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γ-Acyloxy-ε-Caprolactones: Synthesis, Ring-Opening Polymerization vs. Rearrangement by Means of Chemical and Enzymatic Catalysis

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Summary: γ-Acyloxy-ε-caprolactones (**3a–d**) were prepared in two steps starting from 4-hydroxy-cyclohexanone (**1**). In the first step acylation of the hydroxyl group occurs and in the second step ring enlargement by Baeyer-Villiger oxidation. If this order of reaction is inverted rearrangement occurs in the Baeyer-Villiger oxidation of 4-hydroxy-cyclohexanone leading to γ-hydroxyethyl-γ-butyrolactone. Using the first procedure γ-acetyloxy- (**3a**), γ-benzoyloxy- (**3b**), γ-acryloyloxy- (**3c**), and γ- methacryloyloxy-ε-caprolactone (**3d**) were prepared. These monomers and for comparison reasons ε-caprolactone and γ-methyl-ε-caprolactone were polymerized by means of chemical and enzymatic catalysis. The results were different depending on the monomer structure and catalyst used. In the presence of a chemical catalyst, all the monomers, except γ-acetyloxy-ε-caprolactone, undergo controlled ring-opening polymerization. γ-Acetyloxy-ε-caprolactone (**3a**), however, rearranges to a large extent under polymerization conditions to give γ-acetyloxyethyl-γ-butyrolactone (**6a**). In the presence of an enzyme (Novozyme 435, Lipase B from *Candida antarctica* (CALB) immobilized on a macroporous resin) all γ-acyloxy-ε-caprolactones partly rearrange to result the corresponding γ-acyloxy-γ-butyrolactones, while ε-caprolactone and γ-methyl-ε-caprolactone yield the corresponding polymers, the latter even in a stereoselective manner as reported earlier in the literature. A molecular dynamic study was performed with **3a** and **3b** as substrates to gain information on the substrate recognition displayed by CALB. A mechanism for the chemically and enzymatically catalyzed reactions of γ-acyloxy-ε-caprolactones is proposed.

Keywords: enzyme and chemical catalysis; ring-opening polymerization; γ-Acyloxy-ε-caprolactones

Introduction

In recent years, much attention has been devoted to functional biodegradable polymers as biomaterials for medical and pharmaceutical application and as ecological, environmentally friendly materials.[1–4] Aliphatic polyesters and polycarbonates prepared from cyclic monomers via ring-opening polymerization are an important class of biodegradable polymers. Polymers derived from lactide, glycolide, ε-caprolactone and trimethylene carbonate and recently from functional carbonates and lactones are gaining more and more interest and importance for many fields of application.[5–19]

For the controlled or living ring opening polymerization of cyclic esters and cyclic carbonates the initiators most often used are metal alkoxides and metal carboxylates with special emphasis on aluminium alkoxides and tin carboxy-

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lates.[20–21] Unimolecular and bimolecular side reactions – intra- and intermolecular transesterification reactions – are suppressed kinetically and are not depriving the polymerization process from its living character. Enzymatic polymerization catalyzed by Lipase B from Candida Antarctica (CALB) provides an alternative synthetic method for polyesters and polycarbonates. So far lactones of various ring sizes and differently substituted 6-membered cyclic carbonates were subjected to the lipase catalyzed ring-opening polymerization using low molecular weight and polymeric mono- and multifunctional initiators.[22–29]

Further advances in this field require well designed new cyclic monomers with functional groups that contribute to challenging properties, without interacting with the active species in the propagation step of the polymerization. In the past our group has studied the ring-opening polymerization of 2-acetoxymethyl-2-methyltrimethylene carbonate (AMTC) and 2-methoxycarbonyl-2-methyltrimethylene carbonate (MMTC).[17]

With lithium alcoholates as the active site linear polymers without branching were obtained, while with aluminium alcoholate as the active site no polymerization was observed. This was explained by intramolecular complexation of the active species with the adjacent ester group, cf. the structures (1) and (2) shown below. Due to this complexation a new monomer has no chance to interact with the active species which is a prerequisite for the chain growth reaction.

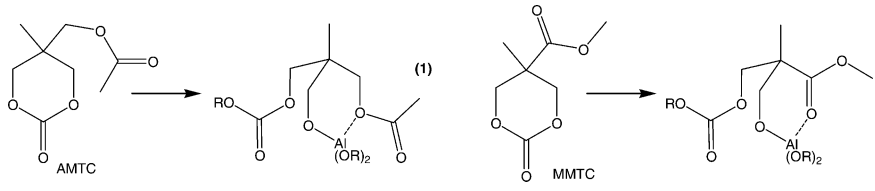
In this investigation we focussed on the ring-opening polymerization of γ-acyloxy-ε-caprolactones. It is expected that the rate of degradation of these polymers and copolymers with ε-caprolactone finely can be tuned due to the nature of the acyl group and the concentration of the γ-acyloxy-ε-caprolactone repeating units. The expectation is based on the fact that the hydrolysis of the ester side chains or thermal treatment of the polymers releases the corresponding acid from the respective acyloxy side chain, which serves as a catalyst for further degradation.

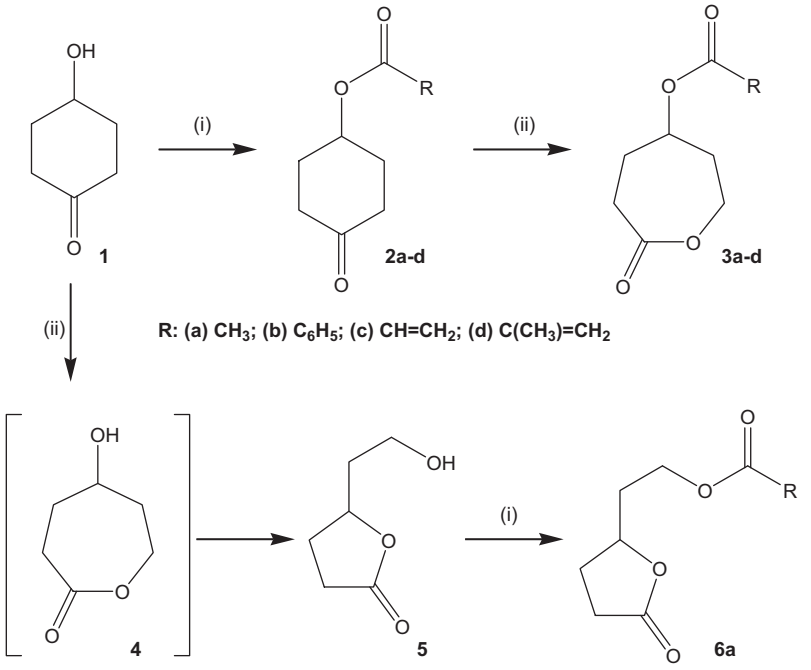
The present communication reports first results on the synthesis and polymerization of γ-acetyloxy-, γ-benzoyloxy-, γ-acryloyloxy-, and γ-methacryloyloxy -ε-caprolactone by means of chemical and enzymatic catalysis.

Results and Discussion

Our goal was to polymerize acylated γ -hydroxy-ε-caprolactones **3a–d** (Scheme 1) by means of chemical and enzymatic catalysis and to compare the two procedures. It was expected that enzymatically catalysed ring opening polymerization occurs enantioselectively leading to an isotactic polymer as was shown for γ-methyl-ε-caprolactone,[30] while for chemically catalyzed ring opening polymerization the polymers obtained should be atactic.

The monomer synthesis (Scheme 1) was performed in two steps with 4-hydroxycyclohexanone (**1**) as the starting material. Two procedures were followed with acylation and Baeyer-Villiger oxidation as the key steps. The first procedure starts with the acylation of 4-hydroxy-cyclohexanone (**1**) followed by Baeyer-Villiger oxidation. This approach was successful leading to the monomers **3a–d** with high purity. In the Baeyer-Villiger oxidation leading to γ-acryloyloxy- (**3c**), γ-methacryloyloxy-ε-



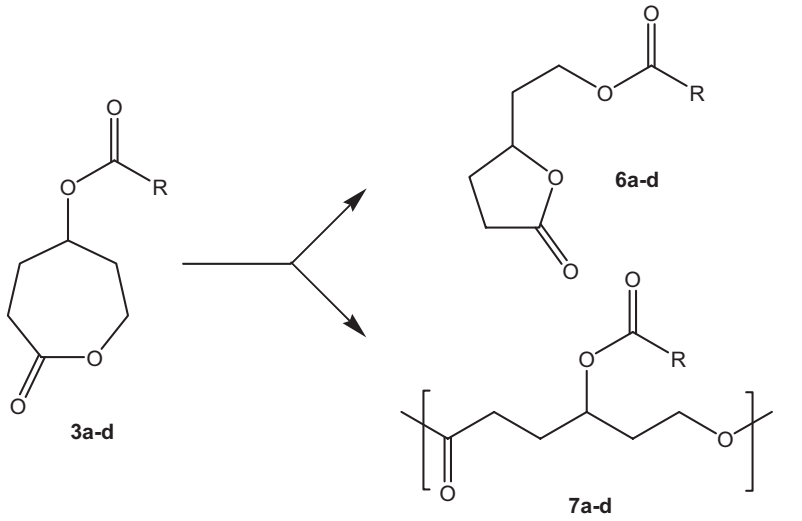


Scheme 1.
Synthesis of γ-acetyloxy- (**3a**), γ-benzoyloxy (**3b**), γ-acryloyloxy (**3c**), γ-methacryloyloxy-ε-caprolactone (**3d**), and γ-acetyloxyethyl-γ-butyrolactone (**6a**): (i) acylation, (ii) Bayer-Villiger oxidation.

caprolactone (**3d**), however, special attention had to be paid to the reaction conditions in order to avoid epoxidation of the C,C-double bond. The second procedure starts with the Baeyer-Villiger oxidation of 4-hydroxy-cyclohexanone (**1**). The final product of this reaction, however, was γ-hydroxyethyl-γ-butyrolactone (**5**). Obviously, γ-hydroxy-ε-caprolactone (**4**) formed spontaneously rearranges to yield the thermodynamically more stable γ-butyrolactone derivative **5**, which upon reaction with acetylchloride gave the corresponding acetate **6a**.[31]

First attempts to polymerize γ-acetyloxy-ε-caprolactone (**3a**) in a controlled way by chemical catalysis failed; instead of the expected polymer a product mixture, with γ-acetyloxyethyl-γ-butyrolactone (**6a**) was obtained as one of the major products, (Scheme 2). Representative experimental conditions are shown in Table 1.

Polymerization of **3a** in toluene solution with aluminium isopropoxide as the initiator (No.1) showed at 25 °C a monomer conversion of 75%; the product, however, was a mixture of rearranged lactone **6a** (40%) and polymer **7a** (35%). At 80 °C after 15h (No.2) the monomer was consumed quantitatively leading to a mixture of 82% rearranged lactone **6a** and 18% of a mixture of linear oligomers. The result with dibutyl magnesium as initiator at 80 °C in toluene solution (No.3) was similar. Polymerization with zinc octoate and tin octoate as catalysts and 3-phenylpropanol as initiator in toluene solution (No.4 and 5) occurred with lower rate; at 25 °C only 8% of the monomer were converted and at 90 °C and 24 h the conversion increased to 55%, the main product, however, being again the rearranged lactone **6a**. Polymerization in bulk at 100 °C with zinc octoate as a catalyst and 3-phenylpropanol as the initiator (No. 6) after 5h showed beside residual monomer 17% a mixture of linear oligomers **7a** and 45% of the rearranged lactone **6a**. After 48 h at 100 °C (No. 7) the



Scheme 2.
Ring-opening polymerization vs. rearrangement of γ-acyloxy-ε-caprolactones.

only product was the rearranged lactone **6a**. Polymerization in bulk with tin octoate as a catalyst and 3-phenylpropanol (No. 8) or poly(ethylene glycol)-monomethyl ether ($MPEG_{2000}$, $M_n = 2000$) as the initiator (No. 9) shows the same tendency: the starting monomer rearranged and no block copolymer was detected.

In order to prove that these results are monomer specific we applied our experimental procedure to ε-caprolactone (CL) as the monomer. Using tin octoate/3-phenylpropanol and aluminium isopropoxide as the initiator we found controlled polymerizations confirming the results reported in the literature,[32] with tin

Table 1.
Polymerization of γ-acyloxy-ε-caprolactones **3a–d** by means of chemical catalysis.

No.	M	Cat.	Init.	M/I	Conditions	Product ratio in %[a]		
						3	**7**	**6**
1	**3a**	$Al(O_iPr)_3$		50	toluene, 25 °C, 24 h	25	35	40
2	**3a**	$Al(O_iPr)_3$		37	toluene, 80 °C, 15 h		18	82
3	**3a**	Bu_2Mg		37	toluene, 80 °C, 15 h		10	90
4	**3a**	$Zn(Oct)_2$	R-OH	67	toluene, 25 °C, 24 h	92		8
5	**3a**	$Sn(Oct)_2$	R-OH	50	toluene, 90 °C, 24 h	45	10	45
6	**3a**	$Zn(Oct)_2$	R-OH	50	bulk, 100 °C, 5 h	38	17	45
7	**3a**	$Zn(Oct)_2$	R-OH	67	bulk, 100 °C, 48 h			100
8	**3a**	$Sn(Oct)_2$	R-OH	67	bulk, 100 °C, 48 h	14	13	73
9	**3a**	$Sn(Oct)_2$	$MPEG_{2000}$	23	bulk, 130 °C, 24 h			100
10	**3b**	$Al(O_iPr)_3$		30	toluene, 25 °C, 24 h		100	
11	**3b**	$Al(O_iPr)_3$		30	toluene, 90 °C, 24 h			100
12	**3b**	$Zn(oct)_2$	R-OH	30	toluene, 90 °C, 48 h	35	65	
13	**3b**	$Zn(oct)_2$	R-OH	30	bulk, 130 °C, 24 h		100	
14	**3c**	$Al(O_iPr)_3$		30	toluene, 25 °C, 24 h		100	
15	**3d**	$Al(O_iPr)_3$		27	toluene, 25 °C, 24 h		100	

[a] The product ratio was determined by means of NMR spectroscopy; ROH = 3-phenyl- propanol; $MPEG_{2000}$ = poly(ethylene glycol)-monomethyl ether ($M_n = 2000$).

octoate as the catalyst and $MPEG_{2000}$ as the initiator the expected block copolymer was obtained.

At this point we came to the conclusion that γ-acetyloxy-ε-caprolactone (**3a**) shows some special features during polymerization, which are the result of the acyloxy substituent. In the literature the only acyloxy-ε-caprolactone studied with respect to ring-opening polymerization using chemical catalysis is γ-acryloyloxy-ε-caprolactone (**3c**). We prepared this monomer as well as γ-methacryloyloxy-ε-caprolactone (**3d**) and γ-benzoyloxy-ε-caprolactone (**3b**) and studied their polymerization (Table 1). A controlled polymerization of all three monomers occurred at 25 °C in toluene solution using aluminium isopropoxide as the initiator (No. 10, 14, and 15). At 90 °C (No. 11), however, **3b** was fully converted to the rearranged monomer **6b**. With zinc octoate/phenylpropanol at 90 °C in toluene (No. 12) after 48 h 65% of **3b** was converted to the polymer **7b**, and at 130 °C (No. 13) the only product detected was polymer **7b**.

NMR analysis of the polymers **3b**, **3c**, and **3d** obtained via ring-opening polymerization using chemical catalysis shows a uniform microstructure.

In the spectrum of the monomer distinct signals for protons of the CH_2 groups adjacent to the endo-cyclic ester group indicate a frozen conformation of the ring at the conditions of the measurement [for **(3d)**: $\delta = 2.51–2.63$ (m, 1H, CH_2–CO–), 2.88–3.01 (m, 1H, CH_2–CO–), 4.19 (ddd, 1H, CH_2–O–), 4.48 (ddd, 1H, CH_2–O–)]. In the polymer these two CH_2 groups show only one signal shifted to higher field proving the free rotation of the main polyester chain [for **(7d)**: $\delta = 2.27–2.40$ (m, 2H, CH_2–CO–), 4.02–4.17 (m, 2H, CH_2–O–)]. In addition the signals of the vinyl protons are present, proving that no side reactions involving these groups occurred.

SEC Analysis of selected experiments summarized in Table 2 show on the basis of polystyrene standards a polydispersity index $PDI \leq 1.3$, which is in accord with a controlled polymerization. The molecular weight of the polymer samples **7b**, **7c**, and **7d** prepared under similar conditions ($[M]/[I] = 30$) and at quantitative monomer conversion varies between 4000 and 5200.

First polymerization experiments with Novozyme as the catalyst were performed with ε-caprolactone and γ-methyl-ε-caprolactone as monomers as a reference. The polymerization of both monomers was reported in the literature and the results obtained were reproduced. Polymerization of ε-caprolactone with Novozyme as the catalyst and 3-phenylpropanol or $MPEG_{2000}$ as the initiator lead to the expected homo and block polymers – poly(ε-caprolactone) and poly(ethylene oxide)-*block*-poly(ε-caprolactone) – with control of molecular weight and molecular weight distribution. Polymerization of γ-methyl-ε-caprolactone with Novozyme as the catalyst and 3-phenylpropanol as the initiator revealed that up to a monomer conversion of ca. 50% only one enantiomer was consumed leading to

Table 2.
Polymerization of γ-acyloxy-ε-caprolactones **3a–d** by means of chemical catalysis; results obtained by SEC analysis in THF solution.

No.[a]	M	Monomer, [M]/[I] Polymerization conditions	7a–d (Yield %)[b]	M_n	M_w	M_w/M_n
1	**3a**	**3a**, **50** $Al(O_iPr)_3$, toluene, 25 °C, 24h	**7a** (35)	2100	2800	1.32
10	**3b**	**3b**, **30** $Al(O_iPr)_3$, toluene, 25 °C, 24h	**7b** (100)	4700	5700	1.20
12	**3b**	**3b**, **30** $Zn(oct)_2$/ROH, toluene, 90 °C, 48h	**7b** (65)	2100	2600	1.19
13	**3b**	**3b**, **30** $Zn(oct)_2$/ROH, bulk, 130 °C, 24h	**7b** (100)	4100	5200	1.27
14	**3c**	**3c**, **30** $Al(O_iPr)_3$, toluene, 25 °C, 24h	**7c** (100)	5200	6700	1.28
15	**3d**	**3d**, **27** $Al(O_iPr)_3$, toluene, 25 °C, 24h	**7d** (100)	4000	5000	1.25

[a] The numbers correspond to those of Table 1;
[b] Determined via NMR analysis.

isotactic poly(γ-methyl-ε-caprolactone) as reported in the literature.[27,33]

For comparison reasons all other monomers **3b–3d** were polymerized at 25 °C and 70 °C. Using γ-benzoyloxy-ε-caprolactones (**3b**) and 3-phenylpropanol as the initiator at 25 °C after 72 h the monomer conversion was 32% (No 5) and at 70 °C a monomer conversion of 64% was obtained (No. 6). In both cases oligomers and no rearrangement was observed.

Using γ-acryloyloxy-ε-caprolactones (**3c**) and 3-phenylpropanol as the initiator at 25 °C after 72 h the monomer conversion was 95% (No 7). However, in this case 75% of rearranged monomer was observed beside 20% of oligomers. For this monomer no experiment was performed at 70 °C. Using γ-methacryloyloxy-ε-caprolactones (**3d**) and 3-phenylpropanol as the initiator at 25 °C after 72 h no conversion and after 168 h 45% conversion was observed (No. 8 and No. 9). At 70 °C at the same monomer to initiator ratio as used for No.8 and No.9 the monomer conversion was 94%, with 82% of linear oligomers and 12% of rearranged monomer (No. 24).

By increasing the monomer to initiator ratio from [M]/[I] = 30 to 50 the monomer conversion slows down (No. 25) the product ratio, however, remains nearly unchanged.

Molecular Modeling

In order to gain information on the substrate recognition displayed by *Candida antarctica* lipase B (CALB) towards the γ-ester and the lactone ester of γ-acyloxy-ε-caprolactones (**3a–d**), a molecular dynamics (MD) study was performed. The γ-acetyloxy-ε-caprolactone (**3a**) and the γ-benzoyloxy-ε-caprolactone (**3b**) were chosen as substrates, since **3a** resulted exclusively in the rearrangement product **6a** and **3b** in the polymer **7b** (Table 3, No.1,2 and 5,6). Both substrates (acyl donors) were covalently connected to Ser105 as tetrahedral intermediates, in order to simulate the transition-state (TS) in the formation of the acyl-enzyme (the activated ester/monomer) complex using the γ-ester carbonyl (resulting in rearrangement products) and the lactone ester carbonyl (resulting in polymers), respectively (Figure 1). The results from the molecular modeling showed that substrates **3a** and **3b** can be accommodated in the active-site of CALB as productive transition-states for both the γ-ester and the lactone ester with the essential hydrogen bonds developed as illustrated in Figure 1. The negatively charged oxygen formed upon attack by Ser(105)-OH at the ester carbonyl is stabilised in the ''oxyanion hole'' of the enzyme (Thr40, Gly106).

Table 3.
Polymerization of γ-acyloxy-ε-caprolactones **3a–d** by means enzymatic catalysis.

No.	M	Novozyme in wt.%	Init.	M/I	Conditions	Product ratio in %[a)]		
						3	**7**	**6**
1	**3a**	10	R-OH	50	toluene, 25 °C, 24h	11		89
2	**3a**	10	R-OH	50	toluene, 70 °C, 24h			100
3	**3a**	6	R-OH	50	bulk, 45 °C, 8h	40		60
4	**3a**		$MPEG_{2000}$	23	bulk, 70 °C, 24h	10		90
5	**3b**	10	R-OH	20	toluene, 25 °C, 72h	68	32 *	
6	**3b**	10	R-OH	50	toluene, 70 °C, 72h	36	64 *	
7	**3c**	10	R-OH	30	toluene, 25 °C, 72h	5	20	75
8	**3d**	10	R-OH	30	toluene, 25 °C, 72h	100		
9	**3d**	10	R-OH	30	toluene, 25 °C, 168h	55	45	
10	**3d**	10	R-OH	30	toluene, 70 °C, 24h	6	82	12
11	**3d**	10	R-OH	50	toluene, 70 °C, 72h	27	59	14

[a)] The product ratio was determined by means of NMR spectroscopy; ROH = 3-phenyl- propanol; $MPEG_{2000}$ = poly(ethylene glycol)-monomethyl ether (M_n = 2000); * the spectrum contains at δ = 166.91 ppm an additional not assigned signal of low intensity.

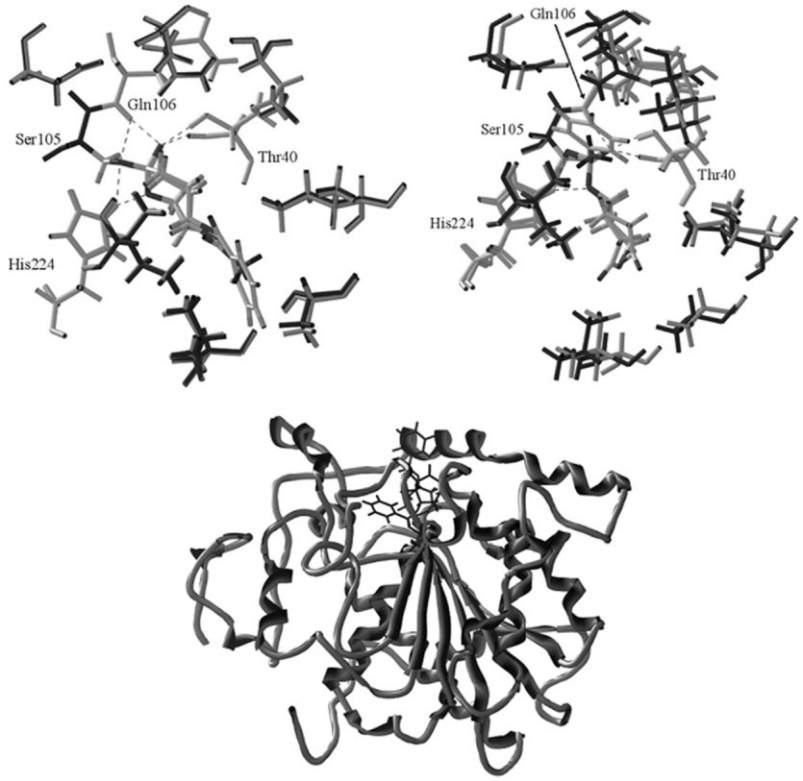


Figure 1.
MD simulated transition-state (TS) structures of γ-acyloxy-ε-caprolactones in the formation of the acyl-enzyme in CALB. TS structures (substrate connected to Ser105) colored by atom-type. Catalytic base/acid (His224) and oxy-anion hole residues (Gln106, Thr40) in yellow. Binding-site residues in CALB colored in green (γ-benzoyloxy-ε-caprolactone TS structures) and in blue (γ-acetyloxy-ε-caprolactone TS structures). 3a: The lactone ester TS of γ-acetyloxy-ε-caprolactone (binding site residues in blue) and γ-benzoyloxy-ε-caprolactone (binding site residues in green). The methyl group in the γ-acetyloxy group is colored in purple. 3b: The γ-ester TS of γ-acetyloxy-ε-caprolactone (binding site residues in dark grey) and γ-benzoyloxy-ε-caprolactone (binding site residues in grey). The methyl group in the γ-acetyloxy group is colored in purple. 3c: Ribbon structure (backbone) of CALB with the simulated TS structures of γ-benzoyloxy-ε-caprolactone in the γ-ester TS and in the lactone ester TS.

In addition, hydrogen bonds are created between the general base/acid (His224) and the oxygen of Ser105 (nucleophile) and the oxygen of the alcohol leaving group of the substrates. In the lactone ester TS the two substrates occupy the same site in the enzyme and the γ-acyloxy side-chains point toward the entrance of the active site (Figure 1a and 1c). The benzoyloxy group is located near the enzyme surface. In the contrast, in the γ-ester TS the γ-acyloxy groups are situated deep in the active site (Figure 1b and 1c).

The different products achieved with substrates **3a** and **3b** using CALB thus can not be rationalized by analysing the MD simulated TS structures. However, further analysis of the MD simulations showed an increased rearrangement in the enzyme backbone structure (as compared with the starting structure) when the γ-benzoyloxy-ε-caprolactone, as compared with γ-acetyloxy-ε-caprolactone, is docked in the γ-ester TS as seen in Figure 1b.

In addition, analysis of the root-mean-square (rms) deviation of the protein

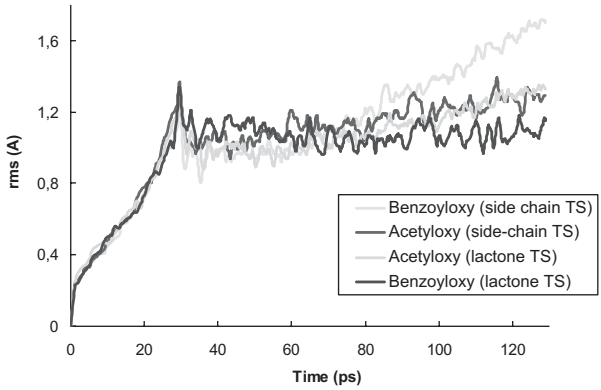


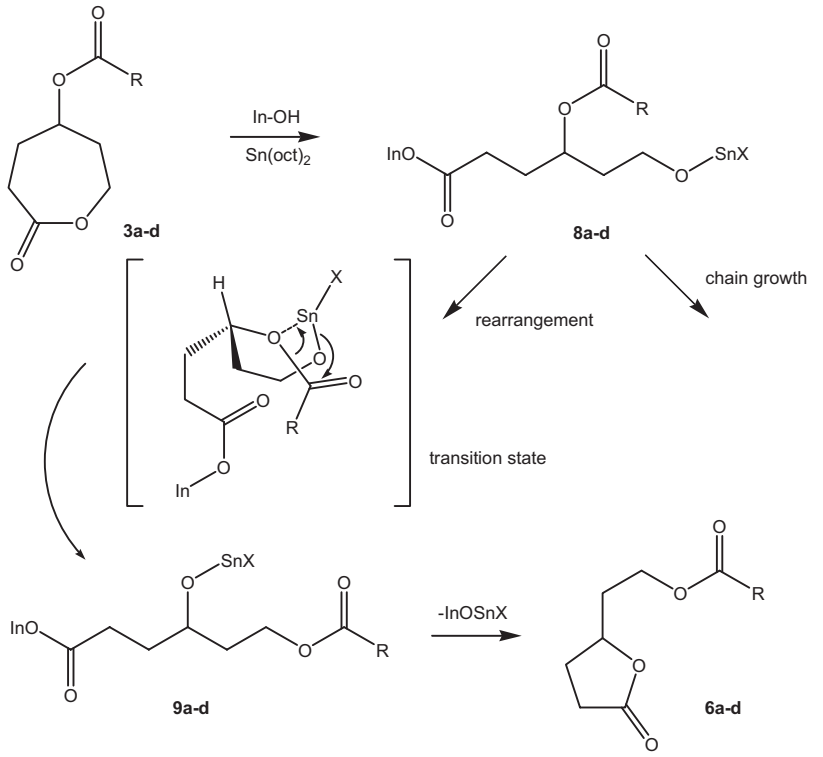
Figure 2.
The RMS distance from the starting structure of the enzyme backbone atoms in the MD-simulations as a function of time.

backbone during the simulations showed larger structural changes for the γ-benzoyloxy ester TS as compared with the other three ester TS structures (Figure 2). This indicates that the lipase needs to make larger structural rearrangements in order to accommodate the benzoyloxy group as compared with the acetyloxy group in the γ-ester TS. In the lactone ester TS the enzyme structures of the two substrates are similar throughout the simulation (Figure 1a and 2). These structural changes observed during the simulation indicate unfavourable interactions in the binding of the γ-benzoyloxy ester TS in the enzyme and offer an explanation for the different products achieved for the γ-benzoyloxy and the γ-acetyloxy substrate.

Mechanistic Consideration

Polymerization of γ-acetoxy-ε-caprolactone (**3a–d**) using different chemical catalysts, different initiators and different reaction conditions showed no uniform reaction course; beside the chain growth reaction leading to linear polymers, rearrangement of the monomer takes place. Scheme 3 summarizes our mechanistic view using tin octoate as a catalyst and an alcohol (In-OH) as the initiator giving an explanation for the observed results. In the first step the catalyst activates the initiator which then reacts via nucleophilic attack with one of the carbonyl groups of the monomer. Reaction with the exocyclic carbonyl group results in an activated γ-hydroxy-ε-caprolactone **4*** (cf. Scheme 1) which would induce the rearrangement. Nucleophilic attack at the endocyclic carbonyl carbon inducing ring opening via acyl-oxygen cleavage and formation of the intermediate **8a–d** (Scheme 3) is expected to be favoured compared to a nucleophilic attack at the exocyclic carbonyl carbon due to the ring strain (cisoid conformation of the functional group). Chain growth reaction occurs if the active species in **8a–d** reacts with monomer. However, intramolecular complexation of the active site by the ester group in γ-position leads to a transition state for an intramolecular rearrangement reaction.

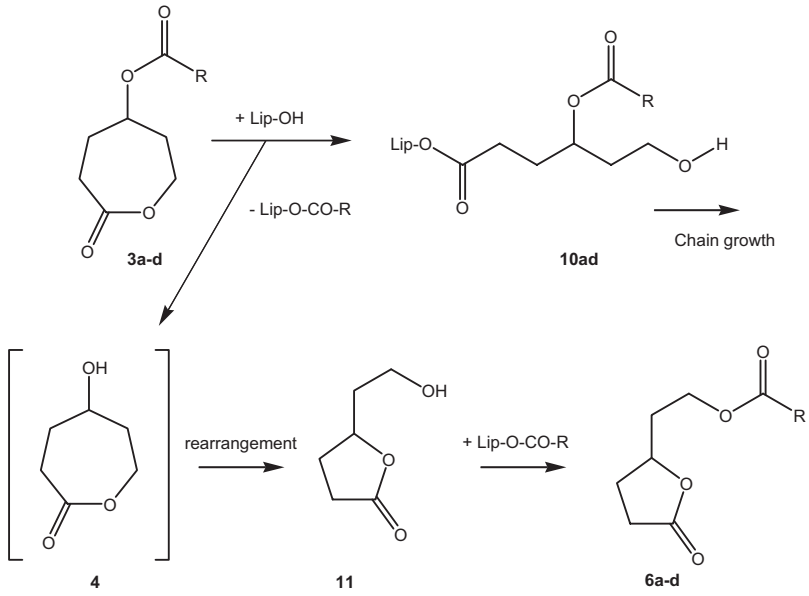
In the rearranged product (cf. structure **9a–d**) the active site and the acyloxy group have changed their position: the acyloxy group is located at the primary carbon atom and the active species at the secondary carbon atom. It is expected that ring closure via nucleophilic attack of the active species in **9a–d** at the carbonyl carbon in γ-position leads to the formation of γ-acetyloxyethyl-γ-butyrolactone (**6a–d**) which is thermodynamically more stable.



Scheme 3.
Mechanistic proposal of the rearrangement of γ-acyloxy-ε-caprolactones under polymerization conditions using tin octoate as a catalyst.

Finally the question must be answered, why the γ-acyloxy-ε-caprolactones **3a–d** give different results with respect to the product ratio polymer/rearranged monomer. The answer to this question is related to the ability of the R group in the acyl moiety to donate electrons or to withdraw electrons. The mobility of the acyl group is higher for electron donating R groups: this means that in the case of γ-acetyloxy-ε-caprolactone **3a** rearrangement will be preferred compared to γ-benzoyloxy-ε-caprolactone **3d**. Finally, for the same monomer upon increasing the temperature, rearrangement will be favoured due to lower selectivity under more severe conditions.

Polymerization of all γ-acyloxy-ε-caprolactones (**3a–d**) using Novozyme as a catalyst showed a non-uniform reaction course, too: the monomers were partly converted to γ-acyloxyethyl-γ-butyrolactones (**6a–d**) and partly to linear oligomers, the product ratio being dependent on the chemical nature of the acyl group (R-CO) and on temperature. However, our mechanistic interpretation for the rearrangement is different from that presented for the chemically catalyzed conversion (Scheme 4). If the Lipase used reacts preferentially or exclusively with the exocyclic ester group via transesterification, γ-hydroxy-ε-caprolactone (**4**) and enzyme activated acetate is formed. It is known that γ-hydroxy-ε-caprolactone is unstable and is readily converted to γ-hydroxyethyl-γ-butyrolactone (**11**). This reacts with the enzyme activated acetate resulting in the thermodynamically stable end product **6a**. If the Lipase used reacts preferentially or exclusively with the exocyclic ester group via transesterification the enzyme activated monomer **10** is formed which is a prerequisite for polymer formation.



Scheme 4.
Mechanistic consideration of the rearrangement of γ-acyloxy-ε-caprolactones under polymerization conditions using enzymatic catalysis.

Conclusion

γ-Acyloxy-ε-caprolactones were successfully prepared in two steps starting with 4-hydroxyl-cyclohexanone. The resulting monomers **3a–d** are thermodynamically less stable than their structural isomers the γ-acyloxyethyl-γ-butyrolactones **6a–d**. In order to avoid isomerization during polymerization mild reaction conditions were successfully applied. Polymers with γ-acyloxy-ε-caprolactone repeating units **7a–d** were successfully prepared. In a forthcoming paper the properties of polymers with such repeating units will be presented.

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