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Polymerization-induced phase separation in gradient copolymers

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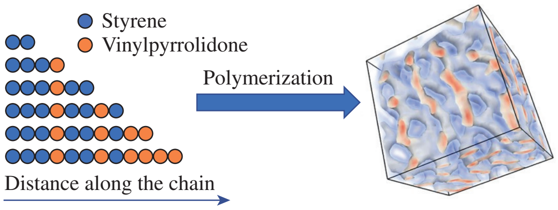
Gradient copolymers of styrene and *N*-vinylpyrrolidone, obtained in bulk using the reversible deactivation radical polymerization process under the action of TEMPO nitroxide, can form microphase-like separated structures directly in the reaction medium without any additional treatment or solvent. The morphology of the resulting product is highly dependent on the monomer feed composition.



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Structured block copolymer systems have attracted much attention due to many applications, including targeted drug delivery systems, nanoreactors, nanolithography, nanostructured membranes and emulsion stabilizers (for diblock copolymer micelles).[1] It is well known and theoretically substantiated that low-dispersity block copolymers can form micelles of different morphology[2,3] and microphase separation in bulk.[4–6] However, when using classical diblock copolymers, the preparation of such a system usually requires a complex multi-step procedure, including a two-step synthesis, purification and annealing. To overcome these difficulties, the method of polymerization-induced self-assembly (PISA) can be used.[7–11] The standard approach of this solution two-step method is to grow a second polymer block on a pre-synthesized homopolymer precursor. The growing block is solvophobic and tends to precipitate, but the first block, being solvophilic, stabilizes the micelles. Is it possible to achieve microphase separation in the bulk directly during polymerization? The answer to this question can be yes when using gradient copolymers instead of conventional block copolymers.

Gradient (tapered) copolymers are a particular class of macromolecules that exhibit a gradual change in monomer composition from predominantly one species to another.[12–14] To obtain a copolymer with a pronounced gradient structure in a one-step process, a difference in the reactivity ratios *r* is required.[15–17] It is assumed that gradient copolymers are not capable of structuring during polymerization since the gradual change in composition with the growth of the chain prevents the separation of components into distinct phases. However, there are many examples of microphase structuring of gradient or tapered copolymers after purification and casting into films.[18–20] Recently, the first work on one-step PISA in a solution using the concept of gradient copolymers has been performed,[21,22] and our computer simulations have theoretically predicted that under certain conditions, gradient copolymers can also form microphase structures during living copolymerization in the bulk.[23] In this work, we report the first experimental attempt to demonstrate PISA during the synthesis of gradient copolymers in bulk without solvent.

As a suitable monomer pair for this research, we chose the styrene (S)–*N*-vinylpyrrolidone (VP) system as one of the most convenient for studying microphase structuring during polymerization. Firstly, the activity of monomers differs by three orders of magnitude ($r_S = 6.3$, $r_{VP} = 0.01$),[24] and secondly, the PS and PVP homopolymers are incompatible with each other, which is a necessary condition for microphase separation. Theoretical calculations of the local composition along the copolymer chain for different ratios of VP monomer in the S–VP reaction mixture can be performed using a standard terminal model,[25,26] representing a simple Markovian process in the space of sequences. Similar results were presented[23] for different polymerization ratios. This shows that this pair of monomers can form gradient copolymers, which in their structure with an almost pure VP block at the end resemble ‘true’ diblock copolymers [Figure 1(*b*)]. Therefore, in such systems, one can expect the appearance of microphase separation, probably directly during the polymerization reaction.

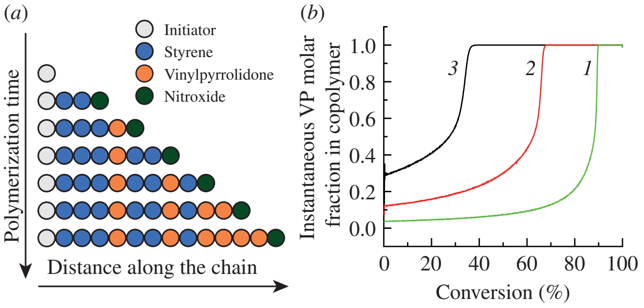

Figure 1 (*a*) Schematic representation of the formation of a gradient copolymer for VP fraction of 0.5 in the feed mixture and (*b*) instantaneous VP fraction in P(S–VP) copolymers for VP fractions of (*1*) 0.2, (*2*) 0.5, and (*3*) 0.8 in the feed mixture, determined from the terminal kinetic model with $r_S = 6.3$ and $r_{VP} = 0.01$.

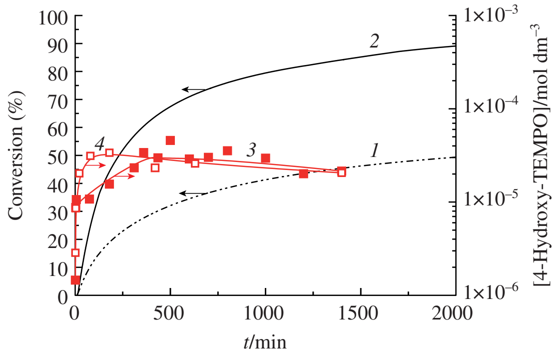

Figure 2 Integral kinetic curves of S and VP copolymerization under the action of AIBN/4-hydroxy-TEMPO (*1*) in the absence and (*2*) in the presence of Ac_2O. Change in the concentration of 4-hydroxy-TEMPO during copolymerization of S and VP under the action of AIBN/4-hydroxy-TEMPO (*3*) in the absence and (*4*) in the presence of Ac_2O. Conditions: [AIBN] = 5 mM, [4-hydroxy-TEMPO] = 6 mM, S/VP = 50:50, [Ac_2O] = 0 and 10 mM at 120 and 130 °C, respectively.

Earlier, we showed the possibility of obtaining gradient copolymers in the S–VP system using controlled TEMPO-mediated radical polymerization.[12] The polymerization mechanism in this system can be represented as follows. Since S is much more active than VP, the former polymerizes much faster than the latter. As a consequence, short ‘living’ macromolecules consist almost only of S units at the early stages of polymerization. Due to the rapid consumption of this monomer, its amount in the reaction mixture depletes, and, therefore, its share in the portions of monomer units that are attached to growing ‘living’ chains also decreases, and, accordingly, the share of VP increases. By the end of copolymerization, almost pure VP remains in the monomer mixture, and the macromolecules attach VP units. As a result, gradient macromolecules will be formed, the ‘head’ of which is enriched with S, and the ‘tail’ with VP [Figure 1(*a*)].

Under typical conditions of nitroxide-mediated polymerization† (S/VP ratio of 50:50, 5 mM AIBN, 6 mM 4-hydroxy-TEMPO, 120 °C), the copolymer yield is only 60% due to the formation of ‘dormant’ VP–nitroxide adducts. We found that introducing a 10 mM acetic anhydride (Ac_2O) additive and increasing the reaction temperature to 130 °C accelerate the process and simultaneously increases the conversion to 90–95% (Figure 2).

The change in the concentration of free nitroxide during copolymerization was analyzed by the ESR method, and it was shown that copolymerization under these conditions proceeds *via* the mechanism of reversible inhibition. According to Figure 2, the change in the concentration of 4-hydroxy-TEMPO occurs with a dependence characteristic of nitroxide-mediated polymerization. In the initial short period corresponding to the decomposition of AIBN, the concentration of nitroxide drops sharply due to its consumption in reaction with primary growth radicals. Then, within 15 min, a rapid accumulation of 4-hydroxy-TEMPO occurs due to the bimolecular termination of the radicals formed during the decomposition of primary adducts. After that, the system reaches a stationary state at which the concentration of free nitroxide changes weakly. The introduction of acetic anhydride does not strongly affect the concentration of free nitroxide against the background of which polymerization occurs. Copolymerization with the addition of Ac_2O proceeds against a background of 4-hydroxy-TEMPO concentration of ~10^{-5} M. As we have shown earlier,[27] these conditions are typical for implementing the mechanism of pseudo living polymerization. The data of IR analysis (Figure S1) and GPC (Figure S2) of the copolymers confirm this conclusion, see Online Supplementary Materials.

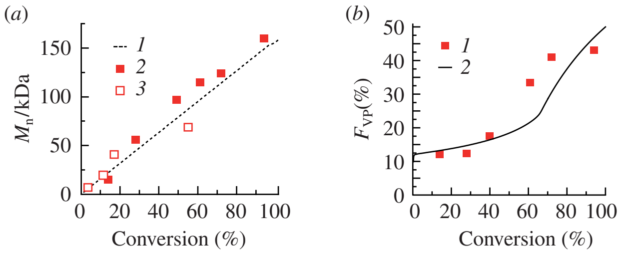

Figure 3 Characteristics of 50:50 S–VP samples: (*a*) dependences of M_n on conversion, including (*1*) theoretical relationship calculated according to the law of living chains, (*2*) experimental data for synthesis in the presence of Ac_2O and (*3*) published data[12] for synthesis in the absence of Ac_2O; (*b*) dependences of the average fraction of VP (F_{VP}) in the copolymer composition on conversion, (*1*) obtained from IR analysis and (*2*) calculated from the data presented in Figure 1(*b*).

The M_n value of the copolymer increased linearly with conversion up to complete polymerization of the monomers [Figure 3(*a*) and Table S1]. The experimental M_n value was close to that calculated according to the law of living chains:

$$M_n = q\,[M]_0\,m\,/\,[\text{4-hydroxy-TEMPO}]_0,$$

where m is the average mass of the monomer unit, q is the conversion, and $[M]$ is the total molar concentration of monomers. This confirmed the living mechanism of chain growth. Note that in the absence of Ac_2O, living growth stops shortly after 50% conversion.[12] It is important that simultaneously with an increase in the M_n value of the copolymer, the proportion of S units decreased, and, accordingly, the fraction of VP units (F_{VP}) in the copolymer increased [Figure 3(*b*) and Table S1], which means the formation of a gradient structure of the chain.

Structure formation during copolymerization in the S–VP system in bulk (without solvent) was studied by transmission electron microscopy (TEM). For this purpose, thin sections (about 100 nm) of the reaction medium polymerized to the maximum conversion were cut using an ultramicrotome. We should emphasize that neither annealing nor purification was used to prepare the samples. Four samples were prepared for further investigation according to the procedure described above, but with a different S/VP ratio – 60:40, 50:50, 40:60 and 30:70. The characteristics of the samples are presented in Figure 4 and Table S2.

Preliminary, we note that the usual statistical copolymer of S and VP, obtained by radical polymerization, is fundamentally different in structure from its gradient analog of the same composition. The statistical copolymer is characterized by disordered macrophase separation with irregular domains of ~1 μm or more. Also, the structure of the gradient copolymer is highly dependent on its composition and degree of conversion. Our samples are homogeneous up to at least 60% conversion (Figure S3).

As can be seen from the microscopy investigation, phase separation with the formation of nanoscale unstructured domains in bulk gradient copolymers P(S–VP) occurs at a conversion above 90% (Figure 4). For sample S/VP (60:40), an almost homogeneous structure is formed, consisting of a dark macrophase interspersed with light spherical inclusions of ~20 nm in size [Figure 4(*a*)]. For the S/VP copolymer of the 50:50 composition, the amount of light phase increases [Figure 4(*b*)]. This copolymer is characterized by the size of inhomogeneities of 50–150 nm,

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† Appropriate amounts of 4-hydroxy-TEMPO and AIBN were dissolved in a mixture of freshly distilled S and VP, the solutions were placed in glass ampoules attached to a vacuum unit, and evacuated to a residual pressure of 3×10^{-3} Torr by repeated freeze–pump–thaw cycles, and then were sealed. The polymerization was carried out at 120 °C. For further analysis, the polymerization products were isolated from the benzene solution by lyophilization *in vacuo*. See Online Supplementary Materials for information on the chemicals and equipment used for the study.

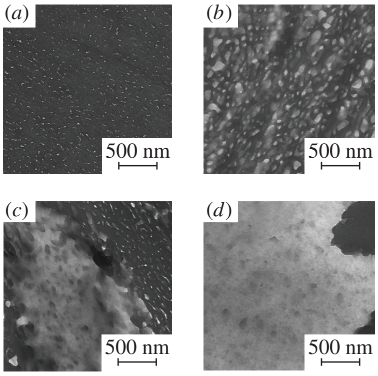

Figure 4 TEM images of ultramicrotome sections of the bulk obtained by copolymerization of S and VP at different S/VP monomer ratios in the feed mixture: (*a*) 60 : 40 (conversion 95%, $Đ$ = 1.5), (*b*) 50 : 50 (conversion 94%, $Đ$ = 2.5), (*c*) 40 : 60 (conversion 94%, $Đ$ = 2.2) and (*d*) 30 : 70 (conversion 97%, $Đ$ = 2.2).

evenly distributed over the entire surface. Further, in sample S/VP (40 : 60), there are two types of inhomogeneity – an extended dark macrophase and an 'amoeba' from the light phase [Figure 4(*c*)]. Both types of macrophases, in turn, are also characterized by microstructured separation and resemble a combination of structures formed in adjacent compositions. It could be assumed that this case is unstable. For sample S/VP (30 : 70) [Figure 4(*d*)], one can observe a light macrophase with small dark spherical inclusions ~50 nm in size, which in some way reflects the case in Figure 4(*a*). Note that the heterogeneity of all these samples is visible not only under the microscope but also visually – the reaction vials become opalescent at high conversions, being transparent at low ones.

It can be assumed that in these gradient copolymers, the dark continuous phase is represented by copolymer segments enriched with S. Such a structure arises at the beginning of the process and forms the basis of the material. Therefore, it is possible to correlate the light regions with the phase formed by the tails of macromolecules enriched with VP units, which have attached to the macromolecule closer to the end of the polymerization process. The regular alternation of light and dark areas observed in all samples indicates the microphase-like separation in these systems. Nevertheless, it is still premature to assert the existence of long-range order in lamellas or cylinders.

In conclusion, we have shown for the first time that gradient copolymers can be used to obtain microphase-like separated structures directly in the reaction medium in one-pot synthesis in bulk without any additional treatment. We have demonstrated that the morphology of the resulting product is highly dependent on conversion and monomer ratio. The described phenomenon can be useful, for example, for casting into sophisticated molds, for the manufacture of nanostructured plexiglass and other composite materials.[28] Thus, it should be thoroughly investigated by our group and other research teams.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.03.045.

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