HYDROXYL GROUP INITIATED RING-OPENING POLYMERIZATION OF *N*-CARBOXYANHYDRIDES

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Synthetic polypeptides and polypeptide-based hybrid polymers are interesting biomaterials for various applications in biomedical field. They are usually prepared by ring-opening polymerization (ROP) of *N*-carboxyanhydride (NCA) monomers derived from α-amino acids. Primary amines are the most commonly used initiators for ROP of NCA, especially for the preparation of hybrid block copolymers. The NCA ring is opened during the initiation by a nucleophilic attack of the primary amine initiator, resulting in a new amine group as the active species for chain propagation. Rate of initiation with primary amine group is usually fast while initiation of ROP of NCA by the hydroxyl group proceeds significantly slower than the chain propagation via formed amine group, leading to uncontrolled polymerization and consequently to poorly defined products. Therefore, the preparation of polypeptide-based hybrid block copolymers demands transformation of significantly more common end-hydroxyl group of a macroinitiator to the amine group, which is usually accomplished through multi-step reactions.

To overcome the issue of slow initiation by hydroxyl group, we have used an acid catalyst during the initiation step, where it plays a double role, i.e. it catalyzes the opening of the NCA ring by the hydroxyl group and simultaneously suppresses further chain propagation by protonating the formed amine group. In this way, we have separated the initiation from the propagation step, and instead performed them in a successive manner. Only after completion of the initiation, the propagation was started by the addition of a base to deprotonate the amine group. This method was successfully applied for the synthesis of homopolypeptides by using alcohol as an initiator as well as polypeptide-based block copolymers by using poly(ethylene glycol) or poly(styrene) macroinitiator terminated with the hydroxyl group. This approach not only expands the pool of possible initiators for ROP of NCA, but also significantly facilities the preparation of polypeptide-based hybrid polymers.