energy of the right-handed α helix (for a particular homopolypeptide) for the sole purpose of demonstrating the relative stability or instability of the right-handed α helix. It is possible that the PPII secondary structure, and/or the ECF secondary structure, might be stable intermediate conformations in the helix $\rightleftharpoons$ coil transition. The ECF conformation was first proposed by Krimm.[20] We have just completed a rather exhaustive study of the helix $\rightleftharpoons$ coil transition in poly(L-glutamic acid) and conclude that ECF is a stable intermediate conformation for this polymer.[21] The data presented in Table IV suggest a helix $\rightleftharpoons$ coil transition for poly-L-histidine as a function of protonation as first suggested by Beychok, *et al.*[22] Further, the most stable side-chain conformation found for the right-handed α helix has side-chain–side chain hydrogen bonds of the type N···H···N formed between residues n and $n + 3$. Infrared studies by Muehlinghaus and Zundel[23] also suggest such hydrogen bonding. One rather surprising result is that poly(L-aspartic acid) should *not* readily undergo a helix $\rightarrow$ coil transition upon deprotonation. The side-chain carboxyl groups are too close to backbone carbonyl oxygens in all but the right-hand α helix to produce a highly destabilizing interaction. Thus, the absence of the single CH_2 unit in the aspartic acid side-chain residue is sufficient to give this homopolypeptide very different properties from poly(L-glutamic acid) which contains the additional CH_2 group. There is some evidence[24–26] which suggests that poly(L-aspartic acid) does not easily undergo the helix $\rightleftharpoons$ coil transition. Poly-L-lysine appears to energetically want to undergo a helix $\rightleftharpoons$ coil transition upon protonation. For all ionizable homopolypeptides, except aspartic acid, the maximizing of the distance between unfavorable side chain–side chain interactions and the maximizing of the exposure of polar groups of the side chains to the aqueous solution induce the helix $\rightleftharpoons$ coil transition.

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Summary

The polymer–solvent hydration shell model presented in this paper for aqueous solution interactions with homopolypeptides yields results consistent with limited experimental data. This model accounts for hydrophobic and hydrophilic bonding, is sensitive to changes in molecular conformation, and is one of the only polymer–solvent models which can be efficiently employed in existing computer algorithms. Extension of the model to include other solvents such as chloroform seems in order in view of the results presented in this report. Inclusion of a temperature dependence into the model would also be useful, since the small size of the solvent molecules makes their dynamic behavior quite temperature sensitive.

Acknowledgment. I am pleased to acknowledge the support, in part, of this work by a National Institute of Dental Research Grant under Program Project No. DE2587.

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Statistical Treatment of the Intramolecular Reaction between Two Functional Groups Connected by a Polymethylene Chain

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Received June 1, 1971

ABSTRACT: In the reaction between two functional groups of $X\text{-}(CH_2)_{n-2}Y$ type molecules, the intramolecular reaction rate constant may be directly proportional to the probability of the distance r between X and Y being smaller than a given value r_0. This probability for n from 6 to 16 was estimated using a rotational isomer model, multiplying an appropriate statistical weight for each conformational state. Then, the cyclization constant, *i.e.*, the ratio of rate constants for intramolecular and intermolecular reactions, was evaluated and compared with experimental values in the esterification of ω-oxy acids reported by Stoll and Rouvé. If all kinds of long-range interactions were ignored, or conformations in which nonbonded skeletal atoms are situated closer than 1.53 Å were rejected, the calculated cyclization constants showed poor agreement with the observed values. However, if the conformations having skeletal overlaps in which the carbon–carbon distance is less than 2.77 Å were rejected, the calculated values agreed well with the observed ones. It was also found that the reasonable value of r_0 was 2.3–2.7 Å, and using these values, the observed alternating property in the cyclization constants was explained.

The dependence of intramolecular reaction rates in $X\text{-}(CH_2)_{n-2}Y$ type molecules upon the number n of the skeletal atoms has been studied by many workers. Among these studies are papers concerning thermal cyclization of dibasic acids,[1] cyclic ketone formation from dinitriles,[2,3] acid-catalyzed lactone formation from ω-oxy acids,[4] etc. In the last example, Stoll and Rouvé[4] determined the cyclization constant, *i.e.*, the ratio of rate constants for intramolecular, k_1, and intermolecular, k_2, reactions. Their values were recalculated by the method developed by Morawetz and Goodman,[5] and are plotted in Figure 1. In this figure, the yield of the intramolecular reaction product in the cyclic ketone for-

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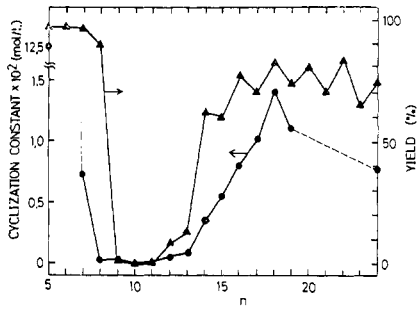

Figure 1. Relative ease of cyclization in $X\text{-}(CH_2)_{n-2}Y$ type molecules: ●, cyclization constant in the acid-catalyzed lactone formation from ω-oxy acids at 354°K in benzene [experimental values originally reported by Stoll, *et al.*,[4] were recalculated by the method developed by Morawetz, *et al.*[5] (eq 9 of ref 5 missed a minus sign)]; ▲, yield of cyclic compound in the cyclization of dinitriles at 313°K in ether.

mation from dinitriles[2,3] is also shown. Figure 1 as well as other works show characteristic features which are summarized as follows. (1) Cyclization is extremely easy for n = 5–7. (2) Cyclization is very difficult for n = 8–13, abruptly becomes easy again for n = 14, and then it becomes constant for $n \geqslant 18$. (3) An even-membered ring is more easily formed than the preceding or the succeeding odd-membered one. The alternating property (3) stated above was also seen in the depolymerization of polyesters and polyanhydrides as reported by Spanagel and Carothers.[6] Since these three features are seen in various reactions of $X\text{-}(CH_2)_{n-2}Y$ type molecules, they seem to be inherent to methylene chains connecting the functional end groups. Therefore, it is expected that these features can be explained by a statistical treatment of the polymethylene chains. The intramolecular reaction rate constant k_1 is expected to be proportional to the probability of ring closure $W(r < r_0)$ defined as probability that the two end groups, X and Y, are within a given distance r_0. Fluendy[7] has already tried to calculate this probability by applying the Monte Carlo method to the polymethylene chain, but his calculation was limited to relatively short chains, and for longer chains the reliability of the result was rather poor. Recently, Morawetz and Goodman[5] pointed out that the Gaussian distribution of the end-to-end distance cannot strictly apply to the estimation of this probability. Similar studies were performed on the ring–chain equilibra of poly(dimethylsiloxane),[8-12] nylon-6,[13] and poly(ethylene terephthalate).[14] Recently it was emphasized[15,16] that in studies on catalysis by various functional polymers and of polymer reactions one of the main problems is the determination of relative reactivities of the substrates distributed along the polymer chain possessing catalytic sites. General kinetic theories for such reactions have been developed[17] in which the dependence of rate constant upon the distance between a substrate and a catalytic group along the chain was taken into account. This problem seems to be directly related to intramolecular reaction. Previously, it was also found that in the polymerization of amino acid *N*-carboxy anhydrides (NCA) initiated by several poly(*N*-alkylamino acids), the terminal catalytic base group reacts most easily with NCA adsorbed on the 7th–12th units from the end of the chain.[18,19] The study of the intramolecular reactions of $X\text{-}(CH_2)_{n-2}Y$ type molecules may be the most basic in this connection; therefore, a statistical treatment of polymethylene chains has been carried out assuming g–t rotational isomer models.[20]

Theoretical Section

Morawetz and Goodman[5] stated that the cyclization constant C corresponds to the effective concentration of Y groups in the neighborhood of the X group attached to the same molecule. Here it is assumed that the change in the electronic states of X and Y groups will occur as the distance r between X and Y groups becomes shorter than r_0. Then the effective concentration in the reaction sphere of radius r_0 can be written as

$$C = k_1/k_2 = 3W(r < r_0)/4\pi r_0^3 N_0 \quad (1)$$

where $W(r < r_0)$ is the ring closure probability, *i.e.*, the probability that $r < r_0$, and N_0 is the Avogadro's number. Equation 1 will apply to a relatively dilute solution of $X\text{-}(CH_2)_{n-2}Y$ molecules in which the intermolecular interactions between the solutes are not extensive so that the molecule can take any positions and directions in the solution. Furthermore, the viscosity of the system should be low so that the diffusion process and the rate of conformational transitions are not the rate-determining steps for intermolecular and intramolecular reactions,[16] respectively. These conditions are satisfied in the experimental work of Stoll and Rouvé[4] to which eq 1 will be applied later.

The ring-closure probability can be written as the ratio of partition functions for the conformational states with $r < r_0$, $Z(r < r_0)$, and for all states, Z_t.

$$W(r < r_0) = Z(r < r_0)/Z_t \quad (2)$$

Neglecting the contribution of vibrational freedom, each partition function is written as

$$Z(r < r_0) = \sum_{r<r_0} \exp(-E_i/RT) \quad (3)$$

$$Z_t = \sum_{\text{total}} \exp(-E_i/RT) \quad (4)$$

where the summation of eq 3 should be made over all the conformational states with $r < r_0$, and E_i is the internal energy of conformational state i. The ring-closure probability can be rewritten in terms of the energy, $\Delta E_c^{\ddagger}$, and entropy, $\Delta S_c^{\ddagger}$, of activation associated with the conformational change.

$$W(r < r_0) = \exp(\Delta S_c^{\ddagger}/R) \exp(-\Delta E_c^{\ddagger}/RT) \quad (5)$$

$$\Delta E_c^{\ddagger} = \langle E(r < r_0) \rangle - \langle E_t \rangle \quad (6)$$

where $\langle E_t \rangle$ is an average energy for all conformational states and $\langle E(r < r_0) \rangle$ is that for the states with $r < r_0$.

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$$\langle E(r < r_0)\rangle = [\sum_{r<r_0} E_i \exp(-E_i/RT)]/Z(r < r_0) \quad (7)$$

$$\langle E_t\rangle = [\sum_{\text{total}} E_i \exp(-E_i/RT)]/Z_t \quad (8)$$

The activation entropy can be obtained by eq 5.

Estimation of Ring-Closure Probability, $W(r < r_0)$

In the succeeding sections, estimations of ring-closure probabilities will be made, by considering no conformational energy differences (treatments 1 and 2) or by taking them into account providing appropriate energy for each dyad sequence (3 and 4), by eliminating conformations having zeroth neighbor skeletal overlaps (1 and 3) or eliminating those having zeroth, first, and second neighbor overlaps (2 and 4). In the course of these treatments, it becomes clear how the results can be improved by the introduction of conformational energy or of long-range interactions.

(1) Diamond Lattice Model Excluding Zeroth Neighbor Skeletal Overlaps without Conformational Energy Difference. If all conformations have equal energies, $W(r < r_0)$ is written as

$$W(r < r_0) = \Omega_n(r < r_0)/\Omega_t \quad (9)$$

where $\Omega_n(r < r_0)$ is the number of conformations with $r < r_0$ and Ω_t is the total number of conformations. Smith[21] assumed that all the skeletal atoms of the polymethylene chain lie on diamond lattice points and constructed all conformations having no zeroth neighbor skeletal overlaps, *i.e.*, excluding conformations in which two skeletal atoms are situated on the same lattice point. He calculated the number of conformations of n-membered cyclic polymethylene chains $\Omega_n(r = 1)$, taking a C–C bond length as unit length, and also the total number of conformations Ω_t of n-membered [$(n-1)$-bonded] polymethylene chains. Using his results, Ω_n ($r \leqslant 1$) can be calculated since $\Omega_n(r = 1) = \Omega_n(r \leqslant 1)$ for even n and Ω_{n-1} $(r = 1) = \Omega_n(r \leqslant 1)$ for odd n. Thus using eq 9, $W(r \leqslant 1)$ was calculated and is plotted in Figure 2 (solid line). The shape of the solid line in Figure 2 is quite different from that of Figure 1, so this preliminary treatment requires revision as shown in the following sections.

(2) Diamond Lattice Model Excluding All Atom Overlaps without Conformational Energy Difference. Smith[22] extended his idea to the exclusion of all atom overlaps including hydrogen atoms. The results of calculation based on this idea are shown in Figure 2 (dashed line). This exclusion of all atom overlaps corresponds to the rejection of gauche(±)-gauche(∓) ($g^{\pm}g^{\mp}$) sequences for chains with $n > 6$ and $g^{\pm}g^{\pm}tg^{\pm}g^{\pm}$-$g^{\pm}g^{\pm}$ sequences for chains with $n > 12$, etc., and leads to the elimination of nonoverlapping cyclic chains for n = 8–13, as also reported by Saunders.[23]

(3) g–t Rotational Isomer Model Allowing for Conformational Energy Differences and Excluding Zeroth Neighbor Skeletal Overlaps. In the previous treatments, calculations were made without considering the conformational energy difference. In this section the energy difference among various conformations was taken into account and special attention was given to the end groups. The structural parameters used here and in following treatments are[20] bond angle = 112°; bond length = 1.53 Å = 1 unit; rotational angle 0° (trans, t), −120° (gauche(+), g^+), 120° (gauche(−), g^-). The energy E_σ attributed to a gauche state and additional energy E_ω assigned to a $g^{\pm}g^{\mp}$ sequence are 500 and 2000 cal/mol, respectively.[20] Here the end group X or Y was regarded as a single sphere equivalent to a skeletal atom, so the $g^{\pm}g^{\mp}$ interaction (E_ω) for the ultimate and penultimate C–C bonds at both ends of the methylene chain was neglected. Calculations were made numbering 1, 2, and 3 to g^+, t, and g^- states, respectively,[24] and searching for the conformations with one end within a distance r_0 of the other, over the $(3^{n-3} + 1)/2$ conformations from 111 ... 1 to 222 ... 2. The conformations from 333 ... 3 to 222 ... 23 are the mirror images of conformations from 111 ... 1 to 222 ... 21,[24] and need not be considered again. In this section, the effect of long-range interaction was taken into consideration excluding the conformations having any carbon–carbon atom pair closer than 1.0 except for the pair of end groups (X, Y). For the selected conformations with $r < r_0$, the partition function $Z(r < r_0)$ and the average energy $E(r < r_0)$ were calculated. During the construction of a polymer chain the possibility that the final end-to-end distance could be smaller than r_0 was checked several times,[25] and the construction was continued only for chains retaining this possibility. Although the time for computation was considerably reduced by this procedure, the total partition function and the total average energy cannot be obtained. However, the calculation constructing all conformations showed the total partition function for n = 6–13 was virtually equal to those neglecting any kind of long-range interactions. Therefore, these quantities were calculated using the following equations.[26]

$$Z_t = \sum_{\omega_n=1}^{3} \{\mathbf{G'G''G}^{n-3}\mathbf{G''}\}_{1,\omega_n} \quad (10)$$

where ω_n = 1, 2, 3 denotes the rotational states (g^+,t,g^-) of the nth unit.

$$\mathbf{G'} = \begin{bmatrix} 1 & \sigma & \sigma \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$\mathbf{G''} = \begin{bmatrix} 1 & \sigma & \sigma \\ 1 & \sigma & \sigma \\ 1 & \sigma & \sigma \end{bmatrix} \quad (11)$$

$$\mathbf{G} = \begin{bmatrix} 1 & \sigma & \sigma \\ 1 & \sigma & \sigma\omega \\ 1 & \sigma\omega & \sigma \end{bmatrix}$$

$$\sigma = \exp(-E_\sigma/RT) \qquad \omega = \exp(-E_\omega/RT) \quad (12)$$

The total average energy is a sum of average energies of each dyad sequence.

$$\langle E_t\rangle = \langle E(\omega_0, \omega_1)\rangle + \langle E(\omega_1, \omega_2)\rangle + \ldots + \langle E(\omega_{n-1}, \omega_n)\rangle \quad (13)$$

where $\langle E(\omega_{k-1}, \omega_k)\rangle$ can be obtained by the following equations.[26]

$$\langle E(\omega_{k-1}, \omega_k)\rangle = \frac{1}{Z_t}\sum_{\omega_n=1}^{3} \{\mathbf{G'G''G}^{k-3}\mathbf{QG}^{n-k-1}\mathbf{G''}\}_{1,\omega_n} \quad (14)$$

for $k \neq 1, 2, n$

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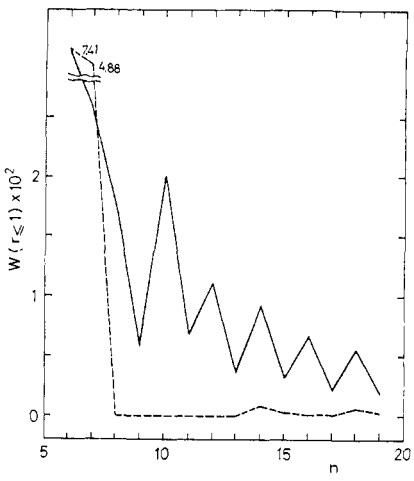

Figure 2. Ring-closure probabilities calculated on a diamond lattice model excluding the zeroth neighbor skeletal overlaps (———), excluding zeroth, first, and second neighbor skeletal overlaps (– – – –).

$$\langle E(\omega_0, \omega_1)\rangle = \frac{1}{Z_{t\omega_{n-1}}}\sum_{1}^{3}\{\mathbf{Q'G''G}^{n-3}\mathbf{G''}\}_{1,\omega_n} \quad (15)$$

$$\langle E(\omega_1, \omega_2)\rangle = \frac{1}{Z_{t\omega_{n-1}}}\sum_{1}^{3}\{\mathbf{G'Q''G}^{n-3}\mathbf{G''}\}_{1,\omega_n} \quad (16)$$

$$\langle E(\omega_{n-1}, \omega_n)\rangle = \frac{1}{Z_{t\omega_{n-1}}}\sum_{1}^{3}\{\mathbf{G'G''G}^{n-3}\mathbf{Q''}\}_{1,\omega_n} \quad (17)$$

Matrices **Q**, **Q'**, **Q''** are

$$\mathbf{Q} = \begin{bmatrix} 0 & E_\sigma\sigma & E_\sigma\sigma \\ 0 & E_\sigma\sigma & (E_\sigma + E_\omega)\sigma\omega \\ 0 & (E_\sigma + E_\omega)\sigma\omega & E_\sigma\sigma \end{bmatrix}$$

$$\mathbf{Q'} = \begin{bmatrix} 0 & E_\sigma\sigma & E_\sigma\sigma \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad (18)$$

$$\mathbf{Q''} = \begin{bmatrix} 0 & E_\sigma\sigma & E_\sigma\sigma \\ 0 & E_\sigma\sigma & E_\sigma\sigma \\ 0 & E_\sigma\sigma & E_\sigma\sigma \end{bmatrix}$$

The calculated probabilities for ring closure are plotted against n in Figure 3. Consideration of the conformational

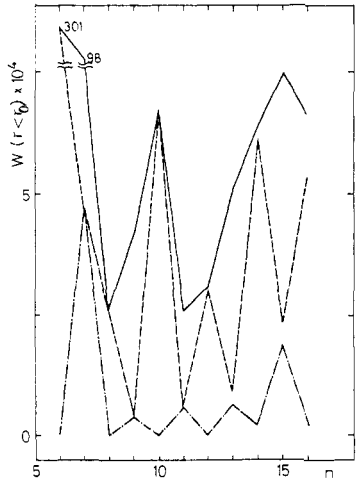

Figure 3. Ring-closure probabilities calculated on a g–t rotational isomer model excluding the zeroth neighbor skeletal overlaps at 350°K: r_0 = 1.75 (———), 1.50 (– – – –), and 1.00 (— · —).

energy difference leads to the result that the probabilities for ring closure increase as n increases from 11 to 17, and this trend is compatible with that actually observed, as shown in Figure 1. The comparison of these results with those neglecting any kind of long-range interactions (not presented here) revealed that such an exclusion of overlapping conformations as performed in this section does not significantly affect the ring-closure probabilities. This is rationalized by the relatively high conformational energies assigned to the rejected conformations. Although the rotational isomer model used here is slightly different from the diamond lattice model, most of the skeletal atoms are situated near the lattice points of the diamond lattice especially for short chains. In this connection, r_0 = 1 in the g–t model is equivalent to adopting only the lattice point occupied by one end group (zeroth neighbor point) as the reactive position of other end group in diamond lattice model. Similarly, r_0 = 1.5 and 1.75 correspond to the inclusion of first and second neighbors, respectively. Furthermore, the exclusion of conformations having any carbon–carbon atom pair closer than 1.0 corresponds to the exclusion of zeroth neighbor overlaps on the diamond lattice model.

(4) Exclusion of Second, First, and Zeroth Neighbor Overlaps. In this section the more severe elimination of overlapping chains will be examined. According to Gō and Scheraga,[27] the smallest possible contact distance between carbon atoms is 2.77 Å and this value corresponds to 1.81 in our units. Therefore, conformations having any nonbonded C–C pairs closer than 1.81 were excluded. This criterion corresponds to the exclusion of zeroth, first, and second neighbor overlaps on a diamond lattice model. In other words, the $g^{\pm}g^{\mp}$ sequences are excluded even at both ends, as in treatment 2. However, when two end groups (X and Y) come closer than 1.50, the distance between an end group (X or Y) and the carbon atom directly connected to another end group (Y or X) is usually less than 1.81. So, if the above rule is applied to end groups, the probability of ring closure $W(r < 1.5)$ will become zero. Therefore, the contact distance was taken to be 1.0 = 1.53 Å for end groups only. This criterion seems to be convincing if we recall a diamond lattice model. When an end group is located at the first neighbor of another end group, the skeletal atom directly connected to the former end group can be located at one of four lattice points, one of which coincides with the latter end groups and three of which are the second neighbor point of the latter end group. Therefore, the criterion used here corresponds to the exclusion of the first case described above. It may be expected that under these severe restrictions most of conformations having their end-to-end distances less than r_0 are rejected owing to skeletal overlaps, as already seen in Figure 2 (dashed line), in which the conformations with $r \leqslant 1$ are treated. The results are shown in Figure 4. As predicted above, the ring-closure probabilities between n = 7 and n = 13 fell to zero even for $r < 1.75$. Comparing Figure 4 with Figure 2 (dashed line), the introduction of conformational energy was found to produce considerable improvement in the results for chains with $n \geqslant 14$. Here again, the total partition function must be evaluated separately. This was achieved by making up all conformations having no skeletal overlaps using the same criterion as adopted in the calculation of $Z(r < r_0)$. To reduce computation time, the total partition function for chains larger than n = 14 was computed using eq 10, 11, and 12, setting $\omega = 0$ and $\mathbf{G''} = \mathbf{G}$.

(27) N. Gō and H. A. Scheraga, *Macromolecules*, 3, 188 (1970).

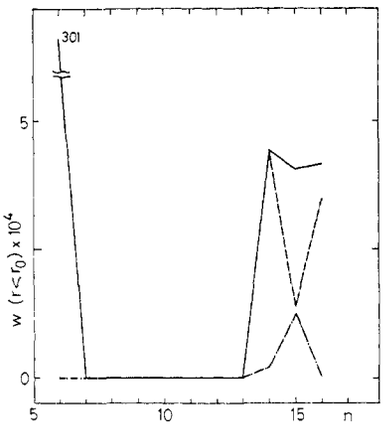

Figure 4. Ring-closure probabilities calculated on a g–t rotational isomer model excluding the zeroth, first, and second neighbor skeletal overlaps at 350°K: r_0 = 1.75 (———), 1.50 (– – – –), and 1.00 (— · —).

The latter method is equivalent to considering all conformations without $g^{\pm}g^{\mp}$ sequences even at both ends, and may be a good approximation to the present case. In fact, the total partition functions calculated by the two methods agreed well with each other at least to four significant figures for $n \leq 13$.

Discussion

Qualitative Comparison between Calculated Ring-Closure Probabilities and the Observed Relative Ease of Intramolecular Reactions. Comparison of Figures 2–4 with Figure 1 can be summarized as follows. (1) When r_0 is taken to be larger than 1.25, the extreme ease of formation of six-membered rings is well accounted for. This large value of $W(r < r_0)$ for $n = 6$ comes from the fact that among the possible 27 conformations two of them correspond to the chair-type conformations of cyclohexane ($g^{\pm}g^{\mp}g^{\pm}$) and have end-to-end distances r = 1.1716 and low conformational energy, 1500 cal/mol. The low energy assigned to chair-type cyclohexane is a result of the elimination of $g^{\pm}g^{\mp}$ interactions for the terminal sequences. If E_ω = 2000 cal/mol is assigned to these terminal $g^{\pm}g^{\mp}$ sequences, the probability of formation of a six-membered ring becomes much less than observed experimentally.

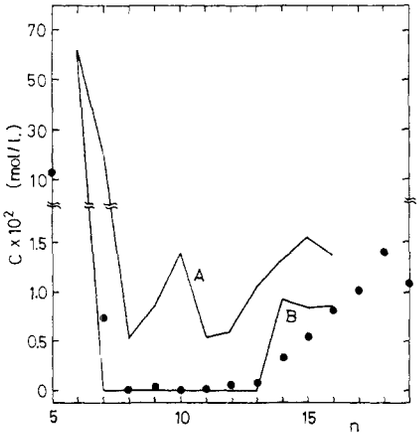

Figure 5. Comparison of the calculated cyclization constants with the actually observed values in the lactone formation from ω-oxy acids. Calculated from $W(r < 1.75)$ obtained (A) by treatment 3, (B) by treatment 4.

(2) The increase in reactivity as n increases from 12 to 18 (Figure 1) can be reasonably explained if the conformational energy difference is introduced to the calculation of ring-closure probabilities.

(3) The observed alternating property of intramolecular reactivities as n increases sequentially also appears clearly in the calculated ring-closure probabilities when r_0 is taken to be 1.50, or $r \leqslant 1$ on a diamond lattice model. Therefore, this alternating property can be explained in terms of geometrical structures of the polymethylene chain determined by the bond angle and the rotational angle. When r_0 is taken to be 1.75, the alternating property in $W(r < 1.75)$ disappeared. Since the observed alternating property is less marked than the calculated one with r_0 = 1.50, the most appropriate ring closure probability would be obtained by multiplying the geometrical probability of ring closure for end-to-end distances between 1.0 and 1.75 by a suitable reactivity parameter. If r_0 is taken to be 1.0, the calculated probability showed the reverse alternating property and indicated no intramolecular reactivity at n = 6, so this value cannot be adopted.

(4) In the treatment excluding only zeroth neighbor skeletal overlap (Figure 3), the calculated ring closure probabilities differed from the observed ones at n = 10. On the other hand, when terminal $g^{\pm}g^{\mp}$ sequences are excluded, as in Figures 2 (dashed line) and 4, the abnormal peak at n = 10 disappeared. The reason for this large ring closure probability is that the conformations $g^{\mp}g^{\pm}g^{\pm}tg^{\pm}g^{\pm}g^{\mp}$ (r = 1.029 3.0 kcal/mol) have relatively low energies because the $g^{\pm}g^{\mp}$ sequences are permitted for both end sequences. Therefore it may be expected that the assignment of any definite structure to both end groups (X, Y) may partially reduce the probability $W(r < r_0)$ for n = 10 even if no second neighbor overlaps are excluded. In the case of acid-catalyzed esterification of ω-oxy acids, for example, the end groups are[28] –X = –C(=O)O^+H_2 and –Y = –OH. Unfortunately, at the present time, no information concerning the rotational energies around these end groups is available and no reasonable estimate of this end effect can be made.

(5) Since the carbon–carbon contact distance adopted in the last treatment, 1.81 = 2.77 Å, is the shortest possible, the last treatment may be most reliable. Indeed, the abrupt increase in ring closure probability at n = 14 is substantiated in Figure 1. The data in Figure 1 also show low reactivity for 8–13 membered chains, whereas the calculation predicts no reactivity in this region. This discrepancy may be eliminated by the use of the appropriate potential function[29] instead of the rigid-sphere model adopted here.

Estimation of Absolute Values of Cyclization Constants. In Figure 1, cyclization constants in the esterification of lactone formation from ω-oxy acids at 354°K, obtained by Stoll and Rouvé,[4] are shown. Using eq 1, the cyclization constants were calculated adopting two different ring-closure probabilities, *i.e.*, $W(r < 1.75)$ in treatment 3 (denoted by A) and that in treatment 4 (denoted by B). Results are compared with the observed values in Figure 5, from which it is seen that treatment A leads to an abnormal peak at n = 10 and cyclization constants which are too large throughout the range of n considered. However, using treatment B, both the absolute values and the general tendency agreed well with the observed values. The observed value at n = 5 is a lower limit, and Stoll and Rouvé[4] stated that this value should

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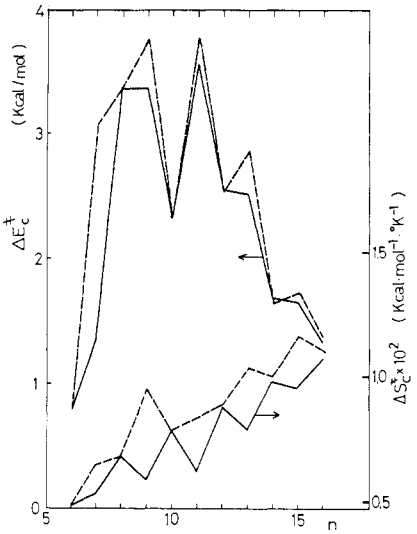

Figure 6. Conformational energies and entropies of activation at 350°K, calculated by treatment 3: r_0 = 1.75 (———), and 1.5 (– – – –).

be increased several times. It should be pointed out that the cyclization constants calculated assuming Gaussian distribution of end-to-end distance[30] were found to be extremely large compared with the observed values. As Morawetz, and Goodman[5] stated, the Gaussian treatment cannot apply to these short chains.

Conformational Energy and Entropy of Activation. To explain the relative ease of the cyclization reaction thermodynamically, the activation energies, $\Delta E_c^{\ddagger}$, and entropies, $\Delta S_c^{\ddagger}$, derived from conformational consideration were calculated by eq 5–8, for treatment 3. The results are plotted in Figure 6. Here, the total average energies were calculated in accordance with the total partition functions, that is, for chains shorter than n = 13, all conformations having no skeletal overlaps were constructed and then total average energies were calculated. For chains longer than n = 14, eq 13–18 were used without modification. As seen in Figure 6, the relative ease of the reaction is explained in terms of conformational energy of activation. On the other hand, the conformational entropy of activation showed rather monotonous dependence on the chain length. Therefore, as far as treatment 3 is concerned, the relative ease of the cyclization reaction is determined mainly by the conformational energy of activation. It was also found that the alternating properties in the conformational entropy were reversed going from r_0 = 1.50 to 1.75. This change can be understood in terms of diamond lattice model, in which r_0 = 1.75 corresponds to taking second, first, and zeroth neighbors of an end group as the reactive conformations and r_0 = 1.50 corresponds to taking first and zeroth neighbors. So, the trend in activation entropies may result from the fact that there can be only even-membered cyclic chains on a diamond lattice.[21–24] On the other hand, energetic consideration shows both values of r_0 lead to the preferred reactivity at even-membered chains.

In this paper, the intramolecular reaction was satisfactorily analyzed in terms of the statistical properties of a chain connecting the two functional groups. Using appropriate energy parameters and introducing long-range interactions, the absolute cyclization constants were estimated. Further, the conformational energies of activation were found to be the origin of the relative ease of cyclizations.

Acknowledgments. The author is deeply indebted to Dr. K. Nagai of the Government Industrial Research Institute, Osaka, for his helpful suggestions, and to Professor T. Higashimura and Dr. Y. Imanishi for their discussion and encouragement throughout the course of this study. The author also wishes to express his appreciation to the Data Processing Center of Kyoto University at which all the computations were performed.

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On Swelling of Natural Rubber in Organic Solvents

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Received April 6, 1971

ABSTRACT: Functions of mixing are considered on the basis of available experimental data in terms of two statistical theories of solutions; the comparison made clearly establishes superiority of the more recent theory developed by Flory and involving three kinds of terms. In elastic contribution to the free energy of swelling, the number ν of network chains per unit volume of rubber appears independent of swelling liquid. A set of relations describing the swelling process involving the more accurate mixing contributions is discussed.

Absorption of liquids by natural rubber was studied experimentally by a number of authors, including careful investigations of Gee and his collaborators[1,2] and also measurements of Mullins.[3] These authors interpreted thermodynamic functions of mixing in terms of an approach usually referred to in the literature as the Flory–Huggins theory; for a description of this approach see ref 4.

Now a more recent theory of liquids and solutions formulated by Flory[5] appears to describe fairly successfully equilibrium properties of pure liquids as well as excess functions of

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