Synthesis of Polyamides and Their Copolymers via Enzymatic Polymerization

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Received January 17, 2015; Accepted March 15, 2015

ABSTRACT: The selective and specific features of enzymes have drawn an enormous amount of attention for use as *in-vitro* catalysts in polymerization reactions. Various studies on the enzymatic synthesis of polyesters, polycarbonates, polysaccharides, polypeptides, and polyamides have been performed and some have been implemented on an industrial scale. Particularly in the synthesis of polyester and polyamides, lipases are the most used enzymes as catalysts for their polymerization. Polyamides are considered to be one of the largest engineering polymer families used in the automotive, electrical and electronics, and consumer goods industries; thus the enzymatic synthesis of polyamides will have a tremendous impact on environmental issues. Therefore, in this article, the enzyme-catalyzed synthesis of polyamides and their copolymers is reviewed with a focus on the type of polymerization the enzyme catalyzes and type of monomer used for the synthesis of polyamides.

KEYWORDS: Enzymatic (co)polymerization, biocatalysis, polyamides

1 INTRODUCTION

Enzymes, also known as biocatalysts, are proteins with catalytic activity that control the rates of metabolic reactions in living cells [1]. Apart from their natural function in living cells, since ancient times enzymes have been used in the preparation of food products such as cheese, beer, wine, vinegar and sourdough, and in the manufacture of commodities such as linen, leather and indigo [2]. Due to the remarkable progress in enzyme discovery, enzyme engineering and biotechnology, more enzymes have been used for a plethora of *in-vitro* applications in organic and polymer synthesis, as well as in the pharmaceutical and other industries [2].

One unique feature of enzymes is their specificity towards a variety of substrates. It was suggested by Fischer in 1894, and postulated as "the lock and key" model, that both enzyme and substrates possess specific complementary shapes so they can fit into each other [3]. This specificity is of tremendous benefit for the use of enzymes in organic synthesis, as well as for pharmaceutical and industry applications. The chiral nature of the enzymes contributes to high enantioselectivity towards substrates and results in the formation of stereo- and regio-chemically defined reaction products [4]. Enzymes reduce the amount of undesirable byproduct formation leading to more efficient reactions, also reducing the waste. Therefore, enzymes are considered environmentally friendly catalysts [1,4].

Over 3000 enzymes have been identified and classified into six enzyme classes (EC) based on the type of reactions they catalyze [5,6]. These enzymes are considered to be highly efficient catalysts for a broad range of organic synthesis transformations and some of them are also suitable for industrial scale applications [6].

EC.1. *Oxidoreductases* catalyze oxidation or reduction reactions.
EC.2. *Transferases* catalyze the transfer of functional groups, such as aldehyde or ketonic, acyl, glycosyl, alkyl, aryl, nitrogenous, etc.
EC.3. *Hydrolases* catalyze the hydrolysis of esters, amides, ethers, carbon-carbon, phosphorus-nitrogen, and so on.
EC.4. *Lyases* catalyze the addition of chemical groups to double bonds, as well as the reverse reaction by removing chemical groups without hydrolysis.

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DOI: 10.7569/JRM.2015.634102

EC.5. *Isomerases* catalyze the rearrangement of isomers via racemization, epimerization, and intramolecular reactions.
EC.6. *Ligases* catalyze the bond formation, but require nucleoside triphosphates for activation of the enzymes.

In nature, enzymatic catalysis typically takes place in aqueous media, whereas most enzymatic catalysis in organic synthesis takes place in organic solvents as a reaction medium because many organic compounds are unstable or insoluble in aqueous environments [7,8]. Changing the reaction medium from an aqueous to an organic solvent may lead to new types of enzymatic reactions. For example, hydrolases catalyze the hydrolysis of esters to their corresponding alcohols and acids in aqueous media. This reaction does not take place in organic solvents due to the lack of water, but the addition of alternative nucleophiles such as alcohols, amines or thiols leads to transesterification, aminolysis, or thiotransesterification, respectively [7]. Enzymatic reactions in organic solvents offer advantages including easy recovery of products, the possibility of using non-polar substrates, avoiding side reactions, increasing the activity (in most cases for lipases), and shifting the thermodynamic equilibrium to favor synthesis over hydrolysis that results in discovering new types of enzymatic reactions [8,9].

Lipases (hydrolase class EC.3) are the most commonly used enzymes in organic synthesis due to their acceptance towards a large variety of substrates, considerable stability in organic solvents, direct use without addition of cofactors, and the fact that many of them are commercially available [8]. *Candida antarctica* lipase B (CAL-B) is one of its most famous proponents and has been used in many organic syntheses. The most well-known immobilized CAL-B is the commercially available Novozym® 435 (N435). N435 is a heterogeneous biocatalyst that consists of physically immobilized CAL-B within macroporous poly(methyl methacrylate) beads, which are known as Lewatit beads, with a particle size of 315–1000 μm and an average pore size of 140–170 Å [10]. N435 has been used as catalyst in chemical synthesis and production of polyesters [11–16], polycarbonates, [11–13], polyamides and their copolymers [11,14,16–18]. In the following section of this article, the discussion focuses on the developments in the enzymatic synthesis of polyamide and its copolymers using enzymes as catalyst.

2 SYNTHESIS OF POLYAMIDES

A polyamide is a polymer that contains a repeating unit linked together with an amide (–CONH–) bond. Polyamides can be found as natural (protein) or synthetic polymers; however, in this article, the discussion will be devoted to synthetic polyamides. According to the composition of their repeating units, polyamides are classified into three types, which are (a) aliphatic, (b) aromatic, and (c) aliphatic-aromatic polyamides, as presented in Figure 1.

Aliphatic polyamides, which are commercially known as nylons, are versatile synthetic fibers and engineering plastic materials due to their high mechanical and heat resistance properties [19]. The first nylon was poly(hexamethylene adipamide) and it was commercialized as nylon-6,6 and used for toothbrush filament by DuPont in 1938 [20]. Another nylon designated nylon-6 was synthesized from ε-caprolactam and was first described in 1938 [21]. Even today, nylon-6,6 and nylon-6 are the most used polyamides. In addition, about two-thirds of the production of nylon-6,6 and nylon-6 is converted to fibers, with the remainder used as engineering plastic materials [19].

The global sales of polyamides (nylon-6 and nylon-6,6) were up to 2.6 million tons in 2006 (around 30% in total market of engineering plastics spanning markets such as the automotive, electrical and electronics, and consumer goods industries) and they are therefore considered to be one of the largest engineering polymer families [22]. The global polyamide market was $22 billion in 2012 and is estimated to reach $27 billion by 2018 [23].

Aromatic polyamide or aramid is known as a high performance material. It has high chemical resistance, superior mechanical and thermal resistance properties compared to aliphatic polyamide [24–28]. Aramid is different from nylon because over 85% of the amide bonds are bound to two aromatic rings [25,29]. The fully aromatic structure and amide linkages in aramid contribute to the stiff rodlike macromolecular chains that interact with each other via highly directional hydrogen bonding, which results in a highly compact intermolecular packing [24,25]. Aramid has been used for several applications, such as high strength and modulus fibers, high temperature resistant coatings, and highly efficient semipermeable membranes [26]. Moreover, commercial aramids, such as poly(*p*-phenylene terephthalamide) (PPPT) under the trade

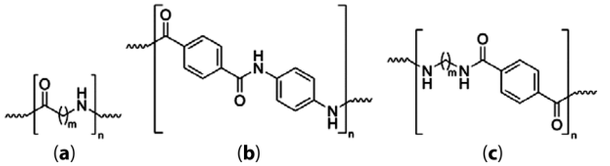


Figure 1 Classification of polyamides based on the composition of repeating units (**a**) aliphatic, (**b**) aromatic, and (**c**) combination of aliphatic and aromatic.

name Kevlar® and poly(*m*-phenylene isophthalamide) (PMPI) are used as electrical insulations, bulletproof body armor, industrial fillers, etc. [24,25,27].

Certain polyamides are synthesized from a combination of aliphatic and aromatic monomers. They are known as aliphatic-aromatic polyamides and mostly have better solubility than aramid and better mechanical and thermal properties than nylon. The commercially available aliphatic-aromatic polyamide polyphthalamides (PPAs) are produced by DuPont. The aromatic structure in PPA gives advantages like higher glass transition temperature (T_g), higher melting temperature, and lower adsorption of moisture and solvent compared to nylon [30]. The PPAs have mainly been used as engineering thermoplastics in automotive components [30]. Another example of application in the intumescent flame retardant (IFR) of polypropylene (PP) is using poly(hexamethylene terephthalamide) (PA6,T) as a carbonization agent. Studies showed that PA6,T has promising flame retardancy properties [31] compared to using nylon-6 as a carbonization agent [32].

The industrial synthesis of most polyamides is carried out by a melting process. The use of elevated temperature reactions leads to thermal degradation and undesired polymer products [27,33]. Polymerization under the polymer's melting temperature (~ 215°C) can be performed by using anionic polymerization methods in the synthesis of nylon-6. However, the polymerization involves the use of alkali metal catalysts such as Na, NaH, C_2H_5MgBr, $LiAlH_4$, etc. [19].

Due to increasing environmental concerns, many efforts in the development of green chemistry have taken place in recent decades and one of them is the use of enzymes as green catalysts. The enzymatic synthesis of polymers not only allows the application of milder reaction conditions, but also the use of enzymes as non-toxic catalysts which are derived from renewable resources [11,34]. Enzymatic polymerization is defined as an *in-vitro* synthesis of polymer catalyzed by enzyme and does not follow biosynthetic pathways [35,36].

In Table 1, the comparison of synthesis of nylon-3 and nylon-6 is summarized. By employing the enzyme as catalyst, the polymerization can be carried out in milder reaction conditions, although the resultant molecular weight of the product is lower compared to product from non-enzymatic polymerization. In this article, four different methods for the enzymatic synthesis of polyamides and polyamide copolymers are discussed; (a) polycondensation of A-B monomer, (b) polycondensation of AA and BB monomers, (c) ring-opening polymerization, and (d) enzymatic copolymerization.

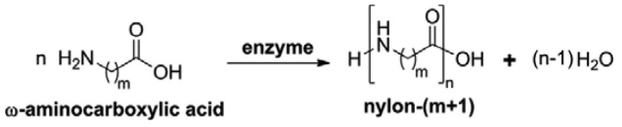
2.1 Polycondensation of A-B Monomer

The A-B type monomer denotes a monomer with two different reactive end groups. Polycondensation of A-B type monomer is also known as self-polycondensation, where groups A and B react with each other [14], as presented in Scheme 1.

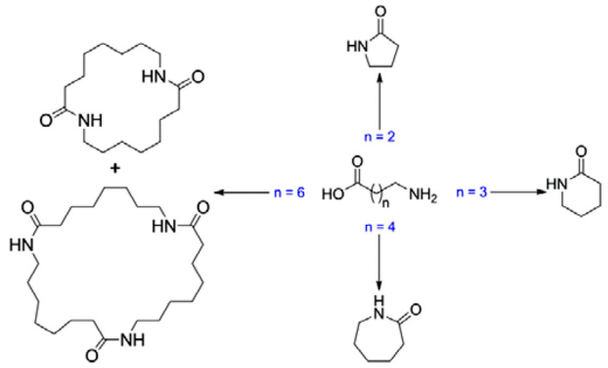
Kong *et al.* [44] have filed a patent application on the method of preparing aqueous polyamide dispersions by lipase-catalyzed condensation of ω-aminocarboxylic acids (C_2–C_{30}). The conventional processes for preparing aqueous polyamide

Table 1 Synthesis of nylon-3 and nylon-6 via conventional chemistry and enzymatic synthesis.

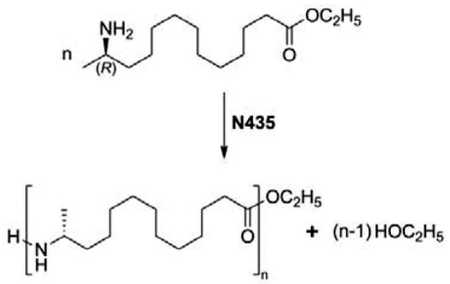
Type	Preparative techniques	
	Non-enzymatic synthesis	**Enzymatic synthesis**
Nylon-3	Polymerization of acrylamide in the presence of strong base catalyst (e.g., *t*-BuOK) in organic solvent (e.g., pyridine) at 80–200°C for 18 h resulted in product yield up to 69% and molecular weight of 80000 g/mol (from light scattering) [37]. Polymerization with this method leads to branched polymers [38]. ROP of β-propiolactam in the presence of *t*-BuP_4 as catalyst in a mixture of DMAC and LiCl for 3 h at 25°C resulted in product yield up to 96% [39].	Ring-opening polymerization (ROP) of β-propiolactam using N435 as catalyst in toluene at 90 or 55°C for 96 h resulted in product yield up to 81% and maximum chain length of 18 units (from MALDI-ToF) [40–42].
Nylon-6	In industry, synthesis of nylon-6 is carried out by polymerization of ε-caprolactam in the presence of water in a continuous multi-step process at a reaction vessel called VK (Vereinfacht Kontinuierlich) tube, which operates at 250°C and 1 atm. Molecular weight of nylon-6 resulted in this process is around M_n = 24–32 kg/mol [43].	ROP of ε-caprolactam is performed in miniemulsions using dispersant (e.g., non-ionic or anionic emulsifiers). The produced nylon-6 had a M_w of 212 kg/mol [44].



Scheme 1 Enzymatic polymerization of ω-aminocarboxylic acid.



Scheme 2 Cyclization of ω-aminocarboxylic using N435 as catalyst in toluene [45].



Scheme 3 Enzymatic synthesis of chiral polyamide using N435 as catalyst carried out by Poulhès *et al.* [46].

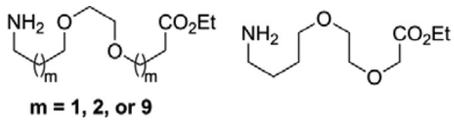


Figure 2 Amino-esters containing ethylene glycol moiety [47,48].

dispersions are generally multistage, technically very complex, and energetically demanding. However, they succeeded in preparing aqueous polyamide dispersion via enzymatic polymerization. They performed the reaction in miniemulsions using dispersants (nonionic or anionic emulsifiers) and addition of water-immiscible solvent up to 60% ($^{w}/_{w}$) (such as toluene). The dispersed phase has an average diameter of ≤ 1 µm in the aqueous medium. Miniemulsions containing lipase (0.5–8% ($^{w}/_{w}$)), dispersants, and water were also prepared and further mixed with the miniemulsions containing aminocarboxylic acids. The reactions were carried out at 60°C and stirred for 20 hours under a N_2 atmosphere.

The cyclization of ω-aminocarboxylic acids of various length (C_3–C_{12}) using immobilized CAL-B (N435) as catalyst has also been reported by our group [45]. It was found that N435 catalyzed the formation of lactams via intramolecular reaction of ω-aminocarboxylic acid and not the predicted polymerization. The resulting products were lactams with different ring sizes (five-, six-, and seven-membered) and macrocylic lactams (dimer and trimer), as depicted in Scheme 2.

Poulhès *et al*. have performed the synthesis of chiral polyamide using amino ester as a monomer [46]. The chiral monomer of (*R*)-amino ester was synthesized prior to use in the polymerization. The polymerization was carried out in diphenyl ether at 80°C using N435 as catalyst for 240 h under reduced pressure (3 mbar), as shown in Scheme 3. They reported that the chiral polyamide had a molecular weight of 1316 g/mol and PDI 1.9. No polyamide was formed in the control reaction (without the addition of N435).

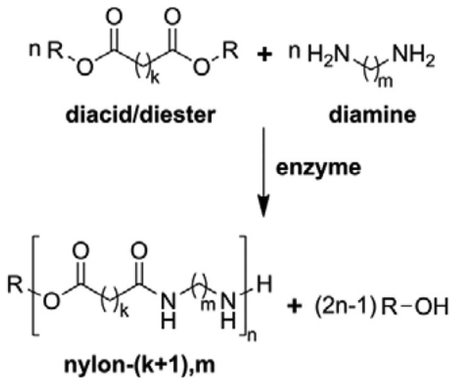
Poulhès *et al.* [47,48] have also reported another enzymatic synthesis of polyamide using an amino-ester containing an ethylene glycol moiety as monomer (Figure 2). All the polymerizations were performed using N435 as catalyst. The presence of the ethylene glycol moiety increases the solubility of the resulting polymer in organic solvent. Moreover, Poulhès *et al*. [48] also observed that by using ω-amino-α-alkoxy-acetate as monomer, 93% conversion can be reached within 30 minutes.

2.2 Polycondensation of AA and BB Monomers

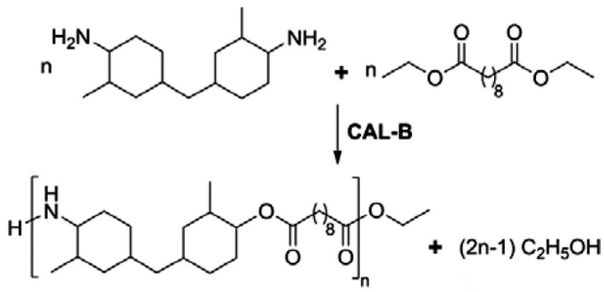
The AA and BB type monomers are difunctional monomers with the same end group, such as diesters, diacids, diamines, etc. An example of the polycondensation of an AA and BB monomer is presented in Scheme 4.

The preparation of high molecular weight polyamides via enzymatic polymerization was first reported by Cheng *et al.* [49]. The polyamides had molecular weights of 3000–10000 g/mol. The reactions were carried out using different dialkyl esters (adipate, malonate, phenylmalonate, or fumarate) and diamines (NH_2-terminated triethylene glycol, triethylene tetraamine, or diethylene triamine) using commercial lipases.

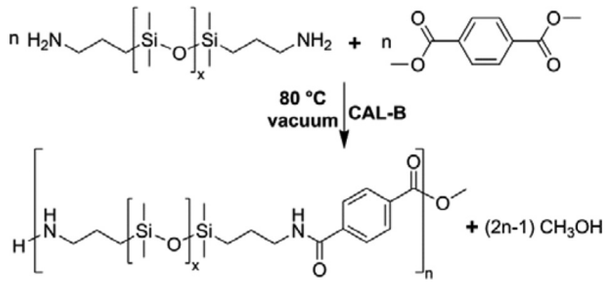
The synthesis of water-soluble poly(aminoamide) has been reported by Gu *et al.* [50]. The poly(aminoamide)s were synthesized using lipase as



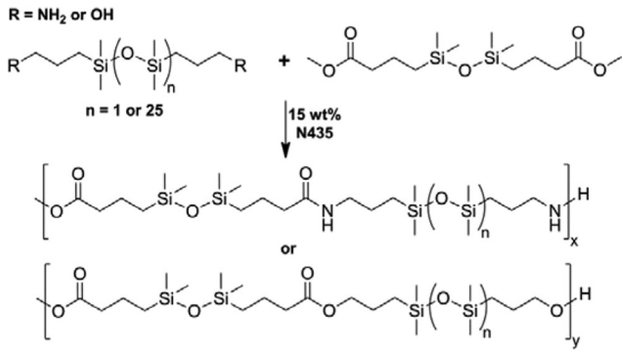
Scheme 4 Enzymatic polycondensation of diacid/diester and diamine.



Scheme 5 Enzymatic synthesis of polyamide in aqueous dispersion.



Scheme 6 Lipase-catalyzed polycondensation of α,ω-(diaminopropyl)-terminated poly(dimethylsiloxane) (APT-PDMS) with dimethyl terephthalate (DMT) carried out in toluene at 80°C for 48–96 h under reduced pressure [54].



Scheme 7 The lipase-mediated synthesis of silicone polyesters and silicone polyamide performed by Frampton *et al.* [55].

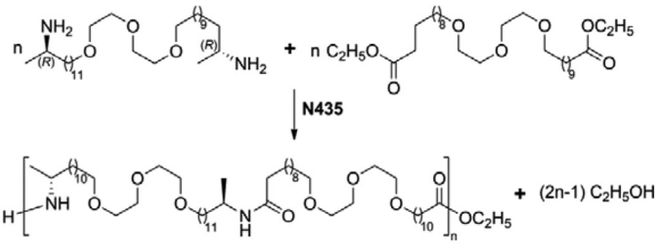
catalyst at 70–90°C. They found that CAL-B (N435) and *Mucor miehei* (e.g., Amano lipase M) showed the highest activities. Various types of poly(aminoamide)s with different molecular weights were produced from these reactions: DETA (diethylene triamine)–adipate polyamide (M_w 8400 and PDI 2.73), TETA (triethylene tetraamine)–adipate polyamide (M_w 8000 and PDI 2.10), and TEGDA (triethylene glycol diamine) polyamide (M_w 4540 and PDI 2.71).

A method for the preparation of aqueous polyamide dispersions via lipase-catalyzed polycondensation has been patented by BASF AG [51]. The AA-BB type of polycondensation is presented in Scheme 5. The reactions were carried out at 60°C at a pH between 3 and 9. The resulting polyamide had a M_w of 5200 g/mol.

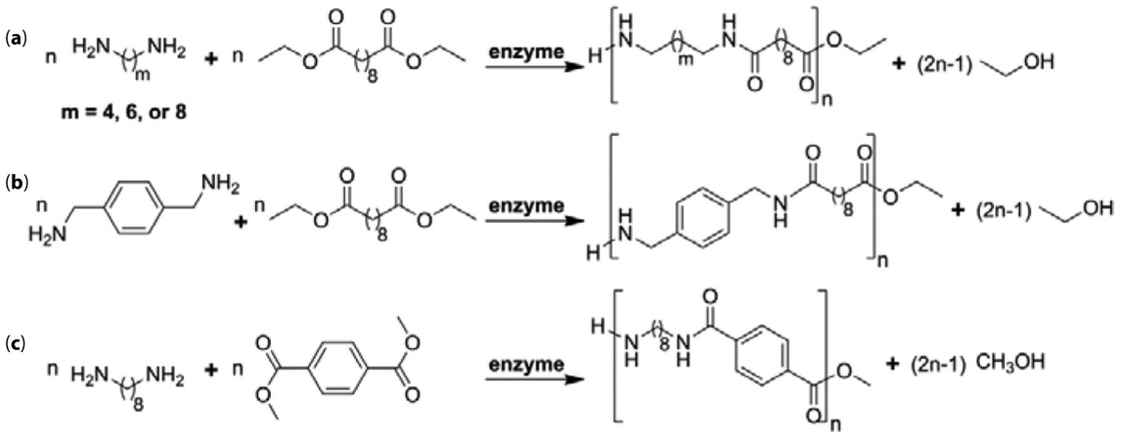
Azim *et al.* [52] have reported the synthesis of oligoamides catalyzed by N435. The reaction was carried out between dialkyl ester (e.g., diethyl allylmalonate) and diamine (e.g., 1,12-dodecanediamine) and the resulting oligoamides had a degree of polymerization (DP) up to 9. Another patent from Panova *et al.* [53] described that the polycondensation of diester and diamine not only resulted in linear polyamides or oligoamides, but also rewsulted in the formation of macrocyclic amide oligomers that could be useful for the subsequent production of higher molecular weight polyamides [53].

The synthesis of silicone aromatic polyamides (SAPAs) was reported by Poojari *et al.* [54], as shown in Scheme 6, where diaminopropyl-terminate poly(dimethylsiloxane) was reacted with dimethyl terephthalate. Two different molecular-masses of APT-PDMS (M_n 1000 and 4700 g/mol) were used and 96 hours reaction time resulted in SAPAs of M_n 5700 and 40000 g/mol, respectively.

The synthesis of silicone polyesters and silicone polyamides were also reported by Frampton *et al.* [55]. In order to gain a better understanding of the optimal reaction conditions for N435, kinetic reactions of formation silicone polyesters and silicone polyamides at different temperatures (35 to 150°C) were studied. In the synthesis of silicone polyesters, the rate constants increased up to 120°C and at 140°C the rate constants declined, which indicates the sign of denaturation of CAL-B. They concluded that incorporating disiloxane unit into diester or diol can greatly increase the temperature at which CAL-B catalyzes reactions. However, the same conclusion cannot be drawn for the synthesis of silicone polyamides, since formation of polyamides was less favored compared to formation of polyesters.



Scheme 8 Enzymatic synthesis of chiral polyamide from AA-BB monomer using N435 as catalyst carried out by Poulhès *et al*. [46].



Scheme 9 Enzymatic syntheses of (**a**) nylons, (**b**) oligo(*p*-xylylene sebacamide), and (**c**) oligo(octamethylene terephthalamide) using immobilized cutinase or N435 as catalyst in one- or two-step reaction [57,58].

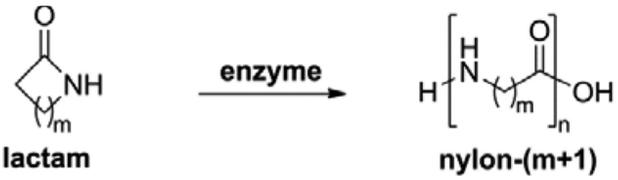
The synthesis of chiral polyamides and polyamides containing ethylene glycol moieties were also reported by Poulhès *et al*. [46–48]. By using AA-BB polycondensation, chiral polyamide was synthesized using N435 as catalyst, as shown in Scheme 8. The reaction was performed in diphenyl ether at 80°C for 240 h under reduced pressure (3 mbar) and resulted in the formation of a chiral polyamide with a yield up to 87% and M_w 19280 g/mol. The crystallinity and thermal properties of the resulted polyamides were determined as well.

Ragupathy *et al.* [56] have reported the syntheses of nylon-8,10, nylon-6,13, nylon-8,13, and nylon-12,13 using immobilized CAL-B as catalyst. The reactions were carried out in one- (in toluene at normal pressure), two- (in dried diphenyl ether at reduced pressure), or three-steps (in diphenyl ether at two-step reduced pressure) enzymatic reactions. By performing three-step enzymatic reactions, yields up to 97% can be reached and a molecular-mass M_n (determined from ^{1}H NMR) up to 5380 g/mol. Detailed studies found that nylon-8,10 had 5 identified microstructures; cyclic, amine-ester, amine-amine, amine-amine, and ester-ester.

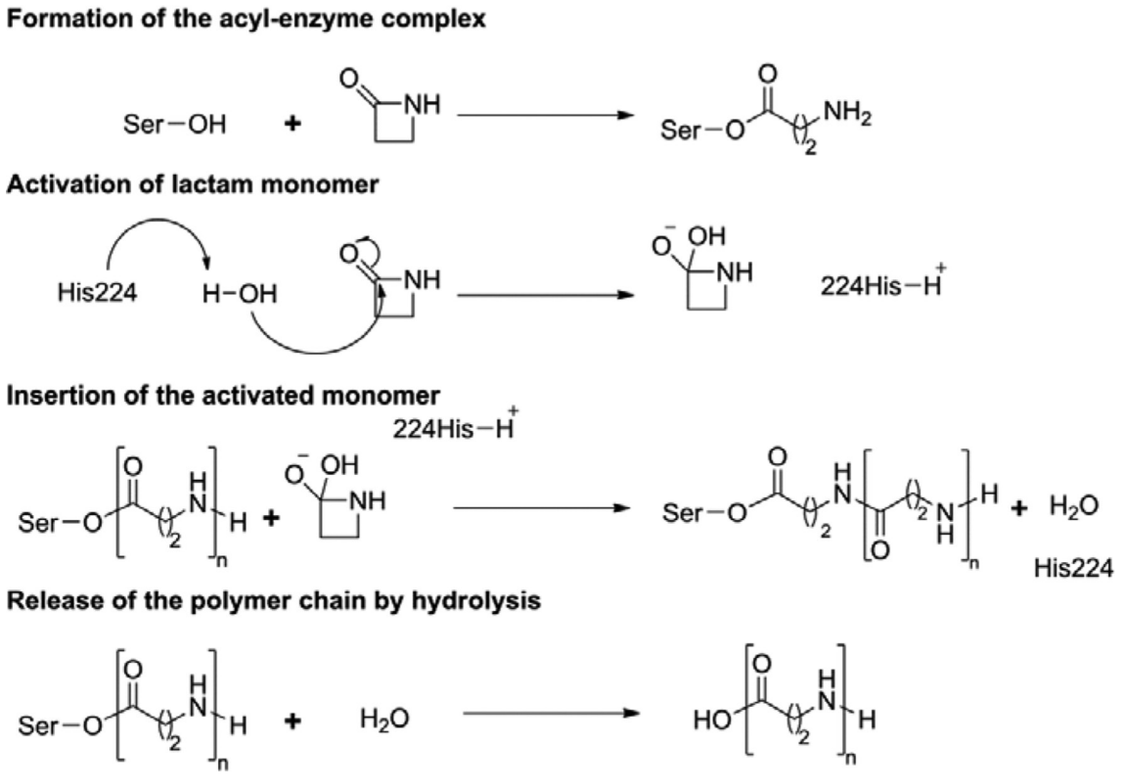
By performing enzymatic polycondensations of AA and BB monomers, our group has reported the syntheses of aliphatic oligomides (nylon-4,10, nylon-6,10, and nylon-8,10) [57] and aliphatic–aromatic oligoamides (oligo(*p*-xylylene sebacamide) and oligo(octamethylene terephthalamide)) [58], as depicted in Scheme 9. The reactions were carried out as one- and two-step reactions using N435 or immobilized cutinase as catalyst. In the synthesis of nylons, the highest maximal degree of polymerization (DP_{max}) is 16 and can be achieved in the synthesis of nylon-8,10 catalyzed by crosslinked enzyme aggregates (CLEA) *Fusarium solani pisi* (*F. solani pisi*) cutinase in a two-step reaction at 70°C. For the synthesis of aliphatic–aromatic oligoamides, the highest DP_{max} of 15 for oligo(*p*-xylylene sebacamide) was observed in the two-step reaction using CLEA cutinase as a catalyst. Although reactions using CLEA cutinase as catalyst showed lower conversion than reactions using CAL-B they resulted in the same or even higher DP_{max}, which indicates the clear potential of CLEA cutinase for enzymatic polyamide polymerizations.

2.3 Ring-Opening Polymerization

Kong *et al.* [44] have reported the preparation of aqueous polyamide dispersions via lipase-catalyzed



Scheme 10 Enzymatic ring-opening polymerization of lactams.



Scheme 11 Mechanism of enzyme-catalyzed ring-opening polymerization of β-lactam developed by Baum *et al.* [42,59] (Reproduced from [41]).

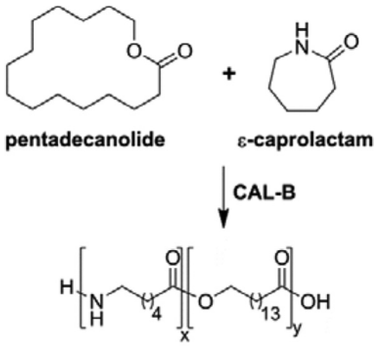
ring-opening polymerization of lactam, as shown in Scheme 10. They used various sizes of lactams, among them ε-caprolactam. They successfully produced poly(ε-caprolactam) (nylon-6) with M_w of 212000 g/mol and M_n of 47000 g/mol.

Mechanistic study on enzymatic ring-opening polymerization of β-propiolactam has been established by Schwab *et al*. [40] and collaborators [42,59]. Its proposed mechanism scheme is summarized in Scheme 11. Schwab *et al*. [40] also reported the synthesis of linear nylon-3 (poly(β-alanine) by lipase-catalyzed ring-opening polymerization β-lactam. The resulting nylon-3 had a low average DP of 8, which is likely caused by low solubility of nylon-3 in the reaction medium. They also performed control experiments with β-alanine as a substrate and confirmed that the ring structure of β-lactam was necessary to obtain the polymer.

2.4 Enzymatic Copolymerization

The enzymatic synthesis of copolymers containing amide bonds or polyamide blocks can be carried out via ring-opening copolymerization, polycondensation, or via a combination of ring-opening and polycondensation in a one-pot reaction. Several selected reports are briefly discussed in this section.

The first report on block copolymer synthesis using enzymatic polycondensation was by Gross *et al.* [60]. They described the synthesis and solid-state properties of polyesteramides with a poly(dimethylsiloxane) (PDMS) block. The polycondensation was carried out with various ratios of dimethyl adipate, octanediol, and diamine-functionalized PDMS (M_w = 875 g/mol). The physical properties of the resultant copolymer varied from hard solids to sticky materials.



Scheme 12 Enzymatic synthesis of aqueous polyamide dispersion by Kong *et al.* [44].

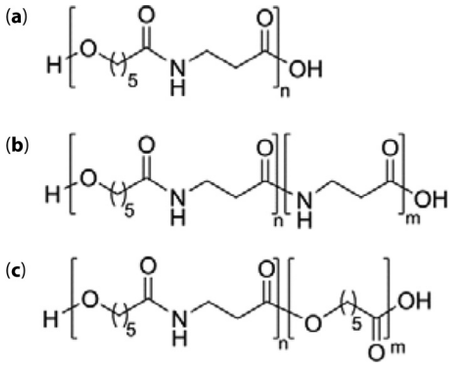
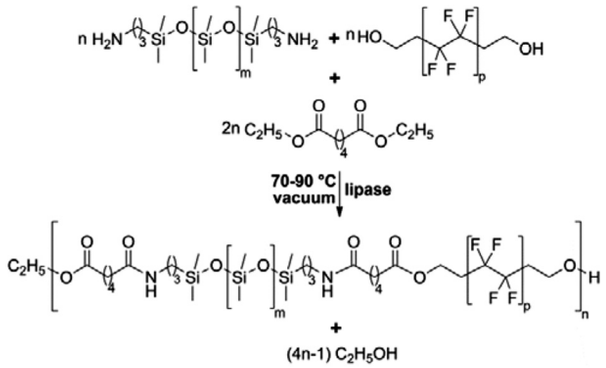


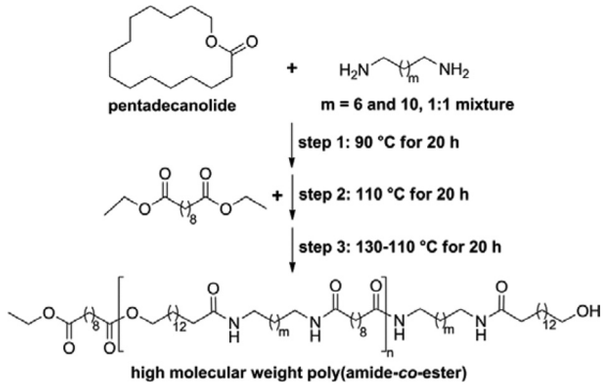
Figure 3 Structures of poly(ε-CL-*co*-β-lactam) which have (**a**) an alternating structure, (**b**) a random structure consisting of repeating unit of oligo(ε-CL), and (**c**) a random structure consisting of repeating unit of oligo(β-lactam).

In the paper discussing the preparation of aqueous polyamide dispersions, Kong *et al.* [44] also produced copolyesteramides. The copolymer was prepared via enzymatic ring-opening copolymerization of pentadecanolide and ε-caprolactam with a ratio of 1:2.3. The produced copolymer had amide and ester bonds in its backbone chain, as shown in Scheme 12. The copolymer had a M_w of 16600 g/mol and two melting points at 97°C and ~ 210°C.

The synthesis of polyester amides by ring-opening copolymerization of ε-caprolactone and β-lactam using CAL-B as catalyst was reported by our group [61]. Variation of the feed ratios of ε-CL/β-lactam (25:75, 50:50, and 75:25) was performed at 90°C in toluene for 72 h. The products contain poly(ε-CL-*co*-β-lactam) and the homopolymers of poly(ε-CL) and poly(β-lactam), respectively. Poly(ε-CL-*co*-β-lactam) has an alternating and random structure consisting of alternating repeating units with oligo(ε-CL) and/or oligo(β-lactam), as shown in Figure 3. The highest fraction of alternating copolymers resulted from the reaction with a feed ratio of 50:50.



Scheme 13 Lipase-catalyzed synthesis of silicone fluorinated polyesteramides (SFAPEPs) by transesterification and amidation of α,ω-aminopropyl terminated poly(dimethylsiloxane) (APDMS) and 3,3,4,4,5,5,6,6-octafluoro 1,8-diol (OFOD) with dimethyl adipate (DEA), respectively, by Palsule *et al.* [62].



Scheme 14 Synthesis of poly(amide-*co*-ester)s by N435-catalyzed polymerization carried out by Ragupathy *et al.* [56].

Palsule *et al.* [62] have reported the synthesis of silicone fluorinated aliphatic polyesteramides (SAFPEAs) using immobilized CAL-B as catalyst, as shown in Scheme 13. They proposed that SAFPEAs have the potential for a variety of low surface energy applications. The SAFPEAs are viscous materials due to the presence of highly flexible silicone segments in the backbone chain. SAFPEAs with a silicone content above 15% no longer exhibit crystallinity.

The synthesis of poly(amide-*co*-ester)s (PEAs) via a combination of ring-opening polymerization and polycondensation in a one-pot reaction has been performed by Ragupathy *et al.* [56]. By using a three-step polymerization process, as described in Scheme 14, molecular weights up to M_n of 17550 g/mol can be obtained, with melting points of approximately 164°C.

A compilation of polycondensation of A-B monomer catalyzed by enzyme is summarized in Table 2.

Table 2 Enzyme catalyzed synthesis of polyamides.

Polycondensation of A-B Monomer			
Monomer	**Enzyme**	**Media**	**Ref.**
ω-Aminocarboxylic acids (C_2–C_{30}) Aminocarboxamides (C_2–C_{30}) Aminocarbonitriles (C_2–C_{30})	*Pseudomonas cepacia*, *Burkholderia platarii*, or *Candida antarctica* lipase B free and immobilized form (N435)	Aqueous, mixture of water and non-polar organic solvent	[44]
ω-Aminocarboxylic acids (C_3–C_{12})	N435	Toluene	[45]
(R)-ethyl 12-aminotridecanoate	N435	Diphenyl ether	[46]
Amino-esters contain ethylene glycol moiety (*i.e.*, ethyl 2-(2-(4-aminobutoxy)ethoxy)acetate, ethyl 3-(2-(3-aminopropoxy)ethoxy)propanoate, ethyl 4-(2-(4-aminobutoxy)ethoxy)butanoate, or ethyl 11-(2-(11-aminoundecyloxy)ethoxy)undecanoate	N435	Bulk, glyme, or diphenyl ether	[47, 48]
Polycondensation of AA and BB monomers			
Diethylene triamine and different alkyl esters (adipate, malonate, fumarate, or phenylmalonate)	N435 or Palatase	Bulk	[34, 49, 50]
Dimethyl adipate and different diamines (diethylene triamine, triethyelene tetraamine, NH_2-terminated triethylene glycol)	N435, *Pseudomonas fluorescens*, *Candida rugosa*, *Pseudomonas sp.*, *Mucor javanicus*, or *Aspergillus niger*	Bulk	
Diamine and diacid Type of diamine: 1,6-diaminohexane 1,12-diaminododecane 2,2-dimethyl-1,3-diaminopropane Isophoronediamine 1,4-diaminocyclohexane 3,3′-diaminodicyclohexylmethane 4,4′-diaminodicyclohexylmethane 3,3′-dimethyl-4,4′-diaminodicyclohexylmethane *m*-xylylenediamine *p*-xylylenediamine Type of diacid: butanedioic acid hexanedioic acid decanedioic acid terephthalic acid or isophalic acid	*Pseudomonas cepacia*, *Burkholderia platarii*, or *Candida antarctica* lipase B free and immobilized form (N435)	Aqueous, mixture of water and non-polar organic solvent	[51]
Diethyl adipate and α,ω-(diaminopropyl) polydimethylsiloxane	N435	Bulk	[60]
Diethyl sebacate and 1,8-diaminooctane (DAO) Ethylene tridecanedioate (ETD) and DAO ETD and 1,6-diaminohexane ETD and 1,12-diaminododecane	N435	Toluene or diphenyl ether	[56]

(*Continued*)

Table 2 cont.

Diethyl 3,3′-(2,2′-oxybis(ethane-2,1-diyl)bis(oxy)) dipropanoate and 3,3′-(2,2′-oxybis(ethane-2,1-diyl) bis(oxy))dipropan-1-amine Diethyl 11,11′-(2,2′-oxybis(ethane-2,1-diyl)bis(oxy)) diundecanoate and 11,11′-(2,2′-oxybis(ethane-2,1-diyl)bis(oxy))diundecan-1-amine Diethyl 11,11′-(2,2′-oxybis(ethane-2,1-diyl) bis(oxy))diundecanoate and *(R)*-13-(2-(2-((*R*)-12-Aminotridecyloxy)ethoxy)tridecan-2-amine Diethyl 2,2′-(ethane-1,2-diylbis(oxy))diacetate and 11,11′-(2,2′-oxybis(ethane-2,1-diyl)bis(oxy)) diundecan-1-amine	N435	Bulk, glyme, or diphenyl ether	[46-48]
1,3-bis(3-carboxypropyl)-1,1,3,3-tetramethyldisiloxane dimethyl ester and 1,3-bis(3-aminopropyl) tetramethyldisiloxane 1,3-bis(3-carboxypropyl)-1,1,3,3-tetramethyldisiloxane dimethyl ester and α,ω-(diaminopropyl) polydimethylsiloxane			
Diethyl sebacate and aliphatic diamine (1,4-diaminobutane, 1,6-diaminohexane, or 1,8-diaminooctane)	N435, immobilized *F. solani pisi* cutinase on Lewatit beads, or CLEA *F. solani pisi* cutinase	Toluene or diphenyl ether	[57]
Diethyl sebacate and *p*-xylylenediamine Dimethyl terephthalate (DMT) and 1,8-diaminooctane DMT and *p*-xylylenediamine	N435, immobilized *F. solani pisi* cutinase on Lewatit beads, or CLEA *F. solani pisi* cutinase	Toluene or diphenyl ether	[58]
Ring-Opening Polymerization			
Lactams (C_3–C_{15})	CAL-B	Aqueous	[44]
β-propiolactam	N435	Toluene	[40-42]
Enzymatic Copolymerization			
Diethyl adipate, 1,8-octanediol, and α,ω-(diaminopropyl)polydimethylsiloxane	N435	Bulk	[60]
Pentadecanolide and ε-caprolactam	CAL-B	Mixture of hexadecane and deionized water	[44]
Diethyl adipate, fluorinated alkane diol (FAD), and α,ω-(diaminopropyl)poly(dimethylsiloxane) Four different types of FAD: 2,2,3,3-tetrafluoro 1,4-butanediol 2,2,3,3,4,4-hexafluoro 1,5-pentanediol 2,2,3,3,4,4,5,5-octafluoro 1,6-hexanediol 3,3,4,4,5,5,6,6-octafluoro 1,8-octanediol	N435	Bulk	[62]
Pentadecanolide, 1,8-diaminooctane, 1,12-diaminododecane, and diethyl sebacate	N435	Diphenyl ether	[56]
β-Propilactam and ε-caprolactone	N435	Toluene	[61]

3 CONCLUSIONS AND FUTURE PERSPECTIVE

The use of enzymes offers many advantages, such as reducing the need for extensive protection and de-protection steps in complicated reactions and preventing undesired byproducts. Furthermore, using enzymes in organic solvents leads to new types of reactions that are not feasible with conventional chemistry (e.g., synthesis of novel monomers, oligomers, or polymers).

In this perspective, we have reviewed the recent developments in the field of enzymatic synthesis of polyamides and their copolymers. New types of polyamides and their copolymers have been synthesized in recent years, which prove that using enzymes in organic solvents can lead to new types of reactions and results and new types of products.

In the near future it can be expected that new enzyme systems will be introduced into this field that are currently used for the enzymatic polymerization of polyester. Furthermore, attempts to overcome the solubility issue of polyamides and to increase molecular weight must be considered in the future, for instance, by using untraditional solvent systems such as ionic liquids or supercritical CO_2. With these it will be possible to not only discover new types of products but also to move towards practical applications.

ACKNOWLEDGEMENT

The authors wish to thank the Ubbo Emmius Programme of the University of Groningen for financial support.

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