

SYNTHESIS AND CHARACTERIZATION OF AMPHIPHILIC GRAFT COPOLYMER CONTAINING MICROPHASE SEPARATED AND LONG POLY(ETHYLENE OXIDE) SIDE CHAIN STRUCTURES**

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ABSTRACT

Acryloyl terminated Poly (ethyleneoxide) macromonomers (PEO-A) with different PEO chain lengths have been prepared by deactivation of PEO alkoxide with acryloyl chloride. A new kind of amphiphilic polystyrene-g-poly (ethylene oxide) graft copolymer containing both microphase separated and PEO side chain structures has been synthesized from radical copolymerization of PEO-A macromonomer with styrene. After careful purification by a newly developed method called "selective dissolution", the well-defined structure of the purified copolymers was confirmed by IR, $^1\text{H-NMR}$ and GPC. Various experimental parameters controlling the copolymerization were studied in detail. The results indicated that the feed ratio of styrene to macromonomer (S/M) was the most important determining factor for the composition of the copolymers. A detailed "comb-model" was proposed to describe the molecular structure of the graft copolymers. Finally, this amphiphilic graft copolymers may readily form microphase separated structures as clearly indicated by transmission electron microscopy.

INTRODUCTION

In the last few decades, many efforts have been made to develop truly bio-compatible polymers, including those for blood applications^[1,2]. Unfortunately, there have been very few promising candidates emerging yet, among them are copolymers with either microphase separated structures or long poly (ethylene oxide) (PEO) side chains.

The microphase separated copolymers previously studied as blood compatible materials were essentially composed of A-B-A type amphiphilic block copolymers^[3-5]. On the other hand, since PEO surfaces have many interesting blood contacting properties, a lot of investigators have been stimulated to develop biomaterials based on PEO and study their interaction with blood^[6-8]. It has been found that long PEO chains grafted on a solid surface prevent more effectively the adsorption of blood components, as compared with the cases in which PEO chains are segmented into a block copolymer. Nevertheless, most of the biocompatible copolymers containing PEO side chains did not have any particular ultra-structures such as microdomains^[8]. In spite of its obvious interest, little is known about whether and how surface-induced thrombogenesis will be further minimized if a material exhibiting both types of structures contacts blood.

By using a rigid and hydrophobic PS chain as backbone, on which flexible, hydrophilic PEO chains are grafted, one could create, at a given surface, both

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microphase separated and long PEO side chain structures. Fulfilling the above two structural requirements and with relatively simple chemistry, polystyrene-g-poly(ethylene oxide)graft copolymer (PS-g-PEO) represents a good and simple molecular model for the designing of blood-compatible materials.

Macromonomer technique has been proven to be a desirable way of synthesizing graft copolymers with well-defined "comb-like" structures. However, most of the previous studies laid emphasis only on the synthesis and the copolymerization ability of various macromonomers^[9], yet seldom concerning the aspect of how to control the copolymerization process or how to control the structure of resulted copolymers.

This paper will report the synthesis and characterization of acryloyl (A) terminated PEO macromonomer (PEO-A), and its copolymerization with styrene. The goal of this work is to prepare a series of PS-g-PEO graft copolymers with varying backbone and side chain lengths, as well as different PEO grafting numbers. The morphology of the graft copolymer will also be examined by means of transmission electron microscopy.

EXPERIMENTAL

1. Preparation of PEO-A macromonomer

Ethylene oxide (EO) of high quality with water contamination less than 30 ppm was purchased from Nanjing Zhongshan Chemical Factory, China, and used as received. Sodium alcoholate (NaOEt) was prepared in our Lab just before use through a reaction of sodium with an excess of ethanol. Acryloyl chloride (AC) was also synthesized in our Lab according to the method reported previously^[10]. All other reagents were anhydrous and subjected to further purification when necessary.

PEO-A was synthesized by anionic polymerization of EO using NaOEt as initiator, followed by termination of the alkoxide function of monofunctional "living" PEO chain with AC. The polymerization of EO was performed in toluene at 90 °C in a pressure vessel. Feed ratio of EO to NaOEt was adjusted to get expected number average molecular weight for the macromonomer. Once the polymerization had finished, the system was cooled to 45 °C and the resulted PEO sodium alkoxide was deactivated in situ with AC (AC/NaOEt = 2) for 6 hours. Then the reaction mixture was poured into a large amount of diethyl ether, and the precipitate which contains PEO-A as well as by-product sodium chloride (NaCl) was dissolved into water. This water solution was extracted twice with chloroform to get rid of NaCl, and then the chloroform phase, now containing only pure PEO-A, was precipitated again in diethyl ether and the precipitate recovered. The PEO-A thus obtained was dried at 40 °C under vacuum and finally stored at 0 °C.

The chemical structure of PEO-A was characterized by UV (SHIMADZU UV240), IR (NICOLET FTIR-5DX) and ¹H-NMR (JEOL FX-90Q) spectroscopy. The double-bond functionality of PEO-A, i.e., quantitative introduction of acryloyl groups into PEO chains (mole% of A), was measured using a W_{iii} titration method^[11]. The number average molecular weight ($\overline{M}_n$) and polydispersity index (H) of the macromonomer were estimated by vapor pressure osmometry (VPO) (KNAUER VPO) and gel permeation chromatography (GPC)

(WATERS-208), respectively.

2. Synthesis and purification of PS-g-PEO

PS-g-PEO was synthesized by free radical copolymerization of distilled styrene monomer with the PEO-A macromonomer. 2, 2'-azobisisobutyronitrile (AIBN) was used as initiator and toluene as solvent. AIBN, macromonomer, styrene and toluene were added sequentially into a reaction vessel under nitrogen atmosphere. The feed ratio copolymerization was varied from run to run, but always accurately adjusted to meet different structure requirements for the products. After 24 hours of polymerization at 60 °C, the reaction mixture was precipitated in a large amount of heptane, and the precipitate which contains the copolymer was purified by selective dissolution, a method recently developed in the authors' Lab^[12].

3. Structural characteriation of PS-g-PEO

The chemical structure of the graft copolymers was determined by IR and ¹H-NMR. The $\overline{M}_n$ and polydispersity index of the copolymers were estimated by GPC. The bulk composition of PS-g-PEO was determined by the well-established first derivative UV spectrometry^[13].

4. Morphology of PS-g-PEO

The samples of PS-g-PEO were dissolved in chloroform at a concentration of about 0.5wt%. Then the solution was coated directly on carbon-coated copper grids. After evaporation of the solvent, the thin copolymer films were exposed to the vapor of osmium tetroxide (2 wt% aqueous solution) at 40 °C for about 40 hr. to selectively stain the PS chains. The morphology was observed by means of a transmission electron microscope (JEOL, JEM-200CX).

RESULTS AND DISCUSSION

1. Synthesis and characterization of PEO-A macromonomer

The IR spectrum of PEO-A macromonomer (Fig.1) exhibited the characteristic absorptions of ether linkages at 1120cm⁻¹ and that of carbonyl groups at 1720cm⁻¹. The characteristic peak of double bond at 1640cm⁻¹ was also presents.

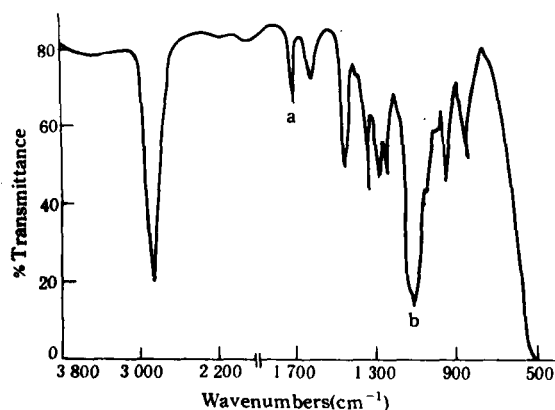


Fig.1 IR spectrum of PEO-A macromonomer (peak a: 1720cm⁻¹, peak b: 1120cm⁻¹)

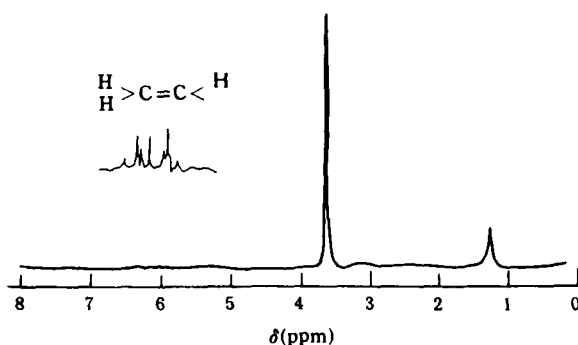


Fig.2 ¹H-NMR spectrum of PEO-A macromonomer

In the ¹H-NMR spectrum (Fig. 2), an strong peak at $\delta=3.6$ due to the methylene groups of -CH₂CH₂O- appeared. Moreover, there were also characteristic peaks around $\delta=6.2$, which can be attributed to the ethenyl groups of

PEO-A.

UV analysis also confirmed the above observation (spectra not presented here). Indeed the macromonomer has an absorbance at 205.5nm, which is consistent with the well-known UV behaviours of conjugated groups, in this case, the acryloyl groups ($\text{CH}_2=\text{CH}-\text{CO}-$). Consequently the obtained PEO-A does have the following expected structure: $\text{CH}_3\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_n\text{COCH}=\text{CH}_2$.

As indicated in Table 1, a series of PEO-A macromonomers with varying chain lengths ($\overline{M}_n=1300-5000$) were obtained. The values of $\overline{M}_n$ determined by VPO were found to be quite close to those predicated theoretically, except for a low molecular weight sample (91-4-8). The double-bond functionality of the resulted macromonomers is also given in Table 1.

Table 1 Characteristics of PEO-A macromonomers

Sample	$\overline{M}_n$ (theoretical)	$\overline{M}_n$ (VPO)	Relative deviation (%)	H^*	mole% of A**
91-4-8	1002	1294	29.14	1.2	40.22
91-4-22	2113	1937	-8.32	1.15	58.4
91-4-26	2747	2727	-0.73	/	72.91
91-3-15	2781	2866	3.06	/	/
91-5-10	2794	2854	0.15	1.25	/
91-5-17	5032	5037	0.01	1.19	89.56

* Polydispersity index. ** mole% of acryloyl group

2. Synthesis and structural identification of PS-g-PEO

The IR and ^1H -NMR spectra of the purified PS-g-PEO are shown in Figure 3 and Figure 4. IR spectrum exhibited the characteristic absorptions of ether linkages at 1120cm^{-1} and those of phenyl rings at 1600 and 1500cm^{-1} . Absorption peaks at 710 and 770cm^{-1} were due to the mono-substituted structure of phenyl rings. ^1H -NMR spectrum showed two peaks at $\delta=6.6-7.2$ due to the phenyl-ring protons, a single peak at $\delta=3.6$ arising from the methylene group in $-\text{CH}_2\text{CH}_2\text{O}-$ units and peaks at about $\delta=1.5$ contributed by methylene and methylidyne groups in $-\text{CH}(\text{C}_6\text{H}_5)-\text{CH}_2-$ units. Thus all characteristic peaks of PS and PEO chains were observed, which are perfectly consistent with the expected macromolecular structure of the graft copolymer.

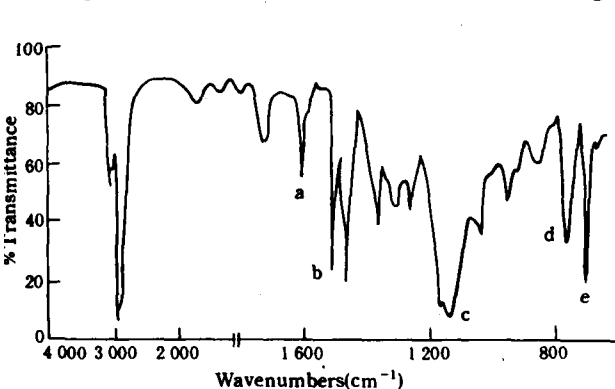


Fig.3 IR spectrum of PS-g-PEO copolymer (wavenumber of peak a, b, c, d and e is 1600, 1500, 1120, 770 and 710cm^{-1} , respectively)

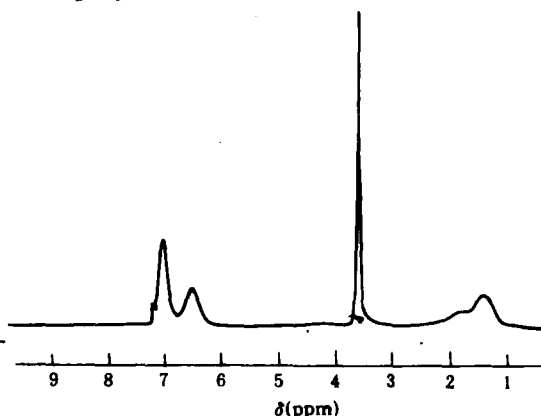


Fig.4 ^1H -NMR spectrum of PS-g-PEO copolymer

3. Control of copolymerization

Various experimental parameters controlling the copolymerization and thereby the structure of the graft copolymer were investigated.

The effects of copolymerization time, solvent, AIBN concentration and feed ratio of styrene to macromonomer (S/M) on the structure of the graft copolymer were investigated. For this purpose, PEO-A macromonomer with $\overline{M}_n$ of about 2800 was used.

It was found that the conversion of copolymerization could be increased by extending the time, but the composition of the graft copolymers kept essentially unchanged (Tab. 2).

Since in radical homopolymerization of styrene, the chain transfer constants to solvent butanone (K_{t1}), toluene (K_{t2}) or benzene (K_{t3}) have the following ratio^[14]: $K_{t1} : K_{t2} : K_{t3} = 100 : 6 : 1$ (60 °C), polystyrene with much higher molecular weight may be expected, if benzene instead of toluene or butanone is used as solvent. However, in the copolymerization of styrene with PEO-A macromonomer, the effect of the solvents on the $\overline{M}_n$ of the copolymers was not so remarkable as should be, only a little increase of $\overline{M}_n$ observed (Tab. 3). This is to say that the process of chain transfer to solvent was not the primary factor in governing the molecular weight of the graft copolymer. Moreover, the effect of AIBN concentration on the $\overline{M}_n$ was also insignificant (Tab. 4). Indeed, how to increase effectively the molecular weight of amphiphilic graft copolymers involving macromonomers, it remains to be a general problem and merits further investigation.

Table 2 Effect of time on the copolymerization (60 °C, $S/M=1:1$, [AIBN]=1%, toluene as solvent, macromonomer: 91-3-15)

Sample	Time (hr.)	Cont* (%)	PS (wt.)%
3-26-2	16	27.69	25.86
3-26-3	24	30.23	24.57
3-26-4	48	33.95	32.44

Table 3 Effect of solvents on the copolymerization (60 °C, 24hr., $S/M=1:1$, [AIBN]=1%, macromonomer: 91-3-15)

Sample	Solvent	Conversion (%)	PS (wt)%	$\overline{M}_n$ (GPC)	H
3-23-1	butanone	30.85	31.47	9021	1.58
3-23-2	toluene	32.10	27.17	10617	1.5
3-26-10	benzene	40.30	27.91	13120	1.6

Table 4 Effect of AIBN concentration on the copolymerization (60 °C, 24hr., $S/M=1:1$, [AIBN]=1%, macromonomer: 91-3-15)

Sample	[AIBN]	Conversion (%)	PS (wt)%	$\overline{M}_n$ (GPC)	H
3-23-2	1%	32.10	27.12	10617	1.5
3-23-5	3%	47.12	31.43	9045	1.43

As shown in Tab.5, the feed ratio of styrene to macromonomer (S/M) was found to be the most sensitive parameter in affecting dramatically the composition

of the copolymers. As S/M increased, the PS content of graft copolymers increased systematically while the PEO grafting numbers decreased at the same time. This increase in PS content was always accompanied by the decrease in PEO grafting number, and vice versa, because the $\overline{M}_n$ of the graft copolymers was found to be essentially unchanged when S/M varied. It is also interesting to point out that this increasing in PS content was gradually slowed down when S/M became higher and higher, finally reaching a plateau with a PS wt% < 80% (Figure 5).

Table 5 Effect of S/M on the copolymerization ($\overline{M}_n$ of the macromonomers was about 2800, 60 °C, 24hr., [AIBN] = 1%, toluene as solvent)

Sample	Macromonomer	S/M	PS(wt)%	$\overline{M}_n$ (GPC)	H	Grafting numbers
3-26-5	91-3-15*	1:2	10.98	11100	1.9	3.5
3-23-2	91-3-15	1:1	27.12	10617	1.5	2.7
3-26-6	91-3-15	2:1	47.45	11101	1.7	2.0
5-21-4	91-3-15	3:1	58.04	9878	1.86	1.4
5-28-5	91-5-10*	5:1	74.61	10679	1.74	1.0
5-28-6	91-5-10	7:1	74.94	10351	1.62	0.9

* See Table 1

In an attempt to establish a quantitative and reproducible correlationship

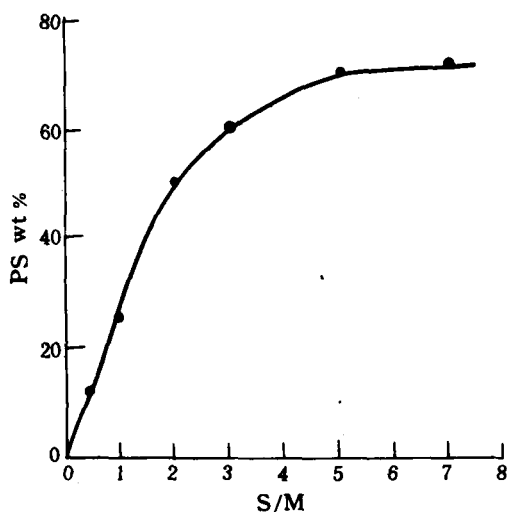


Fig. 5 Effect of feed ratio (S/M) on the composition of PS-g-PEO

between the feed ratio (S/M) and the composition of the copolymers, the same experiment just as above was repeated several times. As shown in Fig. 5, most of the data were indeed quite reproducible and PS(wt)% was about 25, 50, 60, 70 and 72 for S/M = 1:1, 2:1, 3:1, 5:1 and 7:1, respectively. This correlationship is very instructive for the structural controlling of the graft copolymers.

In order to obtain PS-g-PEO with varying PEO side chain lengths, copolymerization of styrene with other three PEO-A macromonomers ($\overline{M}_n$ = 1294, 1937 and 5037) was also carried out. As indicated in Table 6, for all the three PEO chain lengths studied, results similar to those with $\overline{M}_n$ = 2800 were found,

i.e., PS wt% increased as S/M increased, although there were numerical difference from one PEO chain length to another for such feed ratio/composition correlationships. It is astonishing to note that the $\overline{M}_n$ of the graft copolymers was, once again, almost unchanged when PEO chain length varied.

Therefore, two principal conclusions can now be drawn from the above results: (1) the $\overline{M}_n$ of the graft copolymers keeps essentially unchanged regardless of the PEO chain length and the other experimental parameters mentioned above, (2) the composition of the copolymers can be effectively controlled by adjusting the feed ratio of styrene to macromonomer and PS wt% increases

Table 6 Copolymerization of styrene with macromonomers having different PEO chain lengths (60 ℃ , 24hr., [AIBN]=1%, toluene as solvent)

Sample	$\overline{M}_n$ of macromer	S/M	PS (wt)%	$\overline{M}_n$ (GPC)	H	Grafting numbers
4-11-1	1294	1 : 2	32.64	9707	1.67	5.1
4-11-2	1294	1 : 1	45.27	10292	1.77	4.4
4-11-3	1294	2 : 1	51.29	10366	1.58	3.1
4-11-4	1294	3 : 1	58.23	9447	1.86	2.4
5-31-3	1937	1 : 1	51.38	7655	1.64	1.9
5-31-4	1937	3 : 1	60.85	8186	1.76	1.7
5-31-5	1937	5 : 1	70.55	7293	1.7	1.1
5-27-3	5037	1 : 1	23.81	9517	1.47	1.4
5-27-4	5037	3 : 1	50.03	8645	1.62	0.9

systematically as S/M increases.

4. Structural description of the graft copolymers

It is well known that graft copolymers synthesized with macromonomer technique exhibit comb-like structures. Based on the above results, a detailed “comb-model” was proposed to describe the molecular structure of PS-g-PEO.

Because the above obtained PS-g-PEO had almost unchanged molecular weight(around 10000 in most of the cases), the grafting number of the copolymers depended mainly on the composition and PEO side chain length.

Firstly, if we consider a set of graft copolymers with the same PEO side chain length, the average grafting number was controlled only by the composition: the grafting number decreased as the PS wt% of the copolymers increased (Table 5). Thus, the stucture of such a group of copolymers may be depicted schematically by a “composition-dependent” comb-model(Fig.6a).In fact, in lower PS content, the copolymers exhibit a common comb-like structure with shorter

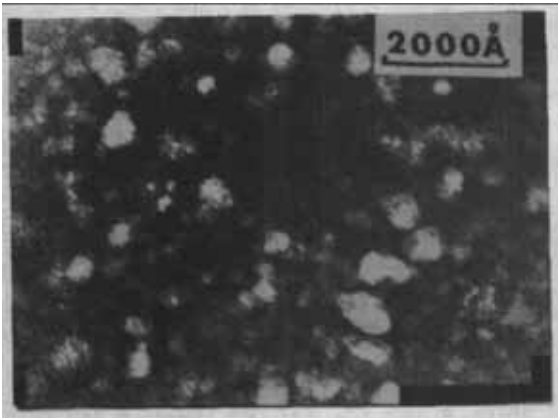
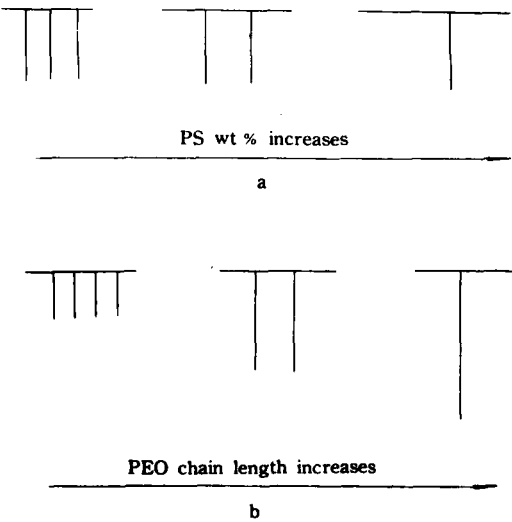


Fig. 6 Detailed comb-model for PS-g-PEO copolymer (a) composition-dependent model ; (b) branch length-dependent model

Fig.7 Transmission electron photograph of a PS-g-PEO copolymer (PSwt%=75)

backbone length and more side chains grafted. As PS wt% increases, the backbone is gradually lengthened and the branch number reduced and finally the copolymers exhibit a "T" shape structure at the highest PS content.

Turning to the second case in which we consider a set of copolymers with comparable compositions but different PEO side chain lengths, the average grafting number was controlled only by the PEO side chain length: the grafting number decreased as the PEO side chain length increased (Table 7). The structure of the copolymers fits now into another type comb-model referred to as "branch length-dependent" comb-model (Fig. 6b). Based on a simple calculation, it was found that the copolymers with comparable compositions but different side chain lengths have comparable backbone lengths. Therefore, the corresponding structure of the copolymers changed progressively from a comb-like shape with a number of shorter branches to a "T" shape with a longer branch.

Table 7 Structural parameters of copolymers with varying PEO side chain lengths (60 °C, 24hr., [AIBN]=1%, toluene as solvent)

Sample	$\overline{M}_n$ of Macromonomer	S/M	PS (wt)%	$\overline{M}_n$ (GPC)	H	Grafting number
4-11-4	1294	3:1	58.23	9447	1.86	2.4
5-31-4	1937	3:1	60.85	8186	1.76	1.7
5-21-4	2866	3:1	58.04	9878	1.86	1.4
5-27-4	5037	3:1	50.03	8645	1.62	0.9
5-31-5	1937	5:1	70.79	7293	1.70	1.1
5-28-5	2854	5:1	74.61	10697	1.74	1.0
5-31-6	1937	7:1	71.05	10557	1.44	1.6
5-28-6	2854	7:1	75.03	10351	1.65	0.9

In summary, the present results demonstrated that PS-g-PEO graft copolymers with different backbone and branch lengths, as well as different grafting numbers can be readily prepared by selecting suitable PEO chain length and by adjusting feed ratio of styrene to macromonomer.

5. Microphase separated structure

The amphiphilic PS-g-PEO graft copolymer may readily form microphase separated structure. As shown in Fig. 7, an "island-sea"-like morphology was observed for a copolymer with PS content of 75wt%. We also found that the feature of the microphase separated structures of PS-g-PEO copolymers depends on their composition and side chain length, the detailed results will be published elsewhere.

CONCLUSION

PEO-A macromonomers with different PEO chain lengths were prepared by deactivation of PEO alkoxide with acryloyl chloride. The radical copolymerization of PEO-A macromonomer with styrene was successful, leading to the formation of amphiphilic PS-g-PEO copolymers. Graft copolymers with different backbone and PEO branch chain lengths, as well as different grafting numbers were readily prepared by adjusting PEO chain length and the feed ratio. A detailed "comb-model" was proposed to describe the molecular structure of the graft copolymers. As expected, this amphiphilic graft copolymer may readily form microphase separated structures.

REFERENCES

- [1] Vorman, L. Leonard, E. F., *ANN. N. Y. Acad. Sci.*, **1977**, 283.
- [2] Cooper, S. L. and Peppas, N. A., "Biomaterials, Advances Chemistry Series 199", A C S , Washington, D. C., **1982**.
- [3] Okano, T.; Aoyagi, T.; Kataoka, K.; Abe, K. and Sakurai, Y., *J. Biomed. Mater. Res.*, **1986**, 20, 919.
- [4] Okano, T.; Uruno, M.; Sugiyama, N.; Shimada, M.; Shinohara, I.; Kataoka, K. and Sakurai, Y., *J. Biomed. Mater. Res.*, **1986**, 20, 1035.
- [5] Yui, T.; Sanui, K.; Ogata, N.; Kataoka, K.; Okano, T. and Sakurai, Y., *J. Biomed. Mater. Res.*, **1986**, 20, 929.
- [6] Bots, J. G.F.; Van der Does, L. and Bantjes, A., *Biomaterial*, **1986**, 7, 393.
- [7] Nose, Y., Kjellstrand, C. and Ivanovich, P., "Progress in Artificial Organ", ISAO Press, Cleveland, **1986**, p. 909.
- [8] Mori, Y.; Nagaoka, S.; Takiuchi, H.; Kikuchi, T.; Noguchi, N.; Tanzawa, H. and Noishiki, Y., *Trans. Am. Soc. Artif. Intern. Organs*, **1982**, 28, 459.
- [9] Rempp, P. F. and Franta, E., *Adv. in Polym. Sci.*, **1984**, 58, 1.
- [10] Rehberg, C. E.; Dixon, M. B. and Fisher, C. H., *J. Am. Chem. Soc.*, **1945**, 67, 208.
- [11] Institute of Polymeric Materials of Fudan University (Shanghai, China) Ed., "Experimental Techniques for Macromolecules", Fudan University (Shanghai) Press, **1983**, p. 275
- [12] Qiu, Yongxing; Yu, Xiaojie; Feng, Linxian and Yang Shilin; *Chem. Res. in Chinese Univ.*, **1992**, 8 (3), 278 — 286 .
- [13] Qiu, Yongxing; Yu, Xiaojie; Feng, Linxian and Yang Shilin; *Makromol. Chem.*, **1992**, 193, 1377.
- [14] Brandrup, J., Immergut, E. H., "Polymer Handbook", 2nd edition, John Wiley and Sons Press, New York, **1974**, p. II-67.