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ARTICLE

Highly Branched and Hyperbranched Glycopolymers via Reversible Addition−Fragmentation Chain Transfer Polymerization and Click Chemistry

Mona Semsarilar, Vincent Ladmiral,† and Sébastien Perrier*

Key Centre for Polymers & Colloids, School of Chemistry, University of Sydney, Sydney, NSW 2006, Australia. *†Present address: Centre for Advanced Macromolecular Design, School of Chemical Sciences & Engineering, University of New South Wales, Sydney, NSW 2052, Australia*

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ABSTRACT: We report a new strategy to synthesize densely functionalized highly and hyperbranched glycopolymers. Our methodology combines living radical polymerization and click chemistry. Hyperbranched "clickable" scaffolds synthesized via RAFT polymerization are functionalized with carbohydrate groups using an array of "click" chemistry reactions, namely Cu(I)-catalyzed Huisgen 1,3-cycloaddition of azides and alkynes (CuAAC), thiol−ene addition, and thiol−yne addition. This simple and flexible method yields glycopolymers of unique structures, which are potential candidates for biomedical applications.

Introduction

For decades, chemists have tried to mimic nature's ability to generate highly ordered structures for molecular materials, which properties are often affected by their macromolecular architectures. In particular, the occurrence of branching in macromolecules is often the source of dramatic variations in their properties and functionality. For instance, amylopectin, the branched version of amylose, does not dissolve in water, while its linear equivalent is highly water-soluble. Synthetically, branched macromolecules are often modeled with dendritic structures.[1−3] Dendrimers are highly ordered macromolecules with well-defined structures, but their synthesis requires several synthesis and purification cycles which is documented to be difficult and time-consuming.[1−5] Alternatives to dendrimers are the highly branched and hyperbranched polymers. The main advantage of these macromolecules over dendrimers is the ease of their synthesis, although their structure is not as perfect as that of their dendritic counterparts. These structures are however receiving a growing interest, for instance, for their potential biomedical applications as drug carrier.[6−8] Similarly to dendrimers, highly branched polymers feature a large number of functional groups distributed throughout their polymeric structure which impart specific physical and chemical properties, a lower intrinsic viscosity and lower glass transition temperature than their linear analogues, and a vastly enhanced solubility due to a low degree of crystallinity and entanglement.[9] A versatile approach to the synthesis of highly branched polymers is via the free radical random copolymerization of a monovinyl monomer with a small amount of a divinyl monomer.[10] The control of the ratio of monofunctional to difunctional monomers and conversion enables to obtain three-dimensional polymer network free of cross-links.[11,12] Moreover, the use of living radical polymerization (LRP) in this approach is an effective method to control the degree of branching and to avoid gelation.[13] Among the various living radical polymerization methods, reversible addition−fragmentation chain transfer (RAFT) polymerization is a well-established, and perhaps the most versatile, LRP method.[14−16] In the free radical copolymerization of monovinyl and divinyl monomers, the presence of a chain transfer agent permits to reduce substantially the molecular weight of the primary chains, and gelation can be suppressed even at high conversion, providing that less than one branching comonomer is incorporated per primary chain. In principle, LRP offers better control over the primary chain length and polydispersity and hence over the branching process.[15]

In some circumstances when a special chemical function is required, the drawback of this approach is the poor availability and compatibility of specific functional monomers.[17] This problem can be circumvented by introducing functionalities via postpolymerization modification. Postpolymerization functionalization can be challenging as it relies heavily on the efficiency and orthogonality of the reactions chosen.[18,19] Click chemistry is one of the most powerful postpolymerization functionalization strategies, and it has been combined with great success with controlled polymerization techniques to synthesize a wide range of functional materials. The Cu(I)-catalyzed Huisgen 1,3-cycloaddition of azides and alkynes[20,21] (CuAAC) is the most widely used example of click chemistry in the polymer synthesis and materials areas.[22−24] Recently, thiol−ene and thiol−yne chemistries have emerged as powerful synthetic tools that have the potential to fall within the realm of click chemistry. The thiol−ene and the thiol−yne reactions proceed rapidly under a variety of experimental conditions and selectively yield the mono- and bis-addition products, respectively.[25] The real strength of these reactions is the broad range of ene and yne substrates that readily undergo hydrothiolation, including activated and nonactivated species.[26] For instance, we have recently shown the use of thiol−yne reaction to produce well-defined hyperbranched polymers.[35]

A range of macromolecules that would benefit from good control over chemical functionalities is the group of glycopolymers. They are an attractive class of materials for biomedical applications, thanks to their hydrophilicity, biocompatibility, and potential cell targeting capability. They also show weak interactions with protein receptors, which is strongly determined by their architecture. LRP techniques have been demonstrated to offer well-defined glycopolymer structures via two different approaches:[27] polymerization of a sugar-containing monomer[28,29] or functionalization of preformed polymers using sugar derivatives.[30]

*Corresponding author: Tel +61 (0)2 9351 3366; Fax +61 (0)2 9351 3329; e-mail s.perrier@chem.usyd.edu.au.

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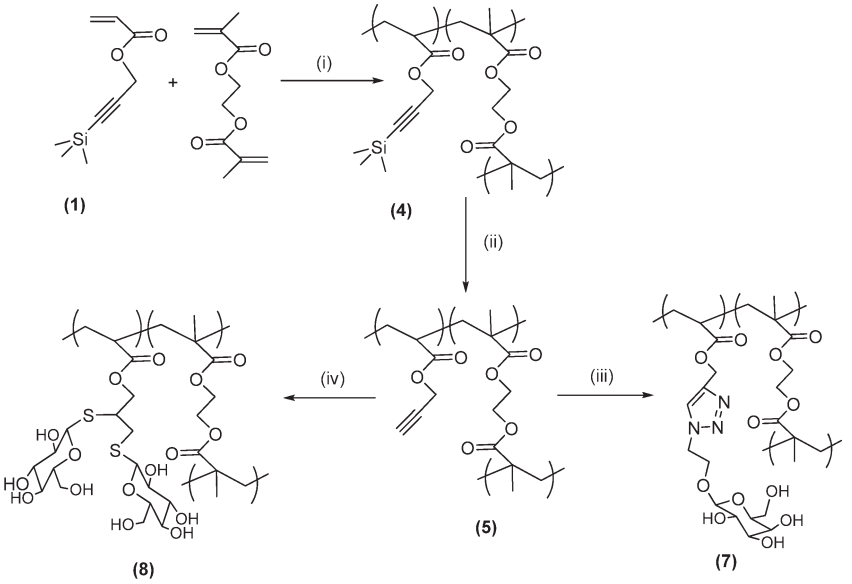
Scheme 1. Synthetic Strategy for the Preparation of Highly Branched Glycopolymers[a]



[a] Conditions and reagents: (i) PABTC, AIBN, toluene, 60 °C; (ii) CH_3COOH, TBAF, THF; (iii) azido-ethyl galactose, $Cu(PPh_3)_3Br$, DIPEA, DMF; (iv) glucothiose, HCl, DMPA, DMF (see Table 1 for molecular weights and PDIs).

Since the library of commercially available glycomonomers is relatively small, and only a number of those are compatible with LRP techniques, postpolymerization functionalization is the most versatile approach to the design of glycopolymers of defined molecular architecture.[31] In the past few years, the combination of demanding applications and novel synthetic techniques has triggered a surge of interest in the synthesis of glycopolymers of complex architectures. However, there is still a need for a simple and flexible method to produce complex glycopolymer architectures. Herein, we report a versatile approach to the synthesis of highly branched and hyperbranched glycopolymers by exploiting the complementarities of reversible addition−fragmentation chain transfer (RAFT) polymerization and click chemistry.

Discussion

This work examines the use of RAFT polymerization in combination with postpolymerization functionalization by click chemistry to synthesize well-defined branched glycopolymers. RAFT polymerization provides the means to synthesize branched polymeric backbones, which are then functionalized via thiol−yne reaction and CuAAC and via thiol−ene reactions, to obtain highly branched and hyperbranched glycopolymers, respectively.

To obtain a highly branched backbone (**4**), 50 equiv of TMSPA monomer (**1**) was copolymerized with 1 equiv of EGDMA in toluene at 60 °C in the presence of PABTC and AIBN, following the procedure reported by Sherrington and co-workers (the Strathclyde route),[10] and adapted for RAFT polymerization.[14−16] The evolution of molecular weight versus conversion, depicted in Figure 1, shows two distinct stages: a linear evolution with conversion up to ca. 65% followed by a sharp increase in molecular weight. The PDI followed the same trend, slowly increasing from 1.1 to 1.6 before 65% conversion then reaching 2.1 at 73% conversion. This behavior suggests that the branching occurred in the later stage of the polymerization as previously reported.[15] The polymerization was stopped after 24 h (93% conversion), and the polymer was isolated by precipitation in a 1:1 water:methanol mixture. The polydispersity of the polymer was 1.9 as indicated by SEC. This value is consistent with a highly branched structure as previously reported by Armes et al.[15,16]

The terminal alkyne-bearing polymer (**5**) was obtained after removal of the trimethylsilyl protecting groups in THF in the presence of TBAF and acetic acid as previously described.[31] Complete deprotection was confirmed by ^{1}H NMR spectroscopy by the complete disappearance of the trimethylsilyl groups signal at 0.2 ppm and the appearance of the terminal alkyne signal at 2.5 ppm.

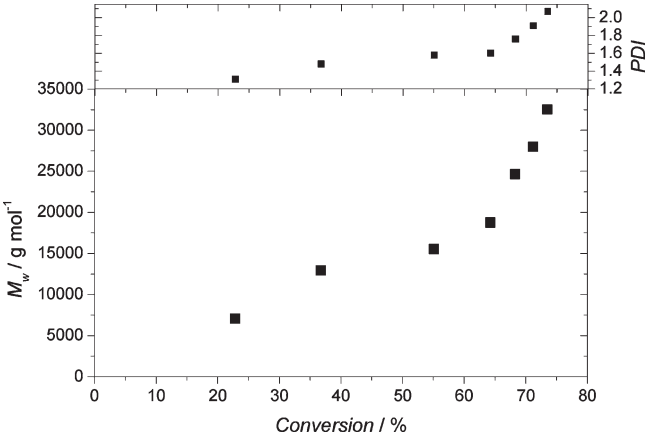


Figure 1. Evolution of molecular weight (M_w against polystyrene standards using universal calibration) and polydispersity (M_w/M_n) with conversion for copolymerization of TMSPA with EGDMA at 60 °C (■).

This deprotected highly branched backbone (**5**) was reacted with an excess of (around 0.45 mmol) glucothiose sodium salt in the presence of HCl and 2,2′-dimethoxy-2-phenylacetophenone (DMPA), a photoinitiator, under UV at room temperature for 8 h to obtain the new highly branched glycopolymer (**8**). The polymer was isolated as a white powder after precipitation, dialysis against deionized water, and freeze-drying. The good solubility in water of the polymer and the appearance of the broad OH band (3100−3700 cm^{-1}) in the FT-IR spectrum along with complete disappearance of the carbon−carbon triple bonds (band at 2100 cm^{-1}) indicate that the addition of glucothiose to the free alkyne did take place with high yield. Close examination of the FT-IR spectrum, however, reveals the presence of carbon−carbon double bonds (small band at 2350 cm^{-1}). This is confirmed by the ^{1}H NMR spectroscopy of the final polymer which shows two peaks at ∼5.5 and 6.15 ppm, suggesting that the

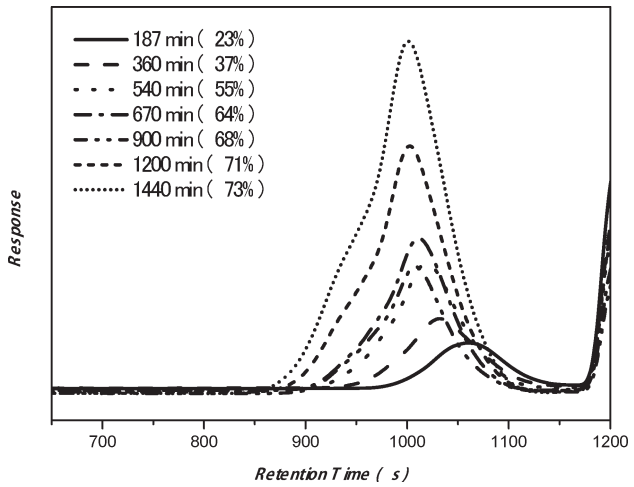


Figure 2. GPC traces (DRI detector) as a function of time for copolymerization of TMSPA with EGDMA at 60 °C.

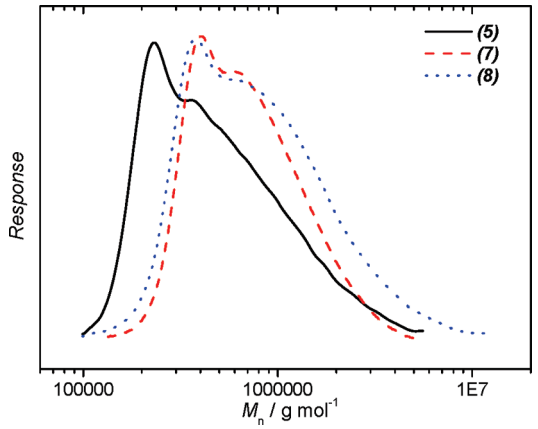


Figure 3. SEC traces of **5**, **7**, and **8** obtained from a DMF-GPC equipped with a DRI detector.

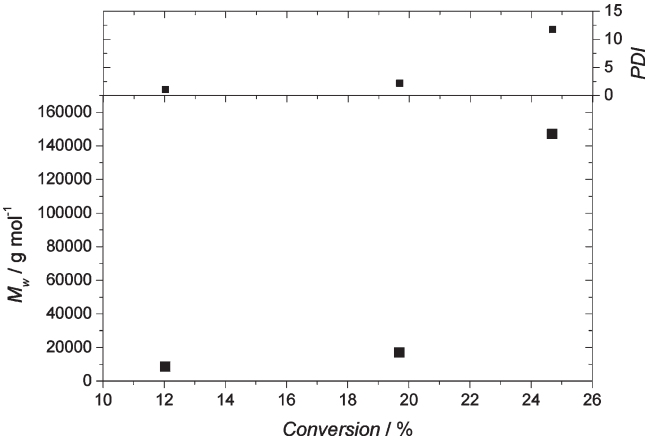


Figure 4. Evolution of molecular weight (M_w against polystyrene standards using universal calibration) and polydispersity (M_w/M_n) with conversion for polymerization of EGDMA with CPDB at 60 °C.

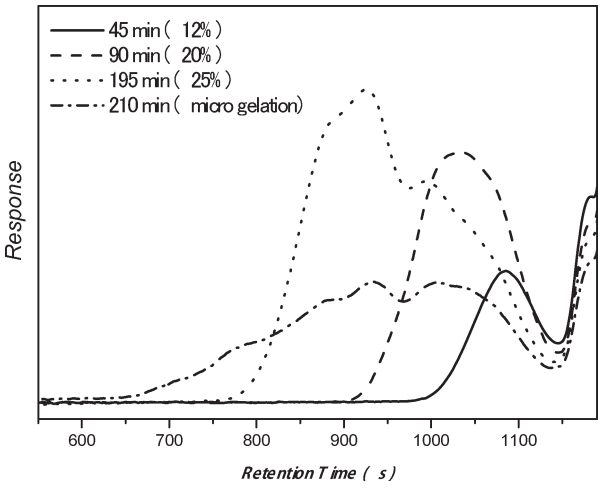


Figure 5. GPC traces (DRI detector) as a function of time for copolymerization of EGDMA with CPDB at 60 °C.

reaction did not proceed to the bis-addition product for every alkyne groups but stopped after the first sugar unit addition leading to the formation of carbon−carbon double bond. Integration of these vinyl peaks indicates that around 10% of the pendent groups are monosubstituted. This could be ascribed to the increase of steric hindrance as the reaction progresses on the highly branched backbone.

The highly branched polymer (**5**) was also submitted to CuAAC with an azido galactose derivative (**3**) [2-azidoethyl-β-D-galactopyranoside]. After 3 days, the copper species were removed with a short alumina column, and the polymer was purified via dialysis against water−methanol. The final galactose-containing product (**7**) was highly soluble in water, and its structure was analyzed by ^{1}H NMR spectroscopy and FTIR analysis. The FTIR spectrum showed the broad absorbance band around 3300 cm^{-1} typical of OH groups as well as the carbon−carbon double bond and carbon−nitrogen bond signals at 2400 and 1000 cm^{-1}, respectively, due to the triazole. The integration of the peak at 8.0 ppm in the NMR spectrum, which corresponds to the proton of the triazole group, confirmed that the reaction proceeded to high yield (85%).

Conjugation of the pyrannose derivatives induced a substantial increase in hydrodynamic volumes of the polymers as shown in Figure 3. The general morphology of the peaks was retained throughout the click procedures, indicating that the reactions did not affect the backbone of the polymeric chains, but the PDI slightly decreased. This could be ascribed to a steric hindrance effect, which impairs the efficiency of the reaction on the higher molecular weight macromolecular chains featuring higher degree of branching. An alternative explanation is the combination of changing polymer interactions with the column and/or solvent in SEC analyses, and fractionation resulting from precipitation, which leads to the observed small decrease in polydispersity index.

To synthesize a hyperbranched backbone (**6**), commercially available EGDMA was polymerized in toluene at 60 °C, using CPDB as RAFT agent (EGDMA:CPDB = 20:1). Contrary to the previous polymerization where the branching took place in the later stages of the reaction, in this case branching starts at the onset of polymerization due to the absence of monofunctional monomer which used to dilute the difunctional species. This produces a higher degree of branching and leads to macrogels at relatively low conversion. To avoid the formation of cross-linked microgels, the polymerization was stopped at 25% conversion, just before the gelation point, and isolated by precipitation. ^{1}H NMR spectroscopy in deuterated chloroform showed an average of 15 monomer units per RAFT agent 11 of which bearing pendent vinyl groups. The hyperbranched structure was confirmed by the multimodal and very broad GPC trace (Figure 5, PDI = 11.8), which also suggests that little loop formation (cyclization) occurs.

This hyperbranched polymer was then used as a scaffold for the clicking of glucose via thiol−ene chemistry. **6** was dissolved in

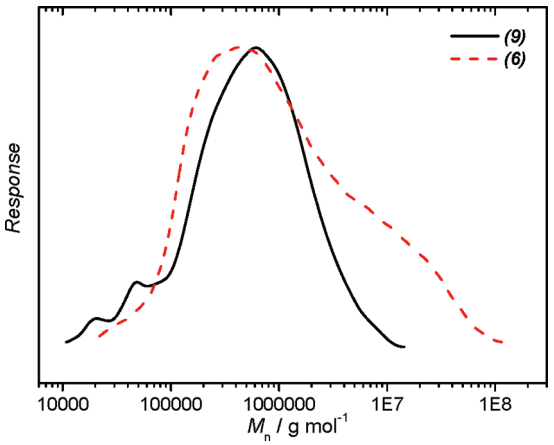
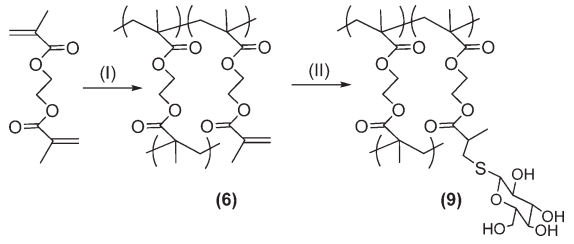


Figure 6. SEC traces of **6** and **9** obtained from a DMF-GPC equipped with a DRI detector.

Scheme 2. Synthetic Strategy for the Preparation of Hyperbranched Glycopolymers[a]



[a] Conditions and reagents: (i) CPDB, AIBN, toluene, 60 °C; (ii) glucothiose, HCl, Me_2PPh, DMF (summary of molecular weights and polydispersity index could be found in Table 1).

Table 1. Summary of Final Conversions, Molecular Weights, and Polydispersities

polymer	convn (%)	M_n (g mol^{-1})	M_w (g mol^{-1})	PDI
4	93	29 000	55 700	1.9
5	100	29 000	62 000	2.1
6	25	15 400	182 100	11.8
7	85	34 400	55 500	1.6
8	>90	33 900	71 000	2.1
9	100	6 000	66 500	11.2

DMF and reacted with glucothiose sodium salt (0.8 mmol) in the presence of HCl and dimethylphenylphosphine (Me_2PPh) at room temperature for 3 days to obtain the corresponding hyperbranched glycopolymer (**9**). The resulting polymer was completely soluble in water in contrast with its precursor. ^{1}H NMR and FTIR spectra (Figures S7 and S8) showed the complete disappearance of the double bonds and the appearance of characteristic signals of the glucopyranose derivative, thus confirming that the thiol−ene reaction preceded with quantitative yield.

Figure 6 shows the GPC traces of the polymer before and after the thiol−ene reaction. The conjugation of the glucose moieties to the hyperbranched backbone induced as expected an increase of the hydrodynamic volume of the polymer (the main peak shifts toward lower retention time), but the shape of the GPC trace was not retained, leading to a much lower PDI. This could be due to the change in interaction between the new structure and the eluent. Although it is possible for the ester groups to cleave during the phosphine-catalyzed click reaction, this has not been observed previously.[32]

Conclusion

In summary, we report the first synthesis of branched glycopolymers following a postpolymerization modification methodology, which combines state-of-the-art controlled radical polymerization technique and click chemistry methods. A highly branched clickable backbone was synthesized using the RAFT copolymerization of TMS-protected alkyne acrylate monomer with EGDMA. Glucose and galactose moieties were then clicked in high yield to this highly branched structure via thiol−yne and CuAAC, respectively. A hyperbranched polymer was prepared by RAFT polymerization of EGDMA. This scaffold was then quantitatively decorated with glucose units via thiol−ene reaction. These methods open the route to the facile synthesis of a variety of branched glycopolymers which could find applications in biomedicine.

Experimental Section

Materials. All the reagents were bought from Sigma-Aldrich and used as received unless otherwise stated.

Analysis. All reactions were carried out under an inert atmosphere of nitrogen. Molar mass distributions were measured using size exclusion chromatography (SEC) on a Polymer Laboratories GPC-50 with a Polymer Laboratories PG-Gel 5 μM guard column and two Polymer Laboratories Mixed-C columns using THF at 1.0 mL min^{-1} as the eluent. The system was equipped with a PL-RI differential refractive index detector and PL-BV 400RT viscometer as well as a Precision Detectors PD2020 light scattering detector. Polystyrene standards were used to calibrate the SEC. Analyte samples contained (0.5 vol %) toluene as the flow marker. Molar mass distributions of the glycopolymers were measured using size exclusion chromatography (SEC) on a system equipped with two PL polar gel M columns and one PL polar gel 5 mm guard column with differential refractive index detection using *N*,*N*-dimethylformamide (DMF)/0.3 M LiBr at 0.5 mL min^{-1} as the eluent. NMR spectra were acquired on a Bruker 300 or 200 MHz in deuterated chloroform or DMSO. All chemical shifts are reported in ppm (δ). The UV irradiation experiments were carried out using a Spectroline ENF-280C/FE (365 nm, 230 V, 0.17 A) UV lamp. Dialysis bags (Spectra/Por Biotech RC) with the molecular cutoff of 2000 were purchased from Spectrum Laboratories Inc.

Synthesis of Acrylic Acid 3-Trimethylsilanyl-prop-2-ynyl Ester (***1***). A three-necked round-bottomed flask equipped with a mechanical stirrer was fitted with a pressure-equalizing dropper and a reflux condenser. The set up was flushed with N_2 and charged with 17.8 g (0.74 mol) of magnesium turnings and 350 mL of dry tetrahydrofuran (THF). Over an hour 55 mL (80.3 g, 0.74 mol) of bromoethane was dropped into the stirring suspension maintaining the temperature at 40 °C. After complete addition, the gray solution was heated to 50 °C for an hour and then cooled down to 5 °C. A solution of 15.2 mL (14.74 g, 0.26 mol) of propargyl alcohol in 25 mL of THF was added slowly to the gray suspension maintaining the temperature at 10 °C. This mixture was then stirred overnight. The resulting solution was cooled down to 5 °C, and 94 mL (79.42 g, 0.74 mol) of chlorotrimethylsilane was dropped over an hour and then the mixture was refluxed for 2 h. The suspension was cooled to 20 °C, and then 300 mL of 1.4 M sulfuric acid was added carefully. After 5 min, 200 mL of ether was added and extracted in a separatory funnel. The organic layer was washed with water and sodium chloride solution. The combined organic layers were dried over magnesium sulfate and concentrated by rotary evaporation. The obtained yellow-brown oil (38 g, 75% yield) was used in the next step with out further purification.

A three-necked round-bottom flask under N_2 was charged with 18.7 g (0.15 mol) of 3-timethylsilyl-2-propyn-1-ol, 50 mL of THF, and 24.5 mL (17.73 g, 0.17 mol) of triethylamine (TEA). The mixture was cooled down to −10 °C, and 13 mL (14.54 g, 0.16 mol) of acryloyl chloride was added dropwise. After complete addition the funnel was rinsed with THF, and the mixture was stirred overnight at room temperature. Upon completion the reaction mixture was filtered (to remove the TEA−chloride

salt), and volatiles were removed by rotary evaporation. The resulting oil was purified by column chromatography on silica gel using hexane:ethyl acetate 9.5:0.5 as eluent. The final product was collected as colorless oil (22.73 g, 85% yield). ^{1}H NMR (300.13 MHz, $CDCl_3$, 298 K): δ (ppm) = 0.18 (s, 9H, $Si(CH_3)_3$); 4.76 (s, 2H, OCH_2); 5.84−5.88 (m, 1H, C=C*H*H); 6.10−6.19 (m, 1H, C=CH*H*) 6.42−6.49 (m, 1H, C*H*=CH_2).

Synthesis of 2-Azidoethyl-2,3,4,6-tetraacetyl-β-D-galactopyranoside (***2***). This product was prepared following the method described by Fazio et al.[33] A round-bottom flask was purged with N_2 and then charged with β-D-galactose pentaacetate (5 g, 12.81 mmol), 25 mL of anhydrous dichloromethane, and 2-azidoethanol (4.6 g, 51.24 mmol) [prepared according to the recipe published by Ladmiral et al.]. While maintaining the temperature at 0 °C, 3.3 mL of $BF_3 \cdot Et_2O$ (3.77 g, 25.62 mmol) was added dropwise. After complete addition the reaction mixture was stirred overnight at room temperature. After dilution with dichloromethane the product was washed with cold water and saturated $NaHCO_3$. The organic phases were combined and dried over $MgSO_4$. The volatiles were removed under reduced pressure a purified using flash column chromatography on silica gel using hexane:ethyl acetate 1:1 as eluent. The final product (3.0 g, 70% yield) was collected as a yellow-brown viscous liquid. ^{1}H NMR (200.13 MHz, $CDCl_3$, 298 K): δ (ppm) = 5.41 (dd, 1H); 5.25 (dd, 1H); 5.19 (dd, 1H); 5.00 (d, 1H); 4.16 (m, 2H); 3.93 (m, 2H); 3.69 (m, 1H); 3.42 (m, 1H); 3.22 (m, 1H); 2.15 (s, 3H); 2.1 (s, 3H); 2..05 (s, 3H); 1.99 (s, 3H).

Deacetylation of 2-Azidoethyl-2,3,4,6-tetraacetyl-β-D-galactopyranoside (***3***). This product was prepared following the method described by Vincente et al.[34] A solution of sodium methoxide (25% in MeOH, 0.50 mL, 2.32 mmol) was added to a solution of 2-azidoethyl-2,3,4,6-tetraacetyl-β-D-galactopyranoside (3.0 g in 25 mL of MeOH, 7.18 mmol). After an hour the solution was acidified with Amberlite IR-120H$^+$ to pH 6. The ion-exchange resin was removed by filtration, and the solvent was evaporated under vacuum. The product was obtained (1.4 g, 78.2% yield) as a yellow-brown viscous liquid. ^{1}H NMR (200.13 MHz, $CDCl_3$, 298 K): δ (ppm) = 5.41 (dd, 1H); 5.25 (dd, 1H); 5.19 (dd, 1H); 5.00 (d, 1H); 4.16 (m, 2H); 3.93 (m, 2H); 3.69 (m, 1H); 3.42 (m, 1H); 3.22 (m, 1H).

General Polymerization Procedures of Typical Reversible Addition−Fragmentation Chain Transfer (RAFT) Polymerization. *Polymerization of Branched Trimethylsilylpropyne Acrylate* (*TMSPA*) (***4***). In a Schlenk tube 2.0 g (10.97 mmol) of TMSPA, 52.0 mg (0.22 mmol) of propionic acidyl butyl trithiocarbonate (PABTC), 3.6 mg (0.02 mmol) of AIBN, and 46.9 mg (0.22 mmol) of ethylene glycol dimethacrylate (EGDMA) were dissolved in 1.16 mL of toluene. The sealed vessel was subjected to several cycles of freeze−pump−thaw. The reaction vessel was placed in a preheated oil bath at 60 °C. The polymerization was quenched after 24 h by cooling and exposure to air. The resulting PTMSPA (93% conversion; M_n = 29 000 g mol^{-1}, M_w = 55 700 g mol^{-1}, M_w/M_n = 1.9) was isolated by precipitating into 50% mixture of methanol−water and drying under vacuum.

Deprotection of Polytrimethylsilylpropyne Acrylate (*PTMSPA*) (***5***). This product was prepared following the method described by Ladmiral et al.[31] The branched trimethylsilyl-protected polymer (300 mg, 1.6 mmol) and acetic acid (150 mg, 1.5 equiv mol/mol with respect to the alkynetrimethylsilyl groups) were dissolved in 20 mL of THF. The resulting solution was purged with N_2 (10 min), and the yellow solution was cooled down to −20 °C. To the stirring solution 2.5 mL of a 1 M solution of TBAF, $3H_2O$ (1.5 equiv mol/mol with respect to the alkynetrimethylsilyl groups) was added slowly via a syringe. The resulting mixture was stirred at this temperature for 30 min and then overnight at room temperature. The reaction solution was passed through a short silica pad in order to remove the excess of TBAF, and the pad was subsequently washed with additional THF. The resulting solution was then concentrated under reduced pressure, and the polymer was precipitated in a mixture of 50% methanol−water and dried under vacuum (M_n = 29 000 g mol^{-1}, M_w = 62 000 g mol^{-1}, M_w/M_n = 2.1).

Polymerization of Hyperbranched Ethylene Glycol Dimethacrylate (*EGDMA*) (***6***). A Schlenk tube was charged with 1.50 g (7.57 mmol) of EGDMA, 83.8 mg (0.38 mmol) of cyanoisopropyl dithiobenzoate (CPDB), 6.2 mg (0.04 mmol) of AIBN, and 0.8 mL of toluene. The sealed vessel was purged with N_2 for 30 min and placed in a preheated oil bath at 60 °C. The polymerization was quenched after 2 h 28 min by cooling and exposure to air. The resulting PEGDMA (25% conversion; M_n = 15 400 g mol^{-1}, M_w = 182 100 g mol^{-1}, M_w/M_n = 11.8) was isolated by precipitating into cold hexane and drying under vacuum.

Clicking Sugar Azide to Alkyne-Containing Branched TMSPA Polymer (***7***). In a glass vial 76 mg of unprotected TMSPA polymer (around 0.69 mmol of alkyne moieties), 156 mg (0.63 mmol) of 2-azidoethyl-β-D-galactopyranoside, and 36 μL (27 mg, 0.21 mmol) of diisopropylethylamine (DIPEA) were dissolved in DMF (5 mL). The vial was sealed and purged with N_2 (10 min.). In a separate vial a solution of 39 mg (0.042 mmol) [$(PPh_3)_3$-CuBr] in 2 mL of DMF was purged with N_2 (5 min). Then the content of the first vial was transferred to the second vial. The mixture was stirred at room temperature for 3 days. Afterward the product was passed through a short neutral alumina pad and dialyzed against 20% methanol−water. Upon freeze-drying the product was collected as an off-white powder (M_n = 34 400 g mol^{-1}, M_w = 55 500 g mol^{-1}, M_w/M_n = 1.6).

Clicking Glucothiose to Alkyne-Containing Branched TMSPA Polymer via Radical-Mediated Thiol−Yne Reaction (***8***). In a glass vial 50 mg of unprotected TMSPA polymer (around 0.45 mmol of alkyne moieties) was dissolved in 1 mL of DMF. To this solution 262 mg (1.2 mmol) of glucothiose salt, 1 equiv of HCl, and 1.54 mg (0.006 mmol) of 2,2′-dimethoxy-2-phenylacetophenone (DMPA) were added. The mixture was purged with N_2 (10 min) and irradiated at 365 nm without stirring for 8 h at room temperature. The reaction mixture was dialyzed against 20% methanol−water. Upon freeze-drying the product was collected as a white powder (M_n = 33 900 g mol^{-1}, M_w = 71 000 g mol^{-1}, M_w/M_n = 2.1).

Clicking Glucothiose to Hyperbranched EGDMA Polymer via Phosphine-Catalyzed Thiol−Ene Reaction (***9***). In a glass vial 200 mg (0.69 mmol of pendent double bonds) of PEGDMA and glucothiose salt (175 mg, 0.80 mmol) along with 1 equiv of HCl were dissolved in 2 mL of DMF. The vial was sealed and purged with N_2 (10 min). Using a microsyringe, 50 μL (0.36 mmol)of dimethylphenylphosphine (Me_2PPh) was added to the reaction mixture and stirred at room temperature for 3 days. The product was dialyzed against 20% methanol−water. Upon freeze-drying, the product was collected as a white powder (M_n = 6000 g mol^{-1}, M_w = 66 500 g mol^{-1}, M_w/M_n = 11.2).

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Supporting Information Available: Analysis and characterizations (GPC, NMR, FT-IR) of all polymers. This material is available free of charge via the Internet at http://pubs.acs.org.

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