ABSTRACT

Polymersomes, spherical structures with a bilayer membrane composed of amphiphilic block copolymers, are gaining attention as robust alternatives to lipid-based liposomes because they are more stable and their properties can be modulated by the chemical composition of the block copolymers. Their ability to incorporate integral membrane proteins makes them particularly promising for the construction of selectively permeable membranes, an essential feature for mimicking cellular functions. A key challenge is the development of membranes with suitable thickness, fluidity and flexibility. This work focuses on the synthesis of amphiphilic miktoarm stars of the AB_2 type as structural analogues of lipids. The aim was to develop an efficient synthetic strategy and to investigate how the chemical composition and architecture of the amphiphilic block copolymers influence the formation of polymersomes and their properties, in particular the membrane thickness.

For the synthesis of AB_2 miktoarm stars, a serinol-based multifunctional core was used to prepare two hydrophobic arms, i.e. poly(trimethylene carbonate) (PTMC) or poly(propylene oxide) (PPO), and then a hydrophilic arm of polysarcosine (PSar) by sequential ring-opening polymerization (ROP) of the corresponding monomers (trimethylene carbonate or propylene oxide and sarcosine *N*-carboxyanhydride). The main challenge was to ensure the selective initiation of the ROP and the compatibility of the ROP with the selected reaction conditions. By using protecting groups and a carefully selected catalytic system, I was able to control the synthesis of the hydrophobic arms (B), which then served as macroinitiators for the polymerization of sarcosine *N*-carboxyanhydride to form the hydrophilic PSar arm (A) of the AB_2 star. Furthermore, I have shown that carbamate groups or classical amine protecting groups (e.g. Boc and Cbz) are compatible with PPO synthesis when a catalytic system of a phosphazene base and a Lewis acid is used. This approach greatly simplifies the preparation of α-amino-functionalized PPOs.

A series of PSar-*b*-$(PTMC)_2$ and PSar-*b*-$(PPO)_2$ amphiphilic miktoarm stars with different hydrophilic block weight fractions (f_{HF}) and corresponding linear AB and ABA analogues were synthesized. Self-assembly studies showed that AB_2 miktoarm stars form polymersomes over a broader range of f_{HF} and form thinner membranes with more elongated hydrophobic chains compared to their linear analogues, providing greater flexibility in tuning membrane thickness. The developed synthetic method enables the preparation of well-defined PTMC or PPO- and PSar-based miktoarm stars and represents an important contribution to the design of novel polymeric membranes with the potential for the incorporation of membrane proteins and the development of advanced biomimetic systems with applications in biomedicine, environmental and nutritional science.