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Synthesis of Both Linear and Cyclic Polypeptides within an Hour

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Ring-opening polymerization (ROP) of α-amino acid N-carboxyanhydrides (NCAs) is a powerful synthetic methodology for generating well-defined functional polypeptides. However, the conventional procedures require a compromise between obtaining controlled microstructures and employing the optimized polymerization conditions. Specifically a versatile method to access sequenced cyclic polypeptides remains challenging due to the difficulty in site-specific cyclization. Herein, a general and highly straightforward strategy for the synthesis of both linear and cyclic polypeptides is reported using air-stable organocatalyst, imidazolium hydrogen carbonate, mediated living polymerization of NCAs. This approach allows for the rapid and controlled polymerization of a variety of NCAs, leading to high conversion within a few minutes under mild conditions. Linear and cyclic block copolypeptides are also accessible simply by controlling the type of initiators and the order of addition of NCA monomers. This organocatalyzed polymerization technique provides a potent protocol for the synthesis of polypeptide topologies of ever-increasing complexity to mimic nature's nanostructure.

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