1. Both the C3 model compounds and the polyamides show no significant conformational change in various solvents such as $CDCl_3$, water, TFE, methanesulfonic acid, and sulfuric acid (from nmr, ORD, CD, and viscosity). In the preferred conformation, the carbonyl groups bisect the cyclopropane ring (from nmr and dipole moment).

2. Both (+)-C6·DSH and V have different conformations in $CDCl_3$ and D_2O (from nmr). (+)-C6·DSH shows no noticeable conformational change in water, TFE, methanesulfonic acid, and sulfuric acid (from ORD, CD, and viscosity). However, the conformation of V varies in the above solvents (from ORD and CD).

Unfortunately, the nmr spectra as well as the ORD and CD spectra did not give us conclusive evidence about the direction of the rotation due to the spirodiamine which rotates the amide bond by 90° either clockwise or counterclockwise.[2] This rotation must occur at random because there seems to be no factor which would determine the direction of the rotation.[2] Therefore, the conformational changes reported here may be due only to the bond connecting the carbonyl groups and the C3 ring or the C6 ring.

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(12) The dipole moment was calculated by assuming that the dipole moment of each amide group was 3.84 D, the angle between the dipole and C–N bond was 39.6°,[1] and the angle C_1C_2H was 115°. The corresponding angles for many cyclopropane derivatives have been shown to be in the range of 110–120°. The calculated dipole moments of II for 110 and 120° are 2.74 and 2.96 D, respectively.

Fluorine Magnetic Resonance Studies of Conformation of Poly(ethylenimines)

Timothy W. Johnson and Irving M. Klotz*

Department of Chemistry, Northwestern University, Evanston, Illinois 60201.
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ABSTRACT: The conformation of derivatives of poly(ethylenimine) in aqueous and in organic solvents has been investigated by fluorine magnetic resonance studies of fluorine-labeled polymers and model small molecules. Fluorine chemical shifts, which are sensitive to molecular surroundings, provide a probe of the local environment in derivatives of poly(ethylenimine). In both aqueous and organic solutions the spectra give evidence of interactions among polymer segments. In aqueous solution long apolar pendant groups on the polymer matrix appear to assemble into clusters. The presence of clusters restricts the range of possible conformations of the polymer. A model is presented that encompasses the observations.

Recent work with poly(ethylenimines)[1,2] has demonstrated the possibility of generating derivatives with dramatic binding[3–5] and catalytic abilities.[6–9] For example, derivatives in which about 10% of the amino groups of poly(ethylenimine) (PEI) have been modified by acylation with an ester of dodecanoic acid or alkylation with 1-iodododecane have a high affinity for small molecules in aqueous solution,[3,4] particularly for anions and for molecules with large apolar segments.[5] PEI derivatives with both apolar binding groups and appropriate nucleophilic groups are catalysts for certain hydrolytic reactions,[6–9] presumably by virtue of the ability of the binding group to constrain the substrate in the vicinity of the catalytic group.

Having demonstrated the possibility of making these polymers, we have undertaken studies to elucidate their structure. Thus we have determined the course of reaction of acylating and alkylating agents with the various (primary, secondary, and tertiary) amino groups.[10] In addition we have probed the local environment of the apolar groups on PEI by fluorine nmr studies of derivatives in which fluorine atoms are part of the apolar substituents.[11] That investigation, based on the high sensitivity of fluorine chemical shifts to local environment, showed that in a derivative in which 5.5% of the PEI residues had been acylated with 10,10,10-trifluorodecanoyl substituents, these groups were distributed between classes of environments, one aqueous and the other micelle like. In the present report we have extended the nmr studies to other fluorine-labeled PEI derivatives, one of which is closely related to polymers used in the binding and catalytic studies. Spectra of various derivatives were obtained both in aqueous solution and in organic solvents. From results in organic solvents we have estimated the degree of exposure of the fluorine labels to these solvents. The observations in aqueous solutions reveal directly the nature of the local environment of the label. The delineation of the nature of the surroundings of the probe molecule places severe limits on the range of possible structures for the entire macromolecule. On the basis of these restrictions a conformational model has been built which encompasses a variety of experimental observations

Table I
Fluorine Chemical Shifts of Model Compounds in Several Solvents

		N-*n*-Propylamide of		
Solvent	1,1,1-Trifluoroalkane[a,b]	3-Trifluoromethylbutyric acid[a]	*p*-Trifluoromethylbenzoic acid[c]	*o*-Trifluoromethylbenzoic acid[c]
50% aqueous PEI-6	2.56			
Dimethyl sulfoxide	2.92	10.34	−17.32	−20.68
Water	3.85	11.17	−16.05[d]	
Ethylenediamine	4.22	11.55		
Dimethylformamide	4.66		−15.61	−19.22
Ethanol	6.04	13.25	−14.30	−18.29
Methanol	6.50		−13.81	−17.76
Hexafluorobenzene	8.83		−11.76	−16.27
δ(ethanol)− δ(dimethyl sulfoxide)	3.12	2.91	3.02	2.39

[a] Chemical shift relative to external 1,1,2-trichloro-3,3,3-trifluoropropene. [b] Some of these data were obtained from ref 12. [c] Chemical shifts relative to external trifluoroacetic acid. [d] *N*-(2-Hydroxyethyl)amide. Concentrations of 0.01 and 0.02 *M* give the same shift, indicating the absence of association effects in this system.

of the properties and behavior of poly(ethylenimine) derivatives.

Experimental Section

***N*-2-Hydroxyethyl-*p*-trifluoromethylbenzamide.** *p*-Trifluoromethylbenzoyl chloride (PCR, Inc.) was allowed to react with a sixfold excess of 2-aminoethanol with cooling in an ice bath. The resulting solid was washed with water and recrystallized from an ethanol–toluene mixture. The amide product after drying in air had a melting range of 116–118°. Its structure was confirmed by its proton nmr spectrum.

The three ring isomers of ***N*-*n*-propyltrifluoromethylbenzamide** were prepared by reaction of the corresponding trifluoromethylbenzoyl chlorides (PCR, Inc.) with an excess of *n*-propylamine. The products after recrystallization had the following melting ranges: ortho, 66–68°; meta, 51.5–53.5°; and para, 103–104°.

***N*-*n*-Propyl-3-trifluoromethylbutyramide.** A 2.4-g (15.4 mmol) portion of 3-trifluoromethylbutyric acid (Pierce Chemical Co.) was dissolved in 15 ml of toluene, and 1.55 g (15.4 mmol) of triethylamine was added. To the stirred mixture, cooled in an ice-salt bath, was added 1.66 g (15.4 mmol) of ethyl chloroformate. The resulting solution was allowed to warm to room temperature. Then it was added with stirring to a solution of 0.91 g (15.4 mmol) of *n*-propylamine and 1.66 g (15.4 mmol) of triethylamine. The amide product was purified by sublimation to yield a substance with a melting range of 31–34°, whose structure was confirmed by proton nmr spectroscopy.

***p*-Nitrophenyl *p*-Trifluoromethylbenzoate.** A 1.5-g portion of *p*-trifluoromethylbenzoyl chloride was added to 1.25 g of *p*-nitrophenol in 5 ml of dry pyridine with cooling in ice. The resulting solid was dissolved in methylene chloride, and the solution was washed with water and then dried over sodium sulfate. After filtration the solution was treated with hexane to induce crystallization. The product had a melting range of 93.5–95°, and its structure was confirmed by proton nmr spectroscopy.

***p*-Nitrophenyl *o*-trifluoromethylbenzoate** was prepared by a procedure similar to that used for the para isomer. The product had a melting range of 116.5–118°.

***p*-Nitrophenyl 10,10,10-Trifluorodecanoate.** In a 100-ml flask was placed 3.73 g (16.5 mmol) of 10,10,10-trifluorodecanoic acid, 30 ml of toluene, and 2.3 ml (16.5 mmol) of triethylamine. The mixture was cooled in an ice–salt bath, and 1.32 ml (16.5 mmol) of ethyl chloroformate in 10 ml of toluene was added dropwise with stirring. The resulting solution, after it had slowly warmed to room temperature, was poured with stirring into a mixture of 2.33 g (16.5 mmol) of *p*-nitrophenol, 2.3 ml of triethylamine, and 20 ml of toluene. After 2 hr at room temperature and 16 hr at 4° the mixture was washed twice with aqueous sodium carbonate and once with water. It was then dried over sodium sulfate and evaporated to dryness at reduced pressure. The structure of the final product, which melted at 40–43°, was confirmed by proton nmr spectroscopy.

The preparation of ***p*-nitrophenyl 3-trifluoromethylbutyrate** has been described.[12]

Poly(ethylenimine), PEI-600 (lot no. TAO 4039BCNN), was supplied by the Dow Chemical Co. as a 33% solution in water. To remove the water the following procedure was used. A 30-g portion of the 33% aqueous PEI-600 (10 g of PEI) was placed in a 500-ml round-bottom flask. Water was removed on a rotary evaporator and the residue was dissolved in about 200 ml of absolute ethanol. The resulting solution was rotary evaporated until no more ethanol distilled at a pressure of 15 mm and a pot temperature of 50°. The treatment with ethanol followed by evaporation was repeated twice. The resulting residue was either weighed out as the very viscous liquid or was dispensed volumetrically as a 10% solution in ethanol.

PEI-6 and PEI-18, with molecular weights about 600 and 1800, respectively, were obtained from Dow Chemical Co. as 99% pure viscous liquids.

PEI derivatives were synthesized and isolated by methods previously described.[10] The composition of the derivatives, in 10% solution in deuterium oxide, was determined by proton nmr spectroscopy (with a Varian T-60). Compositions are designated by R_xPEI where R is the residue covalently linked and x is the fraction of residues with R attached.

Fluorine nmr spectra were obtained with a Bruker HX-90 nmr spectrometer operated at 84.67 MHz. Signal-to-noise ratios of the spectra of the polymers were enhanced by computer averaging of spectra. Line widths were measured as apparent widths at half-height. Chemical shifts were obtained relative to external references, trifluoroacetic acid or the stronger resonance of a 2% solution of 1,2-difluorotetrachloroethane in 1,1,2-trichloro-3,3,3-trifluoropropene.[13] The shifts were not corrected for bulk susceptibility differences since, in most cases, we are concerned only with comparison of dilute aqueous solutions of nonparamagnetic materials, which all have essentially the same susceptibility. In cases in which comparison is made between several solvents, the susceptibility correlation is less than any shift difference which is considered significant, or it cancels out in the type of comparison made.

The model of a segment of a PEI derivative (depicted in Figures 3–5) was built at a scale of 1 cm/Å and used a standard 16-lb bowling ball to represent a spherical cluster. The PEI framework was constructed with Push-Fit Models from Nicholson Molecular Models, Reading, England.

Results and Discussion

The fluorine chemical shift observed in any particular substance is determined first by the nature of the compound and the position in which the fluorine is incorporated and second by the character of the solvent which provides the local environment of the dissolved molecule. In previous fluorine nmr studies[14–19] several compounds were examined which had the general structure $CF_3(CH_2)_nX$, where n is an integer greater than four and X is one of a variety of groups containing a hydrophilic segment. These compounds all have the same chemical shifts in a given solvent, *e.g.*, in water at high dilution, and were assumed to have the same (solvent) environment dependence in the chemical shift. In the present study several substances are included which do not fit the general structure given above and whose fluorine chemical shift in a particular solvent is

Table II
Fluorine Chemical Shifts and Line Widths for *o*- and *p*-Trifluoromethylbenzoyl PEI-600 and Related Model Compounds

	Chemical shift, ppm[a]			
Solvent	*N*-*n*-Propyl-*p*-trifluoromethylbenzamide	(*p*-Trifluoromethylbenzoyl)$_{.18}$-PEI-600	Difference	Line width (Hz) for PEI deriv
Dimethyl sulfoxide	−17.32	−16.96	+0.36	30
Ethanol	−14.30	−14.64	−0.34	34
Methanol	−13.81	−14.20	−0.39	40
	N-*n*-Propyl-*o*-trifluoromethylbenzamide	(*o*-Trifluoromethylbenzoyl)$_{.25}$-PEI-600		
Dimethyl sulfoxide	−20.68	−20.59	+0.09	12
Dimethylformamide	−19.22	−19.41	−0.19	21
Acetic acid		−18.97		60
Ethanol	−18.29	−18.90	−0.61	54
Methanol	−17.76	−18.39	−0.63	50
		(*o*-Trifluoromethylbenzoyl)$_{.10}$-PEI-600		
Water		−20.11		40

[a] Relative to external trifluoroacetic acid.

Table III
Fluorine Chemical Shifts and Line Widths for 3-Trifluoromethylbutyryl PEI Derivatives and a Model Amide

Compd	Conditions[a]	Chemical shift, ppm	Line width, Hz
N-*n*-Propyl-3-trifluoromethylbutyramide	Water	0.00[b]	Small
	Ethanol	2.08	Small
(3-Trifluoromethylbutyryl)$_{.09}$PEI-18	2%, pH 9.8	−0.12	22
	2%, pH 6.1	−0.22	
	0.06 *M* SDS	+0.17	26
(3-Trifluoromethylbutyryl)$_{.18}$-PEI-600	2%, pH 8.5	−0.12	26
	2%, pH 7	−0.18	32
	9%, pH 7	−0.22	25
	2%, pH 3	−0.37	43
	2%, pH 7 1.2 *M* NaCl	−0.31	50
	0.06 *M* SDS	+0.23	60

[a] Aqueous solution unless otherwise specified; SDS = sodium dodecyl sulfate. [b] This shift is defined as zero. It is 11.17 ppm upfield from external 1,1,2-trichloro-3,3,3-trifluoropropene.

not the same as that of the 1,1,1-trifluoroalkane compounds. The environmental dependence of these shifts was determined therefore by comparison of the effects of solvents on the chemical shifts. The results are displayed in Table I. For each of the compounds studied the order of the chemical shifts is the same, indicating that the same factors are important in determining the environmental perturbation of the resonance frequency. The chemical shift difference between each compound in ethanol and in dimethyl sulfoxide is given as the last entry in each column. This should be a rough indication of the sensitivity of the various probes to solvent change. The sensitivity to environment so inferred is seen to be about the same for the first three compounds and only somewhat less for the *o*-trifluoromethylbenzamide. It is interesting to note that the sensitivity is greatest for the least hindered trifluoromethyl group and least for the most hindered trifluoromethyl group.

Observed shifts for several of the PEI derivatives in nonaqueous solvents are listed in Table II, relative to that of the appropriate model compound. It is apparent that the shifts in the polymer solution and in the model compound solution are not identical. The displacement of observed shift from that in dimethyl sulfoxide solution is always less for the polymer. This behavior suggests that each fluorine label on the polymer spends some fraction of the time in contact with segments of the polymer other than the one to which it is covalently attached. The observed shift would then be a weighted average of the shifts in the solvent environment and the various environments provided by the other segments, polyethylenimine backbone (solvated) and aromatic pendant groups (solvated). Since the shift in a polyamine environment is to low field[11] and the shift in an aromatic hydrocarbon environment is to intermediate field (between water and ethanol), the contributions of the polymer should be in the direction observed in the attached labels. Regardless of the precise interpretation of these data, it is clear that the fluorine labels experience an environment that is not completely solvent like.

It is somewhat surprising to find these intersegment contacts in what would be expected to be good solvents for the polymer. This interaction very likely arises from the highly branched structure of the polymer, which favors a compact conformation and increases the probability of intersegment contacts. Such contacts would presumably be less important for linear polymers in good solvents. The fluorine nmr method should be applicable to the study of such systems also.

Fluorine nmr results for 3-trifluoromethylbutyryl derivatives are presented in Table III. The *n*-propylamide in water and in ethanol displays doublets whose chemical shift difference is 2.08 ppm. This difference and the inferred environmental sensitivity are close to those for 1,1,1-trifluoroalkanes with long chains. The chemical shifts of the PEI derivatives in water are all below (*i.e.*, downfield from) that found for the model amide in water by from 0.12 to 0.37 ppm. This is in the direction (relative to the aqueous shift) in which one would expect the chemical shift to be perturbed if the pendant fluorines find themselves in a hydrated PEI environment.

The PEI-18 derivative, as a consequence of its smaller molecular weight and its lower degree of substitution, is expected to show less effect of association of the side chains than the PEI-600 derivative. Thus the shift, 10.85 ppm, of the former in solution at pH 6.1 can be taken as an upper limit in the absence of association effects, since association could only raise the shift (upfield). Since higher (more upfield) shifts appear at high pH for both polymers, and even at pH 7 for the PEI-600 derivative, it seems that indeed there is a small amount of clustering of the apolar side chains.

The effect of low pH (*ca.* 3) or high salt concentration is to increase the line width and to lower the chemical shift. The effects of both low pH and high salt are probably manifestations of a locally enhanced concentration of electrolyte, which has been shown to depress fluorine shifts.[15,20] The mechanism of the enhancement of the line widths is not clear.

Spectra of a (*p*-trifluoromethylbenzoyl)$_{.075}$PEI-600 in water at several pH values are displayed in Figure 1. In these spectra the zero of chemical shifts is taken as that of *p*-trifluoromethylbenzoic acid 2-hydroxyethylamide in

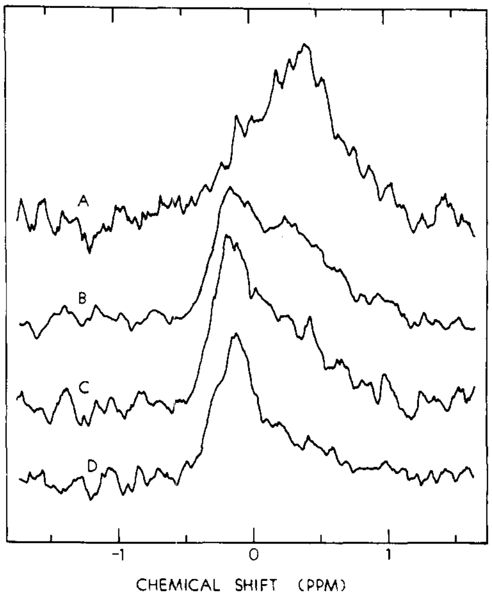


Figure 1. Fluorine nmr spectra of (*p*-trifluoromethylbenzoyl)$_{.075}$PEI-600 in water (2% solution) at pH values (A) 9.2, (B) 8.1, (C) 6.5, and (D) 4.7.

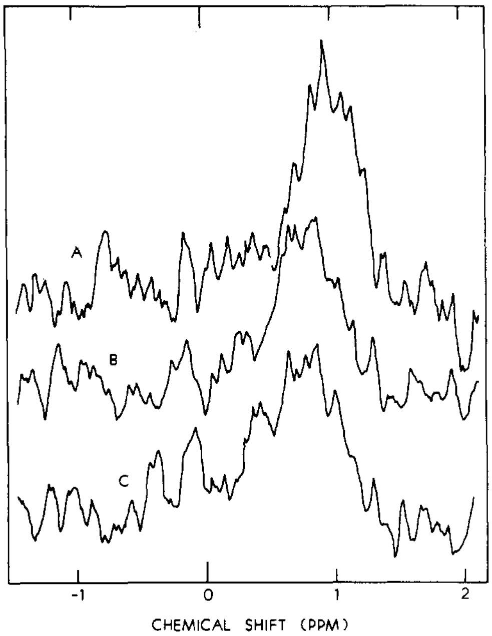


Figure 2. Fluorine nmr spectra of (10,10,10-trifluorodecanoyl)$_{.095}$PEI-600 in water (2% solution) at pH values (A) 9.2, (B) 6.7, and (C) 3.8.

water. Thus resonances to high field from the zero imply a cluster, hydrocarbon-like environment, and shifts substantially below zero reflect an aqueous PEI environment. It is clear that each spectrum can be represented as the superposition of two resonances, one rather broad (*ca.* 60 Hz width at half-height) at 0.3 to 0.4 ppm and the other somewhat sharper (*ca.* 30 Hz width at half-height) at about −0.2 ppm. The form of these spectra is very nearly the same as those previously published for (trifluorodecanoyl)$_{.055}$PEI-600 in water.[11] Thus the low- and high-field resonances respectively may be attributed to fluorines in an aqueous environment modified by the presence of PEI and to fluorines in an environment generated by the association of several of the aromatic residues.

In the case of the low-field resonances, the shift is not nearly as far downfield as is seen[11] in a 50% aqueous PEI solution (*ca.* −1.3 ppm). Thus either the fluorines giving this resonance are in an environment which is mainly water or they oscillate rapidly between a pure water and a concentrated aqueous PEI environment. For all three classes of PEI-600 derivative, trifluoromethylbenzoyl, trifluoromethylbutyryl, and trifluorodecanoyl$_{.055}$, a resonance peak is exhibited downfield to that shown by the corresponding model compound.

The high-field resonance (Figure 1) is not as far upfield as that of fluorine in (trifluorodecanoyl)$_{.055}$PEI-600, where the shift is about 0.7 ppm up from that of model compounds in water. The smaller effect is indeed to be expected on two grounds. First, the solvent chemical shift difference between water and ethanol, for example, is smaller for trifluoromethylbenzoyl compounds. Second, the clustered species that is causing the upfield shift contains aromatic residues, which, on the basis of solvent effects,[20] are not expected to give quite such a high-field resonance as saturated hydrocarbons. In spite of these differences the general implications with respect to the formation of micelle like clusters are essentially the same as for (trifluorodecanoyl)$_{.055}$PEI-600.

The fluorine nmr spectra of (trifluorodecanoyl)$_{.095}$PEI-600 in water at several pH values are shown in Figure 2. In each spectrum there is only one broad resonance (40–60 Hz width at half-height) with chemical shifts from 0.8 ppm at low pH to 1.0 ppm at high pH. In this polymer all of the trifluorodecanoyl side chains spend most of the time in apolar clusters. Furthermore, the clusters, as far as can be determined from positions of the chemical shifts, are similar to those formed by detergent ions. The fact that there is a small pH dependence in the chemical shift suggests that, at least at low pH, there is exchange of some of the apolar side chains between the aqueous and the cluster phases. If one assumes, however, that the chemical shift of the label in the cluster on this PEI derivative is about the same as that in typical detergent micelles,[14–18] then one must conclude that even at low pH nearly all of the apolar residues are within the clusters. In view of the results for (trifluorodecanoyl)$_{.095}$PEI-600, the fact that the shift of the high-field resonance of (trifluorodecanoyl)$_{.055}$PEI-600 is only about 0.7 ppm upfield from the monomer shift implies either that the residues giving that resonance spend a substantial part of the time in an aqueous environment or that the cluster in which they are incorporated is substantially different from the conventional detergent micelle.

The trifluorodecanoyl PEI derivatives have been shown to have binding properties similar to those of the long-chain hydrocarbon derivatives reported previously.[3,4] Thus, in view of the structural and functional similarities between the fluorine-containing PEI derivatives and the other hydrophobic PEI derivatives, we may assume that apolar clusters are also present in the latter. Nevertheless, there may be small differences in their properties. First, the substitution of three terminal fluorines for three terminal protons in a long chain aliphatic hydrocarbon reduces the hydrophobic tendencies of these chains.[14] Thus it is to be expected that (decanoyl)$_{.095}$PEI-600 would have (at any instant) a greater fraction of its apolar side chains in micelle like structures than would (trifluorodecanoyl)$_{.095}$-PEI-600. Second, the basic PEI derivative of primary interest in binding and catalytic studies is (dodecanoyl)$_{.10}$-PEI-600, which has two additional methylene groups per aliphatic chain to increase its hydrophobic tendencies. It is to be expected, therefore, that (dodecanoyl)$_{.10}$PEI-600 will have a greater fraction of its apolar groups in clusters than will (decanoyl)$_{.10}$PEI-600. Thus both changes (hydrogen for fluorine, addition of two methylenes) contribute in the

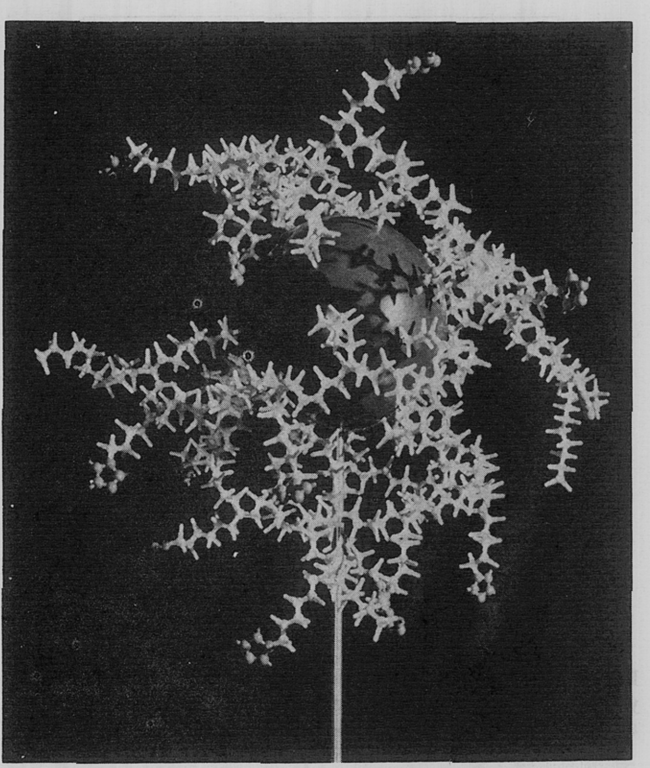
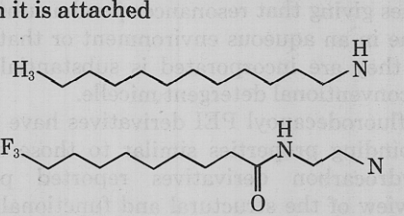


Figure 3. Model of the conformation of a large segment of lauryl imidazolyl PEI in aqueous solution. (See text for details.)

same direction, in favor of the cluster type of environment. Since even in the ^{19}F labeled polymer [(trifluorodecanoyl)$_{.095}$PEI-600], examined by nmr spectroscopy, most of the apolar residues reside in micelle like structures, in (dodecanoyl)$_{.10}$PEI-600 the apolar residues must be so incorporated to an even greater extent, approaching 100%.

In some of the PEI derivatives of interest the apolar group is a dodecyl residue[1] (introduced by alkylation)[8,9] *rather than a dodecanoyl one. In such derivatives there is a* basic amino group adjacent to the apolar group. If we compare the structure of the dodecyl group with the trifluorodecanoyl residue taken together with the ethylenimine residue to which it is attached



we note 12 and 13 atoms, respectively, in the chain backbones. Both residues are attached to basic amino groups. The dodecyl group might have a slightly lower micelle-forming tendency by virtue of its shorter length, but this would probably be more than compensated for by the presence of the fluorines and the polar amide in the other chain reducing its cluster-forming tendencies. Thus again it is to *be expected that* (dodecyl)$_{.10}$PEI-600 *will have at least* as many of its residues in clusters as does (trifluorodecanoyl)$_{.095}$PEI-600, that is, a major fraction would be so incorporated.

The clustering of the apolar pendant groups, which has been clearly revealed by nmr spectroscopy, places rather strong constraints on the type of conformation that the hydrophobic PEI derivatives can assume in aqueous solution. We have built a three-dimensional model that illustrates one type of conformation consonant with these constraints. A photograph of this model giving a full view of a large segment of polymer is displayed in Figure 3. Closer views with added bound molecules are shown in Figures 4 and 5.

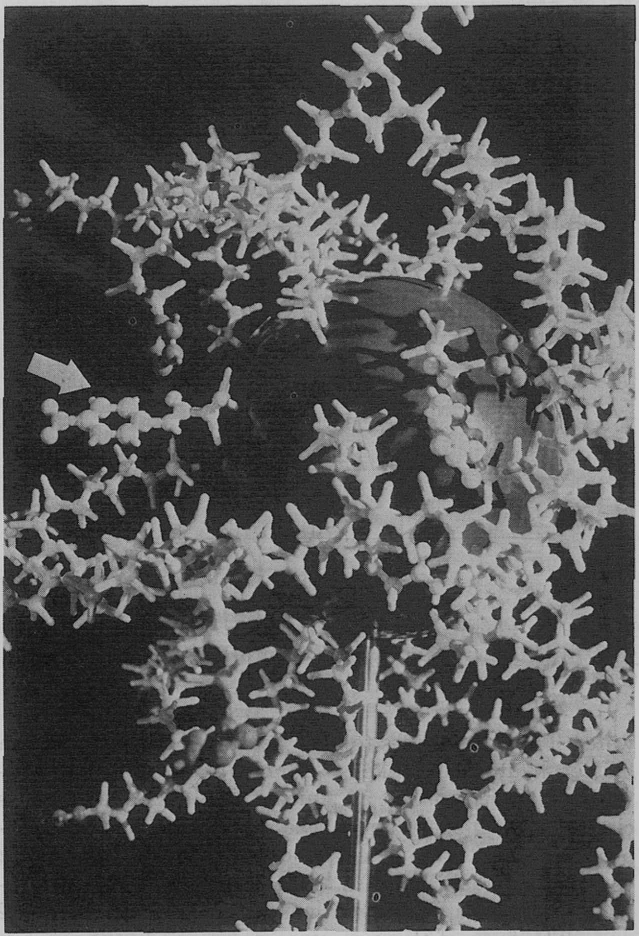


Figure 4. Closer view of the segment shown in Figure 3 with three molecules of bound nitrophenyl caproate added. One of the bound molecules is pointed to by a white arrow; the nitrophenyl group projects out from the domain of the apolar cluster; the caproyl chain is buried in the cluster and hence not explicitly indicated.

In this model the large central sphere represents a cluster of apolar groups. The individual chains in the cluster are not depicted separately, since by analogy with associated apolar chains of detergent micelles they are presumed to be closely packed, with a density about that of a liquid, long-chain hydrocarbon.[21] Thus the cluster is represented as a homogeneous spherical domain since individual chains would not stand out in a uniform region. The number of chains within the cluster is determined by the size of the sphere, which could be chosen over a rather wide range and still be consonant with the constraints of the polymer framework. For construction of this model, clusters were constituted of 20 apolar groups.

The choice of 20 as the number of apolar groups per cluster is somewhat arbitrary. Having built the present model and another using eight apolar groups in a smaller cluster, we conclude that the features of importance are not qualitatively changed by a change in cluster size. In the limit of very large size, the clusters would have to take on a nonspherical shape.[21] Coincident with this, the area per apolar group at the surface of the cluster would be somewhat reduced, eventually to such an extent that the polyamine framework would become crowded. However, before such a condition could be attained, electrostatic effects and solvation effects would presumably stop the further growth of the cluster.

In an average PEI-600 molecule there are over 1000 ethy-

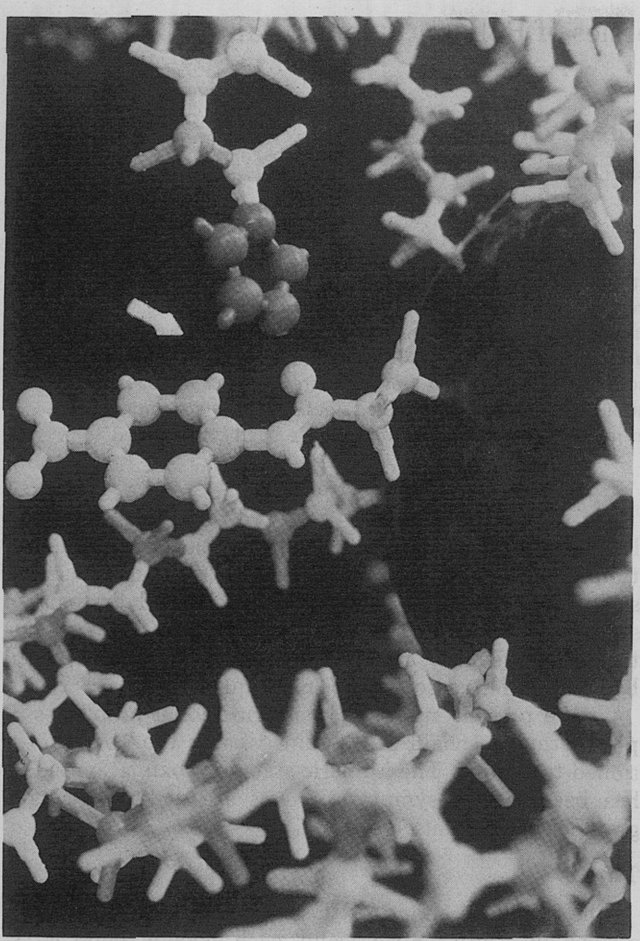


Figure 5. Closeup view of the model (Figures 3 and 4), the arrow showing the proposed close approach of catalytic imidazole groups and bound nitrophenyl caproate.

lenimine residues. Thus in a PEI derivative with 10 mol % apolar groups, there must be over 100 such chains. If we assume 20 chains per cluster, several such aggregates must be present in each macromolecule. The feasibility of such structures with multiple clusters has been confirmed by construction with models of the type shown in Figure 3.

At the surface of an apolar spherical cluster each of the constituent 20 chains is attached to a point on the PEI framework, this depictment corresponding to the covalent linkage of the hydrocarbon side chain to the polymer macromolecular backbone.[22] The PEI framework (Figures 3–5) is represented explicitly in terms of its constituent -CH_2CH_2N- residues, illustrated by the white and gray balls and connectors. Since the sample of PEI used has substantial branching in the macromolecule,[2] there is much latitude in the manner of building the polymer chains. The features of the model being described are not particularly sensitive to the precise manner of assembly of the chains.

Several additional features of the model are noteworthy. First, it is possible to build it without straining chemical bonds or causing unfavorable steric interactions. The polyamine chain is sufficiently long to reach around a cluster, but it is not so long or so bulky as to cause excessive crowding near the surface of the cluster. The spaces at this surface between the polyamine chains (Figures 4 and 5) are likely binding sites for small apolar molecules, since such molecules can be bound at the interface or partially penetrate into the domain of the hydrocarbon sphere in response to favorable apolar interactions. In the model shown in Figure 4, three bound *p*-nitrophenyl caproate molecules have also been included to illustrate possible modes of binding. An arrow points to one of these small molecules. The sites of the other two can be detected by careful comparison of Figures 3 and 4 in the region of the spherical cluster. The regions of the polymer domain that are not occupied by either the framework or bound molecules will contain water and counterions to the charged residues.

In addition to the lauryl groups and the polyamine framework, attached imidazole residues are also represented in the model. These are recognizable as the five-membered gray-atom rings. Since in practice they are linked primarily to primary amines, the imidazole groups in his model are attached at the termini of flexible segments of the polymer, as is apparent particularly in Figure 5. It is readily possible for the imidazole residue to approach a bound substrate molecule, as would be required for its observed catalytic effect.[8]

Nmr spectroscopy thus has provided the necessary insight into the state of the apolar adduct chains of poly(ethylenimine) derivatives.[23] From this information and the bond angles and lengths of the ethylenimine residues of the polymer backbone, it has proved feasible to construct a model whose conformation and flexibility provide a basis for understanding the unusual binding and catalytic properties of this macromolecule.

References and Notes

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