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Synthesis and Properties of Hydrophilized Tertiaryamine Polymers Obtained by Graphitide-Initiated Anionic Copolymerization of a *N,N*-Disubstituted Aminothiirane with Oxiranes

J. Huguet[a]; J. Coudane[a]; M. Vert[ab]; N. Manolova[c]; I. Rashkov[c]
[a] URA CNRS 500 LSM INSA-Rouen, Mont-Saint-Aignan Cedex, France [b] CRBA-URACNRS 1465, Faculté de Pharmacie, Montpellier, France [c] Institute of Polymers Bulgarian Academy of Sciences, Sofia, Bulgaria

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SYNTHESIS AND PROPERTIES OF HYDROPHILIZED TERTIARYAMINE POLYMERS OBTAINED BY GRAPHITIDE-INITIATED ANIONIC COPOLYMERIZATION OF A *N-N*-DISUBSTITUTED AMINOTHIIRANE WITH OXIRANES

J. HUGUET, J. COUDANE, and M. VERT*†

URA CNRS 500, LSM
INSA-Rouen, BP 08
76131 Mont-Saint-Aignan Cedex, France

N. MANOLOVA and I. RASHKOV

Institute of Polymers
Bulgarian Academy of Sciences
1113, Sofia, Bulgaria

ABSTRACT

New functional aliphatic copolymers have been synthesized by anionic ring opening polymerization of *N*-methyl-*N*-sec-butyl-*N*-(thiirane-2-ylmethyl) amine (Me-sBu,ESA) with either trimethylsilyl protected glycidol (TMSGE) or ethylene oxide (EO) using potassium graphitide KC_{24} or sodium metal as initiators. Whenever TMSGE was present, TMSGE chain growing was perturbed by transfer reactions. Branched TMSGE homopolymers and Me-sBu,ESA/TMSGE copolymers were obtained with both the expected 1-3 polyglycidol and the unusual 1-4 poly(3-hydroxyoxetane) enchainments, as shown by ^{13}C NMR. Copolymers of different compositions obtained by varying the Me-sBu,ESA/TMSGE feed composition from 85/15 to 35/65 or the Me-sBu,ESA/EO one from 76/24 to 64/36 were amorphous and random, as shown by DTA and ^{13}C NMR studies. Copolymers with less

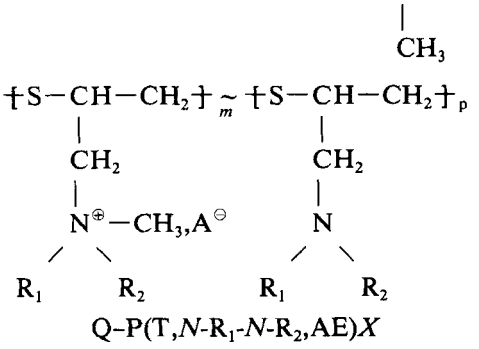
†Present address: CRBA-URACNRS 1465, Faculté de Pharmacie, 15 Ave Charles Flahault, 34000 Montpellier, France.

than 20% of EO or TMSGE-derived units in the chain were soluble in water at pH < 4. Potentiometric titration curves showed the presence of a plateau (for the degree of neutralization $\bar{\alpha}$ in the range $0.15 < \bar{\alpha} < 0.9$) due to phase separation, as in the case of Me-sBu,ESA homopolymers. Copolymers with more than 50% of TMSGE units in the chain were soluble in water at pH < 7 and exhibited normal potentiometric titration curves with pH increasing progressively in the range $0.15 < \bar{\alpha} < 0.9$. From these data, it is concluded that TMSGE- or EO-derived hydrophilic repeat units are unable to promote globular structure, in contrast to quaternary ammonium repeat units.

INTRODUCTION

During the last decades, a growing interest has been devoted to drug carrier systems designed for transport and selective delivery of drugs to specific sites of action or receptors. Carriers based on liposomes, microemulsions, and micro- and nanoparticles are presently regarded as worthwhile potential systems.

A few years ago, we introduced a new carrier system composed of globular macromolecules of the partially quaternized poly[thio-1-(*N*-R_1-*N*-R_2-amino methyl) ethylene]-type, or Q-P(T, *N*-R_1-*N*-R_2.AE)*X*, (Q-P (TDAE)*X* for $R_1 = R_2 = -C_2H_5$ and Q-P),Me-sBu,AE)*X* for $R_1 = -CH_3$ and $R_2 = -CH(CH_3)-C_2H_5$):



Q-P(T,*N*-R_1-*N*-R_2,AE)*X*

where *X* is the percentage of quaternary ammonium groups ($X = 100\,m/(m + p)$) and $A^{\ominus}$ the counterion [1, 2]. Q-P(T,*N*-R_1-*N*-R_2,AE)*X* copolymers were obtained by methylation of some of the tertiary amine pendent groups present in the parent homopolymers synthesized by ring-opening polymerization of the corresponding *N*-R_1-*N*-R_2 aminothiirane monomers [3].

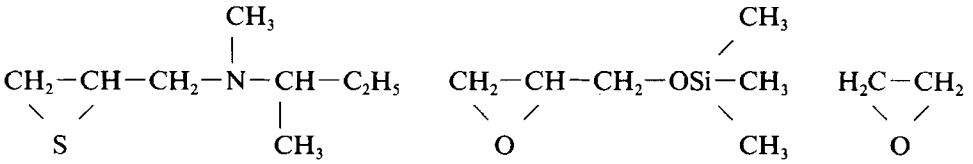
When they are deprotonated, polydibasic Q-P(T,*N*-R_1-*N*-R_2,AE)*X* molecules with $X < 25$ collapse in aqueous solution at pH ~ 7 and take on a globular compact conformation stabilized by permanent quaternary ammonium charges, which are located at the surface and maintain the monomolecular globules dispersed in water. The core of these globules ($\phi \sim 80$ Å) is presently considered as mostly composed of the hydrophobic tertiary amine residues. Protonation of these tertiary amine residues by addition of an acid causes a globule-to-coil cooperative transition [1, 2]. The first theoretical approach to such a phenomenon was recently derived on the basis of weakly charged hydrophobic polyelectrolytes [4].

It was further shown that the core of the globules is able to dissolve and

entrap water-insoluble lipophilic molecules such as steroids. This temporary entrapment was called molecular encapsulation by comparison with the physical entrapment within particles [5, 6]. Radiolabeled ^{75}Se nor-cholestenol molecularly encapsulated in Q-P(TDAE)12 globules was administered to rabbits via intramuscular and intravenous routes. A slow release of the steroid with no toxicity was found after i.m. injections [7]. In contrast, a high toxicity due to lung capillary bed embolization was observed immediately after i.v. injections and was assigned to the presence of the cationic charges which triggered proteins and blood cells aggregation [8].

From these data, globular Q-P(TDAE)*X* copolymers appeared to be acceptable drug carriers from a physicochemical viewpoint. However, the blood coagulation observed after i.v. administration precluded any real therapeutic use. Therefore, we decided to look for macromolecular compounds that had similar physicochemical properties but were less toxic. In a first approach, it was decided to replace the quaternary ammonium groups by nonionogenic hydrophilic repeat units in polyaminothiirane chains [9].

This paper reports the synthesis of new functional copolymers resulting from the ring opening copolymerization of *N*-methyl-*N*-sec-butyl-*N*(thiirane-2-ylmethyl)-amine (Me-sBu,ESA), with glycidol and ethylene oxide (EO) selected as suitable hydrophilic comonomers for replacing hydrophilic quaternary ammonium residues present in Q-P(T,*N*-R_1-*N*-R_2,AE)*X* copolymers. Under the conditions of anionic polymerization, the primary alcohol group present in glycidol had to be protected. Trimethylsilylation leading to trimethylsilylglycidyl ether (TMSEG) was used because the silylated protecting group can be readily cleaved under mild acidic conditions [10, 11].



Homopolymerizations and copolymerizations were achieved by a graphite intercalation compound KC_{24} known to be able to polymerize ethylene oxide [12] and by sodium mirror, which can lead to high-molecular-weight polyaminothiiranes from *N*-R_1-*N*-R_2,ESA monomers [2, 3]. Structural characteristics of the resulting polymeric compounds were investigated by ^{13}C NMR in organic solvent and in acidic aqueous solution where tertiary amine residues are protonated. Physicochemical properties in aqueous solutions, especially the protonation-deprotonation reaction on the recovered copolymers, were discussed on the basis of the molar fraction of the comonomers units incorporated in polymer chains.

EXPERIMENTAL

Reagents

Potassium graphitide KC_{24} was prepared by the Herold method (13) from Madagascar graphite with particle sizes of 100–125 μm.

Monomers

Me-sBu,ESA was prepared by reaction of potassium thiocyanate on corresponding amino-oxirane, whereas TMSGE was obtained by reaction of chlorotrimethylsilane on glycidol according to methods described in Refs. [3] and [14], respectively. Both monomers were vacuum-distilled twice and stored under vacuum in polymerization tubes equipped with breakseals. Both compounds were 99.8% pure according to gas chromatography.

Ethylene oxide was dried over calcium hydride and *n*-butyl lithium.

Homo- and Copolymerizations

Homo- and copolymerizations with KC_{24} were carried out in bulk in sealed apparatus under high vacuum (10^{-4} mmHg) according to the experimental procedure already described for ethylene oxide [12]. KC_{24} was introduced first, followed by the monomers. The mixture was then allowed to stir in a thermostated oil bath for the polymerization time. In the case of TMSGE homopolymerizations, the polymerized mixture was dissolved in 30 cm^3 of methanol acidified by concentrated HCl (1 cm^3). The graphite was removed by filtration. Polyglycidol was precipitated by acetone as a colorless, rubbery product. In the case of aminothiirane homo and copolymerizations, the polymerized mixture was dissolved in 40 cm^3 toluene. The polymer solution was then filtrated to eliminate the initiator residue. The filtrate was concentrated under vacuum up to 20 cm^3. The polymer was precipitated by adding 200 cm^3 methanol. After two successive solubilizations in 15 cm^3 toluene followed by precipitation with 150 cm^3 methanol, the recovered polymer was turned to its polyhydrochloride form by addition of dry gaseous HCl into the last methanol mixture containing the precipitated polyamine. HCl was allowed to bubble up to complete dissolution of the polymer. After solvent removal, the polyhydrochloride was dried under vacuum at 80°C for 24 h. For runs 8 and 9 (Table 2), 20 cm^3 methanol was added to the 20 cm^3 polymer toluene solution. Copolymers were obtained as white powders by precipitation into 300 mL acetone under stirring.

Homo- and copolymerizations with Na mirror were carried out in bulk under high vacuum (10^{-6} mmHg) according to the procedure using breakseal-equipped tubes similar to those described for thiiranes polymerization [15]. TMSGE and Me-sBu,ESA monomers were distillated once separately on a sodium film and collected on the same sodium film during the second distillation. Experimental details for polymerization as well as for polymer isolation were the same as reported above for the copolymerization.

Techniques

Gas chromatograms were recorded with a Perkin Elmer 8500 gas chromatograph equipped with a 12AQ2/BP1 capillary column by using 0.03 μL (or mm^3 monomer samples.

FTIR spectra were obtained from thin films prepared from benzene solutions casted on an Irtran 2 plate. The IR spectra were recorded by using a Perkin Elmer 1760 FTIR spectrophotometer.

100 MHz ^{13}C NMR spectra were recorded at 30° or 50°C by a Brucker AM 400 spectrophotometer.

Intrinsic viscosity [η] was measured in 0.1 *M* aqueous KCl at 25°C on an automatic viscometer.

Molecular weights of acetylated polyglycidol were evaluated by size-exclusion chromatography in dioxane using a Waters apparatus equipped with μ-styragel columns and refractive index detection. Polystyrene standards were used for calibration.

Molar masses of aminothiirane homopolymers in their hydrochloride form were evaluated in 0.1 *M* KCl using a Laser Light Scattering Chromatix KMX 6 apparatus.

Differential Thermal Analysis (DTA) thermograms were recorded with a Perkin Elmer DSC 4 microcalorimeter using samples of about 10 mg and a heating rate of 10°C min^{-1} from − 50° to 150°C. Indium was used to standardized temperatures.

Potentiometric titrations curves were recorded using a Tacussel ionoprocessor II. Aliquots of polyamine in the hydrochloride form *m* (in mg) were dissolved in 50/50 0.05 *M* aqueous KCl/acetonitrile mixture (30 cm^3) and titrated by KOH. From the volume *v* (in cm^3) of KOH needed to reach the potential wave, one deduced m_1, the weight of aminothiirane hydrochloride in the sample ($m_1 = v \times 10^{-3} \times 195.5$), and then, *Xp*, the molar fraction of the comonomer repeat unit from: $Xp = M_1 (m - m_1)/M_1 (m - m_1) + M_2 m_1$, M_1 and M_2 being the molar weights of comonomer repeat units.

RESULTS AND DISCUSSION

Homopolymerization of TMSGE

The anionic homopolymerization of TMSGE was performed in bulk on sodium mirror or in the presence of potassium graphitide KC_{24} (Table 1). Polymers were obtained as protected polyglycidols and were converted to polyglycidol by acid

TABLE 1. Homopolymerization of TMSGE and Me-sBu,ESA, Initiated by KC_{24} or by Sodium Films

Run	Monom.	Init.	[Init] (mol%)	Temp. (°C)	Time (days)	Yield (%)	[η][a] (100 $cm^3 g^{-1}$)	MW $\times 10^{-3}$	I
1	TMSGE	KC_{24}	1.5	80	5	25	0.21	—	—
2	TMSGE	KC_{24}	1.5	70	10	16	0.19	39[b]	1.66
3	TMSGE	Na	3.0	50	7	30	0.36	58[b]	1.27
4	Me-sBu,ESA	KC_{24}	1.5	Room	3	85	1.65	300[c]	—
5	Me-sBu,ESA	Na	≃3.0	Room	3	90	1.8	325[c]	—

[a][η] as determined in 0.1 *M* KCl on free glycidol or on the hydrochloride form of the tertiary amine polymer.

[b]By SEC in dioxane on the acetylated polyglycidol.

[c]By SALLS in 0.1 *M* KCl on the hydrochloride form of the tertiary amine polymer.

hydrolysis in methanol. The resulting polymers were colorless elastomers ($T_G \sim -8°C$) soluble in water and in methanol but insoluble in acetone and in aromatic solvents. It was not possible to determine directly molecular weights on polyglycidols because of their insolubility in the organic solvents generally used for SEC analyses. Thus, hydroxyl groups were acetylated by means of an excess of acetylchloride. Acetylated polymers were soluble in dioxane in which determinations of molecular weights were achievable (Table 1). Polyglycidols were obtained with very low yields, although the values of intrinsic viscosities $[\eta]$ in 0.1*N* KCl, which ranged from 0.2 to 0.36 x 100 $cm^{-3} \cdot g^{-1}$, indicated significant molecular weights. Polymerization rates and degrees of conversion were always much lower than those reported for polymerizations initiated by R_3Al/H_2O/acetylacetone [16] or $ZnEt_2/H_2O$ initiator systems [10, 17]. Raising the polymerization temperature to 80°C did not increase the polymerization rate or the yield.

In Fig. 1, comparison is made of the ^{13}C NMR spectra of the polyglycidols prepared by TMSGE homopolymerizations using KC_{24} and sodium mirror. For the sake of comparison, the spectrum of a polyglycidol obtained by homopolymerization of TMSGE initiated by 1:1 $ZnEt_2/H_2O$ is presented on the same figure. The ^{13}C NMR spectrum polyglycidol polymerized with 1:1 $ZnEt_2/H_2O$ (Fig. 1a) was similar to those of polyglycidols obtained from racemic TMSGE with an aluminum chelate [16] or from a partially optically active TMSGE with 1:1 $ZnEt_2/H_2O$ [17]. Three main signals were observed at 81.8, 71.0, and 62.8 ppm, which were respectively assigned to the C_2, methine and C_1, methylene carbon atoms of the main chain and to the C_3, methylene pendant carbon atom which bears the hydroxyl group. In contrast, the ^{13}C NMR spectra of glycidol polymerized with KC_{24}- or Na-initiated systems appeared much more complex. In both cases, additional peaks were detected in the 60- to 80-ppm region (Fig. 1b and 1c). Similar additional peaks were also observed in the case of KOH or ter-BuOK-initiated polymerization of R or RS trimethylsilyl glycidyl ether [18]. In this case, the extra peaks were correlated to transfer reactions leading to two types of highly branched enchainments, i.e., a 1-3 polyethylene oxide-type, $-[O-\underset{|}{CH}-CH_2]-$, and a 1-4 poly(3-hydroxyoxetane)-type, $-[O-CH_2-\underset{|}{CH}-CH_2]-$, and to diol-type end-groups. Transfers were identified as simple rearrangements of the usual propagating secondary alkoholate species to primary ones due to nucleophilic displacement of the $SiMe_3$ group according to the following scheme [18]:

$$-CH_2-\underset{|}{CH}-O^{\ominus} \rightleftharpoons -CH_2-\underset{|}{CH}-OSiMe_3$$
$$\qquad\qquad\quad CH_2OSiMe_3 \qquad\qquad\quad CH_2O^{\ominus}$$

Comparison of the ^{13}C NMR spectra of graphitide and sodium mirror-derived homopolymers with the spectra of polyglycidols initiated by the 1:1 $ZnEt_2/H_2O$ complex (Fig. 1a) or by KOH [18] showed that polymerization led to spectra with features comparable to those of KOH-initiated polyglycidol and not to that obtained by the modified organometallic initiators. ^{13}C NMR assignments were made with respect to four basic repeat units, namely (1-3)N, (1-3)B, (1-4)N according to the following scheme:

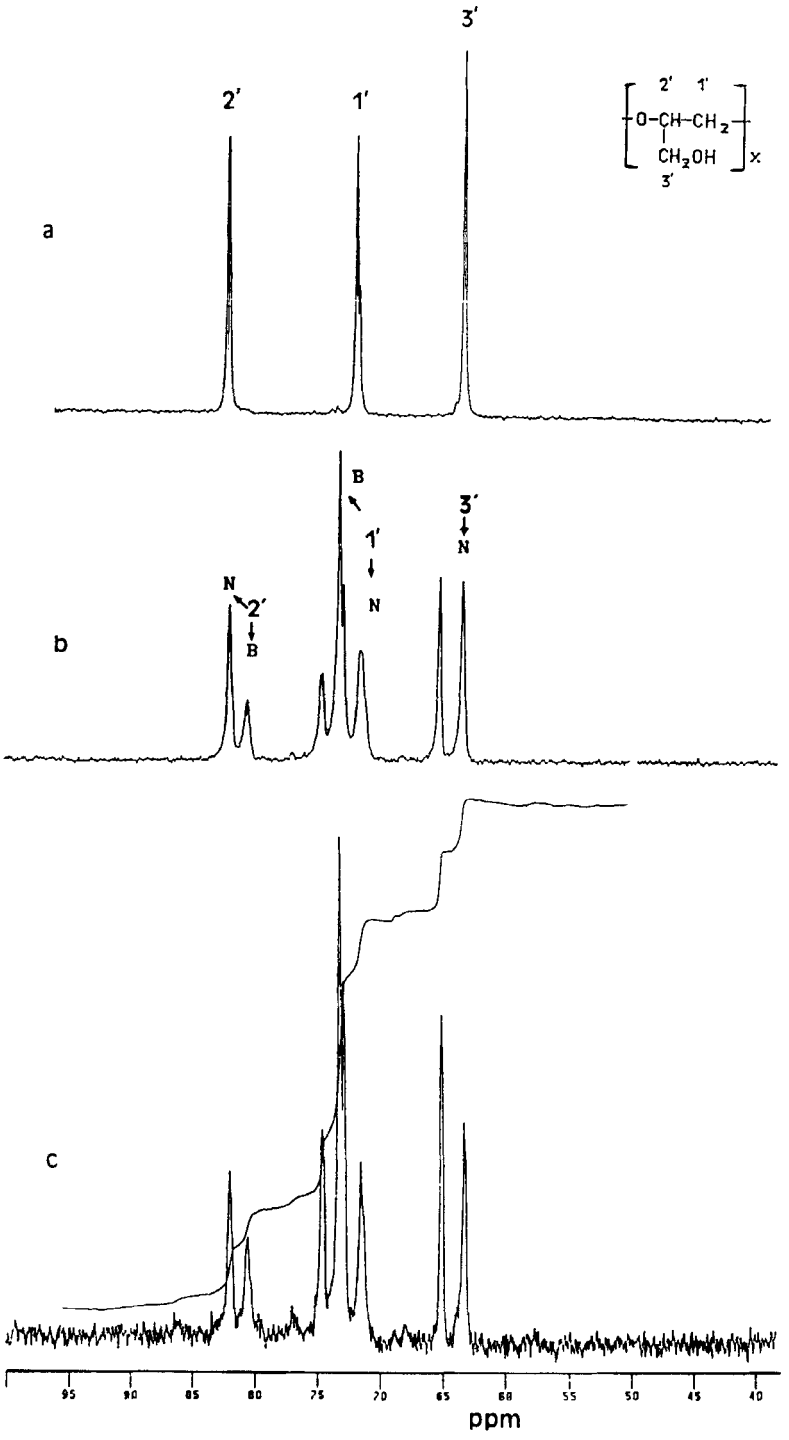
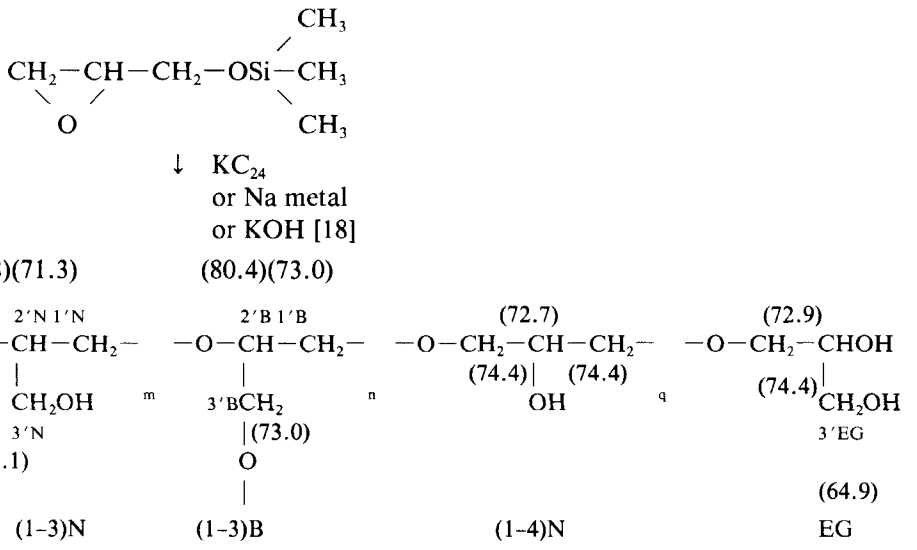


FIG. 1. ^{13}C NMR spectra in D_2O (at 30°C) of polyglycidol obtained by TMSGE polymeration initiated by (a) 1 : 1 $ZnET_2/H_2O$; (b) KC_{24}; (c) sodium mirror.



N for normal chain unit
B for branched structures
EG for diol-type end-groups

For example, the ^{13}C NMR spectrum of the glycidol-containing homopolymers obtained by KC_{24}-initiation exhibited three signals located at 71.3, 81.8,. and 63.1 ppm, which corresponded to the $C_{1'N'}$, $C_{2'N'}$, and $C_{3'N'}$ carbon atoms of the normal (1-3)N enchainment found in 1:1 $ZnEt_2/H_2O$-initiated polyglycidols (Fig.1a and Ref. 17). The two peaks detected at 80.4 and 73.0 ppm corresponded to the $C_{2'B}$ methine carbon atom and to the $C_{1'B}$ and $C_{3'B}$ methylene carbon atoms of the (1-3)B branches present in KOH-initiated polyglycidols [18]. The three signals located at 74.4, 72.9, and 64.9 ppm were matched to the CH_2, CHOH, and CH_2OH carbon atoms of pendent diol groups as referred to in Ref. [18]. The extra peak detected at 72.7 ppm was shown to be a CH by off-resonance decoupling studies and was assigned to the CHOH carbon atom of the (1-4)N enchainment. The existence of diverse units is probably due to the use of a polymerization temperature ranging from 50° to 80°C. At such temperatures, intramolecular migrations of $SiMe_3$ protecting group to the nearest propagating oxyanion are favored.

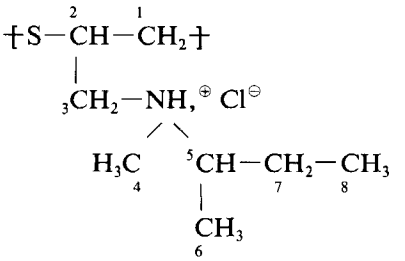
The proportion of the four different typical enchainments was directly deduced from peak integrations of some of the carbon atoms detected in the NMR spectra. For example, in the case of KC_{24}-initiated polymerization (Fig. 1b), the proportion of (1-3)N-type repeat units, ca. 56%, was deduced from the relative weights of $C_{2'N}$ peak located at 81.8 ppm and of CHOH repeat units located at 72.7 and 72.9 ppm. From the $C_{2'B}$ and $C_{2'N}$ peaks located at 80.4 and 81.8 ppm, respectively, one can deduce that (1-3)B-type repeat units accounted for 35%, (1-4)N-type accounting for 9% by difference. On the other hand, the relative intensities of the 62.8 ppm resonance ($C_{3,N}$), which corresponded to pendent (1-3)N CH_2OH groups and those of the 64.9 ppm resonance ($C_{3'EG}$), corresponding to (1-3)B pendent CH_2OH carbon atoms, were almost equal. Therefore, it is concluded that macromolecular chains contained a high proportion, ca. 50%, of pendent diol end-groups, a finding in good agreement with the existence of many short branches.

In the case of the Na-initiated TMSGE polymerization, similarly located resonances were detected but with slightly different relative intensities, which led to 48% of (1-3)N-type, 46% of (1-3)B-type, and 6% of the (1-4)N-type enchainments.

Homopolymerization of Me-sBu,ESA

Me-sBu,ESA homopolymerization initiated by KC_{24} gave rise to yields and intrinsic viscosities (Table1) similar to those reported for polymerization on sodium mirrors [2], thus showing that high-molecular-weight polyaminothiiranes can be readily obtained using graphitide-type initiators. Me-sBu,ESA-derived tertiary amine polymers were soluble in benzene and toluene, but precipitated in methanol. For the sake of preservation, they were turned to their polyhydrochloride form (P(T,Me-sBu,AE),HCl), which can be kept in a desiccator for a long time without degradation[3].

The ^{13}C NMR spectrum of the KC_{24}-derived P(T,Me-sBu,AE) (run 4) in the free amine form in $CDCl_3$ is shown in Fig. 2a and that of the hydrochloride form in D_2O in Fig. 2b. Correlation between the different peaks and the various carbon atoms was done by off-resonance decoupling and by comparison with the resonance of the corresponding polyaminothiirane obtained with the $ZnEt_2/H_2O$ initiator system [19].



In $CDCl_3$, the tertiary amine polymer obtained from KC_{24} and that prepared by $ZnEt_2/H_2O$ showed similar spectra [19]. For both compounds, C_1 and C_2 main chain carbon atoms as well as C_7 and C_8 side chain methylene and methyl carbon atoms appeared as singlets at 35.1, 46.4, 26.4, and 11.6 ppm, respectively. The C_3, C_4, and C_5 atoms, which are directly attached to the nitrogen atom, gave rise to two well-resolved doublets located at 58.5-57.5, 37.3-35.9, and 60.9-60.2 ppm, respectively, because of the presence of two asymmetrical centers in each repeat unit. The same situation was observed for the C_6 carbon atom bonded to the side-chain chiral C_5, which gave a doublet at 13.4-13.25 ppm.

As shown in Fig. 2b, the protonation of tertiary amine groups caused dramatic changes in the local environment of the nitrogen atoms. In particular, C_3. C_4, and C_5 signals split into well-resolved multiple resonances and moved to 57.8-55.1, 41.5-39.3, and 67.8-64.3 ppm, respectively. In the same manner, C_6 and C_7 carbon atoms gave rise to well-separated triplets, which were shifted to 15.7-13.9 and 27.0-25.0 ppm, respectively. Only C_8 gave a singlet located at 12.2 ppm. On the other hand, main-chain C_1 and C_2 appeared as complex resonances at 44.0 and 35.7 ppm, respectively, in agreement with some stereosensitivity. However, decomposition of the fine structures in terms of triads was not reasonably feasible.

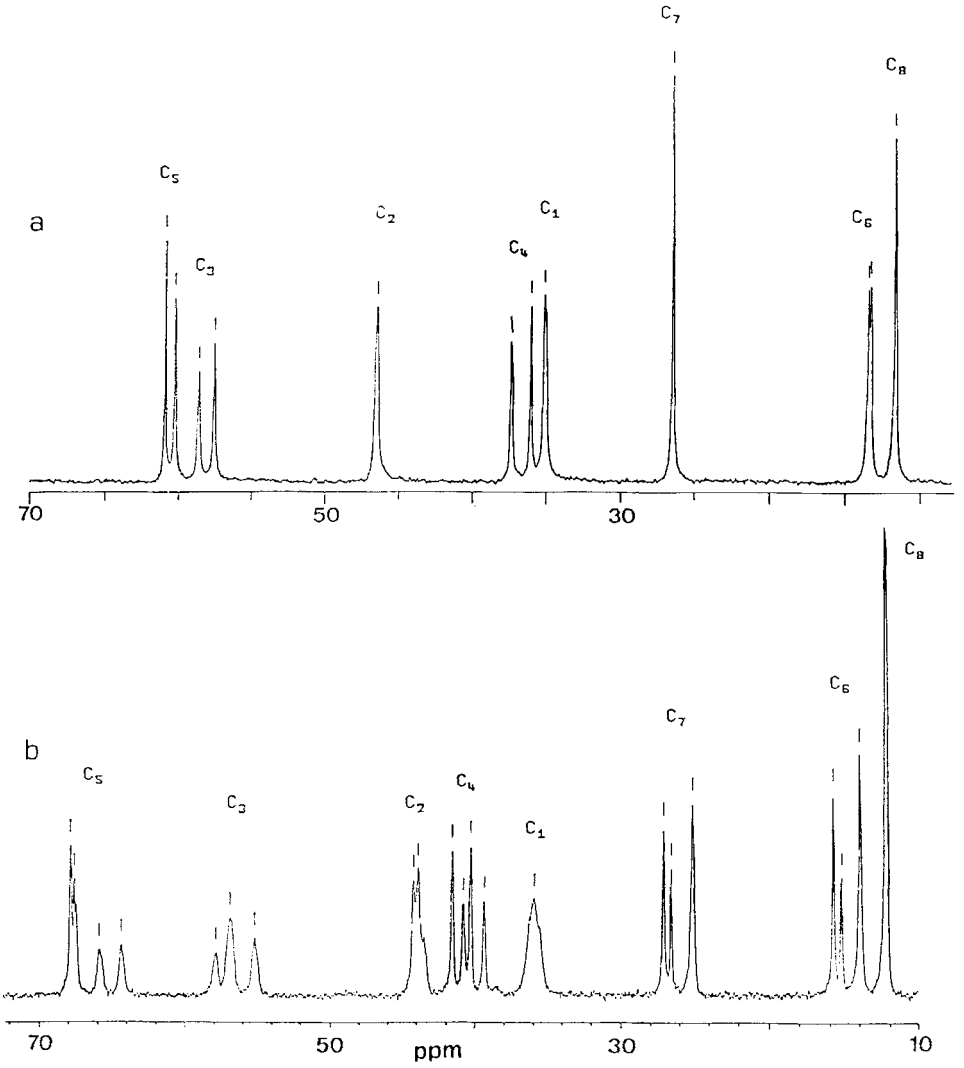


FIG. 2. ^{13}C NMR spectra (at 30°C) of P(T,Me-sBu;AE) obtained with KC_{24} initiator: (a) free amine form in $CDCl_3$; (b) hydrochloride form in D_2O.

These features were common to all P(T,Me-sBu,AE),HCl regardless of the initiator. It is noteworthy that the hydrochloride forms showed splittings of some resonances, especially those surrounding protonated nitrogen atoms. It is likely that the electric repulsion between the protonated tertiary amine groups leads to extended and highly solvated polymer chains. The charged nitrogen atoms are preferentially exposed to the aqueous environment, whereas their hydrophobic aliphatic substituents interact with the backbone, limiting the free rotations of these substituents. This limitation, which generates different local configurational and electrostatic environments, could account for the observed peaks splittings.

Copolymerization

KC_{24}-initiated copolymerizations of Me-sBu,ESA with TMSGE or EO comonomers were carried out in bulk at 70–75°C under different conditions (Table 2). In the case of Me-sBu,ESA/TMSGE mixtures, yields and viscosities decreased as the content of TMSGE increased in the feed. For Me-sBu,ESA/EO mixtures, copolymers were obtained in high yields but with low viscosities. Under their amine form, all the Me-sBu,ESA/TMSGE copolymers were soluble in toluene and dioxane and insoluble in methanol, in agreement with the behavior of the P(T,Me-sBu,AE) tertiary amine homopolymer. In contrast, those polymers derived from feeds with glycidol contents higher than 45% (runs 9 and 10) were insoluble in toluene and dioxane and soluble in methanol, as in the case of homopolyglycidol. Copolymers IR spectra exhibited vibrations characteristic of the Me-sBu,ESA homopolymers, with additional bands corresponding to the contribution of the comonomer. For example, the IR spectrum derived from the 50/50 Me-sBu,ESA/TMSGE monomer mixture showed two broad bands at 3400 and 1120 cm^{-1}, respectively corresponding to ν_{-OH} and ν_{C-O} vibrations of glycidol repeat units, whereas those derived from the Me-sBu,ESA/EO 64/36 mixture showed a weak band located at 1120 cm^{-1}, corresponding to the ν_{C-O} vibration of ethylene oxide units.

The ^{13}C NMR spectrum of the copolymer derived from Me-sBu,ESA and EO (run 12) is shown in Fig. 3 as a typical example. This spectrum exhibited signals comparable to those of the corresponding homopolythiirane (Fig. 2), with two well-resolved additional peaks at 74.25 and 71.9 ppm. These extra resonances were attributed to CH_2 carbon atoms C_t' of ethylene oxide units, thus proving the exis-

TABLE 2. Copolymerizations of Me-sBu,ESA with TMSGE or EO Initiated by Potassium Graphitide KC_{24}

Run	[Init] (mol%)	Temp. (°C)	Time (days)	Yield[a] (%)	$[\eta]$[b] (100 $cm^{-3}g^{-1}$)
[Me-sBu,ESA]/[TMSGE]					
6	85/15	1.4	75	3	71	0.37
6 bis	85/15	1.5	70	12	76	0.30
7	70/30	1.4	75	3	59	0.17
8[c]	66/33	~3.0	50	15	51	0.36
9	52/48	1.9	75	3	50	0.06
10	35/65	1.5	75	3	52	0.045
[Me-sBu,ESA][EO]					
11	76/24	1.5	70	4	70	0.14
12	64/36	1.47	70	4	80	0.24

[a]Calculated for the hydrochloride form of aminothiirane unit and expressed in mass % with respect to monomer weights.

[b]$[\eta]$ was determined on hydrochloride form of aminothiirane unit in 0.1 *M* aqueous KCl.

[c]Initiated by Na mirror.

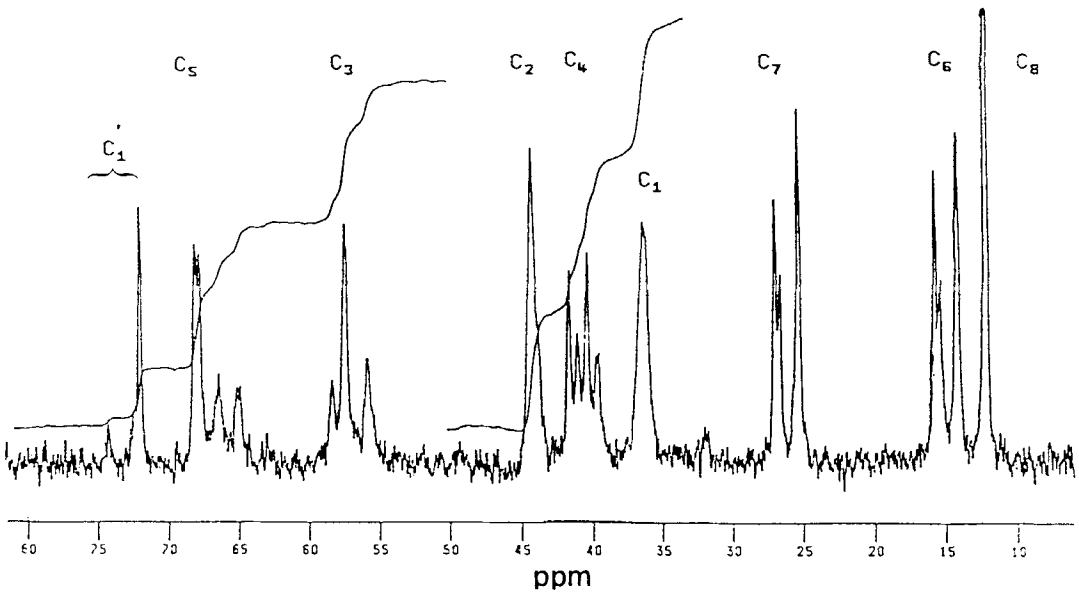


FIG. 3. ^{13}C NMR spectrum in D_2O (at 30°C) of initial 64/36 Me-sBu,ESA/EO copolymer.

tence of a random distribution of the $-[O-CH_2-CH_2]$ and $-[S-CH-CH_2]-$ comonomer repeat units. From the relative intensities of these peaks, it was deduced that 20% m_1m_1 and 80% m_1m_2 dyads were present in copolymer chains (m_1 being the ethylene oxide repeating unit and m_2 the aminothiirane one).

The ^{13}C NMR spectra of copolymers 6, 7, and 10 (Table 2), which were synthesized from Me-sBu,ESA/TMSGE monomers, are shown in Fig. 4. These NMR spectra exhibited resonances typical of Me-sBu,ESA-containing polymer chains. They also showed peaks that are characteristic for KC_{24}-derived polyglycidol chains, a finding that confirms the occurrence of transfer reactions similar to those reported for TMSGE anionic homopolymerization [18]. It is noteworthy that the NMR peaks, especially those of ether units, were composition-dependent. On the other hand, peaks corresponding to C_1 and C_2 of aminothiirane repeat units broadened when the relative amount of Me-sBu,ESA in the feed decreased (Fig. 4c). The broadening of these resonances might be due to small chemical shifts corresponding to changes in sequence distributions suggesting a random copolymerization. The presence of random structure is supported by DTA data obtained for copolymers in which the thioether-based repeat units were in the free amine form. DTA thermograms of these copolymers showed only one glass transition temperature. Copolymers T_G values varied between the T_G values of homopolymers and depended on the composition. For example, T_G of compounds 6 and 7 (Table 2) were −27°C, i.e., similar to the value characteristic of the polyamine ($T_G \sim -28$°C). Those corresponding to compounds 9 and 10 with higher amounts of TMSGE shifted to −20°C.

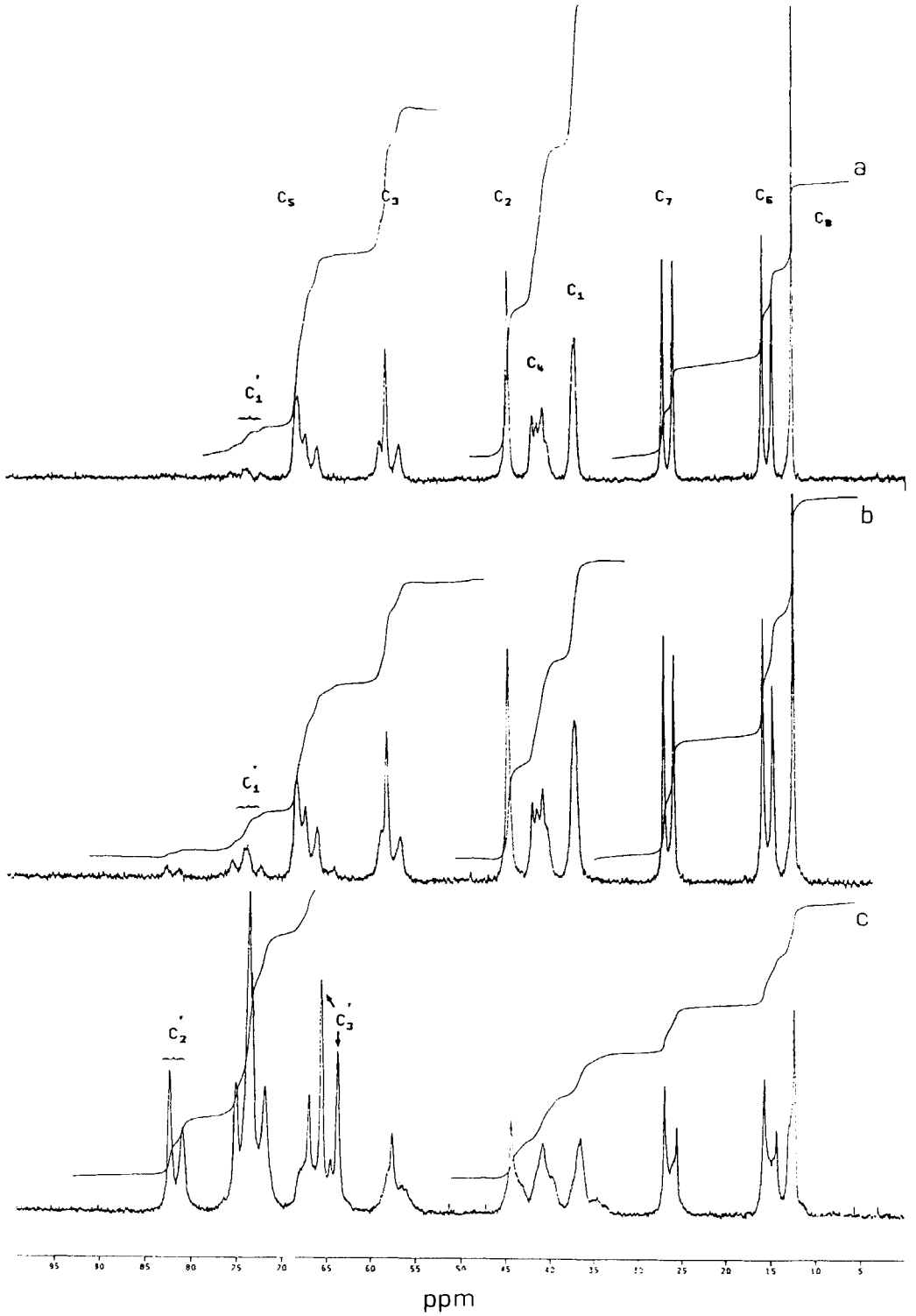


FIG. 4. ^{13}C NMR spectra of Me-sBu,ESA/TMSGE-derived copolymers prepared from different initial monomers compositions: (a) 85/15; (b) 70/30; (c) 35/65.

Determination of Copolymer Compositions

The copolymer gross compositions were evaluated from ^{13}C NMR spectra and from potentiometric titrations curves of their amine salt form. Table 3 presents the *Xi*, *Xp*, and *Xc* values, where *Xi* is the initial molar fraction of TMSGE or EO monomers in mixtures, *Xp* and *Xc* being the same ratio as deduced from potentiometric titration curves and from ^{13}C NM spectra. respectively.

Xp and *Xc* values agree well. However, some discrepancies are observed between *Xp*, *Xc*, and corresponding *Xi*. Therefore, it is likely that both copolymerizations do not proceed at random, but no further investigation of this point has yet been made.

Physicochemical Properties of Copolymers in Aqueous Solutions

The aim of this study was to detect whether glycidol or ethylene oxide can give rise to an effect similar to that of the quaternary ammonium groups insofar as globule formation is concerned. Accordingly, the hydrochloride forms of the different copolymers were titrated with a KOH solution. Resulting titration curves are presented in Fig. 5. Copolymers with ca. 80% repeat units derived from Me-sBu,ESA (runs 6, 7, 8, 11, and 12 in Table 3) behaved similarly. The pH remained almost constant in the $0.15 < \bar{\alpha} < 0.85$ region ($\bar{\alpha}$ being the degree of neutralization of the protonated tertiary amine groups, $\bar{\alpha} = [KOH]_{added}/[>NH,^{\oplus}Cl^{\ominus}_{total})$, as usually observed for partially quaternized Q-P(T,*N*-R_1-*N*-R_2,AE)X [1, 2]. However, the plateau of pH was due to precipitation, as in the case of the corresponding homopoly(aminothiiranes), and not to a coil-to-globule transition. Indeed, macroscopic precipitation was observed above $\bar{\alpha} \sim 0.2$. Copolymers with more than 50% TMSGE-derived units behaved as expected for typical polyelectrolytes with no buffering effect (pH plateau), and precipitation was observed above $\bar{\alpha} \sim 0.9$ only.

None of the Me-sBu,ESA/TMSGE and Me-sBu,ESA/EO copolymers exhibited both buffering effect and water solubility considered typical of the presence of

TABLE 3. Molar Fractions (*X*) of the Ether Repeat Units in Me-sBu,ESA/TMSGE and Me-sBu,ESA/EO Copolymers

run	*Xi*[a]	*Xp*[b]	*Xc*[c]
6	0.15	0.12	0.14
7	0.30	0.19	0.20
8	0.33	0.22	0.24
9	0.48	0.51	0.54
10	0.65	0.58	0.60
11	0.24	0.14	0.12
12	0.36	0.17	0.18

[a] *Xi* initial.

[b] *Xp* determined by potentiometric titration in 0.05 *M* aqueous KCl/acetonitrile solution (V/V; 50/50).

[c] *Xc* determined by ^{13}C NMR.

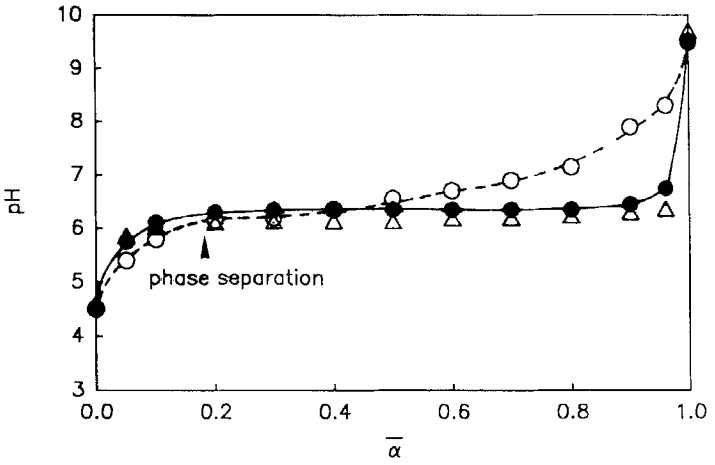


FIG. 5. Effect of copolymer compositions on neutralization curves of the hydrochloride derivatives of copolymers (Cp = 1. 10^{-2} $M.l^{-1}$ in 50/50 0.05 M KCl/acetonitrile solution, $\bar{\alpha}$ being the degree of neutralization of hydrochloride form of the tertiary amine group). With 80% of Me-sBu,ESA-derived repeat units: ●——●, runs 6,7,8; △——△, runs 11 and 12; with more than 50% TMSGE: ○- - -○, runs 9 and 10.

globular macromolecules as referred to the case of partially quaternized polyaminothiiranes. Indeed, copolymers having 20% of EO- or glycidol-derived hydrophilic moieties were hydrosoluble in acidic medium only and precipitated when 10% of *N*-repeat units were deprotonated, i.e., at pH about 6.5, whereas 5% of methylated residues was enough to solubilize Q-P(T,Me-sBu,AE)5 in water regardless of pH. Therefore, neutral hydrophilic residues appear as unable to stabilize a globular microphase as charged quaternary ammonium ones do.

CONCLUSION

The present work shows that polymerization of Me-sBu,ESA with protected glycidol (TMSGE) using KC_{24} as an initiator gives rise to copolymers bearing pendent tertiary amine and alcohol groups. A transfer reaction of trimethysilyl groups between primary and secondary alcohol groups with isomerization leads to branched systems. The copolymers from Me-sBu,ESA/TMSGE or Me-sBu,ESA/EO monomers are soluble in water in the protonated form only and are insoluble at neutral regardless of the composition of the copolymer chains. Finally, this work shows that it is not possible to stabilize tertiary amine polymer chains in a globular state by introducing neutral hydrophilic repeat units. It also seems essential that a suitable amount of electrostatic charges provided by partial *N*-alkylation be present, as in the case of Q-P(*N*-R_1-*N*-R_2)X.

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