Stimuli-Responsive Star Polymers

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ABSTRACT: Stimuli-responsive star polymers gain more and more interest over the last decades due to their unique properties compared to their linear counterparts. The branched structure for instance has influence on the responsive behavior of these polymers. This review offers an overview of stimuli-responsive star polymers generated by different polymerization techniques, e.g. anionic and controlled radical polymerization (CRP). Beside conventional branched homopolymers different other types like block copolymers, miktoarm star copolymers, core crosslinked star polymers (CCS) and comb polymers are also presented. Furthermore their responsive behavior in solution or immobilized on a substrate, and their applications are outlined. © 2013 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2013**, *51*, 2980–2994

KEYWORDS: atom transfer radical polymerization; block copolymers; living polymerization; reversible addition fragmentation chain transfer (RAFT); star polymers; stimuli-sensitive polymers

INTRODUCTION During the past decades the use of stimuli-responsive (synthetic) polymers e. g. mimicking biopolymers and biological systems became a very important field of research.[1,2] Stimuli-responsive polymers are able to undergo significant property changes as a reply to relatively small external or internal variations of the environmental conditions (stimuli). Therefore, these polymers are also named "stimuli-sensitive," "smart," "intelligent," or "environmentally sensitive." The nature of the environmental stimulus can be classified into three categories: physical, chemical and biomedical stimuli.[3] The response of the material can have miscellaneous forms: a change in shape and dimension of the polymer material, altering its mechanical, optical or electrical properties as well as changes in permeability can be observed. Smart polymers in solution can also show a macroscopic phase separation as response to a stimulus.[4] The architecture of smart polymer systems covers not only different polymer geometries but also several orders of magnitude in size. Both, the ability to respond to various stimuli and the numerous possible architectures, are prerequisites for tailor-made polymeric systems for a broad range of applications covering the fields of drug-delivery,[5] diagnostics,[6] biotechnology,[7,8] sensors,[9,10] micromechanical and optical systems[11] as well as coatings and textiles.[12,13]

The effects of branching on stimuli responsive polymers are an important issue since the polymer topology can have a significant influence on the response behavior. The hyper-branched structure of poly(*N*-isopropyl acrylamide) (PNIPAAm), as an example, led to reduced lower critical solution temperatures (LCST) as compared to linear ones, which was primarily attributed to an increased contribution of hydrophobic end groups.[14] Turbidimetry indicates a clear effect of chain architecture as well.[15,16] Other branched structures are star polymers with multiple arms linked to a central core.[17–19] Their preparations have been mainly demonstrated by precise polymerization techniques, in which much effort has been devoted to achieve high degrees of control over the arm-lengths, arm numbers, and architectural branching points.[20]

STAR-SHAPED STRUCTURES

Much interest has been directed to investigate the syntheses and properties of well-defined macromolecules with complex architectures.[21] Star polymers are one example of macromolecules with a precisely controlled architecture containing several linear polymer chains connected at one central core.[22,23] The synthesis of star polymers had first been studied using ionic polymerization.[20] After the development of CRP star polymers have been frequently synthesized using atom transfer radical polymerization (ATRP),[24,25] NMRP[26] and RAFT[27] via three methods: the "core-first" method providing well-defined star macromolecules by growing arms from a multifunctional initiator,[28,29] the "arm-first" method forming stars by crosslinking linear arm precursors using a crosslinker,[30,31] and the "coupling-onto" method attaching linear arm precursors onto a well-defined multifunctional core (Fig. 1).[32] With the "core-first" approach the major

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Agnes Wycisk received her BSc in Chemistry from the University of Paderborn, Germany in October 2007 followed by the Master degree in Chemistry two years later. Since then she has been performing her PhD research work focusing on the controlled synthesis of star polymers and their characterization employing size exclusion chromatography under the supervision of Prof. Kuckling at the University of Paderborn, Germany.
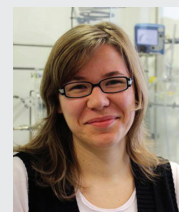
limitation is the limited access to suitable star cores with sufficient functionalities to give polymer stars with larger arm numbers. Although the "arm-first" approach can provide larger number of arms than the "core-first" approach. This technique employs the coupling of preformed macroinitiators in the presence of divinyl compounds also called core cross-linked stars (CCS).

### Star Polymers with Low Molecular Weight Cores

Star polymers are comprised of multiple arms or branches radiating from a central point or core and have been of huge scientific interest since they were first prepared sixty years ago, as a result of their unique physical properties. A variety of small low-molecular compounds are ascribed in literature for the used as core molecules in the "core first" approach.

Homo Polymers

Employing the "core-first" approach a quantity of different initiators can be used for the synthesis of star polymers. The chemical structure of these initiators can either be aliphatic or cyclic and involve generally more than three groups for initiation.[33,34] The synthesis of four-arm PNIPAAm star polymers with different molecular weights was realized using RAFT techniques. The scope of this study was to investigate the effect of polymer architecture and the end group (R group) on the LCST behavior on the PNIPAAm stars. For this reason the LCST of the star polymers was determined first followed by the cleavage of the arms of the stars at the trithiocarbonate linkage by piperidine and a second LCST determination of the linear chains. It was found that the LCST transition of the stars was significantly lower in comparison to linear PNIPAAm polymers and may be explained by the presence of the hydrophobic star core and the benzyl end group. This effect showed molecular weight dependence and diminished once the number of repeating units was

greater than 70. The cleaved linear PNIPAAm chains exhibited identical LCST transitions independent from molecular weight and T_c values were higher than normally obtained for linear PNIPAAm, which might be due to the presence of hydrophilic and hydrophobic units on opposite ends after hydrolysis from the star core.[35]

The strong dependence of the molecular structure on the stimuli-sensitive behavior of the polymers could also be observed by the use of cyclic compounds as core molecules. Cyclodextrins belong to one of the most popular cyclic compounds and many examples are reported in literature using β-cyclodextrin (β-CD) as initiator in combination with PNIPAAm as stimuli-sensitive polymer.[36] The Composition of fully functionalized β-cyclodextrin could be performed by ATRP. The prepared star-PNIPAAm and star-PNIPAAm with cyclodextrin end groups (star-PNIPAAm-CD) exhibit temperature sensitivity and inclusion functionalities. These polymers can self-assembly to form nanosized aggregates above LCST and show molecular recognition capacity. For the normal star polymer molecular recognition was carried out by the interaction of PNIPAAm arms with guest molecules, for the end functionalized star polymer in contrary the molecular recognition is based on the formation of inclusion complexes of CD end groups with guest molecules.[37] Beside the molecular structure of the polymers the inclusion of guest molecules also can influence the LCST of polymers. To investigate the effect of PEG chain length and structure of the adamantyl-containing PEGs on their LCST behavior β-CD-core PNIPAAm star polymers (β-CD-(PNIPAAm)$_4$) were synthesized via ATRP. The use of monoadamantyl-terminated PEGs with different molecular weights as macromolecular guests led to a shift in the LCST form 37.8 °C for MPEG-750-Ad (17 PEG units) to 39.5 °C for MPEG-2K-Ad (48 PEG units). Thus, control over the LCST can be gained by the chain lengths of the PEG block.[38]
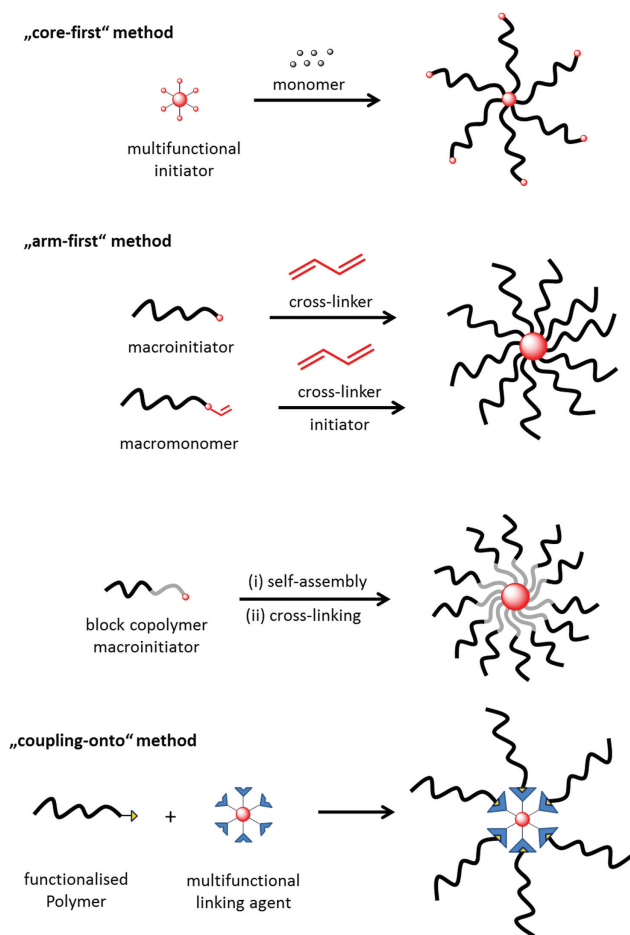
FIGURE 1 Synthetic approaches for the preparation of star polymers using controlled radical polymerization techniques: "core-first"-, "arm-first"-, and "coupling-onto"-approach.

PNIPAAm stars having a hyperbranched polyester (Boltorn H40) core were prepared using reversible addition-fragmentation chain transfer (RAFT) polymerization and possess double phase transition behavior. The polymers exist as unimolecular micelles with a hydrophobic Boltorn H40 core and a shell densely grafted with PNIPAAm brushes. With increasing temperature first the inner part of PNIPAAm brushes collapse in a broad range (20–30 °C), which can be ascribed to the n-cluster-induced collapse resulting from the higher chain density. The second phase transition ascribed to the collapse of the outer part of PNIPAAm brushes takes place above 30 °C.[39] In recent years polyhedral oligomeric silsesquioxanes (POSS, $R_8Si_8O_{12}$), which belong to a class of unique inorganic components, gain more and more interest as potential core molecules for star polymer synthesis. POSS end-capped poly[2-(N,N-dimethylamino)ethyl methacrylate]s (PDMAEMA) were prepared by ATRP using POSS-Br as macroinitiator. Analysis of the self-assembly behavior depending on pH, ionic strength and temperature displays the possibility to change between single and complex micelles (Fig. 2).[40]

Focusing on double stimuli-responsive polymers well-defined star polymers of poly(N,N-diethylaminoethylmethacrylate) (PDEAEMA) with three to eight arms were synthesized via ATRP using "core-first" approach with sugar-based multifunctional initiator. It was found that the pH and temperature-response is analogous to that indicated by PDMAEMA. PDEAEMA exhibits a critical value at which the chains collapse and form aggregates. Its temperature responsive behavior is independent of molecular weight or architecture.[41]

Block Copolymers

Beside conventional AB diblock or ABC triblock copolymers a variety of stimuli-responsive copolymers with complex structures were synthesized using CRP techniques.[42] The preparation of star block copolymers with four arms possessing an interior
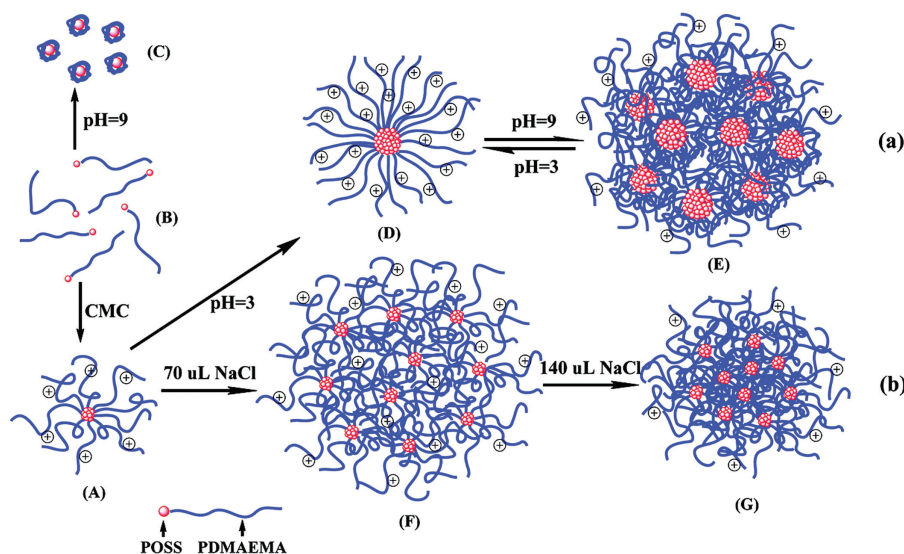
FIGURE 2 Self-assembly process of POSS-PDMAEMA in aqueous solution (Reproduced from Ref. 40, with permission from Copyright © 2011 ACS Publications).
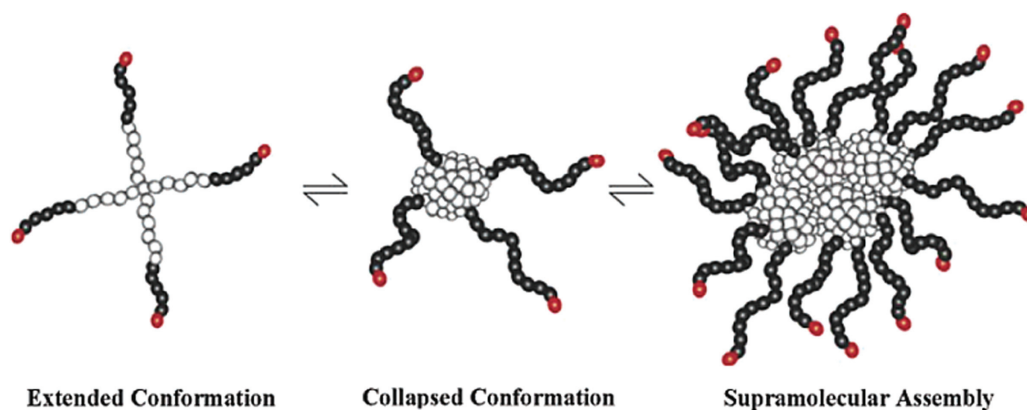
FIGURE 3 Schematic of using four-arm star polymers that form tetrafunctional nanoparticles when the polymer is in a collapsed conformation (Reproduced from Ref. 43, with permission from Copyright © 2006 American Chemical Society).

block comprised of PNIPAAm and an exterior block of PDMAAm was realized via RAFT. These star polymers were observed to form monodisperse supramolecular aggregates in aqueous pH 4 buffer solution when heated above the LCST of PNIPAAm. Using a simple model based on optimal area per headgroup developed for linear block copolymers micelles it was possible to predict the number of star unimers per aggregate in the final structure and the size of those micelles (Fig. 3).[43]

N-isopropylacrylamide/2-hydroxyethyl methacrylate (PNI-PAAm/HEMA) tri-arm star diblock copolymers were generated in methanol via a two-step ATRP method. The polymerization of the first block takes place in a controlled manner regarding to the low polydispersity. The results of the thermo-responsive behavior of the star diblock copolymer solution revealed that introducing a higher ratio of HEMA into copolymers could facilitate the formation of micelles and the occurrence of phase transition at lower temperatures.[44] The synthesis of temperature-responsive hydrogel, composed of star shaped β-CD-g-(PNIPAAm-b-PDMAAm)$_3$ copolymers, was performed via sequential RAFT method, initiated by a β-CD-xanthate as chain transfer agent. Below the LCST of the PNIPAAm segments, the copolymer exists as uniform solution. Above the LCST free-standing hydrogels can be formed rapidly at sufficient concentration. Using Rhodamine B as a molecule to model a typical drug, the in situ encapsulation and release from the hydrogel was analyzed at physiological temperature.[45] To investigate the gelation characteristics and rheological properties of block copolymers with a central hydrophilic poly(ethylene glycol) (PEG) segment and temperature-responsive terminal PNI-PAAm segments, copolymers with various architectures (A(B)$_2$, A(B)$_4$, A(B)$_8$) were prepared. All copolymers of PEG and PNIPAAm form liquid aqueous solutions at low temperature and transfer to relative strong elastic gels upon heating which occurs via a physical crosslinking mechanism. The rheological properties of the gels depend on the molecular structure.[46] Smart hydrogels based on dual stimuli responsive star-block copolymers responding to pH and temperature were prepared via atom transfer radical polymerization (ATRP) employing the "core first" method. They consist of

PDMAEMA inner blocks and outer blocks comprised of poly(di(ethylene glycol) methyl ether methacrylate) (PDEGMA). Above the transition temperature of the PDEGMA outer blocks the stars form flower-like aggregates in dilute solution or free-standing gels at higher concentrations. When the temperature is increased further above the transition temperature of the PDMAEMA inner block, the aggregates start to contract and a weakening was observed for soft gels, whereas for strong gels no influence on the moduli was detected. The minimum polymer concentration for gel formation can be lowered by quaternizing the inner block of the stars, but a second response to stimuli is lost during the procedure.[47]

Referring to homo polymers possessing a hyperbranched polyester core the synthesis of a H40-PNIPAAm-PDMAEMA block copolymer using a Boltorn H40-based macro-RAFT
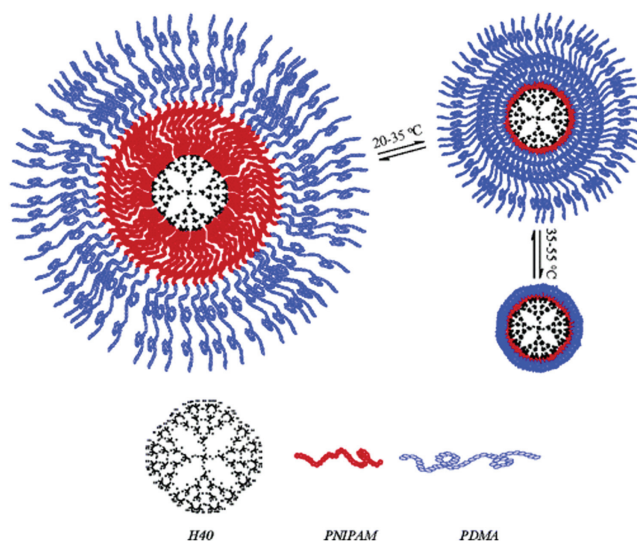
FIGURE 4 Schematic illustration of the thermally induced collapse of H40-PNIPAM-PDMA upon heating through the LCSTs of PNIPAM and PDMA (Reproduced from Ref. 48, with permission from Copyright © 2006 ACS Publications).

agent could also be performed. The dendritic molecules exist as unimolecular core-shell nanostructures with hydrophilic H40 as core, PNIPAAm as the inner shell and PDMAEMA as the corona. The combination of two polymers with different LCST behavior (PNIPAAm: 32 °C, PDMAEMA: 40–50 °C) lead to the formation of dendritic unimolecular micelles that exhibit two-stage thermally induced collapse with increasing temperature (Fig. 4).[48]

The preparation of poly(ε-caprolacton-star-*N*-isopropylacryla-mide) (PCL-*b*-PNIPAAm) could be carried out using hydroxyl-functionalized polyhedral oligomeric silsesquioxanes (POSS) as core to initiate the ROP of ε-caprolactone, followed by ATRP of NIPAAm. These star block copolymers form micelles in aqueous solution and show temperature-dependent hydrophobic drug release behavior.[49] With the intention of tuning the LCST of PNIPAAm via the star approach coupled with the incorporation of pH-responsive blocks octafunctional POSS-cored star-block PAAc-PNIPAAm (POSS-PAAc-*b*-PNIPAAm) copolymers were created via two steps of core-functionalized ATRP. When very short PAAc blocks (POSS-PAAc$_2$-*b*-PNIPAAm$_{11}$) are introduced into the polymer the critical temperature (T_c) of the star polymers varies in a wide temperature range with pH. Whereas, when the PAAc block is relatively long (POSS-PAAc$_8$-*b*-PNIPAAm$_{11}$) pH response disappear owing to the reduced local PNIPAAm chain density.[50]

In addition to star block copolymers comprised of PNIPAAm, other thermo-sensitive blocks have also been investigated. Well-defined block copolymers consisting of four-arm poly(ethylene oxide)-*b*-poly(2-diethylaminoethyl methacrylate) (PEO$_{56}$-*b*-PDEAEMA$_{74}$) were synthesized via ATRP. The investigation of the pH-responsive behavior showed that at high pH spherical core–shell micelles comprising a hydrophobic DEAEMA core surrounded by a four-arm PEO corona were formed. At low pH the micelles dissociated into unimers.[51] A pH-dependence on the micelle morphology could also be observed by four arm star block polymers with a hydrophobic PCL block and hydrophilic PDEAEMA block employed by ROP and ATRP.[52] Focusing also on biocompatible and biodegradable star-shaped polymers the preparation of four-arm star triblock copolymers containing a hydrophobic PCL segment, a hydrophilic poly (oligo(ethylene oxide)475 methacrylate) (POEOMA475) segment and a thermoresponsive poly(di(ethylene oxide) methyl ether methacrylate) (PMEO$_2$MA) segment occurred using ROP and ATRP. These amphiphilic copolymers can self-assemble into spherical micelles in aqueous solution at room temperature (Fig. 5).

The properties of the two series of copolymers (PCL-*b*-POEOMA475-b-PMEO$_2$MA)$_4$ and (PCL-b-PMEO$_2$MA-*b*-POEOMA475)$_4$ were quite different and depended on the sequence distribution of each block along the arms of the star. The first series of star copolymers, with the thermoresponsive PMEO$_2$MA segment on the periphery, could undergo reversible sol–gel transitions between RT (22 °C) and human body temperature (37 °C).[53]
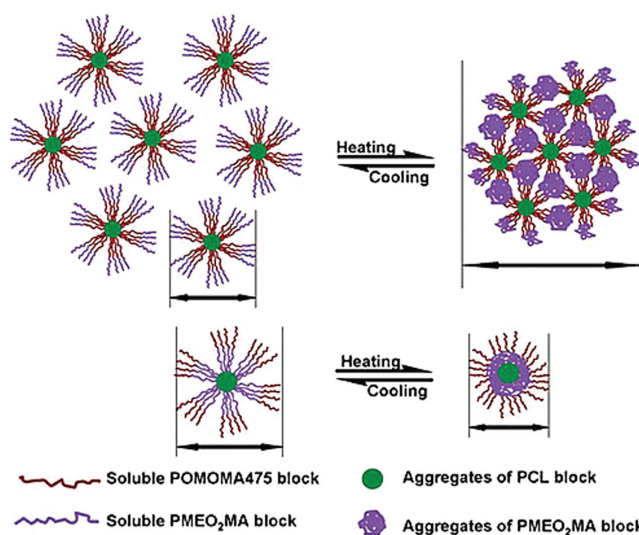

FIGURE 5 Proposed mechanism for the temperature induced self-assembly of thermoresponsive star triblock copolymers in aqueous solution (Reproduced from Ref. 53, with permission from Copyright © 2011 Wiley Periodicals).

Water soluble four- and six-arm star shaped polymers with (bio)degradable hydrophobic cores (PCL) and dense hydrophilic corona (various mPEGMA monomers) were prepared according the previous mentioned procedure. The densely grafted shell [p(mPEGMA)] stabilizes the host-guest complexes and prevent undesired multimolecular aggregation. These systems are able to encapsulate hydrophobic, neutral guest molecules, and release them during the (bio)degradation process of the core under acidic conditions. The dual-stimuli responsiveness of the hydrophobic core to enzymes and pH may facilitate increased control over *in vivo* drug release.[54]

To study the use of star-shaped block copolymers as unimolecular nanocontainers for encapsulation and release experiments five-arm star block copolymers with a hydrophilic poly(ethylene oxide) (PEO) core and a hydrophobic poly(*t*-butyl acrylate) (P*t*BA) shell were prepared by making use of the ATRP technique. Release of the encapsulated guest molecules was performed in acidic media by subsequent hydrolysis of the *t*BA groups to acrylic acid moieties.[55] Recently, the design of novel porphyrin functioned star-shaped amphiphilic PCL-*b*-p(mPEGMA) via the combination of ROP and ATRP were reported. They can easily self-assemble into micelles in aqueous solution via dialysis method and exhibit a controlled drug release by the change of temperature.[56]

Miktoarm Copolymers
Typically miktoarm copolymers (also called asymmetric or heteroarm star polymers) possess various types of polymer arms, that can differ in the molecular weight, the chemical composition and the functional end group, connected to a central core (Fig. 6). Because of their opposed properties, which can be adjusted by the variation of the polymer arms, miktoarm polymers belong to a new and special class of
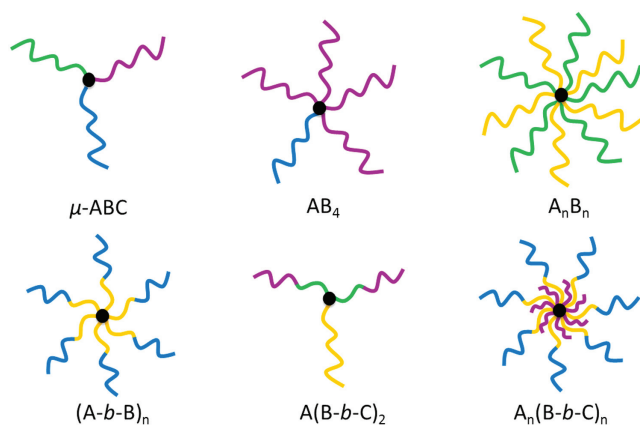
FIGURE 6 Schematic representation of star-shaped segmented polymers: A_nB_n heteroarm star copolymer, AB_4 miktoarm star copolymers, (A-b-B)$_n$ star block copolymer, μ-ABC miktoarm star terpolymer, A(B-b-C)$_2$, and A_n(B-b-C)$_n$ heteroarm star block terpolymers [Reproduced from Ref. 59, with permission from Copyright © 2011 MDPI AG (Basel, Switzerland)].

macromolecules. The various types of asymmetry within the macromolecule allows chemist to create novel morphological nanostructures and self-assembled organizations different from those noted with linear homologs.[57]

Although a lot of different AB_x miktoarm star copolymers are reported in the literature,[58] only a small part show stimuli-responsive behavior in aqueous solution.[59] To investigate the influence on the overall morphologies of the formed aggregates under external stimulus AB_2 type star copolymers combining hydrophilic and hydrophobic blocks within one molecule separated by one branching point were created. The water-soluble miktoarm star polymers own a single polystyrene (PS) block and two ionogenic PAAc or poly(glutamic acid) (PGA)) blocks. First of all, the PS block was prepared using ATRP followed by derivatization of the bromo end-group (with either 1-aminotriethylenetriamine or diethanolamine and bromoesters), polymerization of (1) γ-benzyl-L-glutamate or (2) tert-butylacrylate and hydrolysis of the copolymers. By changing the pH value from 5–12 in aqueous solution formation of narrow sized spherical micelles with the PS part constituting the core and two PGA blocks forming the shell were observed in both cases, although the R_h value under acidic conditions was smaller ($R_h = 11$ nm) than under basic conditions ($R_h = 16$ nm, pH > 12). The difference in size can be explained by the α-helix to coil transition of the electrostatically charged PGA blocks.[60]

Two thermally responsive miktoarm star polymers in which PNIPAAm or poly(oligo(ethylene glycol) methacrylate) (POEGMA) served as the thermo-sensitive building blocks were synthesized. The obtained miktoarm star polymers were comprised of a β-CD core, a PEG arm and about six PNIPAAm or POEGMA arms. Above the LCST of the polymers in aqueous solution, PEG-CD-b-PNIPAAm$_x$ can self-assemble into nano-structures with PNIPAAm as the core and PEG as the corona, whereas PEG-CD-POEGMA$_x$ self-assembled into

nano-architectures possessing hydrophilic surfaces which were constructed by the hydrated oligo(ethylene glycol) side chains of the POEGMA arms. The hydrophobic moiety of the nano-architectures was formed by the methacrylate backbone and the dehydrated oligo(ethylene glycol) side chains of POEGMA. Furthermore, it was found that the thermally induced dehydration of PEG-CD-PNIPAAm$_x$ is completely different from that of PEG-CD-POEGMA$_x$. For the former, the dehydration occurs abruptly and intensively near the LCST of PEG-CD-PNIPAAm$_x$, whereas the dehydration for the latter is gradual and continuous throughout the whole temperature rise. The architecture of the nano-assemblies formed by PEG-CD-PNIPAAm$_x$ or PEG-CD-POEGMA$_x$ was affected by the thermally induced dehydration of the polymers.[61]

The design of miktoarm star polymers using a combination of SET-LRP with other CRP methods is rarely investigated.[62] One example is the synthesis of A_3B miktoarm star polymers composed of PNIPAAm and poly(N-vinylcarbazole) (PNVC). The fluorescent micelle from self-assembly of (PNIPAAm)$_3$(PNVC) are responsive to the temperature, which made it well suited for potential applications as sensitive probe for the microscopic environmental change.[63] The preparation of amphipilic ABC miktoarm star copolymers based on PS, and PEO, poly(methyl acrylate) or PNIPAAm blocks were realized by RAFT techniques and the use of maleic anhydride as a nonhomopolymerizable linking agent. First of all PS with a terminal dithio group was successfully reacted with an excess of maleic anhydride resulting now in a PS with terminal anhydride and dithio group. Polymerization of the second monomer via RAFT techniques and reaction of the anhydride group at the junction of two polymer blocks with PEGM led to miktoarm star polymers with a narrow molecular weight distribution (PD = 1.12–1.18).[64]

The first example of temperature-sensitive core–shell nano-particles were generated from amphiphilic ABC miktoarm star terpolymers. These terpolymers consist of hydrophobic PS, PCL and PNIPAAm and were prepared via a combination of ATRP, ROP, and click reaction (Fig. 7). Because of their chemical composition they should self-assembly in aqueous solution into micelles with a PS/PCL mixed core and a PNIPAAm corona. Moreover these micelles exhibit thermo-responsive size shrinkage induced by the collapse of the PNIPAAm corona upon the LCST. The size of the nanoparticles can be controlled by the PNIPAAm content within the shell. PS$_{43}$(-b-PNIPAAm$_{84}$)-b-PCL$_{55}$ miktoarm terpolymers formed smaller nanoparticles (decreasing from 51 nm at 25 °C to 38 nm at 45 °C) than PS$_{43}$(-b-PNIPAAm$_{52}$)-b-PCL$_{55}$ (75 nm at 25 °C, 65 nm at 45 °C).[65]

Examination of the micellization behavior of double-responsive hydrophilic ABC miktoarm star terpolymers with PEO, PDEAEMA and PNIPAAm arms synthesized employing ATRP and click techniques display interesting activities, which were ascribes as "schizophrenic" micellization behavior. Combination of different polymer arms which exhibit pH-(PDEAEMA) and thermo-responsive (PNIPAAm) behavior within one molecule lead to two different types of micelles
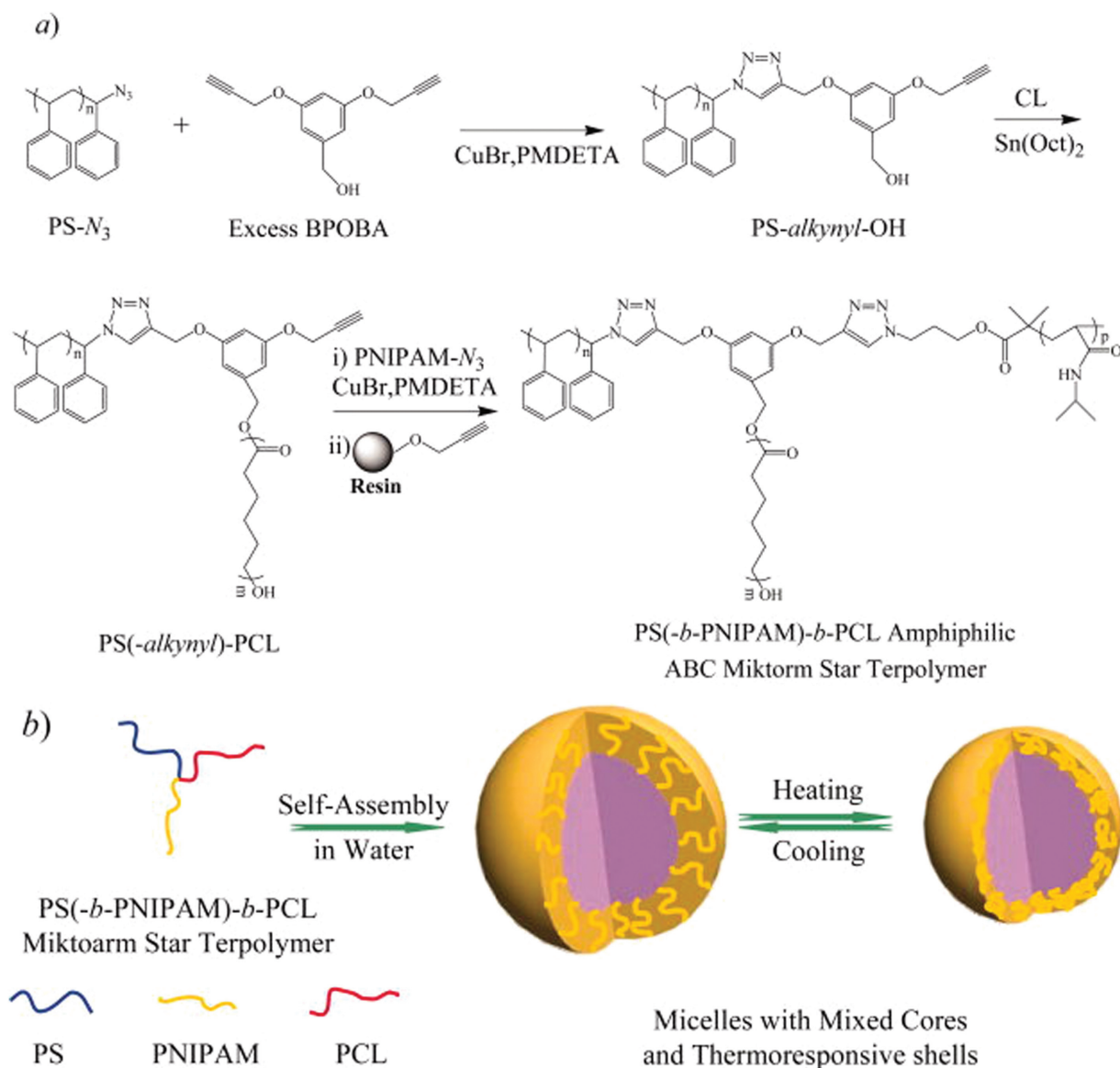
FIGURE 7 (a) Synthetic schemes employed for the preparation of PS(-b-PNIPAM)-b-PCL amphiphilic ABC miktoarm star terpolymer via a combination of ATRP, ROP, and click reactions. (b) Schematic illustration of the fabrication of micelles with mixed PS/PCL cores and thermoresponsive coronas from PS(-b-PNIPAM)-b-PCL amphiphilic ABC miktoarm star terpolymer (Reproduced from Ref. 65, with permission from Copyright © 2009 Wiley Periodicals).

with a hybrid corona in aqueous solution. At pH 4 and 25 °C the PEO(-b-PDEAEMA)-b-PNIPAAm miktoarm terpolymers were dissolved and form unimers, whereas the variation of temperature and pH induced supramolecular self-assembly. Adjusting alkaline pH (pH ∼ 10) and room temperature PDEAEMA-core micelles occurred. Switching to acidic pH at higher temperature (50 °C) micelles with a PNIPAAm-core were formed. Compared to linear ABC triblockcopolymers the PEO(-b-PDEAEMA)-b-PNIPAAm miktoarm star terpolymers seemed to form more compact pH-/ thermo-induced aggregates, which can be explained by their topology.[66] A similar behavior could be observed in Janus-type A_7B_{14} star copolymers of NIPAAm and DEAEMA, (PDEAEMA)$_7$-CD-(PNIPAM)$_{14}$ synthesized by coupling ATRP and click chemistry

techniques, starting from a well-defined β-CD derivative. Upon adjusting solution pH and temperatures, (PDEAEMA$_{30}$)$_7$-CD-(PNIPAAm$_{25}$)$_{14}$ can reversibly self-assemble into two distinct types of polymeric vesicles with "inverted" nanostructures in aqueous solution.[67] The formation of photo-switchable, supramolecular aggregates (called "confused micelles") from miktoarm stars bearing two PEO and three to four PDMAEMA arms was performed in aqueous solution. Utilizing a polymer, which shows both LCST and UCST behavior in the presence of hexacyanocobaltate(III) $[Co(CN)_6]^{3-}$ in water mixture, it was possible to generate micelles at low and also at high temperatures with PDMAEMA as core-forming component. Furthermore the addition of photosensitive $[Co(CN)_6]^{3-}$ allowed the
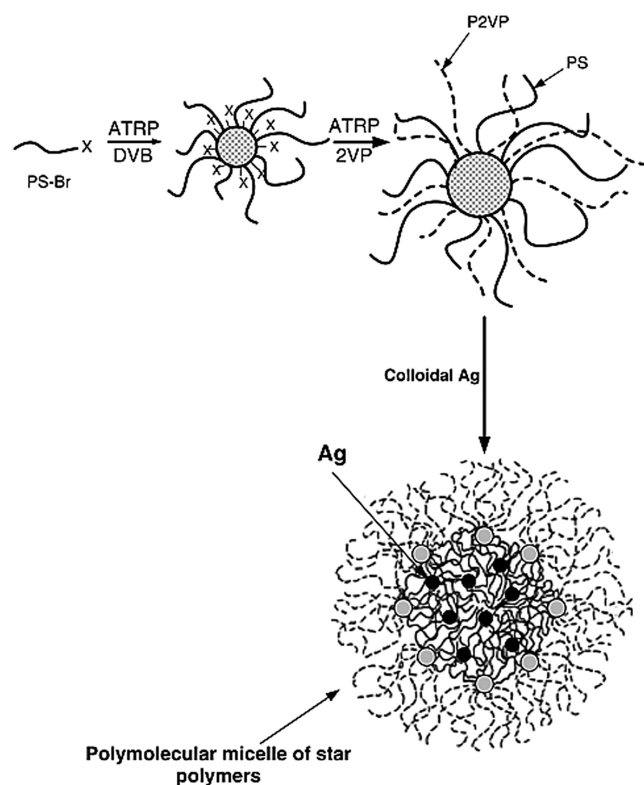
FIGURE 8 Chemical structures of the synthesized PS-*star*-P2VP heteroarm star copolymer (Reproduced from Ref. 71, with permission from Copyright © 2008 Society of Chemical Industry).

introduction of another parameter and therefore the possibility to reverse the mizellization by light.[68]

ABCD-type 4-miktoarm star copolymers of styrene, α-methyl-styrene), tert-butyl methacrylate (tBuMA), and 4-vinylpyridine (4VP) were synthesized via anionic polymerization using 1,3-bis(1-phenylvinyl)benzene (m-DDPE) as the linking molecule. The final product was hydrolyzed to produce a zwitterionic miktoarm star copolymer, which was soluble at lower pH but insoluble in neutral and basic solution.[69] To develop miktoarm star copolymers with an even more complex structure functionalized hyperbranched polyglycerols (MI-HPG) were employed as multifunctional initiator (MI-HPG). Controlled synthesis of heteroarm star copolymers containing thermosensitive PNIPPAm and nonresponsive PDMAAm arms was achieved using sequential RAFT and ATRP techniques. First, the MI-HPG core was prepared from an amine-functionalized polygylcerol, modified with 2-chloropropionamide (ATRP initiator) and 4,4′-azobis(4-cyanovaleric) (azo initator). Polymerization of *N*,*N*′-dimethyl acrylamide (DMAAm) was performed in the next step followed by cografting of PNIPAAm onto the HPG-*g*-PDMA macroinitiator by ATRP. Formation and stabilization of the aggregates were a function of molecular weight of the arms and the PNIPAAm/PDMAAm content of the star polymer.[70]

Smart star polymers grafted on a surface show interesting morphologies. For the purpose of studying the morphological

change of asymmetric amphiphilic PS-P2VP heteroarm star copolymer prepared by ATRP they were diluted in solutions of tetrahydrofuran (THF) and methanol (MeOH). Various aggregate morphologies (spheres, vesicles, rods, large compound micelles, two-dimensional (2D) ring-like and 3D hollow structures) were formed by varying the hydrophilic coil length and the selective solvent content. Silver nanoparticles showed good dispersion behavior in both types of copolymers (Fig. 8).[71]

Studies of the surface micelles of $A_n(B-C)_n$ star terpolymers were performed. The pH-responsive amphiphilic star block terpolymer $PS_n(P2VP-b-PtBA)$ were synthesized by a multistep, one-pot, sequential anionic living polymerization procedure following the "in-out method." They focus on the effect of pH on the morphology of these star-shaped polymers with different architecture (co-/terpolymer), arm/block length (molecular weight of P2VP segments) and number of arms ($n = 9$, 22, and 28). Their results demonstrate a strong pH dependence of the surface aggregation leading to different limiting molecular areas and resulting in distinct surface morphologies for stars with different chemical compositions.[72]

Core Crosslinked Stars (CCS)

Primary focused on star polymers prepared by "core-first" method another promising approach, which involves the coupling of preformed linear chains, containing a dormant chain, with a crosslinkable monomer such as divinylbenzene should be mentioned. Starting with telechelic linear polymer chains, for example, derived from NMRP techniques star copolymers with various numbers of arms and functional groups along the backbone or as chain end groups were accessible. The potential of this approach to star polymers was further demonstrated by employing block copolymers as linear chains.[73]

Although there are many different types of star polymers and methods for their synthesis, recent advances in the field of controlled radical polymerization have enabled the facile production of complex star polymer architectures from a large range of monomer families, without the requirement of highly stringent reaction conditions. In particular, well-defined, nanometer scale core crosslinked star (CCS) polymers, which are readily accessible by controlled radical polymerization techniques, have been increasingly prominent in the scientific literature.[74] However, base-stabilized cationic living polymerization also allowed the quantitative synthesis of star-shaped polymers with a narrow molecular weight distribution via polymer linking reactions and the precision synthesis and self-assembly of stimuli-responsive block copolymers.[75,76] Particular emphasis is placed on the strategy of employing divinyl crosslinkers to introduce branching points into polymer chains during the copolymerization procedures. By rational selection of initiator, monomer and divinyl crosslinker and their polymerization sequence, star-like polymers with a crosslinked core but various arm compositions and site-specific functionalities are formed.[77] CCS polymers, also referred to as core–shell microgel (CSMG) nanoparticles, can be envisaged as permanently crosslinked
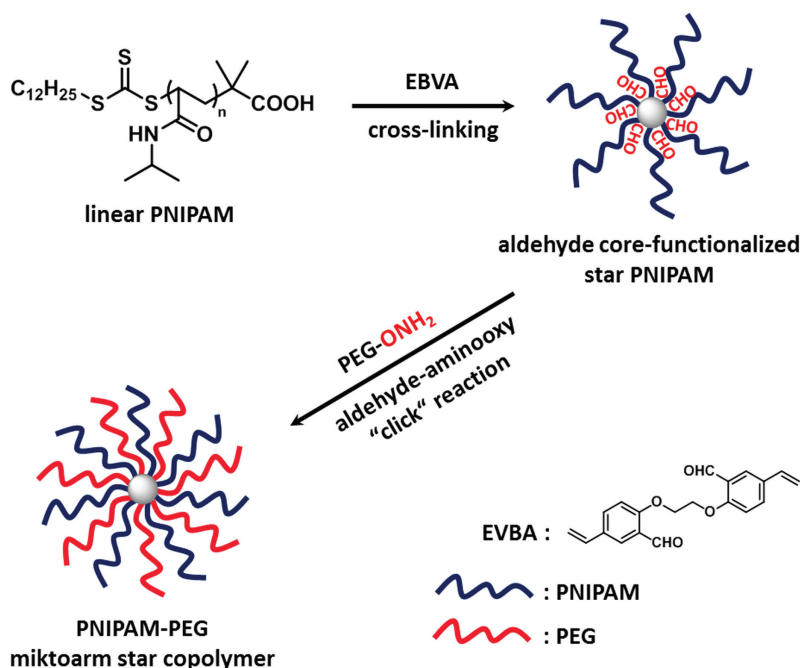
FIGURE 9 Schematic Representation of the Synthesis of PNIPAM-PEG Miktoarm Star Copolymers via Combination of RAFT Polymerization and Aldehyde-Aminooxy Click Reaction.[82]

block copolymer micelles and, as such, afford novel opportunities for chemical functionalization, templating, and encapsulation.[78] Indeed, several research groups reported that CCS polymers containing the arms of PNIPAAm were prepared via the RAFT polymerization method showing interesting behavior.[79] A facile synthetic pathway to PNIPAAm-PEG miktoarm star copolymers with multiple arms has been developed by combining RAFT polymerization and aldehyde-aminooxy "click" coupling reaction. The polymer was then used as a multifunctional coupling agent for the subsequent formation of the second-generation PEG arms via the click coupling reaction between its aldehyde groups and aminooxy-terminated PEGs. Double-hydrophilic copolymers, comprised of two different hydrophilic segments, can self-assemble into micelle-like aggregates in water if one segment becomes hydrophobic upon external stimulus such as a change in solution pH, temperature, and ionic strength.[80] This kind of copolymer has emerged as an important class of polymers due to their potential applications in drug delivery and as intelligent materials.[81] The thermo-responsive behavior of PNIPAAm-PEG miktoarm star copolymer with different PEG arm numbers in water showed thermo induced intermolecular or intramolecular micellization of PNIPAAm-PEG miktoarm star copolymers via controlling the content ratio of PNIPAAm and PEG, forming multimolecular micelles and unimolecular micelles, respectively (Fig. 9).[82] Highly reactive aldehyde functions in the arms of the star polymer could provide the key intermediates to conjugate biomolecules. The conjugation with an aminooxy functionalized BSA model protein was an example of how the star polymer can be utilized to conjugate bioactive molecules, constructing fluorescently labeled "smart" polymerprotein conjugates.[83]

The structural features of stimuli-responsive CCS polymers are defined by a core consisting of crosslinked polymer chains surrounded by a corona of polymeric arms. Much of the interest in CCS polymers is as a consequence of their architectures, possessing crosslinked cores which can be utilized as carriers for small molecules such as drugs or fragrances, and coronal chains which help to solubilize and shield the cargo from its external environment. Dual stimuli-responsive water-soluble CCS polymers which are prepared from crosslinking polymer chains possessing amino and aldehyde functions through the formation of dynamic covalent imine bonds have been prepared. The reversible nature of this bond allows the position of the imine equilibrium to be modulated by changing the pH, as imine formation is favored at high pH and disfavored at low pH. Consequently, the assembly and disassembly of aqueous solutions of the CCS polymer can be triggered simply by changing the pH, a process which can lead to the release of hydrophobic dye molecules complexed within the polymer cores.[84]

A new method for synthesis of smart nanohydrogels under additives-free conditions and at high solid content has been presented. The new core–shell nanohydrogels with crosslinked PNIPAAm core and hydrophilic poly(glycidol) (PGl) shell were obtained by photo crosslinking of PGl-b-PNIPAAm copolymers above their phase transition temperature (T_c). As UV-active group, the chromophore 2-(dimethylmaleimido)-N-ethylacrylamide (DMIAAm) was synthesized and successfully incorporated in the PNIPAAm segment, while poly(glycidol) chains were responsible for stability of aggregates above T_c.[85] PBMA-PCEMA block copolymer micelles, consisting of poly(2-cinnamoyloxyethyl methacrylate) (PCEMA) crosslinked core
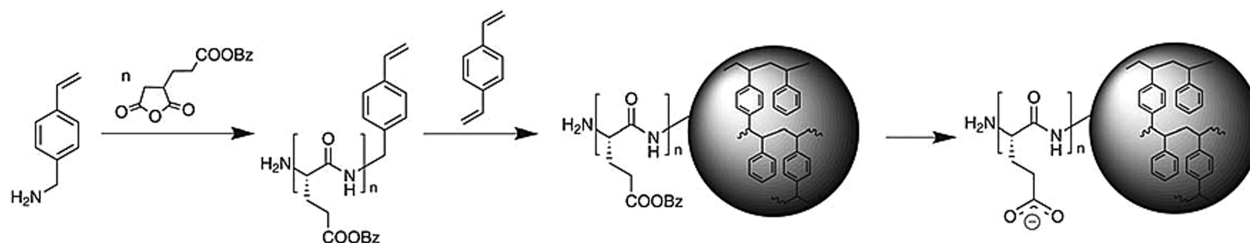
FIGURE 10 Synthesis of peptide star-polymers by the macromonomer approach: (1) Synthesis of PBLG macromonomer with styrene end-groups; (2) Radical polymerization (FRP or RAFT) in the presence of DVB. (3) Crosslinking of block copolymers in the presence of DVB; and (3) Deprotection of PBLG shell (Reproduced from Ref. 90, with permission from Copyright©2010 WileyPeriodicals).

and poly(butyl methacrylate) (PBMA) hairs (shell), are used as model responsive soft colloids, where the core swelling can be tuned by changing solvent quality. The advantage of this particular system is the ability to vary its size (and thus the volume fraction in a suspension of constant mass concentration) by changing the solvent or the temperature, making it responsive in different environments.[86] The synthesis of spherical surface-functionalized organic nanoparticles has been accomplished using reactive diblock copolymer micelles as precursor. Well-defined poly(4-vinylbenzocyclobutene-b-butadiene) diblock copolymers were prepared using living anionic polymerization, and micelles of these diblock copolymers were formed. Thermal crosslinking of benzocyclobutene pendants at the core of the micelles was accomplished at different temperatures. Ozonolysis of the crosslinked micelles produced insoluble nanoparticles with aldehyde functional groups at the surface.[87]

Thiol-yne photochemistry was applied for simultaneous functionalization and crosslinking of the core of poly(2-(3-butinyl)−2-oxazoline)-block-poly(2-ethyl-2-oxazoline) micelles in water to yield functional star polymers. The micelles of poly(2-(3-butinyl)−2-oxazoline)-block-poly-(2-ethyl-2-oxazoline) were simultaneously functionalized and crosslinked by thiol-yne photochemistry in water to yield well defined star polymers. Star polymer samples with core-confined carboxylate or amine groups exhibited stimuli-responsive properties and were sensitive to changes in temperature, pH, ionic strength, and nature of the salt.[88]

Free radical and RAFT polymerization of poly(benzyl-L-glutamate) (PBLG) macromonomers in the presence of divinyl benzene produced star polymers of various molecular weights, polydispersity, and yield depending on the reaction conditions applied. The highest molecular weight (M_w) of 10,170,000 g/mol was obtained in a free-radical multibatch approach. It was shown that the PBLG star polymers can be deprotected to obtain poly(glutamic acid) star polymers, which form water soluble pH responsive nanoparticles. Synthetic polypeptides are of interest because they are synthetically readily accessible by the controlled ring-opening polymerization of amino acid N-carboxyanhydrides (NCA).[89] Star polymer formation occurs through propagation when the CRP is continued from the macroinitiator in the presence of multifunctional

monomers connecting a precise number of arms to a central core molecule. An alternative to the macroinitiator route is the macromonomer (MM) approach. In this method, the number of initiating sites and arms are independently controlled. Therefore, the number of initiating sites per star polymer may be smaller than the number of arms when a lower molar ratio of initiator to MM is used. Lower number of initiating sites in the star core decreases the possibility of star–star reactions and results in the formation of star polymers with narrow molecular weight distribution (Fig. 10).[90]

A poly(n-butyl acrylate)-based star polymer was synthesized by ATRP using a modified core-first method. Further polymerization of a disulfide (SS) crosslinking agent bis(2-methacryloyloxyethyl) disulfide from the arm end produced a SS crosslinked star polymer. The disulfide functionality could be cleaved via reducing reactions, generating individual stars containing SH groups at the chain ends. The transformation between SS-crosslinked star and SH-star was reversible via repetitive reduction and oxidation. The results showed that SS-functionalized star polymers respond to reduction oxidation conditions, indicating that the disulfide bonds do cleave and re-form. These stimuli responsive star polymers have potential utility as intelligent polymeric materials such as self-healing materials (Fig. 11).[91] A similar approach for the synthesis of well-defined multistar assemblies (in which the stars contain crosslinked cores) involving the ATRP of macroinitiators (MIs) and crosslinker with the use of telechelic macroinitiators (TMIs) as the connecting blocks was also described.[92]

A series of disulfide-core-crosslinked poly(ethylene glycol)-poly(amino acid)s star copolymers were synthesized through one-step ring-opening polymerization of L-phenylalanine N-carboxyanhydride (LPheNCA) and L-cystine N-carboxyanhydride (L-CysNCA) with amino group terminated poly(ethylene glycol) monomethyl ether (mPEG-NH$_2$) as macroinitiator. The *in vitro* release results revealed that the release behaviors could be adjusted by glutathione concentration, and poly (amino acid)s content and composition.[93] Well defined, narrow polydispersity, "arm-first" star polymers were made by RAFT polymerization using poorly soluble crosslinked cores for a range of polymers POEGA, PNIPAAm, and PtBA. The approach described in this article involves a highly efficient
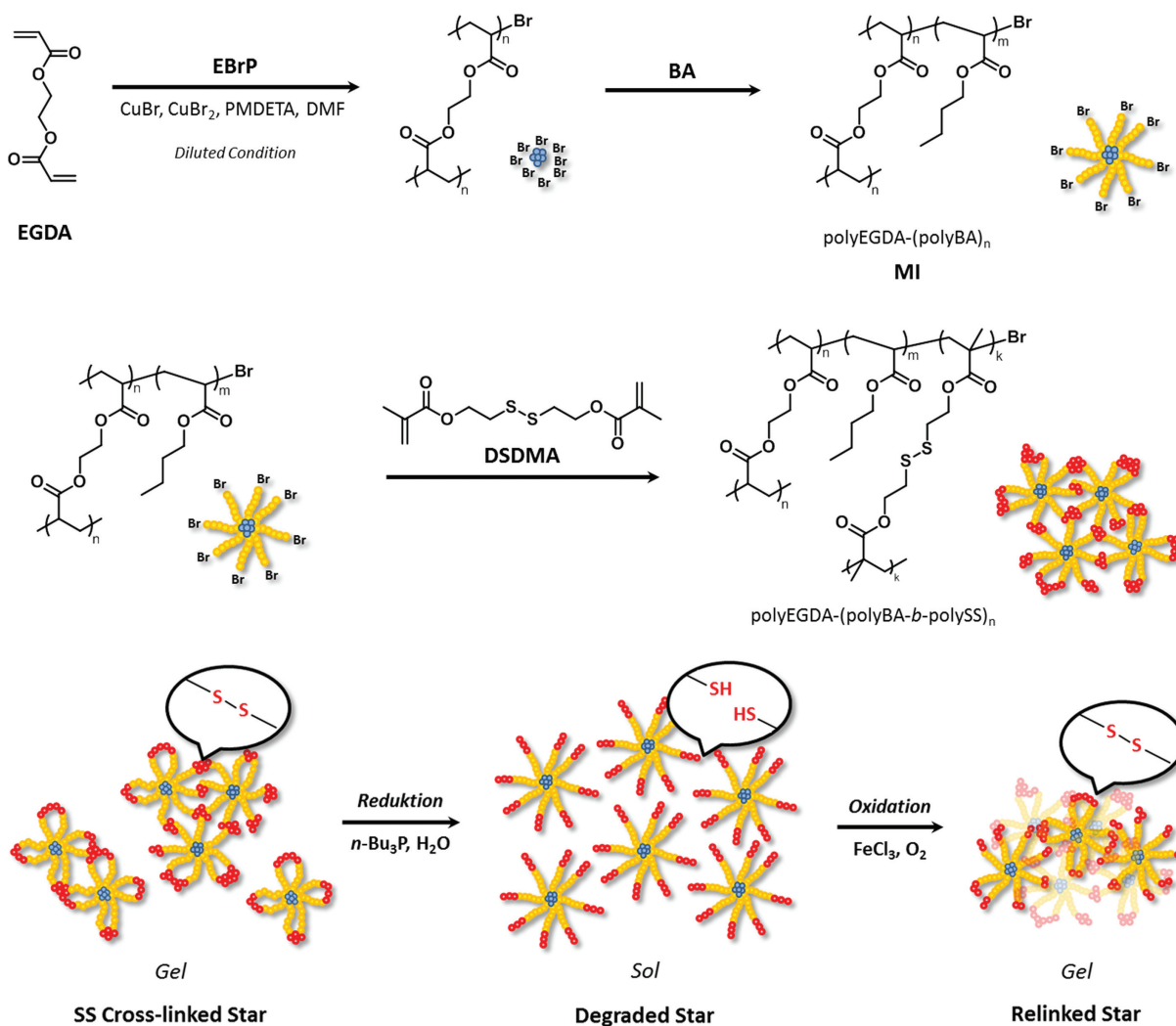
FIGURE 11 Synthesis of SS-functionalized star polymer (top) and reduction and oxidation of SH/SS-functionalized star polymers (bottom).[91]

incorporation of arms into the star polymer structures (close to quantitative yields for molecular weight arms less than 20,000 g/mol). In contrast, when a fully solvent compatible crosslinked core is used, a significantly reduced incorporation of arm polymers into the star structures and molecular weight broadening were observed.[94]

Multifunctional microgel-core star polymers with ruthenium catalysts are designed as catalyst-bearing nanoreactors to improve activity, controllability, and functionality tolerance in living radical polymerization. Multifunctional ligands are efficiently incorporated into the core of star polymers by sequential tandem procedures: (1) ruthenium-catalyzed living radical polymerization, (2) in situ core hydrogenation, and (3) core-ruthenium removal. Typically, the star polymer ligands comprising multiple phosphines and amines within the core cooperatively enclose a ruthenium complex (>100 per core). As a result, the in-core pseudo hetero *P,N*-chelation of the ruthenium complexes not only showed high activity for methyl methacrylate but also high tolerance to

unprotected methacrylic acid.[95] Statistical copolymers are reactivated to prepare amphiphilic block copolymers and star polymers with crosslinked core. The LCST is maintained by varying the architecture; however, the LCST originated behavior changes due to self-aggregation. Statistical copolymers and short block copolymers show complex aggregation, whereas midsize block copolymers and star polymers show shrinkage of aggregate dimensions.[96]

Comb Polymers

The direct dispersion approach is a convenient and simple method to form star shaped polymer structures. Therefore, amphiphilic comb copolymers are dispersed in aqueous solution to yield nanoobjects. Amphiphilic PDMS-containing poly(ether amine) (PDMS-g-PEA) synthesized through one-pot condensation polymerization of commercial di-epoxy and amine monomers could be dispersed directly in aqueous solution to form stable uniform-sized nanoobjectes with a diameter of about 16 nm, whose aggregation is responsive to temperature, pH and ionic strength with tunable cloud point

(T_c).[97] PDMS-g-PEA nanoparticles are composed of hydrophobic PDMS and PPO as their core and a hydrophilic part (EO co PPO) as the outer shell. The hydrophilic outer shell optimizes the surface contacting with water and prevents the star shaped nanoparticle from aggregating further. With an increase in temperature, the hydrogen bonds between the water molecules and the hydrophilic part are destroyed. The outer shell becomes less hydrophilic, leading to the aggregation of PDMS-g-PEA nanoparticles. The responsive nanoparticles of PDMS-g-PEA possessed the unique selective encapsulation of water-soluble dye.

As a hybrid of star and comb structure a series of water-soluble star brush copolymers with four arms consisting of PEO as the backbone and PAAc as side chains with different grafting density were prepared by sequential anionic copolymerization and then ATRP.[98] Comb structures can also be used to prepare double responsive polymers. The results for chitosan- based materials have recently been highlighted.[99] Poly(2-vinylpyridine) (P2VP) containing functionalized end groups was synthesized using nitroxyl-mediated radical polymerization with a hydroxy-functionalized stable free radical. The transformation of the hydroxy groups to an acrylic ester led to the formation of macromonomers. A free-radical copolymerization of these macromonomers with NIPAAm gave a graft copolymer with a PNIPAAm backbone and P2VP side chains.[100] The preparation of temperature-responsive colloidal nanogels with a pH-responsive shell could be achieved by photo-cross-linking of PNIPAAm graft terpolymers. The resulting solutions of nanogel with temperature responsive core and chemically bounded P2VP arms exhibited more stability upon heating and low pH as compared to the corresponding PNIPAAm nanogels. A large transition of the average hydrodynamic diameter of the gels could be observed by increasing either the temperature above 32 °C or the pH above 5.[101]

Application of Stimuli-Responsive Star Polymers

Star polymers with globular architecture and multiple arms are among the simplest forms of polymers with branched topologies. The combination of their unique architecture and high local densities of active functional groups makes star polymers unique candidates for a diverse range of applications, including drug delivery[102] and advanced coatings. Their unique solution properties and high functionality also make them attractive building blocks for the preparation of nanostructured thin films.

Specifically, two types of highly defined, high charge density star polymers with oppositely charged arm structures were prepared: PDMAEMA star and PAAc star polymers with crosslinked cores. Star polymers with precisely controlled structures were synthesized via ATRP using the one-pot arm-first method. By exploiting the electrostatic interactions between the polyelectrolyte arms, the PDMAEMA star and PAAc star polymers were integrated within alternating multilayer thin films using layer-by-layer (LbL) assembly to generate all-star polyelectrolyte LbL films. The prepared star/star

multilayer films illustrate nonuniform and nanoporous structures, which result from the characteristic architecture of star polymers.[103] In solution PAAc star polyelectrolyte displayed pH-responsive behavior, as studied by dynamic light scattering, where a reversible size change was observed in response to pH changes. At pH 8–10, the acrylic acid segments are fully charged, adopting a more stretched conformation, and larger diameters (~30 nm) were observed. When the pH decreases, and associated protonation of the acid segments occurs, the PAA chains adopt a more coiled conformation, and the diameters decrease to ~23 nm at pH 2. At pH 11, the star polymer adopted a stretched conformation and smoother films were obtained, whereas at pH 2, grain domains were visible and comparatively rougher films were formed.[104] Heteroarm star block copolymers made from seven PS and seven P2VP arms were grafted onto a solid substrate to fabricate a responsive polymer surface consisting of a densely packed monolayer of copolymer molecules. The grafted layer demonstrates a two-level hierarchical response upon external stimuli combining core–shell transitions of single stars with cooperative transitions of the interacting arms between "dimple" and "ripple" morphologies of the monolayer. The response allows for the switching of the surface properties upon changing solvent selectivity or pH of the aqueous environment.[105] The assembly of structures, molecule by molecule, into a defined macroscopic or mesoscale object is known as the "bottom-up" approach to nanomanufacturing. A bottom-up route to unimolecular micellar star polymers using ruthenium-catalyzed ring-opening-metathesis polymerization (ROMP) is used to provide a controlled templating effect during the thermal cure of amorphous silsesquioxane derivatives. The unimolecular nature of the polymeric micellar materials eliminates the complex dynamic assembly characterizing most amphiphilic systems. Porogen burnout results in nanoporous films where the pore sizes and distributions reflect the dimensions of single polymer molecules.[106]

Amphiphilic star polymers offer substantial promise for a range of drug delivery applications owing to their ability to encapsulate guest molecules.[107] Star polymers whose core consisted of either PS or PnBA, having different glass-transition (T_g) values, were used as macroinitiators in the polymerization of the cationic DMAEMA. Glassy state of the star-shaped architecture decreased the DNA transfection compared with the rubbery polymer structures.[108] Cation-condensed microgel-core star polymers with PEG-based arms were designed as unimolecular polycationic nanocapsules (hosts) to encapsulate and stimuli-responsively release hydrophilic and anionic dyes (guests) in water. The efficient dye encapsulation is due to the high concentration of quaternary ammonium cations in the core.[109] Poly(oligoethylene glycol) methyl ether acrylate was polymerized via RAFT, and then chain extended in the presence of both a crosslinker and vinyl benzaldehyde (VBA), yielding monodisperse star polymers. The sizes of the stars are typically around 20 nm, a size ideal for tumor site accumulation via the enhanced permeation retention effect. The presence of aldehyde groups in the core was exploited to

attach doxorubicin. The drug loading was controlled by the amount of VBA incorporated (until 28 wt % in drug). The doxorubicin release was studied at pH = 5.5 and 7.4; conditions representative of endosomal and extra cellular environments. In vitro studies revealed that the doxorubicin-conjugated star polymers had a level of cytotoxicity comparable to that found for free doxorubicin.[110]

CONCLUSIONS

In recent years, the continuous development of the controlled polymerization methods enabled a great progress of macromolecular engineering. Of particular interest has been the development of star-shaped macromolecules with special architectures, for example, different kinds of blocks in different topologies showing stimuli-responsive behavior. Such polymers, for example, are able to mimic biopolymers and biological systems. The spontaneous self-organization of those polymers by a variety of stimuli, for example, temperature and pH value have led to the formation of micellar aggregates with differing properties compared to their linear counterparts. The effects of branching on stimuli responsive polymers are an important issue since the polymer topology can have a significant influence on the response behavior. Morphological variations can be achieved by varying the arm length or composition. For instance, if the stimuli-responsive block constitutes the inner part of the star aggregation to larger self-assemblies occur, whereas for star block copolymers with an outer stimuli-responsive block self-organization to a 3D network can be observed. Three different methods have been established to synthesize star polymers: the "core-first" method providing well-defined star macromolecules by growing arms from a multifunctional initiator, the "arm-first" method forming stars by crosslinking linear arm precursors using a crosslinker, and the "coupling-onto" method attaching linear arm precursors onto a well-defined multifunctional core. Because of the large diversity of macromolecules adopting star architecture, the establishment of structure-property relationships such as, number of arms, arm length, segment topology, and specific functionality of each arm/block, with the self-assembly and responsive properties in aqueous media, will need much more work to be devoted to this topic to fully understand these relationships. The combination of their unique architecture and high local density of active functional groups makes star polymers unique candidates for a diverse range of applications, including drug delivery and advanced coatings. Hence, the goal of designing stars with tunable properties for specific applications currently remains an attractive challenge.

REFERENCES AND NOTES

1 D. Roy, J. N. Cambre, B. S. Sumerlin, *Prog. Polym. Sci.* **2010**, *35*, 278–301.

2 D. Kuckling, *Colloid Polym. Sci.* **2009**, *287*, 881–891.

3 A. S. Hoffman, P. S. Stayton, V. Bulmus, G. Chen, J. Chen, C. Cheung, A. Chilkoti, Z. Ding, L. Dong, R. Fong, C. A. Lackey, C.

J. Long, M. Miura, J. E. Morris, N. Murthy, Y. Nabeshima, T. G. Park, O. W. Press, T. Shimoboji, S. Shoemaker, H. J. Yang, N. Monji, R. C. Nowinski, C. A. Cole, J. H. Priest, J. M. Harris, K. Nakamae, T. Nishino, T. Miyata, *J. Biomed. Mater. Res.* **2000**, *52*, 577–586.

4 D. Schmaljohann, *Adv. Drug Del. Rev.* **2006**, *58*, 1655–1670.

5 A. K. Bajpai, S. K. Shukla, S. Bhanu, S. Kankane, *Progr. Polym. Sci.* **2008**, *33*, 1088–1118.

6 J. J. Lai, K. E. Nelson, M. A. Nash, A. S. Hoffman, P. Yager, P. S. Stayton, *Lab Chip* **2009**, *9*, 1997–2002.

7 M. A. Cohen Stuart, W. T. S. Huck, J. Genzer, M. Müller, C. Ober, M. Stamm, G. B. Sukhorukov, I. Szleifer, V. V. Tsurkruk, M. Urban, F. Winnik, S. Zauscher, I. Luzinov, S. Minko, *Nat. Mater.* **2010**, *9*, 101–113.

8 H. G. Börner, H. Kühnle, J. Hentschel, *J. Polym. Sci. Part A: Polym. Chem.* **2010**, *48*, 1–14.

9 M. Guenther, D. Kuckling, C. Corten, G. Gerlach, J. Sorber, G. Suchaneck, K.-F. Arndt, *Sens. Actuators* **2007**, *126*, 97–106.

10 C. Wang, A. Javadi, M. Ghaffari, S. Gong, *Biomaterials* **2010**, *31*, 4944–4951.

11 A. Fernández-Barbero, I. J. Suárez, B. Sierra-Martín, A. Fernández-Nieves, F. J. de las Nieves, M. Marquez, J. Rubio-Retama, E. López-Cabarcos, *Adv. Colloid. Interface Sci.* **2009**, 147–148, 88–108.

12 I. Tokarev, M. Motornov, S. Minko, *J. Mater. Chem.* **2009**, *19*, 6932–6948.

13 P. M. Mendes, *Chem. Soc. Rev.* **2008**, *37*, 2512–2529.

14 A. P. Vogt, B. S. Sumerlin, *Macromolecules* **2008**, *41*, 7368–7373.

15 S. Carter, B. Hunt, S. Rimmer, *Macromolecules* **2005**, *38*, 4595–4603.

16 S. Carter, S. Rimmer, R. Rutkaite, L. Swanson, J. P. A. Fairclough, A. Sturdy, M. Webb, *Biomacromolecules* **2006**, *7*, 1124–1130.

17 G. Lapienis, *Prog. Polym. Sci.* **2009**, *34*, 852–892.

18 K. Matyjaszewski, P. J. Miller, E. Fossum, Y. Nakagawa, *Appl. Organomet. Chem.* **1998**, *12*, 667–673.

19 D. Taton, Y. Gnanou, R. Matmour, S. Angot, S. Hou, R. Francis, B. Lepoittevin, D. Moinard, J. Babin, *Polym. Int.* **2006**, *55*, 1138–1145.

20 N. Hadjichristidis, M. Pitsikalis, S. Pispas, H. Iatrou, *Chem. Rev.* **2001**, *101*, 3747–3792.

21 W. A. Braunecker, K. Matyjaszewski, *Prog. Polym. Sci.* **2007**, *32*, 93–146.

22 N. Hadjichristidis, H. Iatrou, M. Pitsikalis, J. Mays, *Prog. Polym. Sci.* **2006**, *31*, 1068–1132.

23 A. Blencowe, J. F. Tan, T. K. Goh, G. G. Qiao, *Polymer* **2009**, *50*, 5–32.

24 M. Kamigaito, T. Ando, M. Sawamoto, *Chem. Rev.* **2001**, *101*, 3689–3745.

25 N. V. Tsarevsky, K. Matyjaszewski, *Chem. Rev.* **2007**, *107*, 2270–2299.

26 S. Abraham, J. H. Choi, C.-S. Ha, I. Kim, *J. Polym Sci. Part A: Polym. Chem.* **2007**, *45*, 5559–5572.

27 M. Stenzel-Rosenbaum, T. P. Davis, V. Chen, A. G. Fane, *J. Polym Sci. Part A: Polym. Chem.* **2001**, *39*, 2777–2783.

28 S. Angot, K. S. Murthy, D. Taton, Y. Gnanou, *Macromolecules* **1998**, *31*, 7218–7225.

29 H. Gao, K. Matyjaszewski, *Macromolecules* **2008**, *41*, 1118–1125.

30 X. Zhang, J. Xia, K. Matyjaszewski, *Macromolecules* **2000**, *33*, 2340–2345.

31 Y. Amamoto, Y. Higaki, Y. Matsuda, H. Otsuka, A. Takahara, *J. Am. Chem. Soc.* **2007**, *129*, 13298–13304.

32 H. Gao, K. Min, K. Matyjaszewski, *Macromol. Chem. Phys.* **2007**, *208*, 1370–1378.

33 J. Li, H. Xiao, Y. S. Kim, T. L. Lowe, *J Polym. Sci. Part A: Polym. Chem.* **2005**, *43*, 6345–6354.

34 B. Mendrek, B. Trzebicka, W. Walach, A. Dworak, *Eur. Polym. J.* **2010**, *46*, 2341–2351.

35 R. Plummer, D. T. J. Hill, A. K. Whittaker, *Macromolecules* **2006**, *39*, 8379–8388.

36 J. Xu, S. Liu, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 404–419.

37 Y.-Y. Liu, Y.-B. Zhong, J.-K. Nan, W. Tian, *Macromolecules* **2010**, *43*, 10221–10230.

38 Z.-X. Zhang, X. Liu, F. J. Xu, X. J. Loh, E.-T. Kang, K.-G. Neoh, J. Li, *Macromolecules* **2008**, *41*, 5967–5970.

39 S. Luo, J. Xu, Z. Zhu, C. Wu, S. Liu, *J. Phys. Chem. B* **2006**, *110*, 9132–9139.

40 L. Ma, H. Geng, J. Song, J. Li, G. Chen, Q. Li, *J. Phys. Chem. B* **2011**, *115*, 10586–10591.

41 A. Schmalz, M. Hanisch, H. Schmalz, A. H. E. Müller, *Polymer* **2010**, *51*, 1213–1217.

42 C. Ni, G. Wu, C. Zhu, B. Yao, *J. Phys. Chem. C* **2010**, *114*, 13471–13476.

43 R. H. Lambeth, S. Ramakrishnan, R. Müller, J. P. Poziemski, G. S. Miguel, L. J. Markoski, C. F. Zukoski, J. S. Moore, *Langmuir* **2006**, *22*,6352–6360.

44 Z. Cao, W Liu, G. Ye, X. Zhao, X. Lin, P. Gao, K. Yao, *Macromol. Chem. Phys.* **2006**, *207*, 2329–2335.

45 H. Zhang, Q. Yan, Y. Kang, L. Zhou, H. Zhou, J. Yuan, S. Wu, *Polymer* **2012**, *53*, 3719–3725.

46 H.-H. Lin, Y.-L. Cheng, *Macromolecules* **2001**, *34*, 3710–3715.

47 A. Schmalz, H. Schmalz, A. H. E. Müller, *Soft Matter* **2012**, *8*, 9436–9445.

48 J. Xu, S. Luo, W. Shi, S. Liu, *Langmuir* **2006**, *22*, 989–997.

49 C. Ni, G. Wu, C. Zhu, B. Yao, *J. Phys. Chem. C* **2010**, *114*, 13471–13476.

50 Y. Bai, J. Wei, L. Yang, C. He, X. Lu, *Colloid Polym. Sci.* **2012**, *290*, 507–515.

51 E. He, P. Ravi, K. C. Tam, *Langmuir* **2007**, *23*, 2382–2388.

52 X. Zhang, Y. Xiao, M. Lang, *J. Macromol. Sci. Part A: Pure Appl. Chem.* **2012**, *49*, 124–130.

53 W. Zhu, A. Nese, K. Matyjaszewski, *J. Polym. Sci. Part A: Polym. Chem.* **2011**, *49*, 1942–1952.

54 O. G. Schramm, M. A. R. Meier, R. Hoogenboom, H. P. van Erp, J.-F. Gohy, U. S. Schubert, *Soft Matters* **2009**, *5*, 1662–1667.

55 D. Kul, L. M. van Renterghem, A. A. R. Meier, S. Strandman, H. Tenhu, S. S. Yilmaz, U. S. Schubert, F. E. du Prez, *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 650–660.

56 T. Ren, A. Wang, W. Yuan, L. Li, Y. Feng, *J. Polym. Sci. Part A: Polym. Chem.* **2011**, *49*, 2303–2313.

57 T. Higashihara, M. Hayashi, A. Hirao, *Prog. Polym. Sci.* **2011**, *36*, 323–375.

58 N. Hadjichristidis, *J. Polym. Sci. Part A: Polym. Chem.* **1999**, *37*, 857–871.

59 Z. Iatridi, C. Tsitsilianis, *Polymers* **2011**, *3*, 1911–1933.

60 J. Babin, C. Leroy, S. Lecommandoux, R. Borsali, Y. Gnanou, D. Taton, *Chem. Commun.* **2005**, 1993–1995.

61 C.-G. Mu, X.-D. Fan, W. Tian, Y. Bai, X. Zhou, *Polym. Chem.* **2012**, *3*, 1137–1149.

62 X. Tang, X. Liang, Q. Yang, X. Fan, Z. Shen, Q. Zhou, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 4420–4427.

63 W. Zhang, W. Zhang, Z. Zhang, Z. Cheng, Y. Tu, X. Zhu, *J. Polym. Sci. Part A: Polym. Chem.* **2010**, *48*, 4268–4278.

64 X.-S. Feng, C.-Y. Pan, *Macromolecules* **2002**, *35*, 4888–4893.

65 Y. Zhang, H. Liu, H. Dong, C. Li, S. Liu, *J. Polym. Sci. Part A: Polym. Chem.* **2009**, *47*, 1636–1650.

66 Y. Zhang, H. Liu, J. Hu, C. Li, S.Y. Liu, *Macromol. Rapid Commun.* **2009**, *30*, 941–947.

67 Z. Ge, J. Xu, J. Hu, Y. Zhang, S. Liu, *Soft Matter* **2009**, *5*, 3932–3939.

68 F. A. Plamper, J. R. McKee, A. Laukkanen, A. Nykänen, A. Walther, J. Ruokolainen, V. Aseyev, H. Tenhu, *Soft Matter* **2009**, *5*, 1812–1821.

69 X. Wang, J. He, Y. Yang, *J. Polym. Sci. Part A: Polym. Chem.* **2007**, *45*, 4818–4828.

70 K. Ranganathan, R. Deng, R. K. Kainthan, C. Wu, D. E. Brooks, J. N. Kizhakkedathu, *Macromolecules* **2008**, *41*, 4226–4234.

71 Y.-Y. Yu, W.-C Chien, S.-T. Chen, *Polym. Int.* **2008**, *57*, 1369–1376.

72 I. Choi, R. Gunawidjaja, R. Suntivich, C. Tsitsilianis, V. V. Tsukruk, *Macromolecules* **2010**, *43*, 6818–6828.

73 A. W. Bosman, R. Vestberg, A. Heumann, J. M. J. Fréchet, C. J. Hawker, *J. Am. Chem. Soc.***2003**, *125*, 715–728.

74 A. Blencowe, J. F. Tan, T. K. Goh, G. G. Qiao, *Polymer* **2009**, *50*, 5–32.

75 S. Aoshima, T. Yoshida, A. Kanazawa, S. Kanaoka, *J. Polym. Sci. Part A: Polym. Chem.* **2007**, *45*, 1801–1813.

76 S. Aoshima, S. Kanaoka, *Adv. Polym. Sci.* **2008**, *210*, 169–208.

77 H. Gao, K. Matyjaszewski, *Prog. Polym. Sci* **2009**, *34*, 317–350.

78 B. Wei, P. A. Gurr, A. O. Gozen, A. Blencowe, D. H. Solomon, G. G. Qiao, R. J. Spontak, J. Genzer, *Nano Lett.* **2008**, *8*, 3010–3016.

79 G. Zheng, C. Pan, *Polymer* **2005**, *46*, 2802–2810.

80 D. Kuckling, A. Döring, F. Krahl, K.-F. Arndt, In Polymer Science: A Comprehensive Reference, K. Matyjaszewski, M. Möller, Eds.; Elsevier BV: Amsterdam, **2012**; Vol. *8*, 377–413.

81 J. J. Yan, W. X. Ji, E. Q. Chen, Z. C. Li, D. H. Liang, *Macromolecules* **2008**, *41*, 4908–4913.

82 Z. Wu, H. Liang, J. Lu, *Macromolecules* **2010**, *43*, 5699–5705.

83 K. Yang, H. Liang, J. Lu, *J. Mater. Chem.* **2011**, *21*, 10390–10398.

84 A. W. Jackson D. A. Fulton, *Chem. Commun.* **2011**, *47*, 6807–6809.

85 S. Mendrek, A. Mendrek, H.-J. Adler, A. Dworak, D. Kuckling, *Macromolecules* **2009**, *42*, 9161–9169.

86 B. Loppinet, G. Fytas, D. Vlassopoulos, C. N. Likos, G. Meier, G. J. Liu, *Macromol. Chem. Phys.* **2005**, *206*, 163–172.

87 G. Sakellariou, A. Avgeropoulos, N. Hadjichristidis, J. W. Mays, D. Baskaran, *Polymer* **2009**, *50*, 6202–6211.

88 N. ten Brummelhuis, H. Schlaad, *Polym. Chem.* **2011**, *2*, 1180–1184.

89 N. Hadjichristidis, H. Iatrou, M. Pitskalis, G. Sakellariou, *Chem. Rev.* **2009**, *109*, 5528–5578.

90 F. Audouin, R. J. I. Knoop, J. Huang, A. Heise, *J. Polym. Sci. Part A: Polym. Chem.* **2010**, *48*, 4602–4610.

91 J. Kamada, K. Koynov, C. Corten, A. Juhari, J. A. Yoon, M. W. Urban, A. C. Balazs, K. Matyjaszewski, *Macromolecules* **2010**, *43*, 4133–4139.

92 J. F. Tan, A. Blencowe, T. K. Goh, I. T. M. Dela Cruz, G. G. Qiao, *Macromolecules* **2009**, *42*, 4622–4631.

93 J. Ding, F. Shi, C. Xiao, L. Lin, L. Chen, C. He, X. Zhuang, X. Chen, *Polym. Chem.* **2011**, *2*, 2857–2864.

94 J. Ferreira, J. Syrett, M. Whittaker, D. Haddleton, T. P. Davis, C. Boyer, *Polym. Chem.* **2011**, *2*, 1671–1677.

95 T. Terashima, A. Nomura, M. Ouchi, M. Sawamoto, *Macromol. Rapid Commun.* **2012**, *33*, 833–841.

96 L. A. Picos-Corrales, A. Licea-Claverie, J. M. Cornejo-Bravo, S. Schwarz, K.-F. Arndt, *Macromol. Chem. Phys.* **2012**, *213*, 301–314.

97 C. Di, X. Jiang, R. Wang, J. Yin, *J. Mater. Chem.* **2011**, *21*, 4416–4423.

98 P. Li, Z. Li, J. Huang, *Macromolecules* **2007**, *40*, 491–498.

99 A. S. Carreira, F. A. M. M. Gonçalves, P. V. Mendonça, M. H. Gil, J. F. J. Coelho, *Carbohydr. Polym.* **2010**, *80*, 618–630.

100 S. Wohlrab, D. Kuckling, *J. Polym. Sci. Part A: Polym. Chem.* **2001**, *39*, 3797–3804.

101 D. Kuckling, C. D. Vo, S. E. Wohlrab, *Langmuir* **2002**, *18*, 4263–4269.

102 R. S. Navath, B. Wang, S. Kannan, R. Romero, R. M. Kannan, *J. Controlled Release* **2010**, *142*, 447–456.

103 B.-S. Kim, H. Gao, A. A. Argun, K. Matyjaszewski, P. T. Hammond, *Macromolecules* **2009**, *42*, 368–375.

104 L. A. Connal, Q. Li, J. F. Quinn, E. Tjipto, F. Caruso, G. G. Qiao, *Macromolecules* **2008**, *41*, 2620–2626.

105 R. Lupitskyy, Y. Roiter, C. Tsitsilianis, S. Minko, *Langmuir* **2005**, *21*, 8591–8593.

106 E. F. Connor, L. K. Sundberg, H.-C. Kim, J. J. Cornelissen, T. Magbitang, P. M. Rice, V. Y. Lee, C. J. Hawker, W. Volksen, J. L. Hedrick, R. D. Miller, *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 3785–3788.

107 D. E. Poree, M. D. Giles, L. B. Lawson, J. He, S. M. Grayson, *Biomacromolecules* **2011**, *12*, 898–906.

108 A. M. Alhoranta, J. K. Lehtinen, A. O. Urtti, S. J. Butcher, V. O. Aseyev, H. J. Tenhu, *Biomacromolecules* **2011**, *12*, 3213–3222.

109 K. Fukae, T. Terashima, M. Sawamoto, *Macromolecules* **2012**, *45*, 3377–3386.

110 J. Liu, H. Duong, M. R. Whittaker, T. P. Davis, C. Boyer, *Macromol. Rapid Commun.* **2012**, *33*, 760–766.