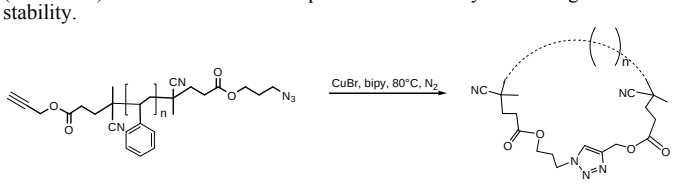
ACCESS TO CYCLIC POLYSTYRENE VIA A COMBINATION OF REVERSIBLE ADDITION FRAGMENTATION CHAIN TRANSFER (RAFT) POLYMERIZATION AND CLICK CHEMISTRY

Anja S. Goldmann[1], Pierre-Eric Millard[1], Damien Quémener[2], Thomas P. Davis[2], Martina H. Stenzel[2], Christopher Barner-Kowollik[1,§], and Axel H. E. Müller[1]

[1]Makromolekulare Chemie II, Universität Bayreuth, D-95440 Bayreuth, Germany. E-Mail: axel.mueller @uni-bayreuth.de
[2]Centre for Advanced Macromolecular Design, School of Chemical Engineering and Industrial Chemistry, The University of New South Wales, Sydney, NSW 2052, Australia. E-Mail: m.stenzel@unsw.edu.au
[§]new address: Institut für Technische Chemie und Polymerchemie, Universität Karlsruhe, 76128 Karlsruhe, Germany. E-Mail: christopher.barner-kowollik@polymer.uni-karlsruhe.de

Introduction

Numerous synthetic methods have been explored for optimizing the control over polymer architecture as a prerequisite to manipulating the material properties. In particular, cyclic polymers have become increasingly attractive over the past years due to their unique architecture and their novel properties (due to the absence of endgroups). However, several challenges exist in controlling the molecular weight and polydispersity in order to obtain well-defined cyclic macromolecules. Significant efforts have been dedicated to preparation and characterization of cyclic homopolymers *via* anionic polymerization,[1-7] nitroxide-mediated polymerization,[8, 9] or the combination of "click" chemistry with ATRP[10] or RAFT polymerization.[11-14] 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 high chemical stability.



Scheme 1. Click-cyclization procedure of telechelic polystyrenes.

Experimental

The synthesis of the azido dithiobenzoate RAFT agent (Scheme 2) was undertaken according to the previously reported protocols.[15, 16] 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.

Results and Discussion

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 an azido dithiobenzoate RAFT agent[15] followed by the exchange of the Z-group with an alkyne-functionalized initiator (Scheme 2).

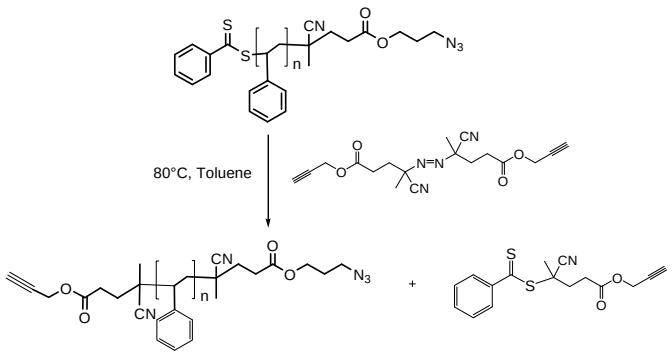
To facilitate the cyclization of the PS chain by click coupling, the dithioester endgroup was modified with the required alkyne functionality as shown in Scheme 2. The insertion of the alkyne group at the PS chain end was accomplished by the removal of the dithiobenzoate endgroup from the polymeric chains according to the method described by Perrier and coworkers[17]. 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.

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, size-exclusion and liquid adsorption chromatographies as well as IR spectroscopy were used. The SEC trace (Figure 1A) of the cyclized PS shows a shift to higher elution volumes due to the more compact structure of the macrocycles[12, 18] 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. 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.

Table 1. RAFT Polymerizations of Styrene with the Azido Dithiobenzoate Click-RAFT Agent in Bulk at 60°C

Exp.	[Mon]:[CTA]:[Ini]	Time (min)	$M_{n,th}$ [c] (g mol^{-1})	M_n [a] (g mol^{-1})	*PDI* [a]	Conv. [b] (%)
1	150:5:1	1260	5100	5300	1.08	30
2	150:5:1	590	3200	3500	1.09	17.5
3	150:5:1	820	3500	3700	1.19	20
4	250:5:1	330	2800	2900	1.11	13
5	500:5:1	180	2500	1900	1.08	9

[a] measured by size-exclusion chromatography (SEC) using polystyrene standards in THF. [b] determined by gravimetry. [c]The theoretical number average molecular weight was calculated according to the equation, $M_{n,th}=M_M \times$ conv. $\times [M]_0/[CTA]_0 + M_{CTA}$ where 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.



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

Liquid chromatography at critical conditions of adsorption (LACCC) in Figure 1B shows the 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 – 10000 g mol^{-1} were used to find the critical conditions, THF/hexane = 43:57 (v/v) on an RP column set. Both 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 end groups 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 of the alkyne group. These dead polymers also show up for the cycle but their amount does 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).

Intrinsic viscosities were obtained from SEC measurements in THF using an online viscosity detector. The Mark-Howink plots of log[η] versus log M for linear and cyclic PS samples result in straight though not quite parallel lines (Figure 1C). 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.[7, 19] From the viscosity measurements a contraction factor of $g' = [\eta]_{cyc}/[\eta]_{lin}$, can be

calculated. The value obtained by us in the good solvent THF, g′= 0.70 - 0.74, is consistent with previous results obtained for polymers in solution.

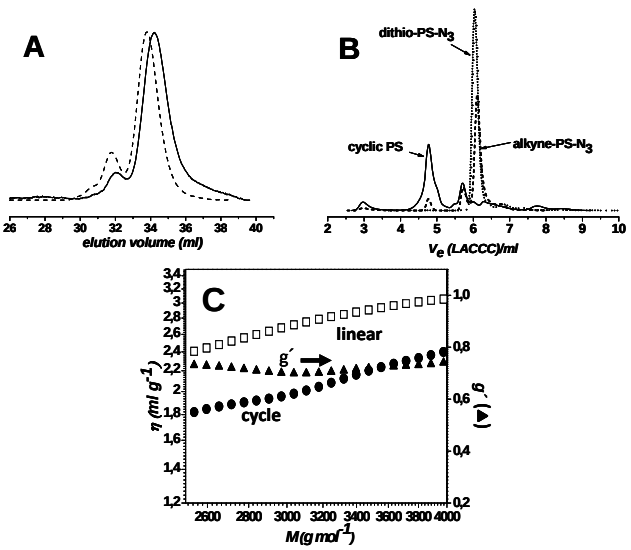


Figure 1. (A) SEC trace of linear alkyne-PS-N_3 (Exp. 1, M_n = 5300 gmol^{-1}, dotted line) and of cyclic alkyne-PS-N_3 (M_n = 4300 gmol^{-1}, solid line). **(B)** LACCC chromatograms at critical conditions of alkyne-PS-N_3 (ELSD detector) for linear dithio-PS-N_3 precursor (dotted line, Exp.1), linear alkyne-PS-N_3 (dashed line) and cyclic polystyrenes (solid line) measured by SEC with viscosity detection in tetrahydrofuran. (**C)** 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'.[20]

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.

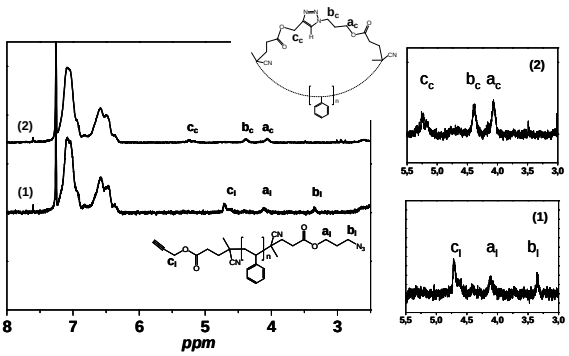


Figure 2. ^{1}H NMR for the heterotelechelic linear alkyne-PS-N_3 (Exp.1) **(1)** and the cyclic product **(2)**.

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 δ = 3.3 ppm (b_l) to δ = 4.3 ppm (b_c) (**Figure 2**) due to triazole formation. The disappearance of protons c adjacent to the alkyne moiety for the linear poymer chain at δ = 4.7 ppm (c_l) and the appearance of a new peak at δ = 5.2 ppm (c_c) are also observed, which results as a effect of the formation of the heterocycle. The proton of the triazole ring was detected at δ = 8.0 ppm with a Bruker DPX 300 instrument.

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 dithio moiety of the polymeric chains was carried out efficiently by using an alkyne-modified initiator, leading to the appropriate endgroup modifications of polystyrene for the click chemistry. Intramolecular cyclization was successfully carried out. The present route towards ring shaped polymers represents a versatile approach for the preparation of cyclic polymers.

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