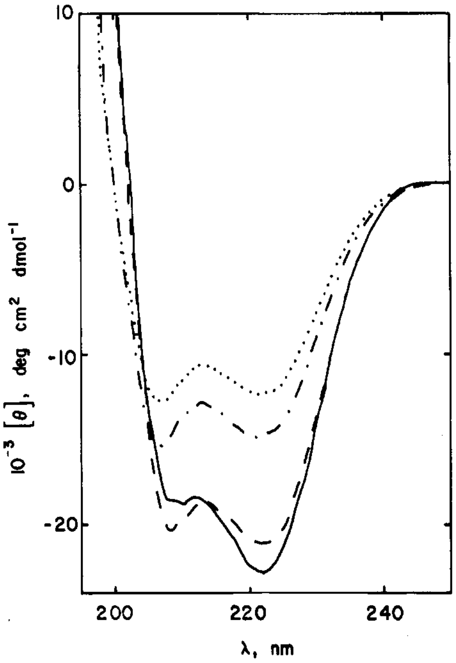

Figure 2. Circular dichroism of the copolymer of highest molecular weight (80 000) at 15 °C when the concentration of NaDodSO$_4$ is zero (solid line), 0.0059 M (dashed line), 0.011 M (dot-dash line), and 0.046 M (dotted line).

the vicinity of 0.008 M. This concentration is in excellent agreement with the values reported for the cmc by other techniques.[31]

Figure 1 also depicts emission data when the lysine-(hydroxybutyl)-L-glutamine copolymer with M_w of 56 × 10^3 is present at concentrations of 0.024 and 0.052 mg/mL. The onset of micelle formation, as revealed by the blue shift of the maximal emission from pyrene-1-carboxaldehyde, commences at somewhat lower NaDodSO$_4$ when the copolymer concentration is 0.052 mg/mL. The transition is completed at a NaDodSO$_4$ concentration that is nearly independent of the concentration of the copolymer. There is no evidence of another transition at NaDodSO$_4$ concentrations above 0.01 M.

The results depicted in Figure 1 reveal a micellization that differs in two respects from that seen in the presence of a copolymer of arginine and hydroxybutylglutamine. First, there is a slight increase in the cmc and little evidence for broadening of the transition, in the presence of the arginine copolymer. The lysine copolymer broadens the transition in a manner that tends to decrease the concentration at the midpoint of the transition. The second difference is the appearance of another transition at about 0.02 M NaDodSO$_4$ in the presence of the arginine copolymer. No evidence for a second transition is apparent in Figure 1. The origin of the different behaviors produced by the lysine and arginine copolymers is unknown. It might be related to the fact that the arginine copolymer contained nearly twice as large a mole fraction of cationic residues and was studied at a higher copolymer concentration (0.38 mg/mL).

The arrows in Figure 1 denote the NaDodSO$_4$ concentrations selected for extensive circular dichroism studies. The copolymer concentration in the CD measurements was 0.01–0.03 mg/mL. The lowest NaDodSO$_4$ used lies slightly below the onset of the transition detected by pyrene-1-carboxaldehyde when the copolymer is in this concentration range. Under these circumstances, it is monomeric NaDodSO$_4$ that is available for interaction with the copolymer. The next arrow denotes a NaDodSO$_4$ concentration that lies slightly above the completion of the transition detected by pyrene-1-carboxaldehyde, and the third arrow is far above this concentration. The three NaDodSO$_4$ concentrations denoted by the arrows in Figure 1 match quite closely the concentrations used in the study of the arginine-(hydroxybutyl)glutamine copolymer.[26]

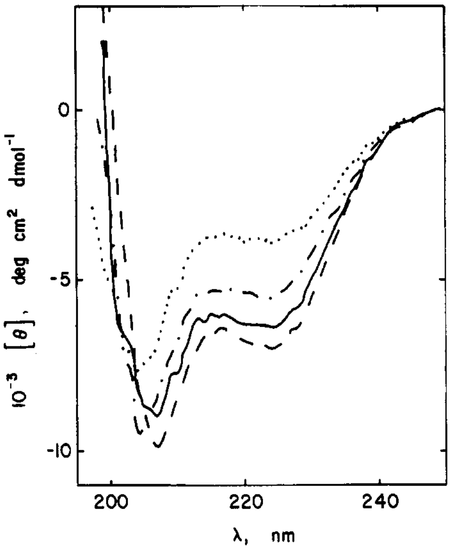

Figure 3. CD of the copolymer of highest molecular weight (80 000) at 68 °C when the concentration of NaDodSO$_4$ is zero (solid line), 0.0059 M (dashed line), 0.011 M (dot-dash line), and 0.046 M (dotted line).

Circular Dichroism. CD spectra in water or NaDodSO$_4$-containing solvents at two temperatures, 15 and 68 °C, for the fraction of highest molecular weight are depicted in Figures 2 and 3, respectively. At 15 °C, the spectra clearly are similar to those observed previously by Dygert et al.[29] and indicate the presence of the right-handed α-helix mixed with statistical coil. The amount of helix decreases upon addition of NaDodSO$_4$, as indicated by the changes in the magnitude of $[\theta]_{222}$. The presence of thermally induced helix-coil transitions in each solvent is evident upon comparison of Figures 2 and 3. The order for the amount of helix remaining at 68 °C is 0.0059 M NaDodSO$_4$ > water > 0.011 M NaDodSO$_4$ > 0.046 M NaDodSO$_4$. This order is also seen in the other fractions at this temperature. The melting curves for the fraction with M = 45 000, expressed as f versus T, are depicted in Figure 4.

Figure 5 shows in detail the response of the fraction with M_w = 31 000 to increasing concentrations of NaDodSO$_4$. Also depicted are results[26] obtained with a copolymer of (hydroxybutyl)-L-glutamine and L-arginine that has nearly the same molecular weight (32 000). The compositions are somewhat different, with the mole fractions of the guest being 0.069 and 0.12 for Lys and Arg, respectively. For both copolymers at 20 °C, $[\theta]_{222}$ becomes less negative with increasing concentration of NaDodSO$_4$ at low concentrations but becomes independent of concentration above about 0.009 M, which is only slightly higher than the commonly accepted critical micelle concentration of 0.008 M.[31] The helix content of the copolymers is reduced by an increase in the concentration of NaDodSO$_4$ monomers. However, it is unaffected by an increase in the concentration of NaDodSO$_4$ micelles. Under these conditions, the helix content of homopoly[(hydroxyalkyl)-L-glutamines] is very nearly independent of NaDodSO$_4$ concentration.[27,28] Therefore one can conclude that the behavior seen in Figure 5 is due to the conformational consequences of the interaction of individual molecules of NaDodSO$_4$ with isolated Lys or Arg residues in the host-guest copolymers.

Table II
Values of σ and s for Lys in Water

t, °C	$\sigma = 10^{-4}$ [a]	$\sigma = 10^{-2}$ [a]	Lifson[b]	Allegra[b]	host[c] $\sigma = 6.7 \times 10^{-4}$
5	1.15 (0.73)[d]	1.29 (0.72)	0.866 (0.63)	0.883 (0.64)	1.038 (0.70)
15	0.98 (0.60)	1.07 (0.62)	0.916 (0.57)	0.924 (0.58)	1.025 (0.62)
25	0.92 (0.50)	0.87 (0.49)	0.939 (0.51)	0.944 (0.51)	1.015 (0.55)
35	0.84 (0.39)	0.77 (0.40)	0.940 (0.45)	0.943 (0.45)	1.007 (0.49)
45	0.77 (0.28)	0.63 (0.27)	0.930 (0.36)	0.932 (0.36)	0.996 (0.39)
56	0.67 (0.20)	0.51 (0.19)	0.915 (0.29)	0.917 (0.30)	0.988 (0.33)
68	0.67 (0.15)	0.50 (0.15)	0.897 (0.21)	0.899 (0.21)	0.975 (0.24)

[a] Values in these two columns were obtained from the data reported in this paper. [b] Interpolated (and extrapolated) from the data in Table IV of ref 29 with $\sigma = 10^{-4}$. [c] Computed from the data in ref 33. [d] Values in parenthesis are the helix contents corresponding to the given values of σ and s.

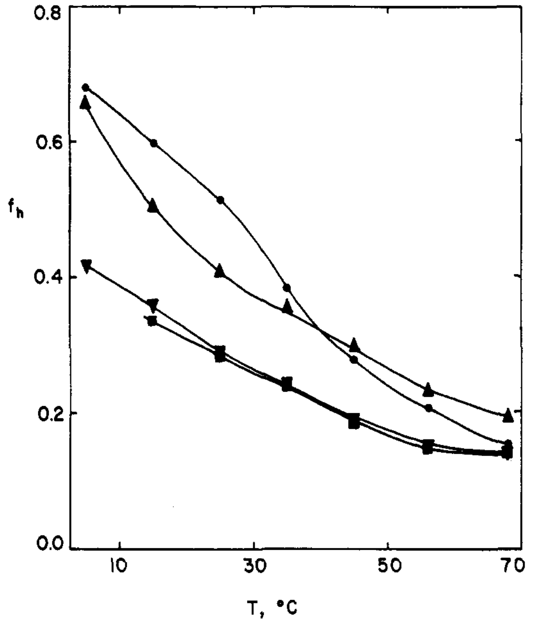

Figure 4. Temperature dependence of the helix content for the fraction with a molecular weight of 45×10^{-3}. The concentration of $NaDodSO_4$ is zero (●), 0.0059 M (▲), 0.011 M (▼), and 0.046 M (■).

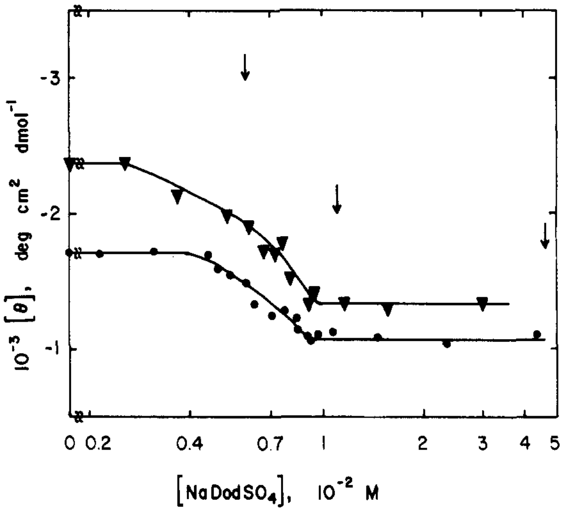

Figure 5. Behavior of $[\theta]_{222}$ for two host–guest copolymer at 20 °C. Circles denote data obtained with the lysine–(hydroxybutyl)glutamine fraction with a molecular weight of 31×10^3, and triangles denote data obtained with an arginine–(hydroxybutyl)glutamine fraction[26] with a molecular weight of 32×10^3. The mole fractions of Lys and Arg are 0.069 and 0.12, respectively.

The $NaDodSO_4$ concentration range depicted in Figure 5 is much different from that required for the conformational transition in the cationic *homo*polymers at comparable polypeptide concentrations. When poly(L-arginine) is present at a concentration of 10^{-4} mol of residues/L, the transition from statistical coil to α helix is sharp and centered at a $NaDodSO_4$ concentration of 10^{-4} M.[35] In contrast, the onset of the reduction in the helix content in the Arg copolymer in Figure 5 is not detectable until the $NaDodSO_4$ concentration is well above 10^{-3} M. In the case of poly(L-lysine), the transition from statistical coil to β sheet occurs at 10^{-4} M $NaDodSO_4$ when the concentration of lysyl residues is 1.17×10^{-4} M.[19] The detergent-induced change in helix content in the Lys copolymer in Figure 5 requires that the concentration of $NaDodSO_4$ be well above 10^{-3} M. The greater charge density in the cationic homopolymers may contribute to their strong interaction with $NaDodSO_4$ at lower detergent concentrations. This increased charge density also has an influence on the conformational effect produced by $NaDodSO_4$. This detergent stabilizes the α helix in poly(L-arginine),[35] but it destabilizes the α helix in the arginine–(hydroxybutyl)–L-glutamine copolymers in which the mole fraction of Arg is 0.12.[26]

Statistical Weights. Values of σ and s for (hydroxybutyl)-L-glutamine residues were those determined by von Dreele et al.[33] These values were used for the analysis of all data, including the sets obtained in the presence of $NaDodSO_4$, because the thermally induced helix–coil transitions of the uncharged poly[(hydroxyalkyl)-L-glutamines] are affected very little by the presence of this detergent.[27,28]

The analysis of the data obtained in the absence of $NaDodSO_4$ was performed with σ for Lys fixed at four values, 10^{-4}, 10^{-3}, 10^{-2}, and 10^{-1}. In the order of increasing σ, the computed values of τ, as defined in eq 3, are 0.086, 0.084, 0.080, and 0.187. For the particular samples studied here, the best fit to the data is obtained with $\sigma = 10^{-2}$, but fits of nearly the same quality are obtained with any σ in the range 10^{-4} to 10^{-2}. The fit experiences significant deterioration when σ becomes as large as 10^{-1}. Table II presents the best values of s when σ is 10^{-4} or 10^{-2}. In both cases, s is found to be greater than 1 at 5 °C, decreases monotonically as the temperature increases, and passes through the value $s = 1$ at a temperature in the range 14–19 °C. The calculated dependence of s on σ is lower at the smaller value of σ, which is expected because helix–coil transitions become more cooperative as σ decreases.

The numbers in parentheses following the values of s in Table II are helix contents calculated for random copolypeptides. The mole fraction of Lys is 0.06, the degree of polymerization is 260, and the host is (hydroxybutyl)-L-glutamine. The Lys content and degree of polymerization are the averages for the samples described in Table I, and the values of σ and s used for (hydroxybutyl)-L-glutamine[33] are listed in the last column of Table II. Inspection of the helix contents calculated with the best values of s for Lys when σ is 10^{-4} and 10^{-2} shows that they

Table III
Values of σ and s for Lys in 0.011 M NaDodSO$_4$

t, °C	σ 10^{-4}	σ 10^{-2}	t, °C	σ 10^{-4}	σ 10^{-2}
5	0.58	0.53	45	0.64	0.48
15	0.56	0.52	56	0.69	0.50
25	0.58	0.53	68	0.69	0.55
35	0.62	0.53			

describe very nearly the same melting curve. At no temperature do the calculated helix contents differ by more than 0.02, an amount that is well within the experimental error in the measurement. Hence it is not surprising that nearly identical values of τ are obtained with these two sets of σ and s.

The values of σ and s for Lys have been reported previously, on the basis of the analysis of melting curves for host–guest copolymers in which the mole fraction of Lys ranged from 0.05 to 0.20.[29] The value of σ was 10^{-4}, which is in reasonable agreement with the results reported in Table II because the quality of the fit is little different for $\sigma = 10^{-4}$ or 10^{-2}. However, there is a greater difference in the values reported for s. Two nearly identical sets of s, based on the Lifson and Allegra theories, were tabulated at intervals of 10 deg over the range 0–60 °C.[29] The values of s obtained by linear interpolation or extrapolation from the two nearest temperatures are presented in Table II, along with the values of the helix content calculated for the host–guest copolymer with degree of polymerization of 260 and mole fraction Lys of 0.06. The best appreciation of the significance of the results presented in Table II is probably obtained by comparison of the helix contents calculated for the host–guest copolymer with those calculated for the host homopolymer (last column). If the guest is assigned the values reported earlier,[29] i.e., those listed in the columns headed by Lifson and Allegra of Table II, the helix content of the host–guest copolymer is always slightly lower than that of the host homopolymer. The difference in helix content is in the range 0.06–0.07 at 5 °C to 0.03 at 68 °C. If, on the other hand, the guest is assigned the values that provide the best description of the fractions listed in Table I, the helix content of the host–guest copolymer is very slightly larger (0.02–0.03) than that of the host homopolymer at 5 °C and somewhat smaller (0.09) than that of the host homopolymer at 68 °C. The maximum difference between helix contents of host–guest copolymers and the host homopolymer in Table II is 0.14, and the average difference is 0.056. It is difficult to obtain reliable values of σ and s for Lys when the mole fraction is only 0.06 because the small amount of Lys produces only a small difference in the melting curves. The previous study[29] surmounted this problem by characterization of samples with a larger mole fraction of Lys.

In view of the preceding discussion, it should not be surprising to find that it is difficult to establish the value of σ uniquely for the present samples in the presence of NaDodSO$_4$. Table III presents two sets of results when the NaDodSO$_4$ concentration is 0.011 M, which corresponds to the middle of the three arrows in Figures 1 and 5. The values of τ when σ for Lys is assigned as 10^{-4}, 10^{-3}, 10^{-2}, and 10^{-1} are 0.070, 0.066, 0.063, and 0.071, respectively. The best fit to the data is obtained when σ is 10^{-2}, but fits of nearly equivalent quality are obtained with the other values of σ. The values of s in Table III are similar to those reported in Table II when the temperature is 56 or 68 °C, and they are smaller than those in Table II at lower temperatures. If σ has the value 10^{-2}, the values of s are in the range 0.43 ± 0.03 when the NaDodSO$_4$ concentration is 0.046 M. At 0.0059 M NaDodSO$_4$, the values of s decrease monotonically from 1.14 at 5 °C to 0.67 at 68 °C, very similar to the values in the absence of NaDodSO$_4$.

The addition of NaDodSO$_4$ to an aqueous solution has been found to produce a decrease in the value of s for isolated Arg residues in host–guest copolymers in which the host is (hydroxybutyl)-L-glutamine.[26] When the detergent concentration is 0.0115 M, the values of s for Arg are in the range 0.71 ± 0.03 and show little dependence upon temperature over the range 5–68 °C. In a qualitative sense, the results obtained earlier with Arg are similar to those reported here with Lys. In both cases, the addition of NaDodSO$_4$ produces a marked reduction in s for the isolated cationic residues; i.e., the helix is destabilized. The influence of NaDodSO$_4$ on the isolated cationic residues is qualitatively different from that seen when the cationic residues occur at higher concentration. A random copolypeptide of Lys and Ala, in which each residue is present at a mole fraction of 0.5, undergoes a transition from random coil to α helix upon the addition of NaDodSO$_4$.[20] When present at this mole fraction, the value of s for Lys apparently experiences an increase upon the addition of the anionic detergent. Consequently one might imagine that the value of s for a cationic residue, when present as the guest in a copolymer with a nonionic host, will be strongly correlated with the mole fraction if the measurements are performed in the presence of NaDodSO$_4$ at a concentration near its cmc.

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Registry No. (Hydroxybutyl-L-glutamine)(L-lysine) (copolymer), 115207-16-4; lysine *N*-carboxyanhydride, 51875-11-7; hydroxybutyl-L-glutamine *N*-carboxyanhydride, 115207-15-3.

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Configurational Properties of Finite Cyclic Alkanes

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ABSTRACT: The dependence of local chain configurations on the number of bonds, n, has been examined for cyclic alkanes. Discrete enumeration is used for identification of all nonintersecting rings with $6 \leq n \leq 22$ on a tetrahedral lattice. Rotational isomeric state theory provides the information for infinitely large rings. Interpolations suggest the behavior of rings of intermediate size, $22 < n < \infty$. Ensembles are weighted in various ways, including (1) all rings weighted equally; (2) $\sigma = 0.43$, which incorporates the butane effect; and (3) $\sigma = 0.43$ and $\omega = 0.034$, which incorporates both the butane and pentane effects. Probabilities are evaluated for occupation of all rotational isomers and for all pairs of rotational isomers at successive bonds. The dominant ring configurations at $6 \leq n \leq 22$ are identified.

Introduction

The configurational characteristics of cyclic alkanes undergo drastic changes as the number of bonds, n, increases from six to infinity. This conclusion follows immediately from the observation that the cyclic chain with $n = 6$ does not have any bond in a trans state, but the majority of the bonds occupy trans states as n becomes infinite. The occupancy of rotational states in infinitely large cyclic polyethylenes is easily calculated from the known behavior of large linear polyethylene chains.[1,2] The calculation presents a more difficult problem for rings that contain 10–100 bonds. Nevertheless, the results for chains of 10–100 bonds are of interest because it is here that the bulk of the transition from cyclohexane to an infinitely large cyclic polyethylene takes place. This transition range is important for several reasons, including its use for deducing the configurational origin of various spectroscopic transitions observed in cyclic alkanes. The diamond lattice rings described here will be used in the analysis of the vibrational spectra of cycloalkanes $C_{14}H_{28}$, $C_{16}H_{32}$, and $C_{22}H_{44}$.[3] Calculations have been performed for cyclic polyethylenes with even n, $6 \leq n \leq 22$. These calculations cover a range that adequately defines an extrapolation to the known limits for infinitely large rings. Therefore, the motivation for this work is somewhat different from the driving force in previous studies of the dimensions of unperturbed[4] and perturbed[5–7] rings, probability for ring closure,[8,9] or rate of intramolecular cyclization.[10–12] The motivation is more closely related to the description of the local configurations that are consistent with ring closure.[13–17]

Methods

All possible configurations were examined for linear chains that are confined to a tetrahedral lattice and have an even number of bonds in the range 6–22. Average properties were computed for those chains that have an end-to-end distance of zero but do not otherwise intersect. This averaging was achieved using several different values of σ and ω, which are the statistical weights for first- and second-order interactions in the rotational isomeric state model developed for linear polyethylene by Abe et al.[7] These combinations of statistical weights are presented in Table I. The first pair of statistical weights considers all configurations to be of equal energy, the second pair penalizes gauche states in the manner expected for polyethylene at 300 K, and the third combination also invokes the penalty for the "pentane effect" in the manner expected at that temperature. The fourth, fifth, and sixth combinations invoke the butane and pentane effects in the manner expected at temperatures of 350, 400, and 450 K, respectively.

Table I
Combinations of Statistical Weights Used

σ	ω	comment
1.000	1.000	configurations equally weighted
0.432	1.000	butane effect, 300 K
0.432	0.034	butane and pentane effects, 300 K
0.487	0.056	butane and pentane effects, 350 K
0.533	0.081	butane and pentane effects, 400 K
0.572	0.106	butane and pentane effects, 450 K

Averages of configuration-dependent properties for unperturbed linear chains were evaluated by using standard matrix methods.[1,2,18]

Results and Discussion

Occurrence of Nonintersecting Cyclic Chains. The configuration partition function for the unperturbed chain is denoted by Z[1,2] and is calculated as

$$Z = \{(1 - \lambda_2)\lambda_1^{(n-1)} + (\lambda_1 - 1)\lambda_2^{(n-1)}\}/(\lambda_1 - \lambda_2) \qquad (1)$$

$$\lambda_1, \lambda_2 = \{1 + \sigma + \sigma\omega \pm [(1 - \sigma - \sigma\omega)^2 + 8\sigma]^{1/2}\}/2 \qquad (2)$$

where λ_1 and λ_2 are the eigenvalues of the statistical weight

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