holds for $l = 0$ also. The multiplicity of solutions is due to the arbitrariness as to what is called layer zero; i.e., if for one solution φ_{lo} is the concentration on layer l, there is another solution with the same free energy for which $\varphi_{l-1,o}$ is the concentration on layer l.

For values of φ_{0o} not corresponding to a minimum of the surface tension there is a less than optimal degree of mixing in the layers. The situation is best visualized by considering the more symmetric system of the interface between two immiscible polymers, A and B. The lattice model for this system has been discussed in detail elsewhere,[5] but we will only delve into a quite intuitive aspect of the problem here. There are two solutions to the equations governing this interfacial structure. In the first we have a symmetry about the plane between layers 0 and 1 in the sense that

$$\varphi_{lA} = \varphi_{1-l,B} \qquad \text{(III.6)}$$

where φ_{lK} is the fraction of cells in layer l occupied by units of polymer K. The second solution to the equations has symmetry about the layer $l = 0$, with

$$\varphi_{lA} = \varphi_{-l,B} \qquad \text{(III.7a)}$$

a special case of which is

$$\varphi_{0A} = \varphi_{0B} = \tfrac{1}{2}$$

These two solutions can be embedded in a continuum of possible density profiles resulting from fixing φ_{0A} and relaxing the equation corresponding to eq III.1. In this case we find that the profile corresponding to eq III.6 is a true solution, corresponding to a minimum of the surface tension γ. On the other hand, the solution with $\varphi_{0A} = \frac{1}{2}$ is a surface free energy maximum corresponding to the most mixing in the layers. While the solvent–polymer solution interface is not symmetric like the polymer–polymer interface, still it is clear that certain degrees of mixing are more favorable than others with respect to free-energy minimization.

For the broad interface we see in Figure 11 that the surface tension vs. concentration of solvent in layer zero, φ_{0o}, is quite shallow in its oscillations, only $0.000\,006 k_B T$ per cell. If one is not at an optimal value of φ_{0o} the approach to the solution tends to be quite slow. The way to get around the difficulty is to not leave the adjustments of φ_{0o} to the vagaries of the iterative procedure. Rather, one fixes φ_{0o}, in which case the rest of the solution $\{\varphi_{lo}\}$, $\{\xi_l\}$ rather quickly converges. Then one varies φ_{0o} until the minimum on a curve such as Figure 11 is located.

In mean field theory one accepts only the solution corresponding to the free-energy minimum, but in reality there will be common fluctuations involving states of $0(k_B T)$ away. Therefore, for broad interfaces it can be inferred that the values of concentration found on each layer will be subject to significant fluctuations. This will show up as a further broadening of the interface, for example in x-ray scattering experiments. The values of the surface tension should be less affected. The actual evaluation of free energies to be associated with fluctuations requires that one allow for inhomogeneity in the direction parallel to the interface, which is beyond the scope of this paper, although perhaps not beyond the power of the methods employed.

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Intrachain Reaction of a Pair of Reactive Groups Attached to Polymer Ends. I. Intramolecularly Catalyzed Hydrolysis of a Terminal *p*-Nitrophenyl Ester Group by a Terminal Pyridyl Group on Polysarcosine Chain

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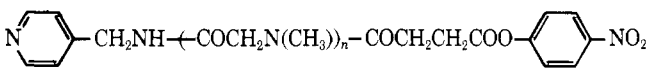
ABSTRACT: The hydrolysis of *p*-nitrophenyl ester groups catalyzed intramolecularly by pyridyl groups, with the two groups attached to two ends of a polysarcosine chain, was investigated. The intrachain reaction rate constant was determined as a function of the degree of polymerization of 5 to 35 at three different temperatures. The rate constant was larger for shorter chains and at higher temperatures. This reaction was compared with the cyclization reaction proceeding on a polymethylene chain taking into account the difference in the inherent reactivity of the end groups. The polysarcosine chain was found to be two or three times more efficient than the polymethylene chain for the intrachain reaction. Activation parameters, $\Delta H_c^{\ddagger}$ and $\Delta S_c^{\ddagger}$, characterizing the conformational change required for the intrachain reaction, were evaluated. $\Delta H_c^{\ddagger}$ as well as $\Delta S_c^{\ddagger}$ increased with increasing chain length. The compensation plot was linear giving an isokinetic temperature of 93 °C. This suggests the possibility to alter the chain length dependence of the intrachain reaction by varying the temperature.

In an X–Y-type polymer the intrachain reactions of a pair of terminal reactive groups, X and Y, will be affected by the conformational properties of the polymer chain in solution. Most polymer chains are sufficiently flexible and if the reaction has a moderately high activation energy, the intrachain collision between X and Y takes place very frequently before the reaction occurs.[1-3] Under these conditions the rate of intrachain reaction is directly proportional to the ring-closure probability, i.e., a probability for a polymer chain to assume conformations in which the end-to-end distance is sufficiently short for the intrachain reaction. The probability will depend upon the chemical structure, chain length, temperature, and other external factors. In other words, it will be possible to control the intrachain reaction by varying these factors.

In 1935, Stoll and Rouvé investigated the esterification

of ω-hydroxycarboxylic acid ($HO(CH_2)_{n-2}COOH$) and determined the cyclization constant, the rate constant ratio of the intramolecular, and the intermolecular reaction, k_1/k_2.[4] Their results showed a strong dependence of the rate of intramolecular reaction upon the chain length. More recently intrachain reactions were discussed for a ring-chain equilibrium of various condensation polymers,[5] and for intramolecularly catalyzed hydrolyses on polyacrylamide[2,6] and polysarcosine[7] carrying randomly distributed reactive groups. The rate constants for these intrachain reactions were used to treat various polymer reactions with statistical theories.[8] Among these intrachain reactions, the reaction between two terminal groups is most simple and will provide basic information. In this series of investigations the intrachain reactions on the X–Y-type polymers are investigated to obtain data on the ring-closure probability.



I

The present paper deals with the intramolecularly catalyzed hydrolysis on a polysarcosine chain having a terminal *p*-nitrophenyl ester group and a pyridyl group (I). The rate of pyridine-catalyzed hydrolysis of *p*-nitrophenyl ester was determined as a function of the chain length *n*, at three different temperatures. Since the acylation of the pyridyl group by the ester group is the rate-determining step,[9] the intrachain reaction rate can be discussed in terms of the over-all rate of hydrolysis.

Experimental Section

Polymer I was synthesized as follows.[7] Sarcosine *N*-carboxyanhydride (NCA) was polymerized in dimethylformamide solution with 4-aminomethyl pyridine (4-AMP) as initiator. After 1 day the polymer solution was evaporated under reduced pressure. The residual oil was dissolved in pyridine and a threefold excess of succinic anhydride was added to the solution. After 3 h, a threefold excess of di-*p*-nitrophenyl sulfite was added and reacted for 1 day at room temperature. The polymer mixture was poured into ether and the precipitated polymer was collected and washed thoroughly with acetone and ethyl acetate. The amount of the terminal ester group was measured after a complete hydrolysis. The fraction of esterified polymer was 0.8 to 1.0. The number-averaged degree of polymerization, *n*, was calculated from eq 1.[10,11]

$$n = [\text{NCA}]/[\text{4-AMP}] \quad (1)$$

The reliability of eq 1 has been established[12] and was reconfirmed in this study by using the acetylated polymer (II). The number-averaged molecular weight was measured with a Hitachi-117 vapor pressure osmometer with sarcosine dimethylamide as a reference substance. The observed molecular weights of polymers produced at the NCA to 4-AMP ratio of 10 and 20 were 959 and 1517, respectively, whereas the theoretical values according to eq 1 are 861 and 1572, respectively. The polymerization of sarcosine NCA with 4-AMP followed the first-order kinetics. This fact and the applicability of eq 1 suggest that the Poisson-type molecular weight distribution was obtained for the polymer.[10,12]

II

4-(*N*-Acetylaminomethyl)pyridine (4-AcAMP) was synthesized by acetylating 4-AMP with an acetic anhydride–pyridine mixture, and recrystallized from ethyl acetate, mp 88.0 °C. The hydrolyses were carried out in phosphate buffer at pH 6.1 (μ = 0.067).[7] Reactions were followed by recording the absorbance of *p*-nitrophenol liberated (320 nm).[7] The concentration of the ester group was about 2.5 × 10^{-5} M. The fraction of neutral pyridyl group of 4-AcAMP was measured spectroscopically.[2,6] The fraction was 0.93 ± 0.01 at pH 6.1 over the temperature range of 15 to 35 °C. In the following discussions rate constants are *not* corrected for the fact that a portion of the pyridyl group is protonated and, therefore, not catalytically active. For the correction the observed rate constant should be multiplied by 1.0/0.93.

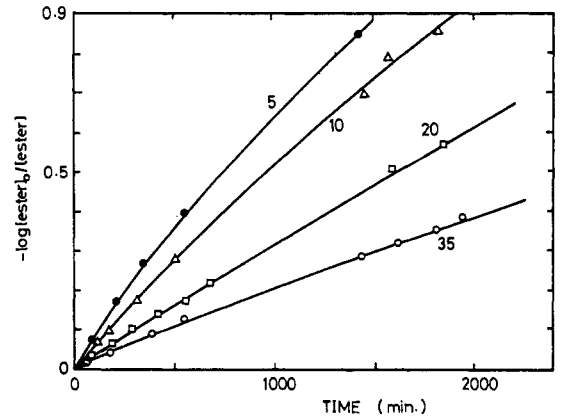


Figure 1. First-order plot for the hydrolysis of polymer I having four different chain lengths *n*: 25 °C, pH 6.1, $[\text{ester}]_0 \simeq 2.5 \times 10^{-5}$ mol/l.

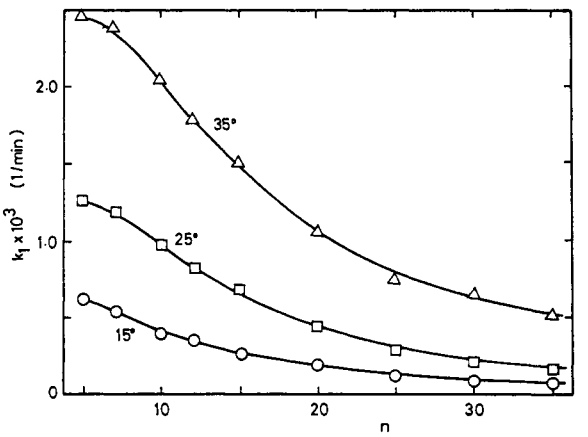
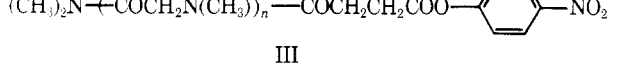


Figure 2. Dependence of intrachain reaction rate constant k_1 on the chain length *n* at three different temperatures, pH 6.1

Results and Discussion

Hydrolysis. Hydrolyses of polymer I having chain length *n* of 5 to 35 were carried out at 15, 25, and 35 °C. Typical first-order plots at 25 °C are shown in Figure 1. Hydrolysis proceeded faster as the chain length decreased. The plots in Figure 1 are slightly convex. This may be accounted for by the molecular weight distribution of the polymer I. Initially, the reaction proceeds mostly on shorter chains which are more reactive than the longer ones. In fact, the curvature was more marked with the shorter chains, where the chain length dependence of the rate constant was more marked (see Figure 2). The spontaneous hydrolysis and the base-catalyzed hydrolysis of polymer III obeyed strictly first-order kinetics up to at least 90% conversion.



III

From the initial slope of the first-order plot in Figure 1 the observed rate constant, k_{obsd}, was determined for the hydrolysis of polymer I. According to eq 2, k_{obsd} consists of three terms where k_1, k_s, and k_2 represent the rate constant for the intrachain catalysis, spontaneous hydrolysis, and intermolecular catalysis, respectively, and [Pyr] is the concentration of the terminal pyridyl group.

$$k_{obsd} = k_1 + k_s + k_2[\text{Pyr}] \quad (2)$$

Table I
Rate Constants for Spontaneous Hydrolysis k_s and 4-AcAMP-Catalyzed Hydrolysis k_2 of Polymer III (pH 6.1)

	n	15 °C	25 °C	35 °C
k_s, min^{-1}	10	8.0×10^{-5}	2.6×10^{-4}	7.4×10^{-4}
	20	8.0	2.7	7.4
	30	8.6	2.7	7.4
k_2, l./(mol min)	10		5.0×10^{-2}	
	20	2.1×10^{-2}	5.2	1.1×10^{-1}
	30		5.0	

Table II
Cyclization Constants k_1/k_2 (mol/l.) for Polysarcosine Chain and Polymethylene Chain

Ring no.	Polysarcosine[a]	Polymethylene[b]
18		1.4×10^{-2}
19		1.1
21	2.3×10^{-2} ($n = 5$)	
24		0.78
27	2.3 ($n = 7$)	
36	1.9 ($n = 10$)	

[a] Present work at 35°C in phosphate buffer. [b] Data from the esterification of ω-hydroxycarboxylic acids at 80°C in benzene.[4]

k_s is equivalent to the rate constant for uncatalyzed hydrolysis of polymer III. The intermolecular catalysis can be estimated from the hydrolysis of polymer III catalyzed by 4-AcAMP. The latter reaction was carried out with two different concentrations of 4-AcAMP, and k_2 was determined. The values of k_s and k_2 are shown in Table I. Since the concentration of the pyridyl group is as low as 10^{-5} M, the contribution of intermolecular catalysis in the reaction described in Figure 1 is negligibly small as compared to intramolecular catalysis. It should be noted in Table I that virtually no difference of the inherent reactivity of the ester group attached to the polymer end was observed for different chain lengths.

The intrachain reaction rate constant k_1 was calculated according to eq 2 and is plotted in Figure 2 as a function of chain length n. The values of k_1 increased with decreasing chain length and increasing temperature.

Cyclization Constant. The present results were compared with those in other systems in terms of the rate constant ratio of the intramolecular reaction against the corresponding intermolecular reaction. Regardless of the nature of the reaction, intrachain reactions must pass through a macrocyclic transition state. In this regard the rate constant ratio (cyclization constant) is related to the effective concentration of one terminal group in the neighborhood of the other.[13] The ratios are shown in Table II, where an intrachain reaction between groups attached to the ends of polymethylene chains was referred to for comparison. For the latter reaction the esterification of ω-hydroxycarboxylic acids investigated by Stoll and Rouvé[4] was chosen, and the cyclization constant was calculated using the kinetic theory of Morawetz and Goodman.[13] If a comparison is made for rings of similar size, the cyclization constant for a polysarcosine chain is two or three times greater than that for polymethylene chain. Although the polysarcosine chain which has planar amide bonds appears to be less flexible than polymethylene chain, the former was more apt to undergo intramolecular reactions than the latter. It should be stressed here that the flexibility of the polymer chain deduced from the average quantities, such as $\langle r^2 \rangle$, is *not* simply related to the intrachain reactivity or the ring-closure probability.

Activation Parameters. Figure 3 shows the Arrhenius plot for the intrachain rate constant k_1. A good linear relationship was observed for all polysarcosine chains. The activition parameters calculated from Figure 3 contain a contribution from the conformational change of polymer chain ($\Delta H_c^{\ddagger}$ and $\Delta S_c^{\ddagger}$) and from the formation of the new bond ($\Delta H_e^{\ddagger}$ and $\Delta S_e^{\ddagger}$), when terminal groups come into contact with each other. The latter contribution probably does not depend on the chain length.

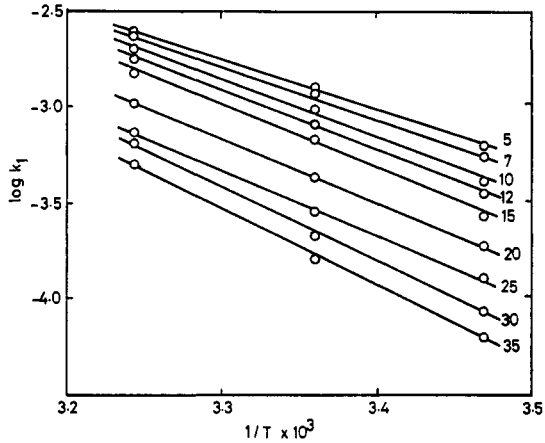


Figure 3. Arrhenius plot of the intrachain reaction rate constant k_1. Numbers shown in the figure are the chain length n.

$$\Delta H_1^{\ddagger} = \Delta H_c^{\ddagger} + \Delta H_e^{\ddagger}$$
$$\Delta S_1^{\ddagger} = \Delta S_c^{\ddagger} + \Delta S_e^{\ddagger} \quad (3)$$

$\Delta H_e^{\ddagger}$ and $\Delta S_e^{\ddagger}$ were evaluated from the activation parameters for the bimolecular rate constant k_2, with the following two assumptions. (1) There is no long-range interaction between a pyridyl group and a *p*-nitrophenyl ester group. (2) The reaction between a pyridyl group and an ester group takes place when these appraoch each other to within $r_0 = 4$ Å,[3] for both the intramolecular and the intermolecular reaction. A small change in the value of r_0 does not affect the following discussion. The Arrhenius plot for k_2 gave a straight line, and $\Delta H_2^{\ddagger} = 14.1$ kcal/mol and $\Delta S_2^{\ddagger} = -17.2$ eu. According to the assumption (1), $\Delta H_e^{\ddagger}$ is equal to $\Delta H_2^{\ddagger}$. On the other hand, $\Delta S_2^{\ddagger}$ is divided into two terms: an entropy change for the bimolecular encounter $\Delta S_b^{\ddagger}$ and that for the electronic change $\Delta S_e^{\ddagger}$.

$$\Delta S_2^{\ddagger} = \Delta S_b^{\ddagger} + \Delta S_e^{\ddagger} \quad (4)$$

$\Delta S_b^{\ddagger}$ can be estimated as follows. If one considers a solution containing two noninteracting particles A and B, the concentration of A (or B) in the reaction sphere of radius r_0 around B (or A) is $4\pi r_0^3 N_a[A][B]/3000$ (M), where N_a represents the Avogadro's number. Thus the "association constant" for the noninteracting particles is $4\pi r_0^3 N_a/3000$ (M). Therefore,

$$\Delta S_b^{\ddagger} = R \ln \frac{4\pi r_0^3 N_a}{3000} = -3.6 \text{ eu} \quad (5)$$

Essentially the same treatment was made by Koshland using the lattice method.[14]

By using these values the activation parameters for the conformational change are now calculated as follows.

$$\Delta H_c^{\ddagger} = \Delta H_1^{\ddagger} - 14.1 \text{ kcal/mol}$$
$$\Delta S_c^{\ddagger} = \Delta S_1^{\ddagger} + 13.6 \text{ eu} \quad (6)$$

The results are shown in Figure 4. $\Delta H_c^{\ddagger}$ as well as $\Delta S_c^{\ddagger}$ increased with increasing chain length. As the rate constant itself decreased with increasing chain length, the chain length dependence of the intrachain reaction is mainly gov-

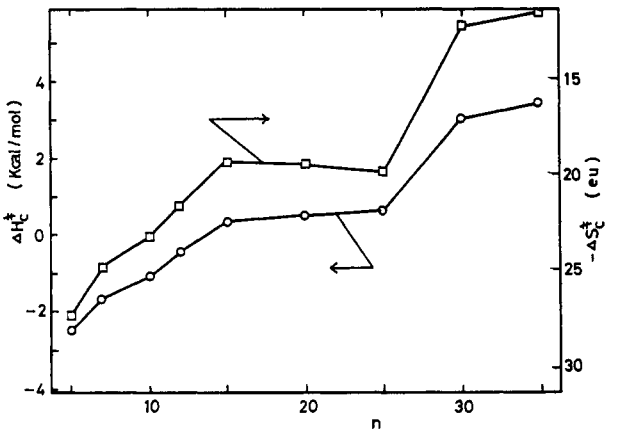


Figure 4. Activation parameters for the conformational change in the intrachain reaction plotted against the chain length n.

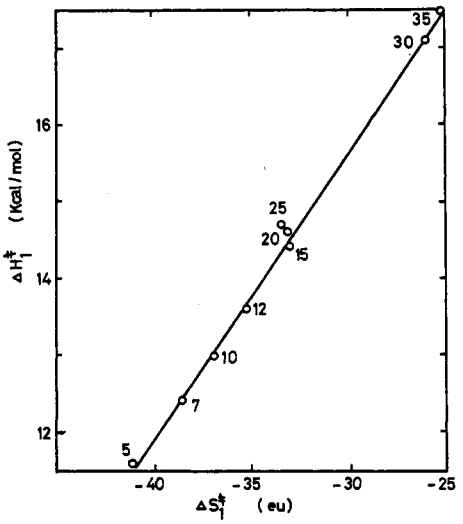


Figure 5. Compensation plot of total activation parameters for the intrachain reaction. Numbers in the figure show the chain length n.

erned by the activation enthalpy required for the conformational change. This result is in contradiction to our expectation. The ring-closure probability or the intrachain reactivity was expected to be governed by the number of cyclic conformations having nearly identical conformational energies. Thus the entropy term was expected to be the dominant factor, and this was expected to be a decreasing function of the chain length. This expectation was supported by a Monte Carlo calculation for the ring-closure probability of the polysarcosine chain, which will appear in the next paper of this series.[15] However, these considerations were *not* in accordance with the experimental results. For the moment we cannot offer any definite explanations for the discrepancy. However, solvation seems to play an important role in determining the activation parameters. For example, in a preliminary experiment on intrachain charge-transfer interactions of groups attached to a polysarcosine chain,[16] the chain length dependence of the thermodynamic parameters for the intrachain association observed in ethanol was opposite to those observed in chloroform.

As for the values of $\Delta H_c^{\ddagger}$ and $\Delta S_c^{\ddagger}$, there have been no reported values available for comparison. $\Delta H_c^{\ddagger}$ assumed negative values for short chains. This indicates that the cyclic conformations are energitically more stable than the other conformations for short polysarcosine chains.

Compensation Relationship. The plot of $\Delta H_1^{\ddagger}$ against $\Delta S_1^{\ddagger}$ is shown in Figure 5. A linear relationship was observed between these two quantities. This implies that the same reaction mechanism is operating irrespective of the chain length. The isokinetic temperature, the slope of the linear plot, was 93 °C. Thus, the intrachain reaction should become independent of chain length at 93 °C. Furthermore, the intrachain reaction will proceed faster for longer chains above 93 °C. Although this has not actually been confirmed, this suggests the possibility to control the intrachain reaction on the basis of the thermodynamic property of the polymer chain. To ensure this, it is hoped to carry out the reaction at higher temperatures, but so far the difficulty due to an increased rate of spontaneous hydrolysis prevented us from carrying out this experiment.

To conclude, the polysarcosine chain was found to be sufficiently flexible to bring about intrachain reactions. The chain length dependence of the activation parameters was determined, and the possibility of controlling the chain length dependence of the intrachain reaction by varying the temperature was suggested. As demonstrated in this paper physical properties of a polymer chain in solution affect various aspects of the intrachain reaction. Therefore, a study of an intrachain reaction provides new information on the conformational properties of a polymer chain.

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