Protonation studies of multifunctional polymers with a poly(amido-amine) structure

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The protonation of some poly(amide-amines) has been studied in aqueous solution by both ^{13}C n.m.r. and potentiometric methods. In particular ^{13}C n.m.r. chemical shifts were plotted as a function of pH. In all cases the curves show points of inflexion at pH values which can be predicted from potentiometric pK values. 1,4-Diacyl piperazine groups are present in the main chain of the poly(amino-amine). We found that 50% *cis* and 50% *trans* isomers with respect to the carbonyls were present in aqueous solution; the *cis/trans* ratio is independent of pH. Only 'apparent' constants were found in the previously described polymeric acids and bases; however, 'real' basicity constants could be determined for the poly(amido-amines) studied in the present work. Moreover, the protonated monomeric unit site could be determined exactly by both potentiometric and ^{13}C n.m.r. methods.

INTRODUCTION

A new class of multifunctional polymers, poly(amido-amines)[1] show interesting properties as complexing agents for natural muco-polysaccharides[2,3]. They are also capable of forming stable complexes with several heavy metal ions[4].

In order to obtain a better knowledge of the structure of these complexes, as well as of the mechanism of complex formation, it is necessary to study the behaviour of poly(amido-amines) towards protonation. We have undertaken a study in aqueous solution using potentiometric and n.m.r. methods.

EXPERIMENTAL

Materials

Poly(amido-amines) I and II (*Table 1*) were prepared as described[1].

Poly(amido-amine) III was prepared by dissolving 1.45 g of *N,N',N''*-trimethyl-diethylenetriamine[5] in 10 ml of methanol, adding 1.94 g of bis-acryloylpiperazine[6], and allowing the reaction mixture to stand at room temperature for 1 week, with occasional stirring. The reaction mixture was then poured into an excess of ether. The precipitated polymer was purified by dissolving in chloroform and reprecipitating with ether, yield 2.93 g (86%). Poly(amido-amine) III is a sticky, non-crystalline material. It is soluble in chloroform, alcohols, acetone, and water, but insoluble in ether and aliphatic hydrocarbons. The sample used had $[\eta]$ = 0.27 dl/g (in chloroform at 30°C). Analysis: found, C = 60.02%, H = 9.96%, N = 20.38%; $(C_{17}H_{33}N_5O_2)_x$ requires C = 60.15%, H = 9.80%, N = 20.60%.

Model IV has been prepared in 85% yield by allowing *N,N'*-dimethylene diamine to react with *N*-acryloyl morpholine in a 2:1 molar ratio in methanol solution. After standing for 2 days at room temperature, the reaction mixture was evaporated to dryness *in vacuo*. The residue was crystallized by rubbing under n-heptane, and then recrystallized from a 4/1 ether/benzene mixture, m.p. 81°C (hot stage, uncorrected). Analysis: found C = 58.3%, H = 9.17%, N = 15.12%; $C_{18}H_{34}N_4O_4$ requires C = 58.35%, H = 9.25%, N = 15.12%.

Diacetylpiperazine was prepared according to ref 7.

Methods

Potentiometric titrations were performed according to a previously described procedure[8], using a Beckman Research potentiometer, an Ag/AgCl reference electrode, a glass electrode, and a salt bridge containing 0.1 M NaCl solution.

For each determination the cell was filled with ~100 ml of 0.1 M NaCl solution, containing a known amount of amine. The solution was titrated with 0.1 M hydrochloric acid solution, added through a Metrohm Dosimat E 415 automatic piston burette.

The Miniquad 76A program used to calculate the equilibrium constants, has been described previously[9]. Basicity constants were calculated from data taken from at least two different titration curves for each compound (*Table 1*).

^{13}C n.m.r. spectra were run on 0.1 M solutions at room temperature on a Bruker XG90 spectrometer operating at 22.63 MHz. The spectral conditions were as follows: pulse width, 4 μsec; points, 16K; width, 6000 Hz; acquisition time, 1.360 sec.

All chemical shifts were determined with an external reference and converted to the TSP (trimethylsilylpropionate);

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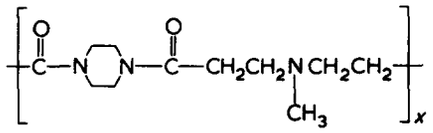
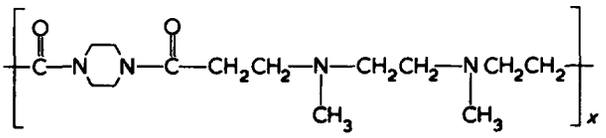
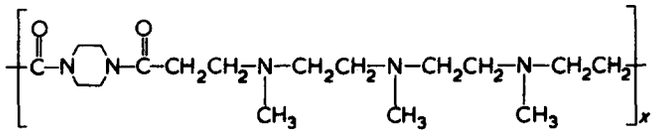
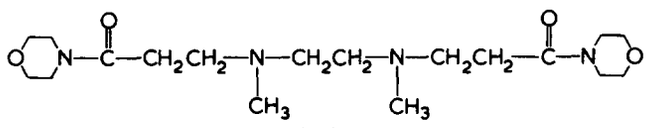
Table 1 Experimental details of the potentiometric measurements

Compound	Curve	Initial conc. ($M \times 10^3$)	Range $-\log[H]^+$	Number of points
I  (I)	1	1.858	9.2–2.5	41
	2	1.760	9.2–2.5	46
	3	2.033	9.2–2.4	50
II  (II)	1	1.828	9.0–2.9	48
	2	2.095	8.6–2.8	50
III  (III)	1	0.0507	9.5–3.0	49
	2	0.0314	9.6–2.9	39
IV  (IV)	1	1.093	9.3–2.8	40
	2	1.072	9.3–2.8	48
	3	2.211	9.1–2.6	48

TSP (at low pH values) was corrected due to its own pH dependence[10]; no shift of the locking frequency with respect to the external reference was found.

RESULTS

Potentiometric titration

The basicity constants of the poly(amido-amines), and of the model compound, are reported in *Table 2*. The number of the basicity constants is equal to the number of aliphatic nitrogen atoms present in the monomeric unit. Attempts to increase the number of basicity constants were rejected by the computer.

A gradual decrease of log K with stepwise protonation is observed for all polymers with two or more basic groups in their monomeric unit; the same is true for the model compound. This behaviour parallels that of all aliphatic non-macromolecular polyamines[11].

The basicity constants of *Table 2* refer to the protonation of the amine nitrogens. The protonation of the amidic nitrogens occurs in the very low pH region, which was not reached in our titrations.

For purposes of comparison, the corresponding protonation constants of some[12,8,13] aliphatic amines are also reported in *Table 2*. It may be noted that in each stage of neutralization the K values of our compounds (I to IV) are decidedly lower.

Among the first protonating constants, the lowest one is that of polymer I, containing only one tertiary amino group in its monomeric unit. On the other hand, the first protonation constants of II and III are equal. It may be observed that in the monomeric unit of both II and III two equivalent basic sites are present. If log K_1 values of these polymers are corrected for the statistical effect (i.e. they are diminished by log 2), they become essentially identical to the log K value of polymer I.

In the second stage of protonation the most favourable conformation occurs when the protons are as far apart as possible[14]. As a consequence, the pK_2 of III is greater than that of II. This is due to the greater distance between the protonated groups, and also to the shielding effect of the intermediate N–CH_3 group. As expected, the third protonation constant of polymer III is the lowest of all constants. This is mainly due to electrostatic repulsion, since the third proton must approach a nitrogen located between two already protonated nitrogen atoms. The third protonation constant of III is similar to that of 2,5,8-trimethyl-2,5,8-triazanonane (*Table 2*).

The protonation constants of model IV are similar, but slightly higher than those of the corresponding polymer II. A calorimetric study is being undertaken to ascertain if the lower basicity of the polymer is due to an enthalpic or entropic effect.

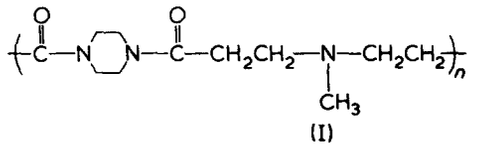
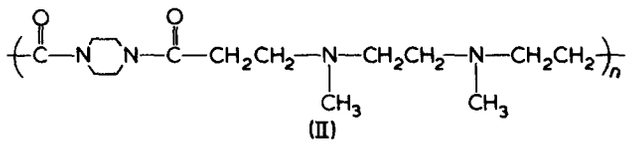
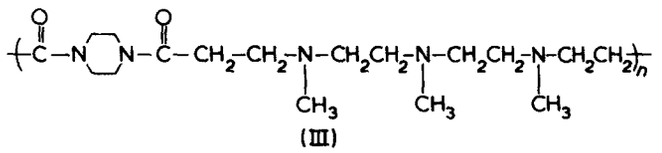
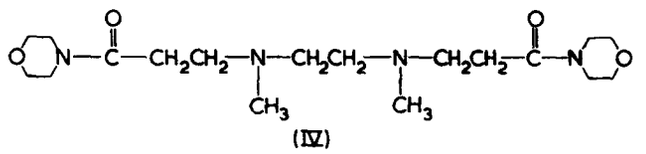
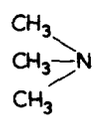
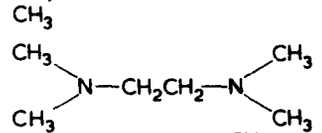
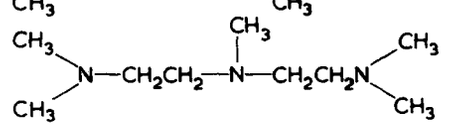
^{13}C n.m.r.

The ^{13}C n.m.r. spectrum of polymer I, with labelled signals is shown in *Figure 1*. At room temperature, four different signals are present for the C atoms of the piperazine ring, respectively at 44.18. 44.57, 47.84 and 48.13 ppm. At 50°C these signals colalesce two by two, and at 70°C a complete coalescence is observed for all four into a single broad resonance at ~16 ppm.

This behaviour indicates the presence of two different conformers, *cis* and *trans*, respectively (see *Figure 2*), in a ratio of about 1:1. ^{13}C n.m.r. spectra show that this ratio does not change between pH 1 and 10.

In order to confirm the above explanation, the ^{13}C n.m.r. spectrum of diacetyl piperazine, has been run using water as

Table 2 Basicity constants of poly(amido-amines), and of some models at 25°C in 0.1 M NaCl

		$\log K_1^a$	$\log K_2^a$	$\log K_3^a$
I	 (I)	7.79 (2)		
II	 (II)	8.09 (2)	4.54 (5)	
III	 (III)	8.08 (2)	6.94 (5)	1.8 (4)
IV	 (IV)	8.248 (4)	4.80 (1)	
		9.79[b]		
		9.281[c]	6.130[c]	
		9.22[d]	8.41[d]	2.09[d]

[a] The values in parentheses are the standard deviations; [b] ref 13; [c] ref 8; [d] ref 12;

solvent (*Figure 3*). Four different peaks of equal intensity, at 48.51, 48.22 and 43.85 ppm due to the piperazine C atoms are present. No variation of the relative intensities was observed in the pH range 1–10. The difference between our data, and previous results obtained by other authors[15,16] may be attributed to solvent effects. It has been found that in $CDCl_3$ or C_6H_5OH there is a variation in the *trans/cis* ratio.

The plot of the chemical shifts of different resonances for polymer I as a function of pH is shown in *Figure 4*. A half neutralizaton pH value can be obtained corresponding to the basicity constant. It is worthwhile to notice the strong effect of the protonation in the γ position on the chemical shift of the carbonyls.

The ^{13}C n.m.r. spectrum of polymer II at pH 10.2, with the corresponding assignments, is shown in *Figure 5*. As in polymer I, the relative amounts of *cis* and *trans* conformers (*Figure 2*) is the same and does not depend on the pH.

A plot of ^{13}C chemical shifts as a function of pH is shown in *Figure 6*. It can be observed that the C, D and G signals (due to the carbonyls and to D and G methylenes) clearly show the effect of a two-step protonation.

The basicity constants obtained by the potentiometric method and by ^{13}C n.m.r. from the half neutralization pH values (8.5 and 4.8), are in close agreement.

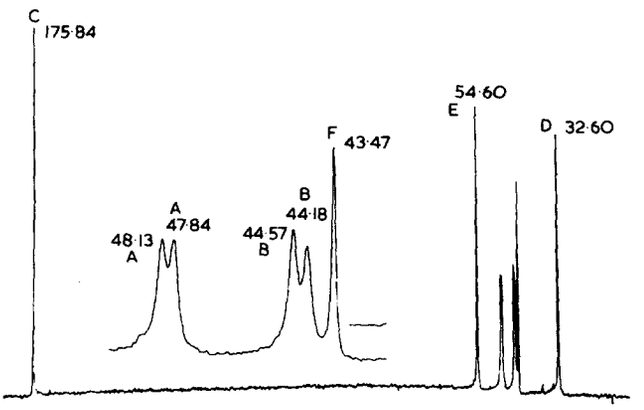
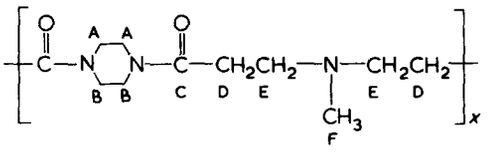


Figure 1 ^{13}C n.m.r. spectrum in water of polymer I, with signal attributions



The assignment of G and E peaks due to the methylenes is tentative and was made observing that in a situation of fast exchange, as demonstrated by the number of observed signals, G methylene resonances are subject to a regular β

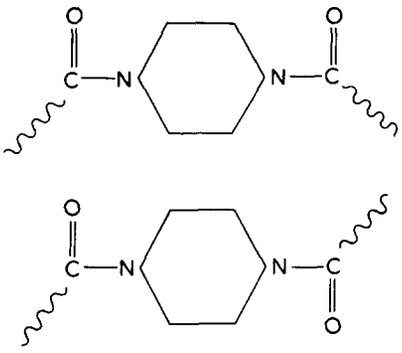


Figure 2 *Cis* and *trans* isomers of substituted diacyl piperazines

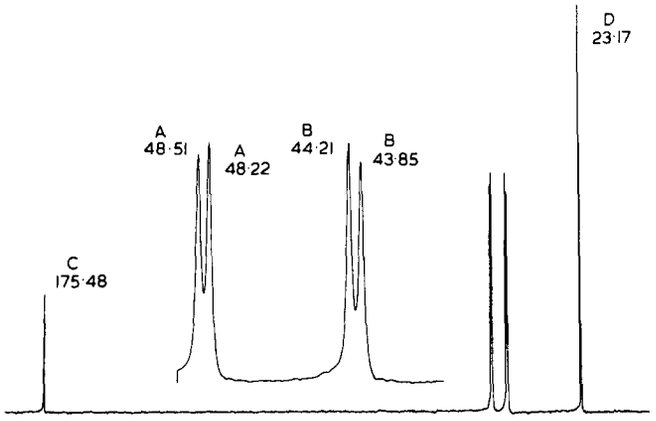


Figure 3 ^{13}C n.m.r. spectrum in water of diacetyl piperazine, with signal assignments

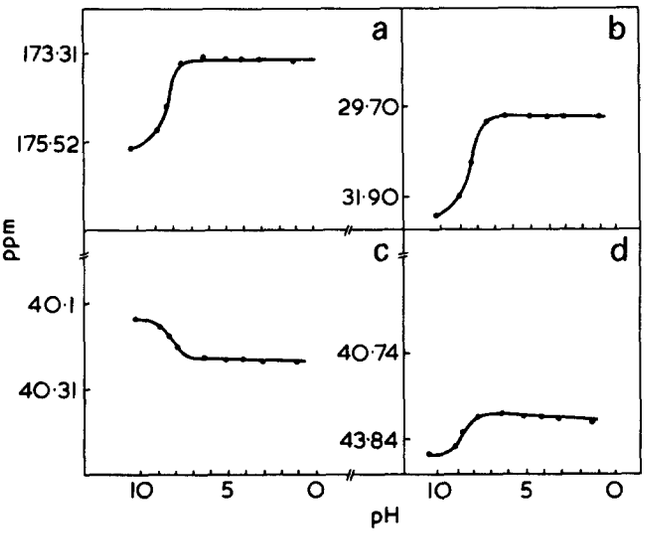


Figure 4 Polymer I ^{13}C n.m.r. shift variation in ppm as a function of pH value: (a) C; (b) D; (c) E; (d) F carbon atoms

effect, while the E methylenes should show a less regular α effect[17].

Titration plots relative to the F N–CH_3 signal and to E methylenes show a different behaviour. The *N*-methyl signal shows a normal upfield shift in the pH range 10–5.5 units, while the sigmoid is reversed in the pH range 5.5–4 when the second protonation occurs. The signal attributed to E methylenes does not show any shift in the pH range 10–7 while a paramagnetic shift is observed in the pH range 7–4.

A possible explanation of this behaviour is that some conformational variation might occur.

The fact that the number of signals does not change in the pH range 10–5 indicates a fast exchange of protonation between the two amine nitrogens; this exchange can easily occur in a folded-chain conformation[18]. At pH 4.8, when the second protonation occurs, the exchange is no longer stabilizing, electrostatic repulsion prevails and a conformational variation from a folded to a zig-zag path may occur. This interpretation is in agreement with a previously proposed model for *N*-methyl piperidines[18].

The ^{13}C spectra of model IV as a function of pH in the range pH 10–1 essentially do not differ from those of polymer II; chemical shift plots as a function of pH values are shown in *Figure 7*.

The close correspondence between the data of polymer II, and that of model IV, gives an indication that during protonation no interaction occurs between neighbouring monomeric units.

The ^{13}C n.m.r. spectrum of polymer III at pH 10.3, with peaks labelled, is shown in *Figure 8*. As far as the carbonyl tautomerism is concerned, polymer III shows the same pattern as for polymers I and II, and for model IV.

A plot of the ^{13}C n.m.r. chemical shifts as a function of pH is shown in *Figure 9*. The basicity constants obtained

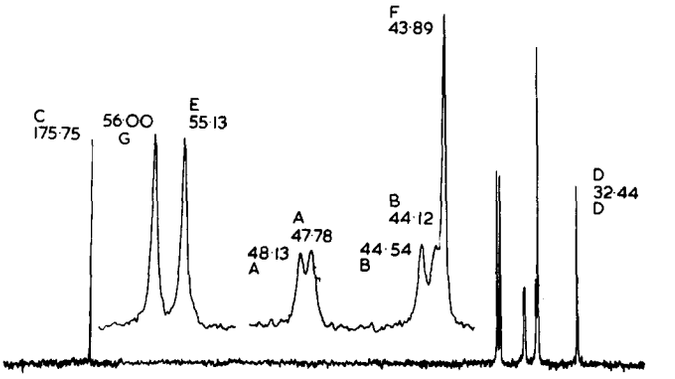
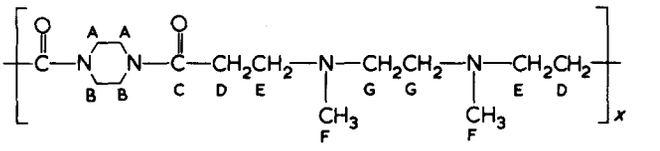


Figure 5 ^{13}C n.m.r. spectrum in water of polymer II, with signal assignments



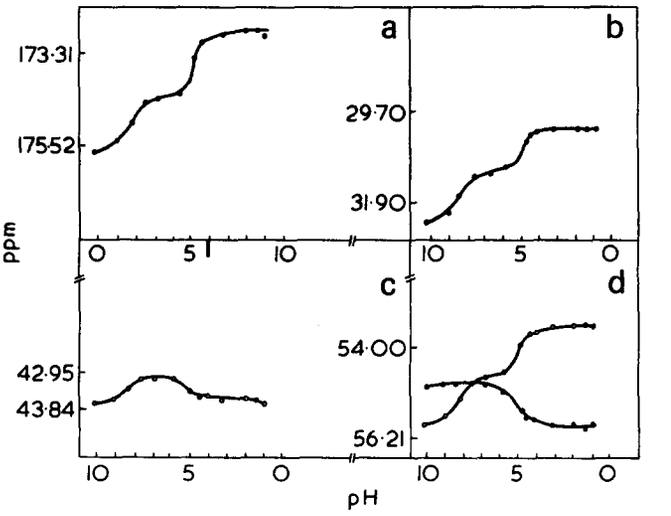


Figure 6 Polymer II ^{13}C n.m.r. shift variation in ppm as a function of pH value. (a) C; (b) D; (c) F; (d) G(○), E(●)

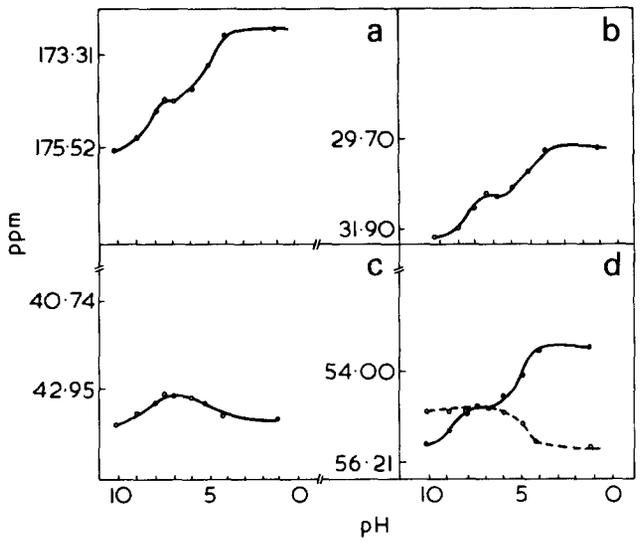
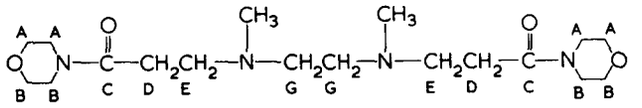


Figure 7 Model IV ^{13}C n.m.r. shift variation in ppm as a function of pH value



(a) C; (b) D; (c) F; (d) C(●) and E(○) carbon atoms

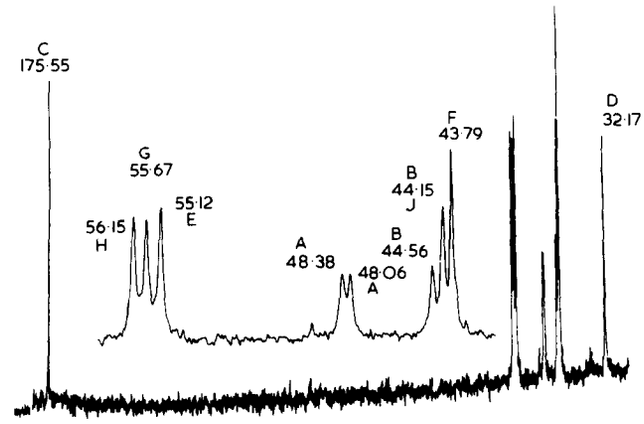
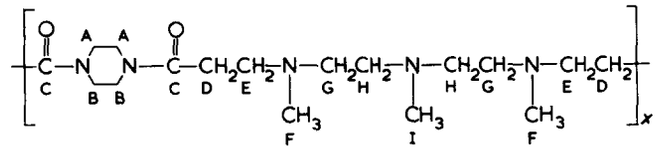


Figure 8 ^{13}C n.m.r. spectrum in water of polymer III, with signal assignments



by the potentiometric method and by ^{13}C n.m.r. (8.2–7.0 and 2.0 ppm) are in good agreement. The signals due to C carbonyls and to B methylenes show a pattern typical of three step protonation. The strong shift of these two signals in the first two protonation steps (pH range 10–7) indicates that the protonation starts on the two external amine nitrogens. Only at the third stage is the inner nitrogen protonated. In this respect it may also be noticed that in the protonation of polymer I, the effect on the carbonyl group located in the γ position with respect to the protonation site is ~2 ppm upfield, i.e. the same effect is present in polymers II and III only after the second protonation step.

This result confirms the above discussed mechanism of protonation, as inferred from the potentiometric basicity constants.

Signals due to *N*-methyl groups can easily be assigned using the intensity ratio. The F methyl resonance signal exhibits an upfield shift in the pH range 10–7 and a paramagnetic shift after the third protonation. Again, as in polymer II, the titration behaviour of this methyl signal indicates that during protonation some conformational variation may occur.

The three signals due to $N-CH_2$ groups may be assigned by observing the regularity of β effects[17,19]. In the first two stages of protonation, H methylene groups are in the β position with respect to the protonation sites; as a consequence, their resonances show the normal 2.5 ppm upfield shift. In the third stage of protonation, G methylenes are in the β position with respect to the protonation site; thus their signals show the normal 2.5 ppm upfield shift (*Figure 8*).

It follows that the third, and more irregular pattern may be attributed to the signals of E methylenes. In any case, the irregular behaviour of shifts due to C atoms in the α position with respect to the protonation site, points to conformation transitions[17–23], possibly more than one. These transitions are probably confined to the level of single monomeric units.

Further studies are in progress, based on LEFS (linear electric field shift) and on conformational analysis[17–23].

CONCLUSIONS

In contrast to most polymeric acids and bases[24] 'real' constants have been determined in the case of poly(amido-amines). This is probably due to the fact that the amine nitrogens of each unit, besides being part of the main chain, are separated from that of neighbouring units by ring structure, namely 1,4-diacylpiperazine groups. Thus, the protonation of an amine nitrogen of a given unit has no influence upon the amine nitrogens of the other units.

Secondly, neat titration curves may be obtained by ^{13}C n.m.r. plotting the chemical shifts of α, β and γ carbon atoms (with respect to the amine nitrogens) *versus* the pH. The pK values obtained by this technique are in close agreement with those obtained by the potentiometric method. Furthermore, in poly(amido-amines) II and III, and in model IV, it is possible to ascertain which nitrogen atom is being protonated at a given pH. In other words, each ionization step takes place at well-determined nitrogen atoms within

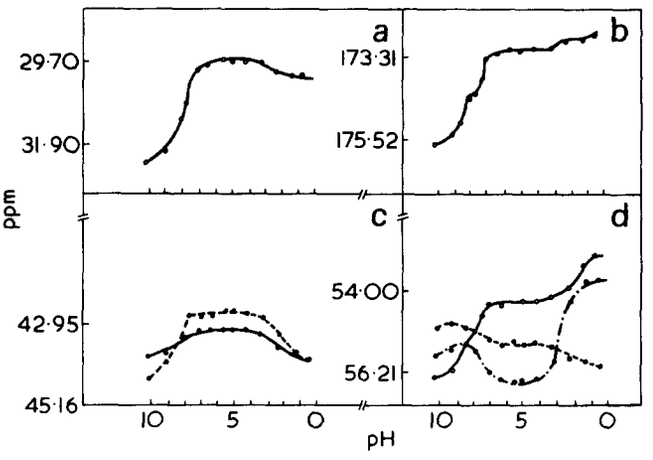


Figure 9 Polymer III ^{13}C n.m.r. shift variation in ppm as a function of pH value for C, D, E, G, H, F, I carbon atoms. (a) D; (b) C; (c) F(●) and I(○); (d) H(○), G (– · – ● – · –) and E (– – ● – –)

the monomeric units, i.e. the protons are not statistically distributed between nitrogen atoms of different types.

Finally, the CO groups of the 1,4-diacylpiperazine rings of the poly(amido-amines) are present in both *cis*- and *trans*-conformations, in approximately 50:50 ratio. The same is true in the case of the non-macromolecular model IV, and of 1,4-diacetylpiperazine.

REFERENCES

1 Danusso, F. and Ferruti, P. *Polymer* 1970, **11**, 88
2 Marchisio, M. A., Longo, T. and Ferruti, P. *Experientia* 1973, **29**, 93
3 Ferruti, P., Arnoldi, D., Marchisio, M. A., Martuscelli, E., Palma, M., Riva, F. and Provenzale, L. *J. Polym. Sci. (Polym. Chem. Edn)* 1977, **15**, 2151
4 Barbucci, R., Conti, F. and Ferruti, P. Italian Pat. Application
5 Langenbeck, W., Augustin, M. and Richter, F. H. *Chem. Ber.* 1961, **94**, 831
6 Danusso, F., Ferruti, P. and Ferroni, G. *Chim. Ind.* 1967, **49**, 271
7 Schmidt, A. and Wichmann, G. *Chem. Ber.* 1891, **24**, 3237
8 Paoletti, P., Barbucci, R., Vacca, A. and Dei, A. *J. Chem. Soc. (A)* 1971, p 310
9 Sabatini, A., Vacca, A. and Gans, P. *Talanta* 1974, **21**, 53
10 de Marco, A. *J. Magn. Res.* 1977, **26**, 527
11 Barbucci, R., Paoletti, P. and Vacca, A. *Inorg. Chim. Acta* 1975, **4**, 302
12 Allison, J. W. and Angelici, R. J. *Inorg. Chem.* 1971, **10**, 2233
13 Christensen, J. J., Izatt, R. M., Vrathall, D. P. and Hansen, L. D. *J. Chem. Soc. (A)* 1969, p 1212
14 Barbucci, R., Fabbrizzi, L. and Paoletti, P. *Inorg. Chim. Acta* 1973, **7**, 157
15 Miron, Y., McGarvey, B. R. and Morawetz, M. *Macromolecules* 1969, **2**, 154
16 Overberger, C. G., Veneski, R. A. Montaudo, G. *J. Polym. Sci. (B)* 1969, **7**, 877
17 Batchelor, J. G., Feeney, J. and Roberts, G. C. K. *J. Magn. Res.* 1975, **20**, 19
18 Marishima, I., Yoshikawa, K., Okada, K., Yonezawa, T. and Goto, K. *J. Am. Chem. Soc.* 1973, **95**, 165
19 Sarneski, J. E., Surprenant, H. L., Molen, F. K. and Reilley, C. N. *Anal. Chem.* 1975, **47**, 2116
20 Horsely, W. J. and Sternlicht, H. *J. Am. Chem. Soc.* 1968, **90**, 3738
21 Batchelor, I. G., Prestegard, I. H., Cushley, R. I. and Lipsky, S. R. *J. Am. Chem. Soc.* 1973, **95**, 6358
22 Batchelor, J. G. *J. Chem. Soc. (Perkin Trans.* 1976, p 1585
23 Batchelor, J. G. *J. Magn. Res.* 1977, **22**, 123
24 Morawetz, H. in 'High Polymers', 2nd Edn, Wiley–Interscience, New York, 1975, vol XXI