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# SYNTHESIS OF THIOL-FUNCTIONAL TELECHELIC POLYCAPROLACTONE VIA THIOL-MICHAEL REACTION

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**ABSTRACT**

*Functional polycaprolactones (PCL) have great potential for opening a new frontier in material design. We report here a method for preparing a thiol end-functionalized telechelic polycaprolactone using a straightforward and highly efficient process via the thiol-acrylate Micheal click addition reaction. Firstly, we esterified PCL diol with excess amount of acryloyl chloride resulting acrylate- end capped polycaprolactone (PCL-diacrylate). Then, thiol-end capped polycaprolactone (PCL-dithiol) was prepared by the reaction between 2,2'-(ethylenedioxy)diethanethiol and PCL-diacrylate in the present of base catalyst (Thiol-ene reaction). Both steps were carried out in the mild condition with high yield. The obtained product was structural analyzed using $^1$H NMR spectroscopy*.

***Keywords:*** thiol-acrylate Michael addition, thiol-functional polycaprolactone.

**TÓM TẮT**

***Tổng hợp polycaprolactone có nhóm tiol cuối mạch thông qua phản ứng tiol-michael***

*Policaprolacton (PCL) chứa nhóm chức năng có khả năng mở ra nhiều hướng đi mới trong thiết kế vật liệu. Trong bài báo này, chúng tôi đưa ra một phương pháp đơn giản và hiệu quả để tổng hợp ra hợp chất chứa nhóm tiol ở cuối mạch đi từ policaprolacton diol. Đầu tiên, nhóm hidroxil của policaprolacton diol sẽ được ester hóa bằng một lượng dư clorur acriloil để tạo ra nối đôi cuối mạch cho PCL. Từ nối đôi này, sử dụng phản ứng tiol-en* (*reaction*) *để phản ứng với 2,2'-(etilenedioxi)dietantiol với sự có mặt của xúc tác baz tạo ra được nhóm tiol cuối mạch. Sản phẩm tạo thành được xác định cấu trúc bằng phổ $^1$H NMR.*

***Từ khóa:*** tiol-acrilat, policaprolacton mang nhóm tiol.

## 1. Introduction

Nowadays, functional polycaprolactone get more interests due to their great potential for application in biomedical as well as in another advanced material. Recently, there are many synthetic routes for the preparation a functional polycaprolactone could be listed here: homopolymerization or copolymerization of functional $\varepsilon$-caprolactone ($\varepsilon$-CL), copolymerization of 2-methylene-1-3-dioxepane with functional vinyl monomer or copolymerization of $\varepsilon$-CL with functional carbonate monomers [1].

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Thiol-functional polycaprolactone has been paid much attention because thiol functional group was well known by their very reactivity [2], [3]. It can be found in addition reaction, nucleophilic reaction, radical reaction and thiol-disulfide coupled reaction, thiol-oxidation and disulfide reduction. Thiol reaction is classified as "click" reaction due to the simple condition and efficiency yielding a single product [4]. Thoroughly, thiol-ene and thiol-yne click reaction have been useful in polymer synthesis. The use of thiol-related chemistry opens a new frontier in material design. For instance, in the year 2017, Natascha Kuhl *et al* introduced a self-healing polymer based on thiol-ene click reaction [5]. They prepared methacrylate monomer featuring a benzyl cyano acetamide copolymerized with butyl methacrylate then crosslinked by the addition of multifunctional thiols. Self-healing experiments revealed scratches could be healed upon heating the polymers to 100 $^{o}$C (150 $^{o}$C) for several hours.

Polymers with thiol functionalities have been successfully synthesized by Martinelle and co-worker [6]. They presented direct routes to thiol-functionalized polymer via the polymerization of $\varepsilon$-CL initiated by 2-mercaptoethanol, in addition, they used *Candida antarctica* lipase B as catalyst due to their chemoselective properties. By using chemoselective enzyme was that protecting and deprotecting steps unnecessary. Leroux and co-worker reported a transformation of PCL diol to PCL dithiol [7], in which PCL diol was esterified with an excess of a dicarboxylic acid containing a disulfide bridge by dicyclohexylcarbodiimide, then reducing disulfide bond to generate thiol groups.

In this study, we present a simple approach to introduce thiol functional polymer within two steps. Polycaprolactone diol was firstly modified by attaching double bond at termini via esterification reaction between acryloyl chloride and -OH groups [8]. Then using 2,2′-(ethylenedioxy)diethanethiol to react with double bond of acrylate groups in the present of base catalyst to generate PCLs dithiol [3]. Both these steps were carried out under mild condition at room temperature.

This synthetic route is an easy approach to introduce thiol group to PCL using cheap and available raw materials. Moreover, the reactions occur under friendly condition, efficiency, and high yield.

## 2. Experiment

### *2.1. Materials*

Poly($\varepsilon$-caprolactone)-diol CAPA 2803 with Mn value of 8000 g mol$^{-1}$ was provided by Acros. Acryloyl chloride (99%), triethylamine (TEA, 99%), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 99%), 2,2′-(ethylenedioxy)diethanethiol (EDT, 99%) were purchased by Sigma Aldrich. All the solvents were purchased from Fisher Chemicals.

### *2.2. Characterization*

$^{1}$H NMR spectra were recorded in deuterated chloroform ($CDCl_3$) with tetramethylsilane as an internal reference, on a Bruker Avance 500 MHz.

### *2.3. Synthesis of Polycaprolactone-diacrylate (PCL-diacrylate)*

PCL (1.5 g, 0.185 mmol) was added to dichloromethane solvent (8 ml) in a round bottomed flask, heating flask up to 50 $^oC$ to dissolve PCL, then cooling down to room temperature. Triethylamine (0.1 mL, 0.742 mmol) was added to solution before adding dropwise acryloyl chloride (0.742 mmol, 0.06 mL) in dichloromethane solvent (4 mL) to the flask. The reaction was performed at room temperature in 24 hours. The resulting solution was washed with distilled water, dried over $K_2CO_3$. The solution was then concentrated to precipitate to remove non-reactive acryloyl chloride. The product as a white powder solid. Yield: 97%.

Polycaprolactone-diacrylate (PCL-diacrylate): $^1$H NMR (500 MHz, $CDCl_3$), δ (ppm): 6.39(d, 1H), 6.12(q, 1H), 5.82(d, 1H), 4.07(t, 4H), 2.3(t, 2H), 1.66(m, 4H), 1.39(m, 2H).

### *2.4. Synthesis of polycaprolactone-diol (PCL-dithiol)*

EDT (40 mg, 0.44 mmol) was added to a solution of PCL-diacrylate (1 g, 0.215 mmol) and DBU (3.3 $\mu$L, 0.022 mmol) in THF solvent (10 mL) for 24 hours at room temperature. The organic solution was precipitated into hexane to remove non-reactive EDT and DBU catalyst, filtered and dried as a white solid. Yield: 100%

Polycaprolactone-diol (PCL-dithiol)*:* $^1$H NMR (500 MHz, $CDCl_3$), δ (ppm): 4.07(t, 4H), 3.75(t, 2H), 3.63(m, 6H), 2.9(t, 2H), 2.82(t, 2H), 2.73(t, 2H), 2.61(t, 2H), 2.3(t, 2H), 1.66(m, 4H), 1.39(m, 2H).

## 3. Results and discussion

PCL diol CAPA 2808 was determined Mn value by $H^1$ NMR. The degree of polymerization x was determined by comparing the integral value between peak m (corresponding to 2 protons of –(R)$CH_2$-CO(O)- and peak i' (corresponding to 4 protons next to -OH groups at termini), to be 76.5. Thus, Mn value of 8809 g.mol$^{-1}$ was calculated [9].

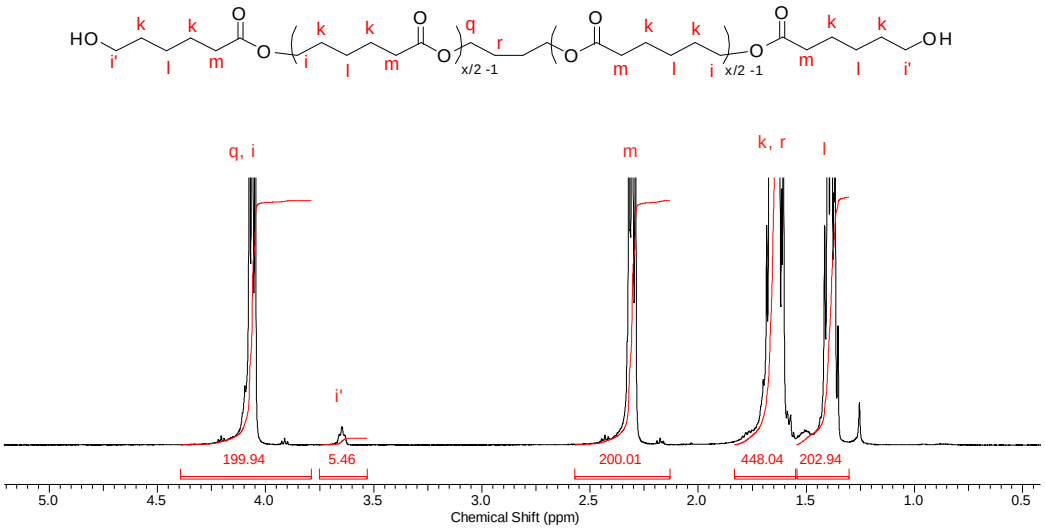
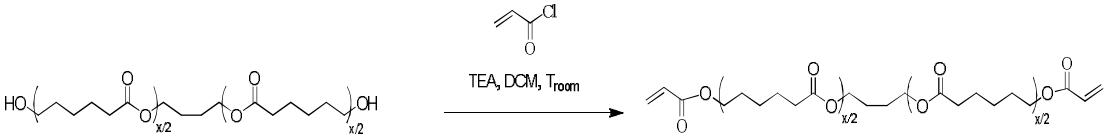



***Figure 1.*** *$^1$HNMR in $CDCL_3$ of poly(ε-caprolactone)-diol with average Mn value given by the supplier of 8000g mol$^{-1}$*

PCL diacrylate was synthesized by a direct esterification between acryloyl chloride and the hydroxy-end functionality in THF at room temperature for 24 hours in the present of TEA as catalyst as shown in Scheme 1. Figure 3 illustrates $^1$H NMR spectra of PCL diacrylate. It is noticeable that peak i' at 3.64 ppm was completely disappear in HNMR spectrum of PCLs-diacrylate. That indicates all -OH groups react with acryloyl chloride and the present of peaks $a_1$ (6.33-6.49 ppm), b (6.03-6.20 ppm) and $a_2$ (5.76-5.88 ppm) corresponding to acryloyl group attached to PCLs [10].




***Scheme 1.*** *Synthesis of polycaprolactone-diacrylate*

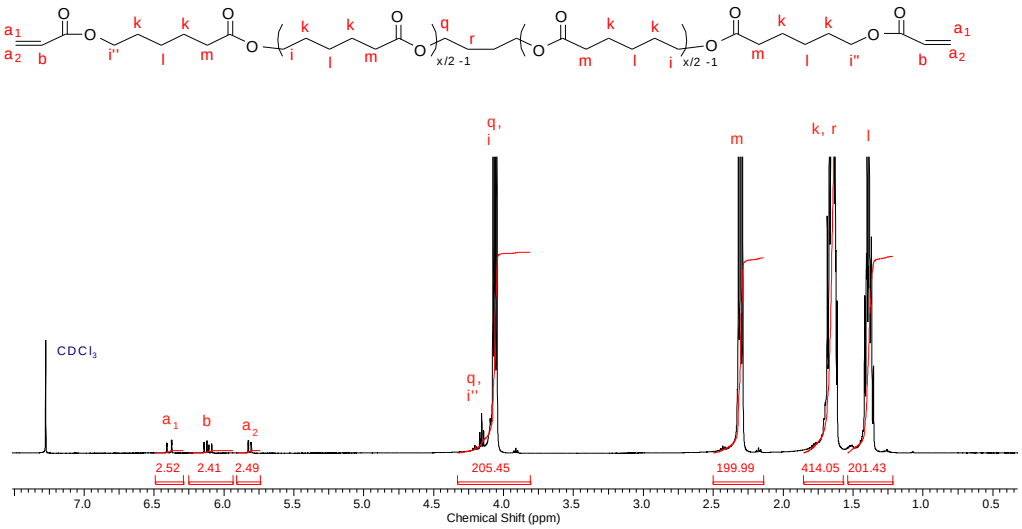
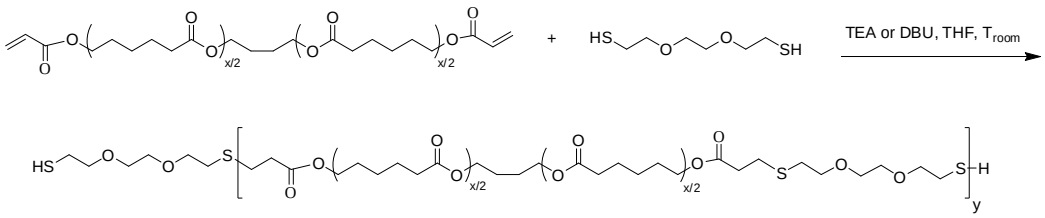
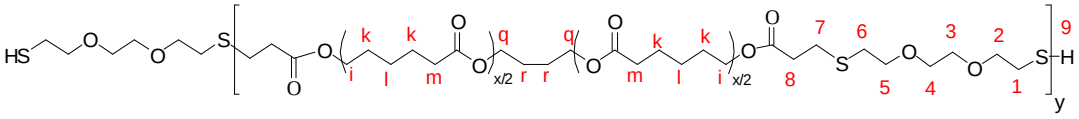



***Figure 2.*** *$^1$HNMR of polycaprolactone-diacrylate in $CDCL_3$*

The thiol-ene reaction between EDT and double bond of PCL diacrylate under DBU catalysis to generate PCL dithiol as shown in Scheme 2. As can be seen in $^1$HNMR of PCL dithiol (Figure 3), signals of double bond (5.76-6.49 ppm) disappear completely and the present of signals of peaks from 1 to 8 assigned to substituted EDT [11]. In particular, this reaction could occur in two situations. The first one, each EDT only react with one PCL-diacrylate to generate thiol-end group. In other case, the free thiol end group would continuously react with another PCL diacrylate and expand polymer [12]. Thus, taking into consideration the integrals of peak 1,7, 8, they have the same intensity, show that each EDT only reacts with one PCL-diacrylate. The degree of polymerization y was 1.




***Scheme 2.*** *Synthesis of polycaprolactone-dithiol*



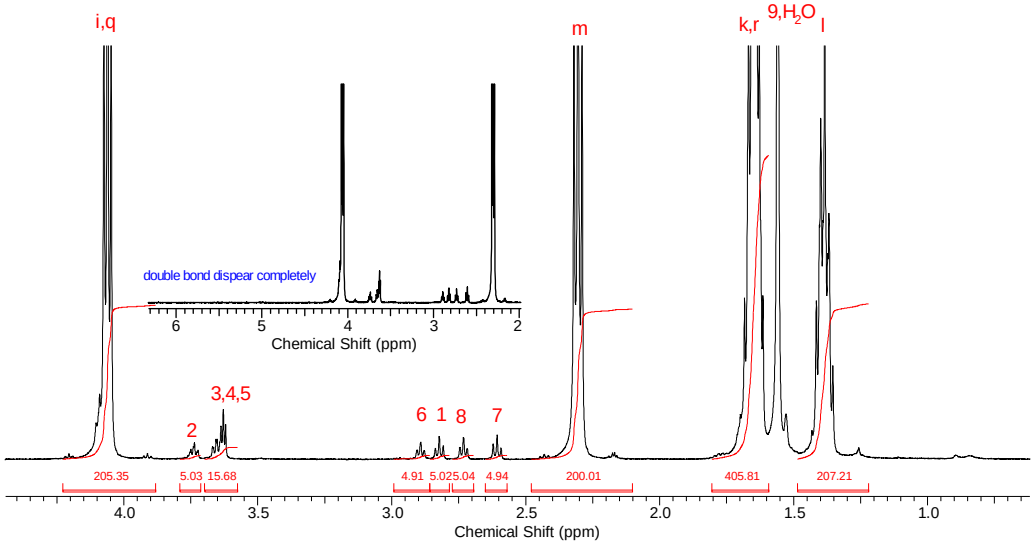



***Figure 3.*** *$^1$HNMR of polycaprolactone-dithiol in $CDCL_3$*

## 4. Conclusion

In conclusion, thiol-functional polycaprolactone was successfully synthesized within two steps with high conversion. The chemical structure of compound was clarified by $^1$H NMR. Futher studies on this compound are currently under work in our laboratory for combining with another subtrates to generate shape memory assisted self-healing polymer.

❖ ***Conflict of Interest:*** *Authors have no conflict of interest to declare.*

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**REFERENCES**


[1] T. Chen., T. Cai, Q. Jin and J. Ji , "Design and fabrication of functional polycaprolactone," *e-Polymers,15*(1), pp. 3-13, 2015.

[2] C.E. Hoyle, A.B. Lowe, and C.N. Bowman, "Thiol-click chemistry: a multifaceted toolbox for small molecule and polymer synthesis," *Chemical Society Reviews*, *39*(4), pp. 1355-1387, 2010.

[3] A.B. Lowe, "Thiol-ene “click” reactions and recent applications in polymer and materials synthesis," *Polymer Chemistry*, *1*(1), pp. 17-36, 2010.

[4] Y. Sato and A. Takasu, "Conversion of diols to dithiols via a dehydration polycondensation with a dicarboxylic acid containing a disulfide and subsequent reduction," *Polymer Journal*, *42*(12), pp. 956, 2010.

[5] N. Kuhl, R. Geitner, R. Bose, S. Bode, B. Dietzek, M. Schmitt, J. Popp, S. Garcia, S. Van der Zwaag and U. Schubert "Self-healing polymer networks based on beversible Michael addition reactions," *Macromolecular Chemistry and Physics*, *217*(22), pp. 2541-2550, 2016.

[6] C. Hedfors, E. Östmark, E. Malmström, K. Hult and M. Martinelle, "Thiol end-functionalization of poly (ε-caprolactone), catalyzed by Candida antarctica lipase B". *Macromolecules*, *38*(3), pp. 647-649, 2005.

[7] B. Lele, and J.-C. Leroux, "Synthesis and micellar characterization of novel amphiphilic A− B− A triblock copolymers of N-(2-hydroxypropyl)methacrylamide or N-vinyl-2-pyrrolidone with poly(ε-caprolactone)," *Macromolecules*, *35*(17), pp. 6714-6723, 2002.

[8] H. Kweon, M. Yoo, I. Park, T. Kim, H. Lee, H. Lee, J. Oh, T. Akaike and C. Cho , "A novel degradable polycaprolactone networks for tissue engineering," *Biomaterials*, *24*(5), pp. 801-808, 2003.

[9] T.T. Truong, S.H. Thai, H.T. Nguyen, V.D Vuong, L.T.T Nguyen, "Synthesis of allyl end-block functionalized poly(ε-caprolactone) s and their facile post-functionalization via thiol-ene reaction," *Journal of Polymer Science Part A: Polymer Chemistry*, *55*(5), pp. 928-939, 2017.

[10] M. Jaiswal, A. Dinda, A. Gupta and V. Koul, "Polycaprolactone diacrylate crosslinked biodegradable semi-interpenetrating networks of polyacrylamide and gelatin for controlled drug delivery," *Biomedical Materials*, *5*(6), pp. 065014, 2010.

[11] F. Jasinski , A. Rannée, J. Schweitzer, D. Fischer, E. Lobry, C. Croutxé-Barghorn, M. Schmutz, D. Le Nouen, A. Criqui and A. Chemtob , "Thiol-ene linear step-growth photopolymerization in miniemulsion: fast rates, redox-responsive particles, and semicrystalline films," *Macromolecules*, *49*(4), pp. 1143-1153, 2016.

[12] N.B. Cramer, and C.N. Bowman, "Kinetics of thiol-ene and thiol-acrylate photopolymerizations with real-time fourier transform infrared," *Journal of Polymer Science Part A: Polymer Chemistry*, *39*(19), pp. 3311-3319, 2001.