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Synthesis of Cyclic Dendronized Polymers via Divergent "Graft-from" and Convergent Click "Graft-to" Routes: Preparation of Modular Toroidal Macromolecules

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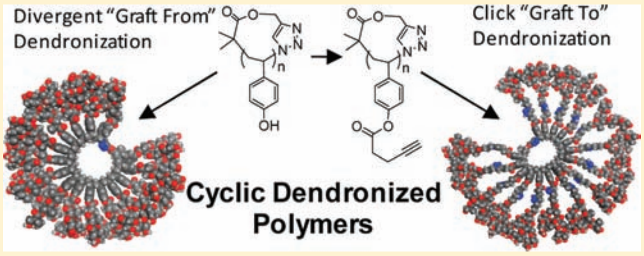
Supporting Information

ABSTRACT: Cyclic dendronized polymers represent a new class of polymers which exhibit a donut-like "toroidal" shape. Two previous unreported methods for preparing this architecture, the divergent "graft-from" and the convergent click "graft-to" approaches, are explored and the resulting products fully characterized. This route is particularly attractive because it enables production of exact linear and cyclic dendronized analogues, enabling direct comparison of their physical properties. In this preliminary work, the divergent "graft from" approach appears to lead to materials with broad PDI at high DP, whereas the "graft to" approach yields more well-defined dendronized cyclic polymers at larger DP. On the basis of reports to date, a combination of click cyclization followed by click "grafting to" provides the most versatile route for the synthesis of cyclic dendronized polymers.



INTRODUCTION

Dendronized polymers represent a unique class of hyperfunctional polymers which exhibit tunable rigidity and shape in addition to control over the length of the polymer backbone.[1,2] They consist of a polymeric backbone in which each repeat unit bears a pendant dendron. The size, steric compactness, and chemical functionality of each dendron on the polymer backbone play a large role in defining the macromolecule's shape and rigidity and therefore, ultimately, its overall physical properties. For large dendrons, the strong steric repulsion between adjacent dendrons inhibits conformational flexibility resulting in a rod-like shape. Dendronized polymers also display a highly functional periphery as a result of the multiplicity of dendron end-groups which largely reside at the surface of these cylindrical macromolecules. These surface functionalities are amenable to chemical modification and therefore provide a rapid means to tune solubility and the strength of other intermolecular interactions. While linear dendronized polymers have been the subject of numerous studies, the properties and applications of other dendronized polymer architectures, such as cyclic dendronized polymers, remain largely unexplored.

There are three general approaches for the synthesis of dendronized polymers: the macromonomer route,[3−11] the "graft from" route,[3,12−16] and the "graft to" route.[17−20] Briefly, the macromonomer approach involves polymerization of a monomer that is already bearing the desired dendritic side chain. This method often suffers from low degrees of polymerization and extremely polydisperse polymers as a result of steric hindrance which discourage interaction between the propagating polymer active site and the polymerizable functionality of the unreacted dendronized macromonomers. The "graft from" approach involves stepwise growth of dendrons outward from the polymer backbone. This technique typically suffers from the same weaknesses as divergent dendrimer syntheses, where the number of functionalities per macromolecule increases exponentially, increasing the probability of incomplete reactions, as well as undesirable side reactions, such as cross-linking. However, for highly optimized dendritic syntheses, such as the polyester dendrons based on bis-MPA,[21−27] or the polyamides,[28] this approach provides a relatively efficient route to well-defined dendronized polymers.[2,12−14] Finally, the "graft to" approach involves a polymer with reactive functional groups along the backbone that are coupled to preformed dendrons with a complementary reactive focal point. This method rarely yields complete dendronization for high generation dendrons because reactive functionalities on the linear polymer can be sterically blocked by dendrons on adjacent repeat units partway through the coupling reaction, in addition to the steric hindrance around the reactive functionality at the focal point of the dendron. However, for highly efficient coupling reactions, such as the Cu catalyzed alkyne−azide click cycloaddition (CuAAC) reaction,[29] sufficient coverage can be achieved to access materials that exhibit the unique properties of dendronized polymers.

Cyclic dendronized polymers are a relatively new polymer architecture which has only been reported within the last 5 years.[30] Preliminary reports from our laboratories have demonstrated for the first time the viability of the divergent route,[31]

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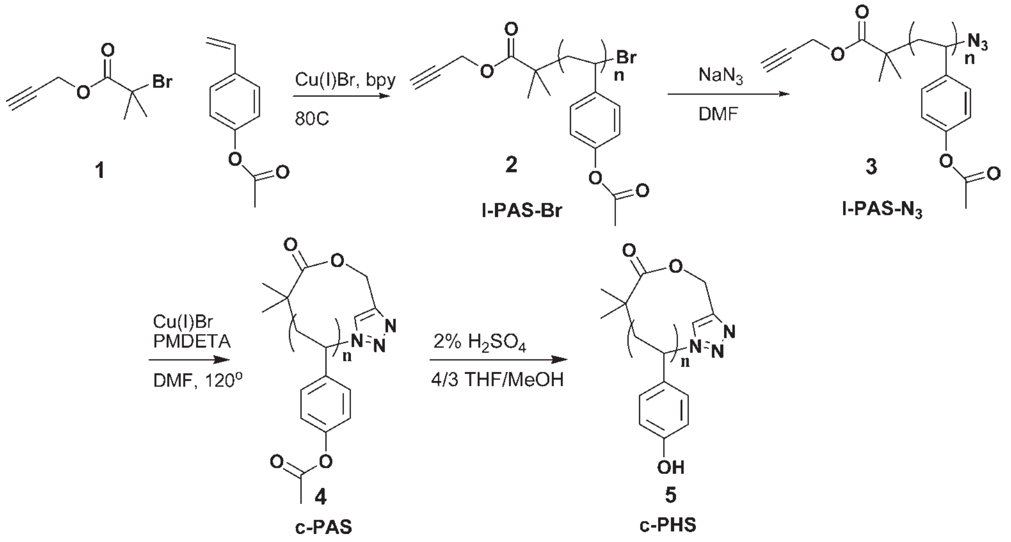
Scheme 1. Synthesis of Cyclic Poly(4-acetoxystyrene) as a Scaffold for Further Functionalization of the Cyclic Architecture



while Boydston et al. have recently reported the first and only reported synthesis of cyclic dendronized polymers utilizing the macromonomer approach.[4] Through the use of a specialized "cyclic" Ru Grubbs type ring-opening metathesis polymerization method,[32−35] Boydston et al. were able to successfully synthesize a second generation cyclic dendronized polymer of extremely high molecular weight, up to 5 MDa, and were also able to visualize the individual polymer rings via Atomic Force Microscopy (AFM). Although this route is notable in that it provides access to cyclic dendronized polymers of sufficient degrees of polymerization (DP) to enable microscopic visualization, broad utilization of this approach is limited due to the relatively challenging synthesis of the unique cyclic Ru catalyst and the products exhibited the relatively broad molecular weight distributions associated with the ring-opening metathesis route.

Explorations within our group have focused on the divergent "graft from" and the convergent "graft to" approaches, in part, because they should offer more synthetic accessibility and versatility, in that a wide range of preformed cyclic polymers can be prepared, and then a variety of different dendrons could be added in subsequent synthetic steps. Recently, a number of research groups have reported improved methods for the synthesis of highly pure simple cyclic polymer backbones consisting of styrenics, acrylates, methacrylates, acrylamides, butadienes, and a variety of polyesters including poly(caprolactone) and poly(lactide).[36−38] Within our laboratory, a technique has been developed for the generation of high purity cyclic polymers employing the slow addition technique of α-alkynyl,ω-azido-heterodifunctionalized linear polymer utilizing highly efficient (CuAAC) coupling.[39−43] This approach offers excellent versatility in both tolerance to functional groups present on the polymer as well as access to a broad range of molecular weight, yet maintains the narrow polydispersity of the linear polymerization techniques used (e.g., atom transfer radical polymerization (ATRP), radical addition−fragmentation chain transfer (RAFT) polymerization, and ring-opening polymerization (ROP)) which have already been the subject of extensive optimization. In this technique, the polymer solution is added at a slow, controlled rate via syringe pump to a solution of Cu(I)Br "click" catalyst to maintain an infinitesimally small concentration of linear precursor throughout the course of the cyclization. Due to the extremely high efficiency of the "click" reaction between a terminal alkyne and an azide,[29] the cyclization reaction affords near quantitative yields of the cyclic polymers, removing the need for tedious purification techniques. As a result of the functional group compatibility of this approach, the facile incorporation of side chain functionality enables the attachment of dendrons via either the "graft from" or the "graft to" approaches.

Herein, we report the first detailed synthesis of cyclic dendronized polymers utilizing both the "graft from" and "graft to" approaches. Each approach produces a styrene-based cyclic polymer backbone with dendritic polyester side chains. In the divergent "graft from" approach, the dendron is grown in a stepwise fashion utilizing iterative esterification and deprotection chemistry. The alternative "graft to" approach consists of the "clicking" of a library of different generation dendrons bearing a single azido-group at the focal point onto a polymer backbone with alkyne side-chains on each repeat unit. This methodology was performed on both linear and cyclic poly(pent-4-ynoyloxy)styrene (*c*-PHS-yne) in order to provide a direct comparison of exact linear and cyclic analogues.

■ RESULTS AND DISCUSSIONS

Divergent "Graft-from" Dendronization of Cyclic Macrocycles. The synthesis of cyclic polymer cores for dendronization utilized the "click" cyclization technique reported recently in our laboratories.[39] 4-Acetoxystyrene was chosen as the monomer unit because poly(4-acetoxystyrene) (PAS) can be readily hydrolyzed to poly(4-hydroxystyrene) (PHS), which is an ideal substrate for divergent dendronization[12] and it has been shown to polymerize via Atom Transfer Radical Polymerization (ATRP) in a controlled fashion to produce polymers with low molecular weight dispersities.[44]

4-Acetoxystyrene was polymerized via ATRP using Cu(I)Br as a catalyst initiating from propargyl 2-bromoisobutyrate **1**, a tertiary α-bromo ester initiator bearing an alkyne to produce a well-defined polymer, **2**, bearing a bromide end-group. The bromo functionality was then converted to an azido end-group by reaction with sodium azide in DMF and the end-modified polymer **3** was isolated by precipitation into hexanes. The linear polymer precursors were then cyclized via a highly efficient intramolecular "click" reaction between the alkynyl group on the α-initiating end of the polymer and the azido group on the ω-terminus of the polymer via a Cu(I)Br catalyst (Scheme 1) to yield macrocyclic polymer **4**.

By using a syringe pump to regulate and optimize the slow addition of the linear precursor **3**, the reactant could be converted to the corresponding cyclic analogue **4** utilizing high dilution to encourage the intramolecular cyclization over intermolecular coupling. The GPC traces of the starting material and crude reaction mixture verified that the linear precursors were converted in a nearly quantitative fashion (Figure 1). A shift to a longer retention time in the GPC of the cyclic polymer was consistent with a more compact cyclic architecture and confirmed that the intramolecular coupling had occurred.[45] The resultant *c*-PAS **4** was then deacetylated either via an acid catalyzed hydrolysis of the phenolic esters using a weakly acidic solution of 1−2% v/v H_2SO_4 in 4/3 THF/MeOH (~0.2−0.4M) or a weakly basic KOH in H_2O/MeOH solution to form the *c*-PHS precursor, **5**, that is necessary for the divergent dendronization procedure.[12,15] This reaction was monitored via ^{1}H NMR by confirming the complete disappearance of the acetate proton signal at 2.1 ppm. Additionally, a control experiment was performed to prove that the linking pivalate lactone ester in the backbone of the cyclic polymer was unhydrolyzed and that ring scission had not occurred to regenerate of the linear precursor (Figure S1 of the Supporting Information, SI). The retention of the cyclic architecture was proven by subsequent reacetylation of the PHS pendant alcohols on the backbone and overlaying the resultant GPC trace onto the original cyclic polymer. The resulting PAS polymer exhibited a monomodal GPC trace that overlaid exactly onto the *c*-PAS, with a notably longer retention time than the *l*-PAS, confirming the cyclic architecture was retained. It is believed that the observed selective hydrolysis of ester side chains results from their phenolic nature

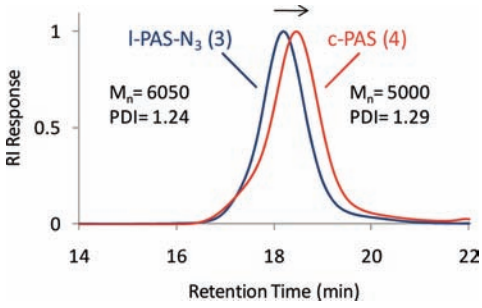
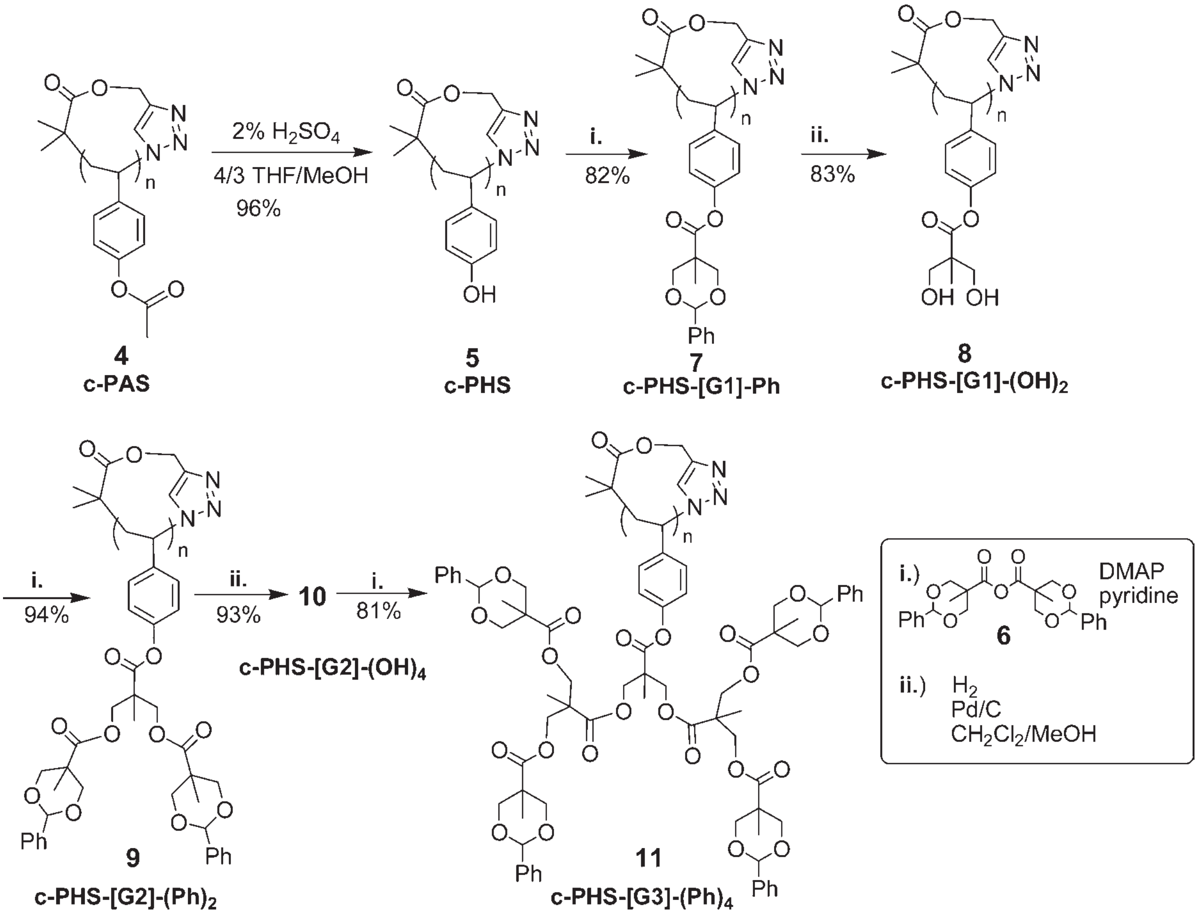


Figure 1. Representative GPC traces exhibiting longer retention time for cyclic poly(4-acetoxystyrene) **4** (red) and linear poly(4-acetoxystyrene) **3** (blue).

Scheme 2. Divergent Dendronization Process Used for Synthesis of Cyclic Dendronized Polymers Employing an Iterative Ester Anhydride Coupling and Pd-Catalyzed Hydrogenolysis Deprotection Step



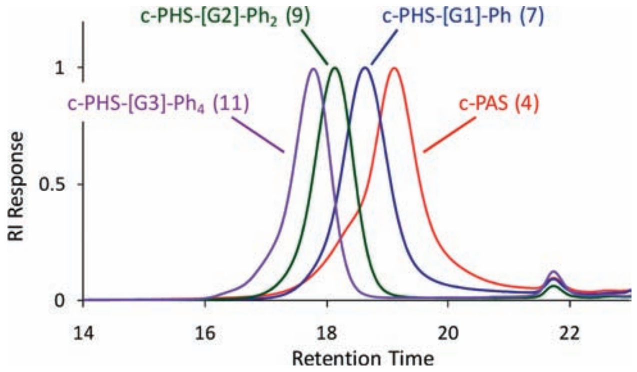


Figure 2. GPC traces of differing generation of poly(ester) based cyclic dendronized polymers produced via an iterative divergent "graft from" dendronization technique.

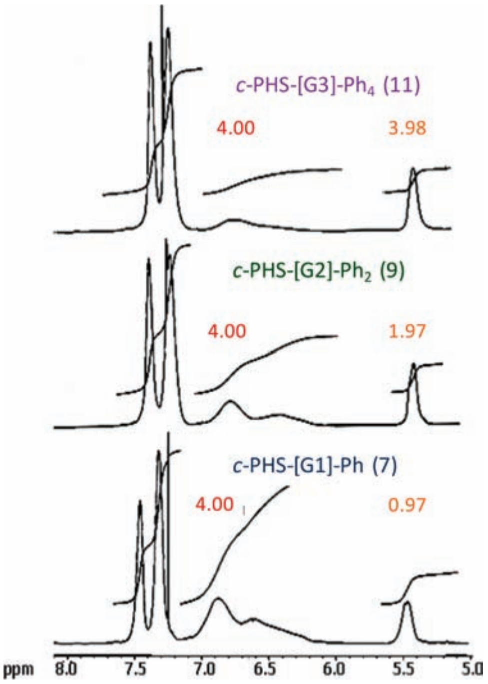


Figure 3. Selected ^{1}H NMR region of first (bottom), second (middle), and third (top) generation cyclic dendronized polymers produce via divergent dendronization showing near quantitative functionalization of the polymeric backbone. Highlighted are the resonances corresponding to the aromatic protons of the *c*-PHS core (6.0−7.15 ppm) and the acetal proton of the benzylidene acetal protecting group (5.35−5.6 ppm).

Table 1. Agreement between Theoretical Molecular Weight and MALDI-TOF MS as Well as GPC Data for Cyclic Dendronized Polymers

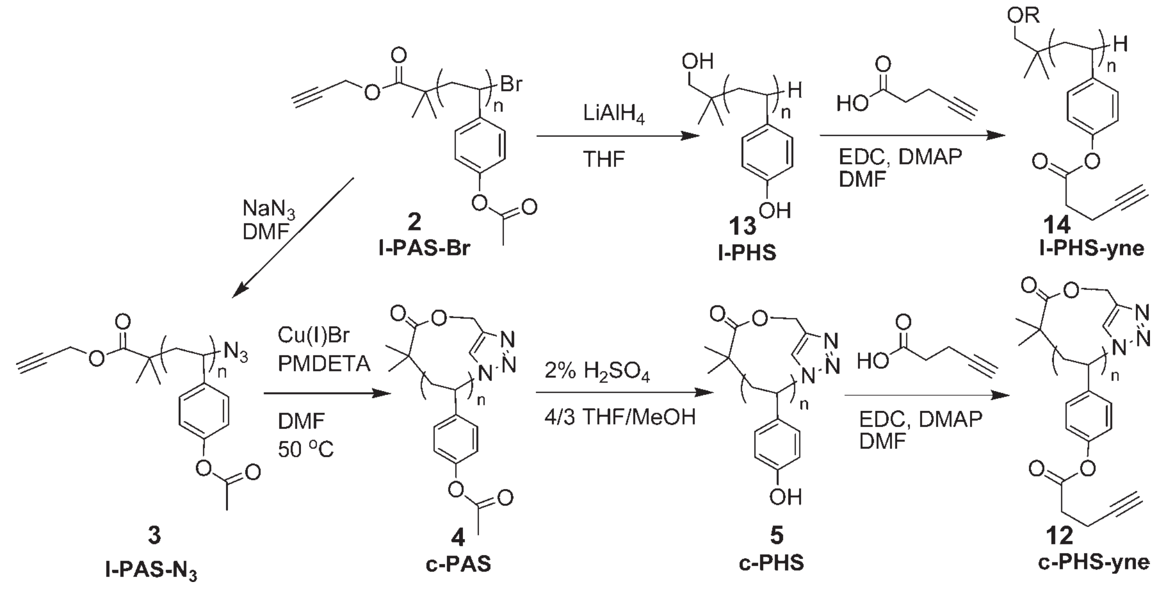
		MALDI-TOF MS		GPC	
	$M_{n,theo}$	M_n	PDI	M_n	PDI
c-PAS	3,300	-	-	3,300	1.17
c-PHS-[G1]-Ph (7)	6,800	6,300	1.14	4,400	1.16
c-PHS-[G2]-Ph$_2$ (9)	13,500	13,000	1.08	6,500	1.13
c-PHS-[G3]-Ph$_4$ (11)	27,000	28,800	1.06	9,600	1.13

as well as the substantial steric hindrance around the pivalate linker on the backbone.

Divergent dendronization of the resultant *c*-PHS **5** was carried out via an iterative procedure of esterification and hydrogenolysis (Scheme 2). First, the alcohol on each repeat unit of **5** was esterified using a benzylidene protected acid anhydride monomer **6** to produce the first generation cyclic dendronized polymer **7**. The cyclic benzylidene acetal was then deprotected via Pd-catalyzed hydrogenolysis to give the corresponding first generation cyclic dendronized polymer **8** with two alcohol surface functionalities per repeat unit. Benzylidene deprotection of the dendron corona was monitored by complete loss of benzylidene aromatic resonances (∼7.2−7.6 ppm) as well as the acetal hydrogen (5.4−5.5 ppm) via ^{1}H NMR. Additional iterations of the nearly quantitative dendron growth and deprotection reactions were verified by a transition to shorter retention times in the GPC for compounds **7**, **9**, and **11** (Figure 2), and by a doubling of the ^{1}H NMR integration values for the benzylidene protecting groups relative to the protons of the styrenic backbone (6.0−7.2 ppm) (Figure 3), as well as a doubling of the MWs in the MALDI-TOF mass spectra (Table 1). GPC traces of each of the cyclic dendronized polymers also show retention of a relatively low polydispersity throughout the dendronization procedure highlighting both the efficiency of this anhydride esterification/deprotection dendronization process and well-defined nature of the products. Molecular weights calculated by the GPC elution volumes were much lower than theoretical molecular weights, but this is expected due to the highly branched and compact nature of the dendronized units (Table 1). This coupling procedure gave excellent results for first, second, and third generation cyclic dendronized polymers with degrees of polymerization of less than ∼30 and upon deprotection, the third generation hydroxylated polymer with 8 hydroxyl units per repeat unit, exhibited modest solubility in water. However, while cyclic polymers remained monomodal at low DP (<30) through the dendronization process to the third generation, larger DP polymers (∼38) that maintained low PDIs for the first two generations, exhibited a loss of monomodality by GPC at higher generations of dendritic growth as noted by an impurity with shorter retention time (Figure S2 of the SI). The appearance of a high molecular weight shoulder has previously been reported during the divergent dendronization of linear polymer cores at high molecular weights using the same benzylidene protected anhydride monomer, and is hypothesized to result from either a covalent cross-linking side-reaction or a noncovalent aggregated assembly in these large, highly functional polymers.[12] We have also observed similar results in our synthesis when attempting to increase the degree of dendronization beyond the third generation for polymers with DP > 30. Divergent dendronization was also explored using acetonide protected bis-MPA monomers, but exhibited a similar loss of monomodality at high molecular weights. In order to explore an alternative route to making well-defined cyclic polymers, as well as expedite the synthetic procedure, an alternative "graft to" approach was investigated where preformed dendrons are attached to the cyclic core via a CuAAC coupling reaction.

Convergent "Graft to" Dendronization of Cyclic Macrocycles. The "graft to" approach utilized the same synthetic route to prepare the *c*-PHS **5** core as the "graft from" approach but carries out the iterative dendritic synthesis on the free dendrons before they are coupled to the core. It has been demonstrated

Scheme 3. Synthetic Methods Outlining the Process for an Exactly Comparable Linear and Cyclic Library of Polymers as Well as Functionalization of the Poly(4-hydroxystyrene) Backbone with 4-Pentynoic Acid for Click Grafting



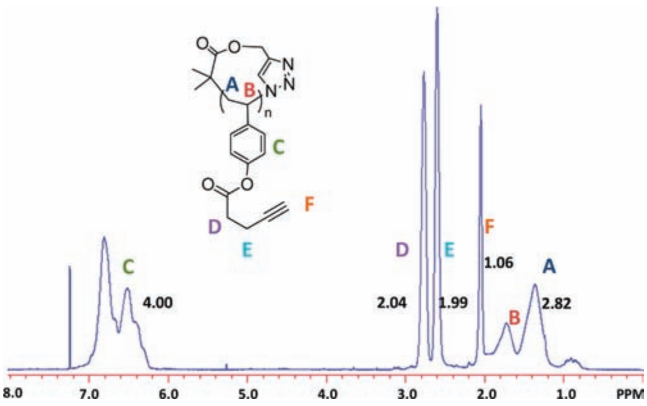


Figure 4. ^{1}H NMR and integration values of the cyclic alkyne functionalized poly(4-hydroxystyrene), *c*-PHS-yne (**12**) indicating near quantitative functionalization of the PHS backbone.

previously that linear dendronized polymers can be produced with high grafting efficiency via "click" coupling of azido-functionalized dendrons as large as the third generation onto alkyne functionalized linear polymer backbones in the presence of a Cu$^{(I)}$ catalyst.[17] Additionally, cyclic polymer brushes have also been reported through a click "graft to" method.[46] This alternative approach, much like the previous "graft from" approach, provides rapid synthetic access to a family of cyclic dendronized polymers, as well as an exactly analogous family of linear dendronized polymers (if the dendronization procedure is carried out on the same batch of linear core **2** before the cyclization step) (Scheme 3). These are attractive synthetic routes for elucidating the effect of the cyclic architecture on physical properties, as the linear and cyclic analogs should have nearly identical molecular weights and side chain structure, differing only in molecular topology.

The cyclic PHS core, **5**, was produced using an identical cyclization and deprotection procedure as described above, whereas the linear PHS core, **13**, was produced through reduction of the acetate functionalities along the polymer backbone as well as the ester functionality of the initiator with LiAlH$_4$. These strong reducing conditions were employed instead of hydrolytic conditions because of the uncertainty of potential side-reactions which may result from the α-carboxylic acid functionality in subsequent steps that would be produced during a simple acidic hydrolysis of the initiating ester.

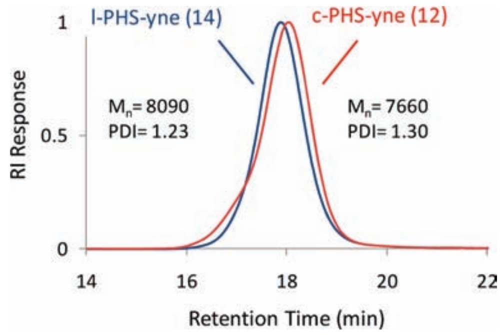
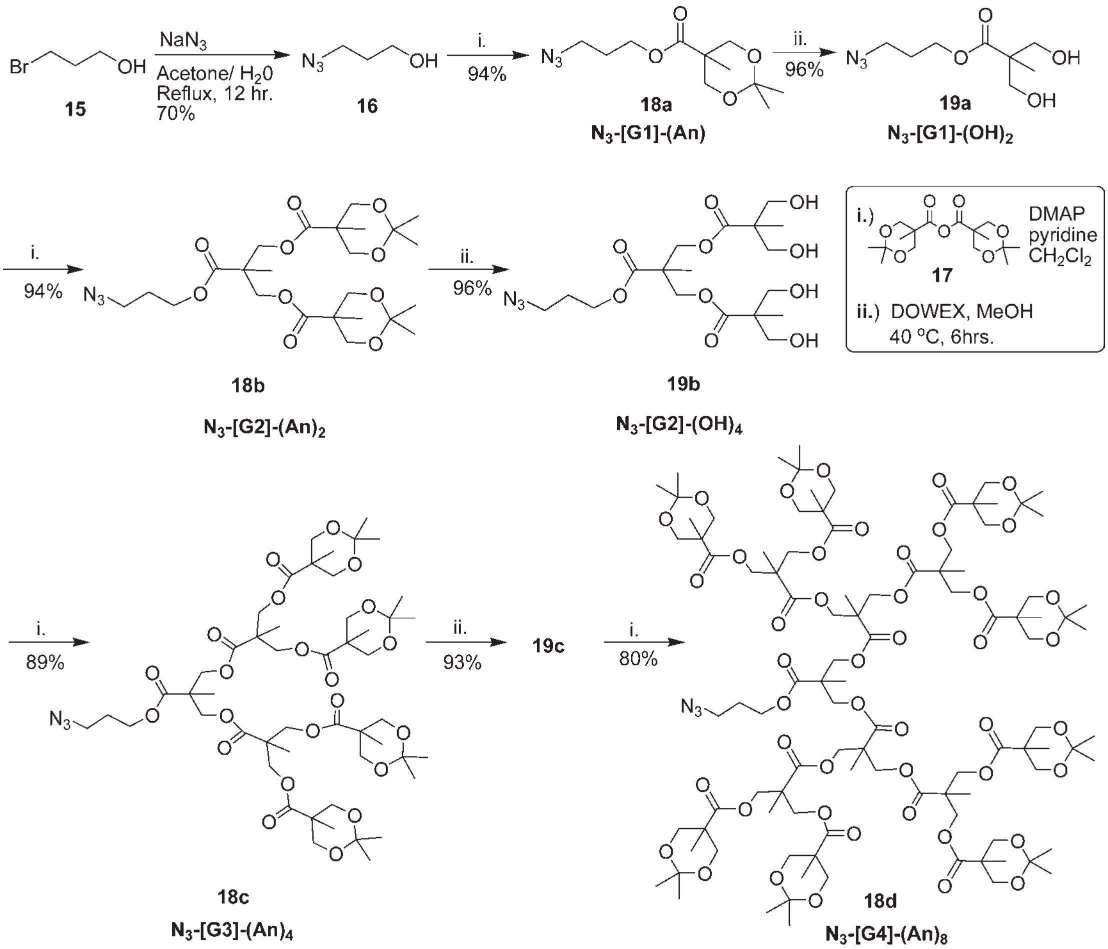


Figure 5. Linear **14** (blue) and cyclic **12** (red) PHS-alkyne scaffolds used for convergent click dendronization.

In order to adapt the parallel linear and cyclic "graft to" approach to our cyclization methodology, *l*-PHS **13** and *c*-PHS **5** were each functionalized with an alkynyl moiety through reaction of the pendant alcohols of PHS with 4-pentynoic acid using *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC) coupling agent (Scheme 3). A combination of MALDI-TOF MS and ^{1}H NMR integration values comparing the aromatic protons of the PHS core (6.20−7.00 ppm) and the methylene units of the formed alkynyl esters (2.70−2.90 ppm) of both the cyclic, **12**, and linear, **14**, alkyne functionalized polymers indicated near quantitative functionalization of the polymer backbone (Figure 4). Additionally, GPC traces verified that both linear and cyclic alkynylated polymer products maintained a narrow

Scheme 4. Divergent Dendronization of 3-Azido-propan-1-ol (16) To Produce a Library of Azido Functionalized Dendrons (18a−d)

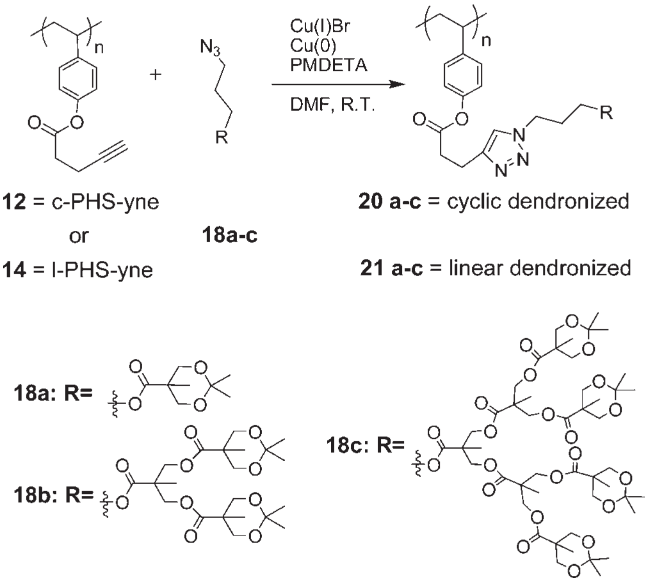


polydispersity and a shorter elution volume compared to their acetate protected counterparts **4** and **2**, respectively. Furthermore, GPC was also able to still resolve differences between the cyclic alkynylated polymer **12** and the less compact linear analogue **14**, as noted by the shorter elution volume of the linear analog (Figure 5).

A library of dendrons with a single azide functionality at the focal point were then prepared via a divergent dendronization procedure using an acetonide protected bis-MPA acid anhydride monomer (Scheme 4).[21,47] The azido group was first introduced by the reaction of NaN_3 with commercially available 3-bromo-propanol **15** to produce 3-azido-propanol **16** which was then esterified with acetonide protected bis-MPA acid anhydride, **17**, to produce the protected first generation azido functionalized dendron **18a**. The acetonide groups on this dendron could then be quantitatively removed using a solid phase acid exchange resin in MeOH to produce the first generation deprotected azido functionalized diol dendron **19a**. The completion of the deprotection reaction could be easily verified by the loss of acetonide resonances at 1.36 and 1.41 ppm in the ^{1}H NMR spectrum. This procedure was repeated in an iterative fashion in order to produce the second (**18b**), third (**18c**), and fourth (**18d**) generation azido functionalized dendrons. The monodisperse nature of the MALDI-TOF mass spectra of the resultant third **18c** and fourth **18d** generation dendron confirmed that complete coupling and deprotection had occurred at each step. For example, in the case of the third generation **18c**, only two peaks were observed in the MALDI-TOF spectrum, the first corresponding to the expect mass of the sodium adduct, 1096.47 ($[M + Na]^+$ theoretical m/z = 1096.50 Da), and the second corresponded to an in-source metastable fragmentation (loss of $-N_2$) that commonly occurs for polymeric azides during MALDI-TOF MS characterization.[48] Lower molecular weight impurities that might result from degradation or incomplete couplings were not observed which indicate that all coupling and deprotection reactions were carried out to completion. In addition, IR spectra of all of the azido-functionalized dendrons exhibited a clear azido stretching frequency at 2100 cm^{-1}, confirming retention of the focal azide functionality throughout the dendronization process.

These azido-functionalized dendrons **18a**−**d** were then "clicked" to the alkynyl functionalized linear (**14**) and cyclic (**12**) polymer cores (Scheme 5). This "click" grafting approach was investigated for first (**18a**), second (**18b**), third (**18c**), and fourth (**18d**) generation azido functionalized dendrons, using a 1.1/1 ratio of azide/alkyne with a Cu(I)Br/PMDETA catalyst in DMF. For the cyclic core, the "click" grafted products **20a**−**c** exhibited increasingly shorter GPC retention times with respect to the increasing generation of dendritic side chains (Figure 6). However, reaction with the fourth generation azido-functionalized dendron exhibited only minimal coupling onto the cyclic polymer

Scheme 5. Convergent "Graft to" Click Coupling Route of a Library of Azido-Functionalized Dendrons (18a−c) onto Both Linear (14) and Cyclic (12) Alkynylated Polymer Cores



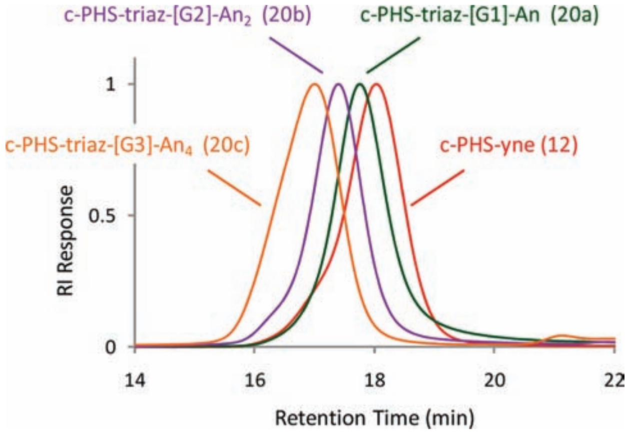


Figure 6. GPC traces of cyclic "click" dendronized polymers **20a**−**c**: *c*-PHS-alkyne **12** (red), *c*-PHS-triaz-[G1]-An **20a** (green), *c*-PHS-triaz-[G2]-(An)$_2$ **20b** (purple), and *c*-PHS-triaz-[G3]-(An)$_4$ **20c** (orange).

core, as judged by GPC, even when using microwave irradiation, elevated temperature, and extended reaction times. This result coincides with the first reported use of CuAAC to dendronize linear polymers, in which Fréchet-type aryl ether dendrons exhibited poor coupling efficiencies above the third generation[17] suggesting that the azido-functionality is sufficiently buried within the dendritic structure at the fourth generation so as to prevent reaction with the polymeric alkynes.

However, unlike the divergent "graft from" approach, the GPC traces remain monomodal even for the higher molecular weight cores, and with dendrons as large as the third generation, suggesting this click "graft to" approach can overcome the complications observed for the divergent "graft from" approach for higher molecular weight dendronized polymers. Similar results were also noted for the click "graft to" approach for the analogous linear dendronized polymer products (Figure S3 of the SI).

A significant advantage to preparing exactly analogous linear and cyclic dendronized polymers is the ability to verify and explore changes in physical properties relative to the architecture of the core that has been dendronized. For example, at the first generation, the cyclic [G1]-dendronized polymer **20a** still shows a notably longer retention time than its linear counterpart **21a**, resulting from the relatively confined configuration of the dendronized cyclic polymer as a result of its ring-like topology (Figure 7). A similar trend is also observed, but less pronounced for the second generation of grafted polymers, namely cyclic [G2]-dendronized polymer **20b** and its linear analogue **21b**. However, the difference is not discernible for the third generation presumably because size of the dendritic side chains for this generation begins to approach the length of the polymer backbones, (DP = 38), yielding similar globular structures regardless of backbone architecture.

These polymers were also characterized in detail by ^{1}H NMR in order to quantify the extent of grafting. ^{1}H NMR spectra of each generation of the cyclic dendronized polymers (**20a**−**c**) are shown in Figure 8. The coupling efficiency was calculated by comparing the integrated values of the protons of the polymeric backbone (aromatic protons at 6−7 ppm) and the proton found on the formed triazole ring (~7.5 ppm). The values for the calculated coupling efficiency are shown in Table 2. It should also be noted that Cu(0) was used as an additive to the "click" reaction in an effort to increase the concentration of the active Cu(I) species for the coupling of both second and third generation dendritic azides onto the polymer backbone. The addition of Cu(0) to the reaction resulted in much higher coupling efficiencies, typically around 10−20% higher than without Cu(0), which have been attributed to the ability of Cu(0) to

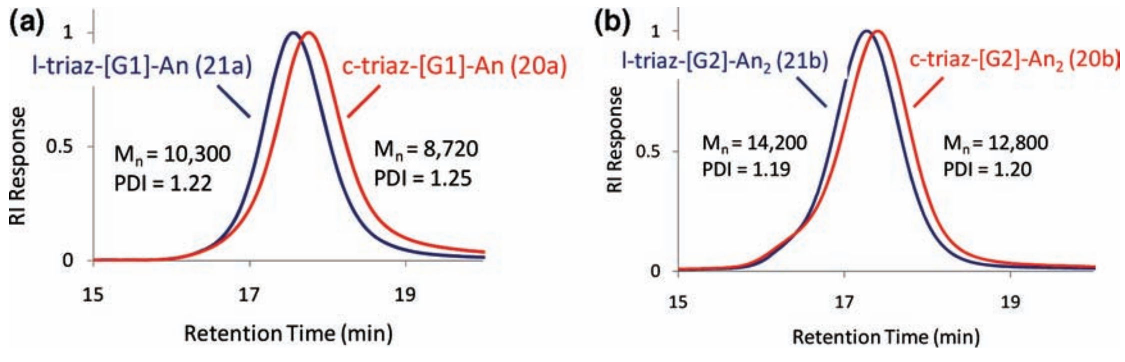


Figure 7. GPC traces of linear (blue) and cyclic (red) first (a) and second (b) generation "click" dendronized polymers, respectively.

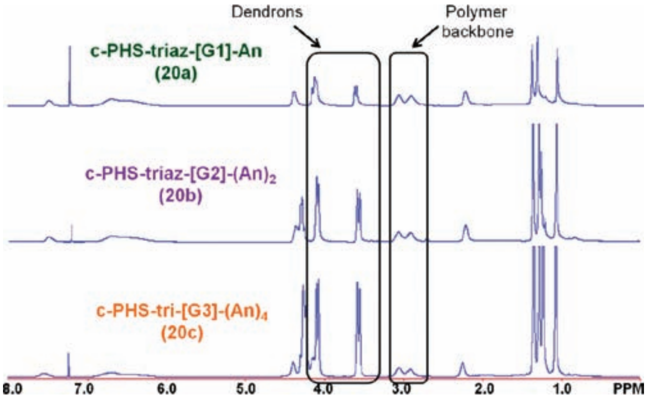


Figure 8. ^{1}H NMR spectra of cyclic "graft to" dendronized polymers of first generation **20a** (top), second generation **20b** (middle), and third generation **20c** (bottom) highlighting growth of dendrons with respect to polymer backbone with increasing generation. Also noted is the presence of the aromatic triazole proton which was used to determine the coupling efficiency of the "graft to" process present at 7.5 ppm.

Table 2. GPC Data and Coupling Efficiency at Each Generation for Both the Linear (21 a−c) and Cyclic (20 a−c) Dendronized Polymers

	GPC Data					
	Linear (21a-c)			Cyclic (20a-c)		
Generation	M_n	PDI	Coupling Eff. (NMR)	M_n	PDI	Coupling Eff. (NMR)
PAS	6,050	1.24	-	5,000	1.29	-
PHS-yne	8,090	1.23	100%	7,660	1.30	100%
PHS-triaz-[G1]-An	10,300	1.22	86%	8,720	1.25	84%
PHS-triaz-[G2]-An$_2$	14,200	1.19	90%*	12,800	1.20	76%*
PHS-triaz-[G3]-An$_4$	19,700	1.18	90%*	19,300	1.22	88%*

* Cu(0) was added during CuAAC.

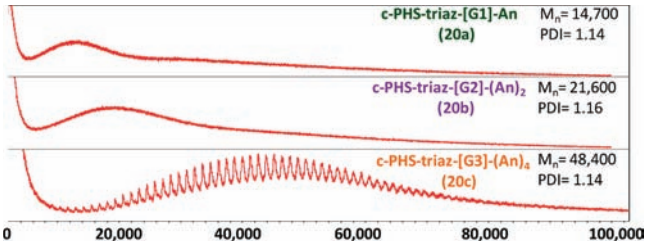


Figure 9. MALDI-TOF mass spectra of first [G1] **20a** (top), second [G2] **20b** (middle), and third **20c** [G3] (bottom) generation cyclic "graft to" dendronized polymers exhibiting an increase in molecular weight upon coupling of higher generation azido-functionalized dendrons (**18a**−**c**). MALDI-TOF mass spectra of analogous series of linear "graft to" dendronized polymers (**21a**−**c**) can be found in the Supporting Information (Figure S4).

regenerate active Cu(I) from the oxidized Cu catalyst. For example, in the case of the second generation dendronization of the linear backbone, a coupling efficiency of 70% was noted without Cu(0), whereas the incorporation of Cu(0) during the "click" reaction showed a coupling efficiency of 90%. Similar results were noted for the third generation dendronization of the cyclic backbone yielding 72% coupling without Cu(0) and 88% with Cu(0).

Table 3. Theoretical and Observed MALDI-TOF MS Data for "Graft to" Coupling Process at Each Generation for Both the Linear (21a−c) and Cyclic (20 a−c) Dendronized Polymers

	MALDI-TOF MS Data				
		Linear (21a-c)		Cyclic (20a-c)	
Generation	$M_{n,theo}$	M_n	PDI	M_n	PDI
PHS-yne	7,400	6,700	1.09	6,800	1.05
PHS-[G1]-An	16,900	15,500	1.11	14,700	1.14
PHS-[G2]-An$_2$	27,000	25,600	1.14	21,600	1.16
PHS-[G3]-An$_4$	47,100	44,400	1.18	48,400	1.14

MALDI-TOF mass spectra also verified the high extent of CuAAC coupling through the third generation of dendrons, based on molecular weight calculations (Figure 9). Because MALDI-TOF MS enables measurement of the absolute molecular weight, the number average molecular weights calculated from the mass spectra nearly double for the first (**20a**) to second generation (**20b**) and double again at the third generation (**20c**). The M_n for MALDI-TOF values observed match closely to the predicted values (Table 3) and in the case of the third generation, the spacing of the crudely resolved peaks agrees with the predicted repeat unit of 1275 Da.

■ CONCLUSIONS

We have developed synthetic methods for the preparation of cyclic dendronized polymers through two routes, namely a divergent "graft from" approach and a convergent "graft to" approach. Both methods rely on the use of a cyclic poly(4-acetoxystyrene) produced via a CuAAC end-to-end intramolecular cyclization reaction performed at high dilution and therefore provide access to exactly comparable linear and cyclic analogues. The "graft from" route was successfully performed via an iterative anhydride esterification reaction followed by catalytic hydrogenolysis of the benzylidene protecting groups on the surface of the dendronized polymers. This method allows for the preparation of cyclic dendronized materials up to the third generation for polymer exhibiting a DP of less than 30; however, for larger polymers, high generation materials with narrow polydispersity were difficult to obtain. The convergent "graft to" method was also explored to produce cyclic polymers by first functionalizing the cyclic polymer backbone "core" with an alkynyl group and subsequently coupling to a library of azido-functionalized dendrons. This method allows for the efficient preparation of up to third generation cyclic dendronized materials showing approximately 90% coupling efficiency at the third generation without loss of monomodality at higher molecular weights. Additionally, a set of analogous dendronized linear polymers can be prepared, and comparison of the GPC retention times exhibited the expected shift to more compact configurations for the cyclic polymers when compared to their linear analogues through the second generation. These results suggest the "graft-to" route is the most versatile of the three routes, in enabling control of the macrocycle diameter, degree of dendronization, and overall molecular weight, while yielding extremely narrow polydispersity cyclic dendronized polymers.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Characterization of all synthetic compounds, data for reacylation of compound **5** as control experiment, example of GPC traces for high DP cyclic dendronized polymers prepared by the "graft from" route, and MALDI and GPC data for linear dendronized compounds **21a**−**c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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