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Access to cyclic polystyrenes *via* a combination of reversible addition fragmentation chain transfer (RAFT) polymerization and click chemistry

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ABSTRACT

The coupling of the reversible addition fragmentation chain transfer (RAFT) polymerization technique with the copper-catalyzed Huisgen 1,3-dipolar cycloaddition ("click chemistry") as a simple and effective way to generate polystyrene (PS) macrocycles is presented. The novel strategy entails the synthesis of linear PS backbones followed by endgroup modification to facilitate click chemistry for the formation of ring shaped polymers. An azido group modified 4-cyanopentanoic acid dithiobenzoate is employed as the chain transfer agent in the RAFT mediated polymerization of styrene to form PS with M_n from 2000 g mol^{-1} to 6000 g mol^{-1} and PDI < 1.2. To facilitate the cyclization of the polystyrene chains by click coupling, the thiocarbonylthio endgroup is removed and concomitantly replaced by an alkyne bearing function. This is carried out *via* the radical decomposition of excess azobis(4-cyano valeric acid) (ACVA) modified with an alkyne endgroup in the presence of the thiocarbonylthio-capped PS. The successful click endgroup modifications of several polystyrenes along with the results from the cyclization of a PS with $M_n = 4300$ g mol^{-1} are discussed in detail. This improved method avoids the presence of thiocarbonylthio functions in the macrocycle, thus considerably increasing the chemical stability of these polymers.

1. Introduction

Numerous synthetic methods have been explored by several groups for optimizing the control over polymer architecture [1–5] as a prerequisite to manipulate the material properties. In particular, cyclic polymers have become increasingly attractive over the past years due to their unique architecture and their novel properties [6] (due to the absence of endgroups), potentially simple bond cleavage [7], bond interchange reactions [8,9] or the formation of catenanes [10–12], rotaxanes [11,13–15] or knots [10,11,16,17]. In the past, cyclic oligomers have been identified as side products in step-growth polymerizations, formed by ring-opening through backbiting reactions [18–20] or ring-chain equilibrium reactions [21]. However, several challenges exist in controlling the molecular weights and polydispersity in order to obtain well-defined cyclic macromolecules. Significant efforts have been dedicated to the preparation and characterization of cyclic homopolymers *via* anionic polymerization using bifunctional initiators and bifunctional coupling agents [22–26]. In an alternative approach, Deffieux and his coworkers [27], employed a coupling reaction under conditions of extreme dilution for the synthesis of vinyl type polymers. Their work involved direct coupling of a heterotelechelic linear polymer precursor previously prepared by living polymerization. In an alternative approach, Cramail and coworkers used linear PS featuring two living endgroups with 1,3-bis(1-phenylethylenyl)benzene (DDPE) as a coupling agent [28]. Hemery et al. detailed a synthetic route to heterotelechelic PS *via* nitroxide-mediated radical polymerization and its cyclization by intramolecular esterification [29]. Some of these earlier syntheses often involve incomplete cyclizations or undesired side reactions which require tedious purification procedures to remove the impurities. Laurent and Grayson [32] demonstrated a strategy to achieve cyclization *via* the combination of ATRP and click chemistry. In their work, PS prepared by ATRP was selected because the terminal benzylic bromide represents a good substrate for a nucleophilic displacement with an azide. The synthetic strategy for the synthesis of cyclic polymers and block copolymers by monomer insertion into a cyclic chain transfer agent was successfully followed by Pan et al. [31]. Monteiro et al. [33] achieved

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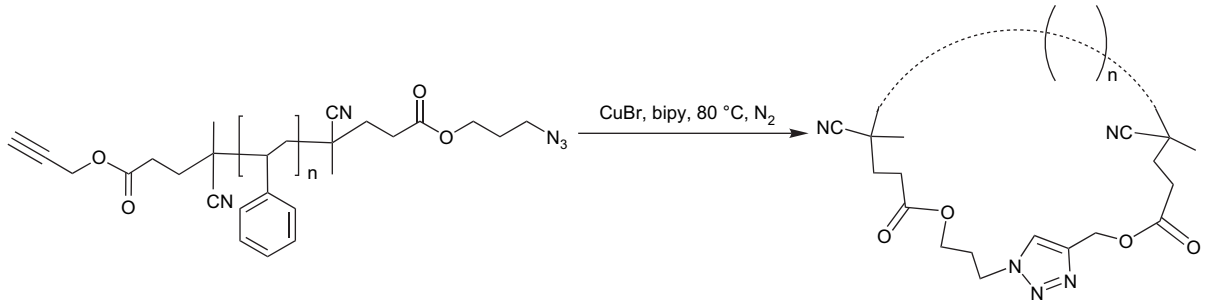


Scheme 1. Click cyclization procedure of telechelic polystyrenes.

formation of unique monocyclic polystyrene chains by polymerizing styrene in the presence of a difunctional RAFT agent and subsequent conversion of the dithioester endgroups to thiols. Monocyclic polymer was obtained by oxidation under dilute conditions. Xu et al. [34] reported the preparation of cyclic poly(*N*-isoproylacrylamide) (PNIPAM) using an approach similar to the one published by Laurent and Grayson [32] by combining ATRP and click chemistry using propargyl 2-chloropropionate as the initiator, followed by reacting with NaN_3 to transform the terminal chloride into azide group. The subsequent end-to-end intramolecular coupling reaction was conducted under high dilution. Recently, Winnik et al. [35] prepared cyclic PNIPAM in aqueous solution synthesized by reversible addition fragmentation chain transfer polymerization (RAFT) carrying an azidoethoxyethyl group on one end. The propargyl group was inserted by a one-pot aminolysis/Michael addition sequence. Click cyclization leads to a polymer with a carbon–sulfur bond in the macrocycle, which makes the ring potentially unstable towards chemical attack.

In comparison, the present approach for cyclization of linear polystyrene chains also provides ready accessibility towards ring closure due to suitable insertion of the prerequisite alkyne and azido functional groups, which are required for click chemistry (Scheme 1) and at the same time provides a macrocyle with higher chemical stability.

In the current study, the RAFT polymerization technique is combined with click chemistry to obtain the ring shaped polymers. RAFT is a particularly attractive approach for synthesizing macrocyclic precursors because of the easy amenability of the azido endgroup functionality using a recently developed azido dithiobenzoate RAFT agent [36] followed by the exchange of the Z-group with an alkyne functionalized initiator (Scheme 2).

The basic mechanism involved in the click reaction, employed for the preparation of our ring shaped polymers, is the copper-catalyzed Huisgen 1,3-dipolar cycloaddition of a terminal alkyne and an azide to form a 1,4-disubstituted 1,2,3-triazole [37]. The challenge in preparing cyclic polymers *via* RAFT was to synthesize the alkyne-terminated initiator to obtain the required end functionality for the click cyclization and to find the best conditions to achieve cyclization in high yields.

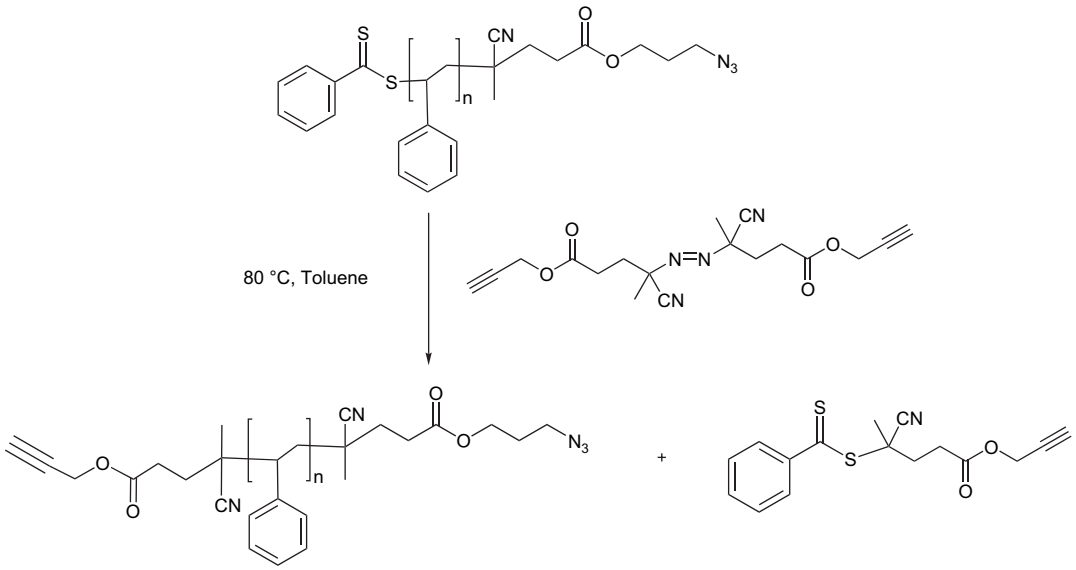
2. Experimental

2.1. Materials

All chemicals and solvents where purchased from Sigma-Aldrich, Acros and Fluka at the highest available purity and used as received unless otherwise noted. Styrene was purified by passing through a basic alumina column. Dimethylformamide (DMF) was dried over molecular sieve or distilled. The thermally decaying initiator 2,2′-azoisobutyronitrile (AIBN, Aldrich, 99%) was purified by crystallization from ethanol. The synthesis of the azido dithiobenzoate RAFT agent (Scheme 2) was undertaken according to the previously reported protocols [36,38].

2.2. Measurements

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker ACF300 300-MHz spectrometer with $CDCl_3$ as the solvent. 2D NMR



Scheme 2. Endgroup modification of the PS chain *via* removal of the thiocarbonylthio functionality to obtain telechelic homopolymers.

measurements (HMBC and HSQC) were performed using a Bruker 500 MHz spectrometer. The SEC setup was performed in pure THF at an elution rate of 1 mL min^{-1} using PSS–SDV gel columns (300 × 8 mm, 5 μm): 10^5, 10^4, 10^3, and 10^2 Å with RI and UV (260 nm) detection. Polystyrene standards were used to calibrate the columns. Samples from preparative SEC were analysed using THF SEC with a precolumn (SDV–Gel (PSS), L: 5 cm, D: 0.8 cm, particle size: 5 μm, pore size: 100 Å) and analytical columns (PL–Gel (PL), *L*: 2 × 60 cm; *D*: 0.8 cm, particle size: 5 μm, pore size 100 Å) with THF as eluent and a flow rate of 0.5 mL min^{-1}. The calibration is based on PS standards. Preparative SEC was carried out on an instrument with a precolumn: SDS (PSS), 5 μm, and analytical columns: PL–Gel (PL), *L*: 30 cm, *D*: 2.5 cm, 10 μm, 10^4 Å, *L*: 30 cm, *D*: 2.5 cm, 10 μm, 10^3 Å, 2 × 10 μm, 100 Å, *L*: 60 cm, *D*: 2.5 cm and *L*: 30 cm, *D*: 2.5 cm. VISCO–SEC was conducted on an Agilent HPLC system (1200 series) with a flow rate of 0.8 mL min^{-1} in THF (HPLC grade) at room temperature. Four detectors were used for the VISCO–SEC: UV (260 nm), RI, Viscometer, Model 250 (Viscotek), (Columns: PSS–SDV, 10^6 Å, 5 μm, 10^5 Å, 5 μm, 10^3 Å, 5 μm). Liquid adsorption chromatography under critical conditions (LACCC) was conducted on a HPLC system at a flow rate of 0.5 mL/min. An evaporative light scattering detector (ELSD, PL-EMD 960) operating at 80 °C with a gas flow rate of 6.8 L/min was used for mass detection. Then 10 μL samples of ca. 0.5 wt% polymer solutions were injected. All measurements were carried out at a constant column temperature of 25 °C. Two reversed phase columns (YMC, 250 × 4 mm) with 5 μm average particle size and 100 and 300 Å pore diameters were used. The critical solvent composition for PS is THF/hexane 43:57 (v/v). Premixing of the mobile phase by weight is necessary for a constant and exact composition. The FT-NIR and ATR-FTIR measurements were performed using a Bruker IFS66\S FTIR spectrometer equipped with a tungsten halogen lamp, a CaF_2 beam splitter and a liquid nitrogen-cooled InSb detector (FT-NIR). For ATR-FTIR a KBr beam splitter was used. Each spectrum in the spectroscopic region of 4000–500 cm^{-1} was calculated from the co-added interferograms of 16 scans with a resolution of 4 cm^{-1}. UV–vis measurements were carried out on a CARY 300 double-beam spectrophotometer.

2.3. Mass analysis

ESI-MS experiments were carried out using a Thermo Finnigan LCQ Deca ion trap mass spectrometer (Thermo Finnigan, San Jose, CA) equipped with an atmospheric pressure ionization source operating in the nebulizer-assisted electrospray mode. The instrument was calibrated with caffeine, MRFA, and Ultramark 1621 (all from Aldrich) in the mass range 195–1822 Da. All spectra were acquired in positive ion mode with a spray voltage of 5 kV, a capillary voltage of 44 V and a capillary temperature of 225 °C. Nitrogen was used as sheath gas (flow: 50% of maximum) while helium was used as auxiliary gas (flow: 5% of maximum). The eluent was a 6:4 v/v mixture of THF/methanol. All reported molecular weights were calculated *via* the program package CS ChemDraw 6.0 and are monoisotopic. MALDI-TOF mass spectra were recorded on a Bruker Reflex III operated in linear mode using a nitrogen laser (337 nm) and an accelerating voltage of 20 kV. Dithranol was used as matrix and silver trifluoroacetate as salt. Samples were prepared from THF solution by mixing matrix (20 mg mL^{-1}), sample (10 mg mL^{-1}) and salt (10 mg mL^{-1}) in a ratio 20:5:1. The instrument was calibrated with a peptide calibration standard from Bruker (part no. 206195) containing a mixture of different peptides in the mass range from $[M+H]^+ = 1047.20$ to $[M+H]^+ = 3149.61$. For the medium range protein calibration standard I was used (part no. 206355) in the mass range from $[M+H]^+ = 5734.56$ to $[M+H]^+ = 16\,952.55$. As titration device a Metrohm automatic 809 Titrando system was used with a 20 mL dosing unit (800 Dosino).

Table 1
RAFT polymerizations of styrene with azido dithiobenzoate click-RAFT agent

Exp.	[M]:[CTA]:[I]	Time (min)	Temp. (°C)	Solv.	$M_{n,th}$ [c] (g mol^{-1})	M_n^a (g mol^{-1})	PDI[a]	Conv.[b] (%)
1	150:5:1	1260	60	–	5100	5300	1.08	30
2	150:5:1	590	60	–	3200	3500	1.09	17.5
3	150:5:1	820	60	–	3500	3700	1.19	20
4	200:1:0.2	510	80	DMF	3100	4800	1.11	13
5	250:5:1	330	60	–	2800	2900	1.08	9
6	500:5:1	180	60	–	2500	1900	1.05	4

[a] The experimental number-average molecular weight, $M_{n,exp}$ and the polydispersity index, PDI, were measured by size-exclusion chromatography (SEC) using polystyrene standards in THF.
[b] Conversion was determined by gravimetry.
[c] The theoretical number-average molecular weight was calculated according to the equation, $M_{n,th} = M_M \times \text{conv.} \times [M]_0/[CTA]_0 + M_{CTA}$ where $M_{n,th}$ is the theoretically calculated molecular weight of the polymer, M_M is the molecular weight of the monomer, $[M]_0$ and $[CTA]_0$ the concentration of the monomer and the concentration of the RAFT agent, M_{CTA} is the molecular weight of the RAFT agent.

2.4. Polymerization procedures

All polymerizations were carried out using the conditions described in Table 1. During the polymerizations, samples were taken at predetermined time intervals so as to monitor the monomer-to-polymer conversion as well as the molecular weight evolution with the monomer conversion. For the described cyclization procedures, linear PS chains with molecular weights in the range from 2000–5000 g mol^{-1} were used.

2.4.1. Synthesis of the alkyne endgroup modified initiator (propargyl initiator) (**1**)

Azobis(4-cyano valeric acid) (ACVA) (1.5 g, 5.35×10^{-3} mol, 1 equiv.) and propargyl alcohol (3.0 g, 5.35×10^{-2} mol, 10 equiv.) were dissolved in a mixture of THF (30 mL) and water (20 mL). This solution was cooled to 0 °C and *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 3.08 g, 1.61×10^{-2} mol, 0.33 equiv.) and 4-di(methylamino)pyridine (DMAP, 0.65 g, 5.35×10^{-3} mol, 1 equiv.) were subsequently added. The mixture was stirred at 0 °C for 2 h and then at ambient temperature overnight. The reaction mixture was washed with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were dried over $MgSO_4$. The product was purified by column chromatography using dichloromethane as the eluent. The volatiles were removed under reduced pressure and the product was isolated as a white powder (1.6 g, 84%). ^{1}H NMR ($CDCl_3$, δ in ppm): 4.7 (t, 4H, C*H*$_2$O), 2.5–2.4 (m, 10H, C≡*H*, CO*CH*$_2$C), 1.72 (s, 3H, CH_3), 1.67 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, δ in ppm): 170.4 (2C, C═O), 117.3 (2C, CN), 77.2 (2C, CH), 75.3 (2C, *C*HCH$_2$), 71.7 (2C, *C*CN), 52.4 (2C, CH_2O), 32.9 (2C, *C*H$_2$CO), 28.9 (2C, *C*H$_2$C), 23.8 (2C, *C*H$_3$); ESI-MS $[C_{18}H_{20}N_4O_4]Na^+$, Calc.: 379.1 g mol^{-1}, found.: 379.1 g mol^{-1}.

2.4.2. Preparation of azide functionalized polystyrenes (dithio-PS-N_3)

A master batch solution of styrene (7.2 g, 6.9×10^{-2} mol), dithiobenzoate RAFT azido (0.05 g, 1.38×10^{-4} mol) and AIBN (0.046 g, 2.80×10^{-4} mol) was prepared and aliquots were placed in a Schlenck tube. The solution was mixed thoroughly and subsequently degassed by four freeze-pump-thaw cycles to remove any residual oxygen. The polymerization reaction was performed at 60 °C unless indicated otherwise. In order to monitor the progress in the polymerization, samples were withdrawn with a gas-tight syringe at predetermined time intervals and the polymerizations were quenched by cooling the solutions at 0 °C in an ice bath. The molecular weights and polydispersity indices were obtained using SEC. The monomer-to-polymer conversion was determined by gravimetry. The residual monomer in the samples taken at predetermined time intervals was evaporated under vacuum at room temperature.

It should be noted that at low monomer conversions, low molecular weights were obtained (<800 g mol^{-1}) which could not be quantified and therefore were omitted from the linear fit (see Fig. 1).

2.4.3. General endgroup modification of dithio-PS-N_3 with propargyl initiator (alkyne-PS-N_3)

In a Schlenck tube, dithio-PS-N_3 (0.1 g, 4×10^{-5} mol) and the alkyne-modified initiator (0.284 g, 8×10^{-4} mol) were dissolved in 3 mL toluene. The solution was degassed by purging with N_2 for 30 min followed by stirring at 80 °C for several hours. The endgroup conversion was indicated by a change in color of the solution from pink to yellow. After completion of the reaction, the solution was cooled to ambient temperature and was added dropwise into cold hexane. The resulting white polymer was filtered and dried.

2.4.4. Click cyclization procedure

To a 250 mL custom-built flask, DMF (180 mL) was added and was degassed using 2 freeze-pump-thaw cycles. To the DMF 0.16 g (1.0×10^{-3} mol) CuBr and 0.45 g (2.0×10^{-3} mol) 2,2′ bipyridyl (bipy) were added . The flask was then resealed and degassed with N_2 while connected to the Titration system (Metrohm, 809 Titrando). The dosing unit containing alkyne-PS-N_3 (0.06 g, 2.0×10^{-5} mol, $M_n = 3000$ g mol^{-1}) dissolved in 20 mL DMF was degassed by bubbling nitrogen. This solution was then transferred to the CuBr/bipy reaction solution at 80 °C *via* a dosing unit at a rate of 0.01 mL min^{-1}. Once the polymer addition to the catalyst solution was completed, the reaction was allowed to proceed at 80 °C for 2 h. After cooling to ambient temperature the DMF was removed and column chromatography in THF was used to remove the catalyst. The crude polymer was precipitated in methanol and dried *in vacuo*.

3. Results and discussion

The dithiobenzoate RAFT agent [36] was designed to entail the prerequisite functionality for the click chemistry. This modified RAFT agent carrying an azide group (azido dithiobenzoate click-RAFT agent, Scheme 2) was employed in the polymerization reaction. RAFT polymerizations of styrene were carried out in bulk at 60 °C using AIBN as the initiator. The azido dithiobenzoate click-RAFT agent has been shown to provide good control of the polymerization of styrene as demonstrated previously by Quémener et al. [36] as well as Gondi et al. [38]. As shown in Fig. 1, the molecular weight increases linearly with the monomer conversion while the polydispersity indices remain less than 1.2 indicating effective living/controlled polymerization leading to homopolymers with molecular weights close to that theoretically expected and low PDI (Table 1).

To facilitate the cyclization of the PS chain by click coupling, the thiocarbonylthio endgroup was modified with the required acetylene functionality as shown in Scheme 2. The insertion of the alkyne group at the PS chain end was accomplished by the removal of the thiocarbonylthio endgroup from the polymeric chains according to the method described by Perrier and coworkers [39]. Using this method, the carboxylic acid groups of azobis(4-cyano valeric acid) (ACVA) were converted to alkyne esters to obtain the modified initiator. The alkyne-modified initiator decomposes in solution to form two propargyl 4-cyanovalerate radicals. These radicals react with the C=S of the thiocarbonylthio moiety in the polymer chain. Under conditions of an excess of the initiator radicals, the equilibrium between the formation of free leaving group radicals (R-group) and the fragmentation of the original attacking radicals, is displaced towards the formation of the R-group radical. The R-group radical can subsequently react with the free initiator radicals and the dithio moiety of the polymer chains with the alkyne initiator fragments is substituted.

The alkyne-modified initiators were characterized by ^{1}H NMR, ^{13}C NMR, 2D NMR (HMBC, HSQC) and ESI-MS spectrometry (see Supplementary data, Fig. S1). The theoretically calculated molecular weights of the alkyne-modified initiator correlate well with the experimental values determined by ESI-MS *i.e.* $M_{n,calc} = 379.1$ g mol^{-1} while $M_{n,exp} = 379.1$ g mol^{-1}.

After the reaction with the alkyne-modified initiator, the polymer was isolated by precipitation in cold hexane resulting in a white powder indicating the removal of the dithio moiety. To confirm this observation, UV–vis measurements were carried out before and after treatment with the alkyne-modified initiator, which indicated the loss of the characteristic peak of the dithiobenzoate moiety (500–510 nm) (Fig. 2). The complete removal of the dithio moiety was further corroborated by the elemental analysis data that resulted in sulfur composition in the modified PS below the detection limit (<10 ppm).

The SEC trace of alkyne-modified PS samples (alkyne-PS-N_3) with different molecular weights is given in Fig. 2a along with that of the unmodified polymer (dithio-PS-N_3), indicating no significant change in the molecular weight upon endgroup functionalization.

The non-modified PS shows a small shoulder at higher molecular weights, which is due to the formation of coupled polymer chains during the synthesis [30]. It can be seen that this shoulder slightly increased in area after the endgroup modification. Such an

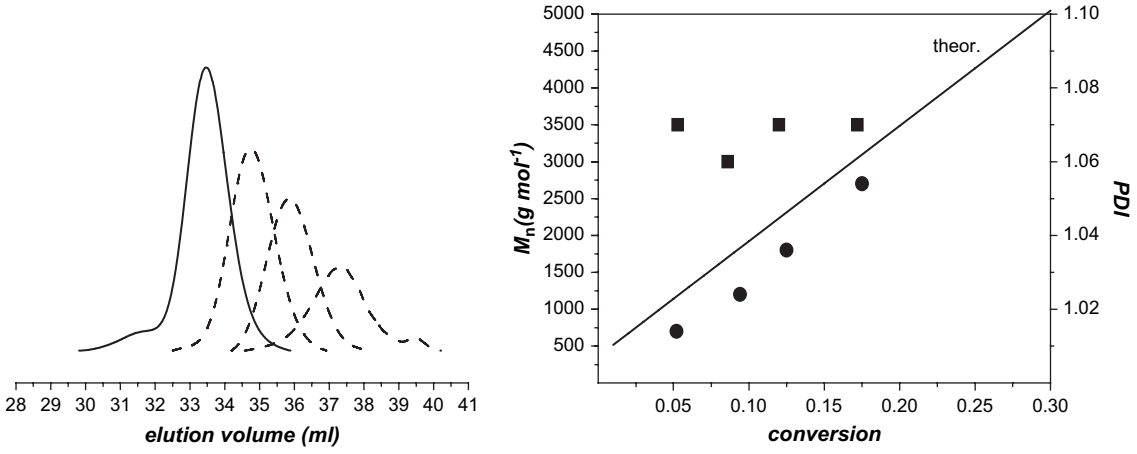


Fig. 1. Left: SEC traces of the evolution of the molecular weight for RAFT polymerization with azide dithiobenzoate RAFT agent at 60 °C (Exp. 2, reaction terminated after 17.5% conversion); right: Evolution of the number-average molecular weight with monomer conversion. The solid line shows the theoretical number-average molecular weight, taking the molecular weight of the transfer agent into account.

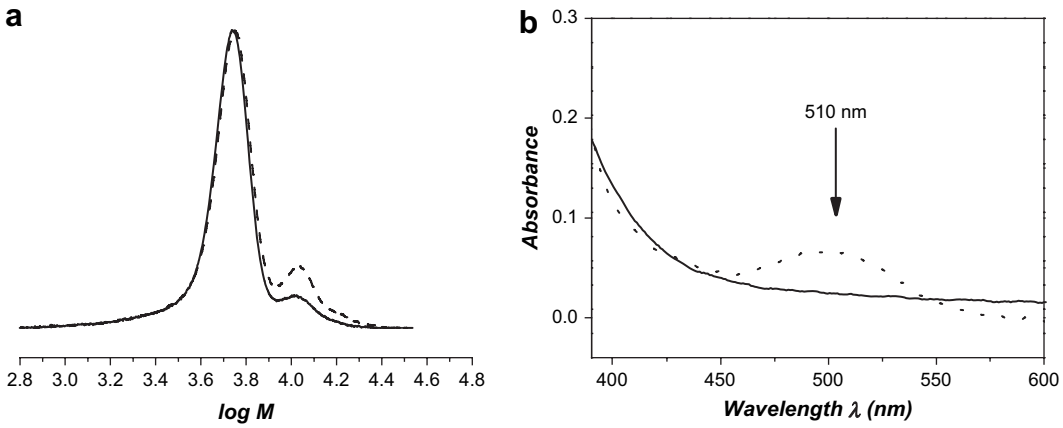


Fig. 2. (a) SEC traces for PS synthesized with azido dithiobenzoate agent (Exp. 1, solid line, $M_n = 5300$ g mol^{-1}, PDI = 1.08) and PS sample after treatment with alkyne functionalized cleavage initiator (dashed line, $M_n = 5300$ g mol^{-1}, PDI = 1.15); (b) UV–vis spectra of dithio-PS-N_3 (dotted line) and after treatment with alkyne functionalized initiator (alkyne-PS-N_3, (solid line)) showing the complete disappearance of the characteristic peak for the dithio moiety at 510 nm in tetrahydrofuran.

observation may be attributed to the coupling of the PS-N_3 radicals generated during the synthesis, leading to a higher molecular weight shoulder in the SEC trace as well as higher polydispersity index.

Linear PS chains with molecular weights below 5000 g mol^{-1}, which did not show coupling during the polymerization, also showed coupling products after the reaction with the alkyne functionalized initiator. Any changes in the reaction conditions, such as increasing the temperature or increasing the amount of the alkyne functionalized initiator, did not reduce the formation of the coupling products. The complete removal of the dithio moiety was further confirmed by ^{1}H NMR spectroscopy (Fig. 3) of the polymers before and after the treatment with alkyne functionalized initiator. The characteristic resonance peaks for the aromatic protons of the dithio moiety ($\delta = 7.3$–8.0 ppm) disappeared completely after reaction with the alkyne functionalized initiator (Fig. 3, insets). Also, a new resonance peak at 4.7 ppm (H_c) could be detected after the reaction which corresponds to the CH_2-group adjacent to the alkyne group.

In principle, during the reaction of a secondary (PS) and a tertiary (cyanovalerate) radical a certain amount of disproportionation might be expected. However, ^{1}H NMR (5000 scans) did not give any hint of the formation of PS with unsaturated endgroup as a disproportionation product. Theoretically, the protons of the terminal double bond of PS should resonate at 5.6 and 6.3 ppm. In this region we did not detect any peaks. In addition, LACCC results (see further below) give further evidence that all dithiobenzoate chain ends were converted to alkynes.

The polymers were subjected to preparative SEC fractionation to separate the coupling product from the main product. Several samples were taken manually at constant intervals and for each sample an SEC trace was taken to identify the region of the main product. All fractions of the main peak were combined and concentrated by solvent evaporation followed by drying. The molecular weight distributions of the purified PS and the coupling product are shown in Fig. 4, which confirms a monomodal distribution of the PS. Thus fractionation is a very efficient method to obtain linear polystyrene with the desirable click functionalities with low polydispersity.

To establish the feasilbility of the polymeric click cyclization, a copper catalysed model click cycloaddition reaction using low molecular weight alcohols (3-azido-1-propanol and propargyl

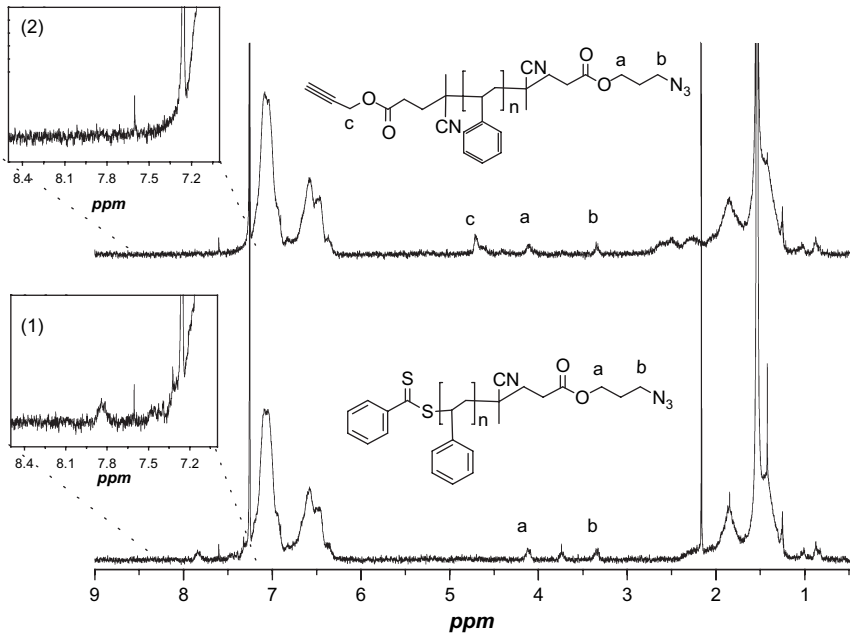


Fig. 3. ^{1}H NMR spectra of (1) dithio-PS-N_3 and (2) alkyne-PS-N_3. Aromatic protons of the dithio endgroup before and after the treatment with alkyne functionalized initiator are shown in the insets.

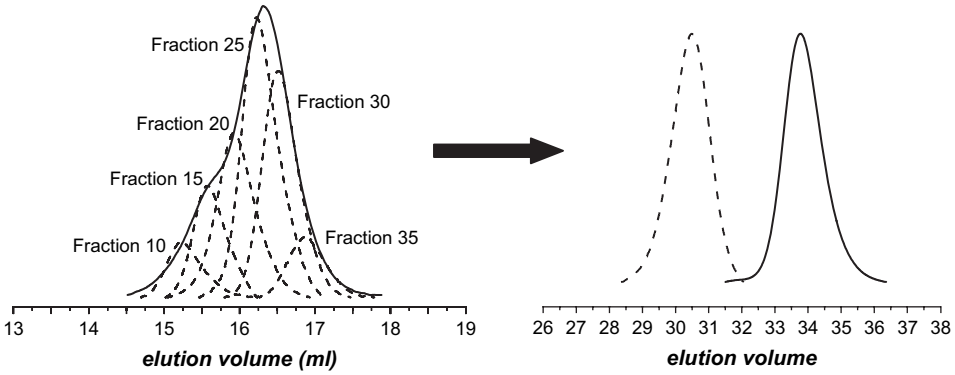


Fig. 4. Separation of coupling product from main product with preparative SEC, Exp. 3; left: original trace and some fractions of the polymer separated by preparative SEC; right: analytical SEC traces of the cumulated fractions 25–35 (solid line) and the coupling product (fractions 1–12; dashed line). Before fractionation: $M_n = 3700\ g\ mol^{-1}$, PDI = 1.19; cumulated fractions 25–35: $M_n = 3000\ g\ mol^{-1}$, PDI = 1.05.

alcohol) was carried out. The click reaction was conducted using copper(I) bromide as catalyst and 2,2′-bipyridyl as ligand in dimethylformamide (DMF) at 80 °C, for 20 h. Conditions similar to this reaction were used for the polymeric click cyclization as well. The progress of the click reaction was monitored by ^{1}H NMR (Supplementary data, Fig. S2) as well as Fourier transform infrared spectroscopy (FTIR) for the condition employed (80 °C). FTIR analysis showed the characteristic peaks at 3300 cm^{-1} (alkyne) and 2100 cm^{-1} (azide) [40] for propargyl alcohol and azidopropanol. The relative concentration of the functional group after reaction can be followed *via* the appearance of the triazole stretches (C═C: 1650 cm^{-1} and ═C–H: 2800 cm^{-1}) and the disappearance of the alkyne- and azide-stretch (3300 cm^{-1} (alkyne) and 2100 cm^{-1} (azide)) indicating a complete conversion of the azido and alkyne endgroups to triazole rings.

After the above-mentioned pre-investigation, cyclization was attempted at 80 °C by the end-to-end ring closure of alkyne-PS-N_3. To verify the successful click cyclization, ^{1}H NMR, SEC and IR spectroscopies were used. The SEC trace (solid line, Fig. 5) of the cyclized PS showed a shift to higher elution volumes due to the more compact structure of the macrocycles [41,34,42] and therefore lower hydrodynamic volume. This shift corresponds to a lower apparent molecular weight due to the ring formation. Both traces show a small peak due to dead polymers formed during endgroup modification (see above). Afer endgroup modification the coupling peak is also shifted towards lower molecular weight which may be attributed to the formation of dimeric cycles. The small peak includes both dead polymers formed during endgroup modification and dimeric cycles. Hence, the small peak is also shifted towards higher elution volume.

Liquid chromatography at critical conditions of adsorption (LACCC) is a powerful method for the characterization of cyclic and linear polymers according to the chemical heterogeneity. Separation of polymers on porous separation phases using mixed mobile phases at critical conditions of adsorption allows the elution of homopolymers independent of their molar mass. Under these conditions, homopolymers can be separated according to the number and nature of functional groups, e.g. endgroups. Because of a better separation, LACCC is more sensitive for a quantitative determination of the topology of the polymer. Pasch et al. [45] and Takano et al. [46] already analyzed cyclic polymers with LACCC. Fig. 6 shows the LACCC traces of the dithio-PS-N_3 precursor, linear alkyne-PS-N_3 and cyclic polystyrenes at critical conditions of alkyne-PS-N_3. Four different alkyne-PS-N_3 with a molecular weight in the range from 2000–10 000 $g\ mol^{-1}$ were used to find the critical conditions, THF/hexane = 43:57 (v/v) on an RP column set.

Both the linear samples, dithio-PS-N_3 precursor (6.0 mL) and alkyne-PS-N_3 (6.1 mL) elute nearly at the same elution volume. However, the cyclic PS elutes significantly earlier (4.7 mL) than the linear counterparts due to the absence of endgroups and therefore loss of the polarity. Alkyne-PS-N_3 exhibit few shoulders due to side reactions during endgroup modification. The shoulder at 5.7 mL can be attributed to the recombination product formed during insertion

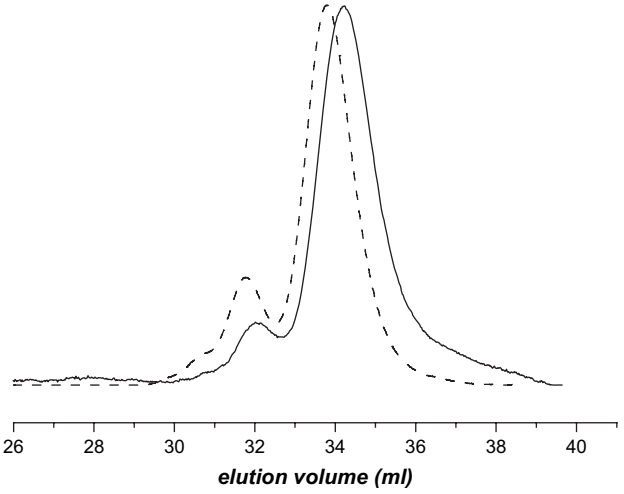


Fig. 5. SEC trace of linear alkyne-PS-N_3 (Exp. 1, $M_n = 5300\ g\ mol^{-1}$, dotted line) and of cyclic alkyne-PS-N_3 ($M_n = 4300\ g\ mol^{-1}$, solid line).

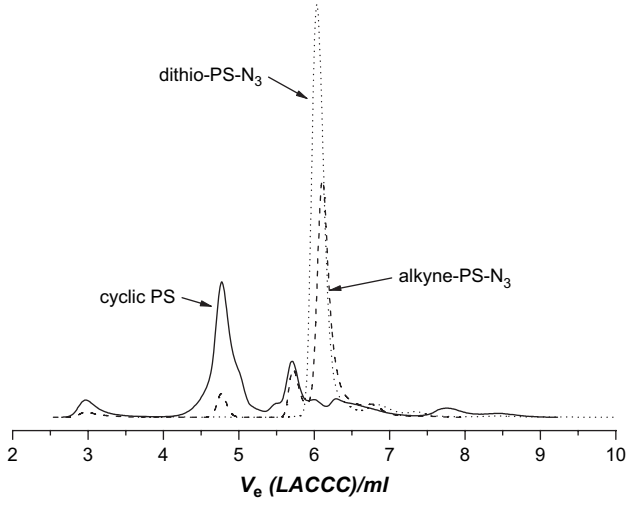


Fig. 6. LACCC chromatograms (normalized by area) at critical conditions of alkyne-PS-N_3 (ELSD detector) for linear dithio-PS-N_3 precursor (dotted line, Exp.1), linear alkyne-PS-N_3 (dashed line) and cyclic polystyrenes (solid line).

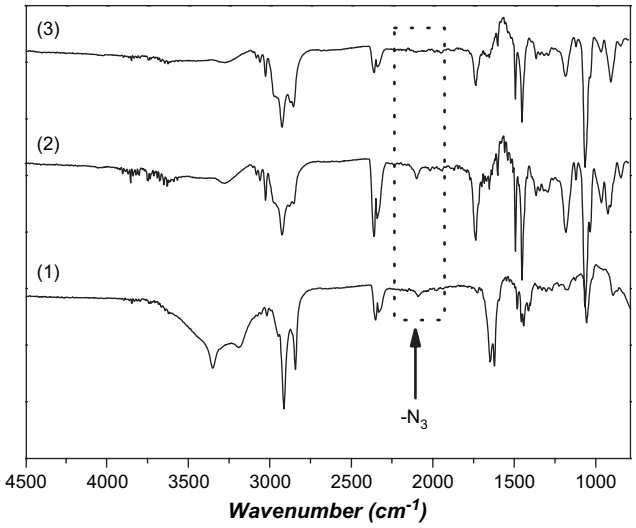


Fig. 7. ATR-FTIR spectra for (**1**) dithio-PS-N_3 (Exp.1), (**2**) alkyne-PS-N_3 and (**3**) cyclic PS showing the loss of the azido group at 2099 cm^{-1}.

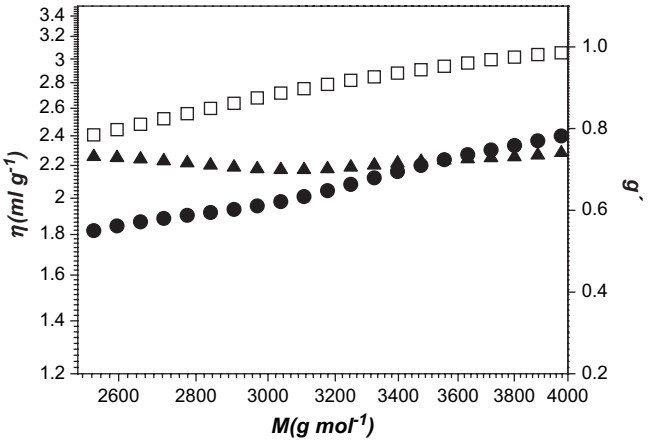


Fig. 9. Mark–Houwink plots of intrinsic viscosity versus molecular weight, for linear (□, Exp.1) and cyclic (●) polystyrenes measured by SEC with viscosity detection in tetrahydrofuran; (▲): contraction factors, g'.

of the alkyne group. These dead polymers also show up for the cycle but their amounts do not increase. This liquid chromatography method clearly underlines the formation of cycles accompanied by the disappearance of the linear polymer, indicating that the linear polymer quantitatively carried the azide. A shoulder in the peak of the cyclic polymer might be attributed to cycles of double molecular weight (from cyclization of a condensate of two alkyne-PS-N_3).

MALDI-TOF measurements were carried out to determine the absolute molecular weight. Identical absolute molecular weights were detected for the linear precursor (Exp. 1, $M_{w,lin} = 3150$ g mol^{-1}) and the cyclized PS ($M_{w,cyc} = 3200$ g mol^{-1}), which corroborates the successful ring formation. Unfortunately, efforts towards characterization of the side products with MALDI-TOF analysis did not give distinct information because of overlapping of several peaks.

ATR-FTIR analysis provided further proof of ring formation, where a peak at 2096 cm^{-1}, corresponding to the N_3 group of the dithio-PS-N_3 and alkyne-PS-N_3 completely disappeared in the cycle due to formation of the triazole group (Fig. 7).

NMR measurements provide further evidence for the triazole formation and therefore intramolecular ring closure. The shift of the methylene protons adjacent to the azido group was observed from $\delta = 3.3$ ppm (b_l) to $\delta = 4.3$ ppm (b_c) (Fig. 8) due to triazole formation. The disappearance of protons c adjacent to the alkyne moiety for the linear polymer chain at $\delta = 4.7$ ppm (c_l) and the appearance of a new peak at $\delta = 5.2$ ppm (c_c) are also observed (see Fig. 8), which results as an effect of the formation of the heterocycle. The proton of the triazole ring was detected at $\delta = 8.0$ ppm with a Bruker DPX 300 instrument.

Intrinsic viscosities were obtained from SEC measurements in THF using a viscosity detector. The double-logarithmic Mark–Howink plots of $[\eta]$ versus M for linear and cyclic PS samples result in straight though not quite parallel lines (Fig. 9). The Mark–Houwink exponents are found to be $a = 0.74$ for the cycles and $a = 0.69$ for the linear chains, which is in good agreement with earlier studies of linear and cyclic polystyrenes [28,43]. From the viscosity measurements a contraction factor of $g' = [\eta]_{cyc}/[\eta]_{lin}$, can be calculated, which was predicted by Bloomfield and Zimm [42] and Casassa [44] to be $g' = 2/3$ for θ-conditions. Depending on the nature of the polymer, molecular weight and solvent used, contraction factors in the literature range from 0.64 to 0.71 [22,28,43]. The value obtained by us in the good solvent THF, $g' = 0.70$–0.74, is consistent with these previous results obtained for polymers in solution.

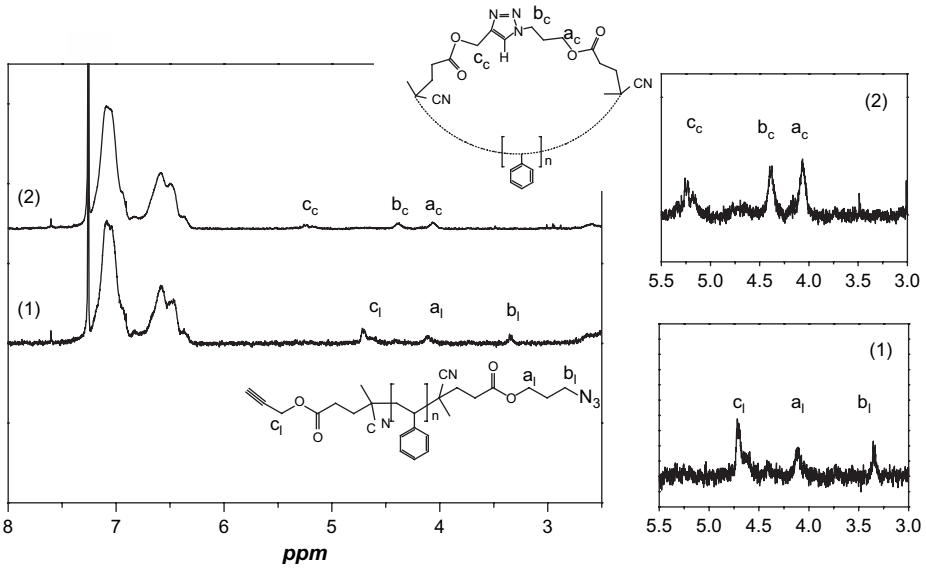


Fig. 8. ^{1}H NMR for the heterotelechelic linear alkyne-PS-N_3 (Exp.1) (**1**) and the cyclic product (**2**).

4. Conclusions

The combination of RAFT and copper-catalyzed Huisgen 1,3-dipolar cycloaddition (click chemistry) is an efficient strategy to synthesize ring shaped polymers. An azido dithiobenzoate click-RAFT agent was employed as chain transfer agent in the RAFT polymerization of styrene resulting in low molecular weight azido-terminated polymers. The exchange of the dithiester endgroup of the polymeric chains was carried out efficiently by using an alkyne-modified initiator, leading to the appropriate endgroup modification of polystyrene for the click chemistry. Intramolecular cyclization was successfully carried out and the ring formation was assertively evaluated by ^{1}H NMR, ATR-FTIR measurements, MALDI-TOF, SEC, VISCO–SEC and LACCC. The present route towards ring shaped polymers represents a versatile approach for the preparation of cyclic polymers and the approach is in principle applicable for polymers derived from acrylates as well, which can be further functionalized to grow polymer brushes on the cyclic backbone. Studies towards such new architecture of ring shaped polymer brushes are currently in progress in our laboratories.

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Appendix. Supplementary data

^{1}H NMR, ^{13}C NMR and 2D NMR spectra of the alkyne functionalized initiator as well as the ^{1}H NMR spectrum of the model click compound. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.polymer.2008.03.017.

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