Macroinorganics. 7.† Property–Structure Relationships for Polymeric Bases Whose Monomeric Units Behave Independently toward Protonation

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ABSTRACT: The protonation of some new poly(amido amines) and their nonmacromolecular model compounds has been studied in aqueous solution by potentiometric and viscosimetric techniques. Sharp basicity constants have been obtained, thus confirming the peculiar behavior of this family of polymeric bases. The behavior of the models is similar to that of the corresponding polymers even if the former are slightly more basic. In order to rationalize the unusual behavior of poly(amido amines), ^{13}C NMR titrations and quantum chemical computations have been performed on some representative poly(amido amines). The resulting model stresses the importance of the stiffening of each monomeric unit upon protonation, due to the formation of intramolecular hydrogen bridges and to electrostatic repulsion between positively charged onium ions, in determining the physicochemical properties of poly(amido amines) even in the absence of direct interactions between groups belonging to different monomeric units. In fact, this stiffening could affect the properties of the whole polymer (conformational transitions) because the joints between different units are very rigid.

Introduction

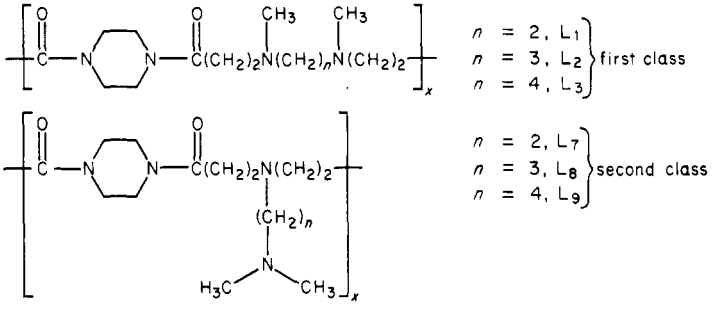
We have recently studied the behavior of a new class of basic tertiary amino polymers, the poly(amido amines), toward both protonation[1] and complex formation.[2] In this respect, these polymers show some peculiar properties. In fact, the monomeric units of these polymers behave independently toward protonation and complex formation,[3] allowing the determination of the precise site of protonation and of "sharp" thermodynamic functions. In a research program designed to gain insight into the origin of this unusual behavior, we have shown that the absence of ring structures between the tertiary amino groups belonging to the different units[2b] and the presence of further amino groups as side substituents[4] do not substantially affect the unusual behavior of poly(amido amines) as polyelectrolytes. On the other hand, recent quantum chemical computations on aliphatic polyamines have shown that the insertion of longer aliphatic chains between the amino groups may lead to a greater conformational freedom.[5] In the case of poly(amido amines) such an effect could give rise, in principle, to larger interactions between different monomeric units and, consequently, to "apparent" thermodynamic functions, as usually found in most polyelectrolytes.[6] Hence, the first part of this paper is devoted to the analysis of the effect on the polymers' behavior of the length of the aliphatic chain between the amino groups present in the monomeric unit. For this purpose, we have studied the stepwise protonation of the two classes of poly(amido amines) in Chart IA.

In order to better ascertain the specific effects due to the macromolecularity, we have also studied a set of nonmacromolecular model compounds whose structures closely correspond to those of the polymers (Chart IB).

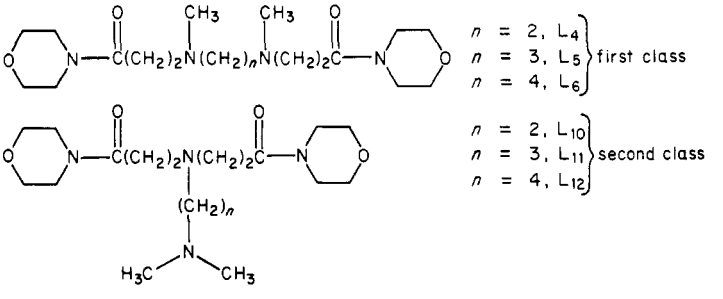
The protonation of the compounds in Chart IB has been studied by means of potentiometric, ^{13}C NMR, viscosimetric, and quantum chemical techniques. The results have been used to relate the behavior of poly(amido amines) to their structure. An attempt has been made to rationalize the unusual behavior of poly(amido amines) in terms of possible conformational transitions induced by protonation. This has been done in order to analyze possible effects of the macromolecularity on the physicochemical properties of poly(amido amines) even in the absence of direct interactions between different monomeric units.

Chart I

A. Poly(amido amines)



B. Nonmacromolecular Model Compounds



Experimental Section

Materials. Polymers L_1[1a] and L_7[4a] and modes L_4[1a] and L_{10}[4a] have been previously described.

† Part 6 is ref 2b.

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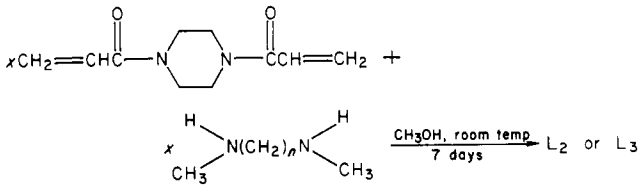
Table I
Basicity of Poly(amido amines) and Their Corresponding Nonmacromolecular Models at 25 °C in 0.1 M NaCl

polymers	log K_1 [c]	log K_2 [c]	models	log K_1 [c]	log K_2 [c]
L_1 [a]	8.09	4.54	L_4 [a]	8.248	4.80
L_2	8.172 (6)	6.691 (9)	L_5	8.729 (2)	6.909 (6)
L_3	8.715 (8)	7.689 (9)	L_6	9.062 (3)	7.841 (6)
L_7 [b]	8.87	4.10	L_{10} [b]	9.05	4.35
L_8	8.755 (8)	6.30 (2)	L_{11}	9.212 (5)	6.605 (10)
L_9	9.196 (6)	7.189 (17)	L_{12}	9.523 (4)	7.465 (12)

[a] Reference 1a. [b] Reference 4b. [c] The values in parentheses are standard deviations.

The other polymers of the first class were synthesized by polyaddition of *N,N'*-dimethylpropylenediamine (L_2) or *N,N'*-dimethylbutylenediamine (L_3) to 1,4-diacryloylpiperazine according to the following scheme:

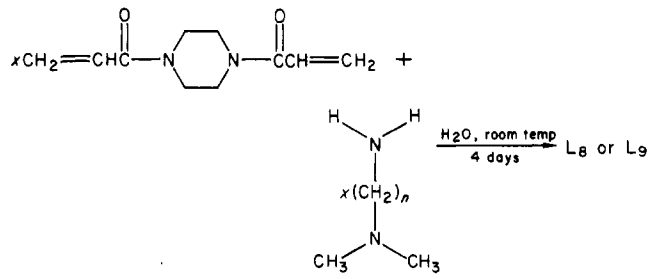


At the end of the reaction the mixtures were evaporated to dryness in vacuo, and the polymers were purified by dissolving in chloroform and reprecipitating with ether. Both polymers were solid.

The intrinsic viscosities of the polymers (in chloroform at 30 °C) were 0.20 and 0.16 dL/g, respectively. Their elemental analyses gave the following results: L_2, Calcd for $C_{15}H_{28}N_4O_2 \cdot H_2O$: C, 57.30; H, 9.62; N, 17.82. Found: C, 57.77; H, 9.98; N, 17.88. L_3, Calcd for $C_{16}H_{30}N_4O_2 \cdot 3H_2O$: C, 52.72; H, 9.55; N, 15.37. Found: C, 53.00; H, 9.81; N, 15.84.

The corresponding models L_5 and L_6 were synthesized in a similar way, starting from the same amines and *N*-acryloylmorpholine in a 1:2 molar ratio. After isolation they slowly crystallized (mp: L_5, 34 °C; L_6, 39.5 °C. Their elemental analyses gave the following results: L_5, Calcd for $C_{19}H_{36}N_4O_4 \cdot H_2O$: C, 56.69; H, 9.52; N 13.92. Found: C, 56.78; H, 9.55; N, 14.16. L_6, Calcd for $C_{20}H_{38}N_4O_4 \cdot {}^1/_2H_2O$: C, 58.94; H, 9.64; N, 13.75. Found: C, 58.81; H, 9.75; N, 13.94.

The polymers of the second class were synthesized by polyaddition of *N,N*-dimethylpropylenediamine (L_8) or *N,N*-dimethylbutylenediamine (L_9) to 1,4-diacryloylpiperazine according to the following scheme:



They were isolated as in the previous cases and purified by dissolving in chloroform and reprecipitating with *n*-hexane. They were both sticky, noncrystalline materials.

The intrinsic viscosities of the polymers, measured as above, were 0.18 and 0.16 dL/g, respectively. Their elemental analyses were as follows: L_8, Calcd for $C_{15}H_{28}N_4O_2 \cdot H_2O$: C, 57.30; H, 9.62; N, 17.82. Found: C, 57.80; H, 9.19; N, 18.17. L_9, Calcd for $C_{16}H_{30}N_4O_2 \cdot H_2O$: C, 58.51; H, 9.82; N, 17.06. Found: C, 58.2; H, 10.0; N, 17.0.

The corresponding models L_{11} and L_{12} were synthesized in a similar way, starting from the same amines and *N*-acryloylmorpholine in a 1:2 molar ratio. They were viscous oils and gave the following analyses: L_{11}, Calcd for $C_{19}H_{40}N_4O_4 \cdot 2H_2O$: C, 53.75; H, 10.47; N, 13.20. Found: C, 54.0; H, 10.0; N, 13.5. L_{12}, Calcd for $C_{20}H_{42}N_4O_4 \cdot H_2O$: C, 57.11; H, 10.55; N, 13.32. Found: C, 57.0; H, 11.0; N, 13.1.

Other Reagents. CO_2-free NaOH solution was prepared, stored, and standardized as described elsewhere.[7] Stock solutions of 0.1 M NaCl were prepared from sodium chloride (C. Erba, ACS grade) and used without further purification as the ionic medium for potentiometric measurements.

Emf Measurements. Potentiometric titrations were performed with a digital potentiometer, an Orion 9101-00 glass electrode, a silver/silver chloride electrode, and a salt bridge containing 0.1 M NaCl solution. The output voltages (mV) were automatically recorded with a Printina Gay alphanumeric printer. The titration vessel was thermostated at 25.0 ± 0.1 °C. A stream of nitrogen, presaturated with water vapor by bubbling through a 0.1 M NaCl solution, was passed over the surface of the solution. For the titrations, the NaOH or HCl solutions were dispensed from a Metrohm Multidosimat piston buret graduated in hundreths of a milliliter. $E°$ calibrations were performed before and after each titration. The concentration of hydrogen ion was calculated from the emf values (in mV) by means of the formula

$$[H^+] = \exp(E - E°)/25.693$$

No attempt was made to correct the data to zero ionic strength or to apply activity coefficient corrections since under the solution conditions used here the ligands do not contribute very much to the ionic strength and the ionic strengths were quite high. The independence of log K on α has been demonstrated by plotting pH + log $[\alpha/(1-\alpha)]$ vs. α for several points of the titration curve over the whole range of pH investigated. The basicity constants reported in Table I have been obtained by using the program MINIQUAD 76A[7,8] and by utilizing all of the points of several titration curves (≃160 points).

NMR Spectra. ^{13}C spectra (16000-Hz width) with ^1H broad-band noise decoupling conditions were obtained for 0.1 M D_2O solutions at 300 K with a WH-270 spectrometer equipped with an Aspect 2000 computer operating at 68.77 MHz. A pulse width of 5 μs with a relaxation delay of 1 s was used. All chemical shifts were determined with Me_4Si as external reference. The pH values were measured with a Radiometer digital pH meter and were not corrected for isotope effects.

Viscosity Measurements. The viscosity measurements, either in chloroform or in water, were performed with a Cannon Ubbelohde 50E998 viscosimeter having a flow time of 90 s for chloroform at 30 °C and 210 s for aqueous 0.1 M NaCl at 25 °C. Corrections for kinetic energy and rate of shear were found to be negligible. The specific viscosities (η_{sp}) were determined in the concentration range 10^{-3}–10^{-2} M. In the determination of the intrinsic viscosities, plots of η_{sp}/c were extrapolated at $c \rightarrow 0$ by means of least-squares.

Pure CO_2-free water was used throughout, and the solutions were used immediately after preparation. The solutions were titrated with a 0.1 M hydrochloric acid solution added through a Metrohm Dosimat E415 automatic piston burette. At least two complete titrations were carried out for each polymer. The salt concentration was 100 times that of the polymer.

Conformational Analysis. In view of the great number of computations to be performed to get conformational maps of several fragments in the different protonation steps, it was not possible to use a refined ab initio method. On the other hand, it is well-known that empirical force field methods are not yet very reliable in the case of polyfunctional compounds[9] and, in particular, the problem of the lone pairs appears not to be solved satisfactorily.[5] Hence, we have chosen the PCILO method,[10] optimizing the bond polarities for each conformation. The PCILO method has been chosen in view of the good agreement usually

obtained with both experimental and ab initio results for molecular conformations.[11] In particular, it has been shown that in the case of secondary or tertiary amines (or onium ions), the PCILO method works better than other semiempirical methods;[5] the acetylcholine results may be considered as a positive check of such a statement.[11,12] Following previous suggestions (see, for example, ref 13), the compounds studied in this paper have been analyzed by means of simpler fragments. This allows a clear-cut analysis of the relationships between structural modifications and conformational characteristics. Dihedral angles around single bonds are defined and labeled according to IUPAC nomenclature rules.[14]

Standard values were used for bond lengths and angles[15] and the methyl groups bonded to nitrogen atoms have been frozen at their staggered conformations. The conformational space has been generally spanned in steps of 30°, but regions around the energy minima have been investigated in greater detail. In the figures only some specific sections of the multidimensional energy surface are reported; the conclusions are drawn, however, from the whole set of results. All computations were performed on the UNIVAC 1100/80 at the University of Naples, using a modified version of the PCILO program.

Results

Basicity Constants. The basicity constants of all the polymers and models studied in the present work are reported in Table I. All basicity constants of the polymers are "real" and not "apparent" ones. This has been demonstrated in every case by plotting log k vs. α (protonation degree). These plots, not reported here, show that the number of basicity constants for each polymer is equal to the number of basic nitrogens present in the monomeric unit.

As a general trend, it may be observed that the basicity constants increase as the number of methylene groups present between the aminic nitrogens increases. This is in agreement with all previous data on diamines[16] and is mainly due to the increased distance of the other amino group, either free or protonated, from the basic center being studied. The effect of the insertion of methylene groups on basicity does not depend on a variation of the +I effect since in primary dialkylamines the basicity constants do not increase with chain length but only show small fluctuations around a fixed value.[17]

A more detailed analysis of the data of Table I shows that the log k_1 values of polymers having n (number of methylene groups between the aminic nitrogens) = 2 and 3 are almost equal. This is rather surprising, since their nonmacromolecular models do not behave in that way. Moreover, in all diamines previously studied, the biggest difference in pK_1's occurs between ethylenediamine and trimethylenediamine.[16] In the four series of compounds, however, the log K_2 values regularly increase with increasing n. The difference between the log K_2's of compounds belonging to the same series and having different n's is always rather large (>1 log unit); as expected, the distance of the nitrogen to be protonated from an already protonated one has a large effect on its basicity.

By considering the corresponding terms of the four series of compounds, we may observe that polymers and models having the tertiary amino groups present both in the main chain and as side substituents have log K_1's higher than those of their linear counterparts. On the contrary, their log K_2's are lower. On the other hand, all basicity constants of the polymers are lower than those of their nonmacromolecular models. This is in agreement with our previous studies and may be related to more favorable entropy effects in the case of the models.[18]

Viscosimetric Titrations. The η_{sp}/c's of the two classes of polymers at various neutralization degrees are shown in Figure 1. It may be observed that in the linear polymers, the plots η_{sp}/c vs. α show two jumps, corresponding to the neutralization points of the two basic nitrogens. On the contrary, in the case of "branched" polymers, the corresponding plots do not show noticeable variations of η_{sp}/c over the whole range of α.

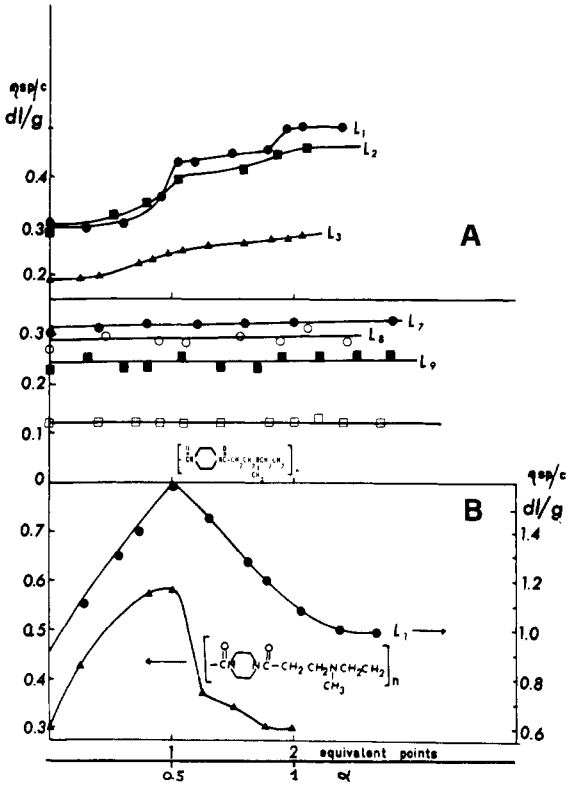


Figure 1. Viscosimetric titrations of polymers in 0.1 M NaCl (A) and pure water (B).

In other words, the viscosities of the linear polymers are constant at low charge density, then suddenly increase when the charge density reaches a value corresponding to the first equivalent point, are constant for a tract, and then again suddenly increase in the proximity of the second equivalent point.

In linear polymers, the above phenomena are most evident when $n = 2$. As n increases and the chain becomes more flexible, the jumps decrease in intensity, the second one almost completely disappears, and η_{sp}/c becomes increasingly smooth with decreasing pH. In "branched" polymers the screening effect caused by the high concentration of the salt is sufficient to depress the extension of the macroion which should take place as its charge is increased.

A titration of the polymers in aqueous salt-free solution showed a different behavior: at a low degree of neutralization, the viscosity increased with increasing neutralization degree until it reached a maximum at $\alpha \simeq 0.5$. From that point on, the viscosity decreased with increasing α, reaching a low value, similar to that formed at very low degrees of neutralization, at $\alpha \simeq 1$. This behavior was common to polymers belonging to both classes and similar to that of other previously studied polymers.[19]

NMR Spectra. The ^{13}C NMR titration of the linear polymer with $n = 2$ (L_1) has been previously reported.[1] In order to allow a comparison between the two classes of polymers we have performed a similar study on its "branched" isomer (polymer L_7). The ^{13}C spectrum at pH 9.8 (free base) is reported in Figure 2.

In analogy with L_1, two doublets are present at room temperature for the C atoms of the piperazine ring, respectively at 41.47, 41.85 and 45.04, 45.36 ppm. For both

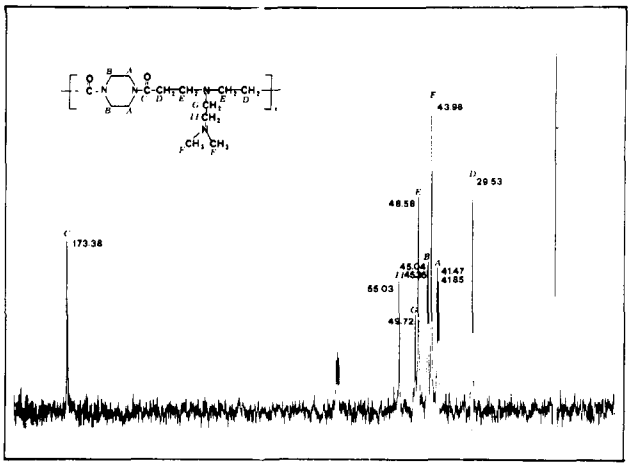


Figure 2. ^{13}C NMR spectrum of polymer L_7 at pH 9.8 (free base). The resonances not labeled are those of $CDCl_3$ (triplet) and Me_4Si.

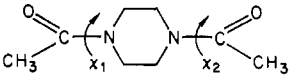
L_1 and L_7, there is a tendency of the signals to coalesce into a single broad band as temperature is increased. This indicates that the carbonyl groups of the two sides of the piperazine ring can assume a cis or trans relative disposition with about the same probability. ^{13}C NMR spectra show that in both cases this trend is pH independent. The resonance at 173.38 ppm has been assigned to the carbonyl carbon C, in agreement with the results of the previous study on L_1.[1]

The resonance at 29.53 ppm has been assigned to the D carbons on the basis of the shielding effect of the carbonyl group, and the resonance at 43.98 ppm has been assigned to the terminal methyl groups F on the basis of its intensity. More care has to be paid to the E, G, and H resonances. Due to higher intensity, the 48.58-ppm resonance has been assigned to the E carbons, in agreement with its multiplicity. The resonances at 49.72 and 55.03 ppm have been assigned to the G and H carbons, respectively, because the G carbon is nearer the E carbon, reflecting a similar chemical environment. This is once again in agreement with previous studies on isomeric polymers.[1,18] Plots of the chemical shifts of different resonances as a function of pH are shown in Figure 3. Resonances C, D, and H show an upfield shift over the entire pH range; the G resonance has a very large shift in the pH 7.5–10 range. Finally, the F and E resonances show a bell-shaped chemical shift dependence, with an upfield shift in the pH 7.5–10 range and a downfield shift in the pH 1–7.5 range. The estimated values[1] of log K_1 and log K_2 are 8.5 and 4.5, respectively, in good agreement with the potentiometric titration results. The regular β effects[20] (2–2.5-ppm upfield shifts[1]) of the G carbon in the first protonation step and of the D carbon in the second protonation step are in agreement with the previous suggestion[4] that the first protonation occurs on the side nitrogen atom.

Also interesting is the behavior of the carbonyl carbon C: in polymer L_1 this resonance showed two steps[1] corresponding to the first and second protonations while for polymer L_7 only one step was observed (Figure 3) at the pH value corresponding to the second protonation. This behavior could be due to the formation of intramolecular hydrogen bridges between the carbonyl group and the onium ions belonging to the main chain. The side aminic group of polymer L_7 is too distant from the carbonyl group to give rise to significant interactions; as a consequence no upfield shifts of resonance C are observed upon the first protonation in this case.

The close correspondence between data of polymers and corresponding model compounds for the pairs L_1–L_4[1] and L_7–L_{10} gives an indication that during protonation no interaction occurs between neighboring monomeric units.

Conformational Analysis. The pH-dependent conformational modifications of poly(amido amines) have been investigated by means of the following fragments (shown in their TT, TTTT, or TTT conformations):



1

This fragment allows the analysis of the joints between different monomeric units.

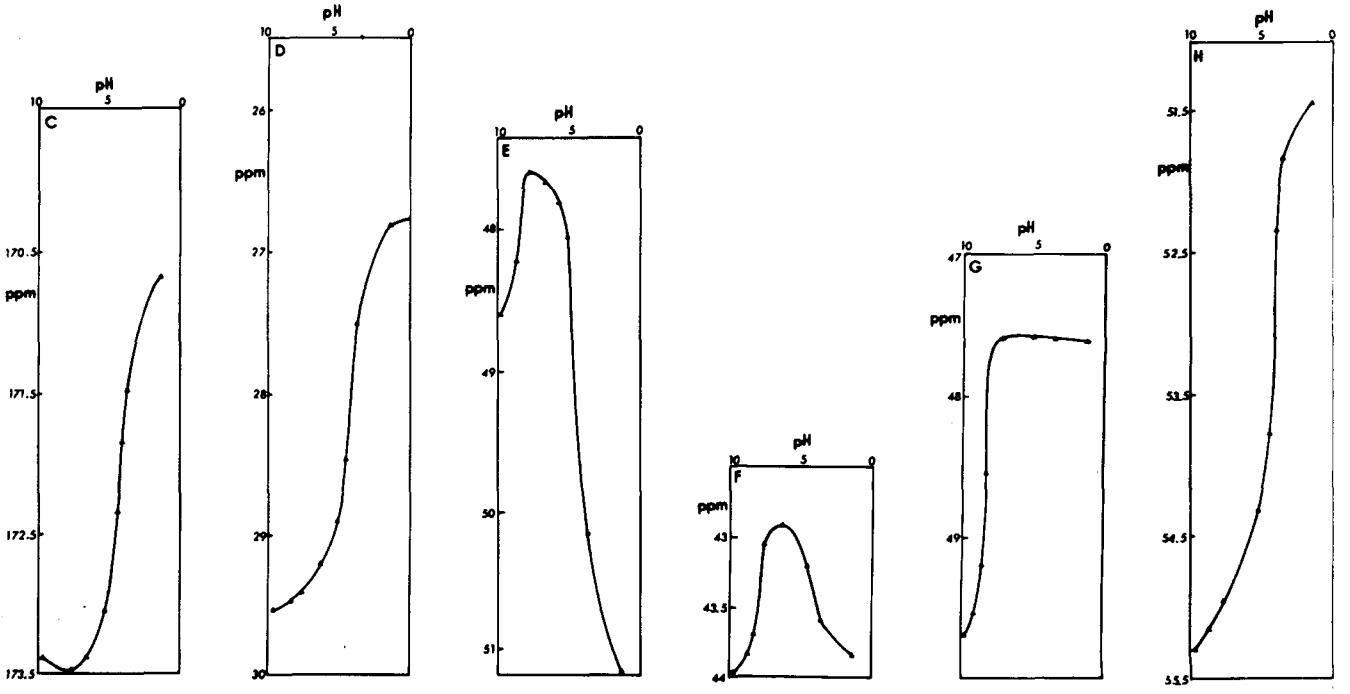
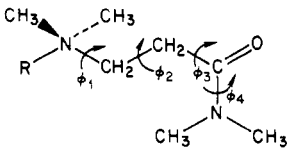
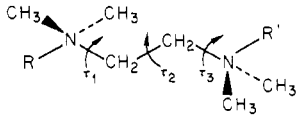


Figure 3. Plot of the ^{13}C chemical shifts of polymer L_7 as a function of pH. The resonances are labeled as in Figure 2.



2
R = lone pair or H

This fragment allows the analysis of the interactions between aminic and amidic groups in the first class of polymers. According to some test computations, the side amino groups present in the second class of polymers, in both the neutral and protonated forms, do not show any appreciable interaction with amidic groups. Hence these interactions have not been further investigated.



3
R, R' = lone pair or H

If the steric hindrance of a CH_2 group is considered to be approximately that of a methl group, this fragment simulates interactions between vicinal aminic groups in both classes of polymers.

As for the first fragment, our computations show that the carbonyl groups are frozen in the mean plane of the diacylpiperazine ring for better conjugation of the amidic group despite the higher steric hindrances involved in this conformation. Furthermore, the carbonyl groups do not interact with each other. Hence they have the same probability of being in a cis or trans relative orientation. On these grounds, in the second fragment ϕ_4 has been frozen in a T conformation.

The second fragment shows a rather large conformational freedom in the nonprotonated form with respect to all the dihedral angles (Figure 4). Only regions corresponding to $\phi_3 \simeq 180°$ are always forbidden and this is due to strong steric repulsion between a methyl group of the amidic nitrogen and the methylenic group bonded to the aminic nitrogen. As for ϕ_1, energy minima always correspond to conformations of the methyl groups bonded to the aminic nitrogen staggered with respect to the rest of the molecule.

Protonation of the aminic nitrogen causes a dramatic reduction of the conformational freedom (Figure 5). This is due to the formation of a strong hydrogen bond between the onium ion and the amidic group, which strongly stabilizes the conformations at $\phi_2 = \pm 60$. The requirement that the H atom of the "onium" ion point toward the amidic group strongly limits the allowed conformations for ϕ_1 and ϕ_3 and this implies a stiffening of the monomeric unit when the protonated nitrogen belongs to the main chain. A section $E(\phi_2)$ of the energy surface (with ϕ_1 and φ_3 at their best values) is reported in Figure 6A,B.

In the neutral form, fragment 3 shows a large conformational freedom.

As for fragment 3, the variations of the dihedral angles τ_1 and τ_3 upon protonation are very similar to those of ϕ_1 and ϕ_3 in fragment 2. Hence we report only sections $E(\tau_2)$ for τ_2 and τ_3 at their best values (Figure 6C–E). In the neutral form, fragment 3 shows a large conformational freedom even if the antiperiplanar conformation of τ_2 is the most stable (Figure 6C). The first protonation favors the synclinal conformation of τ_2, which allows the best compromise between the formation of an effective intramolecular hydrogen bridge and steric repulsions (Figure

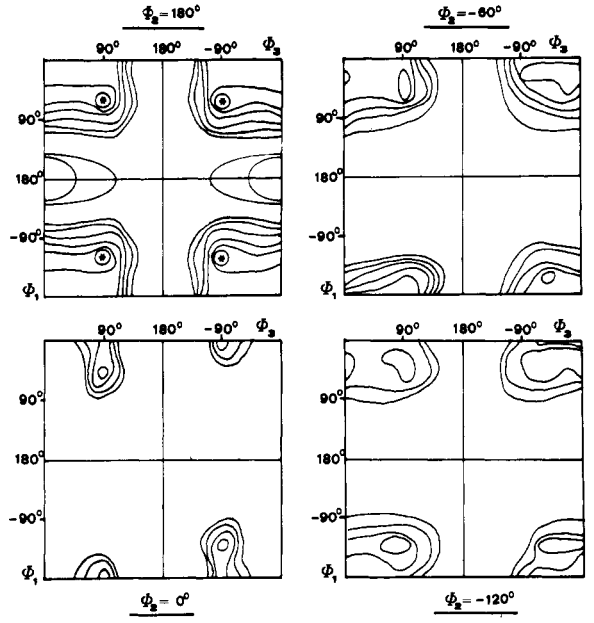


Figure 4. Conformational energy as a function of ϕ_1, ϕ_2, and ϕ_3 for fragment 2 in its neutral form. The isoenergetic curves are spaced 1 kcal/mol and the reported maps contain all the conformations whose energies are less than 5 kcal/mol above the absolute minimun (marked with an asterisk).

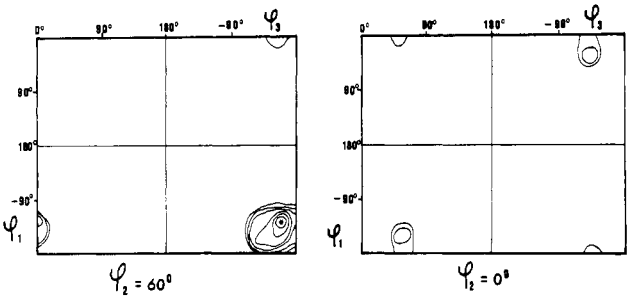


Figure 5. Same as Figure 4 for fragment 2 in its protonated form.

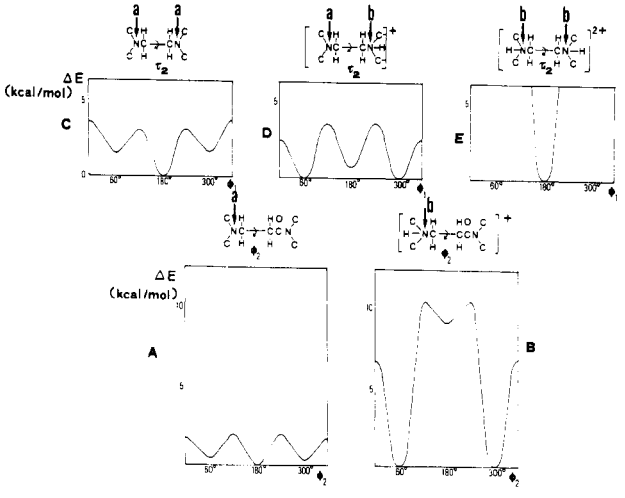


Figure 6. Sections $E(\phi_2)$ (fragment 2) and $E(\tau_2)$ (fragment 3) of the multidimensional energy surface in the various protonation steps.

6D). After the second protonation, the two positively charged onium ions are frozen in a fully extended conformation ($\tau_2 = 180°$) due to the strong electrostatic repulsions (Figure 6E). Increasing the number of methylenic groups between aminic nitrogens has practically no effect

on the neutral molecule. On the contrary, it allows a greater conformational freedom after the first and, especially, the second protonation. As a matter of fact, in all protonation steps the conformational map of the compound with $n = 4$ closely resembles that of the corresponding hydrocarbon.

Finally, we point out that a comparison of the hydrogen bridges formed upon the first protonation in fragments **2** and **3** shows that the stabilization of crowded conformations is much more effective in the former case (10 vs. 1 kcal/mol, Figure 6B,D) due to the reduced bulkiness and higher electronegativity of the acceptor group.

Discussion

On the basis of the results reported in previous sections, it is now possible to discuss the structural modifications induced by stepwise protonation and their effects on the physicochemical properties of poly(amido amines).

Cooperative effects between different monomeric units upon protonation can originate from at least two effects: (1) pH-dependent modifications of electronic density at a basic nitrogen due to inductive effects from neighboring units and (2) pH-dependent conformational variations.

As for point 1, in previous papers[1b,21] we have shown that the protonation enthalpies strongly depend on the electron population of the nitrogen which undergoes protonation. Both quantum chemical computations[1b,22] and thermochemical data[18,22] show that no inductive effects are present between different monomeric units, as both electron populations and protonation enthalpies are essentially equal for the polymers and the corresponding nonmacromolecular models. This is because the piperazine rings block information about variations in electronic distributions between neighboring units.

More attention must be devoted to point 2 because conformational variations (i) could lead to direct interactions between groups belonging to different units or (ii) could involve only each single monomeric unit. This last effect affects the properties of the whole polymer because the joints between different units are very rigid (see the preceding section).

Both ^{13}C NMR results[1] and quantum chemical computations show that no significant interactions exist between groups belonging to different monomeric units. Even the carbonyl groups on the two sides of the diacylpiperazine ring do not show any appreciable interaction with each other and have about the same probability of being in a cis or trans relative disposition, irrespective of pH.

It remains to analyze the possible conformational transitions induced by protonation within each monomeric unit. The general trend is that successive protonation reduces the conformational freedom of each unit and, hence, of the whole polymer. This is in agreement with the experimental result that protonation entropies of polymers are always lower than those of the corresponding nonmacromolecular models.[1]

All of the polymers in the neutral form most likely have a random coil structure due to the great number of accessible conformations about the same energy. In fact, vicinal amino groups have a large conformational freedom and the same applies even more to relationships between amino and carbonyl groups (Figure 4A,D). The protonation leads to stronger limitations to the conformational freedom with respect to the free base (Figure 4B,C,E).

As for the first class of polymers, the first protonation leads to the formation of a strong hydrogen bond between "onium" ions and carbonyl groups belonging to the same monomeric unit. When the first protonation of all the monomeric units is complete, the above effect strongly reduces the conformational freedom of the whole polymer, which tends to assume a rigid structure; this explains the jump of η_{sp}/c at $\alpha = 0.5$.

The reduction of conformational freedom obviously decreases with the lengthening of the aliphatic chain in each monomer: this explains the slight reduction of the first jump of η_{sp}/c with increasing n (i.e., the number of methylenic groups between the aminic nitrogens).

The second protonation leads to an electrostatic repulsion between the positively charged onium ions belonging to the same monomeric unit, and this effect further drives the polymer to a rigid, more extended conformation. Consequently, a second jump is observed in the curve of η_{sp}/c vs. α at $\alpha = 1$. Lengthening the aliphatic chain connecting the aminic nitrogens allows a larger conformational freedom even after the second protonation step, due to lower electrostatic repulsions between more distant "onium" ions. Accordingly, the second step in the viscosimetric titrations tends to disappear with increasing n.

According to both ^{13}C NMR and the potentiometric data in the second class of polymers, the first protonation occurs on the side nitrogen. As a consequence, no effective hydrogen bridges can be formed between the very distant "onium" ion and carbonyl group. Both ^{13}C NMR and quantum chemical results agree on this point, and this explains why the first protonation has no influence on the specific viscosity of these polymers whatever the value of n. The second protonation involves the aminic nitrogen of the main chain.

The interactions between onium groups are the same as for the polymers of the first class, but only an onium ion (the one belonging to the main chain) can interact with either of the two neighboring carbonyl groups. This leads to a greater conformational freedom, and hence the viscosimetric titrations do not show any jump even after the second protonation step.

The results for the polymer having only one amino group in each monomeric unit (no step in the viscosimetric titration) (Figure 1) provide an independent check of the general rule that significant conformational transitions upon protonation are to be expected only when the number of aminic nitrogens equals the number of carbonyl groups and they are at an appropriate distance within each monomeric unit. The viscosimetric data obtained in salt-free solution, however, have not been interpreted because formation of aggregates under these conditions cannot be excluded.

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Length Distributions and the Alignment Transition of Polymers Formed by Linear Reversible Polymerization

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ABSTRACT: The equilibrium distributions of polymer lengths and orientations are calculated for reversible linear polymerization, assuming that the free energy of monomer addition is independent of polymer size. The anisotropy of the equilibrium state at high concentrations has two aspects. (1) In the absence of anisotropy in the interactions between molecules, the system is isotropic with respect to monomer orientation, but the average polymer length is greater along the axis of alignment than orthogonal to it. (2) In the presence of anisotropic interactions between molecules, the orientation of monomers is also anisotropic. The phase diagram differs somewhat from that calculated earlier for an approximation of a reversibly polymerizing system in which all the polymers were constrained to be of identical, albeit reversibly changeable, length. In particular, noninteracting polymers do not form as dense an anisotropic phase as was predicted earlier. However, the temperature dependence of the phase behavior of the present freely reversible system and that of the former constrained reversible system are qualitatively similar to one another and qualitatively distinct from that of irreversibly polymerized systems. In particular, there exists for the reversibly polymerized systems, in contrast to the irreversibly polymerized systems, a temperature below which, for positive enthalpies of polymerization, or above which, for negative enthalpies of polymerization, no phase transition occurs. The maximum concentration of the isotropic phase is found to depend primarily on the free energy of polymerization, to be relatively insensitive to the nature of interparticle interactions, and to have a temperature dependence which is qualitatively similar to that observed for sickle cell hemoglobin. The distribution of polymer lengths in the isotropic phase is significantly different from that observed for sickle cell hemoglobin, presumably due to the relative instability of subnuclear hemoglobin aggregates which is not incorporated into the present model. The minimum concentration of the anisotropic phase is found to depend strongly on both the free energy of polymerization and the interparticle interactions and, in general, has a complicated temperature dependence.

Introduction

A variety of proteins associate reversibly to form long polymers. Among these are tubulin, actin and actin-like proteins, tobacco mosaic virus protein, and sickle cell hemoglobin. The excluded volume dependent nonideality associated with the highly asymmetric shapes of such polymers can induce spontaneous alignment and phase separation. This phenomenon is entropically driven; it is modified by, but not dependent upon, the nature of the interparticle interactions.[1]

Lattice models for monodipserse hard rods[2,3] have successfully explained the main features of the observed phase behavior of α-helical polypeptides[4-9] and *p*-phenylene polyamides.[10-13] Such synthetic systems are relatively simple to describe because the polymer length is fixed and the approach to equilibrium involves adjustment of polymer orientation only. In contrast, proteins form polymers which may reversibly change length so that equilibration involves the joint optimization of polymer lengths and orientations. The lattice models of Flory[2] and DiMarzio[3] have previously been used to describe reversibly polymerizing systems by assuming a narrow length distribution.[14,15] Thus, the number of degrees of freedom in the approach to equilibrium was limited to two (average polymer length and average polymer orientation) by imposing the constraint that the polymers were of uniform, albeit adjustable length. We will hereafter refer to this as constrained reversible polymerization. In the present treatment, based on DiMarzio's lattice model, this artificiality is removed and no constraints whatever are placed on the polymer lengths. It is therefore possible to calculate the expected equilibrium *distribution* of lengths, as well

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