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REVIEW ARTICLE

Synthesis of Glycoconjugated Branched Macromolecular Architectures

By Atsushi NARUMI[1] and Toyoji KAKUCHI[2,]*

The applications developed by polymer chemistry using saccharides have significantly expanded, thus it is required that continuous efforts be made to develop routes for preparing glycoconjugated polymers as well as utilizing sugar resources for the polymer synthesis. We now provide an overview focusing on the preparations of the vinyl polymers with three-dimensional structures utilizing functionality of saccharides and the syntheses of glycoconjugated branched vinyl polymers. As the first topic, we describe that star-like reversed-type polymeric aggregates have been generated by end-functionalized polymers with saccharides, in which the functionalities of malto-oligosaccharides have been utilized to control the sizes of the hydrophilic and hydrophobic domains of the aggregates. The second section describes the star polymer syntheses with the arm numbers regulated by the functionalities of glucose, inositol, sucrose, and cyclodextrins. In the last half sections, the preparations of a new class of glycoconjugates have been reviewed, which includes glycopolymer stars, hyperbranched glycopolymers, star microgels with a glycoconjugated periphery or core, and poly(vinyl saccharide) microgels.

KEY WORDS: Glycoconjugate / Glycopolymer / Star Polymer / Reversed Micelle / Hyperbranched Polymer / Microgel /

Saccharides have been recognized as important in polymer chemistry as elements for molecular and cell recognitions, strong and bio-harmless hydrophilic segments, chirality sources, and inexhaustible raw materials independent of oils. Thus, there have been numerous reports on the polymers related to saccharides especially during the past two and a half decades[1–12] as well as in the very recent years,[13–16] asymmetric polymerizations with saccharides generate main-chain chiral polymers,[17,18] and enzymatic polymerizations produce bioresorbable plastics from sugar resources.[19,20] A noteworthy progresses in the research field of glycoconjugated polymers during the past decade include the adaptation of precise polymerizations. Anionic polymerizations,[21] cationic polymerizations,[22] ring-opening metathesis polymerizations (ROMP),[23,24] and anionic ring-opening polymerizations[25] have produced glycopolymers with well-defined structures and block copolymers with the glycopolymer segments. More extensively, controlled radical polymerizations[26–34] have been applied as versatile synthetic methods for the well-defined glycopolymer, which include the cyanoxyl-mediated free-radical polymerizations,[35–37] the nitroxide-mediated controlled radical polymerization (NMP),[38–44] the atom transfer radical polymerization (ATRP),[45–50] and the reversible addition-fragmentation chain transfer (RAFT) polymerization.[51–54] For the controlled radical polymerizations, the synthesis of well-defined glycopolymers without protection and deprotection procedures[35–37,47,48,51–54] and the miniemulsion polymerization of glycomonomers[55] are current topics. A multivalent saccharide array was demonstrated for the linear and also the three-dimensional macromolecules.[56–60] Cyclodextrins have been utilized in polymer synthesis.[61] The strategies to prepare hyperbranched polysaccharides,[62,63] the synthesis of glycopolymers by post-polymerizations,[64] and the surface initiated polymerizations of the monomers featuring saccharides[16,65] have been developed. Attention has focused on glycoconjugated polymers that include sulfated saccharide-based polymers for glycosaminoglycan mimetic biomaterials,[35] glycopolymer-polypeptide hybrids for glycopeptides mimics,[37] glycoconjugated polymeric nanoparticles with therapeutic interest,[66,67] glycopolymer nanofibrous sticks for protein separations,[68] thermoresponsive glycopolymers for the control of bacterial aggregation,[15] cationic glycopolymers for DNA delivery,[69] saccharide imprinting gels for artificial antibodies,[70,71] and saccharide arrays on the backbone of π-conjugation polymers for biosensors.[72–74] As a consequence, the applications developed by polymer chemistry with saccharides have significantly expanded, therefore, it is required that continuous efforts be made to develop routes for preparing glycoconjugated polymers as well as utilizing saccharide resources for the polymer synthesis.

We now provide an overview focusing on the preparations of the vinyl polymers with three-dimensional structures utilizing saccharide functionalities and the syntheses of a new class of glycoconjugates such as branched vinyl polymers featuring saccharide segments. As the first topic, we mention that star-like reversed-type polymeric aggregates are generated by end-functionalized polymers with saccharides. The use of the functionalities of malto-oligosaccharides provides a route for imparting a definite magnitude of hydrophilicity in the

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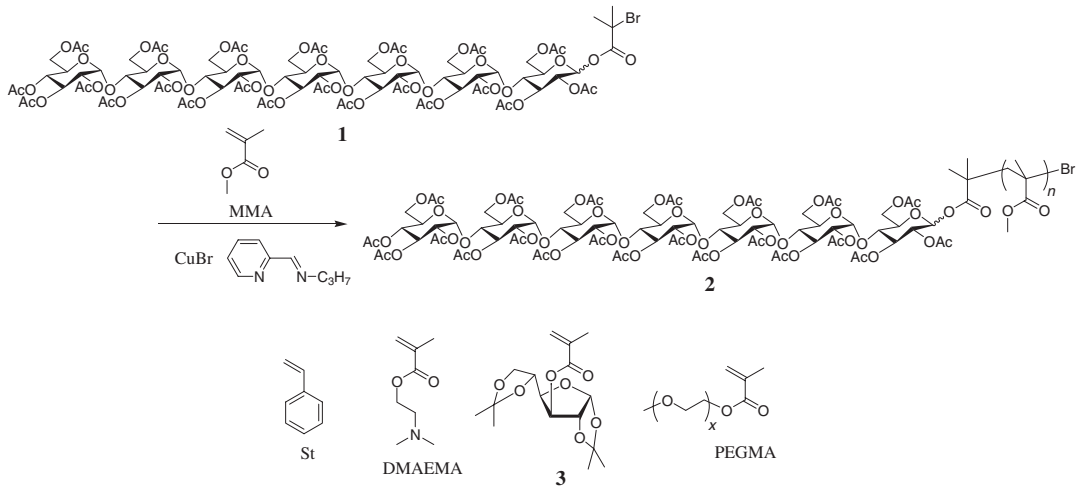
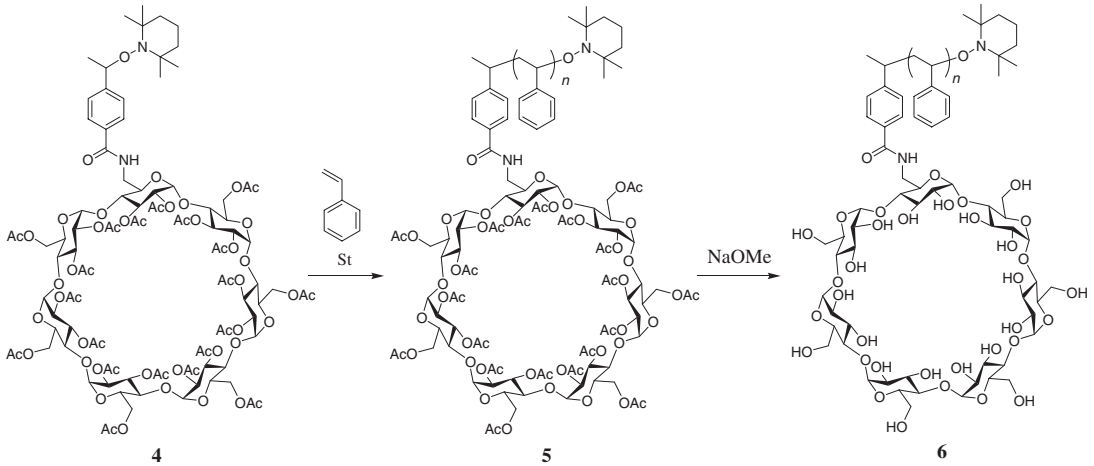
chain-end, which has advantage for tuning the size of hydrophilic/hydrophobic domain for the reversed-type polymeric aggregates. The second section describes the star polymer syntheses utilizing saccharides. The functionalities of glucose, inositol, sucrose, and cyclodextrins are used to produce star polymers with regulated arm numbers. Both the end-functionalized polymers and the star polymers viewed here were designed using living radical polymerization techniques. The living radical polymerizations have also allowed the construction of a new family of glycoconjugates, *i.e.*, branched vinyl polymers featuring saccharides. In the last half section, we review the synthesis of the glycoconjugated vinyl polymers with branched structures, such as glycopolymer stars, hyperbranched glycopolymers, star microgels with a glycoconjugated periphery or core, and poly(vinyl saccharide) microgels.

END-FUNCTIONALIZED POLYMER WITH SACCHARIDE GENERATING STAR-LIKE POLYMERIC REVERSED MICELLE

By anionic polymerizations, Hirao and co-workers[75] reported that monosaccharides were introduced into the chain-ends of polystyrene (PSt) using benzyl chloride derivatives containing acetal-protected monosaccharides as terminating agents. Furthermore, they reported that the end-functionalized PSt's with a 2, 4, 6, 8, and 12 monosaccharide residues were successfully prepared by an "iterative" approach using 1,1-diphenylethylene derivatives with 2 or 4 monosaccharide residues.[75,76] The resulting polymers showed an aggregation property to generate a reversed polymer micelle, in which the aggregation number depended on the number of the introduced monosaccharide



Scheme 1. Structure of maltoheptaose-based ATRP initiator **1** and polymerizations of methyl methacrylate (MMA) using CuBr and *N*-(*n*-propyl)-2-pyridylmethanimine producing end-functionalized polymers with oligosaccharides **2** and the structures of the other monomers polymerized by **1**, such as styrene (St), dimethylaminoethyl methacrylate (DMAEMA), the sugar-carrying methacrylate **3**, and poly(ethylene glycol) methyl ether methacrylate (PMGMA).



Scheme 2. Polymerization of styrene (St) with 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-adduct featuring acetylated *β*-cyclodextrin **4** and subsequent deprotection producing end-functionalized polystyrene (PSt) with *β*-cyclodextrin **6**.

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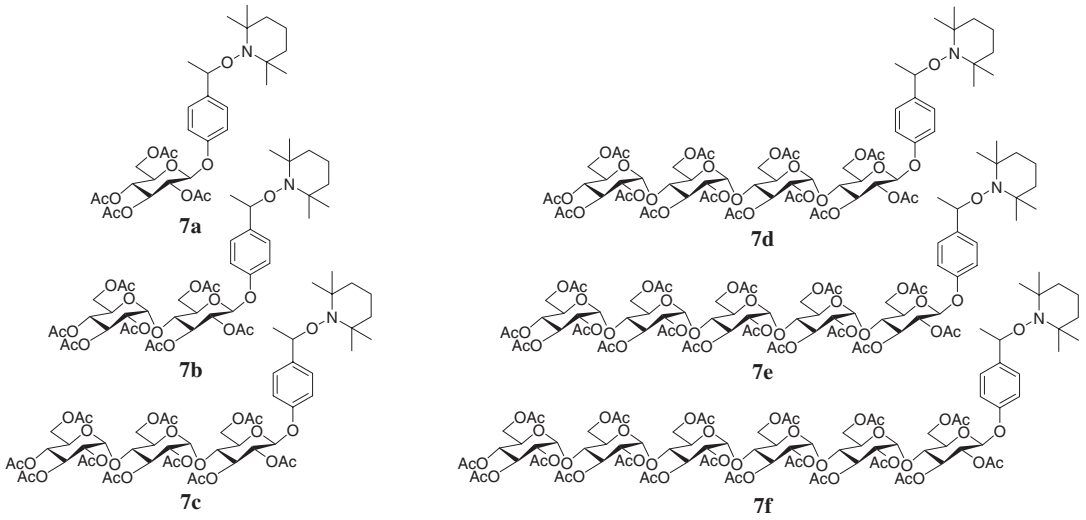
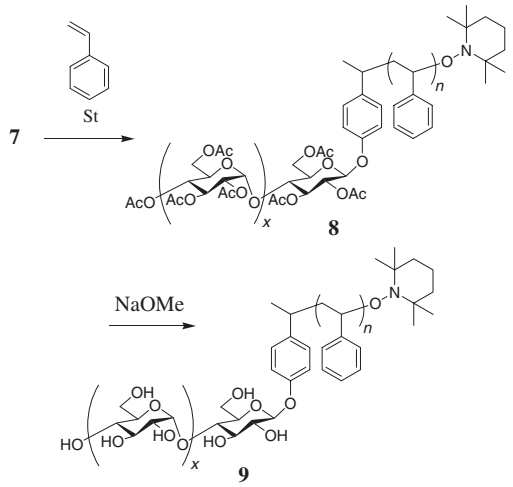


Scheme 3. Structures of the 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-adducts featuring acetylated saccharides based on glucose, maltose, maltotriose, maltotetraose, maltopentaose, and maltohexaose, **7a**, **7b**, **7c**, **7d**, **7e**, and **7f**, respectively.

residues. On the other hand, initiators for the living radical polymerizations featuring oligosaccharides can provide a direct route to generate polymers with excellent end-functionality. Haddleton and Ohno[77] reported that 2-bromoisobutyl ester derivative featuring an acetylated maltoheptaose **1** was prepared and used as the initiator for the atom transfer radical polymerization (ATRP) with CuBr/*n*-propyl-2-pyridylmethanimine (Scheme 1). The polymerization of methyl methacrylate (MMA) was shown to proceed in a living fashion to produce the end-functionalized poly(methyl methacylate) (PMMA) with acetylated oligosaccharides **2**. Styrene (St), dimethylaminoethyl methacrylate (DMAEMA), the sugar-carrying methacrylate **3**, and poly(ethylene glycol) methyl ether methacrylate (PMGMA) were polymerized by **1** to prepare the corresponding end-functionalized polymers.

End-functionalized polymers with oligosaccharides *via* the nitroxide-mediated radical polymerization (NMP) have been reported by us.[78] 2,2,6,6-Tetramethylpiperidinyloxy (TEMPO)-adducts featuring acetylated β-cyclodextrin peracetate **4** was used as the initiator for the polymerization of St to produce the end-functionalized PSt with the acetylated β-cyclodextrin **5** (Scheme 2). After deacetylation, the resulting polymer **6** formed a reversed-type polymeric micelle with a PSt shell and saccharide core in a good solvent for PSt. The average aggregation numbers of the reversed-type polymeric micelle ranged from 42 to 125, thus an excellent end-modification was attained by oligosaccharides.

We used the functionalities of glucose and a series of α-1,4-linked oligosaccharides composed of glucopyranose units, *i.e.*, malto-oligosaccharides.[79] TEMPO-adducts with saccharides, such as glucose, maltose, maltotriose, maltotetraose, maltopentaose, and maltohexaose, **7a**, **7b**, **7c**, **7d**, **7e**, and **7f** (Scheme 3), respectively, were prepared by the glycosylation of 4-ethylphenol with the corresponding glycosyl trichloroacetimidates, followed by the addition of TEMPO. St was polymerized by initiators **7** to produce the well-defined end-



Scheme 4. Polymerization of styrene (St) with **7** and subsequent deacetylation producing end-functionalized polystyrenes (PSt's) with saccharides **9**, which contain 4, 7, 10, 13, 16, and 19 hydroxyl groups with glucose, maltose, maltotriose, maltotetraose, maltopentaose, and maltohexaose ($x = 0$, 1, 2, 3, 4, 5, respectively).

functionalized PSt with acetyl saccharides **8** (Scheme 4). It is known that a carbohydrate consisting of an α-1,4-linked glucopyranose, *i.e.*, amylose, is insoluble in water due to the formation of highly ordered structures such as helical ones though they possess numerous hydroxyl groups. However, malto-oligosaccharides are free from such ordered structures, thus behaving as efficient water-soluble chain-ends. In addition, the functionalities of malto-oligosaccharides with 7, 10, 13, 16, and 19 hydroxyl groups for maltose, maltotriose, maltotetraose, maltopentaose, and maltohexaose, respectively, provide a route for introducing a definite degree of hydrophilicity. After deacetylation, the glycosylated PSt's **9** generated polymeric reversed micelles with the molar masses and average aggregation numbers ranging from 75,000 to 926,000

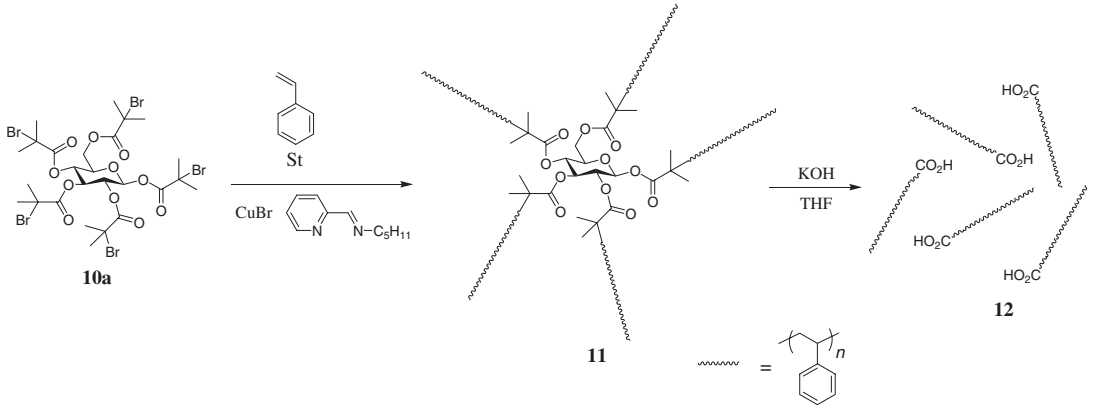
and from 7 to 146, respectively. The sizes of the hydrophilic and hydrophobic domains of the aggregates were independently tunable by controlling the degree of polymerization and the selection of the saccharides. We have now focused on applications of this strategy combined with a film forming process as a potential route for constructing a nonionic hydrophilic nanospot on the polymeric materials made by poly(vinyl chloride)s.

STAR POLYMER SYNTHESIS WITH SACCHARIDE

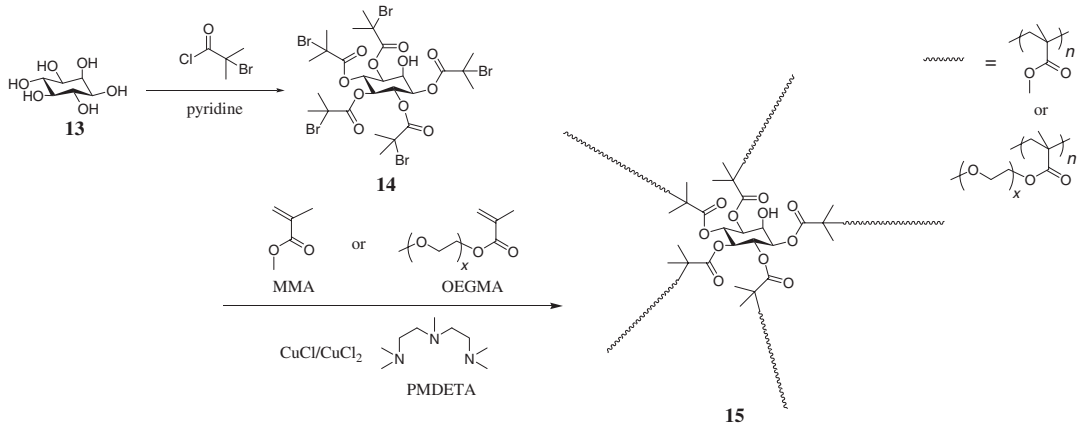
The living radical polymerizations provide routes to construct star polymers *via* two approaches: 1) synthesis of multifunctional initiators and subsequent polymerizations, namely the "core-first" method,[80–87] and 2) preparation of living arm polymers and subsequent linking reaction using a difunctional cross-linking reagent, namely the "arm-first" method.[88–94] It should be noted that ATRP with "click chemistry"[95] has been attracted attention for star polymer syntheses in recent years.[96,97] For the core-first method, saccharides are attractive in terms of their functionality with a definite number of hydroxyl groups. Furthermore, saccharides are abundant, available at low prices, and can be hydrolyzed to produce free arms so that we can well characterize the original star polymers. Haddleton and co-workers[98] reported that glucose derivative with five ATRP-initiating sites **10a** was prepared and used as the initiator for the polymerization of St using CuBr and *N*-(*n*-pentyl)-2-pyridylmethanimine (Scheme 5). The polymerization produced the PSt star **11** and the core of the star polymer was hydrolyzed by potassium hydroxide to characterize the resulting free arms **12**.

Recently, Kimani and Moratti[99] reported that *meso*-inositol **13** was modified into the initiator for ATRP (Scheme 6). Due to steric hindrance, one of the six hydroxyl groups was not esterified. MMA and oligoethylene glycol methacrylate (OEGMA) were polymerized using ATRP with $CuCl/CuCl_2$/pentamethyldiethylenetriamine (PMDETA) to produce the star polymers with five arms and one hydroxyl group in the core **15**.

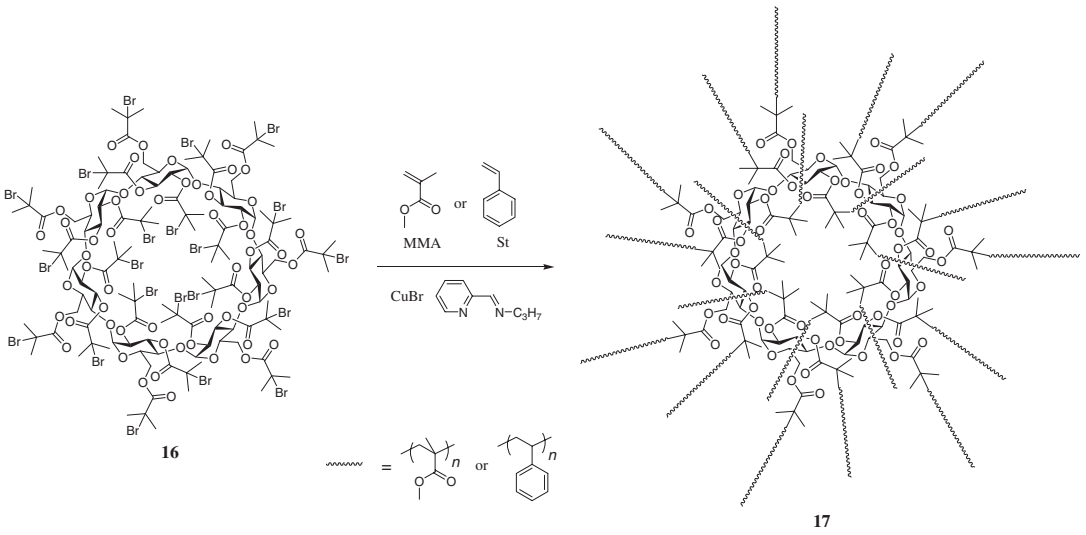
Cyclodextrins should be a suitable core-molecule, because they are cyclic molecules with multiple and definite numbers of hydroxyl groups. Haddleton and co-workers[100] reported that β-cyclodextrin derivative with 21 2-bromoisobutyl ester moieties **16** was prepared and used as the initiator for the ATRP of MMA and St to prepare the star (PMMA's) with 21-arms **17**



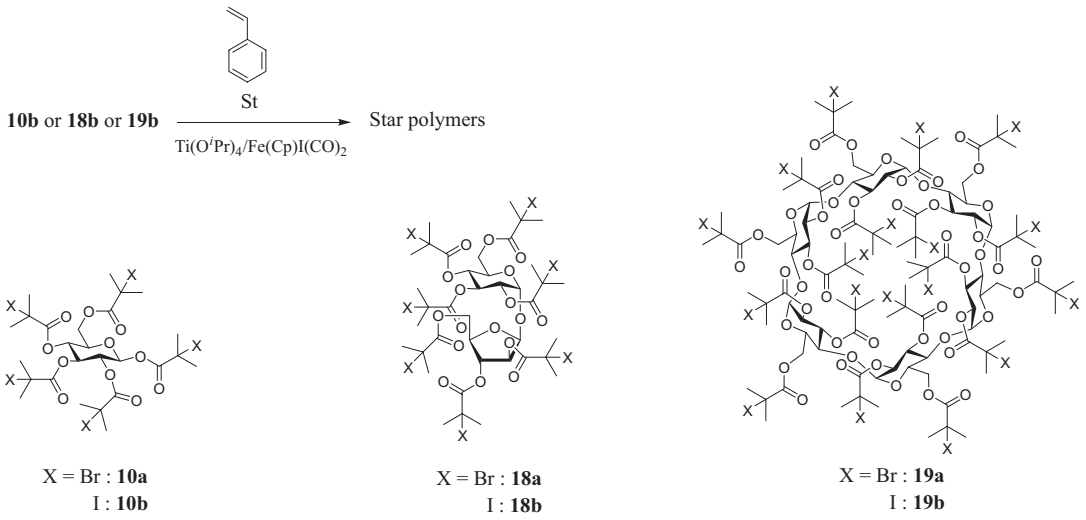
Scheme 5. Structure of glucose-based pentafunctional ATRP initiator **10a** and polymerization of styrene (St) using CuBr and *N*-(*n*-pentyl)-2-pyridylmethanimine producing the star polymer **11**, followed by hydrolysis to characterize the free arm **12**.



Scheme 6. Synthesis of *meso*-inositol-based pentafunctional ATRP initiator **14** and polymerization of methyl methacrylate (MMA) and oligoethylene glycol methacrylate (OEGMA) using $CuCl/CuCl_2$/pentamethyldiethylenetriamine (PMDETA) producing the star polymers with five arms and one hydroxyl group **15**.



Scheme 7. Structure of β-cyclodextrin derivative with 21 2-bromoisobutyl ester moieties **16** and polymerization of methyl methacrylate (MMA) or styrene (St) using CuBr and *N*-(*n*-propyl)-2-pyridylmethanimine producing the cyclodextrin-core star polymers **17**.

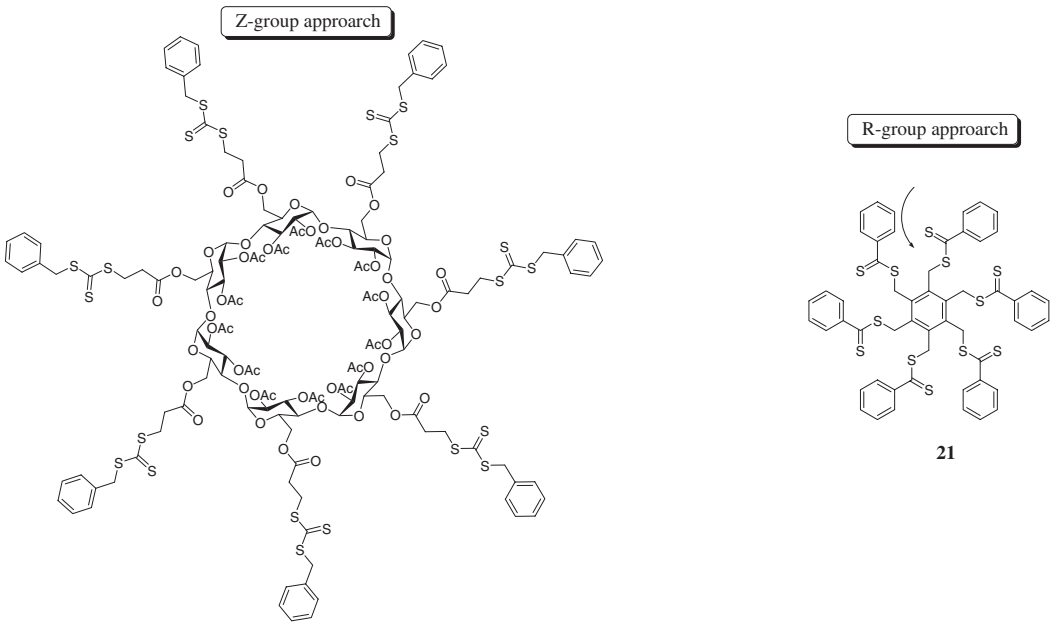


Scheme 8. Structures of glucose, sucrose, and α-cyclodextrin-based initiators, **10**, **18**, and **19**, respectively, and polymerization of styrene (St) with **10b**, **18b**, and **19b** through half-metallocene iron carbonyl complex coupled with titanium(IV) isopropoxide ($Ti(O^iPr)_4/Fe(Cp)I(CO)_2$) producing star polymers.

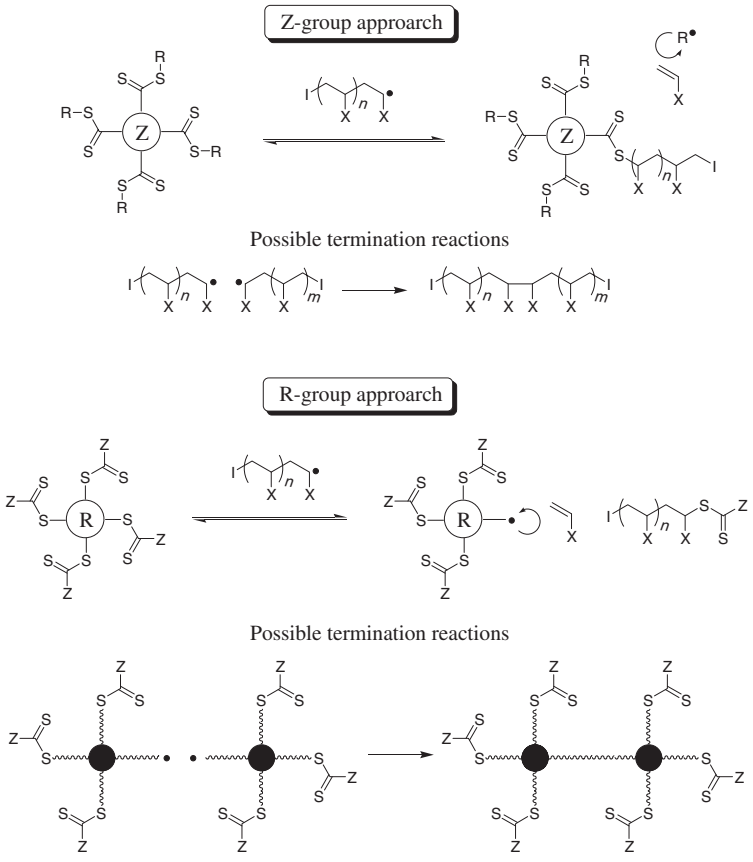
(Scheme 7). The star block copolymer was prepared by subsequent polymerization of *n*-butyl methacrylate onto the PMMA stars.

Stenzel and co-workers[101] reported that saccharide-based multifunctional initiators for the iron-mediated radical polymerization[102] were prepared and utilized for the star polymer synthesis. Glucose, sucrose, and α-cyclodextrin were reacted with bromoisobutyl bromide to obtain **10a**, **18a**, and **19a** (Scheme 8), followed by treatment with sodium iodide. The resulting iodinated compounds, **10b**, **18b**, and **19b** were used as the initiators for the polymerization of St by a half-metallocene iron carbonyl complex coupled with titanium(IV) isopropoxide to produce PSt stars with 5, 8, and 18 arms. The star structure of the polymers was verified by a molecular weight analysis of the PSt arms which was obtained by hydrolysis of the cores. They concluded that the iron system using **10b**, **18b**, and **19b** resulted in narrower molecular weight distributions as compared to the copper systems using **10a**, **18a**, and **19a**.

Müller and co-workers[103] reported that the poly(*tert*-butyl acrylate) stars with 5, 8, and 21 arms were synthesized by **10a**, **18a**, and **16**, respectively. The respective star polymers were modified by acidic treatment into star-shaped poly(acrylic acid). They demonstrated that the titration curves of the poly(acrylic acid) stars are shifted towards a higher pH with the increasing arm numbers. Reynard and co-workers[104] reported the optimized experimental conditions for the peracetylation of β-cyclodextrin. The polymerization of *tert*-butyl acrylate using the ATRP consisting of **16**/CuBr/pentamethyldiethylenetriamine (PMDETA) was carried out to provide poly(*tert*-butyl acrylate) stars exhibiting an arm number close to the theoretical value of 21.



Scheme 9. Structures of trithiocarbonate heptafunctional β-cyclodextrin **20** and hexakis(thiobenzoylthiomethyl)benzene **21**.

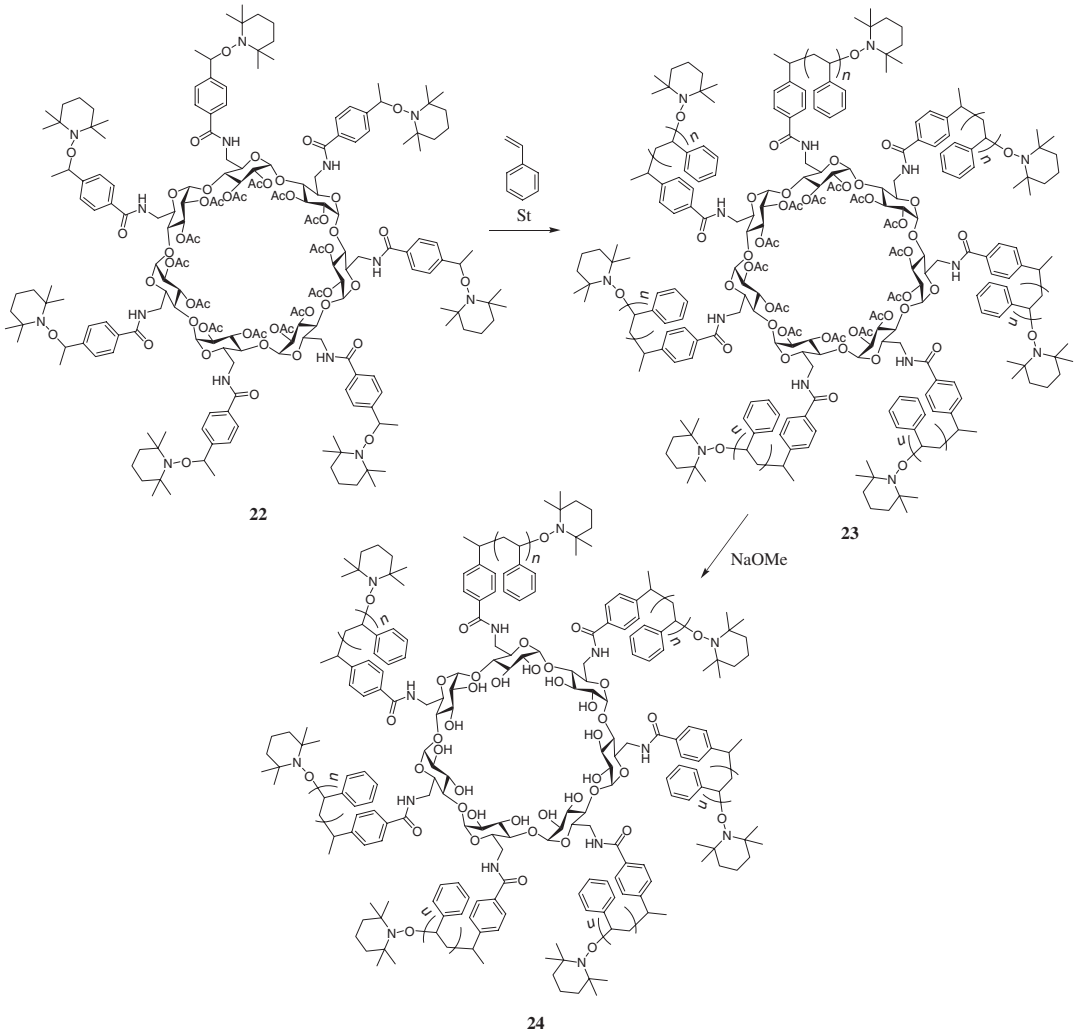


Scheme 10. Mechanisms for Z-group and R-group approaches for the star polymer syntheses through reversible addition-fragmentation chain transfer (RAFT) polymerization demonstrated by Bernard *et al.*[108]

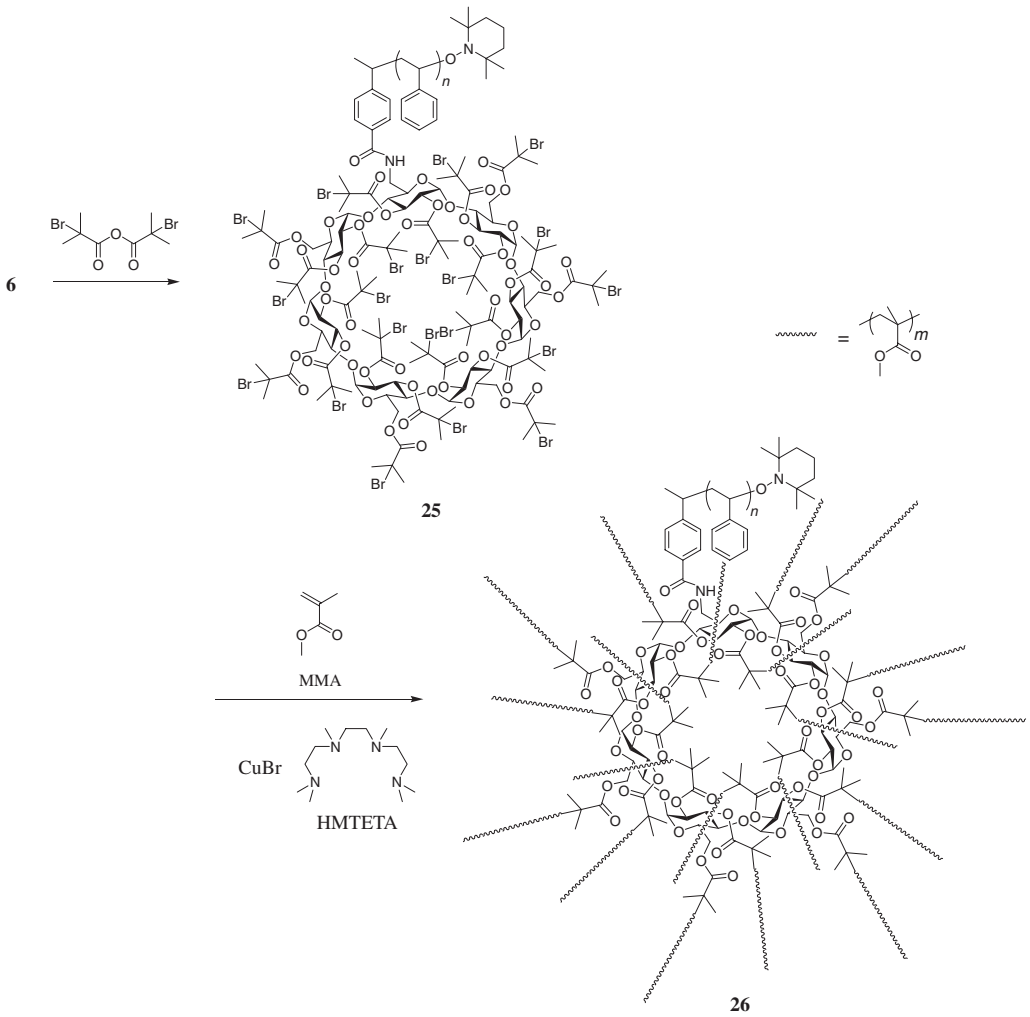
Xiao and co-workers[105] reported that 2-(dimethylamino)-ethyl methacrylate (DMAEMA) was polymerized using ATRP consisting of **16**/CuBr/2,2-dipyridyl in an aqueous medium to produce a poly(DMAEMA) star with 21 arms. Polymers with a medium molecular weight possessed the highest apparent charge density and the largest average particle size. This class of cationic star-like polymers has attracted attention due to its potential applications in the biomedical field and can be also synthesized by another method.[106]

Reversible addition-fragmentation chain-transfer (RAFT) polymerizations using β-cyclodextrins for the star polymer synthesis were reported by Stenzel and Davis.[107] A cyclodextrin-based heptafunctional trithiocarbonate **20** (Scheme 9) was synthesized and used as the chain transfer agent (CTA) for the RAFT polymerization of St. The polymerization was shown to proceed in a living manner to afford a seven-armed star PSt. This approach was fundamentally different from the star polymer synthesis using hexakis(thiobenzoylthiomethyl)-benzene **21** (Scheme 9)[101] that they previously reported. The former approach based on **20** involves attaching the xanthate functionality to the core *via* a nonfragmenting covalent bond (Z-group approach). The latter by **21** involved attaching the xanthate functionality to the core *via* a fragmenting covalent bond (R-group approach) as shown in Scheme 10.[108] They summarized the advantages and disadvantage for both systems and concluded that the systems using the Z-group approach with β-cyclodextrin seems to be better for the star polymer synthesis and suitable for generating star block structures.[107]

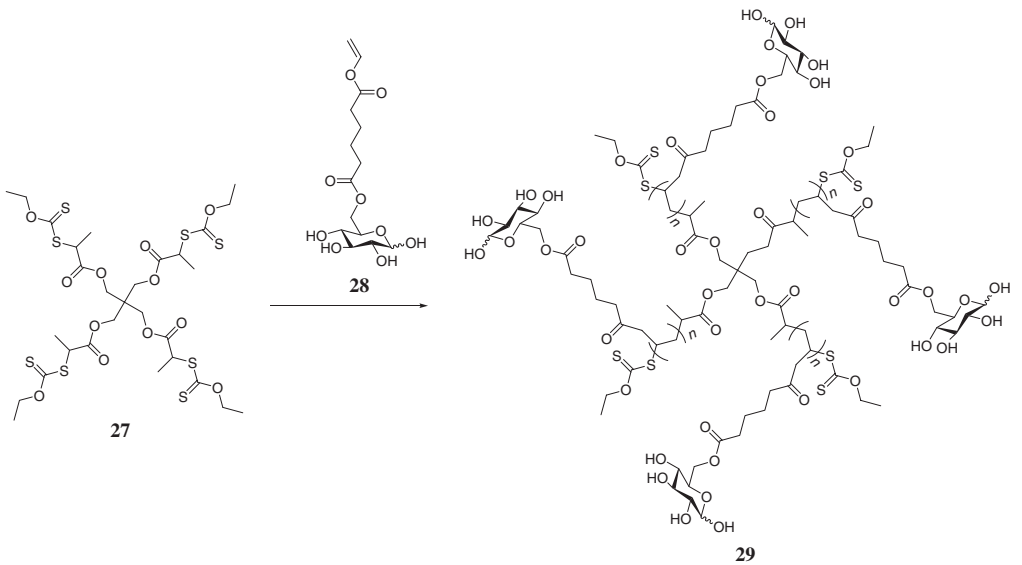
The nitroxide-mediated radical polymerization (NMP) using a cyclodextrin for the star polymer synthesis was reported by us.[109] Seven of the primary alcohols in β-cyclodextrin were modified by 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) adducts followed by acetylation to produce the initiator **22** (Scheme 11). The main product obtained through the polymerization of St with **22** was assigned to the star PSt with seven-arms and an acetylated β-cyclodextrin core **23**. The star polymer **23** was modified by deacetylation into the



Scheme 11. Structure of β-cyclodextrin-based heptafunctional 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-adduct **22** and polymerization of styrene (St) with **22**, followed by deacetylation to produce the star PSt with seven arms and multiple hydroxyl groups **24**.



Scheme 12. Synthesis of end-functionalized PSt with 20 2-bromoisobutyl ester moieties **25** and subsequent polymerization of methyl methacrylate (MMA) using CuBr and 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) producing a 21 heteroarm star polymer consisting of one polystyrene (PSt) and 20 poly(methyl methacrylate) (PMMA) arms and *β*-cyclodextrin core **26**.



Scheme 13. Structure of multifunctional reversible addition-fragmentation chain transfer (RAFT) agent **27** and polymerization of 6-*O*-vinyladipoyl-D-glucopyranose **28** producing glycopolymer star **29**.

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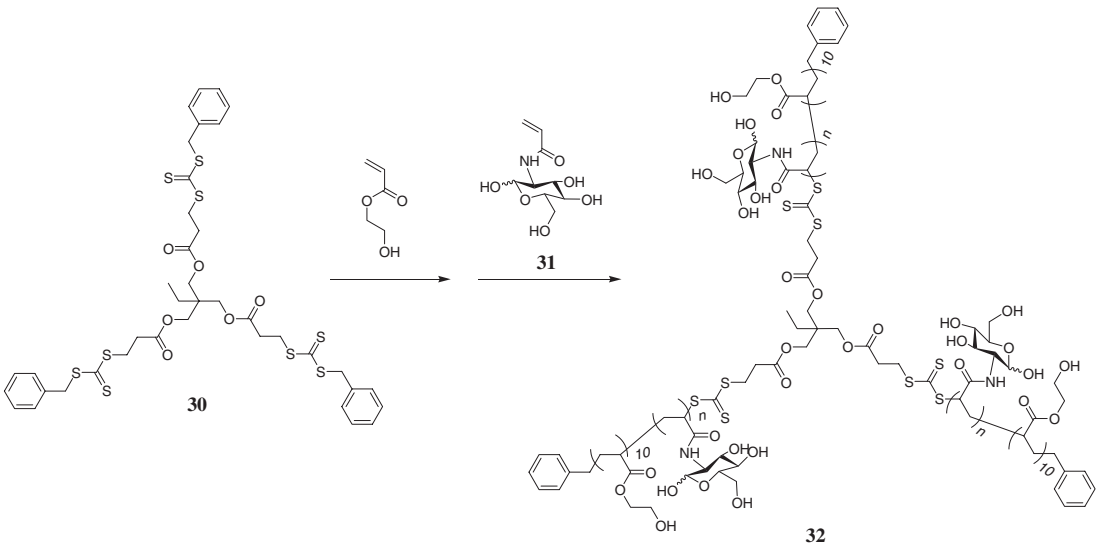


Scheme 14. Structure of trifunctional reversible addition-fragmentation chain transfer (RAFT) agent **30** and polymerization of hydroxyethyl acrylate and acryloyl glucosamine **31** producing 3-arm glycopolymer star **32**.

core-functionalized one with 14 hydroxyl groups **24**, which formed star-star polymeric aggregates in a good solvent for PSt.

We reported that the heteroarm star polymer with the arms of one PSt and 20 PMMA was prepared using the combination of NMP and ATRP (Scheme 12).[110] End-functionalized PSt with the β-cyclodextrin **6**, which was prepared through the NMP and deprotection (procedures are shown in Scheme 2), was reacted with 2-bromoisobutyric anhydride to obtain the end-functionalized PSt with 20 2-bromoisobutyl ester moieties **25**. Subsequently, the ATRP of MMA using CuBr and 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) was performed on **25**. The product was assigned to the AB_{20}-type star polymers with a β-cyclodextrin-core **26** by characterization of the arm polymers separated by the treatment with sodium methoxide.

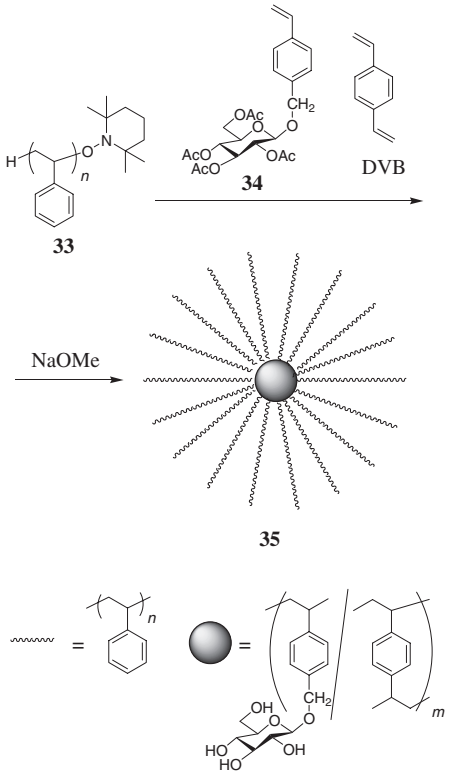
GLYCOPOLYMER STARS

Star polymers with the arms of polymers with pendant saccharides, *i.e.*, glycopolymer stars, were synthesized by Bernard and co-workers[108] using the "core-first" method based on RAFT polymerizations. The R-group approach (Scheme 10) using the multifunctional RAFT agent **27** was applied to the polymerization of 6-*O*-vinyladipoyl-D-glucopyranose **28** (Scheme 13), suggesting that it is possible to create biodegradable glycopolymer architectures **29**.

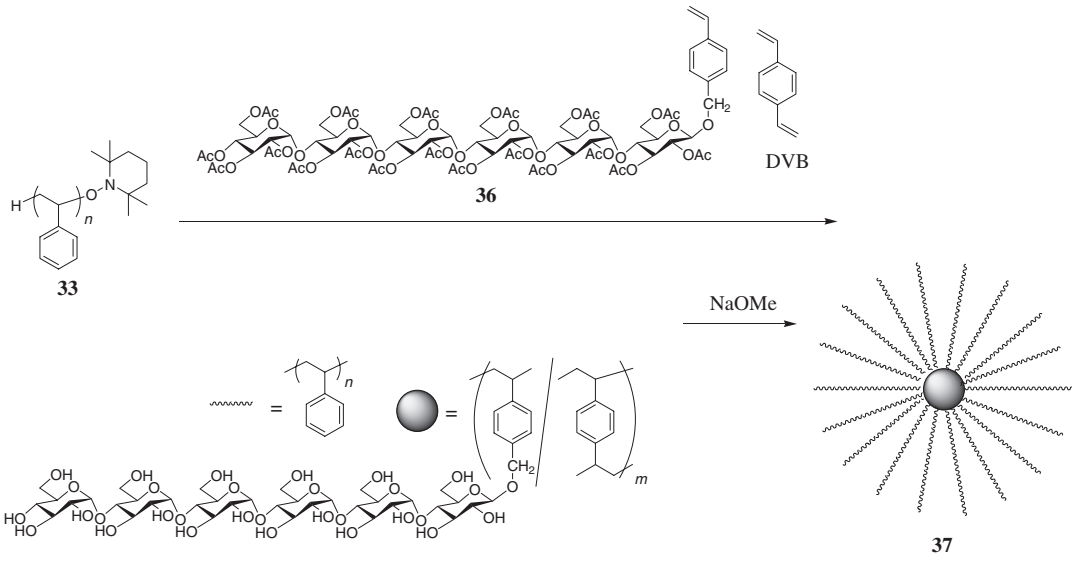
Bernard and co-workers[111] reported that a star glycopolymer was prepared using the Z designed trifunctional RAFT agent **30** (Scheme 14). After the growth of short blocks of poly(hydroxyethyl acrylate) to improve the water-solubility, acryloyl glucosamine **31** was polymerized in an aqueous solution. The polymerizations proceeded in a controlled manner affording well-defined 3-arm poly(acryloyl glucosamine) stars **32**.

STAR MICROGEL WITH GLYCOCONJUGATED CORE AND PERIPHERY

As already described, the synthetic routes for star polymers *via* the living radical polymerization systems include the

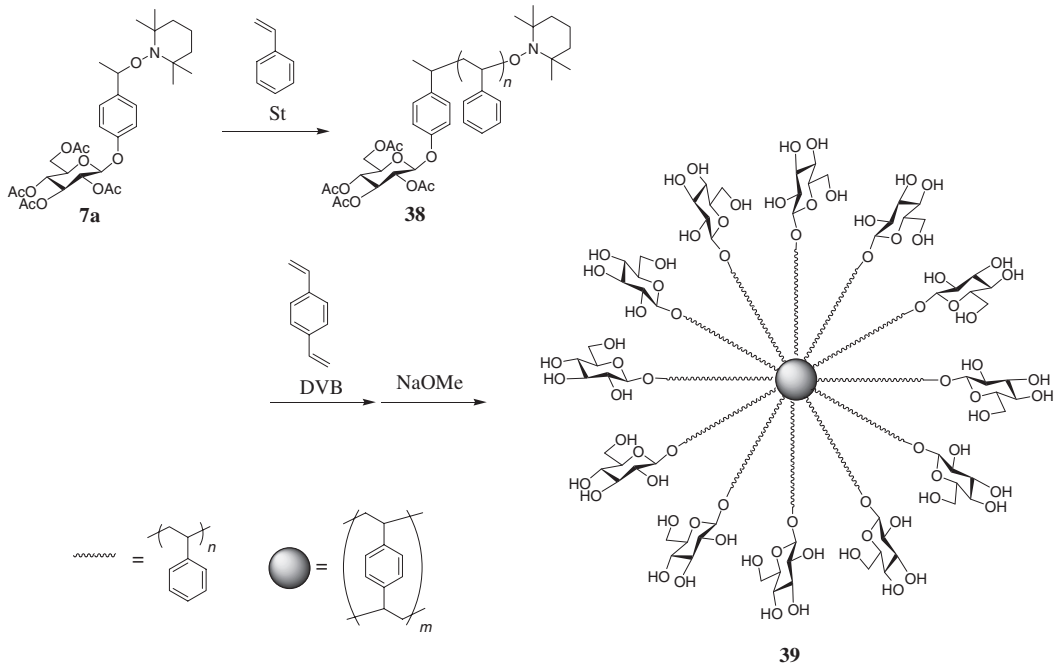


Scheme 15. Coupling reaction of 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-terminated polystyrene (PSt) **33** with divinylbenzene (DVB) in the presence of vinyl monomer featuring acetylated glucose **34**, followed by deprotection to produce the star microgel with PSt arms and glucose-conjugated core **35**.



Scheme 16. Coupling reaction of 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-terminated polystyrene (PSt) **33** with divinylbenzene (DVB) in the presence of vinyl monomer featuring acetylated maltohexaose **36**, followed by deprotection to produce the star microgel with PSt arms and maltohexaose-conjugated core **37**.

preparation of living arm polymers and the subsequent linking reaction using a difunctional cross-linking reagent, namely the "arm-first" method. We reported that the coupling reactions of TEMPO-terminated PSt **33** with divinylbenzene (DVB) occurred in the presence of vinyl monomers featuring acetylated glucose **34** (Scheme 15).[112] In this reaction, a few units of DVB and **34** add to **33** to form short block copolymers with pendant vinyl groups along with saccharides. The pendant vinyl groups are then polymerized by reactive chain-ends in another polymer chain to produce a star PSt with a DVB microgel core with acetyl glucose. The obtained star polymer was modified by deacetylation into the star-shaped PSt with glucose-conjugated core **35**. Similar procedure utilizing vinyl monomers featuring acetylated maltohexaose **36** produced the star-shaped PSt with maltohexaose-conjugated core **37** (Scheme 16).[112] The obtained star polymer with highly hydrophilic cores exhibited an encapsulation ability toward the water-soluble molecules. The encapsulation ability remarkably increased by increasing the saccharide contents.



Scheme 17. Synthesis of end-functionalized polystyrene (PSt) with acetylated glucose **38** and its coupling reaction with divinylbenzene (DVB), followed by deprotection to produce star microgel with PSt arms and glycoconjugated periphery **39**.

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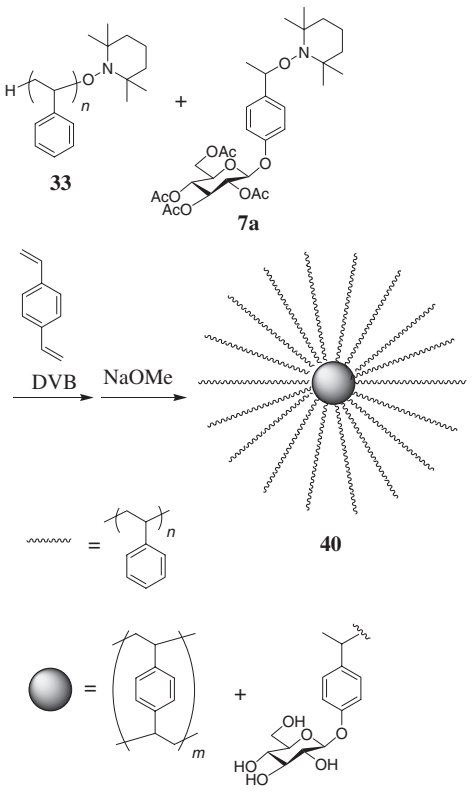


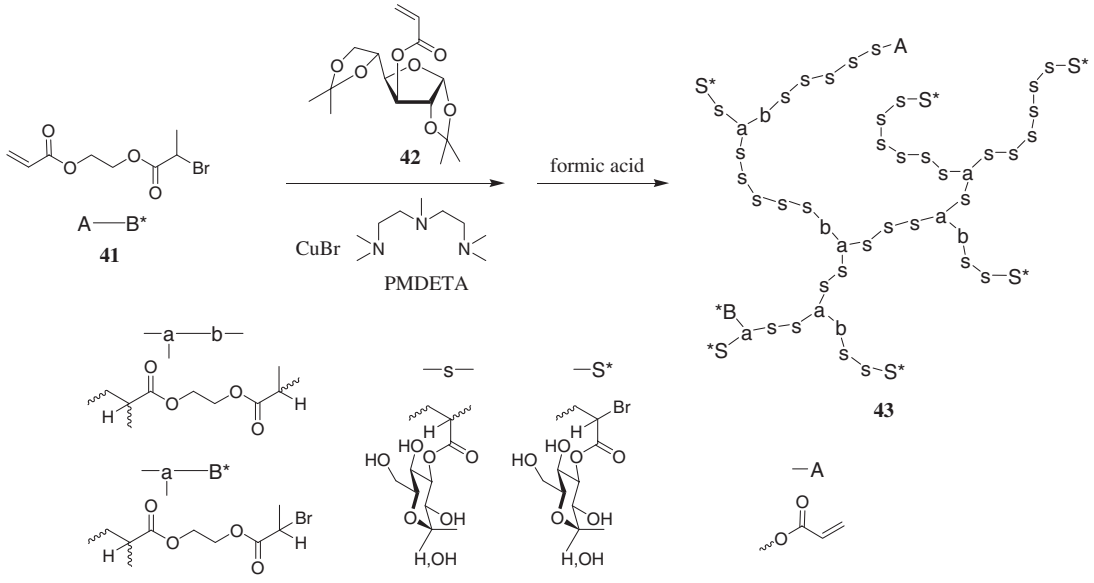
Scheme 18. Coupling reaction of 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-terminated polystyrene (PSt) **33** with divinylbenzene (DVB) in the presence of TEMPO adduct featuring acetylated glucose **7a**, followed by deprotection to produce star microgel with PSt arms and glycoconjugated core **40**.

Glycoconjugation in not only the core, but also in the periphery was demonstrated using the TEMPO-adduct featuring acetylated saccharide **7a** (Scheme 17).[113] St was polymerized with **7a** to afford the living PSt with acetyl glucose in the initiating chain-end **38**. The coupling reaction of **38** was performed with DVB, followed by deacetylation to generate the star-shaped PSt with glucose in the periphery **39**. Core-glycoconjugations were also demonstrated by this approach using **33** and **7a** (Scheme 18). The resulting glycoconjugated star PSt **39** and **40** showed the ability to entrap a polar molecule in their hydrophilic periphery or interior, respectively, in the good solvents for PSt.

HYPERBRANCHED GLYCOPOLYMER

The synthesis of hyperbranched glycopolymers was reported by Müller and co-workers,[114] which was based on the self-condensing vinyl copolymerization (SCVCP)[115,116] of vinyl saccharides. The acrylic AB* inimer, 2-(2-bromopropionyloxy)ethyl acrylate **41**, was polymerized with the sugar-carrying acryloyl monomer **42** *via* ATRP using CuBr/pentamethyldiethylenetriamine (PMDETA) (Scheme 19). The resultant polymers were treated by formic acid to remove the protective isopropylidene groups, producing the water-soluble hyperbranched glycoconjugated poly(acrylate) **43**. They also reported that the sugar-carrying methacrylate **3** (structure is shown in Scheme 1) was polymerized by the methacrylic AB* inimer *via* ATRP initiating bis(triphenylphosphine)nickel(II) bromide ($(PPh_3)_2NiBr_2$), followed by deprotection to give the methacrylate-type glycoconjugated hyperbranched polymers.[117]

This strategy was applied to modify the chemical functionalities of the solid surfaces. Hyperbranched glycopolymers were grafted from a silicon wafer with a covalently attached initiator layer of the fragments of the 2-bromoisobutyl ester moieties using SCVCP of the methacrylic AB* inimer and **3**.[118] The randomly branched copolymer surfaces possess a characteristic architecture, topography, and surface tuning properties.

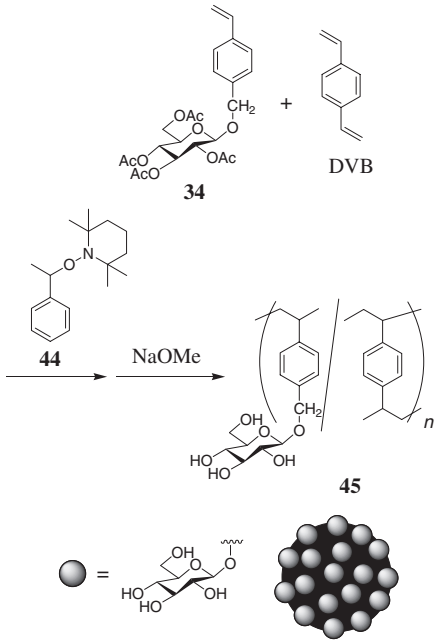


Scheme 19. Self-condensing vinyl copolymerization (SCVCP) with 2-(2-bromopropionyloxy)ethyl acrylate **41** for sugar-carrying acrylate **42** by CuBr and pentamethyldiethylenetriamine (PMDETA), followed by deprotection to produce hyperbranched glycopolymers **43**.

Removal of the protective isopropylidene groups generated hydrophilic surfaces, and there are significant differences in the wettability between the randomly branched and linear polymer brushes.

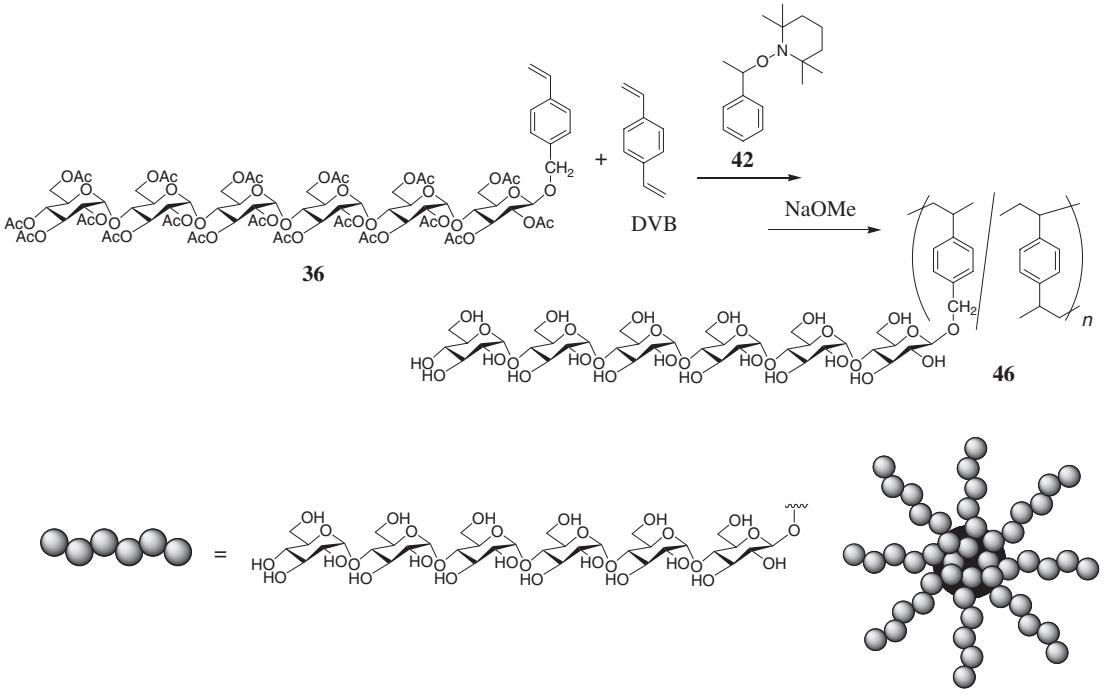
POLY(VINYL SACCHARIDE) MICROGEL

The microgel is a class with a three-dimensional macromolecular architecture defined as a cross-linked polymer particle being able to exist as a stable solution in appropriate solvents.[119,120] Microgels have been synthesized by the conventional free-radical copolymerization of monovinyl monomers and divinyl monomers in suitable solvents under dilute conditions, while Solomon and co-workers[121,122] demonstrated that the living radical polymerization was an efficient method for the controlled synthesis of microgels. We demonstrated that **34** was copolymerized with divinylbenzene (DVB) using the TEMPO adduct **44** (Scheme 20).[123] Visually, the polymerizations homogeneously proceeded to produce products, which passed through a 0.45 μm membrane filter and was able to be characterized by the same method for the soluble polymers. Deacetylation of the products produced the PSt microgels functionalized by 100–300 glucose molecules **45**.



Scheme 20. Copolymerization of vinyl monomer featuring acetylated glucose **34** and divinylbenzene (DVB) with 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-adduct **44**, followed by deprotection to produce polystyrene (PSt) microgel with glucose **45**.

We used the vinyl monomer with the malto-oligosaccharide **36** in this strategy (Scheme 21).[124] The resulting PSt microgels with maltohexaose **46** possessed a high number of hydroxyl groups of more than 400 in the limited space of diameters within 20 nm and showed a higher hydrophilic property that produced stable solutions in the mixed solvent of 1,4-dioxane and H_2O. The ability of **46** to solubilize fullerene was examined according to the literature procedures.[125] In water containing 30% 1,4-dioxane, **46** solubilized fullerene to produce a stable amber-colored solution, in which the molar ratio of **46** and fullerene ([**46**]/[fullerene]) was approximately



Scheme 21. Copolymerization of vinyl monomer featuring acetylated maltohexaose **36** and divinylbenzene (DVB) with 2,2,6,6-tetramethylpiperidinyloxy (TEMPO)-adduct **44**, followed by deprotection to produce polystyrene (PSt) microgel with maltohexaose **46**.

1/1. The amber-colored solution was cast on a glass plate to produce a brown-colored homogeneous film after dryness. Therefore, the good film-forming property derived from the PSt microgel was combined with an excellent hydrophilic property due to saccharide. Thus **46** has a potential of being used as a special coating with functional but incompatible compounds such as fullerene on the surface of various materials including hydrophilic ones derived from, for example, carbohydrates.

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