Lipase-catalyzed ring opening copolymerization of ϵ -caprolactone and β -lactam

E. Stavila, G. O. R. Alberda van Ekenstein, A. J. J. Woortman, K. Loos*

Department of Polymer Chemistry, Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

Percent yield calculation:

Reaction: ε -CL + β -lactam \rightarrow copolymer + poly(ε -CL) + poly(β -lactam)

For 1:1 ratio of ε-CL and β-lactam

mol ε -CL = mol β -lactam = 1.4 mmol

Due to 1:1, ratio mol repeating unit of copolymer = 1.4 mmol

Theoretical yield of copolymer = mol of repeating unit × molar mass of repeating unit

Theoretical yield of copolymer = $1.4 \times 10^{-3} \text{ mol} \times 185.12 \text{ g/mol} = 0.2592 \text{ gram}$

Yield (%) = (actual yield/theoretical yield) \times 100%

Yield (%) from experiment $1 = (0.1388/0.2592) \times 100\% = 53\%$

Yield (%) from experiment $2 = (0.1228/0.2592) \times 100\% = 47\%$

Average yield (%) from duplicate experiments = (53% + 47%)/2 = 50%

For 1:3 or 3:1 ratio of ε-CL:β-lactam

a. For 1:3

mol ε -CL = 0.7 mmol

mol β -lactam = 2.1 mmol

 ε -CL act as limiting reagent, therefore mol repeating unit = mol ε -CL = 0.7 mmol

Theoretical yield = 0.7×10^{-3} mol × 185.12 g/mol = 0.1296 gram

Yield (%) from experiment $1 = (0.0175/0.1296) \times 100\% = 13.5\%$

Yield (%) from experiment $2 = (0.0140/0.1296) \times 100\% = 10.8\%$

Average yield (%) from duplicate experiments = (13.5% + 10.8%)/2 = 12.1%

b. For 3:1:

mol ε -CL = 2.1 mmol

mol β -lactam = 0.7 mmol

 β -lactam act as limiting reagent, therefore mol repeating unit = mol β -lactam = 0.7 mmol

Theoretical yield = 0.7×10^{-3} mol $\times 185.12$ g/mol = 0.1296 gram

Yield from experiment 1 (%) = $(0.0625/0.1296) \times 100\% = 48\%$

Yield from experiment 2 (%) = $(0.0519/0.1296) \times 100\% = 40\%$

Average yield (%) from duplicate experiments = (48% + 40%)/2 = 44%



Figure S1. ¹H NMR spectrum of poly(ϵ -CL-*co*- β -lactam) in CDCl₃



Figure S2. ¹H NMR of the evaporated ethyl acetate fraction from the ring opening polymerization of ε -CL and β -lactam in different feed ratios of ε -CL: β -lactam (a) 25:75 and (b) 75:25







Figure S4. ¹H NMR spectrum of $poly(\beta$ -lactam) in D_2O



Figure S5. MALDI-ToF spectrum of poly(ε-caprolactone)



Figure S6. MALDI-ToF spectrum of poly(β-lactam)

Symbol adduct	Structures	Mass of end group (amu)
H^+ :		18
H ⁺ :		0
H^+ : \bigotimes	$\begin{bmatrix} 0 & 0 \\ 0 $	71
H^+ :	$H \left[O \xrightarrow{O}_{5} \xrightarrow{O}_{H} \xrightarrow{O}_{nH} \xrightarrow{O}_{nH} \xrightarrow{O}_{OH} \right]$	89
H ⁺ :	$H \left[\begin{array}{c} O \\ O \\ J \\ S \\ H \end{array} \right] \left[\begin{array}{c} O \\ H \\ D \\ H \end{array} \right] \left[\begin{array}{c} O \\ H \\ H \\ H \end{array} \right] \left[\begin{array}{c} O \\ O \\ H \\ H \end{array} \right] \left[\begin{array}{c} O \\ O \\ H \\ H \end{array} \right] \left[\begin{array}{c} O \\ O \\ H \\ H \end{array} \right] \left[\begin{array}{c} O \\ O \\ H \\ H \\ H \end{array} \right] \left[\begin{array}{c} O \\ O \\ H \\ H \\ H \end{array} \right] \left[\begin{array}{c} O \\ O \\ H \\$	160
H^+ : *	$H \left[O \\ O \\ O \\ O \\ H \\ H \\ H \\ H \\ H \\ H \\$	231.1
H^+ : \clubsuit	$H \left[O \left(O \right)_{5} \left(H \right)_{1} \left(H \right)_{1} \left(H \right)_{1} \left(H \right)_{1} \left(H \right)_{4} \left(H \right)_{$	302.2
H ⁺ :	$H \left[O \left(\bigcup_{5}^{O} \bigcup_{n}^{O} \bigcup_{n}^{O} \bigcup_{n}^{O} \bigcup_{n}^{O} \right) \right]_{n} O \left(\bigcup_{5}^{O} \bigcup_{n}^{O} O \right)$	132.1
H ⁺ :	$H \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} OH$	246.1

Table S1. Structures of poly(ε -CL-*co*- β -lactam) resulted from the reaction with feed ratio 50:50 of ε -CL: β -lactam.

Symbol adduct	Structures	Mass of end group (amu)
H^+ : N a^+ :		18
H ⁺ :		0
H^+ : \bigotimes		71
H^+ : \clubsuit N a^+ : \blacklozenge	$H \left[O \xrightarrow{O} \\ 0 \xrightarrow{O} \\ 0 \xrightarrow{O} \\ 0 \xrightarrow{N} \\ 0 \xrightarrow{N} \\ 0 \xrightarrow{O} \\ 0 O$	89
$H^{+}: \bigvee \\ Na^{+}: \bigvee$	$H \left[\begin{array}{c} O \\ O \\ - \end{array} \right] \left[\begin{array}{c} O \\ H \\ - \end{array} \right] \left[\begin{array}{c} O \\ H \\ - \end{array} \right] \left[\begin{array}{c} O \\ H \\ - \end{array} \right] \left[\begin{array}{c} O \\ H \\ - \end{array} \right] \left[\begin{array}{c} O \\ H \\ - \end{array} \right] \left[\begin{array}{c} O \\ - \end{array} \left[\begin{array}{c} O \\ - \end{array} \right] \left[\begin{array}{c} O \\ - \end{array} \left[\begin{array}{c} O \\ - \end{array} \right] \left[\begin{array}{c} O \\ - \end{array} \left[\end{array} \right] \left[\begin{array}{c} O \\ - \end{array} \left[\begin{array}{c} O \\ - \end{array} \right] \left[\begin{array}{c} O \\ - \end{array} \left[\end{array} \left[\begin{array}{c} O \\ - \end{array} \right] \left[\end{array} \\[\end{array}] \left[\begin{array}{c} O \\ - \end{array} \left[\end{array} \left[\end{array} \\ \left[\end{array} \left[\end{array} \right] \left[\end{array} \left[\end{array} \\[\end{array} \\[\end{array} \\] \left[\end{array} \\[\end{array} \\[\end{array} \left[\end{array} \left[\end{array} \\[\end{array} \\[\end{array} \\[\end{array}$	160
H ⁺ ∶ ≭ Na ⁺ ∶ ≭	$H \left[O \left(O \right) \\ O \left(O \right) \\ H \right] \left(O \right) \\ H \right] \left(O \right) \\ H \right] \left(O \right) \\ O \bigg) \\ O \bigg$	231.1
H^+ : $\mathbf{\Psi}$	$H \left[\begin{array}{c} O \\ O \\ J \\ 5 \end{array} \right]_{5} \begin{array}{c} O \\ H \end{array} \right]_{n} \left[\begin{array}{c} O \\ H \\ H \end{array} \right]_{n} \left[\begin{array}{c} O \\ H \\ H \end{array} \right]_{4} O H$	302.2
H ⁺ :	$H \left[O \underset{5}{\overset{O}{}_{h}} \underset{H}{\overset{O}{}_{h}} \underset{n}{\overset{O}{}_{h}} \underset{n}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{}_{h}} \overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{$	132.1
H ⁺ :	$H = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$	246.1

Table S2. Structures list of the symbols for figure S8 and figure S9



Figure S7. MALDI-ToF spectrum of the side product dissolved in formic acid



Figure S8. MALDI-ToF spectrum of poly(ε -CL-*co*- β -lactam) with addition of NaTFA



Figure S9. MALDI-ToF spectrum of poly(ϵ -CL-*co*- β -lactam) from the reaction with feed ratio 75:25 of β -lactam: ϵ -CL



Figure S10. MALDI-ToF spectrum of poly(ϵ -CL-*co*- β -lactam) from the reaction with feed ratio 25:75 of β -lactam: ϵ -CL

Symbol adduct	Structures	Mass of end group (amu)
H ⁺ :		18
H ⁺ :	$H \left[O \left(H \right)_{5} \left(H \right)_{n} \left(H \right)_{$	89
H^+ : N a^+ :	$H \left[\begin{array}{c} O \\ O \\ J \\ D \\ J \\ D \\ J \\ D \\ H \\ D \\ D$	160
H ⁺ :	$H \left[O \underset{5}{\overset{O}{}_{h}} \underset{H}{\overset{O}{}_{h}} \underset{n}{\overset{O}{}_{h}} \underset{n}{\overset{O}{}_{h}} \underset{n}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} O \underset{n}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} O \underset{N}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} O \underset{N}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} O \underset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} O \underset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{}_{h}} O \underset{O}{\overset{O}{}_{h}} \underset{O}{\overset{O}{\overset{O}{}_{h}}} O \underset{O}{\overset{O}{\overset{O}{}_{h}}} O \underset{O}{\overset{O}{\overset{O}{}_{h}}} O \underset{O}{\overset{O}{\overset{O}{}_{h}}} O \underset{O}{\overset{O}{\overset{O}{}_{h}}} O \underset{O}{\overset{O}{\overset{O}{\overset{O}{}_{h}}} O \underset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{$	132.1
H^+ : N a^+ :	$H = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} OH$	246.1
H ⁺ : 🗭	$H \left[O \left(\bigcup_{5}^{O} \bigcup_{H}^{O} \bigcup_{n}^{O} \right) \right]_{n} \left[O \left(\bigcup_{5}^{O} \bigcup_{3}^{O} O \right) \right]_{n} O H$	360.2
H^{+} : #	$H \left[O \left(\begin{array}{c} O \\ 0 \end{array}\right)_{5} \\ H \\ H \\ \end{array} \right]_{n} O \left(\begin{array}{c} O \\ 0 \end{array}\right)_{5} \\ O \\ $	474.2
H^+ : \bigcup	$H \left[O \left(\bigcup_{5}^{O} \bigcup_{H}^{O} \bigcup_{n}^{O} \right) \right]_{n} \left[O \left(\bigcup_{5}^{O} \bigcup_{5}^{O} \bigcup_{5}^{O} O H \right) \right]_{n} \left(O \left(\bigcup_{5}^{O} \bigcup_{5}^{O} \bigcup_{5}^{O} O H \right) \right]_{n} \left(O \left(\bigcup_{5}^{O} \bigcup_{5}^{O} \bigcup_{5}^{O} O H \right) \right)$	588.3
H ⁺ :	$H \left[O \left(\begin{array}{c} O \\ H \end{array} \right)_{5} \left(\begin{array}{c} O \\ H \end{array} \right)_{1} \left(\begin{array}{c} O \\ H \end{array} \right)_{1} \left(\begin{array}{c} O \\ H \end{array} \right)_{1} \left(\begin{array}{c} O \\ H \end{array} \right)_{0} \left(\begin{array}{c} O \\ H$	702.4

Table S3. Structures of poly(ϵ -CL-*co*- β -lactam) from the reaction with feed ratio 25:75 of β -lactam: ϵ -CL

Formation of acyl-ezyme complex:



Scheme S1. Proposed reaction mechanism of CAL-B-catalyzed formation of poly(ε-CL-*co*-β-lactam).



Figure S12. DSC curves of poly(β-lactam)