Synthesis and Characterization of Amphiphilic Polymer Networks Based on Acrylated Poly(ε-caprolactone) and *N*-Vinylpyrrolidone

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ABSTRACT: New amphiphilic polymer networks were synthesized by the free-radical copolymerization of α,ω-diacryl polycaprolactone (DAPCL) and *N*-vinylpyrrolidone (NVP), which was initiated by 0.5% azobisisobutyronitrile at 70°C. The chemical structures of the networks were characterized by proton nuclear magnetic resonance spectrometry. The NVP/DAPCL feed ratio played an important role in the crosslinking process. The synthesized amphiphilic polymer networks exhibited controlled swelling properties in water and organic solvents (ethanol, acetones, and toluene). A porous structure was observed for the amphiphilic polymer networks under a scanning electron microscope. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 105: 2712–2716, 2007

Key words: copolymerization; amphiphilic; networks

INTRODUCTION

Amphiphilic polymer networks (APNs) are polymer networks consisting of both hydrophilic and hydrophobic components.[1–3] APNs have been widely studied because they exhibit unique properties such as swelling in both organic and aqueous media, excellent biocompatibility, adjustable mechanical properties, and controlled release of hydrophobic/hydrophilic drugs.[4,5]

The most convenient method for the preparation of APNs is the free-radical crosslinking copolymerization of a hydrophilic component and a hydrophobic component.[2] Generally, APNs can be synthesized by the copolymerization of a hydrophobic and hydrophilic monomer, a hydrophobic macrocrosslinker and a hydrophilic monomer, or a hydrophobic monomer and a hydrophilic macrocrosslinker.[3] The use of macrocrosslinkers has attracted extensive interest because they provide the ability to separate the polymerization process from the network formation and to produce APNs with controlled structures.[1] Various macrocrosslinkers such as α,ω-diacrylate polyisobutylene,[6–13] α,ω-diacrylated poly(tetrahydrofuran),[14–17] α,ω-diacrylated polylactide (PLA)/poly(ε-caprolactone) (PCL),[18–21] and α,ω-diacrylate poly(2-oxazoline)s[22,23] have been investigated widely for the preparation of APNs. Recently, biodegradable APNs synthesized by the free-radical copolymerization of biodegradable macrocrosslinkers and monomers have attracted much interest.[18–21] Jérôme et al.[20] prepared bioerodible and biocompatible APNs from 2-hydroxyethyl methacrylate and α,ω-dimethacrylate with PLA/PCL, which was synthesized by living cationic ring-opening polymerization. The resulting networks could swell in both organic solvents and aqueous media; thus, they could be loaded with both lipophilic (dexamethasone acetate) and hydrophilic (dexamethasone sodium phosphate) drugs.

PCL is one of the most widely used biodegradable polyesters in biomedical and packaging applications. It is a highly hydrophobic polymer with a slow hydrolytic degradation rate.[24] Poly(*N*-vinylpyrrolidone) (PVP) is a water-soluble polymer with excellent biocompatibility and low cytotoxicity to living tissue.[25,26] In addition, PVP is miscible with many organic solvents, and it interacts with a variety of small molecules in solution because of its amphiphilic nature.[27] As a result, PVP has attracted much attention as a material for use in medicine and pharmaceuticals.[28,29] The combination of the two components (i.e., PCL and PVP) in the synthesis of APNs can result in adjustable properties providing the potential to carry both hydrophilic and hydrophobic drugs. APNs with controllable swelling properties also can be obtained by the variation of the feed ratio of the α,ω-diacryl polycaprolactone (DAPCL) to the *N*-vinylpyrrolidone (NVP) monomer. This article reports a family of novel biodegradable amphiphilic networks synthesized by the free-radical copolymerization of DAPCL and NVP.

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EXPERIMENTAL

Materials

A PCL diol with a molar mass of 4000 g/mol, a gift from Solvay Caprolactones (Cheshire, UK), was dried *in vacuo* before use. Acryloyl chloride was purified by distillation in the presence of hydroquinone. Triethylamine was dried and distilled over calcium hydride. NVP was purified by distillation under reduced pressure. Azobisisobutyronitrile (AIBN) was purified by recrystallization from hot ethanol and dried under a vacuum. The other regents were analytical-grade and were used as received.

Synthesis of DAPCL

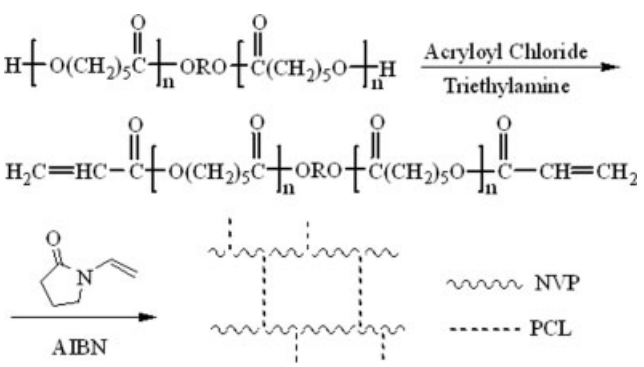
DAPCL was prepared according to the literature.[30] Briefly, 8.000 g (2.0 mmol) of the PCL diol was dissolved in 100 mL of dichloromethane at 40°C; then, 0.455 g (4.5 mmol) of triethylamine and 0.407 g (4.5 mmol) of acryloyl chloride were added, and the reaction mixture was stirred overnight at room temperature. Triethylamine hydrochloride salt was precipitated during the reaction process and was removed by filtration after the reaction was completed. The filtrate was concentrated with a rotary evaporator and poured into *n*-hexane. The white precipitate was collected and dried under a vacuum at room temperature overnight.

Preparation of the APNs

The APNs were synthesized by the free-radical copolymerization of DAPCL and NVP (Scheme 1). DAPCL, NVP, and 0.5 wt % AIBN were added to a glass ampule and vacuum-sealed after three vacuum–nitrogen cycles. The polymerization was carried out at 70°C in an oil bath for 24 h. The crude product was extracted by dichloromethane for 72 h to leach out the reactants and homopolymer. The resulting product was dried at 60°C under a vacuum until a constant weight (W_{gel}) was achieved to ensure the complete elimination of volatile impurities. The gel content was calculated with eq. (1):

$$\text{Gel content} = [W_{gel}/(W_{DAPCL} + W_{NVP})] \times 100\% \quad (1)$$

where W_{DAPCL} is the weight of DAPCL and W_{NVP} is the weight of NVP in feed.



Scheme 1 Synthesis of APNs.

Swelling measurements

The classical gravimetric method was used to measure the swelling ratios. The sample was immersed in one of the four solvents (i.e., water, ethanol, acetone, and toluene) for 48 h to reach the swelling equilibrium. After the solvent on the network surfaces was wiped off with moistened filter papers, the weight of the network was measured. Three measurements were taken for each sample, and the swelling ratio was calculated with eq. (2):

$$\text{Swelling ratio} = [(W_t - W_d)/W_d] \times 100\% \quad (2)$$

where W_d is the weight of the dried networks and W_t is the weight of the swollen networks at time t.

Characterization

^{1}H-NMR spectra of the PCL diol, DAPCL, and APNs were recorded on a Mercury VX-300 spectrometer with tetramethylsilane as an internal standard and $CDCl_3$ as a solvent. For the APNs, a 0.500-g sample was swollen for 48 h in $CDCl_3$ in the NMR tube, and the resulting transparent swollen network was used for the measurements.

The morphologies of the dried polymer networks were investigated with a Hitachi scanning electron microscope (Ibaraki, Japan) at 20 kV.

RESULTS AND DISCUSSION

Preparation of the APNs

The ^{1}H-NMR spectra of the PCL diol and DAPCL are shown in Figure 1. DAPCL was synthesized by the reaction of the PCL diol with acryloyl chloride. The differences in these two spectra are the peaks that appear at δ = 5.70–6.50 ppm in the DAPCL spectrum, indicating the incorporation of acrylate groups into the PCL chain.

The copolymerization temperature was set at 70°C, which was above the melting point of PCL (ca. 60°C), to ensure a homogeneous reaction, which is essential for this kind of reaction. The APNs were prepared at six different NVP/DAPCL feed ratios (w/w)—90 : 10, 70 : 30, 50 : 50, 30 : 70, 10 : 90, and 0 : 100—and were designated CN1, CN2, CN3, CN4, CN5, and CN6, respectively. After extraction in dichloro-

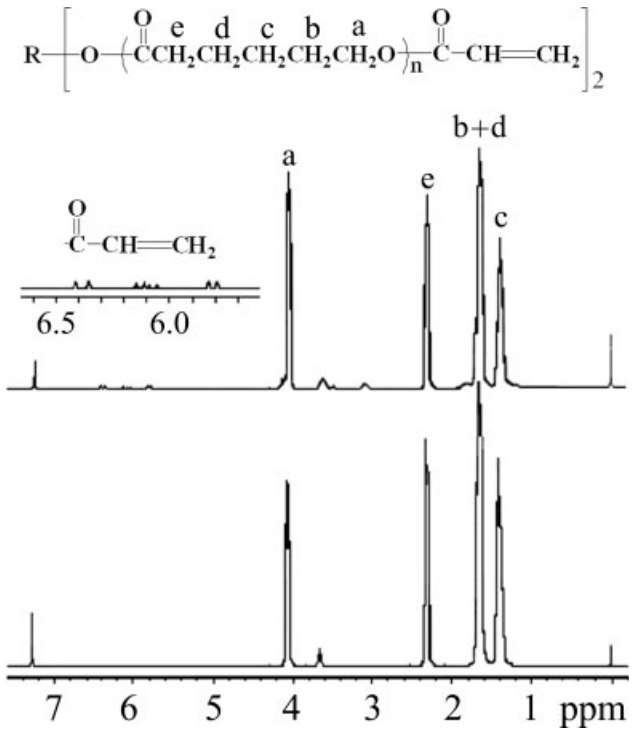


Figure 1 ^{1}H-NMR spectra of DAPCL (top) and PCL diol (bottom).

methane for 72 h to remove all the soluble fractions, the insoluble network consisting of PCL and PVP segments were obtained. As shown in Figure 2, the peak at $\delta = 4.00$ ppm belongs to —OCH_2— of the PCL unit in the network, and the peaks at $\delta = 2.80$ ppm and $\delta = 3.20$ ppm can be assigned to —CH—CH_2 and —N—CH_2— of the NVP unit. The composition of the hydrophobic PCL segment and the hydrophilic NVP segment can be calculated by the integrals of the peak at $\delta = 4.00$ ppm and $\delta = 3.20$ ppm, respectively.

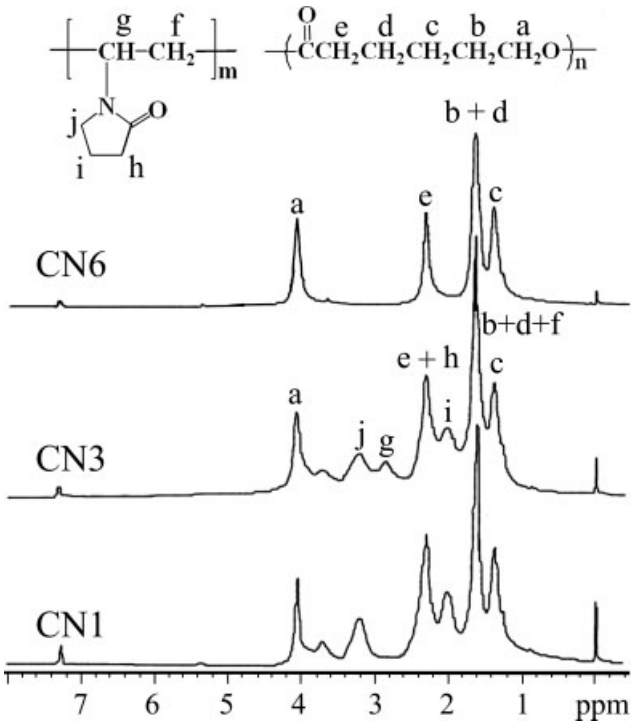


Figure 2 ^{1}H-NMR spectra of NVP/DAPCL APNs.

The gel content and the calculated NVP weight percentage in the APNs as a function of the NVP feed weight percentage are shown in Figure 3. For CN6, the gel content was 54 wt % with the use of only DAPCL as the polymerization monomer. When the NVP feed percentage increased from 0 to 30 wt %, the gel content increased from 54 to 69 wt %. After that, the gel content decreased continuously from 69 to 12 wt % when the NVP feed percentage increased from 30 to 90 wt %. The presence of a maximum gel content, which was obtained at an NVP percentage of 30 wt %, indicates that the crosslinking reaction was highly dependent on the NVP/DAPCL feed ratio and that NVP played an important role in the network formation. The crosslinking efficiency was rather low for the high NVP/DAPCL feed ratio systems, and this can be attributed to the strong tendency for chain transfer of NVP.[31] When the NVP feed percentages were 10, 30, 50, 70, and 90 wt %, the corresponding NVP percentages in the APNs were 8, 27, 40, 46, and 56 wt %, respectively. Although the calculated NVP weight percentages in the APNs increased with the NVP feed weight percentages, it is obvious that the weight percentages of the NVP segments in the resulting APNs were lower than those in the feed. This phenomenon showed that NVP has lower reactivity than DAPCL during the process of network formation. In other words,

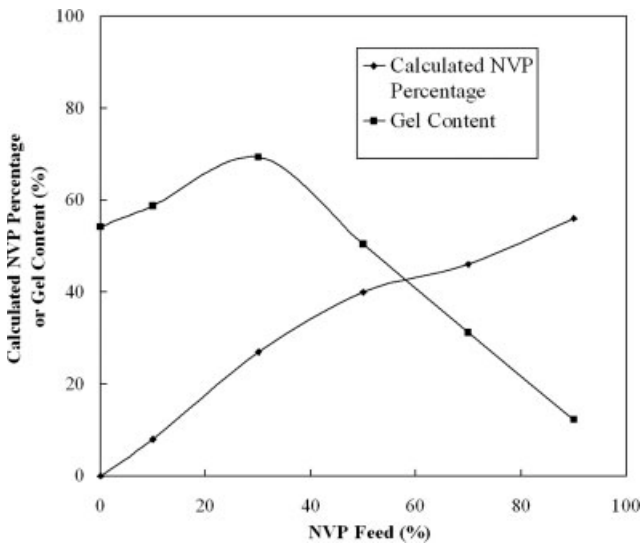


Figure 3 Gel contents and calculated NVP weight percentages in the polymer networks as functions of the NVP feed weight percentage.

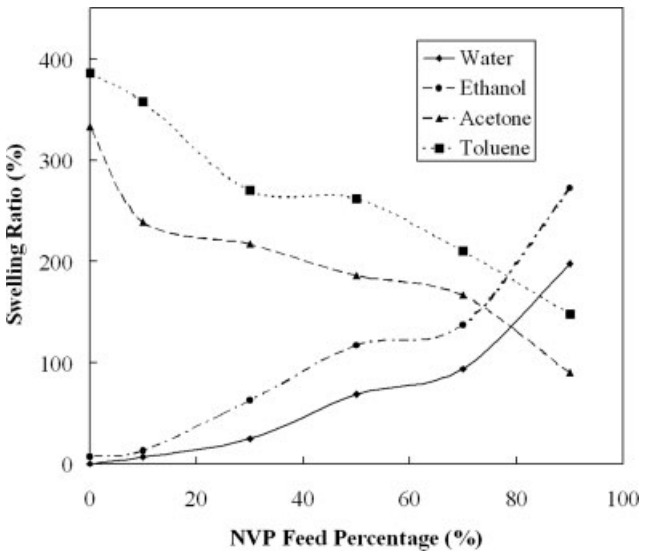


Figure 4 Equilibrium swelling ratios of the polymer networks in water, ethanol, acetone, and toluene (25°C).

the NVP monomers can be incorporated more readily into the NVP homopolymer than into the network, and this leads to lower gel contents at higher NVP feed percentages. For example, at an NVP feed percentage of 90 wt %, most of the NVP converted into the linear homopolymer and subsequently was extracted by a solvent after polymerization, and this resulted in the lowest gel content value.

Swelling studies

APNs have shown their ability to swell in both aqueous media and organic solvents, as reported in the literature.[1] The swelling behavior of APNs is governed by the preferential interaction of each solvent toward one of the two constitutive components of the network, as well as the network composition.[20] In this work, swelling studies of the APNs were performed in solvents with different hydrophilicities: water, ethanol (hydrophilic), acetone (less hydrophilic), and toluene (hydrophobic). Of these four solvents, water and ethanol were good solvents for PVP, but acetone and toluene were poor solvents for PVP.

The dependence of equilibrium swelling ratios in different solvents at room temperature on the composition of the NVP/DAPCL networks is presented in Figure 4. As expected, the polymer networks containing both NVP and DAPCL segments showed amphiphilic behaviors. The composition of the NVP component and PCL component had a great influence on the swelling behavior of the polymer networks in these four types of solvents. For CN6, because the polymer network comprised only hydrophobic PCL segments, it did not swell in water and the hydrophilic ethanol. When the NVP weight percentage in the APNs increased from 0 to 56 wt % (corresponding to the NVP feed percentage from 0 to 90 wt %), the swelling ratios of the networks in water increased from 0 to 198%. This gradual increase in the water uptake with the increase in the hydrophilic component in APNs has been observed in various APN systems, such as PCL/poly(2-hydroxyethyl methacrylate)[20] and poly(2-alkyl-2-oxazoline)/poly(methyl methacrylate).[23] With ethanol as the swelling solvent, the swelling ratios of the networks also showed a gradual increase with the NVP weight percentage, that is, from 0 to 272%. In contrast to the swelling behavior of the APNs in water and ethanol, the swelling ratio in acetone and toluene decreased with an increasing NVP weight percentage (i.e., increased with an increasing PCL weight percentage). When the NVP percentage increased from 0 to 56 wt %, the swelling ratios for

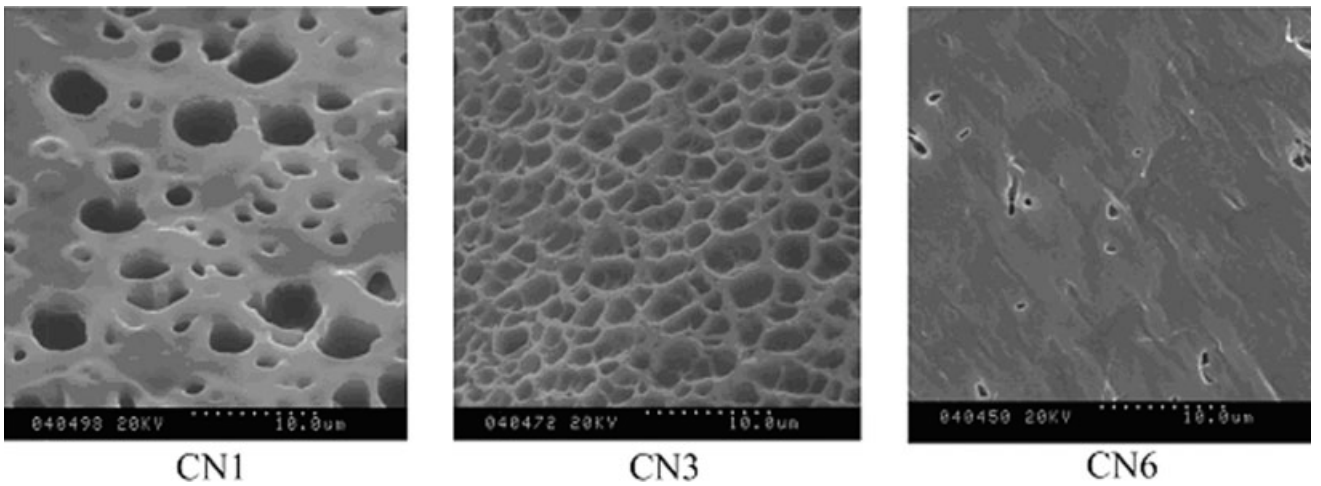


Figure 5 Scanning electron microscopy micrographs of the APNs (CN1, CN3, and CN6).

APNs in acetone and toluene decreased from 333 to 90% and from 386 to 148%, respectively. There were four compositions at which the APNs swelled equally in the hydrophilic solvent (water/ethanol) and hydrophobic solvent (acetone/toluene). Such swelling behavior is typical for APNs containing segments of the opposite philicities.[23]

Morphology of the polymer networks

Figure 5 shows scanning electron microscopy photographs of the dried polymer networks of CN1, CN3, and CN6 with calculated NVP contents of 56, 40, and 0 wt %, respectively. It has been reported that networks prepared with AIBN as a free-radical initiator exhibit a porous structure resulting from the release of nitrogen gas upon the thermal decomposition of AIBN.[20] The surface of the samples appeared to be rough and porous. CN6, consisting of only PCL segments, exhibited a smoother surface with tiny pores. CN1 and CN3 possessed larger and more pores because of their heterogeneous structures as well as the PVP (soluble fractions) leaching effect.

CONCLUSIONS

New APNs with controlled swelling behavior and porous structures were synthesized by the free-radical polymerization of DAPCL and NVP. The gel content strongly depended on the NVP/DAPCL feed ratio. With an increase in the NVP/DAPCL feed ratios, the swelling ratios of the polymer networks increased in water and hydrophilic solvents, such as ethanol, and decreased in less hydrophilic solvents, such as acetone and toluene. The observed phenomena can be attributed to the hydrophilicity of the NVP component and the hydrophobicity of the PCL component in the APNs. Thus, the swelling ratios of the APNs in different solvents could be controlled by the variation of the PCL/NVP composition.

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