# Synthesis of Biodegradable and Biocompatible ABC Triblock Copolymers

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**ABSTRACT:** A facile approach is offered to synthesize well-defined amphiphilic ABC triblock copolymers composed of poly(ethylene glycol) monomethyl ether (MPEO) as A block, poly(L-lysine) (PLLys) as B block, and poly(ε-caprolactone) (PCL) as C block by a combination of ring-opening polymerization (ROP) and click reactions. The propargyl-terminated poly(Z-L-lysine)-*block*-poly(ε-caprolactone) (MPEO-PzLLys-PCL) diblock copolymers were synthesized via the ring-opening polymerization of $N^{\varepsilon}$-carbobenzoxy-L-lysine *N*-carboxyanhydride (Z-L-Lys NCA) in DMF at room temperature using propargyl amine as an initiator and the resulting amino-terminated poly(Z-L-lysine) then used *in situ* as a macroinitiator for the polymerization of ε-caprolactone in the presence of stannous octoate as a catalyst. The triblock copolymers poly(ethylene glycol) monomethyl ether –*block*-poly(Z-L-lysine)-*block*-poly(ε-caprolactone) (MPEO-PzLLys-PCL) were synthesized via the click reaction of the propargyl-terminated PzLLys-PCL and azido-terminated poly(ethylene glycol) monomethyl ether (PEO-$N_3$) in the presence of CuBr and 1,1,4,7,7-pentamethyldiethylenetriamine (PMDETA) catalyst system. After the removal of Z groups of L-lysine units, amphiphilic and biocompatible ABC triblock copolymers MPEO-PLLys-PCL were obtained. The structural characteristics of these ABC triblock copolymers and corresponding precursors were characterized by NMR, IR, and GPC. These results showed the click reaction was highly effective. Therefore, a facile approach is offered to synthesize amphiphilic and biocompatible ABC triblock copolymers consisting of polyether, polypeptide and polyester.
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**Key words:** block copolymers; polyethers; synthesis; ring-opening polymerization

## INTRODUCTION

Amphiphilic block copolymers and their synthesis have received considerable interest not only for their rich morphological structures[1] but also for their potential applications.[2,3] Among these synthetic block copolymers, amphiphilic biodegradable and biocompatible ones are of special interest.[3] Because they possess excellent biodegradable and biocompatible properties, these copolymers can be used for various biomedical applications, such as drug carriers, components of implants, scaffolds, and sutures. Generally, these synthetic block copolymers consist of polylactone, polyether, and polypeptide, which can meet the requirements of biomedical applications. For example, as a typical polylactone, poly(ε-caprolactone) is lack of toxicity, biodegradable and miscible with a wide range of synthetic polymers. Poly(ethylene glycol) (PEO), as a hydrophilic and biocompatible polyether, is widely used in biomedical research and application.[4] Therefore, poly(ε-caprolactone) and poly(ethylene glycol) are often introduced into the copolymers.[5–7] Recently, a growing research interest has been shown in the synthesis of block copolymers comprised of polypeptide segments.[7–18] The probable reasons are as follows: compared with conventional polymers, polypeptide can show well-defined stable secondary conformations, such as α-helices, β-sheets or random coils, depending on the external environment, which plays an important role in the formation of the morphological structures. At the same time, polypeptides also possess excellent properties for biomedical applications, such as low toxicity, biodegradability, and biocompatibility. For example, Motala-Timol et al.[18] reported on the synthesis of PzLLys-PCL diblock copolymers via an *in situ* polymerization method. In short, a combination of the advantages of poly(ε-caprolactone), poly(ethylene glycol) monomethyl ether, and polypeptide may lead to novel biomedical material for the development of bioscience and material science.

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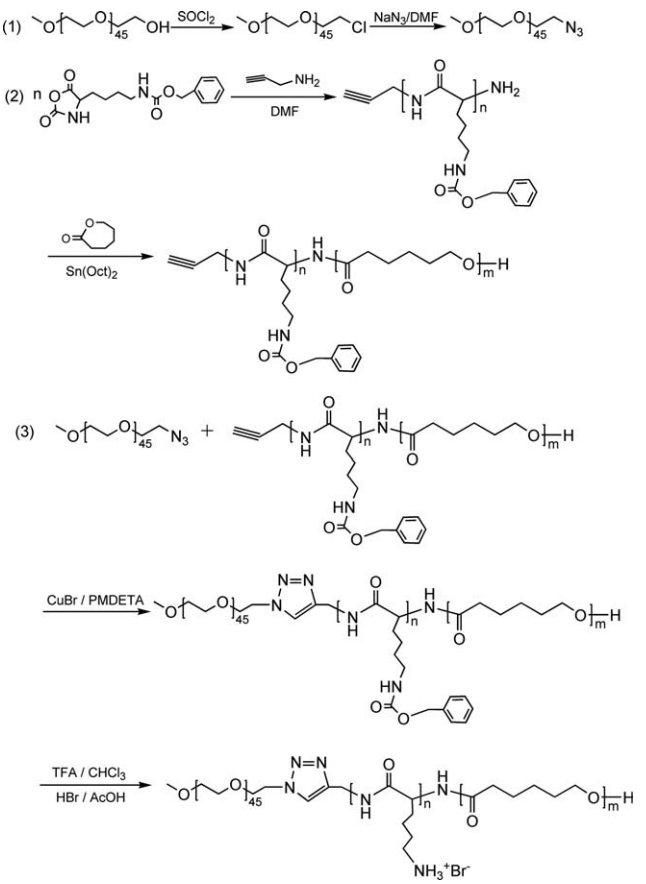
"Click" reaction, defined by Sharpless,[19] has been applied in polymers synthesis[15,16,20–23] and advanced architectural designs[24–28] because of its quantitative yields, mild reaction condition and tolerance of a wide range of functional groups. To date, the combinations of the superior reaction characteristics of click reactions and other polymerization techniques can be applied to prepare polymers with novel structures. Recently, Hua et al.[28] reported that the synthesis of linear-dendron-like poly(ε-caprolactone)-*block*-poly(ethylene oxide) copolymers via the combination of ring-opening polymerization (ROP) and click reactions. Our group[16,29,30] also reported the synthesis of some novel structural ABC triblock copolymers via the combination of click reactions and other controlled polymerization techniques. In this contribution, a series of well-defined amphiphilic triblock copolymers MPEO-PzLLys-PCL were synthesized by the combination of ring-opening polymerization (ROP) and click reactions. Then, amphiphilic and biocompatible ABC triblock copolymers MPEO-PLLys-PCL were obtained from the removal of Z group of L-lysine units in the presence of trifluoroacetic acid and hydrobromic acid. The synthesis of triblock copolymers was shown in Scheme 1. To the best of our knowledge, there have been few reports concerning the synthesis of triblock copolymers comprised of MPEO, PCL, and PLLys segments with PLLys as the middle block.




**Scheme 1** Synthesis of ABC triblock copolymers

## EXPERIMENTAL

### Materials

$N^{\varepsilon}$-carbobenzoxy-L-lysine (H-Lys(Z)-OH) was purchased from GL Biochem (Shanghai). ε-caprolactone(ε-CL, Aldrich, 99%) was distilled over $CaH_2$ *invacuo* before use. Poly(ethylene glycol) monomethyl ether (MPEO-OH) ($M_n$= 2000 g $mol^{-1)}$ was purchased from Aldrich. N,N-dimethylformamide (DMF, Shanghai Chemical Reagent Co., A.R. grade) was dried over $CaH_2$ for 24 h at room temperature, followed by distillation under reduced pressure. The middle fraction was collected and stored over 4Å molecular sieves under an argon atmosphere. CuBr (Shanghai Chemical Reagent Co., A.R. grade) was purified by stirring in glacial acetic acid overnight, filtered, washed with ethanol and then dried in a vacuum oven at 60°C overnight. Thionyl chloride ($SOCl_2$, Shanghai Chemical Reagent Co., A.R. grade) was freshly distilled before use. Sodium Azide ($NaN_3$, Acros, 99%), 1,1,4,7,7-pentamethyldiethylenetriamine (PMDETA, Aldrich, 99+%), Propargyl amine(Acros, 98%), Trifluoroacetic acid (TFA, Shanghai Chemical Reagent Co., A.R. grade), Stannous octanoate($Sn(Oct)_2$, Shanghai Chemical Reagent Co., A.R. grade), Other solvents were purchased from Shanghai Chemical Reagent Company and purified by conventional procedures if needed. $N^{\varepsilon}$-carbobenzoxy-L-lysine *N*-carboxyanhydride (Z-L-Lys NCA) was synthesized according to the literature.[31]

### Characterization

$^1$H-NMR spectra were obtained on a 500 Bruker NMR instrument using $CDCl_3$ as solvent, tetramethyl silane as the internal standard. Fourier Transform Infrared (FTIR) spectra were recorded on a Perkin–Elmer Spectrum one spectrometer at frequencies ranging from 400 to 4000$cm^{-1.}$ Samples were thoroughly mixed with KBr and pressed into pellet form. Molecular weights $M_n$ and polydispersity $M_w/M_n$ were measured on a gel permeation chromatograph (Waters 515C) equipped with three MZ-Gel SD plus column ($10^3$, $10^5$, and $10^6$ Å), using DMF (0.05*M* LiBr solution) as eluent at 40°C with a flow rate of 1 mL/min. The detectors consisted of a multiangle laser light scattering (MALLS) detector (Wyatt Technology Corporation, DAWN HELEOS) with the light wavelength at 690 nm and a RI detector (Wyatt Technology Corporation, Optilab REX).

### Synthesis of propargyl-terminated PzLLys-PCL

The propargyl-terminated PzLLys-PCL was synthesized by ROP of Z-L-Lys NCA in dry DMF using propargyl amine as an initiator and the resulting amino-terminated PzLLys was then used *in situ* as a macroinitiator for the polymerization of ε-CL in the presence of $Sn(Oct)_2$. In a glovebox, Z-L-Lys NCA (4.0 g, 13.1 mmol) was weighted under pure nitrogen, added into a previously dried round-bottomed flask equipped with a magnetic bar, and dissolved with dry DMF (50 mL). Propargyl amine (22 μL, 0.33 mmol) was added into the solution using a degassed syringe after stirring for 10 min. The solution was stirred under pure $N_2$ at room temperature. After 5 days, the polymerization solution was divided into two equal parts. $Sn(Oct)_2$ (1.0 mg, 2.5 mmol) was added to each solution and continuously stirred at 50°C for 20 h, and DMF was then removed by rotary evaporation. Different molar mass of ε-CL was added to each part under pure $N_2$ and the polymerization mixture was stirred at 110°C for 24 h. After the polymerization, the crude product was dissolved in $CH_2Cl_2$ and precipitated into an excess amount of methanol, and purified by reprecipitating three times from tetrahydrofuran (THF) to methanol, filtered and dried at 40°C in a vacuum oven for 48 h. Two samples with the same molecular weight of PzLLys segment and different molecular weight of PCL segment were obtained: $M_n$(GPC) = $1.58 \times 10^4$, $M_w/M_n = 1.35$; $M_n$(GPC) = $1.72 \times 10^4$, $M_w/M_n = 1.28$

### Synthesis of MPEO-$N_3$

MPEO-OH (5.0 g, 2.5 mmol) was dissolved in toluene (50 mL) and the trace water contained in MPEO was removed by azeotropic distillation. After adding dried pyridine(5 mmol), freshly distilled $SOCl_2$(6.0 g, 50 mmol) was added dropwise during 30 min under reflux. The reaction mixture was stirred at 110°C overnight under nitrogen, cooled to room temperature and removed pyridine hydrochloride by filtration. The solution was concentrated by rotary evaporation and the crude product was obtained by precipitating into an excess amount of cold diethyl ether. The chloro-terminated MPEO (MPEO-Cl) was recrystallized from absolute ethanol two times, filtered and dried at 40°C in a vacuum oven for 24 h.

The obtained MPEO-Cl (4.0 g, 2.0 mmol), $NaN_3$ (0.65 g, 10.0 mmol), and DMF (20 mL) were added in a round-bottomed flask. The mixture solution was stirred with a magnetic bar at 90°C overnight under $N_2$ before removal of DMF by rotary evaporation. The solid was dissolved in $CH_2Cl_2$ and the undissolved solid was removed by filtration. The solution was washed three times with water, dried with anhydrous $MgSO_4$, concentrated by rotary evaporation and precipitated in an excess amount of cold diethyl ether. The azido-terminated MPEO (MPEO-$N_3$) was recrystallized from absolute ethanol two times, filtered, and dried at 35°C in a vacuum oven for 48 h. Yield: 85%, $M_n$(GPC) = $2.2 \times 10^3$g mol$^{-1}$,and $M_w/M_n = 1.05$

### Synthesis of MPEO-PzLLys-PCL by a click reaction

A typical procedure for the click reaction was as follows: MPEO-$N_3$ (0.15 g, $2.2 \times 10^3$g mol$^{-1}$, 0.069 mmol), propargyl-terminated PzLLys-PCL (1.0 g, $1.58 \times 10^4$g mol$^{-1}$, 0.063 mmol), CuBr (20.0 mg, 0.14 mmol) and DMF (15 mL) were added into a round-bottomed flask equipped with a magnetic bar. The flask was capped with a rubber plug and purged with pure $N_2$ for 30 min. PMDETA (24.0 mg, 0.14 mmol) was then added by using a degassed syringe. The mixture was stirred for 36 h at 40°C. After the reaction, the reaction mixture was further diluted with THF, removed copper salts through a plugged column of neutral aluminum oxide. The product was precipitated in methanol and purified by reprecipitating three times from THF to methanol and dried at room temperature in a vacuum oven for 48 h. Yield: 80%. $M_n$(GPC) = $1.71 \times 10^4$g mol$^{-1}$, $M_w/M_n = 1.40$.

### Synthesis of MPEO-PLLys-PCL

The ABC triblock polymers MPEO-PLLys-PCL were prepared through the removal of Z groups of L-lysine units in the presence of TFA and hydrobromic acid. A typical procedure was as follows: MPEO-PzLLys-PCL (0.5 g, $1.71 \times 10^4$g mol$^{-1}$, 0.029 mmol) was dissolved in $CHCl_3$ (5 mL), and TFA (34.0 mg, 0.3 mmol) was then added. Under stirring at room temperature with a magnetic bar, a four-fold molar excess of a 33% solution of hydrobromic acid in acetic acid was added to the reaction mixture and then continued stirring for 1.5 h at room temperature. Finally, the reaction mixture was concentrated to a minimum amount by rotary evaporation under high vacuum, and then precipitated in diethyl ether. The product was purified by reprecipitating three times from DMF to diethyl ether and dried at room temperature in a vacuum oven for 48 h. Yield: 92%. $Mn$(GPC) = $1.63 \times 10^4$g mol$^{-1}$, $M_w/M_n = 1.36$

## RESULTS AND DISCUSSION

The ring-opening polymerizations (ROP) of α-amino acid N-carboxyanhydride (NCAs) initiated by nucleophiles or bases have been the most common synthetic technique used for the synthetic polypeptides preparation.[31] In the current study, ROP of Z-L-Lys

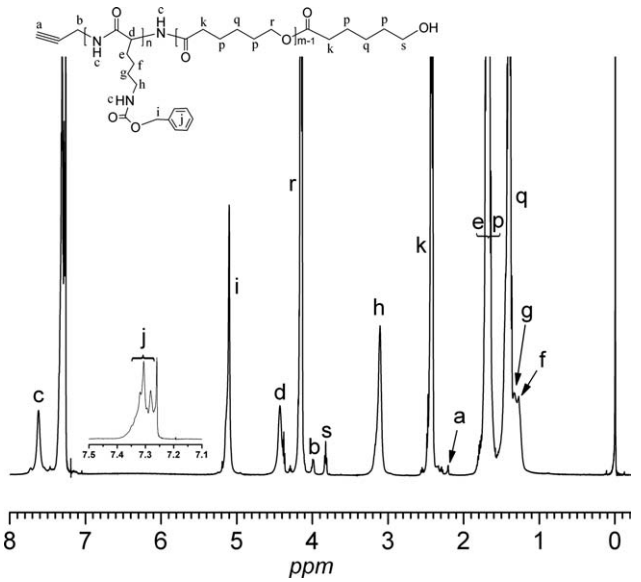



**Figure 1** $^1$H-NMR spectrum of the propargl-terminated PzLLys-PCL$_2$ in CDC1$_3$+15%TFA.

NCA was first carried out in dry DMF using propargyl amine as an initiator. The degree of polymerization of PzLLys can be controlled by the molar ratio of Z-L-Lys NCA to propargyl amine initiator, and PzLLys with appropriate molecular weight contained both propargyl functional group (HC≡CCH$_2$—) and amine functional group (—NH$_2$). It is known that hydroxyl or amine group can initiate the polymerization of ε-CL using stannous organic salt as catalyst.[18,28,32] The obtained PzLLys containing amino-terminal group was used *in situ* as a macroinitiator for the polymerization of ε-CL in the presence of Sn(Oct)$_2$ to obtain the propargyl-terminated PzLLys-PCL block copolymers. To obtain the propargyl-terminated PzLLys-PCL with different molecular weights, the different molar ratio of monomer ε-CL to the obtained PzLLys was varied to control the degree of polymerization of PzLLys-PCL. By GPC measurement, two samples with different number-average molecular weights ($1.58 \times 10^4$ and $1.72 \times 10^4$) were synthesized and their number-average molecular weight increased with increasing molar ratio of monomer ε-CL-to-the obtained PzLLys. The samples were designated as PzLLys-PCL$_n$ ($n$ = 1–2, designating the sample ID). The structural characteristics of propargyl-terminated PzLLys-PCL have been determined by the combination techniques consisting of $^1$H-NMR, IR, and GPC. $^1$H-NMR spectrum of PzLLys-PCL$_2$ recorded in CDCl$_3$+15%TFA is shown in Figure 1. The peaks at 2.20 and 3.98 ppm [Fig.1(a,b)] are ascribed to methine and methylene protons of propargyl residues (**H**C≡C—C**H**$_2$—), respectively. The peaks at 5.09, 4.42, and 3.10 ppm [Fig. 1(i,d,h)] assigned to methylene protons because of the benzylic groups, methine protons and methylene protons adjacent to Z protective groups can be clearly observed in $^1$H-NMR spectrum of the propargyl-terminated PzLLys-PCL, respectively. These peaks at 4.15, 2.42, and 1.40 ppm [Fig. 1(r,k,q)] originated from PCL block can also be clearly observed. The molecular weights of PzLLys block and PCL block in the diblock copolymers PzLLys-PCL can be estimated from integral ratio of resonance peak at 3.98 ppm [Fig. 1(b)] with these at 5.09 and 2.42 ppm [Fig. 1(i,k)], respectively. The molecular weights from GPC and $^1$H-NMR were summarized in Table I. On the other hand, the characteristic absorption peaks of the amido groups at 1652, 1538 cm$^{-1}$ was observed on the FTIR spectrum of the PzLLys-PCL because of the formation of peptide bonds.[18] So, the synthesis of the propargyl-terminated PzLLys-PCL was successful.

Generally, the azido-terminated MPEO (MPEO-N$_3$) can be prepared by two different methods. One

**TABLE I**
**Characterization of Polymers**

| Polymer | [a]$M_{theo}$ g.mol$^{-1}$ | [b]GPC $M_n$ g mol$^{-1}$ | [b]GPC $M_w/M_n$ | $^1$H-NMR $M_n$ g mol$^{-1}$ | $^1$H-NMR wt % MPEO | $^1$H-NMR wt % PzLLys | $^1$H-NMR wt % PCL |
|---|---|---|---|---|---|---|---|
| MPEO-N$_3$ | 2,000 | 2,200 | 1.05 | 1,970 | 100 | – | – |
| [c]PzLLys-PCL$_1$ | 17,320 | 15,800 | 1.35 | 16,000 | – | 57.3 | 42.7 |
| [c]PzLLys-PCL$_2$ | 19,600 | 17,200 | 1.28 | 18,400 | – | 49.8 | 51.2 |
| MPEO-PzLLys-PCL$_1$ | 19,320 | 17,100 | 1.40 | 17,650 | 11.2 | 51.1 | 37.7 |
| MPEO-PzLLys-PCL$_2$ | 21,600 | 18,900 | 1.38 | 20,750 | 9.4 | 45.5 | 45.1 |
| MPEO-PLLys-PCL$_1$ | 17,200 | 16,300 | 1.36 | 15,640 | 13.2 | [d]47.7 | 39.1 |
| MPEO-PLLys-PCL$_2$ | 19,480 | 19,800 | 1.30 | 19,150 | 10.3 | [d]41.5 | 48.2 |

[a] $M_{theo}$ means theoretical molecular weights.
[b] Determined by GPC MALLS in DMF.
[c] PzLLys-PCL was propargyl-functional.
[d] PLLys wt %.

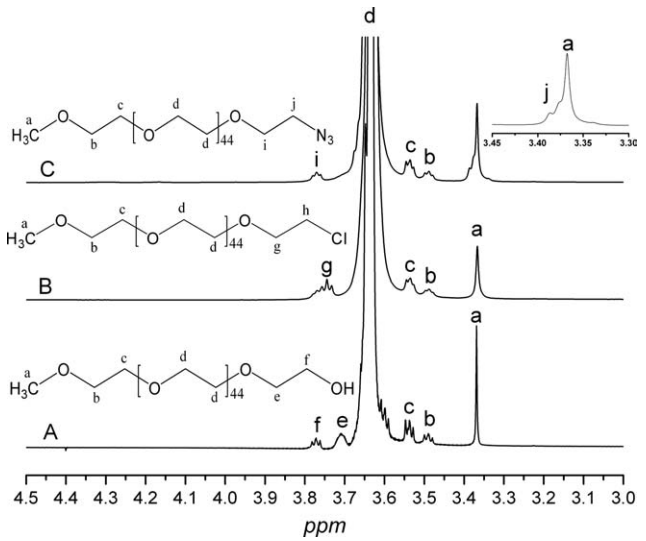



**Figure 2** $^1$H-NMR spectra of (A) MPEO-OH, (B) MPEO-Cl, and (C) MPEO-$N_3$ in $CDCl_3$.

method is that hydroxyl-terminated MPEO (MPEO-OH) is first converted to sulfonate-terminated MPEO by reaction with sulfonyl chloride, followed by transformation of sulfonate chain-end groups into azido groups via reaction with $NaN_3$ in DMF.[28,33] The second method is that chloro-terminated MPEO (MPEO-Cl) is first prepared by reaction with thionyl chloride and MPEO-OH, and then transferred into MPEO-$N_3$ via reaction with $NaN_3$ in DMF.[34] In the contribution, the second method was used to prepare MPEO-$N_3$. $^1$H-NMR spectra of MPEO-OH, MPEO-Cl, and MPEO-$N_3$ are shown in Figure 2. $^1$H-NMR is a very useful and credible tool to verify the structure of polymer. The characteristic signal at 3.77 ppm [Fig. 2(f)] was related to methylene proton neighboring to the hydroxyl group of MPEO—OH and completely disappeared after nucleophilic substitution reaction of the terminal hydroxyl group with thionyl chloride to yield an alkyl chloride. The signal of methylene proton adjacent to chlorine was overlapped by those of methylene protons in MPEO main chain [Fig. 2(d)]. However, compared with that of MPEO-OH [Fig. 3(A)], the FTIR spectrum of MPEO—Cl [Fig. 3(B)] clearly reveals the disappearance of an absorption peak from hydroxyl group at 3270–3661cm$^{-1}$ and the appearance of a new absorption peak at 667cm$^{-1}$, which is characteristic of a terminal chloro group.[34] These results confirm the synthesis of MPEO—Cl is successful. The subsequent azidation reaction of MPEO—Cl with $NaN_3$ led to the formation of MPEO—$N_3$. The resonance peak at 3.39 ppm [Fig. 2(j)] ascribed to methylene proton neighboring to the terminal azido group is clearly observed in $^1$H-NMR spectrum of MPEO—$N_3$. Moreover, after the azidation reaction, the absorption peak at 667 cm$^{-1}$ vanished and the characteristic absorption peak of the azido group at 2105 cm$^{-1}$ [Fig. 3(C)] appeared.[34] These characteristic signals at 3.37, 3.49, and 3.54 ppm corresponding to C***H***$_3$OCH$_2$CH$_2$O—, CH$_3$OC***H***$_2$CH$_2$O—, and CH$_3$OCH$_2$C***H***$_2$O—, respectively, can all be clearly observed in $^1$H MNR spectra of MPEO—OH, MPEO—Cl, and MPEO-$N_3$ (Fig. 2). All of these results confirm that the synthesis of MPEO-$N_3$ is successful.

Finally, using the click reaction, the azido-terminated precursor MPEO-$N_3$ and the propargyl-terminated PzLLys-PCL were reacted to obtain corresponding ABC triblock copolymers MPEO-PzLLys-PCL in the presence of CuBr/PMDETA catalyst system in DMF at 40°C. Triblock copolymers were designated as MPEO-PzLLys-PCLn ($n$ = 1–2, designating the sample ID). After isolation and purification of the samples, GPC curves of triblock copolymers MPEO-PzLLys-PCL are unimodal and symmetrical, clearly shifting toward the higher molecular weight region after the click reaction. At the same time, it is clear that the absence of peaks or shoulder at their corresponding precursors can be observed in the GPC curves of the samples (Fig. 4). Moreover, the structural characteristic of MPEO-PzLLys-PCL was further confirmed by $^1$H-NMR spectroscopy. From the $^1$H-NMR spectrum of the MPEO-PzLLys-PCL$_1$ [Fig. 5(B)], the broad peaks at 7.23, 5.45, 5.00, and 3.10 ppm [Fig. 5(B): a,c,b,g] from PzLLys block, those at 3.36–3.63 ppm [Fig. 5(B):p,q] from MPEO block and those at 4.05, 2.29, and 1.64 ppm [Fig. 5(B): l,h,i+k] from PCL can be clearly observed. After the click reaction, the characteristic absorption peak of the terminal azido group at 2105 cm$^{-1}$ from MPEO-$N_3$ segment disappeared in the IR spectrum of MPEO-PzLLys-PCL$_1$ [Fig. 3(D)]. By $^1$H-NMR

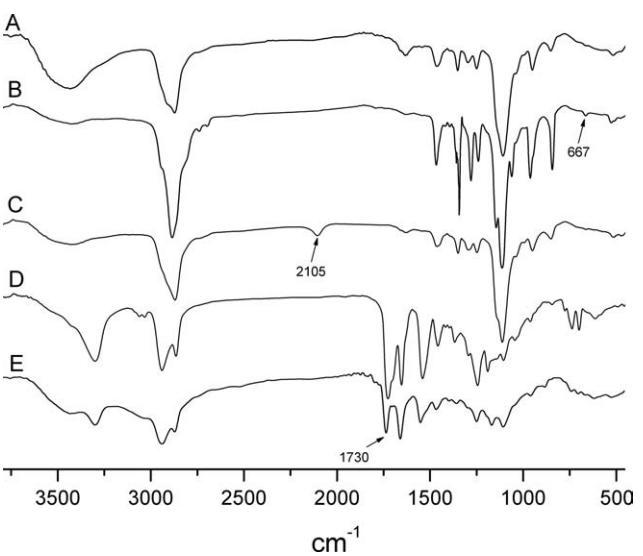



**Figure 3** IR spectra of (A) MPEO-OH, (B) MPEO-Cl, (C) MPEO-$N_3$, (D) MPEO-PzLLys-PCL$_1$, and (E) MPEO-PLLys-PCL$_1$.

measurement, with increasing the molecular weight of triblock copolymers MPEO-PzLLys-PCL from 1.71 $\times$ $10^{-4}$ to 1.89 $\times$ $10^{4}$, MPEO, PzLLys, and PCL segment contents changed from 11.2 to 9.4%, from 51.1 to 45.5%, and from 37.7 to 45.1%, respectively. The triblock copolymers MPEO-PzLLys-PCL were successfully synthesized via the click reaction in the presence of CuBr/PMDETA catalyst system in DMF at room temperature. To obtain MPEO-PLLys-PCL triblock copolymers, the hydrolysis process was employed to remove Z groups of L-lysine units in the presence of TFA and hydrobromic acid. By $^{1}$H-NMR measurement, the peaks at 7.23 and 5.00 ppm, originating from the Z protective groups of PzLLys block segments completely disappeared, and the proton signals of methine and methylene adjacent to amine groups from PLLys block segments were shifted to 4.25 and 2.77 ppm [Fig. 5(C): c,g], respectively. At the same time, it can be clearly observed that the peaks at 3.23–3.36 ppm [Fig. 5(C): p,q] are originated from the MPEO block segments and those at 3.98, 2.24, and 1.52 ppm [Fig. 5(C): l,h,i+k] from PCL block segments, respectively.

Moreover, after the hydrolysis reaction, the characteristic absorption peak of the ester group at 1730 $cm^{-1}$ from PCL segment was clearly observed in the IR spectrum of MPEO-PLLys-$PCL_1$ [Fig. 3(E)]. By GPC measurement, their molecular weights did not obviously decrease (Table I). These results demonstrated that Z groups of L-lysine units were removed completely and the scission of the ester linkage within PCL block segments did not occur. Therefore, MPEO-PLLys-PCL triblock copolymers were successfully obtained. By GPC and $^{1}$H-NMR measurement, with increasing the molecular weight of triblock copolymers MPEO-PzLLys-PCL from 1.63 $\times$ $10^{-4}$ to 1.98 $\times$ $10^{4}$, MPEO, PzLLys, and PCL segment contents changed from 13.2 to 10.3%, from 47.7 to 41.5%, and from 39.1 to 48.2%, respectively. These triblock copolymers possess both amphiphilic property and cationic groups. Meanwhile MPEO, PLLys, and PCL are usually used as biomaterials. Therefore, it is expected that these novel and biocompatible copolymers consisting of MPEO, PLLys, and PCL blocks can be of potential interest as drug carries. This work is currently in progress.

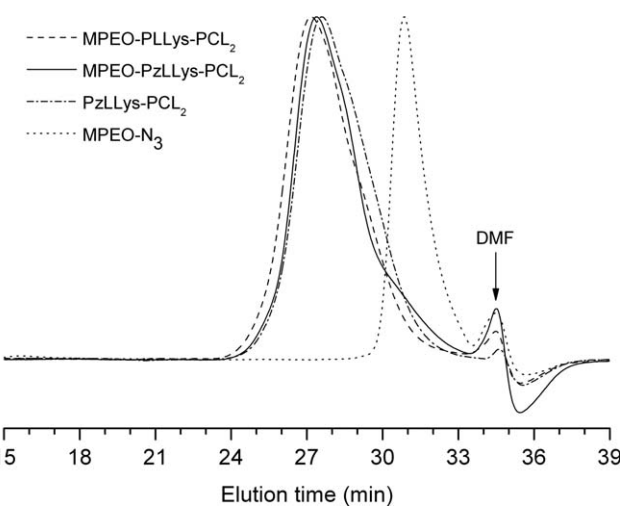



**Figure 4** GPC curves of triblock copolymers and the precursors.

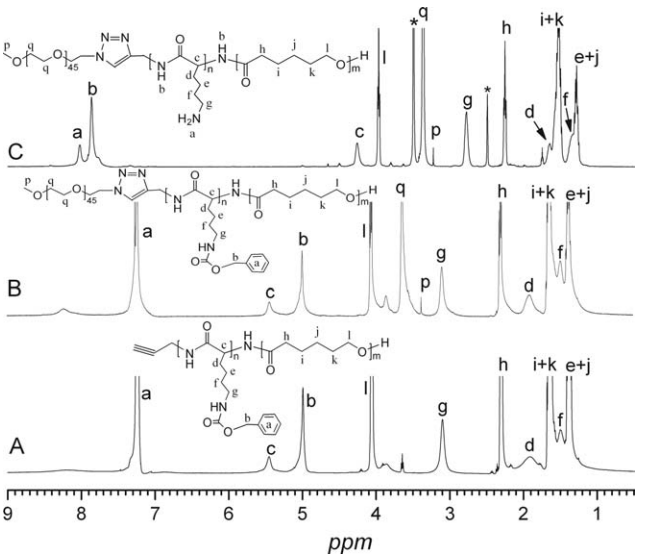



**Figure 5** $^{1}$H-NMR spectra of (A) PzLLys-$PCL_1$, (B) MPEO-PzLLys-$PCL_1$ in $CDCl_3$, and (C) MPEO-PLLys-$PCL_1$ in DMSO-$d_6$.

## CONCLUSIONS

A facile approach for synthesis of ABC block copolymers through the combination of ROP and click reactions was presented in this article. The ABC block copolymers were composed of MPEO, PLLys, and PCL with different molecular weights as A, B, and C block, respectively. ROP was used to synthesize block copolymer PzLLys-PCL, and MPEO was introduced into the block copolymer PzLLys-PCL by a click reaction. After removal of Z protective groups, the well-defined ABC block copolymers with the number-average molecular weights from 1.63 $\times$ $10^{-4}$ to 19.8 $\times$ $10^{-4}$ and a narrow polydispersity from 1.30 to 1.36 were successfully synthesized.

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## References

1. Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Pispas, S.; Avgeropoulos, A. Prog Polym Sci 2005, 30, 725.
2. Adams, M. L.; Lavasanifar, A.; Kwon, G. S. J Pharm Sci 2003, 92, 1343.
3. Kwon, G. S.; Forrest, M. L. Drug Dev Res 2006, 67, 15.
4. Greenwald, R. B. J Controll Release 2001, 74, 159.
5. Allen, C.; Han, J.; Yu, Y.; Maysinger, D.; Eisenberg, A. J Controll Release 2000, 63, 275.

6. Yuan, M.; Wang, Y.; Li, X.; Xiong, C.; Deng, X. Macromolecules 2000, 33, 1613.
7. Deng, M.; Wang, R.; Rong, G.; Sun, J.; Zhang, X.; Chen, X.; Jing, X. Biomaterials 2004, 25, 3553.
8. Wang, L.; Wang, S.; Jian, Z. Polym Adv Technol 2004, 15, 617.
9. Dong, C.-M.; Faucher, K. M.; Chaikof, E. L. J Polym Sci Part A: Polym Chem 2004, 42, 5754.
10. Lin, J.; Zhu, J.; Chen, T.; Lin, S.; Cai, C.; Zhang, L.; Zhuang, Y.; Wang, X.-S. Biomaterials 2009, 30, 108.
11. Meyer, M.; Schlaad, H. Macromolecules 2006, 39, 3967.
12. Rao, J.; Luo, Z.; Ge, Z.; Liu, H.; Liu, S. Biomacromolecules 2007, 8, 3871.
13. Dimitrov, I. V.; Berlinova, I. V.; Iliev, P. V.; Vladimirov, N. G. Macromolecules 2008, 41, 1045.
14. Zhang, X.; Li, J.; Li, W.; Zhang, A. Biomacromolecules 2007, 8, 3557.
15. Agut, W.; Taton, D.; Lecommandoux, S. Macromolecules 2007, 40, 5653.
16. Wang, K.; Liang, L.; Lin, S.; He, X. Eur Polym J 2008, 44, 3370.
17. Huang, C.-J.; Chang, F.-C. Macromolecules 2008, 41, 7041.
18. Motala-Timol, S.; Jhurry, D.; Zhou, J.; Bhaw-Luximon, A.; Mohun, G.; Ritter, H. Macromolecules 2008, 41, 5571.
19. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. Angew Chem Int Ed 2002, 41, 2596.
20. Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. Macromolecules 2005, 38, 7540.
21. Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. Macromolecules 2005, 38, 3558.
22. Opsteen, J. A.; Hest, J. C. M. V. Chem Commun 2005, 1, 57.
23. Laurent, B. A.; Grayson, S. M. J Am Chem Soc 2006, 128, 4238.
24. Whittaker, M. R.; Urbani, C. N.; Monteiro, M. J. J Am Chem Soc 2006, 128, 11360.
25. Lee, J. W.; Kim, B.-K.; Kim, H. J.; Han, S. C.; Shin, W. S.; Jin, S.-H. Macromolecules 2006, 39, 2418.
26. Shen, X.; Liu, H.; Li, Y.; Liu, S. Macromolecules 2008, 41, 2421.
27. Rao, J.; Zhang, Y.; Zhang, J.; Liu, S. Biomacromolecules 2008, 9, 2586.
28. Hua, C.; Peng, S.-M.; Dong, C.-M. Macromolecules 2008, 41, 6686.
29. He, X.; Liang, L.; Xie, M.; Zhang, Y.; Lin, S.; Yan, D. Macromol Chem Phys 2007, 208, 1797.
30. He, X.; Zhong, L.; Wang, K.; Lin, S.; Luo, S. React Funct Polym 2009, 69, 666.
31. Poche, D. S.; Moore, M. J.; Bowles, J. L. Synth Commun 1999, 29, 843.
32. Cao, X.; Li, Z.; Song, X.; Cui, X.; Cao, P.; Liu, H.; Cheng, F.; Chen, Y. Eur Polym J 2008, 44, 1060.
33. Gao, H.; Matyjaszewski, K. J Am Chem Soc 2007, 129, 6633.
34. Deng, G.; Ma, D.; Xu, Z. Eur Polym J 2007, 43, 1179.