

# MODIFICATION OF BIODEGRADABLE ALIPHATIC POLYESTERS BY CLICK CHEMISTRY

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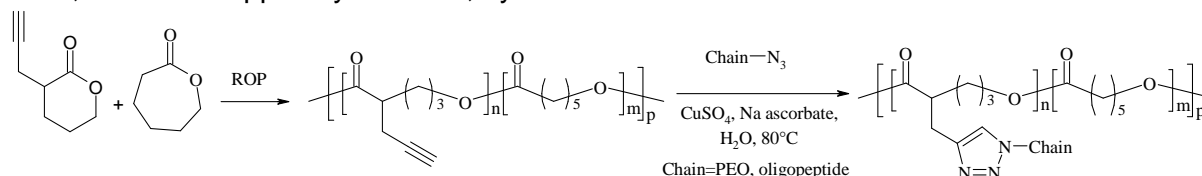
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## Introduction

Nowadays, biodegradable and biocompatible aliphatic polyesters are widely used as environmentally friendly thermoplastics and biomaterials. Nevertheless, the absence of any pendant functional group is a severe limitation for the development of novel applications.

Emrick and coworkers<sup>1</sup> were the first ones to report on the functionalization of aliphatic polyesters by an approach based on the copper-mediated azide-alkyne cycloaddition (CuAAC) (**Figure 1**), which is nothing but the most popular “click” reaction. Firstly, a copolymer of poly( $\epsilon$ -caprolactone) (PCL) bearing pendant alkynes was synthesized by ring-opening polymerization of 3-prop-2-yn-1-yltetrahydro-2H-pyran-2-one and oxepan-2-one ( $\epsilon$ -caprolactone). Finally, pendant alkynes were used for the grafting of an oligopeptide and PEO, both end-capped by an azide, by CuAAC.



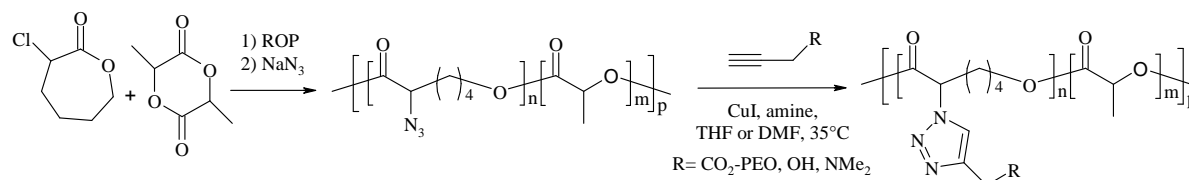
**Figure 1.** Synthesis of functional aliphatic polyesters according to Emrick.<sup>1</sup>

Later on, Riva and coworkers implemented the reverse strategy based on the grafting of functional molecules or chains substituted by terminal alkynes onto PCL bearing pendant azides.<sup>2,3</sup> Up to now, studies dealing with the modification of aliphatic polyesters focused mainly on PCL, most probably because of its low sensitivity to degradation.<sup>4</sup> Besides, a main advantage of CuAAC relies on its completeness even under very mild conditions, which paves the way to the highly efficient derivatization of more sensitive aliphatic polyesters than PCL. This work aims at reporting on the functionalization of copolymers of poly(3,6-dimethyl-1,4-dioxane-2,5-dione) (poly(lactide) or PLA), known to be more sensitive to degradation than PCL.

## Results

Poly( $\alpha$ Cl $\epsilon$ CL-co-LA) copolymers were prepared by ring-opening polymerization of  $\alpha$ Cl $\epsilon$ CL and lactide using 2,2-dibutyl-2-stanna-1,3-dioxepane (DSDOP) as an initiator, followed by the conversion of pendant chlorides into azides by reaction with sodium azide.<sup>2</sup> The hydroxyl groups located at both chain-ends were protected by esterification with acetyl chloride. The grafting of prop-2-yn-1-ol was carried out onto poly( $\alpha$ N<sub>3</sub> $\epsilon$ CL-co-LA) (conditions: CuI, Et<sub>3</sub>N,

THF, 4h, 35°C). The conversion of the CuAAC was close to 100%. Remarkably, the GPC trace remained symmetrical, the polydispersity index did not change ( $M_w/M_n=1.3$ ) and no degradation was thus observed. Interestingly enough, no protection of pendant hydroxyl groups was necessary in order to prevent degradation from occurring.



**Figure 2.** Synthesis of functional copolyesters of lactide.

*N,N*-dimethylprop-2-yn-1-amine was also grafted onto poly( $\alpha$ N<sub>3</sub> $\epsilon$ CL-*co*-LA) (30mol% of  $\alpha$ N<sub>3</sub> $\epsilon$ CL,  $M_n$  (GPC) = 45000,  $M_w/M_n=1.3$ ) under identical conditions (conditions: CuI, Et<sub>3</sub>N, THF, 4h, 35°C). Again, CuAAC turned out to be quantitative. Unfortunately, the GPC trace was no more symmetrical, which is the signature of degradation. In order to overcome this drawback, a new attempt was carried out onto poly( $\gamma$ N<sub>3</sub> $\epsilon$ CL-*co*-LA), the functional group being located in  $\gamma$  position instead of  $\alpha$  position. Indeed, the modification of the position of the functional group is prone to decrease the reactivity of ester bonds,<sup>5</sup> and thus to disfavor degradation. Remarkably enough, the conversion remained close to 100% but, this time, no degradation was observed by GPC even though the chain ends of poly( $\gamma$ N<sub>3</sub> $\epsilon$ CL-*co*-LA) were not protected by reaction with acetyl chloride, which is a further advantage.

## Conclusions

The CuAAC is very efficient to derivatize copolymers of PLA, bearing pendant azides, under very mild conditions, which prevent degradation from occurring. This research paves the way to the macromolecular engineering of polylactide by ring-opening polymerization and CuAAC, which is under current investigation in our laboratory.

## Bibliography

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