ABSTRACT

In this dissertation, previously unreported synthetic route for controlled ring-opening polymerization (ROP) of α-amino acid *N*-carboxyanhydrides (NCA) using hydroxyl group as an initiatior was designed in order to simplify the synthesis of well-defined polypeptides and especially polypeptide-based hybrid block copolymers. In the first part of the work, we developed an efficient synthetic method, where we successfuly used low molecular weight alcohols and hydroxyl-terminated polymers as the (macro)initiators for ROP of NCA. The key idea in overcoming the slow initiation by the hydroxyl group is to prevent chain propagation until the initiation is completed, or in other words, until quantitative conversion of (macro)initiator hydroxyl groups into the primary amine groups is achieved. Methanesulfonic acid (MSA) plays an essential role as an organocatalyst during the initiation step. Namely, MSA efficiently catalyzes opening of the first NCA ring by a hydroxyl group, and at the same time, suppresses further chain propagation by protonation of the formed amine group. Chain propagation was started only after completion of the initiation by the addition of a base, that is *N*-ethyldiisopropylamine, which deprotonates the resulting ammonium groups. In this way formed free primary amino groups allow further chain growth through the normal amine mechanism. This method was successfully applied for the synthesis of not only homopolypeptides by using low molecular weight alcohol as an initiator, but also polypeptide-based hybrid block copolymers by using hydroxyl-terminated macroinitiators.

We further developed a sequential synthesis procedure, combining the MSA-based organocatalyzed ROP of cyclic esters or carbonates, and in the next step, ROP of NCA initiated by the hydroxyl group of the resulting polyester/polycarbonate in order to synthesize the polyester/polycarbonate-*b*-polypeptide hybrid block copolymers in a one-pot manner. This synthetic approach was further extended to ROP of *N*-substituted NCA, especially sarcosine NCA, to prepare the polysarcosine polypeptoids. Due to excellent water-solubility of polysarcosine, the A-B-A amphiphilic block copolymers were synthesized, where A block represents hydrophilic polysarcosine and central B block hydrophobic polypropylene glycol, polyester or polycarbonate. Thus prepared amphiphilic block copolymers reveal well-defined structure and molar mass characteristics and are thus suitable for the preparation of polymeric micelles or polymersomes for potential application in drug delivery systems. In the last part, a possibility of using the thiourea-amine bifunctional organocatalysts for ROP of NCA in combination with alcohol as an initiator was investigated. The results showed that in the presence of thiourea-amine bifunctional organocatalysts, the initiation rate of NCA is slower than the chain propagation, leading to poorly defined polypeptides with broader molar mass distribution.

Keywords: ring-opening polymerization (ROP), α-amino acid *N*-carboxyanhydride (NCA), hydroxyl group initiated ROP NCA, well-defined polypeptides, polypeptide-based hybrid copolymers.