Polymer Bulletin 58, 737–746 (2007)
DOI 10.1007/s00289-006-0697-x

Polymer Bulletin

The template co-crystallization of β-cyclodextrin with polymeric inclusion complex

Irina G. Panova* (✉), Elena V. Matuchina, Irina N. Topchieva***

*Moscow State University, Chemical Department, Leninsky gory, GSP-3, Moscow, 119992, Russia
**Moscow State Pedagogical University, Department of Physics, Malaya Pirogovskaya St. 1, Moscow, 119882, Russia
E-mail: igpan@mail.ru; Fax: (495)9390174

Received: 8 June 2006 / Revised version: 5 October 2006 / Accepted: 13 October 2006

Summary

The study of the crystal formation in aqueous solution of β-cyclodextrin in the presence of the additives of polypropylene oxide in a wide range of macrocycle:polymer molar ratios was carried out. The cyclodextrin separation from the mixture was made by 1) the isothermal crystallization; 2) the rapid crystallization via the precipitation in acetone. The influence of thermodynamic and kinetic factors on the mechanism of crystallization of unbound macrocycles was demonstrated for the first time. It was shown that the isothermal crystallization led to the formation of the mixture of two solids: the channel polymer inclusion complex and unbound β-cyclodextrin in the cage form. The precipitation method at polypropylene oxide content in the initial solutions corresponded to the range of 0,03 - 92% from stoichiometry of the complex resulted in the formation of the structures with the channel organization of macrocycles. Thus, the ability of β-cyclodextrin for the template co-crystallization with the polymeric inclusion complex was demonstrated. These data enable to develop the novel method of creation of the channel nanoporous structure of β-cyclodextrin. The obtained products represent lamellar structures possessing cylindrical nanopores with the diameter of ~ 0,65 nm.

Introduction

Cyclodextrins (CD) are cyclic oligosaccharides consisting of six, seven, and eight glucopyranose units for α-, β- and γ-forms, respectively. They have a porous toroidal-shaped structure with a hydrophobic cavity and hydrophilic rims made of hydroxyl group. One of the most remarkable features of CDs is their ability to form inclusion complexes with small molecules and polymer [1-3]. In recent years CDs have found wide application in supramolecular chemistry as building blocks for the creation of the ordered ensembles with various architectures [2-6].

The striking examples of such substructures are the covalent and noncovalent channel assemblies based on CDs obtained from polymeric inclusion complexes (IC) between cyclodextrins and polyalkylene oxides. The first type represents so-called ”molecular tubes”, the rigid water soluble molecules obtained by the cross-linking of α- or β-CD macrocycles in IC with epychlorohydrin and subsequent removal of the polymer guest [7-11]. The second type, solid channel forms of cyclodextrins, was constructed by us firstly on removing of the included polymer from IC under the action of selective organic solvent that are inert in relation to the macrocycle (the method of supramolecular dissociation) [12]. Thus, CD's channel structures are of interest as high-ordered structures that possess extensive cylindrical nanopores and, therefore, represent a new type of long range receptors for the inclusion of compounds with various chemical natures. As shown in [13], the channel structure based on α-CD is capable to work as a nanoscopic ~~filters~~ for the separation of both small molecules and polymers. According to [14-15], the similar porous structures would have applications in nanotechnology, especially in catalysis, separation technology, biomaterials engineering, and fabrication of nanodevices.

Note that the method of supramolecular dissociation is universal for the preparation of solid channel structures based on all three CD's types, but it is labor-intensive and prolonged in time. Recently a more convenient and faster way was elaborated [13]. It consists in the precipitation of α- and γ-CD from the warm aqueous solutions in suitable organic non-solvent. However, as also shown in [18], this method can not be applied for the preparation of the channel structures based on β-CD, the most commercially accessible and widely used CD. In the present work we demonstrated an effective method for the creation of β-CD$_{chan}$ based on the ability of β-CD molecules for co-crystallization with polymer CD ICs.

Experimental

Materials

β-CD obtained from ICN (USA) was dried in vacuum at 80ºC. Polyethylene oxide (PEO) (Serva) with MM=1000 and polypropylene oxide (PPO) (Wako) with MM=1000 (kindly provided by Prof. J.Inoue) were used without preliminary purification. Acetone was purified by distillation.

The crystallization of β-CD from aqueous solutions containing polypropylene oxide

A weighed portion of β-CD (140 mg) was dissolved in 8 ml of water, and added to 0.5 ml of aqueous solution containing of 1.4×10^{-4} -13.2 mg PPO. These solutions were held for a day at 20ºC. The formed systems (suspensions or solutions) were placed in a crystallizer for full evaporation of water at 20ºC or were precipitated in cold acetone. The formed precipitates were separated on the glass filter, washed two times with 30 ml of acetone and dried in air at room temperature to the constant weight. To obtain the porous structures of solid β-CD prepared by the precipitation method samples were dried in vacuum at 80ºC during 3 days.

Synthesis of the Polymer Inclusion Complex β-CD-PPO

A weighed portion of PPO (20.4 mg) was dissolved in 4 ml of ice water and added to 10 ml of saturated solution of β-CD cooled at 5ºC. The mixture was stirred for an hour and hold at 5ºC for 6 h. The precipitate was centrifuged, washed two times with ice water, and dried in air at room temperature up to the constant weight.

X-ray Diffraction Studies

X-ray diffraction (XRD) patterns were recorded in a transmission mode with a DRON-3M diffractometer (CuK_α radiation, a curved quartz crystal as a monochromator). WAXS patterns were recorded with a URS-55 instrument using a flat-cassette RCV-86 camera (Ni filtered, CuK_α radiation).

^{1}H NMR Investigations

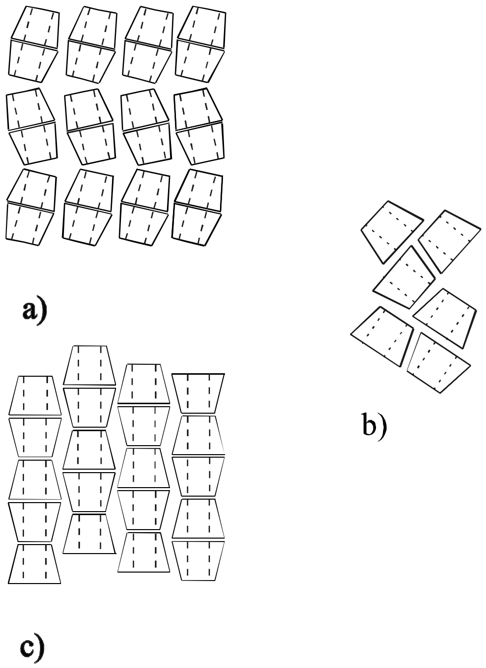
^{1}H NMR spectra were measured at 500 MHz on a DXR-500 NMR-spectrometer at 30°C. The sample concentrations were ~ 10% in DMSO-d_6.

Scanning Electron Microscopy

Electron micrographs were obtained with an Hitachi S-520 scanning electron microscope. The samples were prepared by drawing a drop of suspension of β-CD_{chan} in acetone on a glass surface. The samples were shadowed with Au.

Results and discussion

We first noted the ability of cyclodextrins for co-crystallization with the polymeric inclusion complexes when studying the structural characteristics of the complexes formed by α-CD with polyethylene oxide (PEO) [19]. It was of interest if this behavior may be revealed at the formation of crystal structures in the system "β-CD - poly(propylene oxide)".



Scheme 1. Schematic representation of the arrangement of β-CD molecules in the monoclinic channel lattice (a); cage structure (b) and mesomorphic channel structure (c)

It is well-known that β-CD and PPO form stable and water-insoluble inclusion complexes [20]. Such ICs represent a crystal hydrate having monoclinic lattice characterized by the stoichiometric composition - two propylene oxide units per one macrocycle. Molecules of CD in this structure are arranged parallel to each other in a head-to-head manner forming a channel-like sequence with 2_1 symmetry. One of the proposed versions of the molecular packing in the monoclinic crystal is schematically presented in Scheme 1 (a).

This work is dedicated to the investigation of the crystallization of free β-CD from aqueous solution of β-CD and PPO taken in a wide range of molecular ratios corresponding to the excess of macrocycle. The saturated solution of β-CD (1,8 %) was used. The content of PPO in the initial systems (P) changed from 0,03 to 92% of the stoichiometry of the complex. In a day after the mixing of aqueous solutions of CD and PPO we observed the following picture:

1) if the quantity of PPO (P) was in the range of 0,05 - 92% the formation of the precipitate of the inclusion complex β-CD-PPO was observed.

2) if P corresponded to 0,002-0,05% the solutions became turbid.

3) if P=0,001% the solution remained transparent.

The isolation of CD in the solid state from aqueous solutions was performed using two methods: the isothermal crystallization, i.e. an evaporation of water at 20ºC, (method 1) and the rapid crystallization by the precipitation of the suspensions or solutions in acetone (method 2). The formed solid products were studied by X-ray method. The powder XRD patterns of structures based on β-CD obtained by both methods are displayed in Figures 1, 2 (curves 2-4). The presence of Bragg reflections gives the evidence of the crystalline phase formation in these samples. There is no amorphous scattering in the patterns. Hence, a high degree of crystallinity (more than 90%) was inherent in the obtained samples. In other words, practically all CD molecules were ordered.

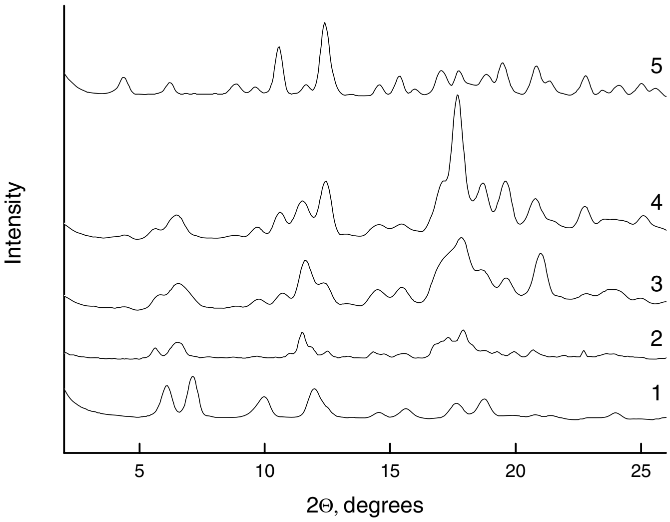


Figure 1. Powder XRD patterns of β-CD-PPO complex with monoclinic channel structure (1); β-CD prepared by method 1 at P=92% (2), P=82% (3), P=62% (4); β-CD with cage structure prepared by the recrystallization from water at 20°C (5)

It should be noted that β-CD itself crystallized from an aqueous solution by the evaporation of water or by the precipitation in acetone is characterized by the cage structure (β-CD_{cage}) in which macrocycles are placed perpendicularly to each other (Scheme 1 (b)). Thus the cavities of CD are blocked from both sides by neighboring macrocycles. The powder XRD patterns of the β-CD_{cage} are presented as the curves 5 in Figures 1, 2. For comparison in the same figures the powder XRD-patterns of crystalline complex based on β-CD and PPO with the channel structure are showed as curves 1.

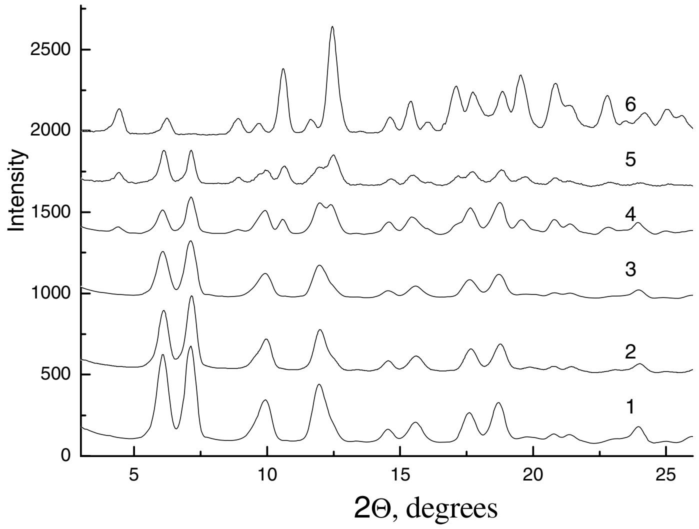


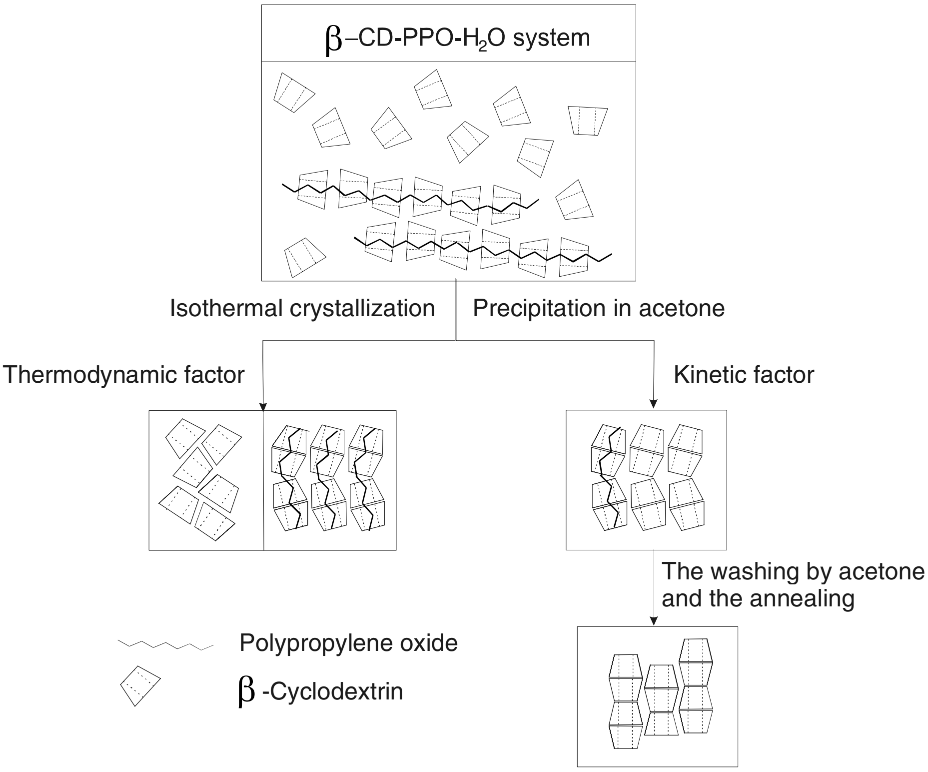
Figure 2. Powder XRD patterns of complex β-CD-PPO with monoclinic channel structure (1); β-CD prepared by method 2 at P=92% (2), P=0,03% (3), P=0,02% (4), 0,001% (5); β-CD with cage structure prepared by the method 2 in the absence of polymer (6)

The comparative analysis of the data presented in Figures 1 and 2 indicated that the phase composition of the solid product depends on two parameters - the PPO content in the initial systems and the crystallization method. The XRD-patterns of products received by the method 1 comprise Bragg peaks inherent to channel and cage forms of β-CD at all used CD : PPO ratios. Hence, the isothermal crystallization leads to the formation of biphasic systems.

The other effect was observed on using the rapid crystallization of β-CD-PPO systems by the precipitation in organic solvent (method 2). The XRD patterns showed only one channel form of β-CD (β-CD_{chan}) for the products received at P in range 0.03-92%. At P=0,02% the Bragg peaks of β-CD_{cage} were observed on the corresponding XRD-pattern (Figure 2 curve 3); their relative intensity growing as the P value decreased. These results testified that the rapid crystallization made it possible to realize the nucleation mechanism of the crystal growth of non-bonded with polymer threaded macrocycles on β-CD-PPO complexes resulting in the formation of the identical crystal lattice. The minimal, "threshold", quantity of the polymer necessary for the production of the only channel form of β-CD amounted nearly 0,03% from stoichiometry.

The formation of only the β-CD_{chan} phase under the precipitation of aqueous solutions of β-CD in an organic solution in the presence of PPO taken in non-stoichiometric ratio may be accounted for by template crystallization probably (Scheme 2). On the basis of these data one can imagine the following mechanism of the formation of channel β-CD structures. The mixing of aqueous solutions of β-CD and PPO resulted in the threading of macrocycles on the polymer chains that leads to the production of IC [20]. Strong H-bonding between neighboring CD stabilizes the linear aggregates playing a part of the crystallization centers for unbound β-CD. Free macrocycles co-crystallize with IC forming the identical channel structures with head-to-head, tail-to-tail conformation of macrocycles. Evidently the mechanism of crystallization of unbounded macrocycles in the conditions of rapid crystallization is controlled by the kinetic factor. If the PPO content in the initial solution decreases below the “threshold" value, the quantity of the nuclei of channel structure becomes insufficient for the "binding" of all free macrocycles. In this case a part of β-CD crystallize in the "cage" form, and the system becomes biphasic.

In discussing the mechanism of the crystallization of β-CD in the system containing PPO by the isothermal method it should be stressed that the equilibrium conditions of the crystallization favored the formation of stable cage structure along with β-CD-PPO inclusion complex. Thus, in this case the thermodynamic factor play the main role (Scheme 2).



Scheme 2. Proposed scheme of the formation of crystal structures in the system “β-CD - polypropylene oxide-water”

As was evident from the foregoing discussion in order to receive β-CD$_{chan}$ using extremely low content of the polymer one should apply the method of rapid crystallization. The precipitation of β-CD from the solution with P=0,03% led to the formation of solid products in which 99,97% of macrocycles were not bounded with the polymer. The molecules of water and acetone may be easily removed by drying. The annealing in vacuum of β-CD$_{chan}$ at 80°C during 2 days resulted in the formation of hollow macrocycles as was confirmed by ^{1}H NMR spectroscopy. Thus we obtained β-CD$_{chan}$ with the hollow pores. The diameter of nanopores corresponds to the diameter of β-CD's cavity ~ 6,5 Å.

It should be noted that the type of packing of macrocycles in the channel lattice has been changed at the drying. The data presented on Figure 3 and our results reported earlier [21] indicate that the arrangement of macrocycles in the annealed β-CD$_{chan}$ corresponds to their mesomorphic 3D-form with hexagonal packing of CD's columns in a basal plane. Molecular packing of β-CD in this structure is schematically shown in Scheme 1 (c).

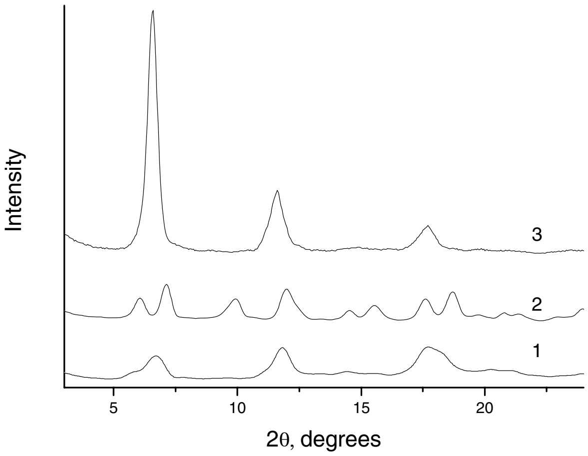
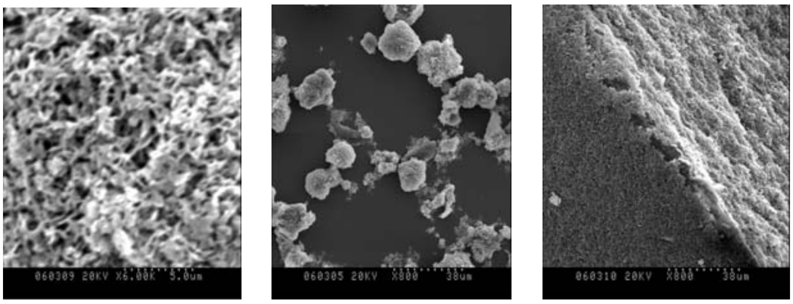


Figure 3. The powder XRD patterns of complex β-CD-PPO with mesomorphic channel structure (1); β-CD$_{chan}$ obtained by the method 2 at P=0,03% (2); β-CD$_{chan}$ after the annealing in vacuum (3)

The same yet unexpected result has been obtained on studying of the system β-CD - polyethylene oxide. It is known that the components of this system do not form stable water-insoluble IC in contrast to the system β-CD – PPO [22-24]. Indeed, the mixing of aqueous solutions of β-CD and PEO didn't result in the formation of the precipitate; solutions remained transparent at all used macrocycle : polymer ratios. In accord with the X-ray analysis the isothermal crystallization of such solutions led to the formation of the mixture composed of β-CD$_{cage}$ and PEO crystals. When the solution of β-CD and PEO taken in stoichiometric ratio was poured in the excess of acetone, the precipitate was formed. The ^{1}H NMR-spectroscopy indicated that the obtained product included molecules of both CD and PEO. According to the X-ray study this precipitate was characterized by the crystal channel structure identical to those of the crystal-hydrate of β-CD-PPO complex. These results evidence indirectly that the mixing of aqueous solutions of β-CD and PEO resulted in the formation of labile water-soluble inclusion complexes that act as nuclei for the crystallization of β-CD_{chan}.

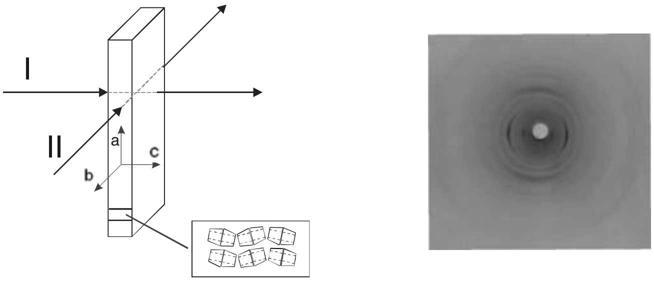
The study of the morphology of the crystallites formed by β-CD_{chan} and the character of their mutual packing in the course of next aggregation was performed using the scanning electronic microscopy (SEM). Figure 4 showed the SEM images of the following samples: a) the crystallites received by drawing of β-CD_{chan} suspension in acetone as a thin layer on a flat glass surface; 2) the powder of β-CD_{chan}; 3) the speciment obtained by drying of the isolated precipitate of β-CD_{chan} on a flat glass surface.



a) b) c)

Figure 4. Micrographs of a thin layer of β-CD_{chan} (a), dry powder of β-CD_{chan} (b), the plate of β-CD_{chan} (c)

It was shown that β-CD_{chan} formed lamellar (layered) structures; lamellae were parallel one to another and perpendicular to the plane of the initial plate. To determine the orientation of β-CD columns in lamellae the flat-camera X-ray method has been used. A thin strip was cut out from a plate of β-CD_{chan} and X-ray patterns were obtained using two directions of the primary beam (Figure 5 (a) relative to the strip plane: perpendicular (I) or along, that is, perpendicular to its edge (II).



a) b)

Figure 5. Positions of the studied strip of β-CD_{chan} during X-ray measurements (a) and X-ray flat-camera pattern of β-CD_{chan} (b)

In the first case, isotropic rings were observed. In the second case, textures were registered: reflections were resolved on the equator and meridian and in the quadrants (Figure 6 (b). Equatorial reflections characterize the arrangement of macrocycles in a basic plane; meridional - define the order of arrangement of macrocycles along the columns [25]. The combination of X-ray and SEM data showed that the columns formed by β-CD molecules were perpendicular to the surface of the precipitate on the plate and hence, were perpendicularly to the lamella planes. Thus, the macrosamples of β-CD_{chan} were characterized by the same orientation of crystallites as the corresponding IC [25].

Conclusions

In this work we have shown for the first time the possibility of the co-crystallization of free unbound with polymer β-CD with the inclusion complex based on β-CD and PPO. It has been demonstrated that polymer ICs are able to act as seeding agents favoring the organization of CD channel structures. It is shown, that the formation of β-CD_{chan} leads to the production of layered structures in which the channels of macrocycles are oriented perpendicularly to the planes of lamella. Removal of guest polymer molecules from β-CD_{chan} presents a method of the synthesis of novel products with cylindrical nanopores.

Acknowledgements. We thank Professor V.I. Gerasimof for helpful discussion of this work. This work was supported by the Russian Foundation for Basic Research, grant no. 04-03-32750.

References

1. Szeitly J (1988) Cyclodextrins and Their Inclusion Complexes. Budapest, Academiai Kiado
2. Harada A (2001) Acc Chem Res 34:456
3. Wenz G (1994) Angew Chem Int Ed Engl 33:803
4. Nepogodiev SA, Stoddart JF (1998) Chem Rev 98:1969
5. Huang L, Tonelli AE (1998) Rev Macromol Chem Phys C38:781
6. Douhal A (2004) Chem Rev 104:1955
7. Harada A, Li J, Kamachi M (1993) Nature 364:516
8. Ikeda T, Ooya T, Yui N (2000) Polym Adv Technol 11:830
9. Ikeda E, Okumura Y, Shimomura T, Ito K, Hayakawa R (200) J Chem Phys 112:4321
10. Topchieva IN, Kalashnikov FA, Spiridonov VV, Mel'nikov AB, Polushina GE, Lezov AV (2003) Doklady Chemistry 390:115
11. Topchieva IN, Kalashnikov FA, Spiridonov VV, Zakharova YuA (2003) Polymer Science Ser A 45:1065
12. Topchieva IN, Panova IG, Popova EI, Matukhina EV, Grokhovskaya TE, Spiridonov VV, Gerasimov VI (2002) Polymer Science Ser A 44:352
13. Rusa CC, Bullions TA, Fox J, Porbeni FE ,Wang X, Tonelli AE (2002) Langmur 18:10016
14. Kleitz F, Marlow F, Stucky GD, Schu'th F (2001) Chem Mater 13:3587
15. Guo CW, Cao Y, Xie SH, Dai WL, Fan KN (2003) Chem Commun 700
16. Dobrzanska L, Lloyd GO, Raubenheimer HG, Barbur LJ (2005) J Am Chem Soc, 127:13134
17. Thallapally PK, Wirsig TB, Barbour LJ, Atwood JL (2005) Chem Commun 4420
18. Panova IG, Matukhina EV, Gerasimov VI ,Topchieva IN (2006) Colloid Journal 68:66
19. Topchieva IN, Tonelli AE, Panova IG, Matuchina EV, Kalashnikov FA, Gerasimov VI, Rusa CC, Rusa M, Hunt MA (2004) Langmuir 20:9036

20. Li J, Harada A, Kamachi M (1994) Bull Chem Soc Jpn 67:2808
21. Popova EI, Topchieva IN, Zhavoronkova EN, Panova IG, Matukhina EV, Gerasimov VI (2002) Polymer Science Ser A 44:72
22. Harada A, Kamachi M (1990) Macromolecules 23:2821
23. Harada A, Li J, Kamachi M (1993) Macromolecules 26:5698
24. Harada A, Okada M, Li J, Kamachi M (1995) Macromolecules 28:8406
25. Panova IG, Matukhina EV, Popova EI, Gerasimov VI, Topchieva IN (2001) Polymer Science Ser A 43:771