Thermodynamic and ^{13}C n.m.r. data on the protonation of polymeric bases whose repeating units behave independently towards protonation

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The protonation of several poly(amido-amines) and their non-macromolecular model compounds has been studied in aqueous solution by ^{13}C n.m.r., potentiometric, and calorimetric techniques. Sharp basicity constants and thermodynamic functions have been obtained with poly(amido-amines), thus confirming the peculiar behaviour of this family of polymeric bases. The behaviour of the models is similar to that of the corresponding polymers. However, they are constantly slightly more basic. This difference is mainly due to the entropy term.

INTRODUCTION

In a previous paper, we have found that some polymers of poly(amido-amine) structure behave unusually towards protonation in aqueous solution[1]. In particular, we have been able to determine 'real' basicity constants, while as a rule only 'apparent' constants can be determined in the case of polymeric bases[2]. This means that in poly(amido-amines), the basicities of the aminic nitrogens of a given unit do not depend on the degree of protonation of the whole macro-molecule. Moreover, by studying the model non-macromolecular compound, we have found that its proto-nation behaviour in aqueous solution is very similar to that of the corresponding polymer[1]. However the basicity con-stants of the model are slightly higher, in spite of the fact that its structure is almost identical to that of the repeating unit of the polymer.

In this paper, we report some results on the protonation of several poly(amido-amines), and of their non-macromolecular models in aqueous solution.

The protonation of the above compounds has been studied by ^{13}C n.m.r., potentiometric and calorimetric tech-niques. The last technique has been used because it is well known that, in polyelectrolytes, the enthalpies of protona-tion generally depend on the overall degree of ionization[2], exactly as the basicity constants do.

EXPERIMENTAL

Materials

Model I

N-acryloylmorpholine (28.2 g) prepared by reacting acryloylchloride with morpholine, was added to a 1 M aqueous solution of methylamine (100 ml).

The reaction mixture was left at room temperature for three days, then extracted several times with chloroform. The chloroform extracts were dried (Na$_2$SO$_4$), and evapo-rated to dryness *in vacuo*. The product crystallized by rubbing under n-hexane, and was recrystallized from a 2:3 (by volume) benzene:n-hexane mixture, m.p. 75°C, with 90% yield.

Analysis found C 57.2%, H 8.2%, and N 13.4%, com-pared with calculations for C$_{15}$H$_{27}$N$_3$O$_4$ which gave C 57.5%; H 8.7% and N 13.3%.

Model III

14.1 g *N*-acryloylmorpholine was added to a solution of 4.1 g anhydrous piperazine in 25 ml methanol. The reaction mixture was left at room temperature for two days. The product precipitated out in a crystalline form. It was col-

Table 1 Experimental details of the potentiometric measurements at 25°C in 0.1 M NaCl

	log K	Curve	Initial conc. (M × 10³)	Range −log[H⁺]	Number of points
Model I	8.066 (6)	1	1.600	9.3—2.4	35
		2	1.776	9.3—2.5	29
		3	2.194	9.5—2.7	37
Model II	7.124 (2)	1	1.585	7.8—2.7	54
	3.289 (8)	2	1.614	8.0—2.7	52
		3	1.455	8.5—2.7	58
Polymer III	7.01 (1)	1	1.624	8.7—2.7	45
	2.98 (3)	2	1.733	9.0—2.6	68
		3	1.246	9.0—2.7	60

lected by filtration, and recrystallized from a n-heptane: benzene 2:1 (by volume) mixture, m.p. 178°C.

Analysis found C 58.2%, H 8.9% and N 15.0%, compared with calculations for $C_{18}H_{32}N_4O_4$ which gave C 58.7%, H 8.8%, and N 15.2%.

The syntheses of the other compounds listed in *Table 3* had been described previously[1,3].

Reagents

0.1 M CO_2-free sodium hydrochloride solutions were prepared, stored and standardized as described elsewhere[4]. 0.1 M sodium chloride stock solutions were prepared from sodium chloride (Merck, suprapure grade) without further purification, and used as ionic medium for both potentiometric and calorimetric measurements.

Potentiometric measurements

Potentiometric measurements were performed according to a previously described procedure[1,5] using a Beckman Research potentiometer, an Ag/AgCl reference electrode, and a salt bridge containing a 0.1 M NaCl solution. The Miniquad 76A program used to calculate the basicity constants has been described elsewhere[6]. Basicity constants were calculated from data taken from three different titration curves for each compound (*Table 1*).

^{13}C n.m.r. spectra

The n.m.r. spectra were run at room temperature in 0.1 M solutions on a Brucker XH 90 spectrometer operating at 22.63 MHz. The spectral conditions were as previously reported[1].

Calorimetric measurements

The calorimetric measurements were carried out at 25°C, with an L.K.B. 10700-1 flow microcalorimeter using a mixed cell. The reagents were introduced into the calorimeter by means of two Mettler DV-10 high precision automatic burettes equipped with 50 cm cylinders. The flow rate of each burette was regulated by a resistance box. In order to measure the heats of protonation, solutions containing: (a) the hydrochloride of the compound together with a slight excess of hydrochloric acid, and (b) sodium hydroxide, were passed through the flow cell. The amount of the compound to be deprotonated was determined from the relative flow rates of the two burettes. The method of calculating the successive enthalpies of protonation from the microcalorimetric data has been previously described[7]. The heat of formation of water chosen[8,9] was −13.34 kcal mol⁻¹. Experimental details are reported (*Table 2*).

Table 2 Experimental details of microcalorimetric measurements at 25°C in 0.1 M NaCl

Reaction	V_H[a,b] μmol s⁻¹	V_L[a] μmol s⁻¹	R[c] μl s⁻¹	D[d] μcal s⁻¹
Polymer 1 + H⁺				
(i)	0.02443	0.02372	8.391	133.8
(ii)	−0.01719			
(i)	0.02516	0.02442	8.781	131.8
(ii)	−0.02014			
(i)	0.02606	0.02606	7.812	139.7
(ii)	−0.00403			
(i)	0.02773	0.02693	7.969	145.9
(ii)	−0.00314			
Polymer 2 + H⁺				
(i)	0.04659	0.02260	8.921	319.9
(ii)	0.00113			
(i)	0.04659	0.02260	8.779	307.9
(ii)	0.00257			
(i)	0.04652	0.02260	8.641	301.4
(ii)	0.00382			
(i)	0.04655	0.02260	8.516	294.7
(ii)	0.00515			
(i)	0.04652	0.2260	8.396	289.7
(ii)	0.00636			
(i)	0.04652	0.02256	8.181	276.7
(ii)	0.00848			
(i)	0.04653	0.02256	9.783	332.2
(ii)	−0.00773			
(i)	0.04659	0.02256	9.239	327.5
(ii)	−0.00209			
(i)	0.04659	0.02260	9.421	329.2
(ii)	−0.00393			
(i)	0.04659	0.02260	9.065	324.9
(ii)	−0.00033			
Polymer 3 + H⁺				
(i)	0.08997	0.04355	8.768	492.2
(ii)	0.03991			
(i)	0.08544	0.0422	8.726	498.5
(ii)	0.03433			
(i)	0.08290	0.04096	8.796	513.1
(ii)	0.02961			
(i)	0.07621	0.03765	8.805	532.8
(ii)	0.01908			
(i)	0.06882	0.03400	9.054	563.0
(ii)	0.00476			
(i)	0.06401	0.03162	9.029	575.6
(ii)	−0.01297			
(i)	0.06401	0.03162	8.799	512.4
(ii)	0.00015			
(i)	0.06252	0.03089	8.724	564.2
(ii)	−0.00131			
(i)	0.06547	0.03235	9.093	584.1
(ii)	−0.00090			
(i)	0.06543	0.03233	9.331	602.2
(ii)	−0.00365			
Model 1 + H⁺				
(i)	0.02714	0.02645	7.126	138.4
(ii)	−0.00373			
(i)	0.02885	0.02812	8.800	149.5
(ii)	−0.01621			
(i)	0.02795	0.02724	7.247	141.7
(ii)	−0.00292			
(i)	0.02885	0.02812	7.831	148.0
(ii)	−0.00202			
Model 2 + H⁺				
(i)	0.05622	0.02767	8.691	318.9
(ii)	0.00994			
(i)	0.05624	0.02768	9.792	366.9
(ii)	0.00257			
(i)	0.05286	0.02602	9.525	365.6
(ii)	−0.00080			
(i)	0.05292	0.02605	9.539	385.9
(ii)	−0.00082			

(continued)

Table 2 (continued)

Reaction	V_H [a,b] μmol s⁻¹	V_L [a] μmol s⁻¹	R [c] μl s⁻¹	D [d] μcal s⁻¹
(i)	0.05634	0.02774	9.631	361.8
(ii)	0.00436			
(i)	0.05625	0.02769	9.418	346.6
(ii)	0.00633			
(i)	0.05135	0.02528	9.404	355.4
(ii)	−0.00229			
(i)	0.05452	0.02684	9.653	368.1
(ii)	0.00089			
(i)	0.05624	0.02769	8.776	313.1
(ii)	0.01273			
(i)	0.05805	0.02857	9.098	315.2
(ii)	0.01454			

Model 3 + H⁺

Reaction	V_H	V_L	R	D
(i)	0.08949	0.04408	8.788	454.7
(ii)	0.04587			
(i)	0.06820	0.03359	8.959	543.1
(ii)	0.01234			
(i)	0.06339	0.03122	9.442	584.9
(ii)	0.00032			
(i)	0.06193	0.03051	9.355	571.9
(ii)	−0.00099			
(i)	0.06058	0.02984	9.288	559.3
(ii)	−0.00234			
(i)	0.05920	0.02916	9.218	550.3
(ii)	−0.00369			
(i)	0.06064	0.02987	7.351	428.6
(ii)	0.01712			
(i)	0.06064	0.02987	7.630	453.2
(ii)	0.01433			
(i)	0.06047	0.02979	7.475	441.9
(ii)	0.01564			

a total or analytical flow rates of the acid and compound
b the values refer to V_H before (i) and after (ii) mixing. The (ii) values were obtained by subtracting the analytical flow rate of OH⁻ from (i) values
c total flow rate
d heat flow corrected for dilution

RESULTS

^{13}C n.m.r. spectra

The ^{13}C n.m.r. spectrum of model I is similar to that of polymer I, in the pH range 1–10 (*Table 3*). The plot of the chemical shifts of the latter as a function of pH had been previously reported[1]. The same is true for polymer II and model II[1] (*Table 3*).

The plot of the chemical shifts of different resonances for polymer III as a function of pH is shown in *Figure 1*. It may be observed that plots of chemical shifts of carbon atoms (D,E), in β or γ positions in respect to the basic nitrogens, are similar to those of polymer II[1]. However, by considering the carbon atom (F) in α position, a slightly anomalous behaviour with respect to polymer II is observed in the pH range 7–9.

The plot of chemical shifts of different resonances for model III *versus* pH is given in *Figure 2*. It may be observed that this model behaves similarly to that of polymer III, as far as the carbon atoms in β or γ positions are concerned. However the carbon atom (F) in α position in respect to the aminic nitrogen, shows an anomalous behaviour in the pH range 6–8. In fact it is different either in respect to polymer III, or to both polymer II and model II[1]. This effect might be due to a conformational variation of the nitrogen doublet in respect to its immediate neighbours, as previously observed[12]. At very low values, the carbon atoms in the α position to the ethereal oxygen in the morpholine rings become non-equivalent. This is due to their *cis* and *trans* positions in respect to the carbonyl. The difference in their chemical shifts increases by decreasing pH, and reaches a maximum of about 4 Hz at pH 1. This effect is quite small, and is present only in model III.

Thermodynamic changes

The thermodynamic functions relative to the protonation of the poly(amido-amines) and their corresponding non-

Table 3   Thermodynamic functions of protonation in 0.1 M NaCl at 25°C

Compound	Structure[a]	Reaction	log K	−ΔG^{o} [c]	−ΔH^{o} [c]	ΔS^{o} [c]
Polymer I	[−CH₂−CH₂−CO−N◯N−CO−CH₂−CH₂−N−]ₓ, CH₃	L + H⁺	7.79 (2)[b]	10.62 (3)	8.26 (7)	7.9 (3)
Model I	O◯N−CO−CH₂−CH₂−N−CH₂−CH₂−CO−N◯O, CH₃	L + H⁺	8.066 (6)	11.00 (1)	8.41 (2)	8.7 (1)
Polymer II	[−CH₂−CH₂−CO−N◯N−CO−CH₂−CH₂−N−CH₂−CH₂−N−]ₓ, CH₃, CH₃	L + H⁺	8.09 (2)[b]	11.03 (3)	7.35 (12)	12.3 (5)
		LH⁺ + H⁺	4.54 (5)[b]	6.19 (7)	6.09 (11)	0.3 (6)
Model II	O◯N−CO−CH₂−CH₂−N−CH₂−CH₂−N−CH₂−CH₂−CO−N◯O, CH₃, CH₃	L + H⁺	8.248 (4)[b]	11.248 (5)	7.34 (18)	13.1 (6)
		LH⁺ + H⁺	4.80 (1)[b]	6.55 (1)	6.05 (15)	1.7 (5)
Polymer III	[−CH₂−CH₂−CO−N◯N−CO−CH₂−CH₂−N◯N−]ₓ	L + H⁺	7.01 (1)	9.56 (1)	5.71 (9)	12.9 (3)
		LH⁺ + H⁺	2.98 (3)	4.06 (5)	5.24 (9)	−3.9 (4)
Model III	O◯N−CO−CH₂−CH₂−N◯N−CH₂−CH₂−CO−N◯O	L + H⁺	7.124 (2)	9.710 (7)	5.50 (10)	14.1 (3)
		LH⁺ + H⁺	3.289 (8)	4.47 (1)	4.00 (10)	1.6 (4)

a for polymers, structure of the repeating unit
b ref 1
c values in parenthesis are the standard deviations on the last significant figure. ΔG^{o}, −ΔH^{o} are expressed in Kcal mol⁻¹; ΔS^{o} in cal mol⁻¹K⁻¹
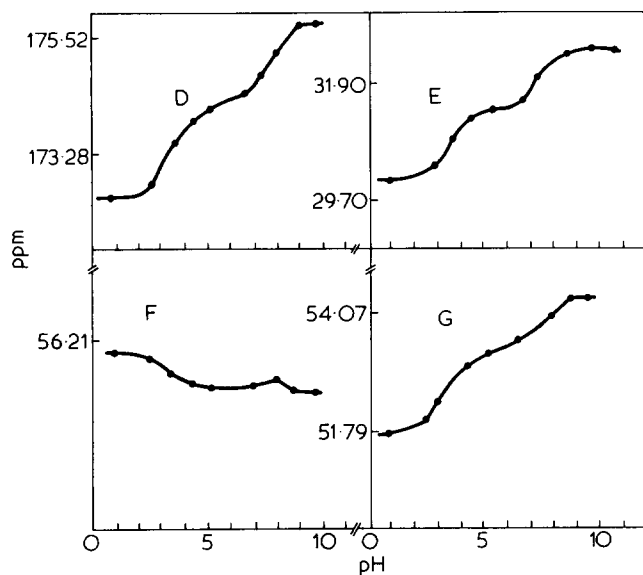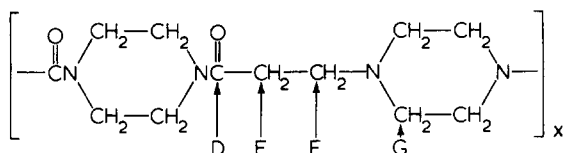
Figure 1 Polymer III ^{13}C n.m.r. shift variation in p.p.m. as a function of pH value

macromolecular models are reported in *Table 3*. As previously reported[1], for each protonation step the basicity constants of the polymers are slightly lower than those of the corresponding models. On the contrary the enthalpy values are quite similar, thus the higher ΔG^0s of the models are due to a more favourable entropy term. The enthalpies are similar to the values obtained for many tertiary mono- and diamines already studied[9]. This apparently means that the diacyl piperazine ring has no influence on the attack of the protons on the aminic nitrogens. This is also supported by ^{13}C n.m.r. spectra which show that the *cis/trans* ratio does not change as a function of pH[1].

For both polymers and models II and III, ΔH_2^0 is lower than ΔH_1^0. This trend, normally found in all the diamines studied until now[9], can be rationalized if we think that the second enthalpy change is affected by the electrostatic repulsion between the positive charges of the nitrogen protonated and the incoming second proton. It is noteworthy, as regards the entropies, that the successive steps in the protonation are accompanied by decreasing entropy change ΔS^0. This trend has been observed previously for other tertiary diamines[9]. It is well known that addition of a proton to a nitrogen atom leads to the liberation of water molecules[10]. The number of solvent molecules bound and oriented by the ammonium ion so formed is less than the number released by the H^+ ion and the amino group. The increase in the number of particles leads to an increase in the translational entropy which is reflected by the markedly positive value of the measured ΔS^o. As protons are added to the molecule, the overall charge of the ion increases, resulting in a much greater retention of oriented water molecules and thus a decreased value of ΔS^o.

By considering polymer III and its corresponding model, the ΔH_2^0 of the polymer is much higher than that of the model, its value being near to ΔH_1^0. This behaviour is anomalous, if compared with the values observed for N,N'-dimethyl piperazine[11], in which the difference $|\Delta H_1^0 - \Delta H_2^0|$ is ≈ 1.8 Kcal mole^{-1}.

CONCLUSIONS

The above results confirm that poly(amido-amines) represent a new class of polyelectrolytes whose behaviour in aqueous solution is quite peculiar: their repeating units behave independently from each other towards protonation. This is confirmed either by considering their n.m.r. and thermodynamic data as such, or by comparing them with the data obtained from the corresponding non-macromolecular models.

The thermodynamic functions ΔG^0, ΔH^0, and ΔS^0 relative to the protonation of poly(amido-amines) are similar to those of their models. The latter compounds are constantly more basic on each step of protonation. In this respect, however, the differences between the polymers and the corresponding models are small, and are due almost entirely to entropy effects.

A less conspicuous retention of oriented water molecules due to the vastly superior hydrophobic chain length is aspected for the polymers. Thus, the attack of the proton provokes a smaller desolvation process and consequently a lower ΔS^0.

In this case of model III the conformational variations which take place during protonation apparently have no influence upon the thermodynamic parameters ΔH^0 and ΔS^0. The values we obtained are in fact of the same order as those reported for N,N' disubstituted piperazines[11].

Polymer III shows a $|\Delta H_2^0|$ value considerably higher than that of the corresponding model. Consequently, with the protonation constants being quite similar, the polymer shows a much lower ΔS_2^0. Since we found by ^{13}C n.m.r. that below pH 6 the variations of chemical shifts as a function of pH are similar for both polymer and model, a possible explanation involves a long range conformational effect which might take place during the protonation of the former.
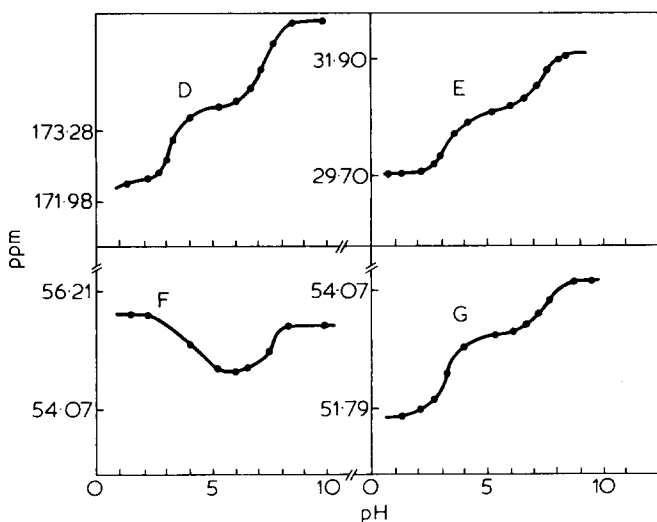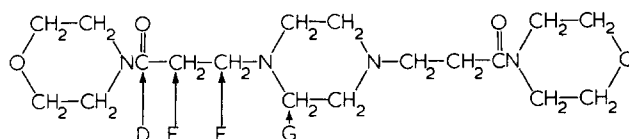

Figure 2 Model III ^{13}C n.m.r. shift variation in p.p.m. as a function of pH value

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