Triblock and Radial Star-Block Copolymers Comprised of Poly(ethoxyethyl glycidyl ether), Polyglycidol, Poly(propylene oxide) and Polystyrene Obtained by Anionic Polymerization Initiated by Cs Initiators

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Summary: The anionic polymerization of ethoxyethyl glycidyl ether (EEGE) initiated by cesium alkoxide was studied. The ring-opening polymerization of EEGE in the presence of cesium alkoxide of 1-methoxy-2-ethanol does not involve any side reactions. The presence of an additional alcohol leads to a significant increase of the initiator efficiency.

Aqueous solutions of poly (ethoxyethyl glycidyl ether) (PEEGE) exhibit lower critical solution temperature (LCST), and the polymer solubility in water is extremely sensitive to its MW. Two novel types of block copolymers based on PEEGE were synthesized: triblock-copolymers of ABA (A'BA') structure, where A is the PEEGE block, A' polyglycidol (PG) and B the polypropylene oxide (PPO) block, and A_2S (A'_2S) and A_4S (A'_4S) heteroarm stars, where S is the polystyrene block.

The synthesis of the ABA block was performed by polymerization of EEGE initiated by bi-functional PPO/Cesium alkoxide macroinitiator. The PEEGE blocks were converted into PG blocks by successful cleavage of the ethoxyethyl group.

Polystyrene/PEEGE and polystyrene/PG three- and five- heteroarm star copolymers were synthesized by a coupling reaction between well-defined chain-end-functionalized polystyrenes carying dendritic benzyl bromide moieties with living anionic polymers of PEEGE with one cesium alkoxide terminal group. The coupling reaction proceeds quantitatively without any side reactions, and thus series of star-branched polymers can be systematically synthesized. Polystyrenes with two or four PG arms have been obtained after the cleavage of the protecting group. The compact structure of these multi-arm star polymers and their amphiphilic character leads to the formation of nanoparticles in aqueous solution with rather uniform size distribution and a mean diameter of 15 nm.

Keywords: block- and heteroarm star copolymers; poly(ethoxyethyl glycidyl ether); polyglycidol; uniform nanoparticles

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Introduction

Glycidol (2,3-epoxy-1-propanol) is a highly reactive monomer bearing both epoxy and hydroxyl functional groups. Both its composition and structure favor the primary to secondary transitions of the alkoxide active sites, as well as the intermolecular transfers during base-initiated polymerization.[1] The polymerization of glycidol has attracted considerable research interest in the past decade. The propagation may evoke side reactions. Both the anionic[2] and cationic[3,4] polymerizations of this monomer lead to hyper-branched polyethers with low polydispersity. In order to obtain linear polymers of glycidol, its hydroxyl group has to be protected by suitable protecting groups. Spassky et al.[5] have shown that ethoxyethyl glycidyl ether obtained in a reaction of glycidol with ethyl vinyl ether can be polymerized by an anionic mechanism. The protective ethoxyethyl group can then be easily removed thus yielding a linear polyglycidol, which is a highly hydrophilic water-soluble polymer due to the polyether structure with a hydroxyl group in each structural repeat unit. We have recently found that low molecular weight PEEGE of Mn = 2000 g/mol is water-soluble below 11°C.[6] Novel high molecular weight copolymers of ethylene oxide and glycidol or EEGE were obtained by anionic precipitation polymerization by using the calcium amide-alkoxide initiating system.[7]

It is well known that materials made of water-soluble block-copolymers consisting of hydrophobic and hydrophilic blocks or of blocks of varying hydrophobicity are being widely applied in the medical field and in processes requiring the stabilization of emulsions or dispersions. The high interest in these copolymers arises mainly from their unique solution and associative properties, which are a consequence of their molecular structure. An essential requirement for many applications is the precise control of the copolymer structure in terms of its composition, molecular weight, molecular weight distribution, and the hydrophilic/hydrophobic balance.

The purpose of this work is to prepare a family of block-copolyethers with a wide range of hydrophobicity. The investigation is focused on EEGE and propylene oxide (PO) polymerization and copolymerization initiated by cesium alkoxide as well as on the coupling of living poly(ethoxyethyl glycidyl) ether chains with functionalized polystyrene.[8] Thus two novel classes of block-copolymers based on PEEGE were synthesized: triblock-copolymers of ABA (A'BA') structure, where A is the PEEGE block, A' is polyglycidol and B is the polypropylene oxide block, and A_2S (A'_2S) and A_4S (A'_4S) heteroarm stars (palm tree), where S is polystyrene block. In the course of this investigation we also gained insight into the mechanism of polymerization and the structure and properties of the aqueous solutions of the resulting block-copolymers. The micellization of these block-copolymers occurs because of two important factors: hydrophobicity of the polystyrene block and the ability of the PPO and the PEEGE blocks to undergo a temperature-induced phase separation from soluble to insoluble state as their aqueous solutions exhibit a lower critical solution temperature. Thus, depending on the solution temperature regime and the chemical modification via deprotection, almost identical block-copolymers can yield quite different species: double hydrophilic, amphiphilic and hydrophobic block-copolymers.

Experimental

Materials

All solvents were purified by standard methods. Poly(propylene glycol) 2000 purchased from Aldrich was vacuum dried.

Ethoxyethyl glycidyl ether (further referred to as protected glycidol) was synthesized from 2,3-epoxy-1-propanol and ethyl vinyl ether according to Fitton et al (9) and fractionated under reduced pressure. A fraction with purity exceeding 99.8 % (GC) was used. Cesium hydroxide monohydrate 99.5 % (Acros Organics) was used as received. 1-Methoxy-2-ethanol was purified by vacuum distillation.

Chain-end-functionalized polystyrene (PS) with two and four benzylbromide moieties was synthesized according to the procedure described previously.[8] The molecular mass characteristics of the polymer precursors are shown in Table 3.

Polymerization procedure

Preparation of poly(ethoxy ethyl glycidyl ether) with cesium alkoxide terminal group (PEEGEOCs)

Cesium hydroxide monohydrate (0.862 mmol) magnetically stirred in a reaction vessel equipped with argon and vacuum lines, was dissolved with an equimolar amount of 1-methoxy-2-ethanol added at 90°C. After stirring for 1.5 h, the system was switched to the vacuum line for 2 h at the same temperature. Then in some cases, an appropriate quantity of additional alcohol was added at 60°C. The polymerization of EEGE was performed by adding the desired amount of monomer to the fresh ROH/CsOH initiator mixture with the chosen molar amounts for the given experiment. The reaction tube was placed in an oil bath at 60 °C and the formation of PEEGE-OCs proceeded for 48 h. At the end of the reaction time, the growing chains were terminated by adding a large excess of methanol. The monomer was then rapidly stripped under vacuum to avoid further polymerization. The resulting polymer was purified by mixing with cation-binding resin followed by filtration.

Preparation of PEEGE-b-PPO-b-PEEGE block copolymers

The polymerization of EEGE initiated by activated PPO 2000 is described elsewhere.[6]

Coupling reactions

Preparation of PS(PEEGE)n (n = 2 or 4)

0.86 mmol of PEEGE-OCs, dissolved in THF, was added to 5 ml THF solution of 0.043 mmol of bi-functional or tetra-functional polystyrene. The reaction was kept for four weeks in ampoule at 50°C. $PS(PEEGE)_n$ was isolated after precipitation of its acetone solution in hexane.

Cleavage of ethoxyethyl protective groups

The procedure described below is similar to a recent method for deprotection of tetrahydropyranyl ethers.[10] A given amount of star-block-copolymer $PS\text{-}PEEGE_n$ or triblock-copolymer PEEGE-PPO-PEEGE was dissolved in MeOH/THF (85:15 v/v). Then $AlCl_3.6H_2O$ was added and the reaction was kept for one hour at room temperature. The EEGE:$AlCl_3$:MeOH molar ratio was 100:1:800. The reaction product was filtered through Hylfo Super Cel® (diatomaceous earth) and the solvents were evaporated under reduced pressure.

Analyses

Polymer samples were analyzed on a Waters size exclusion chromatography (SEC) system equipped with four Styragel columns with nominal pore sizes of 100, 500, 500, and 1000 Å and a differential refractometric detector. THF was used as the solvent at 40 °C at an elution rate of 1ml/min. Toluene was used as an internal standard for indication of elution volumes. Narrow molecular weight distribution polystyrene samples were used as standards for the molecular weight calibration.

The ^1H NMR spectra were recorded at 250 MHz on a Bruker WM 250, using $CDCl_3$, D_2O, CD3OD, and THF-d8 as solvents.

Cloud point (CP) transitions of 2% aqueous solutions of the samples were followed on a Specord UV-VIS spectrometer (Carl Zeiss Jena) switched to transmittance regime at $\lambda = 500$ nm using a thermostated cuvette holder. The solutions were initially equilibrated at 0 ° C before heating them gradually (0.1 °C).

To determine the critical micellization concentration (cmc) aqueous solutions (2 ml) of a block-copolymer in the concentration range from 0.2 to 20 g/l were prepared at 4°C. 20 µl of a 0.4 mM solution of 1,6-diphenyl-1,3,5-hexatriene (DPH) in methanol were added to each of the copolymer solutions. Solutions were incubated in the dark for 16 h at 20 °C. Absorbance spectra in the range of $\lambda = 300$ - 500 nm were recorded on a Specord UV-VIS spectrometer (Carl Zeiss, Jena) at 30°C. The main absorption peak characteristic of DPH solubilized in a hydrophobic domain was observed at 356 nm.[11]

PS-$(PG)_n$ heteroarm star block copolymer nanoparticles were prepared via the solvent exchange method[12] at room temperature. 5 ml of initial solution (10 g/l) of PS-$(PG)_n$ in MeOH/THF (3:1 v/v) was added drop-wise to 10 ml of vigorously stirred bi-distilled water. Then the organic solvents were evaporated under reduced pressure in order to obtain aqueous PS-$(PG)_n$ micellar solutions. Samples for transmission electron microscopy (TEM) were prepared by removing the solvent under vacuum. Measurements were made using a JEM 200 CX apparatus.

Results and discussion

Homopolymerization of EEGE

It is well known that the anionic polymerization of oxirane proceeds with a fast exchange between free hydroxylic compounds and propagating metal alcoxides. Hence, for a sufficiently long period of reaction time the total number of the growing chains corresponds to the overall amount of hydroxylic reactant introduced into the polymerization medium:

$P_n = \alpha[M]/n_{ROH}$,

where n_{ROH} is the number of moles of hydroxylic reactant introduced into the polymerization mixture, α is the monomer conversion, and P_n is the degree of polymerization. The full conversion of the free alcohol is due to the fact that the initial alcohol is a weaker acid than the chain-end alcohol derived from EEGE, thus its alkoxide is a stronger base and presumably more nucleophilic than the alkoxides at the growing chain ends.[13]

The polymerization reaction proceeds under appropriate experimental conditions (anhydrous reactants, Schlenk tube technique under inert atmosphere at 60°C) and with a very high degree of conversion, thus yielding polymers of comparatively low MW distribution (see Table 1). The in situ formation of the active species from $CH_3OCH_2CH_2OH$, and CsOH was studied by varying the relative amount of reactants. Particular attention was paid to the influence of the ROH/Cs^+ ratio on the molecular weight characteristics of the polymer. The efficiency of the MW control implies that the alkoxy end groups introduced in excess with regard to CsOH are all located at the α-end of the resulting macromolecules. Moreover, ^1H NMR analyses indicate almost quantitative conversion of the initial alcohol during the polymerization process.

Table 1- Polymerization of EEGE – 1.3 mmol $CsOH.H_2O$, T=60°C, reaction time = 48 h

Sample	$\frac{[Cs^+]}{[ROH]}$	Monomer (mmol)	Yield (%)	$\overline{Mn}$ Theor.	$\overline{Mn}$ (NMR)	$\overline{Mn}$ (SEC)	$\overline{Mw}/\overline{Mn}$ (SEC)	Initiator efficiency (f)
1	1/3	27.4	100	1026	980	1000	1.26	1.04
2	1/2	27.4	100	1539	1500	1500	1.23	1.02
3	1/1	13.7	100	1539	2400	2700	1.19	0.64
4	1/1	20.0	100	2246	3100	2800	1.17	0.73
5	1/1	27.4	100	3081	4800	5600	1.17	0.64
6	1/1	75.1	86	7253	8200	8000	1.30	0.88

$f = \frac{\alpha[M]}{[ROH].\overline{Pn}}$; α - yield, [M] - monomer quantity (mmol), [ROH] - alcohol quantity (mmol),

$\overline{Pn}$ - average degree of polymerization, determined by ^1H NMR

The presence of an excess of alcohol leads to a significant increase of the initiator efficiency, which exceeds the theoretical value of 1. The effective control of the molecular weight as well as the comparatively low molecular weight distribution and the high initiator efficiency of the cesium-alkoxide clearly show that the anionic ring-opening polymerization of EEGE does not involve any side reactions.

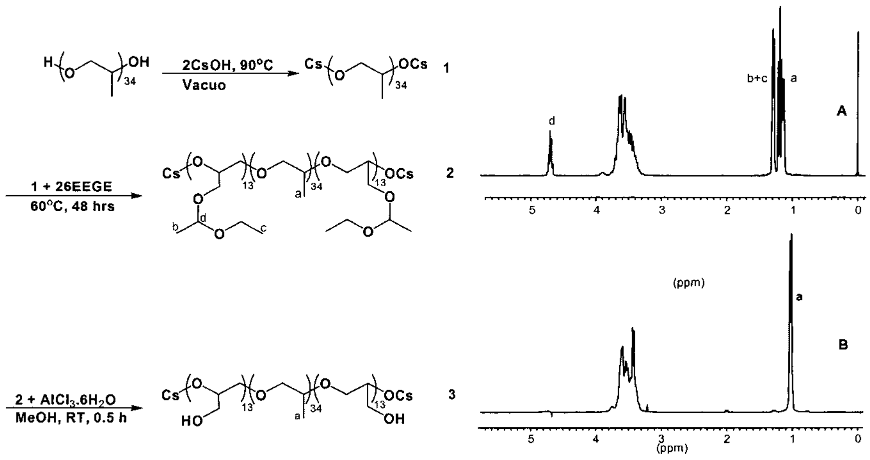
Synthesis and aqueous solution properties of PPO/PEEGE and PPO/PG triblock copolymers

Sequential copolymerization reactions were not performed until now, since it is more difficult to control the structure and the composition of the copolymer obtained. The synthesis begins with preparation of the PPO/Cesium alkoxide macroinitiator, by reacting PPO 2000 with CsOH, as described in Ref. 6.

PEEGE-b-PPO-b-PEEGE block-copolymer was obtained by a direct addition of the second monomer (EEGE) onto the bifunctional PPO macroinitiator. The reaction route is described in Scheme 1.

SEC measurements gave monomodal distribution (Figure 1), which implies that neither PPO nor PEEGE produced any detectable homopolymeric fractions during the copolymer synthesis. The PEEGE blocks were converted into PG blocks by successful cleavage of the ethoxyethyl protective groups (see Scheme 1, NMR spectra). Thus two ABA type tri-block copolymers were obtained with the same length of the blocks, the same central B block of PPO, but with quite different hydrophilic/hydrophobic balance. The results are summarized in Table 2.

The aqueous solution properties of the new block copolymers strongly depend on the role of the central PPO block. When PPO is introduced into water, it develops a hydration shell characterized by an enhanced structuring of the water molecules as evidenced by the negative entropy and enthalpy of mixing.[14] Despite the fact that PPO has the same backbone structure as PEO, an optimal water structure cannot be formed, since the methyl groups of the PO monomer units constitute a steric hindrance. Hence the strain of the water structure results in less hydrogen bond energy as compared to PEO. This is the reason why PPO is partially soluble in water only in the case of low molecular weight polymers. The smaller amount of hydrogen bond energy due to the strain of the water lattice also leads to a LCST property. By increasing the number of methyl groups along the chain it would be expected that the strain in the water structure would increase and thus lead to a less negative value for the heat of mixing and a lower precipitation temperature. Because of the LCST of the PPO block (PPO 2000 has LCST near 19°C) the two new ABA block copolymers are stimuli-responsive. They are water-soluble at temperatures near 0°C, but undergo a temperature induced phase separation from soluble to insoluble state under moderate heating.



Scheme 1. Synthesis of PEEGE-b-PPO-b-PEEGE and PG-b-PPO-b-PG block copolymers and their ^1H NMR spectra: A in $CDCl_3$ and B in D_2O

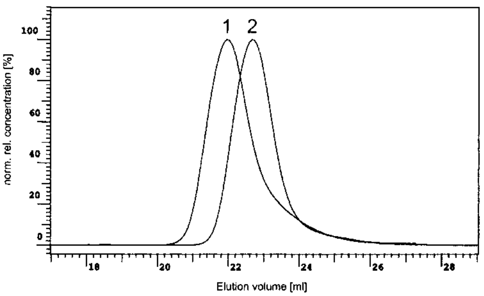


Figure 1. SEC traces of initial PPO macroinitiator (2) and PEEGE-b-PPO-b-PEEGE (1)

PEEGE-b-PPO-b-PEEGE triblock copolymer is built entirely of temperature-sensitive blocks. We have found that PEEGE is more hydrophobic than a PPO block with the same molecular weight.[6] When the central block is more hydrophilic, the tendency for self-assembly of the copolymers is largely weakened as compared to the inverse PPO-b-PEEGE-b-PPO architecture. In contrast, the PG-b-PPO-b-PG copolymer is expected to resemble the association behavior of the most popular nonionic surfactant PEO-b-PPO-b-PEO. At low temperature the aqueous solutions display a double hydrophilic-hydrophilic structure. By raising the temperature the structure becomes amphiphilic, with PPO acting as the hydrophobic block.

The clouding process of both ABA type block copolymers is represented by a sigmoidal curve shown in Figure 2. The thermally induced phase separation leads to a dramatic decrease of the transmittance. As can be seen in Table 2 the CP values and cmc for both structures are quite different. Obviously, the CP and the cmc values of the aqueous solutions of the precursor PEEGE-b-PPO-b-PEEGE are influenced predominantly by the PEEGE blocks. PEEGE, being more hydrophobic can decrease the cmc value. The clouding process in PG-b-PPO-b-PG depends on the PPO block.

Table 2. Characterization of ABA tri-blockcopolymers

Sample	$\overline{Mn}$ (NMR)	$\overline{Mn}$ (SEC)	$\overline{Mw}/\overline{Mn}$ (SEC)	CP (20 g/l) (°C)	cmc (g/l)
$EEGE_{13}PO_{34}EEGE_{13}$	5800	5500	1.2	8	0.12
$G_{13}PO_{34}G_{13}$				21	1.90

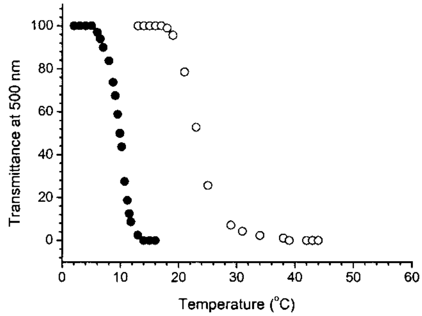
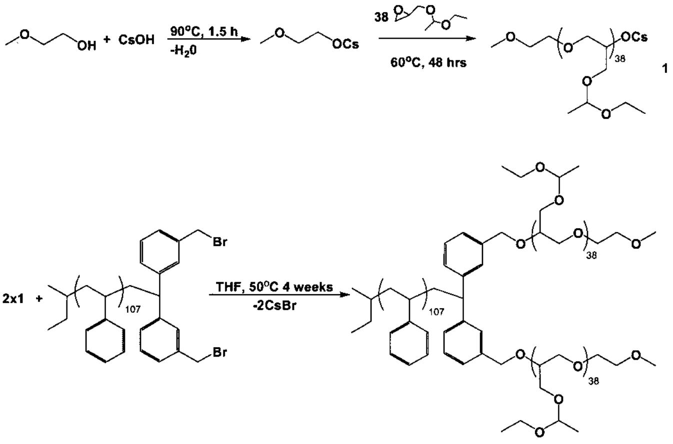


Figure 2. Clouding curves of $EEGE_{13}PO_{34}EEGE_{13}$ precursor (black circles) and $G_{13}PO_{34}G_{13}$ (hollow circles). Concentration =20 g/l

Synthesis of heteroarm star PS(PEEGE)$_n$ and PS(PG)$_n$ copolymers. Formation of nanoparticles.

We attempted to synthesize heterostar-shaped polymers by coupling well defined chain-end-functionalized polystyrenes with 2 and 4 benzyl bromide moieties and living PEEGE. It is well known that the linking reaction in the synthesis of star block-copolymers is usually the slowest, rate-limiting step. Due to the low concentration of alkoxide end-groups on the PEEGE precursor, the reaction was carried out at 50°C with great excess of PEEGE-OCs and for a long period of time (4 weeks). The coupling reactions proceeded quantitatively without any side reactions. This was proved by SEC (Figure 3) and ^{1}H NMR (Figure 4). The reaction route for the synthesis of PS(PEEGE)$_2$ is shown in Scheme 2.



Scheme 2. Synthesis of PS(PEEGE)$_2$ star block-copolymer

Table 3. SEC characterization of PS(PEEGE)$_n$

	PEEGE		PS		PS(PEEGE)n	
	$\overline{Mn}$	$\overline{Mn}/\overline{Mw}$	$\overline{Mn}$	$\overline{Mw}/\overline{Mn}$	$\overline{Mn}_{app}$	$\overline{Mw}/\overline{Mn}$
3 arm	4 500	1.25	11 500	1.02	25 000	1.53
5 arm	4 800	1.36	12 200	1.03	24 200	1.62

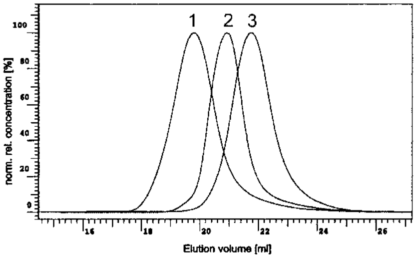


Figure 3. SEC traces of arm precursors (3 – PEEGE, 2 – PSBr$_4$) and the product after the linking reaction 1 - PS(PEEGE)$_4$.

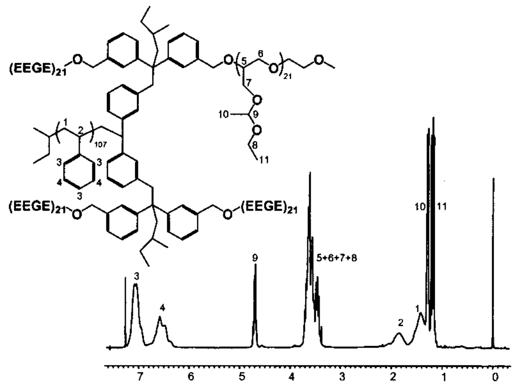


Figure 4. 1H NMR spectrum of heteroarm star-shaped (palm tree) block-copolymer PS(PEEGE)$_4$ in CDCl$_3$

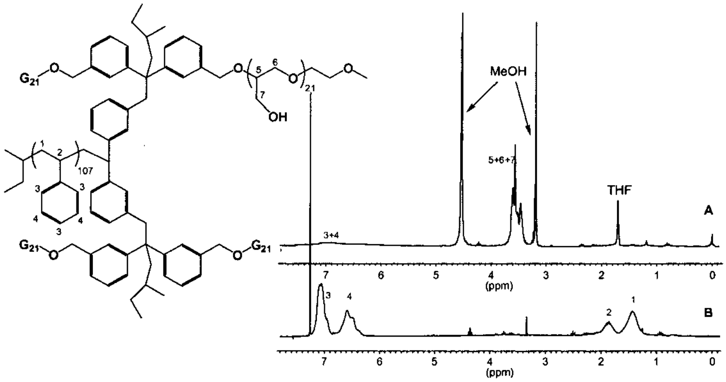


Figure 5. ^{1}H NMR spectra of five arm star-block-copolymers. A – PS(PG)$_4$ in THF-d$_8$/CD$_3$OD; B - PS(PG)$_4$ in CDCl$_3$

The chemical modification of the precursor PEEGE blocks via a deprotection reaction gives access to a new type of heterostar-shaped block copolymers PS(PG)$_n$.

NMR analyses clearly show that CHCl$_3$ is a highly selective solvent for the polystyrene moiety, whereas, the CH$_3$OH/THF mixture is preferred for PG arms (Figure 5).

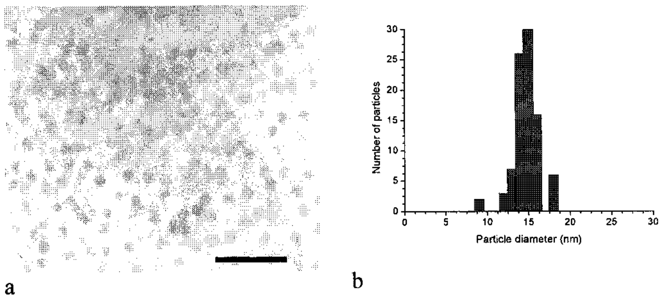


Figure 6 a) TEM micrograph of $PS(PG)_4$ nano-particles, prepared by the solvent exchange method. The bar scale corresponds to 100 nm. b) Size histogram of particles present in a 5 g/l dispersion of $PS(PG)_4$ in H_2O

We used TEM to demonstrate that the $PS(PG)_4$ block copolymers spontaneously form well defined and rather uniform compact spherical nanoparticles in aqueous media. The size distribution (Fig.6b) is monomodal and very narrow. The particle diameters range from 14 to 16 nm. This result supports the fact that in the case of heteroatom star copolymers the association number is considerably lower.[15] The low number of associated unimers could be explained by the fact that each unimer has several stabilizing soluble chains in the micellar shell.

Conclusions

The anionic polymerization of EEGE initiated by cesium alkoxide proceeds as a typical living process without any side reactions. In the PEEGE-b-PPO-b-PEEGE block copolymer each block exhibits a lower critical solution temperature in aqueous media. The PEEG blocks are easily converted into PG blocks. Thus quite different species from an almost identical block polymer backbone can be obtained depending on temperature: double hydrophilic, amphiphilic, and hydrophobic block-copolymers.

Novel polystyrene/polyglycidol heteroarm star block copolymers were synthesized. They form spherical compact and almost uniform micelle-like aggregates in aqueous solution. The polymerization technique used in this study as well as the possibility for the formation of rather short, well defined PEEGE blocks opens the route to the synthesis of a new type of functionalized polymeric micelles.

[1] A. Sunder, R. Hanselmann, H. Frey, R. Muelhaupt, *Macromolecules*, **1999**, *32*, 4240
[2] E.J. Vandenberg, *J.Polym.Sci., Polym.Chem.*, **1985**, *23*, 915
[3] R. Tokar, P. Kubisa, S. Penczek, A. Dworak, *Macromolecules*, **1994**, *2,* 320
[4] A. Dworak, W. Walach, B. Trzebicka, *Macromol. Chem.Phys.*, **1995**, *196,* 1963
[5] D. Taton, A.Le Borgne, M. Sepulchre, N. Spassky, *Macromol.Chem.Phys.*, **1994**; *195*, 139
[6] Ph. Dimitrov, S. Rangelov, A. Dworak, Ch.B. Tsvetanov, *Macromolecules* in print
[7] Ph. Dimitrov, E. Hasan, S. Rangelov, B. Trzebicka, A. Dworak, Ch.B. Tsvetanov. *Polymer,* **2002**, *43*, 7171
[8] A.Hirao, N. Haraguchi, *Macromolecules,* **2002,** *35*, 7224
[9] A. Fitton, J. Hill, D. Jane, R. Miller, *Synthesis,* **1987**, 1140
[10] V.V. Namboodri., R.S. Varma, *Tetrahedron Letters,* **2002**, *43*,1143
[11] P. Alexandridis, J.F. Holzwarth, T.A. Hatton, *Macromolecules,* **1994**, *27*, 2414
[12] C. Allen, D. Maysinger, A. Eisenberg, *Colloids and Surfaces B:Biointerfaces* **1999**, *16*, 3
[13] J. Hine, M. Hine, *J. Am. Chem. Soc.*, **1952,** *74*, 5267
[14] R. Kjellander, E. Florin, *J.Chem.Soc.,Faraday Trans.*, **1981**, I 77, 2053
[15] M. Stepanek, K. Podhajecka, K. Prochazka, Z. Tuzar, W. Brown, *Langmuir* **2000**, *16*, 6868