Special Review

THERMODYNAMIC ASPECTS OF CONFORMATIONAL TRANSITIONS IN SYNTHETIC POLYPEPTIDES

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The helix-coil transition of organic solvent soluble homopolypeptides has been discussed from a largely thermodynamic view-point. The present state and the future prospects are considered.

About two decades ago two key processes in biology, gene replication and protein denaturation, began to be understood in some detail at a molecular level. Each involved one or more conformational changes in the participating macromolecules, the several nucleic acids and a large variety of polypeptides, respectively. These changes between ordered and disordered conformations were understood to be highly co-operative in nature, being processes, that is to say, which occur over a small interval of temperature or other perturbing extrinsic variable. Because of the molecular species involved, these order-disorder transitions are one-dimensional. Thus it became clear that protein denaturation, for example, could be described, from a physical chemical point-of-view, as a smeared, first-order, one-dimensional phase transition. The over-simplification in this description is now apparent; nevertheless the underlying concept is such a general and useful one that refinements are hardly necessary except for the most detailed studies [1].

Following, or concurrent with, the realizations concerning the molecular biological processes referred to above, came two further steps relevant to this discussion: the development of a considerable variety of statistical mechanical descriptions of such processes, all capitalizing on the mathematical simplifications inherent in the one-dimensionality of the model [2], and secondly, the introduction of routes for easily synthesizing homopolymers of α-amino acids, chemically analogous to proteins, of high molecular weight and with an infinite variety of pendant side chains [3]. Many of these synthetic polypeptides were found to assume ordered conformations in solution – the α-helix known to be present in many proteins being the most commonly encountered – and since these conformations could be destroyed by an appropriate change of an external variable – temperature, pH, solvent, etc. – to yield random coils, systems modeling protein denaturation now became available. Indeed the study of conformational transitions in synthetic polypeptides provides some advantages over comparable studies

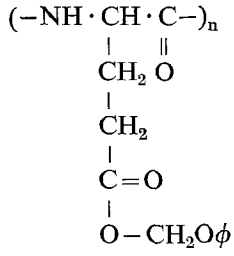
in naturally occurring peptides: total reversibility over many cycles, essentially complete transformation of the macromolecule into one or other of the conformational states, unambiguous dimensionality of the co-operative process, a ready investigation of the effect of molecular weight, and the opportunity to systematically determine the effect of side group structure on the transition. Thus, by an appropriate choice of side group it became possible to synthesize polypeptides displaying the desired phenomena which were soluble in organic solvents, and thereby to separate out electrostatic charge effects on the stabilization and destabilization of the ordered conformation. It became clear at an early stage, from the geometrical structure of the α-helix and from numerous other considerations that hydrogen bonding between residues along the peptide backbone played an important role in the stabilization of the several ordered conformations, and that these and other non-covalent interactions between side groups could be studied in such systems.

Thus conformational (helix-coil) transitions in synthetic polypeptides became of interest from many points of view, and in the past twenty years a considerable body of literature has emerged [1].

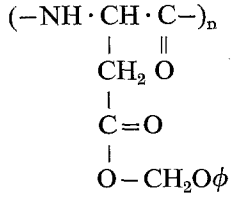
Thermodynamics of helix-coil transitions

In this review we shall be concerned with the helix-coil transition of organic solvent soluble homopolypeptides from a largely thermodynamic view-point. In such systems, the conformational transitions may most conveniently be induced either by a change of temperature or of solvent type. In the most general terms, solvents may be divided into two classes: those which are capable of interacting with the polypeptide backbone in the random -coil conformation, usually by competitive formation of a peptide-solvent hydrogen bond, and which therefore serve to destabilize the helix, and those which are indifferent to the conformational state of the solute. These are termed active and inert solvents respectively.

Structures of two polypeptides which have been quite extensively studied are shown below



Poly-γ-benzyl-L-glutamate
(PBG)



Poly-β-benzyl-L-aspartate
(PBA)

In spite of the minimal differences in the side group in these two polymers their behavior with respect to the stability of the respective α-helices in the presence of active solvent is markedly different. For example around ambient temperature, the PBA α-helix (which, atypically for L-isomers, has left-handed chirality [4]) requires some 6 mole% dichloroacetic acid (DCA) in a DCA-inert solvent mixture to undergo disruption [5]; the corresponding figure for the much stronger PBG α-helix is 70 mole% DCA [6].

The intramolecular (interpeptide) hydrogen bonds stabilizing the α-helix are of course also susceptible to thermal disruption; however, contrary to what might be anticipated, an increase in temperature in the systems under discussion tends to promote the formation of the helical at the expense of the coiled conformation. These so-called inverse thermal transitions can be readily accounted for by considering the solute and solvent system *in toto*: the entropy decrease in the former upon the formation of an ordered structure is balanced by an entropy gain in the active solvent component upon "desorption" from the peptide sites in the random coil.

An important development in helix-coil transition studies was the establishment of methods for estimating the fractional helical content, f_H, in a given solvated polypeptide from optical rotatory dispersion or even optical rotation measurements at a single wavelength [7]. This made it possible to follow the course of a transition from simple polarimetric determinations. The measurement of f_H as a function of temperature (Fig. 1) permits the calculation of the van't Hoff enthalpy ΔH_{VH}. This quantity is related to the co-operativity of the transition and is structure-dependent. In one of the most widely used of the theoretical treatments referred to above, that due to Zimm and Bragg [8], this relationship is expressed simply as

$$\sigma^{1/2} = \Delta H_{cal}/\Delta H_{VH}$$

where ΔH_{cal} is the calorimetric transition heat per mole of peptide residue and σ is equal to $\frac{1}{\bar{n}^2}$, where the $\bar{n}$ is the average number of residues in a helical sequence at the transition mid-point, i.e. at $f_H = 0.5$. Typical values for σ are of the order of 10^{-4}.

An initial estimate of σ was obtained from measurements of the effect of molecular weight on the course of the transition, but it became desirable to measure ΔH_{cal} experimentally, and thus calculate σ directly. The postulated mechanism involving hydrogen bond interactions suggested that ΔH_{cal} would be of the order of a kilocalorie per mole of residue, or less. Since it was appropriate to perform measurements in as dilute a solution as possible – with a polypeptide concentration certainly no greater than 2–3% – it could be readily calculated that a measurement of ΔH_{cal}, although in principle no different from a determination of a heat of fusion, would require instrumentation of unusual sensitivity. In 1964 the first author of this review had available a wide temperature range high precision adiabatic calorimeter designed for the investigation of transitions in solid

synthetic polymers. It was with this apparatus that the first direct measurement of ΔH_{cal}, for the polypeptide, poly-γ-benzyl-L-glutamate (PBG), was achieved, (Fig. 2) [10]. Concurrently, and independently, Ackermann and co-workers, using

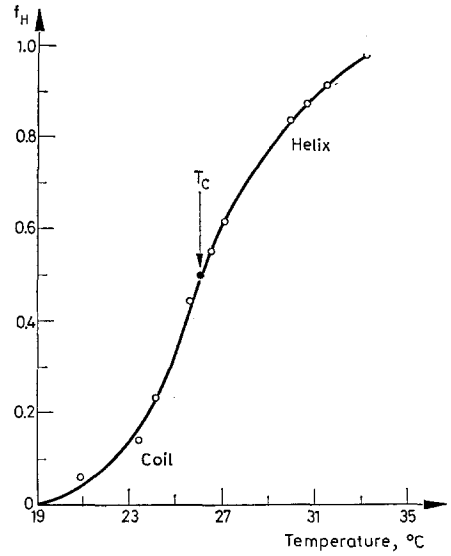


Fig. 1. Fractional helical content, f_H, for poly-γ-benzyl-L-glutamate (PBG) in 75 : 25 (v/v) dichloroacetic acid-1,2-dichloroethane (DCA-DCE) mixture as a function of temperature. Data obtained from optical rotation measurements at 589 nm

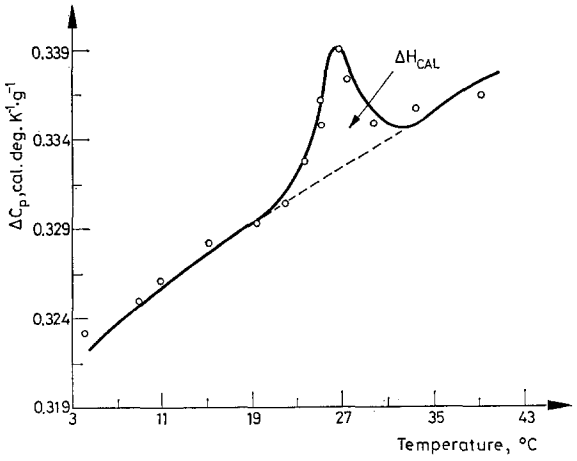


Fig. 2. The heat capacity of a 2 weight % PBG solution (solvent composition 75/25 v'v, DCA-DCE) as a function of temperature. Adapted from reference 10

a twin adiabatic calorimeter in this case designed for heat capacity studies of electrolyte solutions, obtained essentially identical results for the same system [11]. Finally, in about the same period Privalov and his co-workers were beginning a somewhat comparable series of investigations into conformational transitions in proteins, using a differential thermal analysis instrument of unusual sensitivity [12].

Thus it was established that ΔH_{cal} could be determined, albeit with some difficulty, from precision measurements of the heat capacity of the respective polypeptide solutions as a function of temperature [13]. Somewhat later an alternative approach was developed, in which the transition heat was measured by inducing a conformational change in the polypeptide by altering the solvent composition. These isothermal solvent titration experiments could be carried out directly in an appropriate calorimeter or, in yet another variation, the heats of solution of the dry polypeptide in solvents of systematically varied compositions could be determined [14]. Still later developments in the acquisition of ΔH_{cal} data will be discussed below.

Phase boundaries

It has already been mentioned above that an increase in temperature, at a constant solvent composition, induces a coil-to-helix transition for the systems of interest discussed here. It was also soon shown that the transition temperature T_c itself was strongly dependent on solvent composition, increasing with an increase in the mole fraction of active solvent, x_A, in the mixture [15]. Such data permits the construction of a phase diagram – a term used in obvious analogy to the common representation of solid-liquid and solid-solid transitions – by plotting T_c as a function of x_A. It was pointed out already in 1959, that although an inverse thermal transition was almost invariably observed in organic solvent soluble polypeptide systems it was thermodynamically necessary that a "normal", helix-to-coil transition take place at some higher temperature [16]. However, for some years the relationship of the two transitions was unclear, nor could such a transition be found experimentally in spite of at least one study of PBG in several solvents at high temperatures [17].

Recently it was shown that complete phase boundaries for a polypeptide-active/inert solvent system could be calculated from equations derived from a formalization of the model already described qualitatively above [18]. The overall helix-coil transition was resolved into two steps represented symbolically by

$$\ldots\text{HHHCCC}\ldots \rightleftarrows \ldots\text{HHCCCC}\ldots \quad (1)$$

and I

$$\ldots\underset{\mid\;\;\;\mid}{\text{C}\,\text{C}\,\text{C}\,\text{C}\,\text{C}}\ldots + \text{A} \rightleftarrows \ldots\text{CCCCC}\ldots \quad (2)$$

(where in the left-hand chain two C units each carry a bound A, and in the right-hand chain three C units carry bound A: A A → AA A)

In these equations H and C represent an individual peptide residue in the ordered (helical) or coil conformation respectively, A represents an active solvent species capable of binding to a residue in the disordered conformational state. The inert solvent I in the system serves to modify the activity of A. Thus Eq. (1) represents the growth of a coil at the expense of a helical sequence, while Eq. (2) represents a stepwise binding of A to the disordered chain. It was assumed that the species A was distributed randomly amongst the C residues with no lateral interaction. The equations obtained from this model contain the following parameters: the equilibrium constants K_1 and K_2 associated with Eqs (1) and (2) respectively, the activity of A in the mixed solvent system, and the temperature T. The two equilibrium constants can be further resolved into enthalpy and entropy terms, ΔH_1 and ΔH_2, ΔS_1 and ΔS_2, in the normal manner.

The following central equation relating these parameters was derived:

$$RT \ln s = -(\Delta H_1 - T\Delta S_1) - RT \ln\{1 + x_A \exp[(\Delta H_2 - T\Delta S_2)/RT]\} \qquad (3)$$

where s is the overall equilibrium constant between helical and coil residues in the polypeptide, and the activity of A is approximated by its mole fraction, x_A.

Phase boundaries, i.e. curves of T_c as a function of x_A, in terms of the four thermodynamic parameters are calculated by solving Eq. (3) for T as a function of x_A with the condition $s = 1$, i.e. $T = T_c$. The calculated phase diagrams fall basically into two categories, depending on the relation of ΔH_1 to ΔH_2. In the case $|\Delta H_1| \geq |\Delta H_2|$, a single phase boundary is observed dividing a low temperature helical phase domain from a higher temperature coil phase (Fig. 3). With the condition $|\Delta H_1| < |\Delta H_2|$ a slightly more complicated situation prevails in which two branches of the phase boundary may be found separating the helical region from low and high temperature domains in which the coil phase predominates, in the former regime with a high fraction of C "sites" filled by A, whereas for the coil at high temperature a low degree of binding is calculated (Fig. 4a). For certain combinations of values of the parameters the two branches of the phase

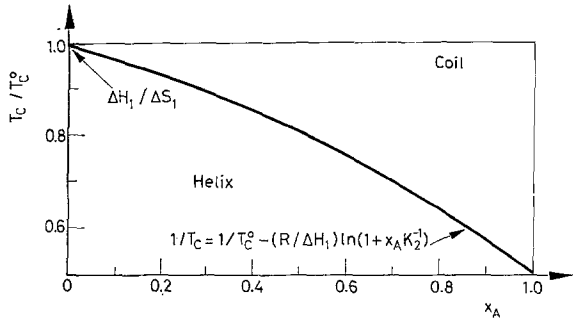


Fig. 3. Schematic of phase diagram calculated for a polypeptide in a binary active/inert solvent system, showing reduced transition temperature T_C/T_C^0 *vs.* mole fraction active solvent, x_A, with $|\Delta H_1| \geq |\Delta H_2|$

boundary will join to produce a closed loop, Fig. 4b. The latter situation is favored by the use of a relatively strongly binding solvent *A*.

The results derived from this model and particularly the calculated phase boundaries, clarify the situation with respect to the solvent dependence of T_c, the inverse thermal transitions, and many of the other experimentally observed features of the helix-coil transition of polypeptides in mixed organic solvents. For example, in most of the systems studied the active solvent has been the more strongly binding type, associated with phase diagrams of the type depicted either in Fig. 4a or 4b, and in these cases the experimentally accessible temperature interval, approxi-

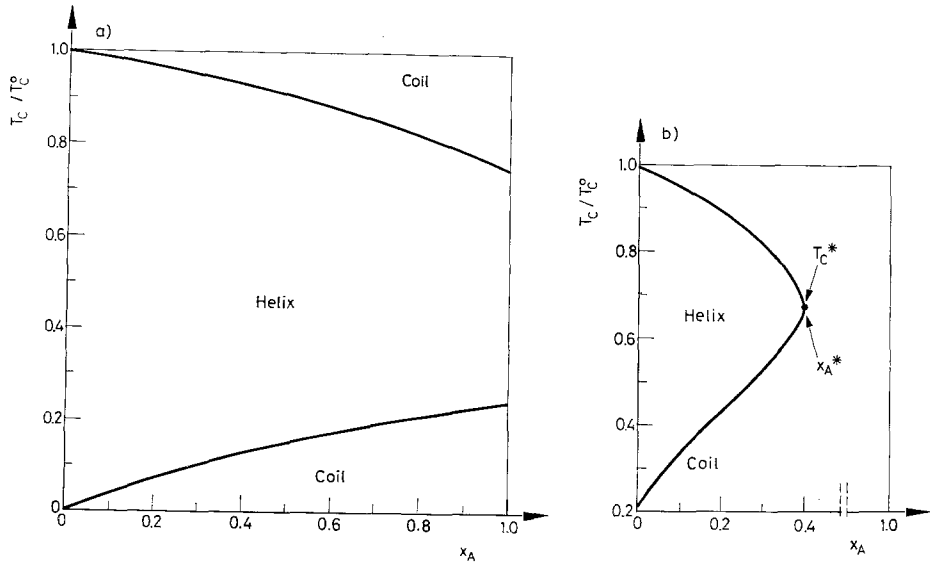


Fig. 4. Schematics of phase boundaries calculated with $|\Delta H_1| < |\Delta H_2|$. The closed loop depicted in 4(b) indicates a stronger interaction of active solvent and polypeptide relative to the two branch phase diagram 4(a) [18]

mately 0° to 100°, happens to coincide with the lower branch or portion of the phase boundary, i.e. that region in which $dT_c/dx_A > 0$. Inverse thermal transitions are therefore observed.* In these cases a higher temperature transition of the helix-to-coil variety is indeed predicted, but is likely to be unobservable because of the experimental problems at high temperatures – polymer degradation, solvent volatilization, etc. However this is largely determined by the intrinsic stability of the particular polypeptide helix, i.e. its transition temperature T_c° in undiluted inert solvent, at $x_A = 0$. Clearly the considerable dispersion in this parameter

* Normally if a "weaker" active solvent were to be used in these systems, the depression in T_c would be too small, and no transition at all would be noted.

must be ultimately traceable to variations in side-group structure and interactions. It was already established that for a known "weak" polypeptide, poly-β-benzyl-L-aspartate (PBA), both normal [19] and inverse [5] transitions could be observed in the experimental window, according to solvent system used. The explanation for this again is that with the weaker active solvents, a phase diagram of the type depicted in Fig. 3 will be found, for the more active solvents, Fig. 4a or 4b type phase diagrams will tend to be observed. Thus if T_c° is low enough (but still, of course, above ambient) then the "normal" transition predicted in Fig. 4a or 4b can be observed. From such considerations we have recently shown that by a careful choice of solvent type and composition it is possible to find conditions in which both inverse and normal thermal transition in PBA are to be found, at a given composition, in the $0° - 100°$ temperature range [20].

The relatively low T_c° for this polypeptide – our most recent estimate is $155 \pm 5°$ – also permits tests of other predictions of the theory and the correctness of certain postulates in the model. For example according to current belief the chlorinated hydrocarbons which typically serve as the inert component in active-inert solvent mixtures should not interact preferentially with either of the allowed polypeptide conformations. Thermodynamically this implies that the phase boundaries for a given polypeptide-active solvent system should coincide regardless of the inert solvent employed. It has already been demonstrated in PBG that this was not the case [16], but it was assumed that the neglect of activity coefficients was responsible. For PBA, a direct test of this point by the measurement of T_c° in different inert solvents is feasible. In actual practice it is preferable to measure the somewhat lower transition temperature exhibited in inert-active solvent mixtures for PBA; this then necessitates only a short, quite reliable, extrapolation to yield T_c°.

Our preliminary results in regard to this point indicate that hitherto supposedly inert solvents do in fact possess some slight activity, as shown by a small spread of observed T_c°'s. A rough measure of this interaction is obtained by the depression of the T_c° from its "asymptotic" value. Formally, peptide-solvent interactions in such cases should be interpreted in terms of two active solvents, say A_1 and A_2, competing for "C" sites along the polymer backbone. The basic theory expressed in equation 3 has recently been modified to take this into account and several cases of transitions of PBG in binary active solvent systems have been experimentally studied. In the general case, where a third, effectively inert, solvent is also present, the equilateral triangle representation of an isothermal section used in ternary phase diagrams is appropriate, (Fig. 5) [21].

Other assertions of the theory can be tested by using different active solvents. The temperature T_c° is equal to $\Delta H_1/\Delta S_1$ and these enthalpy and entropy parameters are, of course, also characteristic of a given polypeptide; thus the derived values should be independent also of the active solvent system in which the experimental data are observed. Data obtained for PBG in two very different active solvents, dichloroacetic acid and 1,3-dichloro-1,1,3,3-tetrafluoropropan-2,2-diol, and ignoring the possible small effects due to different inert components, has largely borne out this contention [22, 23]. An analogous question, which is whether

the interaction of a given active solvent with a polypeptide is unaffected by the nature of the pendant side-group, as may also be implied from the postulated mechanism, has not yet been subjected to a definitive test.

Since the formation of hydrogen bonds of varying types is of the greatest importance in any consideration of the different conformation of solvated polypep-

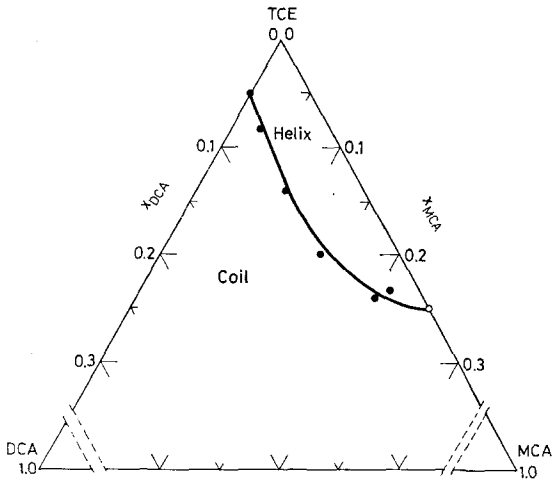


Fig. 5. Isothermal section of three component phase diagram (two active, one inert solvent) for poly-γ-benzyl-L-glutamate in the solvent system, dichloroacetic acid (DCA)-monochloroacetic acid (MCA)-1,1,2,2-tetrachloroethane (TCE). The points are the experimental data and the solid line represents the best fit according to the theory developed in reference 21

tides the opportunity to gain further information on such bonds from isotopic substitution experiments presents itself. Deuteration of polypeptides at the labile amide hydrogen position has been shown to cause a substantial change in the transition temperatures of PBG [24], but direct interpretation is complicated by the fact that the active solvent in such studies e.g. dichloroacetic acid, is necessarily also deuterated [25, 26]. Some simplification can be achieved by using aprotic active solvents and in the single case where this technique has been applied no change in the T_C of PBA could be detected [27]. Further investigations are being undertaken with the objective of assessing the relative contributions of the backbone hydrogen bonds and of side group interactions to the stability of a given polypeptide. The basic assumption is of course that the latter interactions would normally be unaffected by a deuterium-hydrogen substitution in the backbone α-amino group [28].

Experimental considerations

The theoretical framework discussed above contains four parameters, of which two are a function of the polypeptide alone, and two are dependent on the active solvent and (probably) on the polypeptide also. A knowledge of these parameters permits the calculation of the phase boundaries and of a wide variety of other thermodynamic properties of the helix-coil transition. It is of course also desirable to invert the process and to estimate these parameters from experimental data. In principle, this could be done from phase boundary determinations alone, but this procedure does not lead to reliable estimates, and in practice transition enthalpies, preferably as a function of temperature, are additionally required. The calorimetric heat ΔH_{cal} is related to the enthalpies associated with the individual equilibria as follows [18]:

$$\Delta H_{cal} = \Delta H_1 + F_c \Delta H_2$$

where F_c is the fraction of coil residues bonded to A at the mid-point of the transition. F_c and hence ΔH_{cal} are functions of T_c. Procedures for deriving ΔH_1, ΔH_2, ΔS_1 and ΔS_2 which depend on the enthalpy and phase boundary data available in a particular case have been worked out [18].

The determination of ΔH_{cal} therefore assumes an even more important role in the elucidation of the details of the helix-coil transition. The techniques used in the earliest experiments described above suffered uniformly from several disadvantages: relatively complex instrumentation is required, data acquisition is slow and perhaps of insufficient precision, and sample requirements are often burdensome.

A promising alternative approach is the use of commercially available differential scanning calorimeters [29, 30]. This instrumentation with perhaps only relatively modest modifications, can be sufficiently sensitive to make ΔH_{cal} determinations feasible. Recently for example we have used a Perkin–Elmer DSC-2 in measurements of transition enthalpies for the ubiquitous PBG in several solvents over a considerable temperature range [31, 33]. Precisions of the order of $\pm 5-10\%$, comparable to those attained with the older more cumbersome techniques but using polypeptide samples three orders of magnitude smaller were achieved. While still not entirely satisfactory the experimental advantages of these techniques are such as to make these results most encouraging, and further developments are likely.

In summary there are currently available several distinct experimental calorimetric techniques for the direct determination of ΔH_{cal} for conformational transitions in polypeptides and proteins: 1. heat capacity measurements of the respective solutions at constant solvent composition over the appropriate temperature interval using either classical adiabatic calorimeters or commercial scanning instruments, and 2. isothermal measurements of heats of solution of polypeptide films, or of heats of mixing of polypeptide solutions using one or another of the several variations of conduction micro-calorimeter. All of these techniques may yield results accurate to $\pm 5-10\%$. All other factors being equal, ΔH_{cal} is of course

independent of the measurement technique, but it should be noted that apparent discrepancies may be found if account is not taken of the fact that because of the finite transition width incomplete conversion between the two conformational states may occur [34].

It should also be noted that non-calorimetric techniques of determining ΔH_{cal} have been derived [35]. These are based essentially on the determination of the change in f_H with temperature and/or solvent composition and as a function of the molecular weight of the polypeptide, and rely therefore on the availability of sharp fractions of the given polymer in the range $10^3 - 10^5$ daltons. As far as can be judged at present ΔH_{cal} results from these techniques are in fair agreement with those obtained calorimetrically.

Future prospects

While it has been shown that studies of conformational transitions in synthetic polypeptides can be of interest from several points of view a basic motive for such investigations is surely the desire to ultimately account for the secondary, tertiary and quaternary structure of the naturally occurring analogoues, i.e. proteins, both in the solid phase and in solution, on the basis of information regarding non-covalent interactions gleaned from studies of these model compounds. Thus a systematic study of the stability of the α-helix in polypeptides as a function of the chemical structure of the side-group is necessary. We already have shown that quite small changes in the side-group structure have rather profound effects when measured in terms of the parameter T_c°, or ΔH_1 and ΔS_1 [18]. One may therefore predict that such studies of homopolypeptides of systematically varying structure will continue, and in the near future the next level of complexity, in which comparable studies of well-defined copoly-α-amino acids are carried out, will attract increasing attention. In this manner it will indeed eventually be possible to predict the conformational properties of a heteropoly-α-amino acid, both as a function of residue composition and sequence, and of environment.

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References

1. A. RICH and N. DAVIDSON, Structural Chemistry and Molecular Biology, W. H. Freeman and Co., San Francisco, 1968; G. D. FASMAN, Poly α-Amino Acids, M. Dekker, New York, 1967; N. LOTAN, A. BERGER and E. KATCHLSKI, Ann. Rev. Biochem., 42 (1973) 869.
2. D. C. POLAND and H. A. SCHERAGA, Theory of Helix-Coil Transitions in Biopolymers, Academic Press, New York, 1970.
3. C. H. BAMFORD, A. ELLIOT and W. E. HANBY, Synthetic Polypeptides, Academic Press, New York, 1956.
4. E. R. BLOUT and R. H. CARLSON, J. Am. Chem. Soc., 80 (1958) 1259.
5. Y. HAYASHI, A. TERAMOTO, K. KAWAHARA and H. FUJITA, Biopolymers, 8 (1969) 403.

6. P. DOTY and J. T. YANG, J. Am. Chem. Soc., 78 (1956) 498.
7. W. MOFFITT and J. T. YANG, Proc. Natl. Acad. Sci. U. S., 42 (1956) 596.
8. B. H. ZIMM and J. K. BRAGG, J. Chem. Phys., 31 (1959) 526.
9. B. H. ZIMM, P. DOTY and K. ISO, Proc. Natl. Acad. Sci., U. S., 45 (1959) 160.
10. F. E. KARASZ, J. M. O'REILLY and H. E. BAIR, Nature, 202 (1964) 693.
11. T. ACKERMANN and M. RUTERJANS, Zeit. Phys. Chem., 41 (1964) 116.
12. P. L. PRIVALOV *et al.*, Dokl. Akad. Nauk., USSR, 156 (1964) 951.
13. F. E. KARASZ and J. M. O'REILLY, Biopolymers, 3 (1965) 241.
14. A. KAGEMOTO and R. FUJISHIRO, Makromol. Chem., 114 (1968) 139.
G. GIACOMETTI and A. TUROLLA, Zeit. Phys. Chem., 51 (1966) 108.
15. F. E. KARASZ and J. M. O'REILLY, Biopolymers, 5 (1967) 27.
16. L. PELLER, J. Phys. Chem., 63 (1959) 1194.
17. J. S. FRANZEN, J. B. HARRY and C. BOBIK, Biopolymers 5 (1967) 193.
18. F. E. KARASZ and G. E. GAJNOS, J. Phys. Chem., 77 (1973) 1139.
19. T. NORISUYE, K. MISUMI, A. TERAMOTO and H. FUJITA, Biopolymers 12 (1973) 1533.
20. R. P. MCKNIGHT and F. E. KARASZ, Macromolecules, 7 (1974) 143.
21. D. LU and F. E. KARASZ, Macromolecules, (in press).
22. G. E. GAJNOS and F. E. KARASZ, J. Phys. Chem., 76 (1972) 3464.
23. J. SIMON, G. E. GAJNOS and F. E. KARASZ, Analytical Calorimetry, Plenum Press New York, 1974, Vol. 3, p. 443.
24. F. E. KARASZ and J. M. O'REILLY, Biopolymers, 4 (1966) 1015.
25. F. E. KARASZ and J. M. O'REILLY, Adv. in Chem. Series, 63 (1967) 180.
26. F. E. KARASZ and J. M. O'REILLY, Studia Biophysica, 4 (1967) 69.
27. P. DUBIN and F. E. KARASZ, Biopolymers, 11 (1972) 1745.
28. G. E. GAJNOS and F. E. KARASZ, to be published.
29. A. KAGEMOTO and F. E. KARASZ, Analytical Calorimetry, Plenum Press, New York, 1970, p. 147.
30. R. P. MCKNIGHT and F. E. KARASZ, Thermochim. Acta, 5 (1973) 339.
31. J. SIMON and F. E. KARASZ, Thermochim. Acta, 8 (1974) 97.
32. J. SIMON, G. E. GAJNOS and F. E. KARASZ, Proceedings of the VIth ICTA, Budapest, 1974, p. 99.
33. J. SIMON, G. E. GAJNOS and F. E. KARASZ, Polymer J. (Japan) (to be published).
34. F. E. KARASZ and G. E. GAJNOS, Biopolymers, 13 (1974) 725.
35. N. SAYAMA, K. KIDA, T. NORISUYE, A. TERAMOTO and H. FUJITA, Polymer J., 3 (1972) 538.

RÉSUMÉ — On a discuté d'une pointe de vue thermodynamique large la transition helix—non helix des homopolypeptides solubles dans des solvants organiques et considéré la situation actuelle ainsi que les perspectives futures.

ZUSAMMENFASSUNG — Der Helix-Ungeordnete Übergang von in organischen Lösungsmitteln löslichen Homopolypeptiden wurde aus einem breiten Gesichtspunkt diskutiert, gegenwärtige Lage und zukünftige Entwicklungsaussichten erörtert.

Резюме — Рассмотрены спиральные переходы в гомоpолипептидах, растворимых в органических растворителях, с точки зрения макротермодинамики. Рассмотрено настоящее состояние и будущие перспективы исследований в этой области.