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Synthesis of Well-Defined Macrocyclic Poly(δ-valerolactone) by "Click Cyclization"

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ABSTRACT: The living ring-opening polymerization of δ-valerolactone (VL) initiated from 6-azide-1-hexanol using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1-[3,5-bis(trifluoromethyl)phenyl]-3-cyclohexylthiourea (BCT) was carried out to prepare the poly(δ-valerolactone)s ($N_3-PVL-OH$) bearing azide groups at the α-chain ends with $M_{n,NMR}$s (PDIs) of 2600 (1.08), 4700 (1.11), and 9900 (1.09). The acetylene functionality was introduced at the ω-end of $N_3-PVL-OH$ using 5-hexynoyl chloride to afford the telechelic poly(δ-valerolactone) with the azide group at the α-end and acetylene group at the ω-end ($N_3-PVL-C\equiv CH$). The click reaction between the α-azide and the ω-acetylene of $N_3-PVL-C\equiv CH$ in DMF was carried out under the highly diluted condition as [$N_3-PVL-C\equiv CH$] = 0.18 mM, which was monitored by IR and ^1H NMR measurements. The SEC peak of the cyclic-PVL shifted to the lower molecular weight region than that of $N_3-PVL-C\equiv CH$, and the intrinsic viscosity of the cyclic-PVL significantly decreased. In addition, there was no change in the molecular weight of the resulting polymer through the click cyclization, which was confirmed on the basis of the MALDI-TOF MS measurement. Finally, we succeeded in the synthesis of a well-defined cyclic-PVL having a narrow polydispersity (M_w/M_n = 1.09−1.15) and the predicted molecular weight ($M_{n,NMR}$ = 2800−9500) in reasonable yield (60−80%) using the click cyclization.

Introduction

Precisely designed macromolecular architectures,[1] such as block,[2] starlike,[3,4] comblike,[5] eight-shaped,[6] and macrocyclic polymers,[7] have emerged as leading candidates for advanced materials because these polymers show unique characteristics due to their inherent structures; for example, there is some significant difference in the surface structure,[8] viscosity,[9] glass-transition temperature,[10] and hydrodynamic volume between the complex macromolecular architectures and their usual linear analogues.[4,11−14] In particular, a macrocyclic polymer comprised of an "endless" polymer main chain, one of the most interesting materials, makes a distinctively unique topological feature as compared to the other macromolecular architectures.[15] Although the development of the precise synthetic strategy for the macrocylic polymer has attracted much attention, a size controllable synthetic method for macrocyclic polymers is still challenging.

In general, the synthetic strategies of well-defined macrocyclic polymers are essentially classified into two methods: the "ring-expansion polymerization" and "cyclization of linear polymer precursor". Although the former method can exclude the possibility of generating a linear polymer as an unfavorable byproduct, it is time-consuming to synthesize a tailor-made cyclic initiator for cyclic polymer synthesis.[16−18] In addition, this methodology is known to sometimes suffer from the removal of active species involved in a cyclic polymer structure.[17,18] On the other hand, the key step of the latter method is the cyclization of a telechelic polymer between the α- and ω-chain ends to afford the well-defined macrocyclic polymer.[19] Importantly, the cyclization of a telechelic polymer required an extremely high reactivity and selectivity because of the low probability of an encounter between the α- and ω-ends, which has made it difficult to synthesize macrocyclic polymers using the "cyclization of linear polymer precursor" method.[14,20] For overcoming the low possibility of the reaction between the α- and ω-ends, the cyclization in high efficiency should be designed to resemble reactions such as that between polystyryl lithium and silyl chloride, which in turn required the main chain to resist any chemical conditions.[21,22] Thus, the synthesis of macrocyclic polymers via the "cyclization of linear polymer precursor" method was essentially limited to the chemically stable polymers such as the vinyl-type polymers, whereas the cyclization of the chemically weak linear polymeric precursors, such as polyesters, is still a challenging task for polymer chemists.[9,23−28]

From the viewpoint of the reaction efficiency, "click chemistry" has emerged as a leading candidate for the suitable reaction with a high efficiency, high selectivity, and high tolerance to other functional groups, which has improved many polymer syntheses including chain-end functionalization, peptide conjugation, pendant modification, and building of a complex architecture.[29−31] In fact, the combination of the living polymerization technique and "click reaction" has offered a newly developed synthetic method for the well-defined macrocyclic polymer (so-called "click cyclization"); for example, Grayson and co-workers reported the synthesis of macrocyclic polymers including polystyrene, poly(*p*-acetoxystyrene), and poly(methyl acrylate)-*block*-polystyerene using the "click cyclization" technique.[32,33] As a significant advantage of the "click reaction", the reaction condition for the "click cyclization" was milder than that employed in a previous study, which nominates the "click cyclization" as a potentially versatile synthetic strategy of macrocyclic polymers.[34−37]

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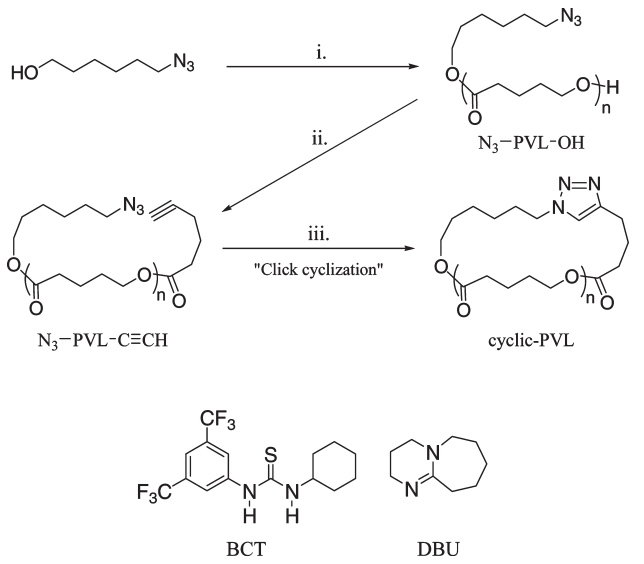
Scheme 1. Synthesis of Macrocyclic Poly(δ-valerolactone)[a]



[a] Conditions: (i) δ-valerolactone, BCT, DBU, toluene, 25 °C; (ii) 5-hexynoyl chloride, DMAP, THF, 25 °C; (iii) Cu(I)Br, 2,2′-bipyridyl, DMF, 120 °C.

When we took it into the account that polyester derivatives were not as chemically stable as other polymers such as vinyl-type polymers due to the inherent reactivity of the ester bonding, this mild reaction conditions of the "click cyclization" should be important for the macrocyclic polyester synthesis. Hence, we aimed to expand the availability of the "click cyclization" technique toward the synthesis of macrocyclic polyester derivatives that still remains a challenging task due to the weakness of the ester bonding.

In this study, we developed the synthesis of a well-defined macrocyclic poly(δ-valerolactone) (PVL) by combining organocatalytic living ring-opening polymerization and "click cyclization". The polymerization of δ-valerolactone (VL) was carried out using 6-azide-1-hexanol as the initiator and 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU)/1-[3,5-bis(trifluoromethyl)phenyl]-3-cyclohexylthiourea (BCT) as an organocatalytic system to afford the end-functionalized poly(δ-valerolactone) with the azido group at the α-chain end and the hydroxyl group at the ω-chain end (N_3−PVL−OH). The reaction of N_3−PVL−OH with 5-hexynoyl chloride was then carried out to afford the telechelic poly(δ-valerolactone) having the azido group at the α-chain end and the acetylene group at the ω-chain end (N_3−PVL−C≡CH). Finally, the resulting N_3−PVL−C≡CH was cyclized by the "click reaction" in the presence of copper(I) bromide (Cu(I)Br) and 2,2′-bipyridyl (bpy) under highly diluted conditions (Scheme 1).

Results and Discussion

Synthesis of Poly(δ-valerolactone) Bearing Azido Group at α-Chain End and Acetylene Group at ω-Chain End (N_3−PVL−C≡CH). In order to exclude the potential contact of organo azide compounds with a heavy metal, we selected an organocatalytic system for the synthesis of a telechelic polyester. The 6-azide-1-hexanol was used as the initiator for the living ring-opening polymerization of VL with DBU and BCT in toluene at ambient temperature. For the polymerization using the $[VL]_0/[initiator]_0/[DBU]_0/[BCT]_0$ ratio of 50:1:2.5:2.5, the conversion of VL reached 99.5% after 3 h, which was directly determined from the ^{1}H NMR spectrum of the aliquots of the polymerization mixtures in $CDCl_3$. The polymerization mixture was purified by reprecipitation and dried under vacuum to give the product as a white solid in 86.7% isolated yield. The SEC trace of the product displayed a symmetrical monodisperse peak with an $M_{n,SEC}$ and M_w/M_n of 4900 and 1.11, respectively. In the ^{1}H NMR spectrum of the obtained polymer, the major signals in the range both from 2.1 to 2.6 ppm and from 3.9 to 4.3 ppm were assigned to the methylene protons adjacent to the ester bond of the PVL main chain, and the remaining high signal in the range from 1.5 to 1.9 ppm was assigned to the inner methylene protons of the polymer backbone, while the sharp triplet signal at 3.27 ppm was assigned to the methylene protons adjacent to the azido group (Figure 1a). In addition, a distinct peak attributable to the azido group was observed at 2098 cm^{-1} in the IR spectrum of the obtained polymer. Thus, the product was assignable to the PVL with an azido end-group (N_3−PVL−OH). The theoretical molecular weight ($M_{n,th}$) of 5100 was similar to the $M_{n,NMR}$ of 4700, and the number-average degree of the polymerization (DP) was calculated to be 46. This value was close to the molecular weight expected from the $[VL]_0/[initiator]_0$ of 50, which showed a high efficiency of the end-functionalization.

The DP values could be controlled by changing the feed ratios. The polymerization was performed using the $[VL]_0/[initiator]_0/[DBU]_0/[BCT]_0$ ratio of 30:1:1.5:1.5. The VL conversion reached 99.2% after 2 h to produce N_3−PVL−OH with an $M_{n,SEC}$ of 4000 and an M_w/M_n of 1.08 in 54% isolated yield. The $M_{n,NMR}$ and DP were calculated as 2600 and 25, respectively. In a similar fashion, for the polymerization using the $[VL]_0/[initiator]_0/[DBU]_0/[BCT]_0$ ratio of 100:1:5:5, the VL conversion reached 99.8% after 5 h to produce N_3−PVL−OH with an $M_{n,SEC}$ of 10 300 and an M_w/M_n of 1.09 in 84% isolated yield. The $M_{n,NMR}$ and DP were calculated as 9900 and 97, respectively. Consequently, we prepared three samples, i.e., N_3−PVL−OHs that feature azido end-groups with $M_{n,NMR}$ values of 2600 (N_3−PVL_{25}−OH), 4700 (N_3−PVL_{46}−OH), and 9900 (N_3−PVL_{97}−OH).

We performed the esterification reaction between the hydroxyl end-group of N_3−PVL_{46}−OH and 5-hexynoyl chloride using DMAP in THF. The reaction was monitored by checking the signal of the methylene protons adjacent to the hydroxyl group in the ^{1}H NMR spectrum. After the reaction was complete (48 h), the mixture was purified by reprecipitation to give the N_3−PVL_{46}−C≡CH as a white solid. Figure 1b shows the ^{1}H NMR spectrum of the resultant polymer. The signal of the methylene protons adjacent to the hydroxyl group observed in the ^{1}H NMR spectrum for N_3−PVL_{46}−OH (Figure 1a) completely disappeared. Alternatively, the signals of the 5-hexynoyl group were observed in the range from 1.8 to 2.5 ppm. In addition, the signal due to the terminal acetylene proton was observed at 1.98 ppm as a narrow triplet. In order to directly characterize the terminal structure, we used MALDI-TOF MS. The MALDI-TOF MS spectrum of N_3−PVL_{46}−C≡CH shows two series of peaks, which have a regular interval of 100.1 for the molar mass that corresponds to the VL unit (Figure 4a). The number-average molecular weight calculated from the MALDI-TOF MS ($M_{n,MS}$) was 4260, which was in good agreement with the $M_{n,NMR}$ of 4800. The series of peaks with the highest intensities were assignable to the N_3−PVL−C≡CH. For example, the peak at m/z = 4465.5 in Figure 4a corresponds to the 42-mer of PVL for the structure of N_3−PVL−C≡CH (4465.2, calcd for $[M + Na]^+$).[38] Thus, the product was assigned as the polymer with an azido group at the α-chain end and acetylene group at the ω-chain end (N_3−PVL_{46}−C≡CH).

Synthesis of Cyclic-Poly(δ-valerolactone) via Click Cyclization. We succeeded in preparing the poly(δ-valerolactone)s bearing an azido group at the α-chain end and acetylene

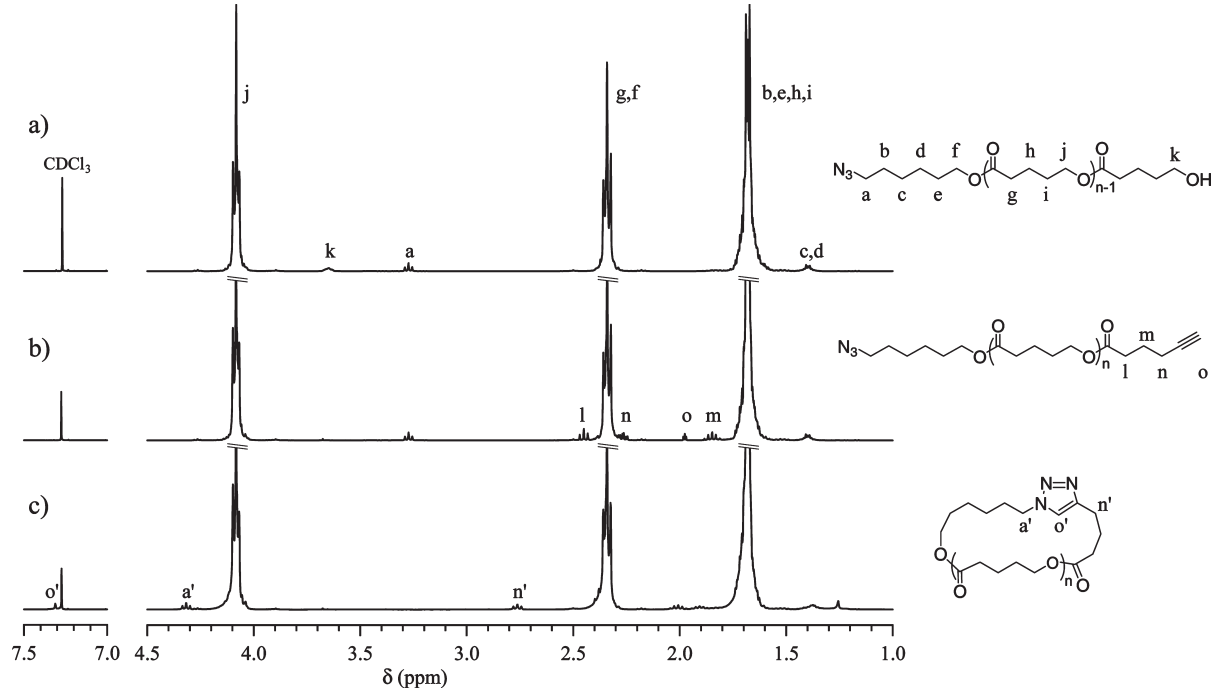


Figure 1. ^{1}H NMR spectra of (a) N_3−PVL_{46}−OH, (b) N_3−PVL_{46}-C≡CH, and (c) cyclic-PVL_{46} in $CDCl_3$.

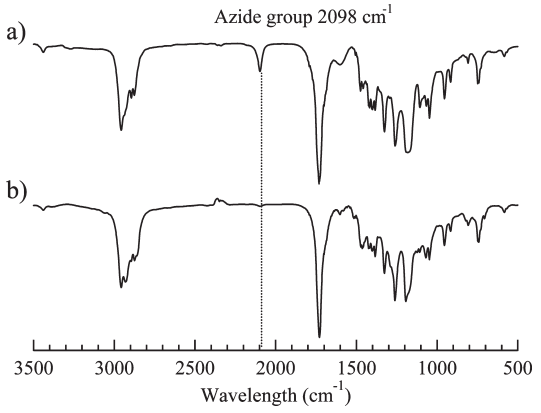


Figure 2. IR spectra of (a) N_3−PVL_{46}−C≡CH and (b) cyclic-PVL_{46}.

group at the ω-chain end (N_3−PVL−C≡CH) having various molecular weights, i.e., $M_{n,NMR}$ of 2700 (N_3−PVL_{25}−C≡CH), 4800 (N_3−PVL_{46}−C≡CH), and 9900 (N_3−PVL_{97}−C≡CH). Among them, N_3−PVL_{46}−C≡CH was used for the further discussion about the click cyclization because it was suitable for various measurements including ^{1}H NMR, IR, and MALDI-TOF MS.

We performed the "click cyclization" of N_3−PVL_{46}−C≡CH using copper(I) bromide and 2,2′-bipyridyl in DMF at 120 °C under highly dilute conditions. The polymer solution was added to the catalyst solution via a syringe pump for 33 h and stirred for an additional 9 h under an argon atmosphere. The reaction was monitored by checking the azido group peak in the IR spectrum.[39] Figure 1c shows the ^{1}H NMR spectrum of the resultant polymer. The signals of the terminal acetylene proton and the methylene protons next to the azido group completely disappeared in the ^{1}H NMR spectrum for N_3−PVL_{46}−C≡CH, as shown in Figure 1c. Additionally, the signal of the methine proton in the triazole ring was observed at 7.31 ppm. Furthermore, the signals assignable to the methylene protons next to the triazole ring appeared at

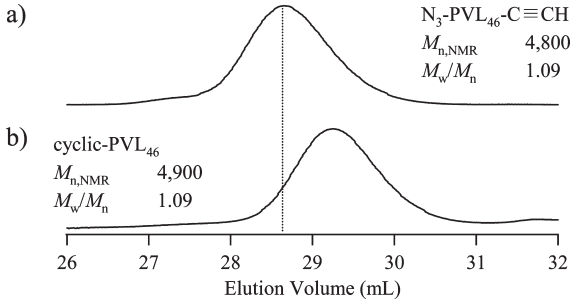


Figure 3. SEC traces for (a) N_3−PVL_{46}−C≡CH and (b) cyclic-PVL_{46}.

Table 1. Synthetic Results of PVL

	yield (%)	$M_{n,NMR}$[a]	M_w/M_n[b]	$M_{n,SEC}$[b]	[η] (mL/g)[c]
N_3−PVL_{25}−OH	54	2600	1.08	4000	9.2
N_3−PVL_{25}−C≡CH	74	2700	1.07	3800	10.1
cyclic-PVL_{25}	80	2800	1.12	2900	4.7
N_3−PVL_{46}−OH	87	4700	1.11	4900	14.5
N_3−PVL_{46}−C≡CH	70	4800	1.09	6800	15.4
cyclic-PVL_{46}	59	4900	1.09	5100	8.0
N_3−PVL_{97}−OH	84	9900	1.09	10300	16.2
N_3−PVL_{97}−C≡CH	93	9900	1.10	10100	17.2
cyclic-PVL_{97}	60	9500	1.15	8100	13.9

[a] Determined by ^{1}H NMR in $CDCl_3$. [b] Determined by SEC in THF using PSt standards. [c] Determined by SEC viscometer in THF.

4.32 and 2.76 ppm. We also confirmed the disappearance of the peak attributable to the azido group in the IR spectrum of the product (Figure 2b). Although these results based on the ^{1}H NMR and IR analyses showed that the "click reaction" smoothly proceeded, the ^{1}H NMR and IR measurements were not sufficient to determine the resultant polymer as the cyclic structure. In other words, the "click reaction" between the α-azido and ω-acetylene groups of the polymer might proceed in an intermolecular pathway and might cause dissociation or an undesirable side reaction.

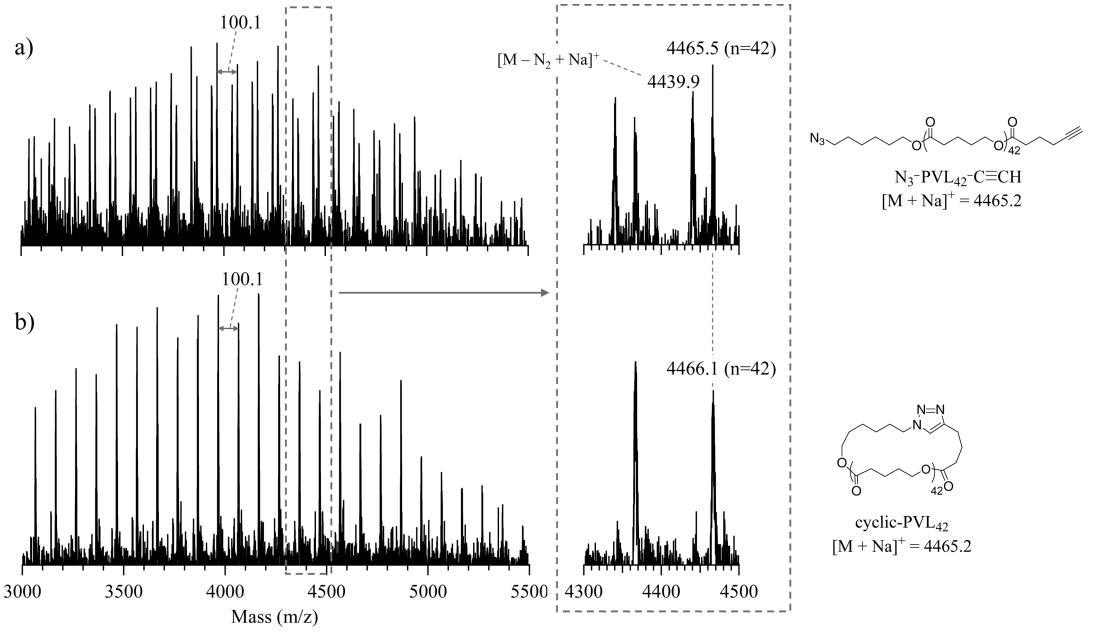


Figure 4. MALDI-TOF MS spectra of (a) $N_3-PVL_{46}-C\equiv CH$ and (b) cyclic-PVL_{46}.

To remove the possibility of the intermolecular click reaction or dissociation, an SEC measurement was performed. The SEC measurement is one of the most powerful analyses for excluding the possibility of the intermolecular click reaction or dissociation. If the intermolecular click reaction proceeded, the SEC curve of the product would shift to the higher molecular weight region because the molecular weight of the resulting product would become at least twice as high as that of the linear precursor. In addition, if the dissociation of the polymer proceeded, the monodispersed sharp trace of the starting material was supposed to become a multimodal one. The SEC traces of both the $N_3-PVL-C\equiv CH$ and resultant polymer are shown in Figure 3. The SEC trace of the product displayed a monodisperse sharp peak in the lower molecular weight region when compared to that of $N_3-PVL_{46}-C\equiv CH$. Furthermore, there was no peak in the molecular weight region higher than that of $N_3-PVL_{46}-C\equiv CH$, strongly supporting the fact that the intermolecular "click reaction" did not proceed. Thus, the "click cyclization" selectively proceeded to afford the cyclic PVL in a reasonable yield.

In addition, the viscosities of each polymer including $N_3-PVL_{46}-OH$, $N_3-PVL_{46}-C\equiv CH$, and the resultant polymer were measured (Table 1). In general, formation of a macrocyclic structure leads to a reduction in the hydrodynamic volume of the polymer and subsequent decrease in viscosity of the solution state. The values of the intrinsic viscosities of $N_3-PVL_{46}-OH$ and $N_3-PVL_{46}-C\equiv CH$ in a THF solution were similar to each other. To be more precise, $N_3-PVL_{46}-OH$ was 14.5 mL/g and $N_3-PVL_{46}-C\equiv CH$ was 15.4 mL/g. As expected, the intrinsic viscosity of cyclic-PVL_{46} was 8.0 mL/g, which was much lower than those of linear polymers, $N_3-PVL_{46}-OH$ and $N_3-PVL_{46}-C\equiv CH$. Therefore, these results also supported that the resultant polymer formed a cyclic structure.

As further evidence, the MALDI-TOF MS measurements of the cyclic-PVL_{46} were performed. MALDI-TOF MS provides detailed information about polymeric materials, which can remove the possibility of any unfavorable side reaction (Figure 4). The MALDI-TOF MS spectrum of the cyclic-PVL_{46} showed only one series of peaks, which have a regular interval of 100.1 for the molar mass that corresponds to the VL unit (Figure 4b). The number-average molecular weight of the cyclic-PVL_{46} calculated from the MALDI-TOF MS ($M_{n,MS}$) was 4290, which was in good agreement with that of 4260 for $N_3-PVL_{46}-C\equiv CH$. In addition, the series of peaks of the resultant polymer was assignable to the cyclic-PVL. For example, the peak of the resultant polymer at m/z = 4466.1 in Figure 4b corresponds to the 42-mer of PVL for the cyclic-PVL structure (4465.2, calcd for $[M+Na]^+$), which was identical to the peak of the polymer before the click reaction at m/z = 4465.5 corresponding to the 42-mer of PVL for the structure of $N_3-PVL-C\equiv CH$ in Figure 4a.[40] Thus, these results clearly showed that the "click reaction" of the α- and ω-chain ends of $N_3-PVL-C\equiv CH$ proceeded in an intramolecular fashion, namely, the "click cyclization", to afford the cyclic-PVL with a good yield and excellent selectivity. It is worth noting here that the polyester backbone survived even at the high temperature of 120 °C under basic conditions.[41]

To confirm the versatility of this strategy, we next demonstrated the "click cyclization" using two polymers with different molecular weights, $N_3-PVL_{25}-C\equiv CH$ ($M_{n,NMR}$ = 2700, M_w/M_n = 1.07) and $N_3-PVL_{97}-C\equiv CH$ ($M_{n,NMR}$ = 9900, M_w/M_n = 1.10). As a result, we succeeded in the synthesis of the well-defined cyclic-PVL_{25} and cyclic-PVL_{97} having a narrow polydispersity (M_w/M_n = 1.12 and 1.15, respectively) and predicted the molecular weight ($M_{n,NMR}$ = 2800 and 9500, respectively) in reasonable yield (80 and 60%, respectively). Therefore, the combination of the living ring-opening polymerization and "click cyclization" turned out to be a very powerful and simple method for macrocyclic polyester synthesis.

Conclusions

In the present study, we succeeded in the synthesis of a precisely designed macrocyclic polyester having a narrow polydispersity and the predicted molecular weight in reasonable yield using the combination of organocatalytic polymerization and click cyclization. This result demonstrates the practical application of "click cyclization" in the synthesis of cyclic polymers that are susceptible to chemical environment and thus decomposes even under mild conditions.

Experimental Section

Materials. Toluene (>99.5%; water content, <0.001%) and dichloromethane (>99.5%; water content, <0.001%) were purchased from the Kanto Chemical Co., Inc., and distilled over sodium benzophenone ketyl and CaH_2 before use, respectively. THF (>99.5%; water content, <0.001%), *N,N*-dimethylformamide (DMF), and CaH_2 were available from the Kanto Chemical Co., Ltd., and used as received. Cu(I)Br and 2,2′-bipyridyl (bpy) were purchased from the Sigma-Aldrich Chemicals Co. and used as received. δ-Valerolactone (VL; 99%, Kanto Chemical Co., Inc.) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; >98%, Tokyo Kasei Kogyo Co., Ltd.) were distilled over CaH_2 under reduced pressure. 4,4′-(Dimethylamino)pyridine (DMAP; >99%) was purchased from the Wako Pure Chemical Industries, Ltd., and purified by recrystallization from toluene. 1-[3,5-Bis(trifluoromethyl)phenyl]-3-cyclohexylthiourea (BCT),[42] 6-azide-1-hexanol,[43] and 5-hexynoyl chloride[44] were prepared according to their literature procedures.

Instruments. The ^{1}H and ^{13}C NMR spectra were recorded using JEOL JNM-A400II instruments. Polymerization was carried out in an MBRAUN stainless steel glovebox equipped with a gas purification system (molecular sieves and copper catalyst) in a dry argon atmosphere (H_2O, O_2 <1 ppm). The moisture and oxygen contents in the glovebox were monitored by an MB-MO-SE 1 and an MB-OX-SE 1, respectively. The size exclusion chromatography (SEC) was performed at 40 °C in THF (1.0 mL min^{-1}) using a Jasco GPC-900 system equipped with set of Waters Ultrastyragel 7 mm columns (linear, 7.8 mm × 300 mm) and two Shodex KF-804 L columns (linear, 8 mm × 300 mm). The number-average molecular weight (M_n) and polydispersity (M_w/M_n) of the polymers were calculated on the basis of a polystyrene calibration. The viscosity of the polymer solution was determined by SEC in THF (1.0 mL min^{-1}) at 40 °C using an Agilent 1100 series instrument equipped with two Shodex KF-804 L columns (linear, 8 mm × 300 mm; exclusion limit, 4×10^5) and a Viscostar viscosity detector (Wyatt Technology). The preparative SEC was performed in $CHCl_3$ (3.5 mL min^{-1}) at 23 °C using a JAI LC-9201 equipped with a JAI JAIGEL-3H column (20 mm × 600 mm; exclusion limit, 7×10^4) and a JAI RI-50s refractive index detector. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) of the obtained polymers was performed using an Applied Biosystems Voyager-DE STR-H equipped with a 337 nm nitrogen laser (3 nm pulse width). Two hundred shots were accumulated for the spectra at a 25 kV acceleration voltage in the reflector mode and calibrated using insulin (TAKARA BIO, Inc.) as the internal standard. Samples for the MALDI-TOF MS were prepared by mixing the polymer (2.0 mg mL^{-1}, 1 μL) and a matrix (2,5-dihiydroxybenzoic acid, 15 mg mL^{-1}, 50 μL) in THF.

Polymerization of δ-Valerolactone. A typical procedure for the polymerization is as follows: VL (3.00 g, 30.0 mmol) was added to a solution of BCT (0.554 g, 1.50 mmol) and 6-azide-1-hexanol (42.9 mg, 0.300 mmol) in toluene. DBU (0.228 g, 1.50 mmol) was then added to the solution to initiate the polymerization. The polymerization was quenched after 5 h by the addition of benzoic acid (180 mg). The polymer was isolated by reprecipitation from CH_2Cl_2 into cold methanol. Yield, 99.8%; SEC (RI): M_n = 10 300 g mol^{-1}, M_w/M_n = 1.09. ^{1}H NMR ($CDCl_3$) ppm: 4.08 (t, CH_2O polymer backbone, CH_2O initiator), 3.65 (bs, CH_2OH, 2H), 3.27 (t, N_3CH_2-, 2H), 2.34 (t, C(=O)CH_2 polymer backbone), 1.70 (m, CH_2CH_2 polymer backbone, $N_3CH_2CH_2$ initiator, CH_2CH_2O initiator), 1.40 (m, $N_3CH_2CH_2CH_2CH_2CH_2$, 4H).

Esterification Reaction of N_3−PVL−OH. A typical procedure for the polymerization is as follows: The precursor (N_3−PVL_{97}−OH) (250 mg, 28.9 μmol) and DMAP (3.53 mg, 28.9 μmol) were dissolved in THF (2 mL). 5-Hexynoyl chloride (18.8 mg, 144 μmol, 5 equiv) was added to the solution. The reaction mixture was stirred for 48 h at room temperature in an argon atmosphere. The obtained polymer (N_3−PVL−C≡CH) was purified by reprecipitation from CH_2Cl_2 into cold methanol. Yield, 93.4%; SEC (RI): M_n = 10 100 g mol^{-1}, M_w/M_n = 1.10. ^{1}H NMR ($CDCl_3$) ppm: 4.08 (t, CH_2O polymer backbone, CH_2O initiator), 3.27 (t, N_3CH_2-, 2H), 2.45 (t, C(=O)CH_2 hexynoate, 2H), 2.34 (t, C(=O)CH_2 polymer backbone), 2.27 (dt, $CH_2C{\equiv}C$, 2H), 1.98 (t, C≡CH, 1H), 1.85 (quin, C(=O)CH_2CH_2 hexynoate, 2H), 1.70 (m, CH_2CH_2 polymer backbone, $N_3CH_2CH_2$ initiator, CH_2CH_2O initiator), 1.40 (m, $N_3CH_2CH_2CH_2CH_2CH_2$, 4H).

Click Cyclization of N_3−PVL−C≡CH. A typical procedure for the polymerization is as follows: DMF (100 mL) was placed in a three-neck flask and degassed by bubbling argon for 30 min. Cu(I)Br (144 mg, 1.00 mmol) and 2,2′-bipyridyl (313 mg, 2.00 mmol) were added to the degassed DMF. A solution of N_3−PVL_{97}−C≡CH (198 mg, 20.0 μmol) in degassed DMF (10 mL) was added to the catalyst solution via a syringe pump at the rate of 0.3 mL/h. The reaction was carried out at 120 °C in an argon atmosphere for 33 h. At the end of the polymer solution addition, the mixture was stirred for another 9 h. After the mixture was cooled to room temperature, DMF was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 (30 mL) and washed with HCl(aq) (3 × 50 mL) and distilled water (2 × 50 mL). The organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. The crude polymer was then purified using preparative SEC (eluent $CHCl_3$). Yield: 60.6%; SEC (RI): M_n = 8100 g mol^{-1}, M_w/M_n = 1.15. ^{1}H NMR ($CDCl_3$) ppm: 7.31 (s, triazole ring, 1H), 4.32 (t, NCH_2, 2H), 4.08 (t, CH_2O polymer backbone, CH_2O initiator), 2.76 (t, C=CCH_2, 2H), 2.34 (t, C(=O)-CH_2 polymer backbone, C(=O)CH_2 hexynoate), 2.01 (quin, C(=O)CH_2CH_2 hexynoate, 2H), 1.70 (m, CH_2CH_2 polymer backbone, $N_3CH_2CH_2$ initiator, CH_2CH_2O initiator), 1.40 (m, $N_3CH_2CH_2CH_2CH_2CH_2$, 4H).

References and Notes

(1) Grayson, S. M.; Fréchet, J. M. J. *Chem. Rev.* **2001**, *101*, 3819–3867.
(2) Lynd, N. A.; Meuler, A. J.; Hillmyer, M. A. *Prog. Polym. Sci.* **2008**, *33*, 875–893.
(3) Hirao, A.; Hayashi, M.; Loykulnant, S.; Sugiyama, K.; Ryu, S. W.; Haraguchi, N.; Matsuo, A.; Higashihara, T. *Prog. Polym. Sci.* **2005**, *30*, 111–182.
(4) Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. *Chem. Rev.* **2001**, *101*, 3747–3792.
(5) Gallot, B. *Prog. Polym. Sci.* **1996**, *21*, 1035–1088.
(6) Tezuka, Y.; Komiya, R.; Washizuka, M. *Macromolecules* **2003**, *36*, 12–17.
(7) Kricheldorf, H. R. *J. Polym. Sci., Part A* **2004**, *42*, 4723–4742.
(8) Ishizone, T.; Han, S.; Hagiwara, M.; Yokoyama, H. *Macromolecules* **2006**, *39*, 962–970.
(9) Culkin, D. A.; Jeong, W. H.; Csihony, S.; Gomez, E. D.; Balsara, N. R.; Hedrick, J. L.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2627–2630.
(10) Li, H. Y.; Jérôme, R.; Lecomte, P. *Polymer* **2006**, *47*, 8406–8413.
(11) Vanden Eynde, X.; Oike, H.; Hamada, M.; Tezuka, Y.; Bertrand, P. *Rapid Commun. Mass Spectrom.* **1999**, *13*, 1917–1923.
(12) Tezuka, Y.; Oike, H. *Prog. Polym. Sci.* **2002**, *27*, 1069–1122.
(13) Adachi, K.; Takasugi, H.; Tezuka, Y. *Macromolecules* **2006**, *39*, 5585–5588.
(14) Schappacher, M.; Deffieux, A. *Science* **2008**, *319*, 1512–1515.
(15) Tezuka, Y.; Oike, H. *J. Am. Chem. Soc.* **2001**, *123*, 11570–11576.
(16) (a) Bielawski, C. W.; Benitez, D.; Grubbs, R. H. *Science* **2002**, *297*, 2041–2044. (b) Boydston, A. J.; Xia, Y.; Kornfield, J. A.; Gorodetskaya, I. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2008**, *130*, 12775–12782.
(17) Shea, K. J.; Lee, S. Y.; Busch, B. B. *J. Org. Chem.* **1998**, *63*, 5746–5747.
(18) Takeuchi, D.; Inoue, A.; Osakada, K.; Kobayashi, M.; Yamaguchi, K. *Organometallics* **2006**, *25*, 4062–4064.
(19) Adachi, K.; Honda, S.; Hayashi, S.; Tezuka, Y. *Macromolecules* **2008**, *41*, 7898–7903.
(20) Schappacher, M.; Deffieux, A. *Makromol. Chem., Rapid Commun.* **1991**, *12*, 447–453.

(21) Vollmert, B.; Huang, J. X. *Makromol. Chem., Rapid Commun.* **1981**, *2*, 467–472.
(22) Hild, G.; Kohler, A.; Rempp, P. *Eur. Polym. J.* **1980**, *16*, 525–527.
(23) With respect to the synthesis of the cyclic polyester using click cyclization technique, Grayson and co-workers have previously reported partially on their ongoing work. Please see: Hoskins, J. N.; Grayson, S. M. *Polym. Mater. Sci. Eng.* **2008**, *98*, 480–481.
(24) Recently, Kricheldorf et al., Jérôme et al., and Waymouth et al. have independently developed the synthesis of the cyclic polyester derivatives using ring-expansion polymerization techniques. For their recent works, please see refs 9 and 25−28.
(25) Li, H. Y.; Debuigne, A.; Jérôme, R.; Lecomte, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 2264–2267.
(26) Kricheldorf, H. R.; Lomadze, N.; Schwarz, G. *Macromolecules* **2008**, *41*, 7812–7816.
(27) Jeong, W.; Hedrick, J. L.; Waymouth, R. M. *J. Am. Chem. Soc.* **2007**, *129*, 8414–8415.
(28) Li, H. Y.; Riva, R.; Kricheldorf, H. R.; Jérôme, R.; Lecomte, P. *Chem.—Eur. J.* **2008**, *14*, 358–368.
(29) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2008**, *29*, 952–981.
(30) Gauthier, M. A.; Gibson, M. I.; Klok, H. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 48–58.
(31) Lutz, J. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1018–1025.
(32) Eugene, D. M.; Grayson, S. M. *Macromolecules* **2008**, *41*, 5082–5084.
(33) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238–4239.
(34) Qiu, X. P.; Tanaka, F.; Winnik, F. M. *Macromolecules* **2007**, *40*, 7069–7071.
(35) Xu, J.; Ye, J.; Liu, S. Y. *Macromolecules* **2007**, *40*, 9103–9110.
(36) Goldmann, A. S.; Quémener, D.; Millard, P. E.; Davis, T. P.; Stenzel, M. H.; Barner-Kowollik, C.; Müller, A. H. E. *Polymer* **2008**, *49*, 2274–2281.
(37) O'Bryan, G.; Ningnuek, N.; Braslau, R. *Polymer* **2008**, *49*, 5241–5248.
(38) The minor peaks including m/z = 4439.9 shown in Figure 4a is assignable to the $[M - N_2 + Na]^+$. This experimental fact that an azido group has undergone decomposition during the ionization process of the MALDI-TOF MS analysis was already reported. Please see ref 33 and the following reference: Hiki, S.; Kataoka, K. *Bioconjugate Chem.* **2007**, *18*, 2191–2196.
(39) To remove a slight amount of the impurity, the mixture was purified by preparative SEC to give the resultant polymer.
(40) Furthermore, the series of peaks due to the decomposition of N_3−PVL−C≡CH during the ionization process of the MALDI-TOF MS measurement was not completely observed (Figure 4b).
(41) The decomposition reaction of polyester main chain during the click cyclization was found when we used THF as solvent. In addition, we performed the click cyclization in DMF at the lower temperatures than 120 °C, at which the click condensation reaction predominantly occurred compared with click cyclization reaction.
(42) Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Lundberg, P. N. P.; Dove, A. P.; Li, H. B.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 7863–7871.
(43) Speers, A. E.; Adam, G. C.; Cravatt, B. F. *J. Am. Chem. Soc.* **2003**, *125*, 4686–4687.
(44) Atkinson, R. S.; Grimshire, M. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1215–1224.