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Synthesis of amphiphilic polycyclooctene-graft–poly(ethylene glycol) copolymers by ring-opening metathesis polymerization

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ABSTRACT

In this paper, a novel monomer of 4-methyl-3-(carbamate)–carbanilic acid-4-cyclooctene ester (MCCCE) was synthesized and characterized by FTIR, NMR and ESI-MS. Polycyclooctene-graft-blocked isocyanate copolymers were prepared by the copolymerization of MCCCE and cyclooctene via ring-opening metathesis polymerization (ROMP). Amphiphilic polycyclooctene-graft–PEG copolymers were prepared by melt mixing the polycyclooctene-graft-blocked isocyanate copolymers with poly(ethylene glycol) (PEG) at 200 °C. The blocked isocyanate group on MCCCE can be dissociated to produce free isocyanate group, which will react with the end hydroxyl groups on PEG molecules. The effects of monomer-to-catalyst, monomer-to-chain transfer agent ratios on molecular weight of the copolymer were detailedly studied. The water contact angle of polycyclooctene-graft–PEG copolymer is much smaller than that of polycyclooctene.

1. Introduction

Poly(ethylene glycol) (PEG) has been widely applied in materials science and biotechnology [1–4] due to its low toxicity and good biocompatibility. Generally, it has also been used to functionalize [5,6] or blend [7,8] with some other polymers in order to improve their biocompatibility. However, for polyolefins, good biocompatible materials can not be obtained by neither surface [9] nor bulk modification [10] because of the relatively low grafting degree of PEG. Ring-opening metathesis polymerization (ROMP) is a powerful and broadly applied method to synthesize many kinds of polymers such as telechelic and end functionalized polymers [11], nonlinear optics polymers [12], chiral polymers [13], liquid–crystalline polymers [14], conjugated polymers [15], hole-transport [16], comb polymers [17], biologically relevant polymers [18–20], and so on. And the Grubbs' catalysts have been extensively used in the ROMP reaction [21], due to their high reactivity, air-stability, and remarkable functional group tolerance.

Recently, Todd Emrick's research group have successfully synthesized polyethylene-graft–PEG by copolymerization of cyclooctene and PEG–cyclooctene macromonomer through ROMP [22,23]. The synthesis of PEG–cyclooctene was adopted by two methods. One method was used by the reaction between 5-hydroxy-1-cyclooctene and succinic anhydride, and then the reaction between succinic acid mono-cyclooct-4-enyl ester and poly(ethylene glycol) monomethyl ether. However, these reaction activities were poor, resulting in long reaction time. The other method was used anionic polymerization to preparing PEG–cyclooctene, whereas the synthesis condition of PEG–cyclooctene was more rigour.In this article, a small molecule monomer: 4-methyl-3-(carbamate)–carbanilic acid-4-cyclooctene ester (MCCCE) was firstly synthesized. Then polycyclooctene-graft-blocked isocyanate copolymers were prepared by the copolymerization of variable amount of MCCCE and cyclooctene via ROMP reaction. Polycyclooctene-graft–PEG copolymers were prepared by melt mixing the polycyclooctene-graft-blocked isocyanate copolymers with PEG at 200 °C through the reaction between the free isocyanate groups reproduced from the dissociation of blocked isocyanate groups in MCCCE and the end hydroxyl groups on PEG molecules. Furthermore, similar copolymers with some other biocompatible grafts, not only PEG, with functional groups may deactivate the Grubbs' catalyst and can not be directly used to undergo efficient ring-opening metathesis polymerization [24] can also be easily prepared via this method.

2. Experimental

2.1. Materials

Cis-cyclooctene was purchased from Acros Organics Co. Ltd. Lithium aluminum hydride (98.3%) and m-chloroperoxybenzoic

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acid (85.3%) were purchased from Tianjin hainachuan science and technology company. 1,5-cyclooctadiene (99%), 1-hexene (97%), ethyl vinyl ether (99%) and Grubbs' generation II catalyst were purchased from Aldrich. Toluene diisocyanate (TDI) was purchased from Shanghai lingfeng chemical regent Co. Ltd. Poly(ethylene glycol) monomethyl ether (M_n = 6000) was obtained from Shanghai chemical regent company. Anhydrous ethanol was purchased from Beijing chemical company. Tetrahydrofuran (THF) was distilled with sodium and benzophenone ketyl, and dichloromethane was distilled with calcium hydride.

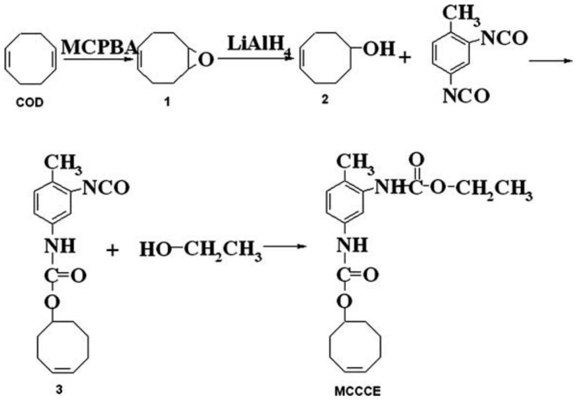
2.2. Characterization

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 300 MHz spectrometer.

Molecular weights and molecular weight distributions were measured on a Waters-2414 gel permeation chromatography (GPC) instrument. The measurements were carried out at 30 °C using THF as the eluent with a flow rate of 1.0 mL/min. The system was calibrated with polystyrene standards.

Mass spectrum was obtained employing A LCQ ESI-MS (Finnigan MAT) (ESI-MS). The spray potential was 5 kV. Full scan spectra were acquired over the mass charge range of 50–2000 and its scanning time was 2.0 s. The mass spectra were obtained by flow injection method with a flowing rate of 5 μL/min. The ion abundance (%) was normalized on the base of one of the peaks assumed as a reference (100%) in each spectrum.

Thermogravimetric test was carried out using a Pyris Diamond TG/DTA thermal analyzer. The experiment was performed in the range of 40–800 °C at a heating rate of 10 °C/min under nitrogen atmosphere.



Scheme 1. Synthesis route of MCCCE.

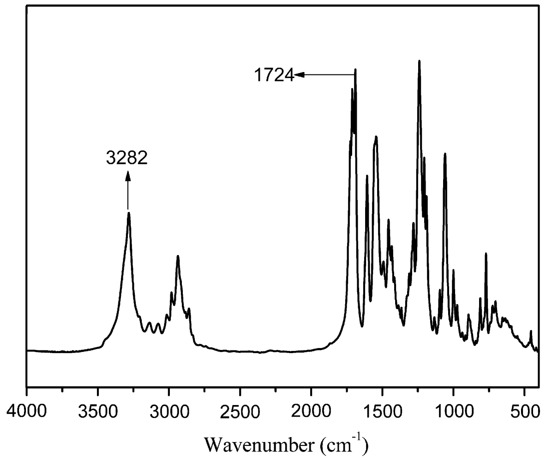
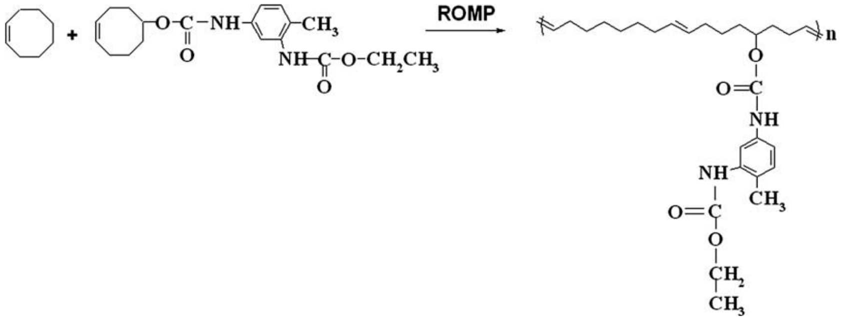
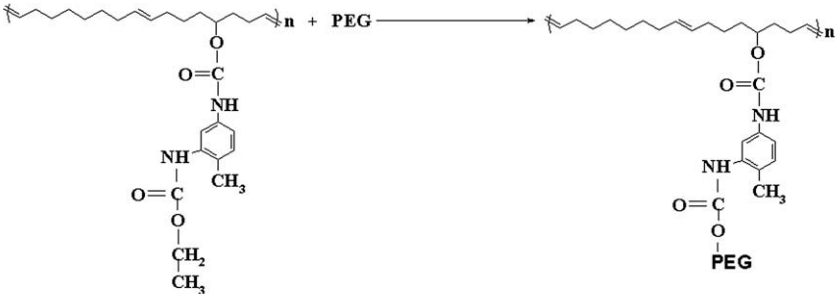


Fig. 1. FTIR spectrum of MCCCE.



Scheme 2. Polymerization of cyclooctene and MCCCE.



Scheme 3. Reaction of blocked polymer and poly(ethylene glycol).

FTIR spectra of both monomers and polymers were recorded using a Bruker Vertex 70 FTIR spectrometer from 4000 to 400 cm^{-1} at a resolution of 2 cm^{-1} for 32 scans.

The determination of contact angle was conducted on a Drop Shape Analyzer DSA100 (KRÜSS company). A droplet of water was put on the surface of a film and the contact angle was

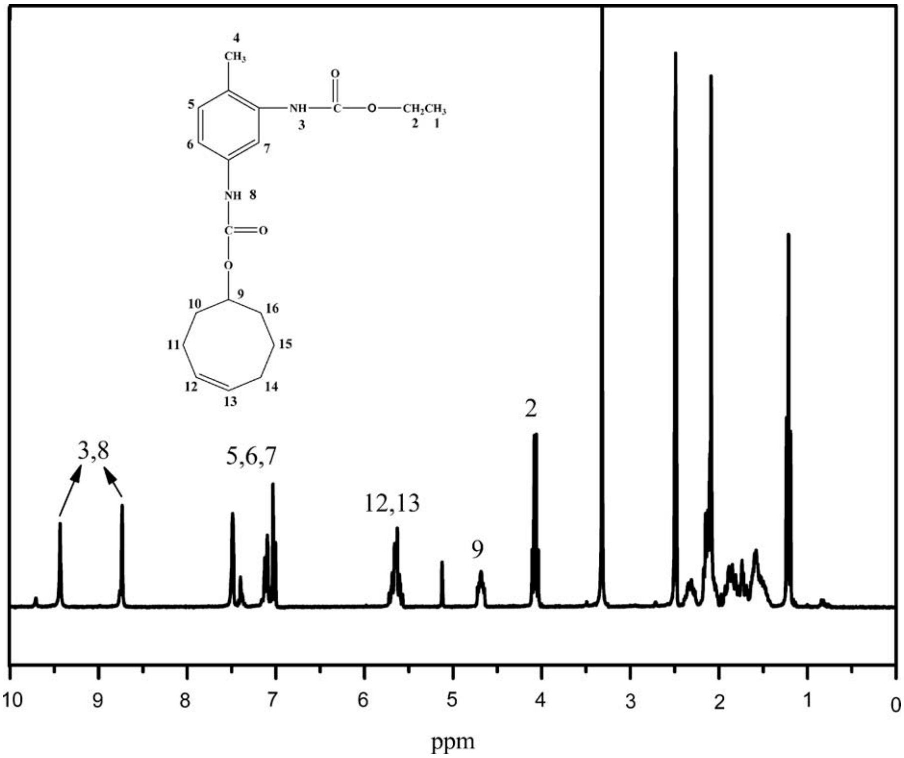


Fig. 2. ^{1}H NMR spectrum of MCCCE.

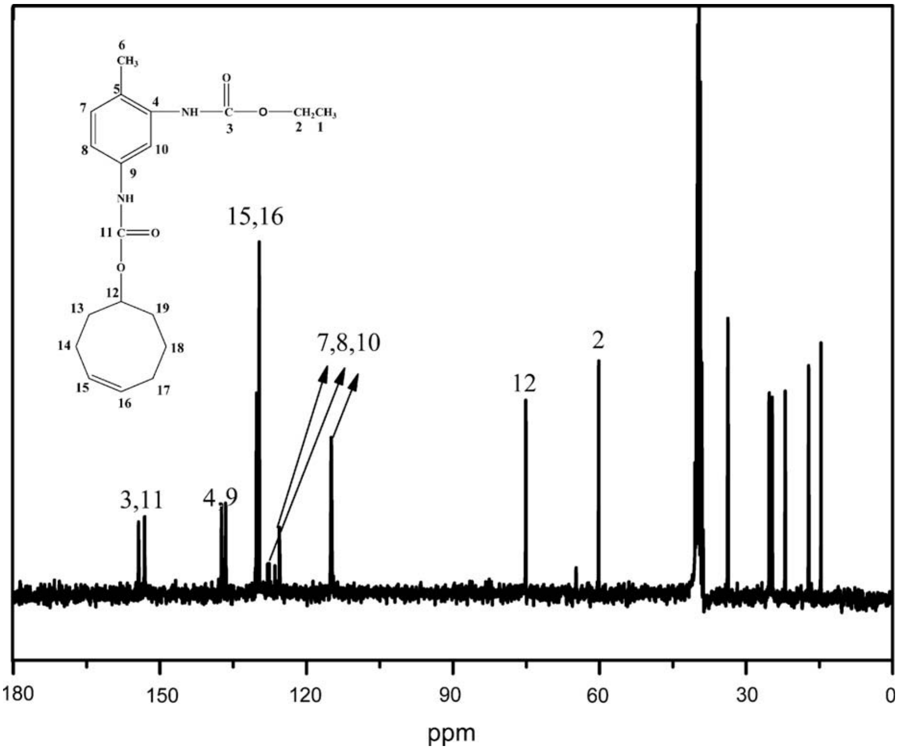


Fig. 3. ^{13}C NMR spectrum of MCCCE.

measured. Ten measurements were carried out for a single sample and the values obtained were averaged.

2.3. Synthesis of 4-methyl-3-(carbamate)–carbanilic acid-4-cyclooctene ester (MCCCE)

The synthesis procedure of MCCCE was shown in Scheme 1. 5-hydroxy-1-cyclooctene was synthesized according to the procedure of literatures reported earlier [21,25].

0.0475 mol 5-hydroxyl-1-cyclooctene was dissolved in 10 mL of dry cyclohexane and added dropwise to a solution of 0.05 mol TDI in 30 mL of cyclohexane at 45 °C under argon atmosphere for 1 h. The reaction stirred for an additional 12 h to obtain Monomer 3. Then the temperature was heated to 65 °C. Anhydrous ethanol 0.05 mol was added slowly into the system for 1 h under argon and then stirred for additional 5 h. Yellow precipitate (MCCCE) was seen when the reaction was completed. The product was purified via column chromatography with 7:3 petroleum ether/ethyl acetate on silica. The yield of MCCCE is 60%.

^{1}H NMR δ (ppm) with DMSO as solvent: 9.4 and 8.7 (two kinds of N***H***), 7.0 to 7.5 (aromatic-***H***), 5.5–5.7 (CH_2—C***H***= in cyclooctene), 4.6–4.7 (—C***H***—O in cyclooctene), 4.0–4.1 (—C***H***$_2$—CH_3).

^{13}C NMR δ (ppm) with DMSO as solvent: 154.36 and 153.12 (***C***=O), 137.40 and 136.53 (NH—***C*** in benzene ring), 130.20 and 129.67 (***C***=***C*** in cyclooctene), 127.65, 125.50 and 114.92 (the other carbon in benzene), 75.09 (—***C***—O in cylooctene), 60.16 (O—***C***H_2—CH_3).

2.4. Polymerization procedure

The ROMP route of MCCCE and cyclooctene was shown in Scheme 2. MCCCE (0.25 mmol), cyclooctene (0.75 mmol), 1-hexene

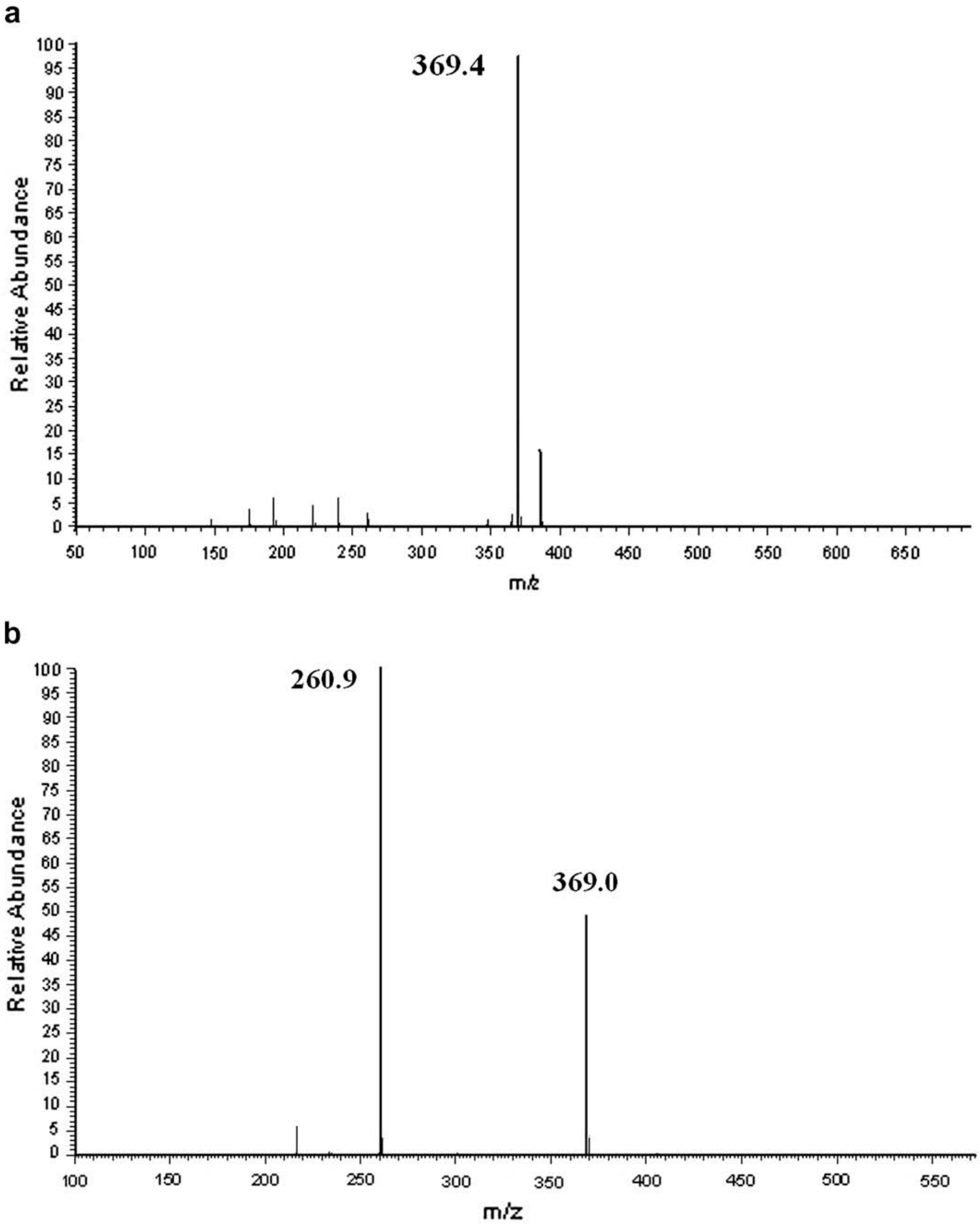


Fig. 4. MS spectra of MCCCE.

(10^{-5} mol) as chain transfer agent and dry dichloromethane (0.8 mL) were added in a dry Schlenk tube under argon. In a separate vial, Grubbs' generation II catalyst (2 μmol) was dissolved with dry dichloromethane (0.2 mL). Both the monomer mixtures and catalyst solution were subjected to two freeze/pump/thaw cycles and then warmed to room temperature. The catalyst solution was added rapidly into the monomer solution and stirred for 3 h. Then ethyl vinyl ether (1 mL) was added to terminate the polymerization, and dichloromethane was added to dilute the polymer solution. The product was precipitated into methanol containing 0.01 wt.% butylated hydroxyl toluene (BHT) and dried under vacuum after filtration, and 0.12 g (70.9% yield) off-white solid (Copolymer 1) was obtained.

The NMR of Copolymer 1 chemical shifts were assigned as follows:

^{1}H NMR δ (ppm): 7.78 and 7.26 (two kinds of N***H***), 7.07, 6.59 and 6.39 (aromatic-***H***), 5.37 (CH_2—C***H***= in polymer chain), 4.84 (—C***H***—O in polymer chain), 4.27–4.14 (—C$\boldsymbol{H_2}$—CH_3).

^{13}C NMR δ (ppm): 154.09 (***C***=O), 137.40 and 136.68 (NH—***C*** in benzene ring), 131.44–129.50 (***C***=***C*** in polymer chain), 121.72–111.35 (the other carbon in benzene), 75.27 (—***C***—O in polymer chain), 61.7 (O—***C***H_2—CH_3).

Reaction between Copolymer 1 and poly(ethylene glycol) was also conducted in schlenk tube as Scheme 3. Copolymer 1 and poly(ethylene glycol) were added into schlenk tube and subjected to five pump/charge argon cycles. Then the reaction was conducted at 200 °C for 1 h and cooled to room temperature. The product was washed with water to remove unreacted poly(ethylene glycol) to constant weight.

3. Results and discussion

FTIR spectrum of MCCCE was shown in Fig. 1. The absorption bands at 3282 cm^{-1} can be ascribed to the stretching vibration of N—H, and the band at 1724 cm^{-1} belongs to the stretching vibration of carbonyl. And the 1456, 1491, 1606 cm^{-1} are skeleton vibrations of benzene ring in MCCCE.

Figs. 2 and 3 are ^{1}H NMR and ^{13}C NMR spectra of MCCCE with DMSO as solvent. The chemical shifts at 9.4 and 8.7 (two kinds of N***H***) in Fig. 2 and 137.40 and 136.53 (NH—***C*** in benzene ring) in Fig. 3 demonstrated that the reactions between TDI and 5-hydroxyl–cyclooctene, or TDI and ethanol have been conducted.

The molecular weight of MCCCE was checked by ESI-MS. As shown in Fig. 4A that 369.4 m/e was the quasi-molecular ion peak of [MCCCE + Na]$^+$. So the molecular weight of MCCCE was 346.4, which was in accordance with the value calculated from its structural formula. Fig. 4B showed the fragmentation peak of the molecular ion. Due to the fact that ESI-MS is a soft ionization process, there were only two main peaks at 369.0 m/e and 260.9 m/e. The peak at 369.0 m/e was attributed to [MCCCE + Na]$^+$ and the peak at 260.9 m/e was from the remaining part of [MCCCE + Na]$^+$ discarded with one cyclooctene group. All the above results demonstrated that the molecule structure of MCCCE follows quite well with that shown in Scheme 1.

The FTIR spectrum of MCCCE after being heated at 200 °C for 1 h was given in Fig. 5. It is obvious that there is a new absorption at 2273 cm^{-1}, which is the characteristic band of free NCO group. This result indicated that the blocked isocyanate group in MCCCE could be dissociated again at high temperature. The TG/DTA result of MCCCE in Fig. 6 showed an original dissociation temperature of MCCCE at 175 °C before the maximal degradation rate appeared at 280 °C, which could be ascribed to the dissociation of block isocyanate group in MCCCE.

Graft Copolymers 1–9 were prepared by ROMP with the appropriate ratio of cyclooctene to MCCCE in dichloromethane, using Grubbs' generation II catalyst. Gel permeation chromatography was used to estimate the molecular weights and molecular weight polydispersity of the graft copolymers by using THF as eluent. The results were presented in Table 1. As expected, the polydispersity (M_w/M_n) of all these samples was estimated (by GPC) to be about two.

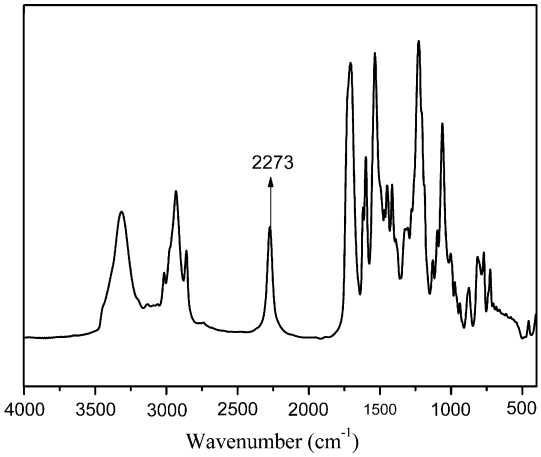


Fig. 5. FTIR spectrum of deblocked MCCCE.

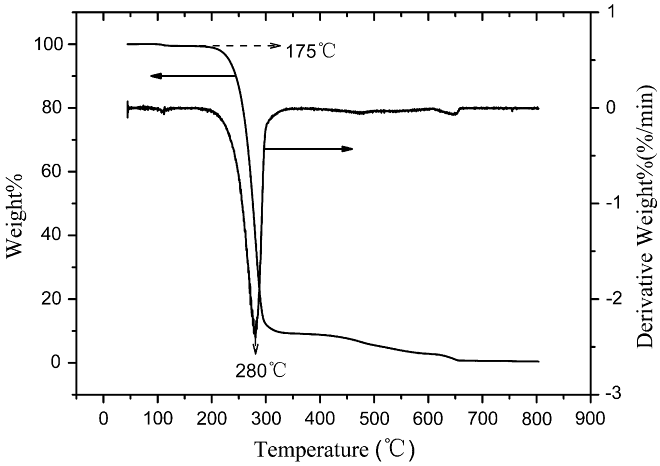


Fig. 6. TG/DTA curve of MCCCE.

From Table 1, it was found that molecular weight of copolymers increased with the increase of monomer-to-catalyst ratios and the decrease of chain transfer agent content. These results were quite similar to the literature [26].

The structure of the copolymer was characterized by ^{1}H NMR and ^{13}C NMR with $CDCl_3$ as solvent. The ^{1}H NMR and ^{13}C NMR spectra of Copolymer 1 were shown in Figs. 7 and 8, respectively. Although the reactivity ratios of cyclooctene and MCCCE are not equal, and the MCCCE content in the copolymer calculated by ^{1}H NMR was less than its addition amount, the content of blocked isocyanate groups in these copolymers are still tunable by changing the MCCCE incorporations.

It was found that there were two major transitions in the TG/DTG curve of Copolymer 1 in Fig. 9. The low temperature transition could be attributed to the dissociation of the blocked isocyanate group in Copolymer 1 and its initial dissociation temperature was 183 °C. This temperature is a little higher than that 175 °C for MCCCE monomer, which indicates that the stability of the

Table 1
ROMP of MCCCE and cyclooctene using Grubbs II catalysts.

Polymers	$[M]$/[Cat]	$[M]$/[hexene]	m_{MCCCE} (%)	$M_n \times 10^{-4}$	PDI	M_{MCCCE} (%)
1	250:1	100:1	25	3.89	2.53	24.21
2	500:1	100:1	25	4.48	2.30	22.77
3	750:1	100:1	25	5.29	2.46	24.23
4	500:1	25:1	25	1.27	1.64	23.32
5	500:1	50:1	25	2.55	2.07	23.64
2	500:1	100:1	25	4.48	2.30	22.77
6	500:1	200:1	25	8.06	2.89	22.03
2	500:1	100:1	25	4.48	2.30	22.77
7	500:1	100:1	50	12.49	2.35	44.08
8	500:1	100:1	75	11.78	2.27	72.27
9	500:1	100:1	100	6.19	2.58	98.60

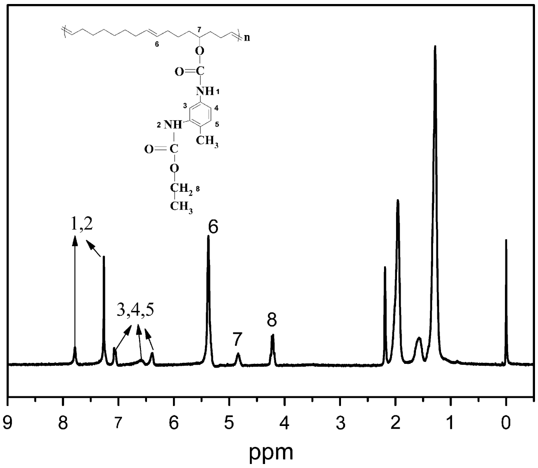


Fig. 7. ^{1}H NMR spectrum of Copolymer 1.

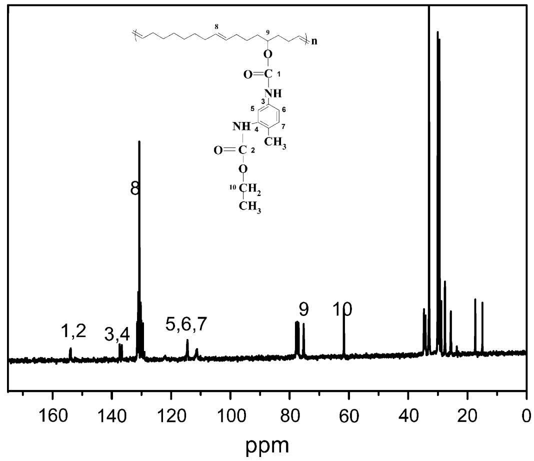


Fig. 8. ^{13}C NMR spectrum of Copolymer 1.

blocked isocyanate group in Copolymer 1 is higher than that in MCCCE monomer. The other transition was the degradation of molecular skeleton and the temperature of maximum degradation rate was 463 °C.

Fig. 10 is the FTIR spectrum of Copolymer 1 and polycyclooctene-graft–PEG graft copolymer obtained from reaction between Copolymer 1 and poly(ethylene glycol). Compared to that of Copolymer 1, two new main peaks appeared in polycyclooctene-graft–PEG copolymer at 3430 and 1110 cm^{-1} which should be

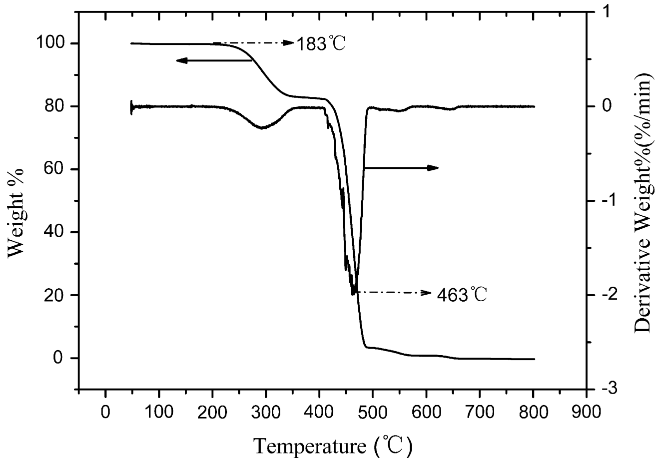


Fig. 9. TG/DTA curve of Copolymer 1.

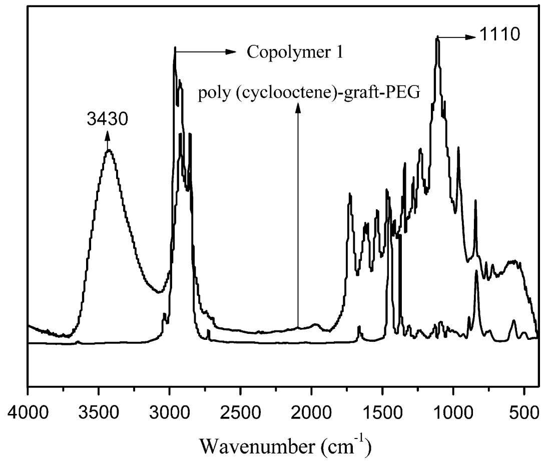


Fig. 10. FTIR spectra of Copolymer 1 and polycyclooctene-graft–PEG.

attributed to O—H and C—O stretch vibration in poly(ethylene glycol) chains. This demonstrated that poly(ethylene glycol) indeed reacted with Copolymer 1 and formed polycyclooctene-graft–PEG graft copolymer.

The contact angles of polycyclooctene-graft–PEG and polycyclooctene were 68.06° and 87.28°, respectively. The hydrophilic molecule chains in polycyclooctene-graft–PEG results in the lower contact angle.

4. Conclusion

In this paper, a novel monomer of 4-methyl-3-(carbamate)–carbanilic acid-4-cyclooctene ester (MCCCE) was synthesized and its structure was characterized by FTIR, ^{1}H NMR and ^{13}C NMR. Molecular weight obtained from ESI-MS was 346.4, which was in accordance with the value calculated from its structural formula. FTIR results of MCCCE heated at 200 °C for 1 h produced a new peak at 2273 cm^{-1}, which demonstrated that it can be dissociated again to produce free isocyanate group. MCCCE can easily copolymerize with cyclooctene to form polycyclooctene-graft-blocked isocyanate copolymers by ring-opening metathesis polymerization with Grubbs' generation II catalyst. The molecular weight of the copolymer increased with either the increase of monomer-to-catalyst ratio or the increase of monomer-to-chain transfer agent ratio. Polycyclooctene-graft–PEG copolymer was prepared by melt mixing the above polycyclooctene-graft-blocked isocyanate copolymer and PEG at 200 °C. The hydrophilic molecule chains in polycyclooctene-graft–PEG results in the lower contact angle than that in pure polycyclooctene.

Acknowledgments

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