Macromolecules 1981, *14*, 1634–1637

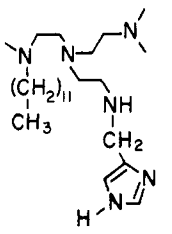
pH-Dependent Esterolysis by Dodecylated Poly(ethylenimine) Derivatives

Curtis S. Lege and James A. Deyrup*

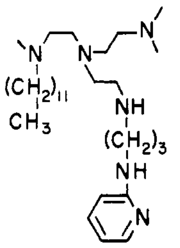
Center for Macromolecular Science, Department of Chemistry, University of Florida, Gainesville, Florida 32611. *Received May 12, 1981*

ABSTRACT: Imidazole, pyridine, and 2-aminopyridine have been attached to partially dodecylated poly(ethylenimine) to yield macromolecular catalysts PEI-D-Im, PEI-D-Pyr, and PEI-D-APyr, respectively. Esterolyses of *p*-nitrophenyl acetate (PNPA) by these catalysts were studied as a function of pH and compared with the previously described esterolyses by the primary amino groups of PEI-D-NH_2. Similar pH dependencies were observed for all four polymers and we conclude that electrostatic effects on nucleophilicity play dominant roles in all our observed pH dependencies. The similar behavior of PEI-D-Pyr and PEI-D-APyr precludes bifunctional catalysis and makes such effects unlikely for PEI-D-Im. Comparisons are made between the above systems and other published accounts of esterolyses by polymeric heterocycles.

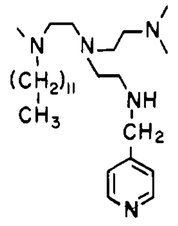
In the previous paper we examined[1] the aminolysis of esters by the amino groups of partially dodecylated poly(ethylenimine) (PEI-D). In this system, pH–rate dependence was entirely accounted for by consideration of both α (fraction of unprotonated nitrogens) and the pH-dependent nucleophilicity of the polymer. In this paper we consider the significance of the pH-dependent nucleophilic behavior of various heterocycles attached to PEI-D. Our selection of heterocycles was based, in part, on an earlier suggestion that cooperative effects of the type shown in Scheme I might be important in esterolyses mediated by certain imidazole-substituted polymers.[2] With this suggestion in mind, imidazole, 2-aminopyridine (which might similarly profit from deprotonation in the transition state), and pyridine (which could not receive such assistance) derivatives of PEI-D were prepared and their esterolyses studied.



PEI-D-Im



PEI-D-APyr



PEI-D-Pyr

Experimental Section

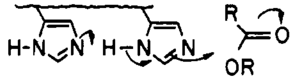
The general synthetic, analytical, and kinetic procedures of the preceding paper were used except as noted.[1] The same PEI-D sample of that paper was utilized in the preparation of the heterocyclic polymers described below.[1] The fraction (Z) of nitrogen atoms attached to the heterocyclic substituents was calculated by careful integration of NMR spectra, eq 1, and the mole unit weight was calculated by eq 2, where X is the number of carbons and Y is the number of nitrogens in the heterocyclic unit.

$$Z = \frac{(\mathrm{C/N})(14.01/12.01) - 2 - 12(0.113)}{X - (\mathrm{C/N})(14.01/12.01)Y} \quad (1)$$

$$\text{mole unit weight} = \frac{(1 + ZY)14.01}{\%\ \mathrm{N} \times 0.01} \quad (2)$$

Dodecyl-4-pyridinylmethyl-poly(ethylenimine) Hydrochloride (PEI-D-Pyr-HCl). Freshly distilled 4-pyridinecarboxaldehyde (bp 191–192 °C under N_2, 0.96 g, 0.0090 mol) was dissolved in 25 mL of absolute ethanol contained in a flask, and PEI-D (25 mL, 0.030 mol) was added to the flask. The cloudy suspension was stirred for 2 h under N_2. A solution of $NaBH_4$ in 50 mL of ethanol (0.13 g, 0.0022 mol) was added to the flask at 0 °C, and the mixture was stirred for 2 h. Four milliliters of concentrated HCl was added to form the polymer salt, which was then isolated by centrifugation. The precipitated polymer salt was washed twice with absolute ethanol. The polymer salt was dialyzed aginst 500 mL of absolute ethanol twice. The ethanolic dialysate was passed through a Sephadex LH-20 column. The salt was reprecipitated from the eluant by addition of HCl. The salt was again isolated by centrifugation and washed twice with absolute ethanol. The polymer salt was dried to give a white powder (1.12 g, 0.00966 mol, 32%). Anal.: C, 45.66; H, 8.32; N, 14.52; Cl, 24.57. Mole unit weight = 115 ± 5; Z = 17 ± 4 (anal.); Z = 12 ± 2 (NMR).

Scheme I



Dodecyl-[3-(2-pyridinylamino)propyl]-poly(ethylenimine) Hydrochloride (PEI-D-APyr-HCl). Ten milliliters of an absolute ethanol solution of *N*-(2-pyridyl)-3-aminopropionaldehyde hydrochloride (0.65 g, 0.0031 mol)[3] was prepared in a 125-mL Erlenmeyer flask with gentle heating. A stir bar and PEI-D (10 mL, 0.012 mol) were added to the flask, and the contents were stirred for 1 h under N_2. Ten milliliters of an absolute ethanol solution of $NaBH_4$ (0.092 g, 0.0024 mol) was added to the reaction mixture. After 1 h of stirring, the reaction mixture was transferred to a tube. The polymer salt was precipitated by addition of 1 mL of concentrated hydrochloric acid, centrifuged, and washed twice with absolute ethanol. The polymer salt was first dialyzed against a stream of deionized water for 24 h and then dialyzed against 500 mL of absolute ethanol overnight. The dialysate was passed through a Sephadex LH-20 column. The polymer salt was reprecipitated by the addition of 1 mL of concentrated hydrochloric acid. The polymer salt was dried, producing an off-white solid (0.35 g, 0.0023 mol, 19%). Anal.: C, 45.66; H, 8.32; N, 14.52; Cl, 24.57. Mole unit weight = 190 ± 50; Z = 46 ± 25 (anal.); Z = 25 ± 5 (NMR).

Dodecyl-4(5)-imidazolylmethyl-poly(ethylenimine) Hydrochloride (PEI-D-Im-HCl). To a solution of PEI-D (25 mL, 0.030 mol) in a sealable tube were added 4(5)-(chloromethyl)imidazole hydrochloride[4] (1.59 g, 0.10 mol), triethylamine (2.5 g, 0.025 mol), and a stir bar. The tube was sealed and maintained at 56 °C in an oil bath for 36 h. After cooling, the tube was opened and the contents were transferred to two test tubes. One milliliter of concentrated hydrochloric acid was added to each tube, forming a heavy precipitate. The tubes were centrifuged, and the supernatant was decanted. The precipitates were washed with absolute ethanol, the tubes were centrifuged, and the supernatant was decanted. The precipitate was dissolved in 20 mL of deionized water and dialyzed against a stream of deionized water for 72 h. The polymer was then dialyzed with 500 mL of absolute ethanol three times. The polymer solution was removed from the dialysis bag and passed through a Sephadex LH-20 column. The salt was reprecipitated with 4 mL of concentrated hydrochloric acid. The

0024-9297/81/2214-1634$01.25/0

salt was dried, producing an off-white solid (1.75 g, 0.0143 mol, 48%). Anal: C, 44.99; H, 7.85; N, 18.15; Cl, 25.29. Mole unit weight = 116; $Z = 26 \pm 4$ (anal.); $Z = 26 \pm 3$ (NMR).

Dodecyl-4(5)-imidazolylmethylisopropyl-poly(ethylenimine) Hydrochloride (PEI-D-Im-Ip-HCl). PEI-D-Im-HCl (0.0300 g) was dissolved in 30 mL of water. This solution was treated with solid $NaBH_4$ to bring the pH up to approximately 7. After freeze-drying, the polymer was suspended in 50 mL of absolute ethanol containing 1 g of acetone by the dropwise addition of 6 N hydrochloric acid and allowed to stir for 12 h to complete hydrolysis of the residual $NaBH_4$. The solution was dialyzed for 24 h. The polymer solution was centrifuged and filtered. The filtrate was freeze-dried, producing a white solid (0.281 g, 94%).

Dodecyl-4(5)-imidazolylmethyl-diisopropyl-poly(ethylenimine) Hydrochloride (PEI-D-Im-Ip_2-HCl). PEI-D-Im-HCl (0.098 g) was dissolved in 10 mL of water. This solution was heated with solid $NaBH_4$ to bring the pH up to approximately 7. After freeze-drying, the polymer was stirred in 20 mL of absolute ethanol containing 1 g of acetone for 1 h. The polymer was suspended by dropwise addition of 6 N hydrochloric acid, and 5 mL of absolute ethanol containing 1 g of acetone was added. After 1 h $NaBH_4$ (0.4 g, 0.01 mol) was added in 10 mL of absolute ethanol followed by suspension of the polymer salt with 6 N hydrochloric acid 1 h later. The reaction mixture was stirred under a stream of N_2 overnight. The polymer was dialyzed against a stream of deionized water for 24 h followed by 0.1 N hydrochloric acid for 3 h. The polymer solution was centrifuged, filtered, and freeze-dried, producing a white solid (0.062 g, 63%).

Relative Concentrations of Imidazole-Containing Polymer Solutions. The relative concentrations of stock solutions of the three imidazole-containing polymers, PEI-D-Im-HCl, PEI-D-Im-Ip-HCl, and PEI-D-Im-Ip_2-HCl, used for kinetics were determined spectrophotometrically. A series of seven solutions was prepared from the PEI-D-Im-HCl stock solution in 1.0 M hydrochloric acid. The absorbance of these solutions, ranging in concentration from 2.24×10^{-5} to 28.0×10^{-5} M in imidazole units, was measured at 210 nm and 25.0 ± 0.3 °C. A Beer's law plot was constructed from these data. The least-squares line passed through 0 (within experimental error, $r = 0.99998$) and had a slope (extinction coefficient) of 6.79×10^3 M^{-1}. Solutions (two each) of the isopropylated imidazole-containing polymers were prepared from the respective stock solutions in the same way (ca. 10^{-5} M) and their absorbances measured. The concentrations of the stock solutions were calculated from the extinction coefficient of the PEI-D-Im-HCl system. The concentrations of PEI-D-Im-Ip-HCl and PEI-D-Im-Ip_2-HCl solutions then were determined relative to PEI-D-Im-HCl.

Pyridine Ionization in PEI-D-Pyr-HCl. The pyridine in PEI-D-Pyr-HCl exhibits a pH-dependent absorbance at 259 nm. In 0.1 N hydrochloric acid solution the extinction coefficient based on two measurements was 5800 ± 400. In 0.1 M Tris buffer solution at pHs 6.71, 7.28, and 7.75 the extinction coefficients were found to be 3020, 3030, and 2970, respectively. These values indicated that the state of ionization of pyridine is not changing over pH 6.71 under these conditions.

Results and Discussion

The polymer systems were prepared from the previously described PEI-D and the appropriate derivatized heterocycle. PEI-D-Im-HCl was prepared by alkylation of PEI-D with 4(5)-(chloromethyl)imidazole.[5] PEI-D-Pyr-HCl and PEI-D-APyr-HCl were prepared by reductive amination of PEI-D using, respectively, 4-pyridinecarboxaldehyde and *N*-(2-pyridyl)-3-aminopropionaldehyde with $NaBH_4$. The fraction of the polymer derivatized was determined spectrally by NMR and by the C/N ratio from elemental analysis.

The second-order rate constants were determined as described in the previous paper and plotted vs. 10–14 values between pH 7 and 9. These plots are depicted in Figure 1. Also shown in Figure 1, for purposes of comparison, is the previously obtained plot for PEI-D-HCl.[1] It is apparent that the reaction rates of PEI-D-HCl are significantly higher than those of the heterocyclic systems.

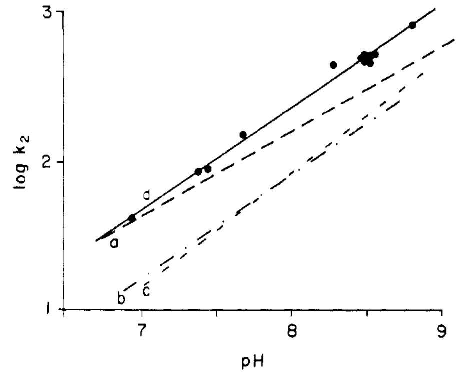


Figure 1. Esterolysis of PNPA by PEI-D-NH_2-HCl compared to esterolysis of PEI-bound heterocyclic systems: (a) PEI-D-Im-HCl (slope = 0.56); (b) PEI-D-Pyr-HCl (slope = 0.74); (c) PEI-D-APyr-HCl (slope = 0.69); (d) PEI-D-HCl (slope = 0.74).

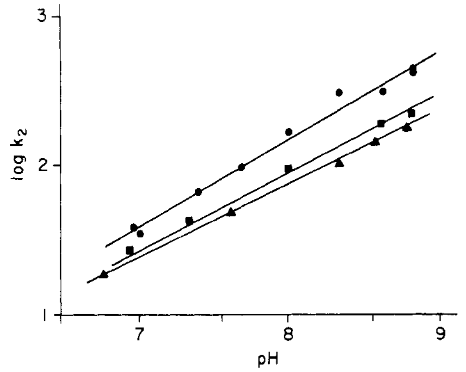


Figure 2. Effects of repetitive isopropylation of PEI-D-Im-HCl on PNPA esterolysis reactivity: (●) PEI-D-Im-HCl; (■) PEI-D-Im-Ip-HCl; (▲) PEI-D-Im-Ip_2-HCl.

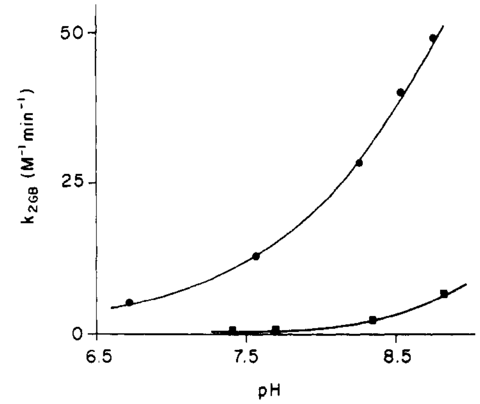


Figure 3. Comparison of PNPA esterolysis rates for (●) PEI-D-Im-Ip_2-HCl and (■) PEI-D-Ip-HCl.

For this reason possible contributions to k_2 by residual primary amines must be considered. Preliminary results suggested that the trinitrobenzenesulfonate reagent might not be a reliable probe for primary amines in the presence of heterocyclic substituents. For this reason we subjected one of the polymers, PEI-D-Im-HCl, to reductive isopropylation via acetone and $NaBH_4$. The initial product, PEI-D-Im-Ip-HCl, was further isopropylated to give PEI-D-Im-Ip_2-HCl. In this manner we expected to remove all residual primary amino groups. Figure 2 indicates the consequence of these isopropylations on the pH–rate profile. Comparison of PEI-D-Im-Ip_2-HCl with PEI-D-Ip-HCl (Figure 3) demonstrates that the rate of the former is significantly greater than the general-base-catalyzed reaction of the polymer backbone with PNPA. It follows, therefore, that the kinetic data on PEI-D-Im-Ip_2-HCl (as

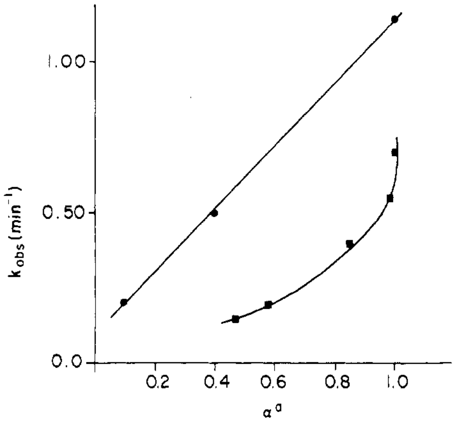


Figure 4. Plot of k_{obsd} against α for the esterolysis of 2,4-dinitrophenyl acetate by (■) poly(4-vinylpyridine) and (●) 4-methylpyridine. Values of k_{obsd} and α determined at 36.8 °C in 50% aqueous ethanol.[8]

well as the other heterocyclic-substituted polymers) represent nucleophilic attack by the heterocycle on PNPA.

The state of ionization of the imidazole in PEI-D-Im-Ip_2-HCl cannot be determined directly by spectrophotometric methods because the amine backbone interferes with the imidazole absorbance. The PEI-D-Pyr-HCl system, however, does not suffer such interference, and the pendent pyridine was found to be completely nonprotonated in the pH range studied. Therefore it is reasonable to assume that the imidazoles in PEI-D-Im-HCl are un-ionized throughout the pH range studied.

Since the imidazole is virtually nonprotonated in the region of interest, its pK_a is undetermined in this region. Without pK_a data a Brønsted plot cannot be constructed. It was shown in the previous paper that the nucleophilicity, and hence the reactivity, of the PEI-D-NH_2-HCl system was related to the pK_a or basicity of the polymer. By analogy one would then expect that the reactivity of the heterocycles would increase with pH as is observed in Figure 2.

The pH dependence of PEI-D-Pyr-HCl is particularly significant because kinetic assistance (as in Scheme I) via deprotonation is not possible. We conclude from the data of this and the previous paper that the amount of charge on these polymers does have a major impact on the nucleophilicity of the substituents whether or not the polymer substituents are significantly protonated in the pH region of interest. All the pH effects observed by us must reflect this phenomenon.

It is possible that cooperative catalysis is also occurring with PEI-D-Im-HCl and/or PEI-D-APyr-HCl. Perhaps a detailed analysis of the pH dependencies (slopes) would support such a contention. It should be noted, however, that the ability of substituents to take part in cooperative catalysis (i.e., accept positive charge) should be affected by the degree of backbone protonation. Unambiguous separation of such effects would be very difficult. We suspect that pH dependencies alone are unlikely to be useful in detecting bifunctional catalysis in synthetic macromolecules of this type.[7]

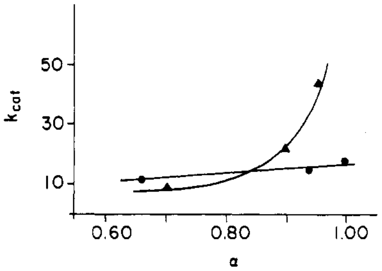


Figure 5. Solvolysis of PNPA catalyzed by poly[4(5)-vinylimidazole] (▲) and imidazole (●). 28.5 (v/v) EtOH-H_2O, u = 0.02, 30 °C.[2]

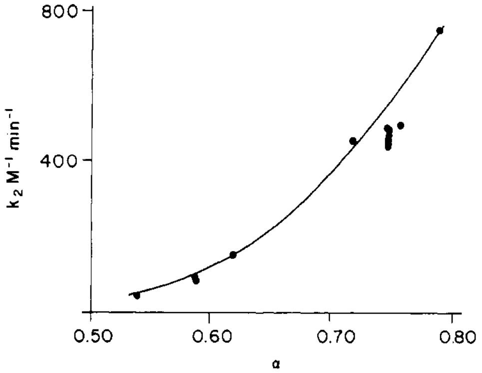


Figure 6. Plot of k_2 against α for the esterolysis of PNPA by PEI-D-NH_2-HCl.

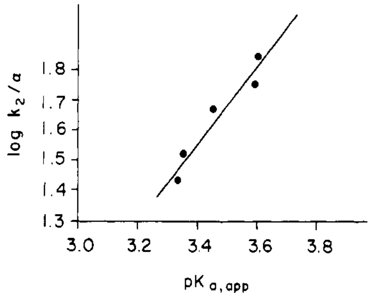


Figure 7. Brønsted plot for the esterolysis of 2,4-dinitrophenyl acetate by poly(4-vinylpyridine). Values of pK_a and k_2 determined at 36.8 °C in 50% aqueous ethanol.[8]

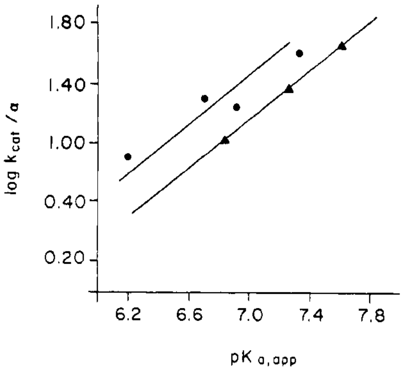


Figure 8. Brønsted plot for the esterolysis of PNPA by (▲) poly[4(5)-vinylimidazole][2] and (●) imidazoles. Values of k_{cat} and $pK_{a,app}$ determined at 30 °C in 28.5% ethanol.[10] Imidazole (●) data from data in ref 10.

With this in mind it is interesting to examine some previously published pH-dependent ratios exhibited by functionalized polymers. Letsinger and Saveride[9] studied poly(4-vinylpyridine)-catalyzed 2,4-dinitrophenyl acetate (DNPA) hydrolysis. They found that although 4-methylpyridine produced the expected linear rate vs. α plot, the poly(4-vinylpyridine) exhibited a curved plot (Figure 4). They qualitatively attributed the curvature in the polymer reaction to decreased nucleophilicity with increasing protonation (decreasing α). Overberger et al.[2] found very similar results in poly[4(5)-vinylimidazole] vs. imidazole catalysis of hydrolysis of PNPA (Figure 5). They attributed the curvature to possible bifunctional mechanisms. The rate vs. α plot for the reaction of PEI-D-NH_2-HCl with PNPA shows a similar curvature

(Figure 6). Since the Brønsted relationship was able to quantitatively account for the PEI-D-NH_2-HCl pH dependence of PNPA esterolysis, it is reasonable to apply the relationship to the above reactions of poly(4-vinylpyridine) (Figure 7) and poly[4(5)-vinylimidazole] (Figure 8). As in the case of the PEI-D-NH_2-HCl reaction with PNPA[1] the Brønsted plots are linear. Note that the poly[4(5)-vinylimidazole] Brønsted slope, 0.8, is precisely that expected from the portion of the small-molecule imidazole plot also shown in Figure 6. The cooperative effect proposed for the polyimidazole esterolyses thus seems unwarranted.[2,12]

Acknowledgment. We are grateful to Dr. John Zoltewicz for helpful discussions. Support for this work was provided by the Division of Sponsored Research, University of Florida.

References and Notes

(1) Lege, C. S.; Deyrup, J. A. *Macromolecules*, preceding paper in this issue.
(2) Overberger, C. G.; St. Piere, T.; Vorchheimer, N.; Lee, J.; Yaroslavsky, S. *J. Am. Chem. Soc.* **1965**, *87*, 296.
(3) Reynaud, P.; Tupin, T.; Delaby, R. *Bull. Soc. Chim. Fr.* **1957**, 718–24.
(4) Turner, R. A.; Huebney, C. F.; Scholz, C. H. *J. Am. Chem. Soc.* **1949**, *71*, 2810.
(5) A similar PEI derivative was prepared by Klotz and co-workers.[6]
(6) Klotz, I. M.; Royer, G. P.; Searper, I. S. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 263.
(7) Bifunctional catalysis by a synthetic macromolecule has been demonstrated in a convincing manner by means of other kinetic analytical approaches.[8]
(8) Kunitake, T.; Okahata, Y. *J. Am. Chem. Soc.* **1976**, *98*, 7793.
(9) Letsinger, R. L.; Saveride, T. J. *J. Am. Chem. Soc.* **1962**, *84*, 3122.
(10) Overberger, C. G.; Morimoto, M. J. *J. Am. Chem. Soc.* **1971**, *93*, 3222.
(11) Bruice, T. C.; Lapinski, R. *J. Am. Chem. Soc.* **1958**, *80*, 2265.
(12) Other possible explanations for the pH dependence of poly[4-(5)-vinylimidazole] have been offered.[13] This interpretation, based on microenvironmental changes caused by alterations in polymer conformations with pH, also appears unnecessary.
(13) Kunitake, T.; Okahata, Y. In *Adv. Polym. Sci.* **1976**, *20*, 159–221.

Polymer Solutions near an Interface. 1. Adsorption and Depletion Layers

P. G. de Gennes

Collège de France, 75231 Paris Cedex 05, France. *Received March 9, 1981*

ABSTRACT: We construct first the equilibrium concentration profiles for a polymer solution near a solid wall (or near the free surface). The wall is characterized by a certain "free energy of sticking", γ_1, which is negative for adsorption and positive for a repulsive surface. We are concerned with the case where γ_1 (per monomer) is small, but where the energy *per chain* is large. (1) For the attractive case (with a good solvent), we find a remarkable, *self-similar* form for the profile which is essentially independent of the bulk concentration. Most monomers are confined in a region of thickness $D \sim |\gamma_1|^{-3/2}$. But the "equivalent hydrodynamic thickness", e_H, is controlled by the longest loops and should scale like the coil size in solution, R_F. (2) We also extend these considerations to *metastable adsorption*. For instance, starting from the above situation, we assume that the polymer in solution is washed out, leaving an adsorption layer; then the solvent is cooled down to a Θ point: the adsorption layer shrinks significantly. In particular, we predict that all large loops disappear. All results now depend on the sample history: if the layer would have been prepared by contact between a Θ solvent and the wall, we would expect e_H comparable to the Θ solvent coil size. (3) For the repulsive case, the exponents describing the *depletion layer* had been constructed earlier through a tentative argument based on the osmotic pressure near the wall. We rederive these exponents here by a more direct scaling method. For all these cases, we construct the scaling form of the interfacial tension and check the associated Gibbs identities.

I. Introduction

1. Two Regimes. When a solution of neutral, flexible polymer chains is put into contact with a solid wall, two regimes can occur: (a) In many cases the polymer sticks to the wall and cannot be desorbed by washing with the pure solvent.[1] (b) In some cases (in particular with grafted surfaces), the polymer is repelled by the wall, and a depletion layer is expected to build up.[2] Similar effects can take place near the free surface of the solution. Roughly, when the surface tension of the pure polymer melt, γ_p, is lower than the tension of the pure solvent, γ_0, we expect adsorption: this occurs for instance with poly(methylsiloxane) in toluene. On the other hand, if $\gamma_p > \gamma_0$, we expect a depletion layer: this appears to be found with polystyrene in toluene. Detailed measurements on the surface tension of these two systems have been carried out recently.[3]

A copious amount of theoretical work has been carried out on these interfacial systems. The early literature on single-chain adsorption in Θ solvents is reviewed in ref 4. Here, however, we shall be concerned mainly with *good* solvents, where theoretical predictions are more scarce. For simplicity, we shall treat mainly the athermal case, having in mind a Flory–Huggins lattice[5] on which the polymer chains are inscribed: the lattice is cubic with a lattice parameter a and a volume per monomer a^3. Each site can be occupied at most by one monomer; the average occupation or volume fraction is called ϕ. The value of ϕ in the bulk we call ϕ_b.

The mean field theory of the profile $\phi(z)$ (at a distance z from the wall) has been constructed by Jones and Richmond in the attractive case[6] and by Joanny and Leibler in the repulsive case.[2] These mean field theories are analyzed in ref 8 and will not be covered here in more detail because the deviations from mean field are often serious.

Beyond mean field, the *single*-chain adsorption has been clarified by a scaling argument.[7,8] But an early attempt by the present author to discuss the *many*-chain adsorption problem[7a] was a failure: because of a mistake in sign

0024-9297/81/2214-1637$01.25/0