FUNCTIONALIZATION AND GRAFTING OF POLYLACTIDE BY CLICK CHEMISTRY

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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 in the biomedical field. In order to tailor or to impart new properties to those polyesters, the grafting of functional groups or polymer chains is required. Emrick and coworkers[1] were the first ones to report on the functionalization of aliphatic polyesters by an approach based on the copper-mediated azide-alkyne cycloaddition (CuAAc). Firstly, a copolymer of poly(ε-caprolactone) (PCL) bearing pendant alkynes was synthesized by the ring-opening copolymerization of α-alkyne-valerolactone and ε-caprolactone (εCL). Finally, the pendant alkynes were used for the grafting of oligopeptide or PEO chains, both end-capped by an azide. Later on, Riva and coworkers implemented the reverse strategy based on the grafting of functional molecules or PEO chains substituted by terminal alkynes onto a PCL bearing pendant azides.[2,3] Up to now, studies dealing with the modification of aliphatic polyesters focused mainly on PCL, most probably because of its low sensitivity to degradation.[4] Nevertheless, the completeness of the CuAAC reaction under mild conditions paves the way to the highly efficient derivatization of more sensitive aliphatic polyesters than PCL. This contribution aims at reporting on the functionalization of copolymers of poly(lactide) (PLA), known to be more sensitive to degradation than PCL and prepared from renewable natural resources.

Results and Discussion

The poly(αClεCL-*co*-LA) copolymers were prepared by the ring-opening copolymerization of α-chloro-ε-caprolactone) (αClεCL) and lactide (LA) using 2,2-dibutyl-2-stanna-1,3-dioxepane (DSDOP) as an initiator, followed by the conversion of the pendant chlorides into azides by the reaction with sodium azide.[2] 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(αN_3εCL-*co*-LA) (conditions: CuI, Et_3N, THF, 4h, 35°C). The conversion of the CuAAc reaction 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 the pendant hydroxyl groups was necessary in order to prevent degradation from occurring.

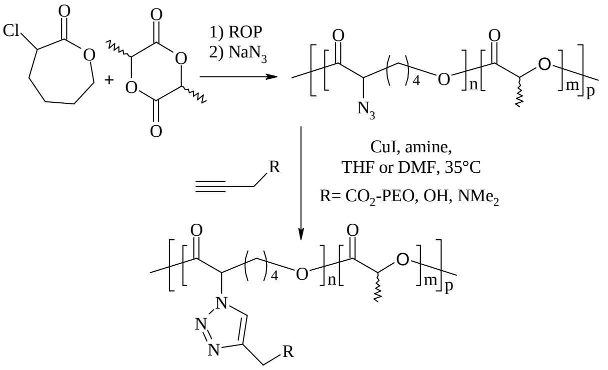

Figure 1. Synthesis of functional copolyesters of lactide.

N,*N*-dimethylprop-2-yn-1-amine was quantitatively grafted onto poly(αN_3εCL-*co*-LA) under identical conditions but with a partial degradation of the copolyester chain. A new attempt was successfully carried out onto poly(γN_3εCL-*co*-LA), as the modification of the substituent position is prone to decrease the reactivity of the ester bonds,[5] and thus to disfavor degradation. PEO-alkyne was also grafted onto PLA-based copolyesters with the purpose to synthesize biocompatible amphiphilic copolymers, which are known to be precursors of drug carriers (micelles) or to be potential surfactant for the stabilization of PLA nanoparticles.

Conclusions

The CuAAc reaction is very efficient to derivatize the 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.

References

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