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Polybiguanides: synthesis and characterization of polybiguanides containing hexamethylene groups

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A series of polymeric biguanide hydrochlorides containing hexamethylene groups has been synthesized by developing methods for melt and solution polymerization, based on the reaction of cyano groups with amine hydrochlorides. These polymers were characterized by solution viscometry, gel permeation chromatography, ^{1}H n.m.r. and i.r. spectroscopy and thermal analyses (d.s.c. and t.g.a.). The presence of some melamine groups in the polymers made by melt polymerization was noticed and identified based on i.r. spectroscopy. The polymer salts obtained were generally hygroscopic and water soluble and lacked crystallinity. The hygroscopicity of the polymers varied with the hydrocarbon groups contained in the chains and the extent and nature of salt formation. The polybiguanide salts in both aqueous and polar non-aqueous solutions showed typical solution viscosity features of polyelectrolytes. The polybiguanides readily formed coloured complexes with copper ions. © 1997 Elsevier Science Ltd.

(Keywords: biguanides; poly(hexamethylene biguanide); polyelectrolytes)

INTRODUCTION

The name polybiguanide is used to describe a diverse group of polymers containing repeating biguanide groups

$$\begin{matrix} & NH & & NH & \\ & \| & & \| & \\ (-NH- & C & -NH- & C & -NH-R-) \end{matrix}$$

in the main chain. The polymeric biguanides, like the corresponding simple bigunides, are quite strong bases, which react with organic and inorganic acids to form the corresponding salts. Polybiguanide hydrochlorides can be synthesized by various routes based on the reaction of cyano groups with amine hydrochlorides[1-3].

A typical aliphatic homopolybiguanide, poly(hexamethylene biguanide hydrochloride) (PHmBG.HCl), is a water soluble and fibre-forming material with good antibacterial properties[4], which has a potential application in wound dressings. It is also an ion-containing polymer which could be the basis for an ion-exchange material. Since non-polymer biguanides form coloured complexes with transition metal ions[5], there are also attractive possibilities for the removal and recovery of metal ions from aqueous solutions.

Although PHmBG.HCl was prepared by Rose and Swain[5] by melt polyaddition, no systematic investigation of the synthesis and characterization of polybiguanides has been reported. In the present paper, solution and melt polymerization are both used for the preparation of polybiguanides, and the effects of polymerization conditions on the polymer structures and the molecular weights are examined. The influence of the hydrocarbon groups in polybiguanides on the hygroscopicity, basicity and thermal behaviour is also evaluated. The solution

behaviour of the homopolymer PHmBG.HCl, in particular its ability to behave as a polyelectrolyte, is investigated.

EXPERIMENTAL

Instrumental techniques

The ^{1}H n.m.r. spectra were recorded in deuterated dimethylsulfoxide (DMSO) either on a Nicolet Fourier-transform 2E 300 MHz spectrometer or on a Jeol JNE FX 200 MHz superconducting spectrometer. Infra-red spectra were obtained with a Perkin Elmer 1725X Fourier-transform i.r. spectrometer using KBr discs. The i.r. absorbance of cyanoguanidine end-groups, whose characteric peak is at 2175 cm^{-1}, was determined in DMSO solutions at a concentration of 0.4 molar repeat unit l^{-1}, by injecting the solutions into a NaCl cell with a pathlength of 0.025 mm. The background absorbance of DMSO solvent was removed as part of this procedure. The relationship between the concentration of cyanoguanidine end-groups and their i.r. peak heights (or peak areas) was established by calibration using DMSO solutions of hexamethylenebiscyanoguanidine (HmBCG) and hexamethylenediamine dihydrochloride (HmDA.2HCl), at various known concen-trations, and showed good linearity. A Pye Unicam SP 1800 u.v. spectrophotometer was used to measure u.v.–vis. bands.

Elemental analyses were carried out using a Carlo Erba elemental analyser (Model 1106). Melting points were determined using a Stanton Redcroft TH600 hot stage equipped with an Olympus polarizing microscope. Solution viscosities of the polymers in DMSO were measured at $25 \pm 0.02°C$ at a concentration of 0.5 g dl^{-1} using an Ubbelohde viscometer. Molecular weights (M_w)

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and molecular-weight distributions (M_w/M_n), based on polystyrene standards, were determined by J. Cunningham of RAPRA Technology Ltd using gel permeation chromatography (g.p.c.) at 120°C in stabilized *m*-cresol with a refractive-index detector and two 30 cm columns of 10 μm 2× PLgel, mixed bed B.

Thermal analysis was conducted under nitrogen with a heating rate of 10°C min^{-1} using a DuPont Model 910 d.s.c. cell with a DuPont 2000 controller. Thermogravimetric analyses were carried out in nitrogen at a heating rate of 20°C min^{-1} using a DuPont 951 t.g.a. analyser with a DuPont 2000 controller.

Materials

Sodium dicyanimide (SDC, 96%), dicyandiamide (DCDA, 99%), hexamethylenediamine dihydrochloride (HmDA.2HCl, 99%), hexamethylenediamine (HmDA, 98%), *p*-phenylenediamine dihydrochloride (PhDA.2HCl, 99%), piperazine dihydrochloride monohydrate (Pip.2HCl, 98%), *N*-methyl-2-pyrrolidinone (NMP, 99%), dimethylsulfoxide (DMSO, 99+%), diethylene glycol (DEG, 98%), acetic acid (AR grade), and methanol (h.p.l.c. grade) were purchased from Aldrich Chemical Co. These compounds were used without further purification.

Monomer preparations

The preparation of biscyanoguanidine monomers was based on the reaction of SDC with diamine dihydrochlorides (*Scheme 1*).

Preparation of HmBCG

SDC (19.58 g, 0.22 mol) and HmDA.2HCl (18.9 g, 0.1 mol) were mixed together with n-butanol (100 ml) in a 250 ml three-necked round-bottomed flask provided with a reflux condenser. The mixture was heated in an oil bath kept at 120–135°C and stirred with a PTFE magnetic follower on a magnetic stirrer hot-plate for about 8 h. A nitrogen atmosphere was maintained during the reaction. Upon completion of the heating period, the suspension was cooled, a larger volume of water was added and stirred vigorously, and then the solid was recovered by filtration. The solid was washed thoroughly with further water, then with ethanol and acetone successively to remove unreacted starting materials and sodium chloride, and finally dried. The crude product was recrystallized from distilled water (1 l) to give crystals of 20.8 g (83.2% yield), m.p. 210–213°C (lit. m.p. 203–205°C[6]; 202–203°C[2,7]). Elemental analysis: calculated for $C_{10}H_{18}N_8$, C 48.0%, H 7.2%, N 44.8%; found, C 47.75%, H 7.25%, N 44.65%. ^{1}H n.m.r. δ (DMSO-d_6); 2.9 (4H, CH$_2$-N), 1.1, 1.3 (8H, -CH$_2$-), 6.0–7.0 (6H, NH). I.r. (KBr): 3372, 3165 (-NH-, =NH, str.), 2175 (-C≡N, str.), 2940, 2857 (-CH$_2$-, str.); 1651, 1621, 1558 (>C=N str/NH def.); 730 cm^{-1} (-CH$_2$-, bending). *n*-Butanol was superior to 2-ethoxyethanol as a solvent for this preparation; water gave no product.

Preparation of p-*phenylene biscyanoguanidine* (PhBCG)

A mixture of 19.58 g (0.22 mol) of SDC and 18.1 g

(0.1 mol) of PhDA.2HCl in water (80 ml) was heated in an oil bath at 110°C for 6 h. The precipitate that formed was filtered off and recrystallized from dimethylformamide (DMF)/H$_2$O (3/2, v/v) in the presence of antioxidant [sodium dithionite (Na$_2$S$_2$O$_4$)] and charcoal to give needle-like crystals (65–70% yield), m.p. 320°C (d) [lit.[8], 314°C (d)]. Elemental analysis: calculated for $C_{10}H_{10}N_8$, C 49.57%, H 4.16%, N 46.2%; found, C 49.25%, H 4.2%, N 45.45%. ^{1}H n.m.r. δ (DMSO-d_6); 6.9 (4H, NH), 7.25 (4H, Ar), 9.0 (2H, NH). I.r. (KBr): 3405, 3326, 3220 (-NH-, =NH, str.), 2182 (-C≡N), 1630, 1562, (>C=N, -C=C-, str./NH def.); 830 cm^{-1} (out of plane, *p*-Ar). Water was superior to *n*-butanol and 2-ethoxyethanol as a solvent for this preparation.

Preparation of piperazine biscyanoguanidine (PipBCG)

A mixture of 19.58 g (0.22 mol) of SDC and 17.7 g (0.1 mol) of Pip.2HCl.H$_2$O in *n*-butanol (100 ml) was heated in an oil bath at 130°C for 10 h. The precipitated crude product was purified by crystallization from NMP/H$_2$O (5/1, v/v) to give crystals (68% yield), m.p. > 380°C (lit.[9] m.p. 300°C). Elemental analysis: calculated for $C_8H_{12}N_8$, C 43.62%, H 5.49%, N 50.89%, found, C 43.85%, H 5.50%, N 50.80%. ^{1}H n.m.r. δ (DMSO-d_6); 3.5 (8H, -CH$_2$-), 7.25 (4H, NH). I.r. (KBr): 3340, 3322, 3216 (-NH-, =H str.), 2169 (-C≡N str.), 1647, 1559, 1523 (N–C>C = N str./NH def.); 1000 cm^{-1} (pip. ring, vibration). *n*-Butanol was superior to 2-ethoxyethanol as a solvent for this preparation.

Polymerizations

Synthesis of poly(hexamethylene biguanide hydrochloride) (PHmBG.HCl). Five methods of synthesis were examined and are outlined below. Quantities, yield and some product properties are listed in *Table 1*.

Method I (Scheme 2, melt): HmDA.2HCl (1.89 g, 10 mmol and HmBCG (2.50 g, 10 mmol) were mixed and ground. The intimate mixture was heated in an oil bath at 165–175°C on a hot-plate for about 12 h under a nitrogen atmosphere, stirring with a mechanical stirrer. After the first 1–2 h of heating, the mixture started to fuse and then gradually turned into a homogeneous viscous liquid. The viscosity of the melt increased and occasionally became so high that further stirring was difficult, so the temperature of the reaction was raised to 180°C. After the desired reaction time, heating and stirring were stopped, and the molten homogeneous liquid was allowed to cool to room temperature. A hygroscopic brittle solid was obtained.

Method II (Scheme 2, solution): A mixture of HmBCG and HmDA.2HCl in NMP (10 ml) was heated at 145–155°C, stirring with a magnetic follower under a nitrogen atmosphere, for about 14 h. After a few hours of heating, the mixture became a clear solution, which gradually formed two transparent layers. PHmBG.HCl was obtained after cooling the mixture, decanting the supernatant upper layer (NMP), hardening the residue by acetone and quickly transferring the solid to a vacuum oven at 60°C for about 2 days. NMP gave results significantly better than those of DEG.

Scheme 1

2 N≡C—N(Na)—C≡N + NH2–R–NH2•2HCl ⟶ N≡C—NH—C(NH)—NH — R — NH — C(NH)—NH—C≡N + 2NaCl

Table 1 Synthesis of polybiguanide hydrochlorides: typical results

Monomers (mmol)			Solvent (ml)	Temp. (°C)	Time (h)	Yield (%)	η_{sp}/c (dl g^{-1})	$\bar{M}_w$	T_g (as made) (°C)
BCG	DA.2HCl								
SDC (10)	HmDA (10)		None	160–170	15	73.1	0.37	—	40–50
SDC (10)	HmDA (10)		DEG	150–160	15	54.7	0.27	—	35–45
HmBCG (10)	HmDA (10)		None	165–175	12	99.1	1.16	2.5×10^5	45–60
HmBCG (10)	HmDA (10)		NMP (10)	145–155	14	68.7	1.10	—	40–52
HmBCG (5)	HmDA (2.5)	PhDA (2.5)	None	170–180	8	98.6	0.32	—	90–110
HmBCG (4)	HmDA (3)	Pip (1)	None	170–180	10	97.1	0.37	—	80–100
HmBCG (10)	PhDA (10)		H$_2$O (15)	100–110	11	76.4	0.54	—	150–165
HmBCG (10)	PhDA (10)		NMP (10)	130–150	8	78.6	0.63	1×10^5	165–180
PhBCG (5)	HmDA (5)		NMP (5)	170–180	8	74.2	0.31	—	160–175
HmBCG (10)	Pip (10)		NMP (10)	150–160	12	84.5	0.36	—	100–120
PipBCG (10)	HmDA (10)		NMP (10)	175–185	15	78.7	0.26	—	110–130

Method III (Scheme 3, *melt*): An equimolar mixture of SDC and HmDA.2HCl was heated at 160–170°C for 15 h, forming an opaque liquid. A brittle solid was obtained on cooling.

Method IV (Scheme 3, *solution*): An equimolar mixture of SDC and HmDA.2HCl was heated in DEG at 150–160°C for 15 h. A suspension formed and the product was isolated by adding acetone and then filtering. The filtrate was hardened by acetone and dried in a vacuum oven at 70–80°C for three days, giving a glass-like solid. DEG gave results slightly better than those of NMP.

Method V (Scheme 4, *melt*): An equimolar mixture of DCDA and HmDA.2HCl was heated at 160–170°C for 16 h to give a glass-like fibre-forming substance with a low viscosity number.

PHmBG.HCl from these procedures was purified in all cases to remove any low molecular weight oligomers by precipitating it from an aqueous solution by addition of sodium chloride until the solution became saturated. However, the product made by Method V failed to form a precipitate from an aqueous solution.

Synthesis of copoly(hexamethylene/p-phenylene biguanide hydrochloride) [*P(Hm/Ph)BG.2HCl*]. *Method VI:* A mixture of 1.89 g (10 mmol) of PhDA.2HCl and

2.50 g (10 mmol) of HmBCG in NMP (10 ml) formed a red solution during 30 min heating at 140°C, then precipitation occurred. After 6 h further heating, the product was cooled, an excess of ethanol was added with stirring, and the solid product was isolated by filtration (yield 79%; η_{sp}/c 0.63 dl g^{-1}). When the same reaction was carried out in water (15 ml), a clear solution was formed on heating under reflux for 1 h and persisted throughout the reaction period of 10 h. The viscous solution was cooled and poured into a large amount of ethanol with vigorous stirring. The precipitate was recovered by filtration and dried in a vacuum oven at 60–80°C for two days (yield 76%; η_{sp}/c 0.54 dl g^{-1}).

Method VII: A heterogeneous mixture of PhBCG and HmDA.2HCl (5 mmol each) in NMP (8 ml) was heated in an oil bath at 170–180°C. It became emulsion-like, but remained of low viscosity. After 8 h, the cooled mixture was added to mixed ethanol/acetone. The precipitate was isolated and dried (yield 74%; η_{sp}/c 0.31 dl g^{-1}).

Synthesis of copoly(hexamethylene/piperazine biguanide hydrochloride) [*P(Hm/Pip)BG.2HCl*]. *Method VIII:* A mixture of HmBCG and Pip.2HCl.2H$_2$O (10 mmol each) in NMP (10 ml) turned clear at first and then gradually separated into two layers, when heated at 150–160°C with stirring using a magnetic
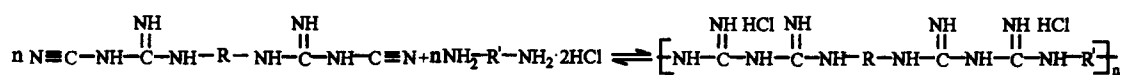
Scheme 2
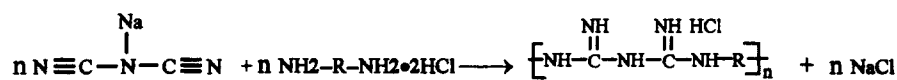
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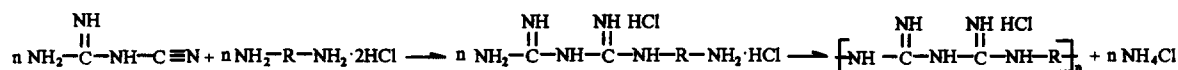
Scheme 4

follower. The product in the lower layer became viscous as the reaction continued. After a 12 h reaction, a transparent solid was obtained after decanting the supernatant upper layer and washing the residues with acetone. P(Hm/Pip)BG.2HCl was dried in a vacuum oven at 60°C for two days (yield 84%; η_{sp}/c 0.36 dl g^{-1}).

Method IX: P(Hm/Pip)BG.2HCl was also prepared in NMP (10 ml) using a mixture of PipBCG and HmDA.2HCl (10 mmol each). The mixture, when heated at 170–180°C for 15 h, became a suspension and gradually deposited a soft product, which lacked mobility even at 185°C. After the reaction, the upper clear layer was decanted and the soft product was recovered, washed with ethanol and acetone, and dried in a vacuum oven at 60°C for two days (yield 79%; η_{sp}/c 0.26 dl g^{-1}).

RESULTS AND DISCUSSION

Polymerization

Homopolymer (PHmBG.HCl). The polymerization was conveniently carried out either in the presence or absence of solvents by reaction of either HmBCG or SDC with HmDA.2HCl, i.e. by polyaddition (*Scheme 2*) or polycondensation (*Scheme 3*), respectively. Viscosity numbers (η_{sp}/c) of the products made by polycondensation with SDC were significantly lower than those of the products obtained by polyaddition with HmBCG (*Table 1*). This is attributable to the relatively low purity of SDC, which is difficult to purify further. The polycondensation of DCDA with HmDA.2HCl (*Scheme 4*), as also reported in the literature[10], was inefficient and gave only low molecular weight products, presumably due to side reactions and incomplete elimination of ammonia.

The homopolymers made by melt or solution polyaddition (Methods I and II) under the best conditions gave similar values of η_{sp}/c (*Table 1*). Higher temperature (> 190°C) melt polymerization resulted in the

formation of branched or cross-linked polymers which formed swollen and sponge-like materials in water or DMSO. Use of a slightly unbalanced mixture of the monomers or of a mixture of HmDA.2HCl and HmDA, instead of HmDA.2HCl, did not influence the molecular weight significantly. The effect of prolonging the duration of melt polymerization on η_{sp}/c was slight, as shown in *Figure 1*. It was found that η_{sp}/c did not continue to increase after reaction for 8 h.

The i.r. spectra (KBr) of all the PHmBG.HCl samples exhibited bands at 3310, 3180 cm^{-1} (−NH−, =NH, =NH$_2^+$, str.) and 1635 and 1550 cm^{-1} (NH, def. conjugated with N$_2$−C=N, str.), besides the absorptions at 2930, 2855, 1470 and 725 cm^{-1} (−CH$_2$−, str., def. and bending) for hexamethylene groups. They are similar to the spectrum of the model compound, hexamethylene bis(hexylbiguanide hydrochloride) (HxBGHmBGHx.2HCl) (m.p. 199–201°C), prepared by the reaction either of HmBCG with hexylamine hydrochloride or of HmDA.2HCl with hexylcyanoguanidine and purified by recrystallization from water and acetone. Typical spectra are shown together in *Figure 2*. This confirms that the polymers contained biguanide linkages. The absorption due to −C≡N at 2175 cm^{-1} in the spectra of PHmBG.HCl can be distinguished using either a KBr disc or a solution. This band was used to follow the change in cyanoguanidine end-group concentration during melt polymerization. The cyanoguanidine end groups, although consumed rapidly in the early stages, did not disappear at the end of the reaction, even in those cases where the homopolymer had a relatively high viscosity number ($\eta_{sp}/c = 1.16$ dl g^{-1}) or was made using either 10% excess of HmDA.2HCl or a prolonged duration of reaction. Their continued presence and the limiting value of η_{sp}/c are attributed to an equilibrium between polymerization and depolymerization, since simple biguanides have been shown to decompose to products containing −C≡N (*Scheme 5*)[11]. In principle, melt polymerization should give an equilibrium more favourable to the polymer than solution polymerization.
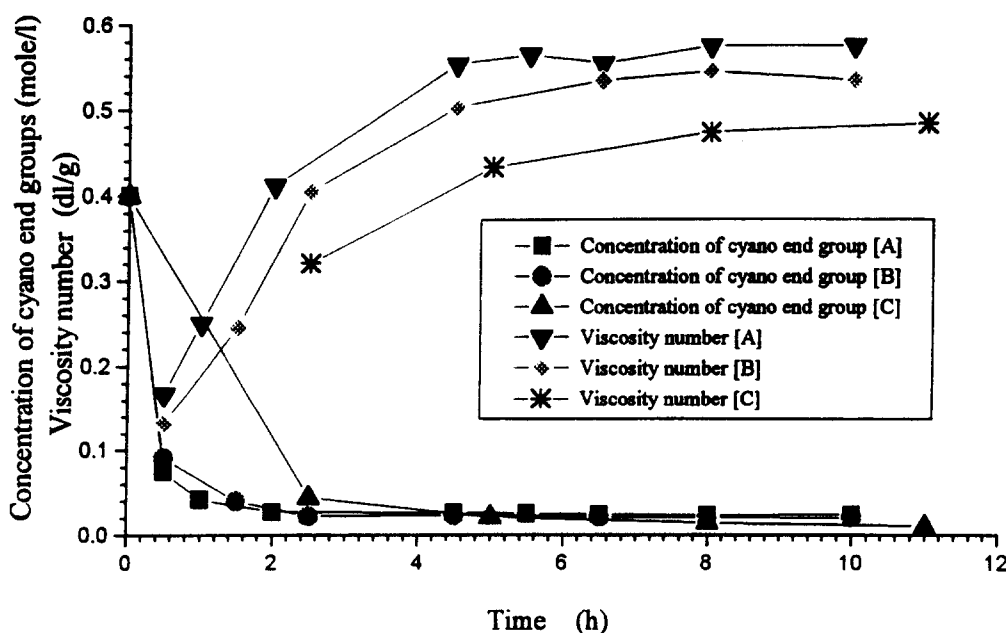

Figure 1 Synthesis of PHmBG.HCl by melt polyaddition at 160–170°C: (A) equimolar HmBCG and HmDA.2HCl; (B) 10 mol% excess of HmDA.2HCl; (C) molar ratio HmBCG: HmDA.2HCl: HmDA (5/4/1.1)
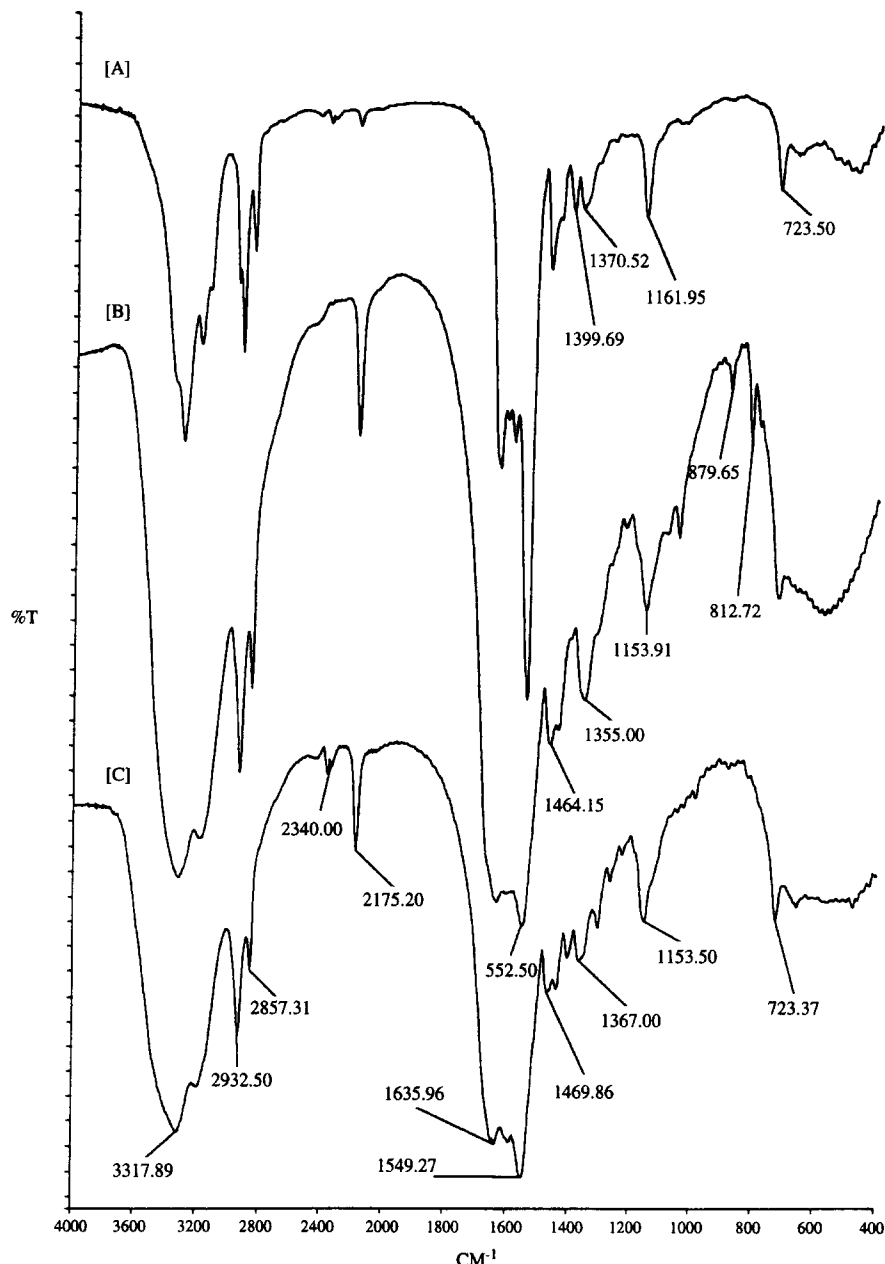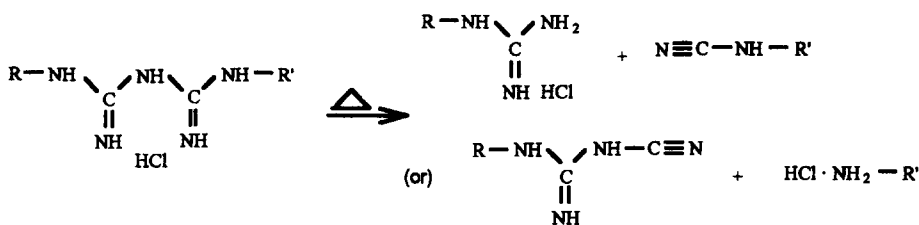
Figure 2 I.r. spectra of PHmBG.HCl and the model compound: (A) model compound (HxBGHmBGHx.2HCl); (B) polymer made in the melt; (C) polymer made in NMP

Scheme 5

All the homopolymers synthesized by melt polymerization exhibited an additional sharp i.r. peak at $812 \pm 5 \, \text{cm}^{-1}$ which appeared even after purification or in their free base form; in contrast, none of the homopolymers produced by solution polymerization gave such an absorption (*Figure 2*). However, this peak did appear if the homopolymer made by solution polymerization was heated further and kept molten at 160°C. The

tendency of cyanoguanidine groups to form substituted melamines in melt reactions, especially at a high temperature, has been reported[12]. Substituted melamine or amino-*s*-triazine structures exhibit characteristic sharp i.r. absorption of medium intensity in the region of 800–825 cm^{-1} and further peaks at 1420 and 1550 cm^{-1} [13]. The i.r. peak at 812 cm^{-1} in the polymers obtained by melt polymerization therefore provides evidence for the
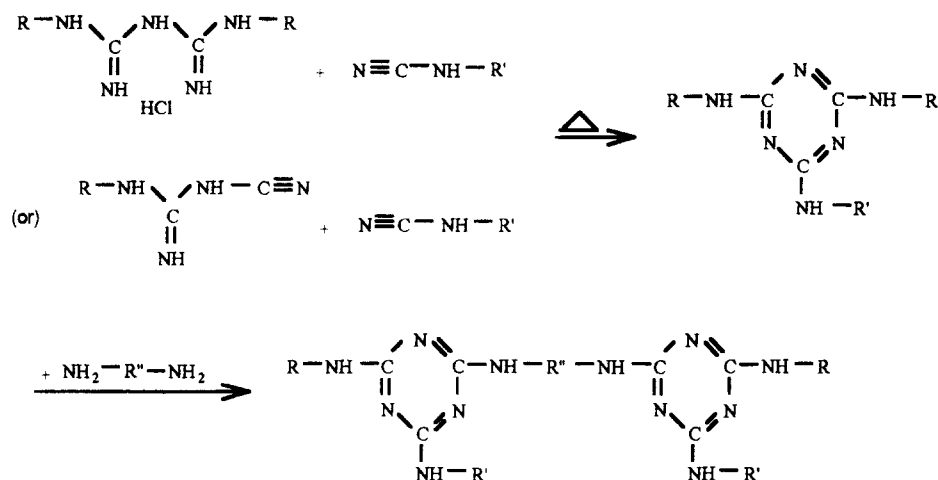
Scheme 6

formation of substituted melamines by cyclization of some biguanide groups through reactions with cyano groups, or less probably by the condensation of cyano groups themselves (*Scheme 6*). Such reactions should lead to chain branching and eventually to cross-linking and insolubilization, as observed at temperatures above 190°C.

The ^{1}H n.m.r. spectra of all these PhmBG.HCl samples showed sharp peaks at δ 1.3 and 1.4 (8H, $-CH_2-$) and δ 3.1 (4H, $-CH_2-N-$), which confirmed that hexamethylene groups were present in the polymer chain, and broad peaks at δ 6–7 (5H, $-NH-$), which resulted mostly from the biguanide groups. The peaks of the protons in the melamine groups, present in the homopolymers by i.r. identification, were not detectable by n.m.r., due to the breadth and variety of the protons attached to the biguanide nitrogens.

Differences in thermal behaviour of the homopolymers obtained by melt and solution polymerization were noted in t.g.a. and d.s.c. traces. According to the t.g.a. traces (*Figure 3*), the sample prepared by solution polymerization (Method II) started to lose weight at about 230°C; in contrast, the sample obtained by melt polymerization (Method I) did not show significant weight loss until above 300°C. The samples both underwent further weight losses to give similar carbonized residues (18%) at 550°C (original carbon content 43.7%). The glass transition temperature ($T_g \approx 45$°C) of the polymer 'as made' by Method II was lower than that ($T_g \approx 50$°C) of the polymer by Method I. The effect of molecular weight on T_g was slight in the range examined and this increase in T_g in the homopolymer made by Method I is therefore attributed to the formation of some melamine groups. Slight differences in the colours of the metal complexes and in the solubilities of the samples made by Methods I and II were also noted.

Copolymer [P(Hm/Ph)BG.2HCl]. By using h.p.l.c. to monitor concentrations of reactants and products in the model reactions of HmBCG with aniline hydrochloride and of PhDA.2HCl with phenylcyanoguanidine (PhyCG)[14], it was confirmed that the aromatic amine hydrochlorides reacted efficiently with cyano groups in the presence of a solvent and that the polymerization could be carried out at a low temperature (about
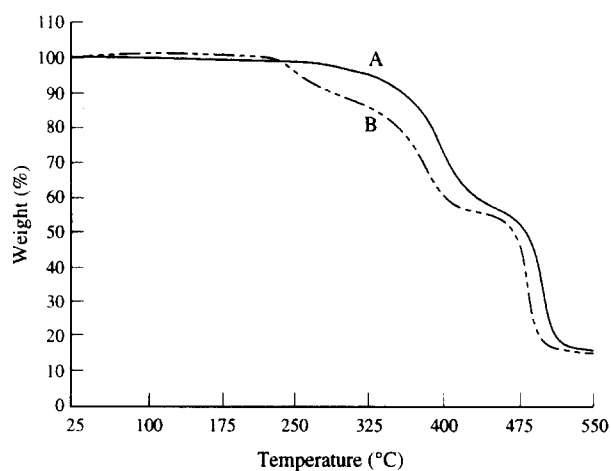

Figure 3 T.g.a. curves of PHmBG.HCl made in (A) the melt and (B) NMP

90°C). Quite high molecular weight samples of P(Hm/Ph)BG.2HCl were obtained via the reaction of HmBCG and PhDA.2HCl in water or NMP (see *Table 1*). In contrast, the polymerization of PhBCG with the non-aromatic salt HmDA.2HCl (Method VII) was less efficient under the same conditions and gave a product with a lower η_{sp}/c (*Table 1*). The η_{sp}/c values did not increase further even in cases where the reaction temperature was raised to 180°C and the duration was increased. The polydispersity ($\bar{M}_w/\bar{M}_n = 7.9$) of the copolymer was much lower than that ($\bar{M}_w/\bar{M}_n = 62.9$) of the homopolymer made in the melt. The latter value is attributed to the higher temperatures prevailing in the melt reaction leading to both chain branching through the formation of melamine groups (as already indicated by the i.r. studies) and chain scission. P(Hm/Ph)BG.2HCl could not be prepared by melting either of the above mixtures at around 200°C due to the infusibility of one or more reactants.

The i.r. spectra of all the P(Hm/Ph)BG.2HCl products exhibited identical bands at 2930, 2855 and 715 cm^{-1} ($-CH_2-$, str., and bending for hexamethylene groups); at 1630–1550, 1545 and 1505 cm^{-1} (HN=C–N$_2$, str./NH def. or C=C ring str.) and at 3310 and 3180 cm^{-1} ($-NH-$, =NH or =NH$_2^+$, str.). A peak at 830 cm^{-1} is

assigned to a characteristic absorption due to the out-of-plane bending in *p*-phenylene groups directly attached to amine or biguanide salts. The peak of the end-groups ($-C\equiv N$) at $2175\,cm^{-1}$ was only just visible, much weaker than that in the homopolymer. This is attributed to the higher reactivity of aromatic amine hydrochlorides with cyano groups and to the lower polymerization temperatures which should prevent thermal depolymerization of the biguanide groups into products containing $-C\equiv N$.

The ^{1}H n.m.r. spectra (*Figure 4*) of P(Hm/Ph) BG.2HCl prepared either in water or in NMP gave identical chemical shifts and showed peaks at δ 1.25 and 1.45 (8H, $-CH_2-$), 3.08 (4H, $-CH_2-N-$) and 7.25 (4H, Ar.) ppm, assigned as shown to the hexamethylene groups and *p*-phenylene groups. Peaks due to the protons attached to the nitrogen in the biguanide groups at δ 6.85, 7.85 and 9.8 ppm (10H, $-NH-$) were broad and difficult to assign. The peaks of solvent DMSO-d_6 and residual water appeared at 2.5 and 3.2 ppm, respectively. A peak at δ 2.04 ppm present in some samples was attributed to residual acetone.

The products prepared in NMP or in water (Method VI) showed little difference in t.g.a. and d.s.c. In d.s.c. traces, slightly different glass transition temperatures were revealed giving $T_g \approx 160°C$ and $T_g \approx 175°C$ for the products 'as made' in water and in NMP, respectively. Similar exothermic processes with a peak at about 265°C were noted in both samples and were assumed to be due to decomposition. Bubbles and discoloration observed at this temperature on a hot stage confirmed the decomposition.

Copolymer [P(Hm/Pip)BG.2HCl]. P(Hm/Pip)BG.2HCl was prepared by the reaction either of HmBCG with Pip.2HCl or of PipBCG with HmDA.2HCl in NMP. The former reaction gave a higher η_{sp}/c (*Table 1*).

The i.r. spectra of these P(Hm/Pip)BG.2HCl samples were identical, and exhibited known absorptions for hexamethylene groups and biguanide linkages. A characteristic peak at $1000\,cm^{-1}$ was assigned to the piperazine ring vibration. The peak at $2175\,cm^{-1}$ due to $-C\equiv N$ was still obvious. The relatively low values of η_{sp}/c are attributed to the relatively low reactivity of piperazine groups with cyano groups, which may also make the reverse reaction more important under these conditions.

The product obtained by Method IX (using Pip.2HCl) showed a slightly higher T_g and a higher carbonized residue than that obtained by method VIII (using HmDA.2HCl). Both samples were observed to begin to bubble at 260°C.

Effect of copolymerization on the properties of poly(hexamethylenebiguanide)

The method of preparation should give rise initially to alternating copolymers, but if the reaction is reversible, randomization will occur. The extent of randomization was not investigated. Since even the homopolymer PHmBG.HCl exhibits little or no crystallinity, the sequence distribution is not expected to have a significant effect upon physical properties.

The hygroscopicity and solubility of the copolymers, especially those containing *p*-phenylene groups, were reduced significantly compared with those of the homopolymer (PHmBG.HCl). The homopolymer is very hygroscopic and soluble in water, DMSO, *m*-cresol and
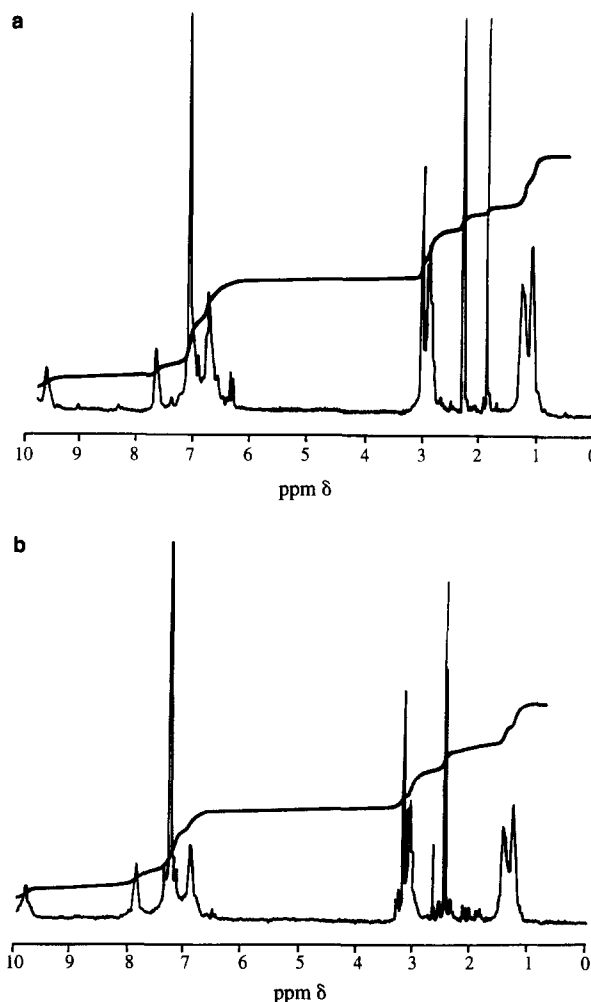
methanol, but only slightly soluble in DMF, NMP, acetic acid, ethanol and brine, where soft, swollen and sticky mixtures were formed. It is insoluble in acetone, ether and toluene. The copolymer P(Hm/Ph)BG.2HCl is soluble in DMSO and hot water, but only swollen in methanol and sparingly soluble in brine; the solubility of P(Hm/Pip)BG.2HCl is slightly lower than that of the homopolymer.

Filaments and films of the copolymer, P(Hm/Ph)BG.2HCl, drawn or cast from a warm aqueous solution, are brittle. In contrast, long, fine and flexible filaments of the homopolymer, PHmBG.HCl, could be drawn readily from an aqueous solution or from a melt, and films were cast easily under pressure. Since the molecular weights of both these polymers were quite high when measured by g.p.c. (see *Table 1*), the brittleness of the copolymer filaments is not likely to be due to low molecular weight. Filaments from both polymers showed some birefringence resulting from orientation.

The d.s.c. traces for the different polybiguanide hydrochlorides revealed that T_g was related to the nature of the hydrocarbon groups present and the thermal history of the polymers. The higher the *p*-phenylene content of the copolymer, the higher the T_g (*Table 1*). It was found that, after the polybiguanide hydrochlorides were kept at 150°C for 20 min and then quenched to $-50°C$, the T_g rose (*Figure 5* and *Table 1*). Exothermic processes in these polymers were seen at around 260°C, where

bubbles and discoloration were also observed on a hot-stage microscope. This confirmed that decomposition was occurring. The thermal stability of the polybiguanide salts was, therefore, not improved by altering the hydrocarbon groups.

The t.g.a. traces for the polybiguanide hydrochlorides showed that the presence of the *p*-phenylene group led to a higher carbonized residue (*Figure 6*). The carbonized residue was highest for P(Hm/Ph)BG.2HCl, which gave 42%, only slightly greater (20%) for P(Hm/Pip)BG.HCl, and lowest (18%) for PHmBG.HCl, whereas their original carbon contents were 44.5, 41 and 43.7%, respectively.

Polybiguanide bases

The free base of the homopolymer (PHmBG) was precipitated from an aqueous solution of its hydrochloride salt on addition of NaOH together with NaCl. After washing with saturated NaCl solution and drying, PGmBG gave $\eta_{sp}/c = 0.85\,dl\,g^{-1}$ in DMSO solution at $0.5\,g\,dl^{-1}$ and pH 11.8 in an aqueous solution at $0.8\,g\,dl^{-1}$ (p$K \approx 10.96$). The basicity was quite strong [compare the corresponding simple biguanides: biguanide (p$K_1 = 11.52$, p$K_2 = 2.93$) and phenyl biguanide (p$K_1 = 10.76$, p$K_2 = 2.13$)[15]]. The free bases of the copolymers were also prepared using similar procedures. However, since the free base copolymers were only sparingly soluble in water, measurement of pH in solution was not possible.

The i.r. spectrum of PHmBG was similar to that of its hydrochloride since the charges on the amino groups of the biguanide were distributed over several nitrogen atoms. PHmBG softened about 40°C, and soon thereafter started to bubble and cross-link; it was also noted to turn brown–yellow on exposure to air. These free base forms therefore showed lower thermal stability and poorer resistance to environmental oxygen than the corresponding polymer salts.

Solution behaviour of homopolymer PHmBG.HCl

Solution viscosity. The viscosity number (η_{sp}/c) of PHmBG.HCl, measured in three solvents of different polarities indicated by the dielectric constants (ε), viz. water (ε 80), DMSO (ε 47) and acetic acid (ε 6.13)/methanol (ε 32) (5/2, v/v), exhibited typical polyelectrolyte features as shown in *Figure 7*. The value of η_{sp}/c depended strongly on the solvents used and their polarity; the higher the dielectric constant, the higher was the value of η_{sp}/c and the greater was the increase of its value at lower polymer concentration.

The application of an empirical relationship based on a simple electrolyte solution[16]:

$$\frac{\eta_{sp}}{c} = \frac{A}{1 + B\sqrt{c}} + D$$

where c is concentration by weight, and A, B and D are empirical constants, was examined. It is supposed that A corresponds to a limiting viscosity number [η] and B is a measure of electrostatic interactions. Since D is usually much smaller than A^{16}, D can be neglected and the relationship can be expressed as

$$c/\eta_{sp} = 1/A + B/A.\sqrt{c}$$

A plot of $1/(\eta_{sp}/c)$ against $\sqrt{c}$, based on data in *Figure 7*, gave poor linearity in poor agreement with the above empirical equation, as shown in *Figure 8*. The intercept values of $1/A$ varied, and did not show the clear link with [η] reported in some cases[17]. In contrast, B/A increases with decreasing dielectric constant of the solvent and corresponds to the electrostatic interactions in solution. This suggested that the above empirical equation was too simple, presumably since the viscosity data were obtained at very low concentrations and were very different from those for a simple electrolyte.

Adding a small amount of water to the DMSO solution significantly affected the viscosity, as shown in *Figure 9*. Rapid increase of η_{sp}/c was observed on the
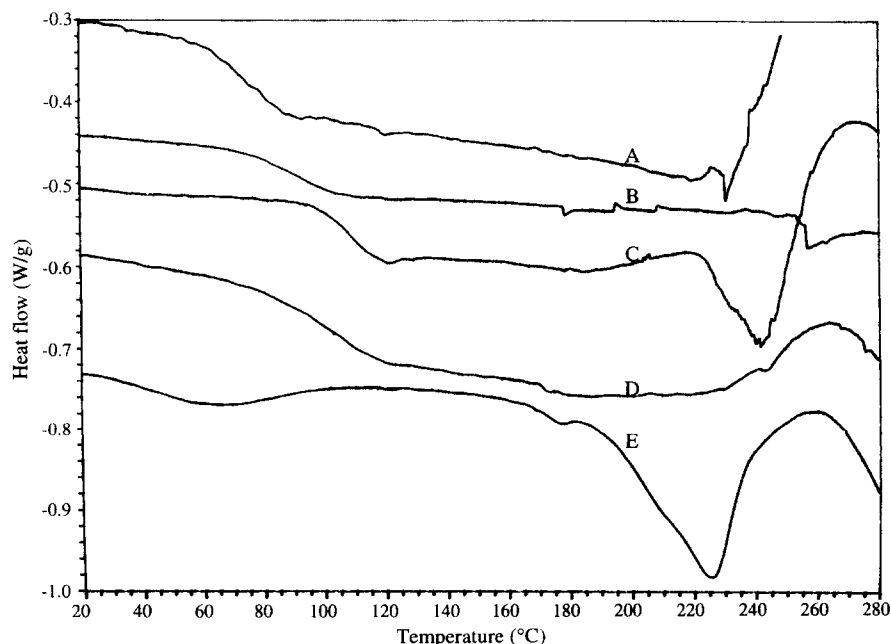

Figure 5 D.s.c. curves of polybiguanides: (A) PHmBG.HCl (made in the melt); (B) P(Hm/Pip)BG.2HCl (7/1) (melt); (C) P(Hm/Pip)BG.2HCl (1/1) (in NMP); (D) P(Hm/Ph)BG.2HCl (3/1) (melt); (E) P(Hm/Ph)BG.2HCl (1/1) (in NMP)
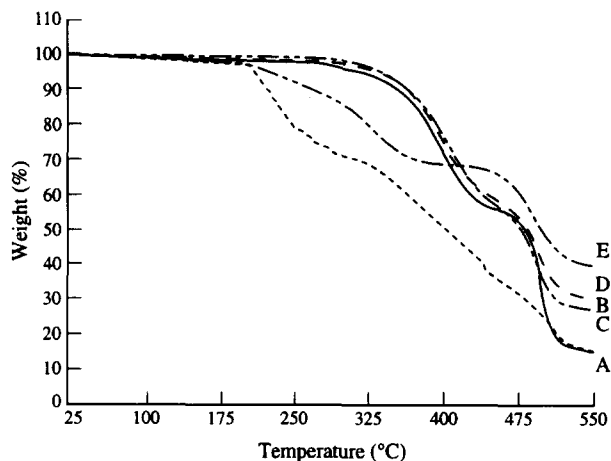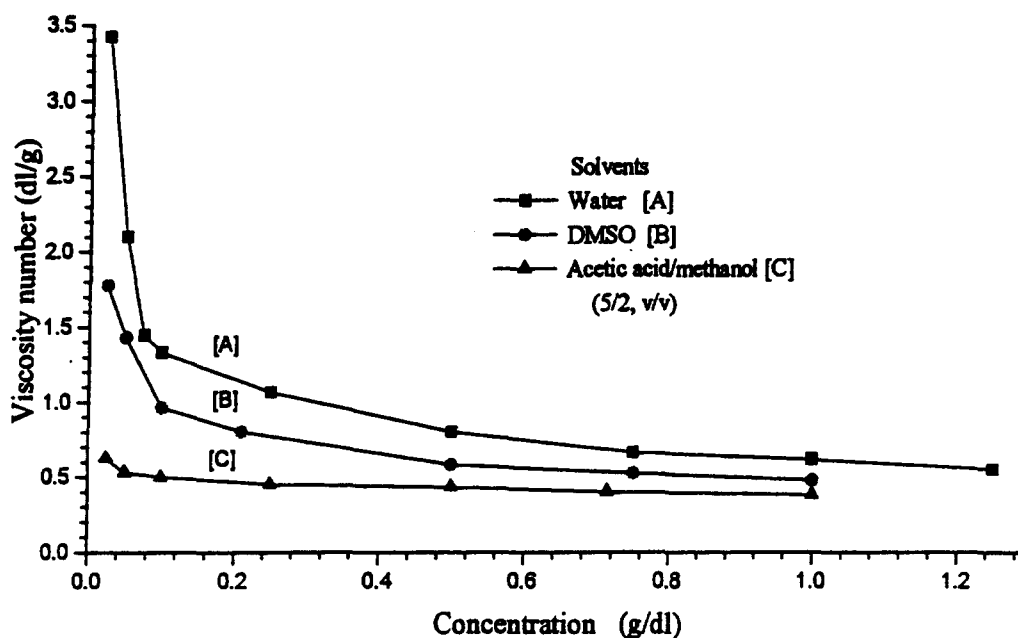
Figure 6 T.g.a. curves of polymers: (a) PHmBG.HCl (made in the melt); (b) P(Hm/Pip)BG.2HCl (7/1) (melt); (c) P(Hm/Pip)BG.2HCl (1/1) (in NMP); (d) P(Hm/Ph)BG.2HCl (3/1) (melt); (e) P(Hm/Ph) BG.2HCl (1/1) (in NMP)

The solution viscosities of PHmBG.HCl samples obtained by Method II were determined at a constant concentration (0.05 M) of an added salt in water, DMSO and acetic acid/methanol (5/2, v/v) and are shown in *Figure 11*. As a result of the effect of the salt on the polyelectrolyte, η_{sp}/c at quite a low concentration of salt exhibits solution behaviour similar to that of non-ionizable polymers and reduces with decreasing concentration of PHmBG.HCl. The viscosity numbers plotted against weight concentration of the polymers were nearly linear and tended to a limiting value at $c \to 0$ (i.e. a limiting viscosity number $[\eta]$). This agrees with the Huggins equation, $\eta_{sp}/c[\eta] + k'[\eta]^2 c$.

However, the value of $[\eta]$ depends not only on the polymer–solvent–temperature system, but also on the nature and the concentration of the added simple salt.

Molecular weight. The homopolymer made by Method I had a g.p.c. polystyrene-equivalent $\bar{M}_w$ of 2.5×10^5 in *m*-cresol. The apparent $\bar{M}_w$ values for

Figure 7 Effect of different solvents on viscosity number, η_{sp}/c, of PHmBG.HCl

first addition of a little water. This is attributed to changes in polarity of the solvent. It indicates that the viscosity number in organic solvents is very sensitive to the presence of water and shows that even a little absorbed water in the hygroscopic polyelectrolyte may cause a marked variation in the viscosity number in a non-aqueous solvent. The importance of keeping the polymer or solvent dry before and during viscosity measurements cannot be too strongly emphasized.

When a simple salt was added to an aqueous solution, η_{sp}/c fell due to the reduced net charge of the polyions and the mutual repulsion of the like charges on the chains. The rate of decrease of η_{sp}/c in aqueous solution fell quickly with the first addition of NaCl, and then showed a slow reduction at a concentration above 0.05 M (*Figure 10*). Further addition of salt led to the separation of PHmBG.HCl. The addition of LiCl to DMSO solution did not affect η_{sp}/c as significantly as addition of NaCl to water.

polyelectrolytes obtained using g.p.c., like the values of η_{sp}/c, are strongly dependent on the ionic strength of the solution, especially in aqueous solution[18]. It is difficult to judge how valid this $\bar{M}_w$ value is for a polybiguanide in *m*-cresol ($\varepsilon \approx 12$), which, although of relatively low polarity, may still give appreciable chain expansion in dilute solution.

Solution stability of PHmBG.HCl. The aqueous solution stability of PHmBG.HCl was investigated by measuring the variation of the solution viscosity number with time in a solution and by elemental analysis and i.r. spectroscopy. In the case of a neutral solution, the solution viscosity did not change on boiling under reflux for 10 h, and the PHmBG.HCl, after precipitation from the boiled aqueous solution by acetone, showed no significant difference in elemental analysis or in its i.r. spectrum compared with the initial sample. In acidic (pH 2.5) and alkaline (pH 13.5) solutions, the initial η_{sp}/c values were
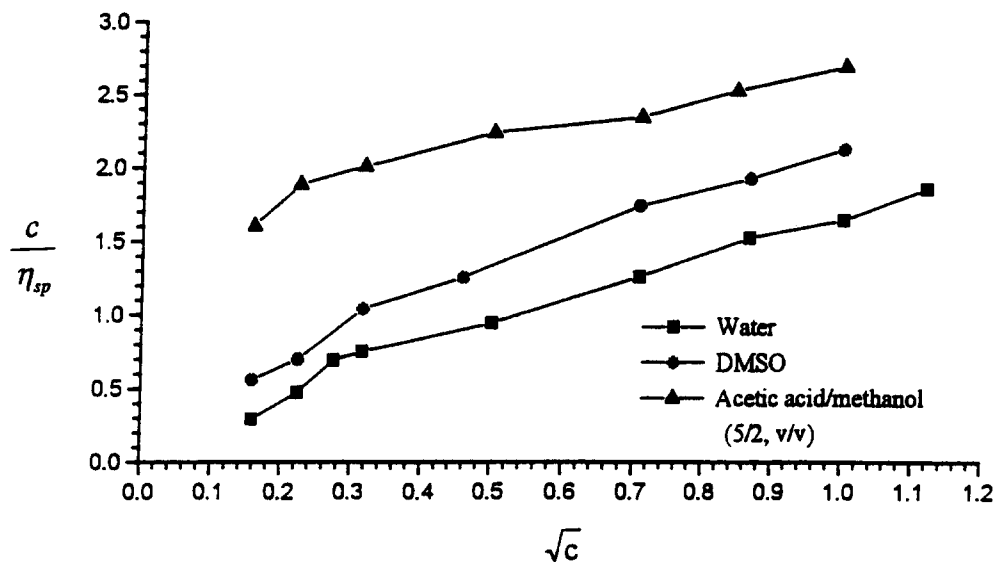
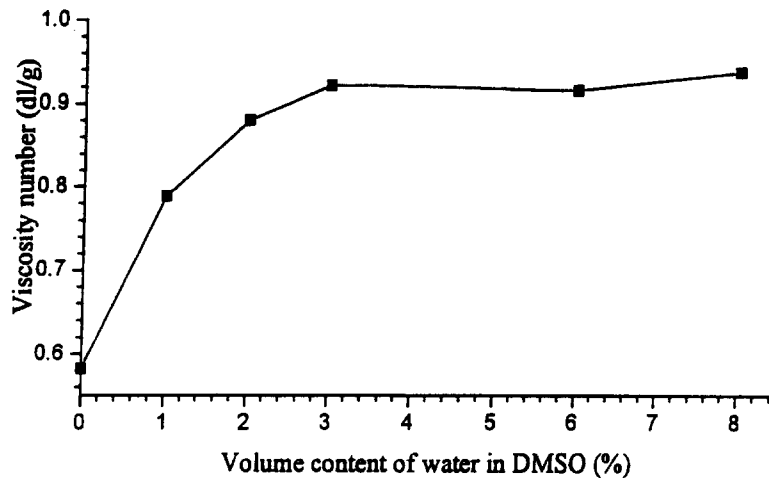**Figure 8** Effect of different solvents on viscosity of PHmBG.HCl

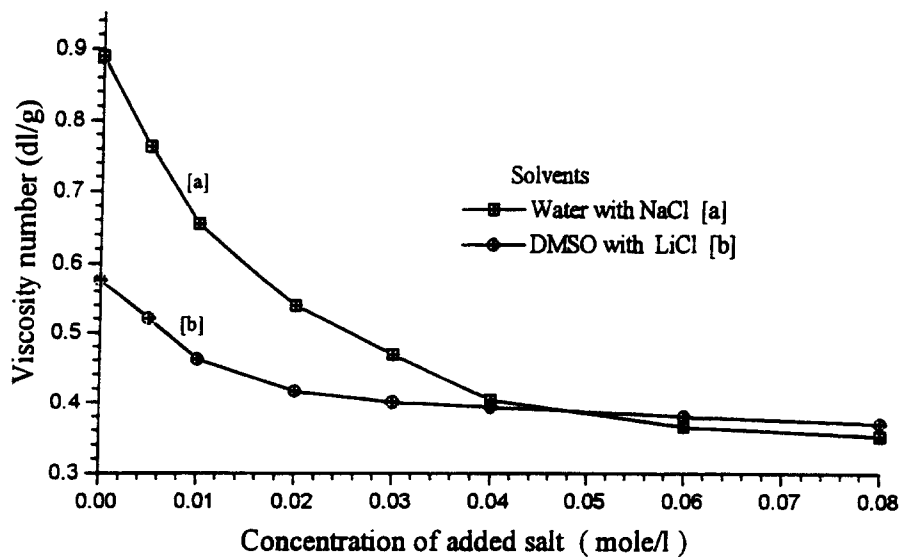**Figure 9** Effect of water content of DMSO on viscosity number, η_{sp}/c, of PHmBG.HCl at $0.5\,\mathrm{g\,dl^{-1}}$

Figure 10 Effect of added salts on viscosity number, η_{sp}/c, of PHmBG.HCl in water and in DMSO at $0.5\,\mathrm{g\,dl^{-1}}$ (Method I)
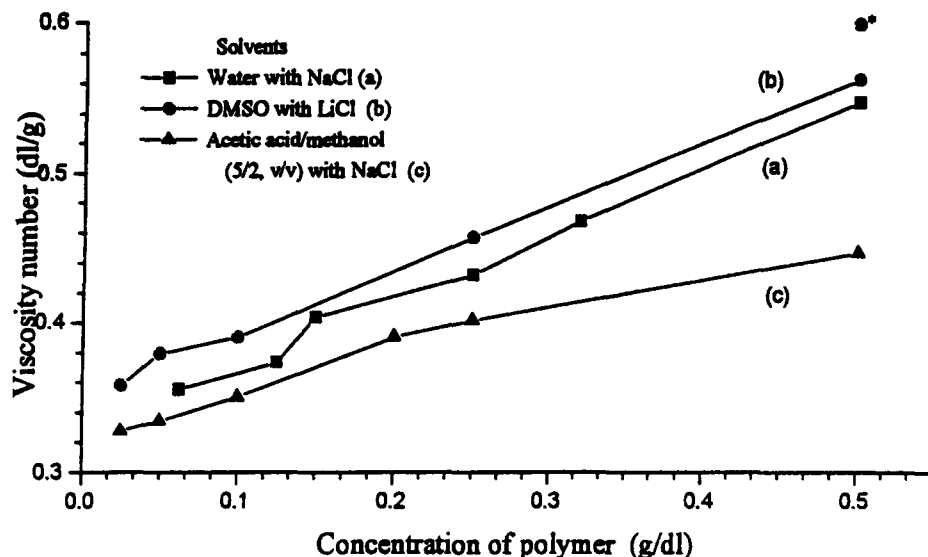
Figure 11 Effect of added salts (0.05 M) on viscosity number, η_{sp}/c, of PHmBG.HCl in various solvents (Method II). *Before the addition of salts

much lower; in one case the added ions (H^+ and Cl^-) suppressed the extension of the positively charged chains and in the other the OH^- ions converted PHmBG.HCl into its free base form, which no longer carries positive ions. However, the solution viscosities of the homopolymer did not decline on standing for 24 h at room temperature at these pH values (*Table 2*). The homopolymer therefore exhibits good stability in hot neutral aqueous solutions and over a wide range of pH values at room temperature.

Complexes with metallic ions

PHmBG and its hydrochloride formed insoluble coloured complexes on reaction with some transition metallic ions: rose-red complex with Cu^{2+}; vermilion-red with Cr^{3+}; off-white with Fe^{3+} and yellow with Ni^{2+}. The properties and stability of the polymeric copper(II) complexes were investigated. When a blue $CuCl_2$ aqueous solution was added to an aqueous solution of PHmBG or PHmBG.HCl, a rose-red colour appeared at first, and a precipitate formed on further addition. It was found by elemental analysis of the rose-red precipitate that two biguanide groups were associated with each copper(II) ion. The same ratio has been found for the complexes formed by nonpolymeric dibiguanides[19]. In the polymers, this association should involve biguanide groups in different chains chelating with the same copper(II) ion, and this will lead to a highly cross-linked structure.

These rose-red copper complexes of PHmBG.HCl, once precipitated, did not redissolve in distilled water. However, they dissolved in dilute acid solutions (H_2SO_4 or HCl at pH < 2.5) with loss of the characteristic colour of the complexes, and in EDTA solution forming a blue solution by transfer of copper(II) ions from the polymeric complex to EDTA. Colourless copper-free PHmBG.HCl was precipitated by adding NaCl to both these solutions and purified by dissolving the solid in methanol, filtering and evaporating the solvent. No changes in η_{sp}/c or in the i.r. spectra of the PHmBG.HCl samples were noted compared with the original.

The rose-red soluble aqueous complexes of PHmBG and its hydrochloride showed an absorption maximum at 515–535 nm in spectrophotometry whose intensity

was found to be linear with the concentration of the complexes. An aqueous solution containing four biguanide units per copper(II) ion, i.e. half the biguanide units complexed with copper, was adjusted to pH 8 by adding PHmBG. Its absorbance at 520 nm was measured at intervals during the addition of strong HCl, until the pH value of the solution reached pH 2, and then while adding 6 N NaOH up to pH 12.8, as shown in *Figure 12*. The polymeric biguanide itself did not give any absorptions at visible wavelengths, and the blue–green colour of copper(II) ions had an absorption maximum above 700 nm.

Solutions decolorized by acidification became rose-red again at about pH 3.0 on adding NaOH solution, and remained coloured above that pH. A lag in the change point of the colour at pH between 2.5 and 3.0 was noted. The stability of the polymeric biguanide copper complex was higher than that of the corresponding simple biguanide complex, which has been reported to be stable only above pH 5[20]. There is reference in the literature to formation of a blue mono-copper complex at pH 4–5 by some non-polymeric biguanides[20], but the polybiguanides did not form a blue complex or show signs of any absorption at 650–670 nm at any pH from 2 to 12.5.

The precipitated copper complex of PHmBG exhibited slight birefringence which disappeared at about 170°C on reaching the glass transition. The complex expanded in volume with bubbling when heated at 240°C and turned black at 320°C. The i.r. spectrum of the complex exhibited an additional peak at 1250 cm^{-1} compared with that of PHmBG.HCl.

CONCLUSIONS

Comparison of five methods of synthesizing poly(hexamethylenebiguanide dihydrochloride) shows that melt

Table 2 Stability of PHmBG.HCl in aqueous solution

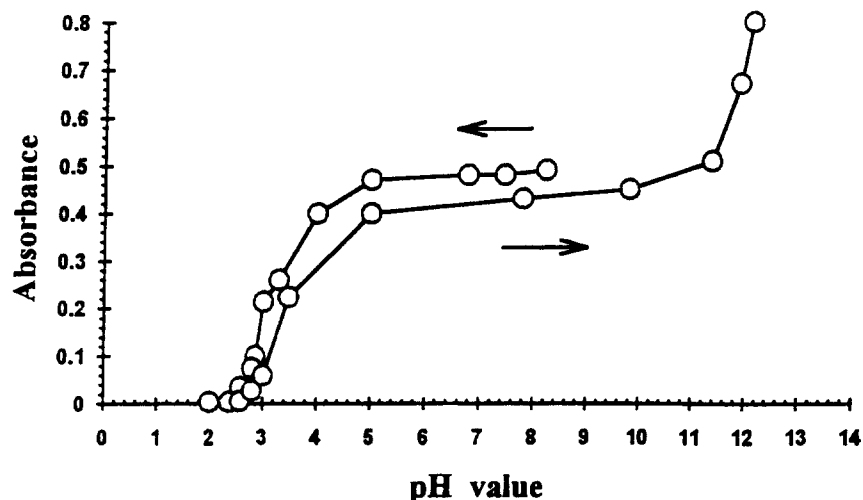| Treatment	pH	η_{sp}/c (dl g^{-1})	pH	η_{sp}/c (dl g^{-1})	pH	η_{sp}/c (dl g^{-1})
Initial value	6.8	0.86	2.5	0.62	13.5	0.41
24 h room temp.		0.87		0.63		0.40
10 h, boil		0.90		—		—

Figure 12 Absorbance of copper complex at 520 nm at various pH values

and solution polyaddition of hexamethylene biscyano-guanidine with hexamethylenediamine give products with the highest solution viscosities. Under the conditions used, melt polymerized products contain significant concentrations in the chain of melamine units, which act as branching sites and in some cases lead to cross-linking. There are indications that the preparative reaction is reversible. The polymer exhibits good stability in hot neutral aqueous solutions and in acidic and alkaline aqueous solutions at room temperature.

The polymeric salt behaves as a polyelectrolyte in aqueous solution, and to a less marked extent in other dipolar solvents.

The polymer forms insoluble coloured complexes with a variety of metallic cations. The insoluble copper(II) complex contains two biguanide groups per copper (II) ions. A soluble coloured complex is stable over a wide pH range.

Copolymers in which 50% of the hexamethylenedi-amino groups are replaced by *p*-phenylenediamino or piperidino groups are best prepared by solution poly-addition using the cyclic diamine dihydrochlorides as reactants.

ACKNOWLEDGEMENTS

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