

Title High Functionalized, Aliphatic Polyamides via CuAAC and Thiol-yne Chemistries

Authors Leen Billiet, Xander K.D. Hillewaere and Filip Du Prez

In: Journal, Volume (Issue), pages, year. European Polymer Journal, 48 (12), 2085-2096, 2012

Optional: http://dx.doi.org/10.1016/j.eurpolymj.2012.08.013

# Highly functionalized, aliphatic polyamides via CuAAC and thiol-yne chemistries

*Leen Billiet, Xander K. D. Hillewaere, and Filip E. Du Prez*[*]

*Department of Organic Chemistry, Polymer Chemistry Research Group, Ghent University, Krijgslaan 281 S4-bis, B-9000 Ghent, Belgium*

**Corresponding author: filip.duprez@ugent.be, Tel: +32 92644503, Fax: +32 92644972*

## *Abstract*

The first step in the synthesis of functionalized polyamides consisted in the introduction of alkyne side groups in several types of linear polyamides by interfacial step-growth polymerization of hexane-1,6-diamine or 4,9-dioxadodecane-1,12-diamine in combination with on one hand adipoyl or sebacoyl chloride and on the other hand an alkyne-containing building block, i.e. 2-methyl-2-propargylmalonic acid dichloride. Both homo- and copolyamides were synthesized, creating a large range of alkyne-containing polyamides with degrees of functionalization ranging between 5 and 100 %. Subsequently, these polyamide chains have been modified with two types of linking chemistries, respectively with azides through the copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition or with thiols through the thiol-yne addition reaction.

## *Keywords*

Aliphatic polyamides, step-growth polymerization, polycondensation, click chemistry, thiol-yne chemistry, functionalization of polymers

# Introduction

Step-growth polymers, made through sequential addition or condensation reactions between two functional groups, cover a huge industrial area. Well known examples are polyesters, polyurethanes, polyurea and polyamides. The polyamides (PAs) form an interesting polymer class with many applications, such as fibers, engineering plastics, films and coatings, due to their good thermal and mechanical properties [1]. One way to prepare them consists of the polycondensation of diamines with dicarboxylic acids or derivatives. The polyamidation equilibrium is much more favorable than that for the formation of polyesters [2]. If the aliphatic PA is thermally stable above its melting temperature, a melt synthetic method is almost exclusively used [1]. However, the reaction temperature in PA synthesis can considerably be reduced by using derivatives of dicarboxylic acids such as diacid dichlorides. They react with diamines at room temperature via the Schotten-Baumann reaction, which can be carried out by solution as well as interfacial polymerization [3].

Like in the case of polyesters [4], the application areas could be broadened with straightforward synthetic strategies to functionalize the polyamide backbone, in order to give them modified physical properties or specific functionalities. As mentioned above, PAs have excellent thermal and mechanical properties, of which many are attributable to the formation of hydrogen bonds between the NH and C=O groups of neighboring macromolecules. This is demonstrated by their solubility in a limited number of solvents (sulfuric acid, formic acid, *m*-cresol), their high melting points even when originating from aliphatic components, and their resistance to hydrolysis. On one hand, the introduction of alkyl side chains on carbon or nitrogen lowers the melting point of polyamides, but at the same time this improves the solubility [3].

The aim of our research was to couple a variable amount of functional compounds with polyamides by making use of some developments in click chemistry during the last decade [5-6]. In this way, for example the solubility or polarity could be modified more extensively to fit the application's needs. Unlike for the polyesters [7-12] and polyurethanes [13-15], it is remarkable that the combination of linear polyamides with click chemistry has not been explored extensively. The research already done in the field of click chemistry on polyamide-containing structures is mainly focused on the Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction for the synthesis and functionalization of polyamide-based dendrimers. Goyal *et al*. synthesized polyamide-based dendrimers possessing both a single aldehyde and azide moiety on their periphery [16]. These dendrimers can be quantitatively functionalized with small organic and biological molecules. The same authors designed and synthesized monofunctionalized polyamide-based dendrimers containing either a terminal azide or alkyne moiety [17]. Lee and coworkers used click chemistry for the coupling of alkyne-functionalized poly(amido amine) (PAMAM) dendrimers. Several multi-azide building blocks, designed and synthesized to serve as the core of the dendrimer, were clicked with the alkyne-functionalized PAMAM dendrons in a convergent strategy resulting in the formation of several kinds of PAMAM dendrimers with different core units in high yields [18]. Ornelas

*et al*. developed a copper-free strain-promoted alkyne-azide cycloaddition (SPAAC) strategy that quantitatively functionalized polyamide-based dendrons and dendrimers with PEG chains under mild reaction conditions without any metal contamination [19]. Amongst others, this SPAAC strategy was further used by the same group to attach aminocyanine dyes to similar polyamide-containing dendrons and dendrimers [20-21]. The combination of peptides and CuAAC click chemistry was applied in dendrimers as well, attaching antimicrobial peptide sequences to polyamide-based dendrimers in medium to high yields [22]. Both linear and cyclic peptide sequence azides were linked to the alkyne functions in the periphery of the dendrimer.

To our knowledge, linear polyamide structures and CuAAC reactions were only combined in three applications. Firstly, Holub *et al.* functionalized azide- or alkyne-modified peptoid oligomers with model compounds using sequential synthesis on a solid support [23]. In this way, peptides could be generated with a variety of functional groups on specific sites in the oligomer scaffold. Secondly, Pipkorn and coworkers have utilized "peptide nucleic acid" like polyamide penta- and heptamers in combination with Diels-Alder click chemistry to couple functional tetrazines to the amide backbones [24]. Finally, Lo *et al.* managed to attach azamacrocycles to lexitropsins, which form a polyamide class of minor groove binders for DNA [25]. This allowed the authors to selectively bind AT-rich oligonucleotides and investigate the influence of DNA-binding on different azamacrocycle-metal complexes.

Thiol-ene click chemistry was used by Kreye *et al.* to polymerize butane-1,4-dithiol with aliphatic amide-containing monomers generated via Ugi multicomponent reactions [26]. This was done in addition to acyclic diene metathesis polymerizations to generate linear polyamides with a high diversity of side chains.

In this research, linear, aliphatic polyamides have been functionalized with two types of functionalization chemistries, nowadays denoted as click chemistries under certain conditions [27]: CuAAC and thiol-yne radical addition reactions. As alkynes are known to react with both azides and thiols [6], suitable building blocks bearing an alkyne function will be synthesized and used in the step-growth polymerization (SGP). The generated polyamides will be extensively characterized by $^{1}$H NMR, $^{13}$C NMR, FTIR, DSC, TGA, SEC and viscosimetry. Subsequently, these alkyne-containing polyamides will be subjected to CuAAC and thiol-yne reactions. The use of thiol-yne chemistry in the field of polyamide functionalization has never been reported.

# Experimental

## *Materials*

Diethyl methylmalonate (DEMM, Acros, 99%), 1,6-hexanediamine (HDA, Aldrich, 98%), 4,9-dioxa-1,12-dodecanediamine (DDA, Aldrich, 97%), ethylenediamine (EDA, Aldrich, ≥ 99%), sebacoyl chloride (SC, Acros, 92%), adipoyl chloride (AC, Acros, 98%), diethylenetriamine (DETA, Acros, 98+%), lithium aluminum hydride (Acros, 95%), propargyl bromide (Aldrich, 80 wt%, stabilized in toluene), 2,2-dimethoxy-2-

phenylacetophenone (DMPA, Acros, 99%), camphorquinone (CQ, Aldrich, 97%), Novozyme® 435 (Aldrich) and thionyl chloride (Acros, 99.7%) were used as received. Solvents were purchased from Acros (HPLC grade) and used without purification, unless otherwise noted. Benzyl azide ($BnN_3$) and α-methoxy-ω-azido-poly(ethylene glycol) with a molecular weight of 550 g/mol ($PEG_{550}N_3$) were synthesized according to the literature [1-2]. Copper(I) bromide (Aldrich, 98%) was purified by stirring with acetic acid, then by filtering and washing with ethanol and diethyl ether, and finally by drying in a vacuum oven at 70 °C. Tetrahydrofuran (THF, Aldrich, 99.9%) and *N,N,N',N''*-pentamethylethylenetriamine (PMDETA, Acros, 99+%) were distilled before use.

## *Measurements*

$^{1}H$ NMR and $^{13}C$ NMR spectra were recorded at 25 °C with a Bruker Avance 300 or a Bruker DRX500 spectrometer. Infrared (IR) spectra were obtained with a Perkin Elmer FTIR SPECTRUM 1000 spectrometer in combination with a PIKE Miracle ATR unit. Gas chromatography (GC) coupled with mass spectrometry (MS) analysis was performed using a Hewlett-Packard GCD-Plus GC/MS (G1800B) instrument with an electron ionization (EI) source. A DB-5MS column from J&W Scientific was used with helium as a carrier gas and a flow rate of 0.7 mL/min. The column was initially set at 70 °C for 3 min, followed by a heating rate of 17.5 °C/min until 315 °C and kept for 3 min at this temperature. The inlet temperature was kept at 250 °C. For electrospray ionization mass spectrometry (ESI-MS), a single-quad MS detector (G1946C) was used. Gel permeation chromatography (SEC) was performed on a Waters instrument with a Waters 2414 Refractive Index Detector, equipped with 3 PSS serial columns (GRAM Analytical 30 Å and 1,000 Å, 10 μm particle size) at 35 °C. Poly(methylmethacrylate) standards were used for calibration and DMA containing LiBr (0.42 $g.L^{-1}$) was used as an eluent at a flow rate of 1 mL/min. Molecular weight and polydispersity index were determined using the Empower software. Thermogravimetric analysis (TGA) was performed with a Mettler Toledo TGA/SDTA851e instrument under air atmosphere at a heating rate of 10 °C/min from 25 to 800 °C. Differential scanning calorimetry (DSC) was performed using a Perkin-Elmer DSC 7 analyzer with TAC 7/DX thermal analysis controller and Pyris software. The DSC scans were recorded under a nitrogen atmosphere in the temperature range from 50 to 300 °C at a heating rate of 20 °C/min. The melting temperature was determined as the temperature of the main peak in the curve obtained from the second heating scan. Viscosimetry measurements were performed in a PM Tamson Instruments TV 4000 viscosimeter bath at 25 °C in combination with a Schott Geräte AVS 300 equipment and a P22 printer. The Ubbelohde had a diameter of 0.8 mm and a K value equal to 0.03 $mm^2/s^2$.

## *Synthesis of 2-methyl-2-propargylmalonic acid dichloride*

As a starting compound for 2-methyl-2-propargylmalonic acid dichloride (MPMAD), diethyl 2-methyl-2-propargylmalonate (DEMPM) was synthesized according to literature [7]. Next, modified literature procedures were used for the synthesis of the diacid dichloride [28-29].

DEMPM (10.00 g, 0.0471 mol) was first hydrolyzed to 2-methyl-2-propargylmalonic acid by dissolving DEMPM in 28 mL of methanol after which NaOH (11.20 g, 0.280 mol) in water (56 mL) was added. This reaction mixture was refluxed for 5 hours at 75 °C. Subsequently, methanol was evaporated under vacuum and concentrated HCl was added to the watery solution until pH = 1. At this point, the yellowish color disappeared. The mixture was extracted three times with diethyl ether after which the combined ether phases were dried over $MgSO_4$. After removal of diethyl ether under vacuum, 2-methyl-2-propargylmalonic acid was obtained as a white powder. Yield: 95 %. $^1$H NMR (300 MHz, DMSO-$d_6$, ppm): δ = 1,35 (s, 3H, C$H_3$), δ = 2,62 (d, 2H, C$H_2$-C≡CH), δ = 2,86 (t, 1H, $CH_2$-C≡C*H*), δ = 12,86 (s, 2H, O*H*). FTIR (ATR, cm$^{-1}$): ν (C=O stretch) = 1716, ν (OH stretch) = 2400-3300, ν (C≡C-H stretch) = 3302.

To convert the dicarboxylic acid into the diacid dichloride, $SOCl_2$ (12.88 mL, 0.1775 mol) and three droplets of DMF were added to 2-methyl-2-propargylmalonic acid (13.2 g, 0.0845 mol). This reaction mixture was refluxed for 24 hours under inert atmosphere and turned dark brown. Subsequently, the diacid dichloride was distilled under vacuum (0.08 mbar) in a double ice-cooled set-up. The two fractions, respectively evaporating at 62-76 °C and 80-85 °C, both contained MPMAD. $^1$H NMR analysis revealed some small impurities in the first fraction, but the second fraction was pure. Yield: 57 %. $^1$H NMR (300 MHz, $CDCl_3$, ppm): δ = 1,78 (s, 3H, C$H_3$), δ = 2,18 (t, 1H, $CH_2$-C≡C*H*), δ = 2,98 (d, 2H, C$H_2$-C≡CH). $^{13}$C NMR (300 MHz, $CDCl_3$, ppm): δ = 20,29 (*C*$H_3$), δ = 26,39 (C-*C*$H_2$-C≡CH), δ = 71,96 (C-$CH_2$-C≡*C*H), δ = 73,96 (*C*-$CH_2$-C≡CH), δ = 75,92 (C-$CH_2$-*C*≡CH), δ = 169,93 (*C*=O). FTIR (ATR, cm$^{-1}$): ν (C=O stretch) = 1776, ν (C≡C-H stretch) = 3302.

## *Synthesis of alkyne-functionalized polyamides*

### Enzyme-catalyzed polymerizations

A representative example of the enzyme-catalyzed polycondensation is mentioned below. Diethylenetriamine (3.095 g, 0.03 mol) was added to DEMM (5.226 g, 0.03 mol) and 0.2 g of Novozyme® 435 catalyst [30]. This reaction mixture was stirred for 24 hours at 80 °C under a nitrogen flow. Thereafter, 15 mL of methanol was added to the solidified mixture and the catalyst was filtered. After removal of the solvent, a yellow-brownish sticky oligomer was obtained.

### Solution and interfacial polymerization

For the solution and interfacial polymerization, the diamine was solubilized in water (0.17 M), together with 2.06 eq. of base (KOH or $Na_2CO_3$). The diacid dichlorides were dissolved in THF or dichloromethane (0.17 M). Both solutions were combined and the formed polymer was either filtered (stirred process) or grasped with tweezers and pulled as a rope (non-stirred process). Subsequently, the polymer was thoroughly washed with water and acetone in order to remove remaining unreacted monomer, base or solvent. The polyamides (PAs) were dried under vacuum at elevated temperatures (40 – 70 °C) prior to further analysis. The $^1$H NMR, $^{13}$C NMR and FTIR data of some samples are provided in the supporting information.

### *CuAAC reaction between alkyne-containing polyamides and azides*

In a round-bottomed flask, the alkyne-functionalized PA (1 equivalent of alkyne functions) was charged with a minimal amount of solvent to dissolve the polymer, an azide (2 equivalents), and the copper catalyst CuBr/PMDETA (0.3 equivalent each according to the alkyne content). The reaction was stirred overnight under nitrogen atmosphere at 40 °C. The resulting modified PA was precipitated in a cooled solvent that is miscible with the reaction solvent. The PA was dried under vacuum overnight before further characterization.

### *Thiol-yne reaction between alkyne-containing polyamides and thiols*

Alkyne-containing PA (IF15*R*, 0.100 g, 7.710 x $10^{-5}$ mol, $M_v$ = 2,500 g/mol) in combination with 5 equivalents of thiol (benzyl mercaptan, 0.048 g, 3.855 x $10^{-4}$ mol) and 0.2 equivalents of photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPA, 4 mg, 1.542 x $10^{-5}$ mol) was placed in a schlenk tube and dissolved in 3 mL of formic acid. The tube was irradiated in an oven equipped with a 365 nm UV lamp in close contact with the flask. The resulting modified PA was precipitated in cold diethyl ether and thoroughly washed with diethyl ether. The modified PA was dried under vacuum overnight prior to $^{1}$H NMR analysis.

## Results and discussion

### *Synthesis of 2-methyl-2-propargylmalonic acid dichloride*

For the synthesis of linear polyamides (PAs) by step-growth polymerization, several types of monomers can be used. PAs can be prepared by the polycondensation of diamines and dicarboxylic acids or by the combination of diamines and derivatives of these acids (e.g. diesters, diacid dichlorides). For safety reasons, the alkyne and thus not the azide functionality was chosen to be incorporated into the monomers.

In **Fig. 1**, the considered synthetic routes for aliphatic alkyne-containing PAs are shown, starting from the readily available diethyl methylmalonate (DEMM). Diethyl 2-methyl-2-propargylmalonate or DEMPM can be easily synthesized via alkylation with propargyl bromide [7]. Starting from this alkyne-containing diester, several other monomers could theoretically be obtained: the alkyne-containing diamide (2-methyl-2-propargylmalonamide, **1**), diamine (2-methyl-2-propargyl-1,3-propanediamine, **2**), dicarboxylic acid (2-methyl-2-propargylmalonic acid, **3**) and diacid dichloride (2-methyl-2-propargylmalonic acid dichloride, **4**). In combination with an appropriate second monomer, aliphatic polyamides are expected to be obtained.

[Fig. 1]

The alkyne-containing diamine **2** is of great interest since it could be combined with any dicarboxylic acid to obtain alkyne-containing polyamides via a melt polycondensation reaction, typically at temperatures ranging from 180 to 300 °C. For the synthesis of this diamine, DEMPM was first converted into the alkyne-containing diamide (2-methyl-2-propargylmalonamide, **1**) with a yield of 52 %. In the following step, this diamide had to be reduced to the diamine by means of $LiAlH_4$. Unfortunately, this reduction failed despite multiple attempts (see supporting information).

A second possibility is the use of 2-methyl-2-propargylmalonic acid (**3**) that can be obtained via the hydrolysis of DEMPM. In theory, both the diester DEMPM and the dicarboxylic acid can be used in a melt polycondensation reaction in combination with a diamine. However, in practice, it is known that malonic acid and its derivatives are not stable at high temperatures and undergo decarboxylation [31-32]. This occurs via a six-membered cyclic transition state in which the acid proton is transferred to the oxygen of the other carbonyl group. The enol produced by decarboxylation undergoes rapid proton tautomerization to yield a carboxylic acid.

The dicarboxylic acid can also be further converted into the diacid dichloride **4**, for which reaction conditions were taken from literature [29]. Originally, the dicarboxylic acid was refluxed in an excess of thionyl chloride ($SOCl_2$, 3.44 eq.), catalyzed by a droplet of DMF. Finally, the crude reaction mixture is distilled under vacuum in order to obtain **4** as a pure colorless oil. Initially, low yields (~ 20 %) were obtained after distillation under vacuum, thus the reaction conditions were adapted to improve the yields. $^1$H NMR analysis of the cold trap revealed that not only the excess of thionyl chloride was distilled off, but also a part of the formed diacid dichloride. This was circumvented by using a smaller excess of thionyl chloride (2.1 eq.), in combination with longer reaction times and additional cooling of the distillation set-up with ice-cooled water. These conditions resulted in pure 2-methyl-2-propargylmalonic acid dichloride (MPMAD) with a yield of 57 %. The GC-MS spectrum showed only one signal at a retention time of 6.78 minutes and MS analysis of this signal proved the pure synthesis of **4** by the presence of fragments at m/z ratios of 157 Da (loss of Cl) and 129 Da (loss of C=O-Cl). The alkyne-containing monomer is stable up to a year at least when kept under cool and dark conditions.

## *Alkyne-containing aliphatic polyamides prepared by SGP*

### Enzyme-catalyzed polymerizations

One of the possibilities to make polyamides is the polycondensation reaction between diesters and diamines (**Fig. 1**). When no catalyst is added, this reaction requires high temperatures (> 270 °C), which could be too high for the alkyne and lead to crosslinking [1]. On the other hand, the use of lipases for the synthesis of small molecules is well known [33-36]. Lipases have also been successfully applied for polyesterification reactions [37-40] and for polymer modification reactions [41-43]. However, there is little known about lipases that can catalyze the reaction between diamines and diesters to form high-molecular-weight PAs. Gu *et al.* explored the use of enzymes as catalysts for polyamide synthesis [30, 44]. They found lipases,

and especially Novozyme® 435 lipase, to be good catalysts in this polycondensation reaction. Novozyme® 435 is a lipase from *Candida Antarctica* yeast cells immobilized on a macroporous acrylic resin and is also often called Candida Antarctica Lipase B or CALB. Recently, this Novozyme® 435 has attracted attention for biodiesel production where the lipase is used for enzymatic transesterification [45-48]. The reaction temperatures used with this catalyst are remarkably lower than in the conventional melt synthesis (70 – 100 °C), but still high enough for the formed EtOH to evaporate.

In this research, both DEMM and DEMPM were mixed with diethylenetriamine (DETA) in different ratios (**Table 1** and **Fig. 2**). The Novozyme® 435 catalyst was dried under vacuum before it was added to the mixture of diester and diamine. According to the conditions of Gu *et al*., 2.4 weight% of lipase was added and the reactions were run for 24 hours at 80 °C under a nitrogen flow (Entries 1-3, **Table 1**). The mixture solidified at the end of the reaction. The reaction was stopped by adding MeOH to solubilize the PA after which the catalyst was filtered. After evaporation under vacuum, a yellow-brown sticky oil was obtained.

[Table 1]

[Fig. 2]

During these polycondensation reactions, only linear PAs are formed because the secondary amine in DETA is not reactive under these mild reaction conditions [30]. All formed PAs were analyzed with FTIR spectroscopy, $^{1}$H NMR and SEC. The IR spectra of Entries 1-3 from **Table 1** clearly show the formation of the amide bond by means of a shift of the C=O stretch signal from 1730 (ester) towards 1640 $cm^{-1}$ (amide) while $^{1}$H NMR analysis in DMSO-$d_6$ shows an amide signal at 7.80 ppm. Although FTIR and $^{1}$H NMR confirmed the polymerization by the presence of amide bonds in Entries 1-3, the analysis of these polyamides by means of SEC (DMA as solvent) revealed that all molecular weights were below the detection limit of the equipment. An ESI-MS (electrospray ionization mass spectrometry) analysis of Entry 1 showed that at best the number of repeating units equals 3, thus only small oligomers were obtained under these conditions.

In an effort to obtain higher molecular weights, recent reaction conditions were followed from literature [49]. Jiang prepared poly(amine-*co*-ester)s from *N*-alkyldiethanolamine and several diethyl esters in two steps. The first step consists of an oligomerization under a nitrogen flow for 24 hours, followed by a polymerization step under vacuum during 3 days. Moreover, 10 wt% Novozyme® 435 catalyst was used instead of 2.4 wt%. At 80 °C, polymers were obtained with a weight average molar mass between 29,500 and 44,500 g/mol [49]. In Entry 4 of **Table 1**, DEMM, DEMPM and DETA were added in the same ratios as in Entry 2 and were reacted according to these conditions. The reaction was finished by adding MeOH, followed by filtration of the catalyst and removal of the solvent by evaporation. Eventually, a sticky brown oil was obtained. $^{1}$H NMR analysis showed the formation of amide bonds by the presence of the signal at 7.80 ppm, but SEC analysis once more revealed low molar masses.

In a last experiment (Entry 5, **Table 1**), the polycondensation between DEMM and DETA was performed without the addition of any Novozyme® 435 catalyst. Remarkably, after analysis with FTIR, $^{1}$H NMR and DMA-SEC, the same results were obtained as when the catalyst was added. Although the catalyst was new and dried before use, it did not reveal its activity in these reactions. Therefore, another strategy was considered for the synthesis of alkyne-containing PAs as described below.

**Solution and interfacial polymerization**

PAs can also be prepared in solution by the Schotten-Baumann reaction at low temperatures. For this purpose, two rapidly reacting monomers, e.g. a diamine and dicarboxylic acid dichloride, are mixed together while stirring in an inert solvent. The released hydrogen chloride is trapped with an acid acceptor, such as tertiary amines or dispersed potassium hydroxide. Although the temperatures used for this type of polycondensation are low (0 - 40 °C), the reaction usually goes to completion after a few minutes. Moreover, at these low temperatures practically no side reactions occur. The disadvantages include the relatively large amounts of solvent that must be handled and large amounts of salts that are formed as by-products [3]. The Schotten-Baumann reaction can also be performed as an interfacial polycondensation. The interfacial technique has the advantage of short reaction times at low temperatures using a simple set-up as well. In this type of reaction, the two components are separately dissolved in two immiscible solvents and the polymerization takes place at the interface of the two liquids. The instantaneously formed thin PA film prevents further diffusion of the two reactants, allowing the polycondensation to continue only when this film is carefully pulled away from the interface as a rope. This non-stirred interfacial polymerization is often called the 'Nylon Rope Trick' [3]. On the other hand, a stirred interfacial method can also be used. For this purpose, the solution of diacid dichloride is dispersed in the aqueous solution of diamine by vigorous stirring. The polycondensation then takes place at the surface of the droplets. Water is especially suitable as solvent for the diamine component, while aliphatic chlorinated hydrocarbons are typically selected for the diacid dichlorides [3].

Several aliphatic PAs with pendant alkyne groups were successfully prepared using the methods mentioned above. For this, 2-methyl-2-propargylmalonic acid dichloride (MPMAD) was combined with readily available monomers (**Table 2**). As a model reaction, the interfacial polymerization of nylon 6,6 was performed (Entry IF1, **Table 2**), starting from 1,6-hexanediamine (HDA) and adipoyl chloride (AC). Potassium hydroxide (KOH) was added as a base in order to neutralize the released HCl. HDA and KOH were dissolved in water, AC in xylene and the two-phase system was magnetically stirred at room temperature.

[Table 2]

Immediately, white precipitates are formed and after 15 minutes, these precipitates were filtered, washed with hot water and dried under vacuum. IF1 was analyzed with FTIR, $^{1}$H NMR, $^{13}$C NMR and Ostwald viscosimetry, showing that indeed nylon 6,6 was obtained with a molecular weight (viscosity average molecular weight, $M_v$) of around 12,000 g/mol. In FTIR, the three characteristic signals according to the amide bond were clearly visible: NH stretch at 3301 cm$^{-1}$, NH bend at 1535 cm$^{-1}$ and C=O stretch at 1633 cm$^{-1}$ [50].

The same polymerization method and work-up was applied for Entry IF2 in **Table 2**, which rendered a colorless and sticky polyamide with 100% alkyne functions. This percentage indicates the amount of MPMAD compared to the added diacid dichloride starting compounds. The structure of IF2 was confirmed by $^{1}$H NMR and $^{13}$C NMR. Since this polyamide was soluble in DMA, the peak molecular weight ($M_p$) was determined using SEC with this solvent. Despite the overnight storage under vacuum at 70 °C, some of the relatively high boiling xylene (139 °C) was still present. Since solvent stripping would be necessary to remove all traces, THF and dichloromethane were used as alternative low boiling solvents (resp. 66 and 40 °C) to dissolve the diacid dichloride (Entry S1 and IF3, **Table 2**). Since THF and water are miscible, Entry S1 is considered as a solution polymerization. This polycondensation reaction rendered a hard to filter PA with a low molecular weight ($M_v$ = 2,000 g/mol). As this was considered to be too low with regard to material properties, the solution polymerization was not further used in this research. On the other hand, the interfacial polymerization (IF3) allowed for easy filtration of a solvent free PA with a much higher molecular weight, which lead to the conclusion that $CH_2Cl_2$ is a suitable solvent. The synthesis of nylon 6,10 was also tested in this solvent (Entry IF4, **Table 2**), using mechanical stirring to avoid obstruction of the stirring process, confirming the previous good results.

Next, the alkyne-containing diacid dichloride MPMAD was used in combination with 1,6-hexanediamine (Entry IF5, **Table 2**). Similar to Entry IF2, no other diacid dichloride is added. After filtration, IF5 was washed with hot water and dried under vacuum prior to further analysis. FTIR, $^{1}$H and $^{13}$C NMR confirmed the structure of the alkyne-containing PA and again $M_p$ was determined using DMA-SEC. Entries IF6, IF7 and IF8 (**Table 2**) were obtained by interfacial copolymerization in which two types of diacid dichloride have been used: the alkyne-containing MPMAD in combination with either AC or SC. Three copolyamides containing 50% of alkyne side groups were formed using, in all cases, 0.5 equivalent of each diacid dichloride in combination with 1 equivalent of diamine. A general reaction scheme for the synthesis is shown in **Fig. 3**.

[Fig. 3]

The final composition of the copolyamides was determined using $^{1}$H NMR in DMSO-$d_6$ or TFA-$d_1$. Therefore, the integration of the signal at 2.01 ppm (CO-C$H_2$, from AC or SC) was compared against the signal in the region 2.99 - 3.07 ppm (NH-C$H_2$, from HDA). The results in **Table 2** reveal that in the stirred interfacial polymerization (Entries IF6, IF7 and IF8), the amount of incorporated MPMAD is 5 to 9% lower than the theoretically expected amount.

Most probably, this can be explained by the sterically more hindered carbonyl group in MPMAD, which could be impeding the nucleophilic attack of the diamine compared to the unhindered carbonyl groups of SC and AC.

Depending on the solubility of the copolyamides, the molecular weight was determined either by DMA-SEC or by viscosimetry in *m*-cresol as solvent. The Mark-Houwink constants for nylon 6,6 ($K = 240 \times 10^{-5}$ mL/100 g and $a = 0.61$) and nylon 6,10 ($K = 13{,}5 \times 10^{-5}$ mL/100 g and $a = 0.96$) in *m*-cresol at 25 °C [51-53] were also used to approximate the viscosity average molecular weight $M_v$ of the copolymers. For IF7, the molecular weight was determined by both methods and a relatively large difference was noticed (**Table 2**). For the other copolymers IF6 and IF8, molecular weights in the same range were obtained. Despite the successful incorporation of the MPMAD monomer, the molecular weight of these copolymers is still in the oligomeric range. Therefore, the next series of experiments consisted in the use of the non-stirred interfacial polymerization, further referred to as the Nylon Rope Trick (NRT).

Four different polyamides were synthesized via the NRT using HDA and SC, with increasing amounts of the MPMAD monomer (**Table 2**). The continuously withdrawn polyamide rope was washed with water and acetone and dried under vacuum prior to further analysis. It has to be noted that in the case of IF11 (40 mol% of alkyne groups), the polyamide rope was not strong enough to be drawn from the reaction mixture. As a result, the major part of the polymer remained at the interface of the reaction mixture as large white flocks. This residual fraction was analyzed as well, and is mentioned in further discussion as IF11*R*.

When the NRT is used as polymerization technique, the polymer composition calculated via $^1$H NMR was in better agreement with the feed values, although the solution is not stirred. Only Entry IF11*R* had an obvious lower amount of incorporated MPMAD. This can be due to the fact that diffusion of the more bulky MPMAD monomer is not supported because the polyamide film is not continuously withdrawn and the process is non-stirred.

Unfortunately, the molecular weights were comparable with the molecular weights of the PAs obtained by the stirred interfacial process and thus remained low. In literature, it is mentioned that the molecular weight for nylon 6,10 obtained by interfacial polymerization is situated between 11,000 and 20,000 g/mol [54]. Therefore, higher molecular weights are expected to be obtained by both the stirred interfacial technique and the NRT after optimization. Nevertheless, both homo- and copolyamides with a desired amount of pendant alkyne groups were synthesized via interfacial polymerization and this without any additional protection or deprotection steps.

The obtained functional polyamides were analyzed with differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) to determine the melting temperature $T_m$ and the degradation temperature at 10% weight loss $T_{d,90}$ respectively. The results of both analyses are shown in **Table 3**.

[Table 3]

The melting temperatures of Entries IF1 (nylon 6,6) and IF4 (nylon 6,10) in **Table 3** correspond well to the theoretical values mentioned in literature (respectively 255 °C and 215 °C) [51]. The other values in **Table 3** show some typical trends for polyamides, *e.g.* that alkyl side chains on carbon or nitrogen lower the melting point [3]. From the Entries IF9, IF10 and IF11*R* it is clear that $T_m$ decreases with increasing amount of MPMAD. This phenomenon is related to the fact that the alkyne side groups hamper the formation of the intermolecular hydrogen bonds between the polyamide functional groups in the backbone. Apart from that, the melting point also lowers with increasing distance between the amide groups because of decreasing hydrogen bond interactions [3]. This is clear from the $T_m$ values of IF1 (nylon 6,6) and IF4 (nylon 6,10). The TGA results reveal that $T_{d,90}$ at 10% weight loss shows a similar trend. From these thermal results it can be concluded that the incorporation of alkyne groups is lowering $T_m$ and $T_{d,90}$.

In addition, the solubility of the polyamides in **Table 3** was tested and it was shown that all polymers were soluble in formic acid, *m*-cresol and to a limited extent in TFA. This is due to the ability of these solvents to break the intermolecular hydrogen bonds [3, 55]. IF5, IF7 and IF8 were also soluble in DMA and DMSO. Other characteristic polyamide solvents such as DMF and NMP only dissolved IF5 and IF8. These polyamides contain a higher amount of alkyne groups hindering hydrogen bond formation, thereby improving their solubility. For further use, the merits of either higher solubility or higher melting and degradation temperature have to be balanced against each other.

## *Functionalization of aliphatic polyamides via CuAAC chemistry*

For the functionalization of the polymers, the Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction between azides and alkynes was used. Therefore, benzyl azide ($BnN_3$) as a model compound and α-methoxy-ω-azido-PEG with a molecular weight of 550 g/mol ($PEG_{550}N_3$) were reacted with the alkyne groups and this in a two-fold excess according to the alkynes to decrease the reaction times. CuBr/PMDETA was applied as catalyst system (0.3 eq. according to the alkyne groups) and the PAs that are insoluble in THF or DMSO were solubilized in *m*-cresol at room temperature (**Table 4**). Especially the coupling with $PEG_{550}N_3$ is expected to modify the solution properties of the polyamides. All the reactions were performed at 40 °C and after overnight reaction, the modified PA was precipitated in a solvent that is miscible with the reaction solvent and afterwards filtered and dried prior to further analysis. As an example, the CuAAC reaction with $PEG_{550}N_3$ is shown in **Fig. 3**.

[Table 4]

$^1$H NMR integrations were used to check the conversion of the alkynes due to the CuAAC reaction. For $BnN_3$ and $PEG_{550}N_3$, respectively the integration of the methylene Ph-C$H_2$ and the O-C$H_2$C$H_2$ signal are used for the calculations. The conversions of the CuAAC reactions are listed in **Table 4**. After clicking, a new triazole signal is expected in the region 7.0 – 8.0

ppm. In illustration of this, the $^{1}$H NMR spectra of IF5 and IF5-C are compared in **Fig. 4**. The alkyne signals *f* and *g* in the bottom spectrum both shift, respectively from 2.66 ppm to 3.11 ppm and from 2.74 ppm to 7.60 ppm (triazole ring, see arrows). Moreover, the original alkyne proton signals have disappeared in the upper spectrum, proving the nearly full conversion of the alkyne groups into triazole rings mentioned in **Table 4**. The small signals in the upper spectrum at 2.26 and 2.72 ppm are satellite signals from DMSO while the signal at 4.44 ppm is coming from traces of remaining $BnN_3$ as an excess was added according to the alkyne groups.

[Fig. 4]

From **Table 4** it is clear that only for the alkyne-containing homopolyamides, conversions higher than 90% could be obtained. When copolyamides are used, much lower conversions were obtained and no clear trend could be observed. Functionalization with the more bulky $PEG_{550}N_3$ seemed to be slightly more limited than with $BnN_3$. Further optimization with other copper salts or higher excess of the azides could be envisaged. Despite these low conversions, the functionalization could be sufficient for specific applications (*e.g.* PAs with antibacterial properties) and it is noteworthy that it is the first time that this kind of functionalization strategy has been applied on polyamides.

Another aspect that was not addressed and might be critical for certain applications, is the potential contamination of the polyamide with residual Cu(I)-catalyst. As suggested by Ornelas and coworkers, both the polyamide and the triazole ring could form complexes with the copper [19]. In their work, a greenish color indicated contamination with copper and ICP-MS analysis revealed a copper content of 0.50 % in their dendrimers. This could be lowered to 0.004 % by using copper wire, sodium ascorbate and sulfonated bathophenanthroline as a catalyst system, but could never be completely removed. For the polyamides investigated in this research, a green color was also noticed in IF5-C, IF6-C and IF7-C, clearly showing that part of the Cu(I)-catalyst was still present. IF2-C had a blue color due to oxidation of Cu(I) to Cu(II) by the precipitation solvent ($H_2O$). IF8-C, IF9-C and IF10-C appeared mostly white after a thorough washing procedure, indicating that purification is in principle possible but laborious.

## *Functionalization of aliphatic polyamides via thiol-yne chemistry*

A metal- and azide-free functionalization strategy that recently has gained a lot of interest is the light-mediated radical thiol-yne coupling reaction [56-58]. Since two thiols are coupled to one alkyne group, it appears to be perfectly suited to create multifunctional polymer structures [59]. All the coupling reactions have been performed with IF11*R*, a copolyamide containing 32% alkyne functions ($M_v$ = 2,500 g/mol). The thiol that has been used is the model compound benzyl mercaptan, each time in excess (5 equivalents) according to the alkyne units. 2,2-Dimethoxy-2-phenyl-acetophenone (DMPA) and camphorquinone (CQ) have been

applied as an ultraviolet and visible-light photoinitiator respectively. CQ is known to be a good initiator in combination with amines and is used a lot for the curing of dental composites [60]. The thiol-yne reactions are listed in **Table 5**. As an example, the reaction scheme of IF11*R*-T5 is shown in **Fig. 5**.

[Table 5]

[Fig. 5]

Entry IF11*R*-T1 and IF11*R*-T2 (**Table 5**) were performed with 0.2 eq. of photoinitiator DMPA and irradiated with a 365 nm UV lamp while stirring. After reaction, the polyamide was precipitated in cold diethyl ether and dried under vacuum. Subsequently, the PAs were analyzed by $^{1}$H NMR in order to evaluate the conversion. The lower conversion in *m*-cresol in comparison to formic acid can be explained by the fact that this solvent competes with the UV absorption of the initiator, thus causing fewer radicals to be generated. When the visible-light photoinitiator CQ (peak absorption at 468 nm [60]) was added in a concentration of 2.5 mg/mL solvent and irradiated at 450 nm, the conversion increased, up to 73% after 90 minutes of irradiation (Entry IF11*R*-T5, **Table 5**). CQ, having a lower molar extinction coefficient compared to DMPA at their individual peak absorption, causes much better depth cure of the sample.

As an example, the comparison of the $^{1}$H NMR spectra of IF11*R* before and after thiol-yne coupling is displayed in **Fig. 6**. Since the methylene signal *m* at 3.72 ppm appears as a singlet instead of a doublet in the free thiol, it can be stated that all present signals are coming from coupled benzyl mercaptan. The aromatic signals *n* between 7.10 and 7.45 ppm in the upper spectrum were used to calculate the conversions mentioned in **Table 5**. The original alkyne signals *f* and *g* in the lower spectrum have almost completely disappeared. The remaining signals originate from methylene protons adjacent to end groups or to functional groups in the vicinity of the polymer chain ends [61]. These signals are clearly visible due to the low molecular weight of the PAs.

[Fig. 6]

DSC and TGA were performed on these thiol-yne modified polyamides in order to see if the modifications affect the thermal properties. It was noted that in all cases the melting temperature decreased by more than 10 °C compared to the alkyne-containing polyamide IF11*R* (**Table 6**). This can again be explained by hampering the formation of hydrogen bonds, which is expected to be larger for the benzyl groups than for the non-modified PA. A steady decrease in degradation temperature at 10% weight loss with increasing conversion of the alkyne groups can be observed, most probably as a result of scission of the thio-ether bonds.

[Table 6]

Although a quantitative functionalization degree could not be obtained, it is the first time that this thiol-yne functionalization strategy has ever been applied on polyamides. Even partial conversions (up to 70 %) can lead to modified properties of the PAs, as can be concluded from the results mentioned above.

# Conclusion

In this report, alkyne-containing aliphatic PAs have been obtained via step-growth polymerization. Therefore, an appropriate building block carrying an alkyne group was synthesized. As the synthesis of an alkyne-containing diamine repeatedly failed, a diacid dichloride was synthesized instead. This diacid dichloride was used in homo- and copolymerizations. It was found that interfacial polymerization gave PAs with higher molecular weights than solution polymerization and that via the Nylon Rope Trick the incorporated amount of alkyne-containing monomer agreed better with the feedstock than in case of the stirred interfacial polymerization. Although the obtained molecular weights were not elevated (2,500 – 6,100 g/mol), both homo- and copolymers with pendant alkyne groups were successfully synthesized and this without any additional protection or deprotection steps. Functionalization of the alkyne-containing polyamides was performed both by CuAAC reactions and by thiol-yne coupling. To our knowledge, it is the first time that these strategies have been applied on nylons. It was found that, when using the CuAAC chemistry, only the alkyne-containing homopolyamides rendered good conversions (over 90%). When copolyamides were used, much lower conversions were obtained. In the examples where thiol-yne coupling was applied, conversions up to 73% were reached. CQ as photoinitiator resulted in higher conversions compared to DMPA. Changes in thermal properties were clearly noted after modification with the thiol-yne chemistry. These results open routes for the design of polyamides with novel physical properties. Further research will be required to optimize the reaction conditions and to introduce other functionalities in the direction of material applications.

# Acknowledgements

The authors thank the IWT (The Institute for the Promotion of Innovation through Science and Technology in Flanders, Belgium) for a PhD scholarship. The Belgian Program on Interuniversity Attraction Poles initiated by the Belgian State, Prime Minister’s office (Program P6/27) and the P2M ESF-program are acknowledged for financial support.

# References

[1] Rogers ME, Long TE. Synthetic methods in step-growth polymers. New York: John Wiley & Sons; 2003.

[2] Odian G. Principles of Polymerization. Fourth Edition ed. Hoboken, New Jersey: John Wiley & Sons, Inc.; 2004.

[3] Braun D, Cherdron H, Rehahn M, Ritter H, Voit B. Polymer Synthesis: Theory and Practice: Fundamentals, Methods, Experiments. Fourth Edition ed. Berlin Heidelberg: Springer-Verlag; 2005.

[4] Williams CK. Synthesis of functionalized biodegradable polyesters. Chem Soc Rev. 2007;36:1573-1580.

[5] Kolb HC, Finn MG, Sharpless KB. Click chemistry: Diverse chemical function from a few good reactions. Angew Chem-Int Edit. 2001;40(11):2004-2021.

[6] Hoyle CE, Lowe AB, Bowman CN. Thiol-click chemistry: a multifaceted toolbox for small molecule and polymer synthesis. Chem Soc Rev. 2010;39(4):1355-1387.

[7] Billiet L, Fournier D, Du Prez F. Combining "Click" chemistry and step-growth polymerization for the generation of highly functionalized polyesters. J Polym Sci Pol Chem. 2008;46(19):6552-6564.

[8] Billiet L, Fournier D, Du Prez F. Step-growth polymerization and 'click' chemistry: The oldest polymers rejuvenated. Polymer. 2009;50(16):3877-3886.

[9] Riva R, Lussis P, Lenoir S, Jérôme C, Jérôme R, Lecomte P. Contribution of "click chemistry" to the synthesis of antimicrobial aliphatic copolyester. Polymer. 2008;49(8):2023-2028.

[10] Riva R, Schmeits P, Stoffelbach F, Jérôme C, Jérôme R, Lecomte P. Combination of ring-opening polymerization and "click" chemistry towards functionalization of aliphatic polyesters. Chem Commun. 2005(42):5334-5336.

[11] Riva R, Schmeits S, Jérôme C, Jérôme R, Lecomte P. Combination of ring-opening polymerization and "click chemistry": Toward functionalization and grafting of poly(epsilon-caprolactone). Macromolecules. 2007;40(4):796-803.

[12] Parrish B, Breitenkamp RB, Emrick T. PEG- and peptide-grafted aliphatic polyesters by click chemistry. J Am Chem Soc. 2005;127(20):7404-7410.

[13] Fournier D, Billiet L, Du Prez F. Click chemistry and step-growth polymerization: the ideal combination for the rejuvination of industrial polymers. New Smart Materials Via Metal Mediated Macromolecular Engineering. 2009:145-164.

[14] Fournier D, De Geest BG, Du Prez FE. On-demand click functionalization of polyurethane films and foams. Polymer. 2009;50(23):5362-5367.

[15] Fournier D, Du Prez F. "Click" chemistry as a promising tool for side-chain functionalization of polyurethanes. Macromolecules. 2008;41(13):4622-4630.

[16] Goyal P, Yoon K, Weck M. Multifunctionalization of dendrimers through orthogonal transformations. Chem Eur J. 2007;13(31):8801-8810.

[17] Yoon K, Goyal P, Weck M. Monofunctionalization of dendrimers with use of microwave-assisted 1,3-dipolar cycloadditions. Org Lett. 2007;9(11):2051-2054.

[18] Lee JW, Kim HJ, Han SC, Kim JH, Jin SH. Designing poly(amido amine) dendrimers containing core diversities by click chemistry of the propargyl focal point poly(amido amine) dendrons. J Polym Sci Pol Chem. 2008;46(3):1083-1097.

[19] Ornelas C, Broichhagen J, Weck M. Strain-Promoted Alkyne Azide Cycloaddition for the Functionalization of Poly(amide)-Based Dendrons and Dendrimers. J Am Chem Soc. 2010;132(11):3923-3931.

[20] Ornelas C, Lodescar R, Durandin A, Canary JW, Pennell R, Liebes LF, et al. Combining Aminocyanine Dyes with Polyamide Dendrons: A Promising Strategy for Imaging in the Near-Infrared Region. Chem-Eur J. 2011;17(13):3619-3629.

[21] Ornelas C, Pennell R, Liebes LF, Weck M. Construction of a Well-Defined Multifunctional Dendrimer for Theranostics. Org Lett. 2011;13(5):976-979.

[22] Rijkers DTS, van Esse GW, Merkx R, Brouwer AJ, Jacobs HJF, Pieters RJ, et al. Efficient microwave-assisted synthesis of multivalent dendrimeric peptides using cycloaddition reaction (click) chemistry. Chem Commun. 2005(36):4581-4583.

[23] Holub JM, Jang HJ, Kirshenbaum K. Clickity-click: highly functionalized peptoid oligomers generated by sequential conjugation reactions on solid-phase support. Org Biomol Chem. 2006;4(8):1497-1502.

[24] Pipkorn R, Wiessler M, Waldeck W, Lorenz P, Muehlhausen U, Fleischhacker H, et al. Enhancement of the Click Chemistry for the Inverse Diels Alder Technology by Functionalization of Amide-Based Monomers. Int J Med Sci. 2011;8(5):387-396.

[25] Lo ATS, Salam NK, Hibbs DE, Rutledge PJ, Todd MH. Polyamide-Scorpion Cyclam Lexitropsins Selectively Bind AT-Rich DNA Independently of the Nature of the Coordinated Metal. PLoS One. 2011;6(5).

[26] Kreye O, Turunc O, Sehlinger A, Rackwitz J, Meier MAR. Structurally Diverse Polyamides Obtained from Monomers Derived via the Ugi Multicomponent Reaction. Chem-Eur J. 2012;18(18):5767-5776.

[27] Barner-Kowollik C, Du Prez FE, Espeel P, Hawker CJ, Junkers T, Schlaad H, et al. "Clicking" Polymers or Just Efficient Linking: What Is the Difference? Angew Chem-Int Edit. 2011;50(1):60-62.

[28] Foster P, Rausch MD, Chien JCW. Synthesis of 2-methylbenz[f]indene and (eta(5)-2-methylbenz[f]indenyl)rhodium dicarbonyl. J Organomet Chem. 1998;569(1-2):121-124.

[29] Neumeier R, Kramp W, Mäcke HR. Chelating agents for forming complexes with radioactive isotopes, metal complexes thereof and use thereof in diagnosis and therapy. In: Patent US, editor.1994.

[30] Gu QM, Maslanka WW, Cheng HN. Enzyme-Catalyzed Polyamides and Their Derivatives. In: Cheng HN, Gross RA, editors. Polymer Biocatalysis and Biomaterials II. Washington: Am. Chem. Soc.; 2008. p. 309-319.

[31] Fox MA, Whitesell JK. Organic Chemistry, Third Edition ed. Boston: Jones & Bartlett Publishers, Inc.; 2004.

[32] Clayden J, Greeves N, Warren S, Wothers P. Organic Chemistry. New York: Oxford University Press, Inc.; 2001.

[33] Karmee SK. Lipase catalyzed synthesis of ester-based surfactants from biomass derivatives. Biofuels Bioprod Biorefining. 2008;2(2):144-154.

[34] Paal TA, Forro E, Liljeblad A, Kanerva LT, Fulop F. Lipase-catalyzed kinetic and dynamic kinetic resolution of 1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid. Tetrahedron: Asymmetry. 2007;18(12):1428-1433.

[35] Paal TA, Forro E, Fulop F, Liljeblad A, Kanerva LT. Lipase-catalyzed kinetic resolution of 1,2,3,4-tetrahydroisoquinoline-1-acetic acid esters. Tetrahedron: Asymmetry. 2008;19(24):2784-2788.

[36] Ghanem A. Trends in lipase-catalyzed asymmetric access to enantiomerically pure/enriched compounds. Tetrahedron. 2007;63(8):1721-1754.

[37] Uyama H, Kobayashi S. Enzymatic synthesis of polyesters via polycondensation. Enzyme-Catalyzed Synthesis of Polymers. Berlin: Springer-Verlag Berlin; 2006. p. 133-158.

[38] Kobayashi S. Recent Developments in Lipase-Catalyzed Synthesis of Polyesters. Macromol Rapid Commun. 2009;30(4-5):237-266.

[39] Kobayashi S, Makino A. Enzymatic Polymer Synthesis: An Opportunity for Green Polymer Chemistry. Chem Rev. 2009;109(11):5288-5353.

[40] Matsumura S. Enzymatic synthesis of polyesters via ring-opening polymerization. Enzyme-Catalyzed Synthesis of Polymers. Berlin: Springer-Verlag Berlin; 2006. p. 95-132.

[41] Ponsart S, Coudane J, des Rieux A, Vert M. Mechanical properties and lipase-catalyzed biodegradation of alpha-methyl, epsilon-caprolactone/epsilon-caprolactone copolymers obtained by chemical modification of poly(epsilon-caprolactone). J Polym Environ. 2003;11(2):31-37.

[42] Mahapatro A, Johnson DM, Patel DN, Feldman MD, Ayon AA, Agrawal CM. Surface modification of functional self-assembled monolayers on 316L stainless steel via lipase catalysis. Langmuir. 2006;22(3):901-905.

[43] Gu QM. Lipase-catalyzed grafting reactions on polysaccharides. In: Gross RA, Cheng HN, editors. Biocatalysis in Polymer Science. Washington: Amer Chemical Soc; 2003. p. 243-252.

[44] Cheng HN, Gu QM, Maslanka WW. Enzyme-catalyzed polyamides and compositions and processes of preparing and using the same. In: Patent US, editor.2004.

[45] Talukder MMR, Wu JC, Fen NM, Melissa YLS. Two-step lipase catalysis for production of biodiesel. Biochem Eng J. 2010;49(2):207-212.

[46] Bisen PS, Sanodiya BS, Thakur GS, Baghel RK, Prasad G. Biodiesel production with special emphasis on lipase-catalyzed transesterification. Biotechnol Lett. 2010;32(8):1019-1030.

[47] Balat M, Balat H. Progress in biodiesel processing. Appl Energy. 2010;87(6):1815-1835.

[48] Calabro V, Ricca E, De Paola MG, Curcio S, Iorio G. Kinetics of enzymatic trans-esterification of glycerides for biodiesel production. Bioprocess Biosyst Eng. 2010;33(6):701-710.

[49] Jiang ZZ. Lipase-Catalyzed Synthesis of Poly(amine-co-esters) via Copolymerization of Diester with Amino-Substituted Diol. Biomacromolecules. 2010;11(4):1089-1093.

[50] Hummel DO. Atlas of Polymer and Plastics Analysis. New York, USA: VCH Publishers; 1991.

[51] Brandrup J, Immergut EH, Grulke EA. Polymer Handbook. Fourth Edition ed. New York: John Wiley & Sons, Inc.; 1999.

[52] Burke JJ, Orofino TA. Nylon 66 polymers .I. Molecular weight and compositional distribution. Journal of Polymer Science Part b-Polymer Physics. 1969;7(1):1-25.

[53] Morgan PW, Kwolek SL. Interfacial polycondensation .13. Viscosity-molecular weight relationship and some molecular characteristics of 6-10 polyamide. Journal of Polymer Science Part a-General Papers. 1963;1(4):1147-1162.

[54] Ultramid's Processing Properties. BASF Tech Bulletin1969.

[55] Zhang L, Zhang XY, Dai Z, Wu JJ, Zhao N, Xu J. Micro-nano hierarchically structured nylon 6,6 surfaces with unique wettability. J Colloid Interface Sci. 2010;345(1):116-119.

[56] Fairbanks BD, Scott TF, Kloxin CJ, Anseth KS, Bowman CN. Thiol-Yne Photopolymerizations: Novel Mechanism, Kinetics, and Step-Growth Formation of Highly Cross-Linked Networks. Macromolecules. 2009;42(1):211-217.

[57] Hensarling RM, Doughty VA, Chan JW, Patton DL. "Clicking" Polymer Brushes with Thiol-yne Chemistry: Indoors and Out. J Am Chem Soc. 2009;131(41):14673-14675.

[58] Lowe AB, Hoyle CE, Bowman CN. Thiol-yne click chemistry: A powerful and versatile methodology for materials synthesis. J Mater Chem. 2010;20(23):4745-4750.

[59] Hoogenboom R. Thiol-Yne Chemistry: A Powerful Tool for Creating Highly Functional Materials. Angew Chem-Int Edit. 2010;49(20):3415-3417.

[60] Mills RW, Jandt KD, Ashworth SH. Dental composite depth of cure with halogen and blue light emitting diode technology. Br Dent J. 1999;186(8):388-391.

[61] Cakir S, Kierkels R, Koning C. Polyamide 6-Polycaprolactone Multiblock Copolymers: Synthesis, Characterization, and Degradation. J Polym Sci Pol Chem. 2011;49(13):2823-2833.

# Figure Captions

**Fig. 1.** General reaction scheme for the synthesis of alkyne-containing monomers suitable for step growth polymerization towards functionalized polyamides.

**Fig. 2.** Scheme for the enzymatic synthesis of a linear PA starting from 0.2 eq. DEMPM, 0.8 eq. DEMM and 1 eq. DETA, catalyzed by 2.4 wt% Novozyme® 435 (Entry 2, **Table 1**).

**Fig. 3.** Scheme for the interfacial copolymerization (**Table 2**) from HDA (in $H_2O$), MPMAD and SC (in $CH_2Cl_2$) at room temperature under mechanical stirring, followed by modification using the CuAAC reaction.

**Fig. 4.** $^1$H NMR spectra of IF5 (bottom) and IF5-C after CuAAC reaction with $BnN_3$ (top) in DMSO-$d_6$ (300 MHz).

**Fig. 5.** The radical thiol-yne addition of benzyl mercaptan and IF11*R* in formic acid under visible light irradiation, catalyzed by camphorquinone.

**Fig. 6.** $^1$H NMR spectra of IF11*R* (bottom) and IF11*R*-T5 after thiol-yne reaction with BnSH (top) in TFA-$d_1$ (300 MHz).

# Tables

**Table 1.** Reaction conditions applied for enzymatic synthesis of linear PAs, catalyzed by Novozyme® 435 lipase.

| Entry | DEMM (eq.) | DEMPM (eq.) | DETA (eq.) | Lipase (wt%) |
|---|---|---|---|---|
| 1 | 1 | 0 | 1 | 2.4 |
| 2 | 0.8 | 0.2 | 1 | 2.4 |
| 3 | 0 | 1 | 1 | 2.4 |
| 4 [a] | 0.8 | 0.2 | 1 | 10 |
| 5 | 1 | 0 | 1 | 0 |

[a] Synthesized according to the further mentioned reaction conditions of Jiang [49].

**Table 2.** Composition and molecular weight of the linear PAs synthesized via (non-)stirred interfacial (IF) or solution (S) polymerization.

| Entry | Diamine[a] | Diacid dichloride[b] | Solvent | Stirring method[c] | Mol% alkyne (feed) | Mol% alkyne (NMR) | $M_p$ (SEC) or $M_v$ (visc) (g/mol) |
|---|---|---|---|---|---|---|---|
| IF1 | HDA | AC | xylene | magn | 0 | 0 | 12,100 ($M_v$) |
| IF2 | DDA | MPMAD | xylene | magn | 100 | 100 | 22,000 ($M_p$) |
| S1 | HDA | AC | THF | magn | 0 | 0 | 2,000 ($M_v$) |
| IF3 | HDA | AC | $CH_2Cl_2$ | magn | 0 | 0 | 35,900 ($M_v$) |
| IF4 | HDA | SC | $CH_2Cl_2$ | mech | 0 | 0 | 13,000 ($M_v$) |
| IF5 | HDA | MPMAD | $CH_2Cl_2$ | mech | 100 | 100 | 5,600 ($M_p$) |
| IF6 | HDA | AC/MPMAD | $CH_2Cl_2$ | mech | 50 | 41 | 3,900 ($M_v$) |
| IF7 | HDA | SC/MPMAD | $CH_2Cl_2$ | mech | 50 | 42 | 5,000 ($M_p$)<br>3,000 ($M_v$) |
| IF8 | DDA | SC/MPMAD | $CH_2Cl_2$ | mech | 50 | 45 | 4,600 ($M_p$) |
| IF9 | HDA | SC/MPMAD | $CH_2Cl_2$ | NRT | 5 | 4 | 3,900 ($M_v$) |
| IF10 | HDA | SC/MPMAD | $CH_2Cl_2$ | NRT | 20 | 19 | 6,100 ($M_v$) |
| IF11 | HDA | SC/MPMAD | $CH_2Cl_2$ | NRT | 40 | 39 | -[d] |
| IF11*R*[e] | HDA | SC/MPMAD | $CH_2Cl_2$ | NRT | 40 | 32 | 2,500 ($M_v$) |

[a] HDA = 1,6-hexanediamine, DDA = 4,9-dioxa-1,12-dodecanediamine.
[b] AC = adipoyl chloride, SC = sebacoyl chloride, MPMAD = 2-methyl-2-propargylmalonic acid dichloride.
[c] magn = magnetic stirring, mech = mechanic stirring, NRT = Nylon Rope Trick.
[d] The yield was too low to determine the molecular weight by viscosimetry.
[e] Residual fraction of IF11 at the interface of the reaction mixture.

**Table 3.** Melting and degradation temperatures of the synthesized PAs.

| Entry | Mol% alkyne (NMR) | $T_m$ (°C) | $T_{d,90}$ (°C) |
|---|---|---|---|
| IF1 | 0 | 254 | 371 |
| IF4 | 0 | 216 | 359 |
| IF5 | 100 | -[c] | 280 |
| IF6 | 41 | -[c] | 371 |
| IF7 | 42 | 156 | 332 |
| IF8 | 45 | 126 | 297 |
| IF9 | 4 | 212 | 372 |
| IF10 | 19 | 191 | 356 |
| IF11 | 39 | 175 | 328 |
| IF11*R* | 32 | 182 | 328 |

[c] No melting peak was observed in the DSC curve.

**Table 4.** CuAAC reactions with the alkyne-containing homo- and copolyamides.

| Entry | Mol% alkyne ($^1$H NMR) | Azide[a] | Solvent | Precipitation Solvent | Conversion (%) |
|---|---|---|---|---|---|
| IF2-C | 100 | $BnN_3$ | THF | water | 92 |
| IF5-C | 100 | $BnN_3$ | DMSO | EtOH | 94 |
| IF6-C | 41 | $BnN_3$ | *m*-cresol | diethyl ether | 24 |
| IF7-C | 42 | $PEG_{550}N_3$ | *m*-cresol | diethyl ether | 6 |
| IF8-C | 45 | $PEG_{550}N_3$ | DMSO | acetone | 2 |
| IF9-C | 4 | $PEG_{550}N_3$ | *m*-cresol | diethyl ether | 29 |
| IF10-C1 | 19 | $BnN_3$ | *m*-cresol | diethyl ether | 33 |
| IF10-C2 | 19 | $PEG_{550}N_3$ | *m*-cresol | diethyl ether | 16 |

[a] All the reactions were run overnight at 40 °C.

**Table 5.** Thiol-yne reactions with the alkyne-containing copolyamide IF11*R*.

| Entry | Solvent | Catalyst | Irradiation time (min) | Conversion (%) |
|---|---|---|---|---|
| IF11*R*-T1 | *m*-cresol | DMPA | 90 | 24 |
| IF11*R* -T2 | HCOOH | DMPA | 60 | 60 |
| IF11*R* -T3 | HCOOH | CQ | 30 | 71 |
| IF11*R* -T4 | HCOOH | CQ | 30 | 71 |

| | | | | |
|---|---|---|---|---|
| IF11*R* -T5 | HCOOH | CQ | 90 | 73 |
| IF11*R*-T6 | HCOOH | CQ | 180 | 69 |

**Table 6.** Thermal properties of the alkyne-containing copolyamide IF11*R*, before and after modification with thiol-yne reactions.

| **Entry** | **Conversion (%)** | **$T_m$ (°C)** | **$T_{d,90}$ (°C)** |
|---|---|---|---|
| IF11*R* | 0 | 182 | 328 |
| IF11*R*-T1 | 24 | 170 | 319 |
| IF11*R* -T2 | 60 | 167 | 290 |
| IF11*R* -T3 | 71 | 170 | 267 |
| IF11*R* -T5 | 73 | 171 | 270 |