Macrocyclic Poly(methyl acrylate) and Macrocyclic Poly(methyl acrylate-*block*-styrene)
Synthesized by Radical Trap-assisted Atom Transfer Radical Coupling

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Abstract:

Dibrominated poly(methyl acrylate) (BrPMABr) was prepared by atom transfer radical polymerization (ATRP), and this unpurified reaction mixture was used directly in a radical trap-assisted atom transfer radical coupling (RTA-ATRC) reaction to achieve cyclic PMA by intramolecular chain-end coupling. When the polymerization-to-cyclization crossover was performed as a one pot-two step sequence simply by the addition of the radical trap 2-methyl-2-nitrosopropane (MNP) and increased amounts of ligand-catalyst complex, cyclic PMA could be formed in yields up to 65% by adjusting the total volume and reactant ratios during the intramolecular RTA-ATRC, based on gel permeation chromatography (GPC) analysis. In analogous intramolecular ATRC trials lacking the radical trap, cyclization was not successful and instead chain extension by continuation of ATRP was observed. When the ATRP reaction mixture containing the BrPMABr precursor was added drop-wise into a redox active solution containing MNP, yields of cyclic polymer were increased up to 85%. The effect of the ligand was studied, with the highest amounts of cyclic product obtained in intramolecular RTA-ATRC reactions using tris[2-(dimethylamino)ethyl]amine (Me₆TREN) as the ligand. Cyclic diblock copolymers were also prepared by this method, using telechelic poly(methyl acrylate-*block*-styrene-*block*-methyl acrylate) (PMA-b-PS-b-PMA) linear precursors prepared by sequential ATRP reactions.

Introduction.

Atom transfer radical polymerization (ATRP) allows the experimenter the ability to carry out polymerizations using a wide array of monomers, solvents, initiators, and ligands.¹⁻¹³ The end result, when an alkyl bromide is chosen as the initiator, is a polymer sample of narrow molecular weight distribution, predictable chain lengths, and chain end functionality in the form of, most typically, a benzyl bromide¹⁴⁻¹⁶ or an α -bromo ester.¹⁷⁻²² While the chain end does little to impart properties on the bulk polymer, its presence is essential for post-polymerization modifications, such as chain extension and diblock formation^{7, 23-26} in a second ATRP reaction. If redox activation of the terminal C-Br bond into a carbon-based radical is done in the absence of monomer, a bimolecular termination reaction between two polymeric radicals can occur, with the result being dimerization if head-to-head coupling is the dominant pathway.²⁷⁻²⁹ This atom transfer radical coupling (ATRC) pathway is summarized in **Scheme 1a**.

Scheme 1: ATRC Pathway Compared to RTA-ATRC Pathway

Mechanistically similar, in radical trap-assisted ATRC (RTA-ATRC) polymer chain ends are activated in the presence of a radical trap, such as a nitroso group, which acts as a protecting group of the chain end radical by converting it into a persistent nitroxide radical. The nitroxide radical subsequently selectively chooses another polymer radical as its coupling partner.³⁰⁻³² As a consequence of the altered mechanistic sequence, RTA-ATRC ultimately accomplishes coupling in a stepwise fashion with both individual steps only first order with respect to the polymer radical chain ends (**Scheme 1b**). In addition to simply producing dimers of polystyrene (PS) from brominated precursors,³³ RTA-ATRC has also been shown capable of producing diblocks by selectively capping one type of polymer radical in the first step, and the resulting nitroxide-capped polymer capturing a second type of polymer radical to form the diblock with an alkoxyamine at the junction of the segments.³⁴ Furthermore, the ability to couple polymer radicals that favor disproportionation as the major radical-radical termination pathway, such as poly(methyl methacrylate) radicals,³⁵ expands the scope of polymers that can participate in coupling reactions when RTA-ATRC is used instead of traditional ATRC.

The synthesis of cyclic polymers by end-to-end coupling of telechelic linear precursors remains the most popular method for their production.³⁶⁻⁴⁴ The installation of compatibly reactive chain ends is typically done post-polymerization. As an example, the conversion of the terminal alkyl bromide into an azide group when an alkyne-containing ATRP initiator is used allows for ring closure by “click” chemistry.⁴⁵⁻⁴⁸ By choosing a dibrominated initiator, ATRP can be used to produce telechelic polymers that can be directly employed in end-to-end coupling reactions either by ATRC⁴⁹ or RTA-ATRC⁵⁰ resulting in cyclic (**Scheme 2**), or even dicyclic, polymers.^{27,51} Ring closing by traditional ATRC to produce macrocycles is problematic due to the following: i) chain end radicals must terminate by head-to-head coupling and ii) chain end radicals must be sufficiently present (large K_{ATRP} value) that a bimolecular reaction is feasible in which each chain end radical has only one allowable partner.

In this contribution, cyclic poly(methacrylate) (PMA) is produced directly from the dibrominated telechelic precursor by intramolecular RTA-ATRC (**Scheme 3**). An additional advantage is that the raw, unpurified ATRP reaction mixture (which contains unconverted monomer) is directly used in the cyclization reaction, making the entire polymerization-to-

cyclization process extremely streamlined and less wasteful. The system is then extended to the cyclization of Br-PMA-PS-PMA-Br linear triblock precursors, resulting ultimately in PS-PMA cyclic diblocks (**Scheme 4**).

Scheme 2: Cyclization by ATRC or RTA-ATRC

Scheme 3. Synthetic Pathway Leading to Cyclic PMA

Experimental

Materials. Copper(I) bromide, (CuBr, Aldrich, 98%) and copper nanopowder (Cu⁰, Acros, 99.8%) were used as received. Ethylene bis(2-bromoisobutyrate) (Eb₂biB, Aldrich, 97%), benzal bromide (Bzb, Aldrich, 97%), chloroform-D (99.8 atom % D, 1% v/v TMS), tris[2-(dimethylamino)ethyl]amine (Me₆TREN, Alfa, 99%) and N, N, N', N', N''-pentamethyldiethylene triamine (PMDETA, Aldrich, 99%) were used as received and stored at 5°C. 2-Methyl-2-nitrosopropane dimer (MNP, Aldrich, 98%) was used as received and stored at -20°C. Methyl acrylate (MA, Aldrich, 99%) and styrene (Sty, Aldrich, 99%) were run over an alumina

purification column to remove inhibitors and stored at -20°C. Tetrahydrofuran (THF) was collected from an Innovative Technology PureSolv solvent purification system.

Synthesis of Cyclic PMA by ATRP and Crossover Directly to Intramolecular RTA-ATRC. To a flame-dried two-neck round bottom flask was added methyl acrylate (2.5 mL, 27.58 mmol), ethylene bis(2-bromoisobutyrate) (99.6 mg, 0.276 mmol), copper(I) bromide (79.2 mg, 0.552 mmol) and a dried magnetic stir bar. The flask was then subjected to three freeze-pump-thaw cycles with the aid of a Schlenk line before placing in a 60°C oil bath. Once equilibrated, PMDETA (116 µL, 0.552 mmol) was added via an argon flushed syringe to initiate the reaction and the solution was stirred for 30 minutes. The reaction was terminated by submersing the flask in an ice bath and opening the flask to the atmosphere. A GPC sample was prepared by diluting several drops of the sample with THF and filtering through 0.45 micron PTFE syringe filter for analysis: $M_n = 2500$, $M_p = 2700$, $\bar{D} = 1.09$. To the same two neck round bottom flask was added CuBr (273.6 mg, 1.66 mmol), Cu⁰ (105.2 mg, 1.66 mmol), MNP (240.5 mg, 1.38 mmol) and 100 mL THF. The flask was then subjected to four freeze-pump-thaw cycles with the aid of a Schlenk line before being placed in a 40°C oil bath. Once equilibrated, PMDETA (576 µL, 2.76 mmol) was added via an argon flushed syringe to initiate the reaction and the solution was stirred for 6 h. The reaction was terminated by submersing the flask in an ice bath and opening to the atmosphere. An aliquot of the solution was removed for GPC analysis: $M_n = 2900$, $M_p = 2100$, $\bar{D} = 1.60$. Trials using a different ligand (Me₆TREN) and ratios of reactants were performed in a similar manner.

Synthesis of Cyclic PMA by ATRP and Crossover Directly to Pseudo High Dilute Intramolecular RTA-ATRC. To a flame-dried two-neck round bottom flask was added methyl acrylate (1.25 mL, 13.79 mmol), ethylene bis(2-bromoisobutyrate) (24.9 mg, 0.0690 mmol), copper(I) bromide (19.8 mg, 0.138 mmol) and a dried magnetic stir bar. The flask was then subjected to three freeze-pump-thaw cycles with the aid of a Schlenk line before placing in a 60°C oil bath. Once equilibrated, PMDETA (29 µL, 0.138 mmol) was added via an argon flushed syringe to initiate the reaction and the solution was stirred for 30 minutes. The reaction was terminated by submersing the flask in an ice bath and opening the flask to the atmosphere. A GPC sample was

prepared by diluting several drops of the sample with THF and filtering through 0.45 micron PTFE syringe filter for analysis: $M_n = 4400$, $M_p = 4700$, $\bar{D} = 1.06$. To the same two neck round bottom flask was added MNP (120.1mg, 1.38 mmol) and 25 ml THF. To a second flame-dried two neck round bottom flask was added CuBr (59.3 mg, 0.4137mmol), Cu^0 (26.3 mg, 0.4137 mmol), PMDETA (173 μ L, 0.827 mmol), a dried magnetic stir bar and 25 mL THF. The flasks were then subjected to three freeze-pump-thaw cycles with the aid of a Schlenk line. The copper containing flask was filled with argon and flushed for 5 minutes before being placed in a 40°C oil bath. The polymer and MNP solution in the other flask was withdrawn into a syringe aseptically under argon and then placed on the syringe pump. Once equilibrated the solution was added at a rate of 3 mL/h (8.27 μ mol/hr). The solution in the flask was left to stir for an additional 2 h after the syringe addition was complete. The reaction was terminated by submersing the flask in an ice bath and opening to the atmosphere. The raw reaction mixture was concentrated by rotovap and an aliquot of the solution was removed for GPC analysis: $M_n = 4400$, $M_p = 3400$, $\bar{D} = 1.49$. Trials using a different ligand (Me₆TREN) and ratios of reactants were performed in a similar manner.

Synthesis of Br-PMA-PS-PMA-Br Triblock by ATRP and Cyclic PMA-PS Diblock by Pseudo High Dilute Intramolecular RTA-ATRC. To a flame-dried two-neck round bottom flask was added methyl acrylate (1.06 mL, 11.7 mmol), bifunctional polystyrene precursor ($M_n = 2800$, 155.2 mg, 0.0586 mmol), copper(I) bromide (16.81 mg, 0.117 mmol), 1 mL THF and a dried magnetic stir bar. The flask was then subjected to three freeze-pump-thaw cycles with the aid of a Schlenk line before placing in an 80°C oil bath. Once equilibrated, PMDETA (25 μ L, 0.117 mmol) was added via an argon flushed syringe to initiate the reaction and the solution was stirred for 20 minutes. The reaction was terminated by submersing the flask in an ice bath and opening the flask to the atmosphere. A GPC sample was prepared by diluting several drops of the sample with THF and filtering through 0.45 micron PTFE syringe filter for analysis: $M_n = 4900$, $M_p = 5200$, $\bar{D} = 1.11$. To the same two neck round bottom flask was added MNP (102.1mg, 1.172 mmol) and 50 mL THF. To a second flame-dried two neck round bottom flask was added CuBr (50.4 mg, 0.352 mmol), Cu^0 (22.3 mg, 0.352 mmol), PMDETA (147 μ L, 0.703 mmol), a dried magnetic stir bar and 50 mL THF. The flasks were then subjected to three freeze-pump-thaw

cycles with the aid of a Schlenk line. The copper containing flask was filled with argon and flushed for 5 minutes before being placed in a 40°C oil bath. The polymer and MNP solution in the other flask was withdrawn into a syringe aseptically under argon and then placed on the syringe pump. Once equilibrated the solution was added at a rate of 6 mL/h (7.03 μmol/hr). The solution in the flask was left to stir for an additional 2 h after the syringe addition was complete. The reaction was terminated by submersing the flask in an ice bath and opening to the atmosphere. The raw reaction mixture was concentrated by rotovap and an aliquot of the solution was removed for GPC analysis: $M_n = 5500$, $M_p = 4300$, $\bar{D} = 1.46$. Trials using the one-pot RTA-ATRC technique were also performed to prepare cyclic diblocks. This was performed in a similar manner except all reactants were placed in one Schlenk flask.

Measurements. Polymer samples were analyzed on an EcoSec Gel Permeation Chromatography (GPC) system (Tosoh Biosciences LLC) connected to a PC with EcoSec data analysis software. The instrument was equipped with a dual flow RI detector, UV detector, two TSK gel Super HZ3000 columns, and temperature controlled at 40°C with a steady flow rate of 0.35 mL/min THF. A seven point polystyrene calibration curve was used for comparison to determine the polymer molecular weight characteristics. A Varian 400 MHz FT-NMR was utilized to gather ^1H NMR data at room temperature that was used to calculate percent monomer conversion of polymer samples prepared in deuterated chloroform (CDCl_3). A Thermo Fischer Scientific Inc. Exactive 1.1 bench top orbitrap mass spectrometer equipped with Thermo Xcalibur 2.1.0 was used to analyze linear and cyclic polymers using electrospray ionization (ESI) in negative ion mode over a scan range of 400.00-4000.00Da. Samples were run in 50:50 THF: ACN as well as 100% THF.

The calculated molecular weights of the isolated cycles in the $z=1$ series are obtained by equation 1:

$$MW_{theo} = MW_I + (n * MW_{MA}) + MW_n + MW_{Na^+ - 2H} \quad (1)$$

while calculated molecular weights of the isolated cycles in the $z=2$ series are obtained by equation 2:

$$MW_{theo} = \frac{MW_I + (n * MW_{MA}) + MW_n + MW_{Na^+ - 3H}}{2} \quad (2)$$

where MW_I is the molecular weight of the initiator mass that is incorporated into the polymer (Eb_2biB minus the mass of the two bromines), MW_{MA} is the molecular weight of the MA monomer, MW_n is defined as the molecular weight of the radical trap MNP, and $MW_{Na^+ - (2 \text{ or } 3)H}$ accounts for the sodium ion associated with the polymer and the charge.

RESULTS AND DISCUSSION

Cyclization of linear precursors by ATRC or RTA-ATRC relies on activation and coupling of halogenated polymer chain ends prepared by ATRP (**Scheme 2**). In the case of mono- or di-brominated PS precursors, both ATRC or RTA-ATRC can easily create dimers or cyclic polymers due: i) to the K_{ATRP} value allowing for PS radicals to be formed in concentrations conducive to a bimolecular reaction, ii) and to head-to-head coupling being the dominant termination pathway. The challenge taken on in this work is to produce cyclic polymers by end-to-end coupling of a halogenated polymer historically problematic in ATRC reactions due to its unfavorable K_{ATRC} ,^{27, 51} while keeping the entire process as streamlined as possible.

Preparation of cyclic PMA in a one pot – two step sequence

The ATRP of methyl acrylate was carried out using the bifunctional initiator ethylene bis(2-bromoisobutyrate) (Eb_2biB), CuBr as the catalyst, and PMDETA as the ligand with ratios of $[MA]:[Eb_2biB]:[CuBr]:[PMDETA]=100:1:2:2$ to afford telechelic PMA ($BrPMABr$). The polymerizations were allowed to proceed for 30 minutes to produce polymers with number-average molecular weight (M_n) values between 2000 to 7500 Da and dispersity ($\mathcal{D}$) values <1.2 (**Table 1**, Trials 1-6).

Table 1. Results of One-Pot Intramolecular RTA-ATRC using BrPMABr Precursors Prepared by ATRP											
BrPMABr Precursor ^a				ATRC, RTA-ATRC Products ^b					Cyclization Conditions		
Trial	M_n^c	M_p^d	$\mathcal{D}^e$	M_n^c	M_p^d	$\mathcal{D}$	$\langle G \rangle^f$	% C ^g	$[BrPMABr]^h$	CuBr:Cu ⁰ :MNP:PMDETA ⁱ	
1 ^l	2200	2300	1.06	2700	2900	1.07	1.26	NA	2.758	25:25:0:50	
2	2000	2200	1.09	1600	1700	1.92	0.74	55%	5.516	6:6:5:10	

3	2500	2700	1.09		2900	2100	1.60	0.77	60%	2.758	6:6:5:10
4	2200	2300	1.18		2500	2000	1.39	0.87	65%	1.379	6:6:5:10
5	2900	3000	1.06		3400	2300	1.75	0.76	55%	2.758	25:25:10:50
6	7500	9200	1.14		10600	7000	1.45	0.76	60%	2.758	25:25:2.5:50

^aTelechelic poly (methyl acrylate) (BrPMABr) was prepared by ATRP at 60°C for 45 min using the ratios [MA]:[Eb₂biB]:[CuBr]:[PMDETA]=100:1:2:2.

^bATRC and RTA-ATRC product after 6 h of reaction time at 40°C.

^cNumber-average weights obtained by GPC calibrated with linear PS standards, expressed in Da.

^dPeak molecular weights obtained by GPC calibrated with linear PS standards, expressed in Da.

^eDispersity values obtained by GPC calibrated with linear PS standards.

^fG-value obtained by dividing the RI-GPC M_p values of the RTA-ATRC or ATRC product by the M_p of the linear BrPMABr precursor.

^gPercent of BrPMABr precursor that underwent intramolecular coupling and formed cyclic product, as estimated by areas under RI-GPC trace.

^hConcentration of BrPMA-Br in mM for RTA-ATRC or ATRC reaction.

ⁱRatios of CuBr catalyst, Cu⁰ reducing agent, MNP radical trap, and ligand compared to BrPMABr initiator.

^jATRC one-pot intramolecular coupling attempt (no radical trap was present).

The ATRP reaction solutions were used directly (with no isolation or purification of the PMA precursor or removal of monomer) in RTA-ATRC reactions by adding the radical trap MNP and increasing the dilution to varying extents, in an attempt to favor intramolecular end-to-end coupling and thus PMA cycles. The RTA-ATRC reactions were performed in 50-200 mL of THF with CuBr as the catalyst, copper metal as the reducing agent and PMDETA as the ligand with typical ratios of [BrPMABr]:[CuBr]:[Cu⁰]:[PMDETA]=1:6:6:12 (**Table 1**). In the case of the ATRC reaction performed with no radical trap (**Table 1**, trial 1), the peak molecular weight (M_p) value after ATRC increased indicating intramolecular coupling did not occur; rather it is likely that polymerization by ATRP continued. This is expected and consistent with results obtained in the attempted dimerization of unpurified, monobrominated PMA chains using traditional ATRC.⁵³ In the analogous RTA-ATRC reactions of BrPMABr with the addition of the radical trap MNP, a shift to longer retention times on GPC chromatograms indicated that cyclization of the PMA precursors was occurring (**Table 1**; trials 2-6 and **Figure 1**). Consistent with cyclic products compared to the linear precursors from which they were derived, <G> values of approximately 0.8 were observed when analyzed by GPC (the ratio of M_p values of the cyclic to linear precursor).⁵⁴ Trials with increased dilution volumes resulted in the largest percent of cyclic product, as determined by GPC (**Table 1**, Trials 2-4). Trials with increased amounts of catalyst, reducing agent, and ligand at a constant volume did not have a significant effect on the amount of intramolecular versus intermolecular coupled product (**Table 1**, trials 3 vs 5-6).

Streamlined preparation of cyclic PMA under pseudo high dilute conditions

RTA-ATRC reactions to prepare cyclic PMA polymers were next attempted using syringe addition to achieve pseudo high dilute conditions, with the raw ATRP reaction mixture, MNP, and THF added via syringe into a redox-active solution containing THF, CuBr catalyst, Cu⁰ reducing agent, and PMDETA or Me₆TREN as the ligand. This method allowed for greater dilution in the intramolecular RTA-ATRC reaction without the use of higher total volumes of THF, while still affording the experimental leniency of using the unpurified ATRP reaction mixture. Preparation of linear BrPMABr precursors was performed in a similar manner as was done in the one-pot reaction trials: using ATRP with typical ratios of [BrPMABr]:[CuBr]:[Cu⁰]:[PMDETA]=1:6:6:12. Results of the pseudo high dilute cyclization reactions are summarized in **Table 2**. As was seen with the one pot RTA-ATRC reactions of BrPMABr, a shift to longer retention times upon GPC analysis indicated the formation of cyclic product when PMDETA was used as the ligand (**Table 2**; trials 2-8 and **Figure 2a**). GPC analysis indicated $\langle G \rangle$ values of approximately 0.8, again consistent with cyclization. Carrying out intramolecular RTA-ATRC under pseudo high dilute conditions compared to the one pot method, under otherwise analogous conditions, led to a modest increase in cyclization (**Table 2**, trial 1 vs 2). Increasing the amount of catalyst, reducing agent, and radical trap increased the

extent of cyclization (**Table 2**, trials 3-4), consistent with these conditions creating a scenario where the participants in the rate limiting step in the intramolecular coupling sequence were available in higher concentrations (**Scheme 2**, k_1). Reducing the amount of ligand-metal catalyst and reducing agent while keeping the nitroso radical trap concentration high continued to produce high amounts of cyclic product (**Table 2**, trials 6-8), while analogous trials but with reduced amounts of nitroso coupling agent adversely affected the extent of cyclization (**Table 2**, trial 5).

In the case of Me₆TREN, the percentage of cyclic product in a one pot reaction sequence matched that when PMDETA was used, despite the increased redox activity of Me₆TREN (**Table 2**, trials 1 vs 9). Performing the RTA-ATRC reaction under pseudo high dilute conditions led to increased cyclization in all cases with Me₆TREN as the ligand (**Table 2**, trials 10-14 and **Figure 2b**). Compared to cyclization reactions using PMDETA as the ligand, higher degrees of cyclization were achieved with lowered amounts of ligand, catalyst, and reducing agent, with the percent of cyclic product most closely related to addition rate (**Table 2**, trials 10-14). This is consistent with Me₆TREN creating a higher concentration of PMA radicals due to its increased redox strength, and the participation of these radicals in an intramolecular reaction is tied to dilution.

Table 2. Results of Pseudo High Dilute Intramolecular RTA-ATRC by Addition of BrPMABr Precursors and Radical Trap to Cyclization Flask

BrPMABr Precursor ^a				RTA-ATRC Products ^b					Cyclization Conditions			
Trial	M _n ^c	M _p ^d	Đ ^e	M _n ^c	M _p ^d	Đ ^e	<G> ^f	% C ^g	THF (mL) ^h	Addition Rate (μmol/h) BrPMABr ⁱ	CuBr:Cu ⁰ :MNP:Ligand ^j	Ligand Type
1	2700	2900	1.06	3600	2300	1.68	0.80	50%	50	One Pot	6:6:5:10	PMDETA
2	3800	3700	1.18	4400	3100	1.48	0.83	60%	50	33.1	6:6:5:10	PMDETA
3	2600	2800	1.07	2800	2200	1.60	0.78	65%	50	33.1	25:25:10:50	PMDETA
4	3700	3900	1.06	3600	3000	1.44	0.81	70%	50	33.1	25:25:20:12	PMDETA
5	3000	3100	1.07	4400	2500	2.15	0.78	40%	50	11.0	6:6:2.5:12	PMDETA
6	5000	5300	1.06	5300	4100	1.47	0.80	70%	50	16.6	6:6:20:12	PMDETA
7	6000	6400	1.06	6800	5200	1.38	0.81	70%	50	8.3	6:6:20:12	PMDETA
8	4200	4400	1.06	4400	3400	1.49	0.77	70%	25	8.3	6:6:20:12	PMDETA
9	4400	4700	1.06	5300	3600	1.66	0.78	50%	50	One Pot	6:6:5:12	Me ₆ TREN
10	5100	5500	1.07	5100	4300	1.42	0.79	70%	50	33.1	6:6:10:12	Me ₆ TREN

11	5000	5300	1.07		5000	4000	1.54	0.77	70%	50	27.8	6:6:10:12	Me ₆ TREN
12	5000	5200	1.05		4900	4100	1.47	0.78	75%	50	16.6	6:6:10:12	Me ₆ TREN
13	5000	5400	1.07		5100	4200	1.40	0.78	80%	50	12.5	6:6:10:12	Me ₆ TREN
14	2400	2600	1.08		2400	2000	1.38	0.78	85%	50	8.3	6:6:10:12	Me ₆ TREN

^aTelechelic poly (methyl acrylate) (BrPMABr) was prepared by ATRP at 60°C for 45 min using the ratios [MA]:[Eb2biB]:[CuBr]:[PMDETA]=100:1:2:2.

^bRTA-ATRC product after 6 h of reaction time at 40°C.

^cNumber-average weights obtained by GPC calibrated with linear PS standards, expressed in Da.

^dPeak molecular weights obtained by GPC calibrated with linear PS standards, expressed in Da.

^eDispersity values obtained by GPC calibrated with linear PS standards.

^fG-value indication of cyclic product formed by dividing the exact RI-GPC M_p values of the RTA-ATRC product by the M_p of the linear BrPMABr precursor.

^gPercent of BrPMABr precursor that underwent intramolecular coupling.

^hAmount of THF in reaction flask.

ⁱAddition rate in micromoles per hour of BrPMABr.

^jRatios of CuBr catalyst, Cu⁰ reducing agent, MNP radical trap and ligand compared to BrPMABr initiator.

The cyclic products formed by RTA-ATRC were also analyzed by electrospray ionization – mass spectrometry (ESI-MS), with the m/z of major series found to be nearly identical to the predicted values for the MNP-containing cycles (**Figure 3**). In addition to the major series ($z=1$, *), a second set of peaks ($z=2$, *) can be seen at lower mass-to-charge (m/z) ratios. The $z=2$ series of peaks matches the calculated molecular weight of the PMA cycles also seen in the

main series, with calculations shown in the Experimental Section. For example, the $z=2$ peak on the ESI-MS spectrum of 1272.13 Da matches well with the calculated value of 1273.74 Da (for 26 MA units in the cycle). This offers direct evidence of the cyclic structure and is consistent with the intramolecular RTA-ATRC mechanism shown in **Scheme 3**.

Synthesis of Cyclic Diblocks from Br-PMA-PS-PMA-Br linear triblocks

Due to the success of preparing cyclic PMA by intramolecular RTA-ATRC, this method was applied to the formation of cyclic diblocks with PMA chain ends. Cyclic diblocks offer an intriguing set of properties, and methods leading to their synthesis are currently of interest.⁵⁵⁻⁵⁷ In order to accomplish this, triblock copolymers composed of polystyrene (PS) and PMA segments were prepared by consecutive ATRP reactions. ATRP of styrene (Sty) was carried out to initially prepare bifunctional polystyrene (BrPSBr) using benzal bromide (Bzb) as the initiator, CuBr as the catalyst, and PMDETA as the ligand with initial ratios of [Sty]:[Bzb]:[CuBr]:[PMDETA]=50:1:1:1. The reactions were carried out for 2 hours resulting in number-average molecular weight (M_n) values between 2000 to 3000 Da and dispersity ($\mathcal{D}$) values <1.2. Monomer conversions, as determined by ^1H NMR, were less than 40%.

The triblock Br-PMA-PS-PMA-Br was prepared using BrPSBr as the macroinitiator in a subsequent ATRP chain extension reaction to add PMA segments to each end of the PS segment, with methyl acrylate as the monomer, CuBr as the catalyst and PMDETA as the ligand with initial ratios of [MA]:[BrPSBr]:[CuBr]:[PMDETA]=100:1:2:2. The polymerizations were allowed to proceed for 20 minutes resulting in number-average molecular weight (M_n) values between 3600 to 4900 Da and dispersity ($\mathcal{D}$) values <1.2 (**Table 3**, trials 1-5). Monomer conversions were less than 50% for the PMA segments.

Next RTA-ATRC reactions to prepare cyclic PS-PMA diblocks were performed under pseudo high dilute conditions in which the unpurified triblock, MNP and THF were added via syringe into a flask containing THF, CuBr catalyst, Cu⁰ reducing agent and PMDETA (**Scheme 4**). As seen with previous RTA-ATRC reactions of BrPMABr, a shift to longer retention times upon GPC analysis indicated that coupling of the triblock precursors to form cyclic product had occurred (**Table 3**; trials 2-5). Consistent with cyclic products compared to the linear precursors from which they were derived, <G> values of approximately 0.8 were observed when analyzed by GPC. Shifting from a one pot cyclization (**Figure 4a**) to pseudo high dilute conditions led to a modest increase in the percentage of cyclic product (**Table 3**, trials 1 vs 2). Increased concentrations of MNP and slower addition rates resulted in the largest percent of cyclic product, as determined by GPC (**Table 3**, trials 3-5 and **Figure 4b**). Higher eq of copper catalyst and ligand did not translate into larger yields of cyclic product (**Table 3**, trials 1,2 v 3-5). By adjusting redox components in the cyclization flask, the amount of cyclization could be increased up to 80% when addition rates were slow (**Table 3**, trial 5 and **Figure 4b**). This method of PMA-PS cyclic diblocks differs from previous reports of its preparation using α -alkyne and ω -azide linear diblock precursors.⁵⁷

Scheme 4: Synthetic Pathway to Cyclic PS-PMA Diblocks

Table 3. Results of RTA-ATRC of Br-PMA-PS-PMA-Br to Make Cyclic Diblocks

Br-PMA-PS-PMA-Br Precursor ^a				RTA-ATRC Products ^b					Cyclization Conditions ^h	
Trial	M _n ^c	M _p ^d	Đ ^e	M _n ^c	M _p ^d	Đ ^e	<G> ^f	% C ^g	Addition Rate(μmol/h) Br-PMA-PS-PMA-Br ⁱ	CuBr:Cu ⁰ : PMDETA:MNP ^j
1	4900	5200	1.12	6000	4300	1.49	0.82	60%	One pot	25:25:50:5
2	3800	4000	1.10	4400	3200	1.57	0.80	65%	5.3	25:25:50:5
3	3600	4000	1.17	3900	3200	1.56	0.79	65%	14.1	6:6:12:20
4	4900	5200	1.11	5500	4300	1.46	0.82	70%	7.0	6:6:12:20
5	4300	4800	1.11	4400	3900	1.43	0.81	80%	5.3	6:6:12:20

^aTriblock macroinitiator (Br-PMA-PS-PMA-Br) was prepared by ATRP at 80°C for 20 min using the ratios [MA]:[BrPSBr]:[CuBr]:[PMDETA]=100:1:2:2.

^bRTA-ATRC product after 6 h of reaction time at 40°C.

^cNumber-average weights obtained by GPC calibrated with linear PS standards, expressed in Da.

^dPeak molecular weights obtained by GPC calibrated with linear PS standards, expressed in Da.

^eDispersity values obtained by GPC calibrated with linear PS standards.

^fG-value indication of cyclic product formed by dividing the exact RI-GPC M_p of the RTA-ATRC product by the M_p of the linear BrPMABr precursor.

^gPercent of BrPMABr precursor that underwent intramolecular coupling.

^h100 mL of THF was used in all cases in the cyclization flask.

ⁱAddition rate in μmoles of Br-PMA-PS-PMA-Br per hour.

^jRatios of CuBr catalyst, Cu⁰ reducing agent, PMDETA and MNP radical trap compared to BrPMABr initiator.

Conclusions. Cyclic PMA was prepared in an efficient polymerization-to-cyclization sequence in which the unpurified ATRP reaction mixture containing the telechelic PMA was employed directly in an intramolecular RTA-ATRC reaction. The highest yields of cyclic polymer were obtained when the linear precursor was added drop-wise via syringe into a redox active THF solution using Me_6TREN as the ligand. Cyclization by intramolecular ATRC (lacking the radical trap) was unsuccessful using the same process; instead continuation of ATRP was observed. The identity of the cyclic polymer containing the MNP radical trap was confirmed by ESI-MS. The polymerization-to-cyclization process was applied to the synthesis of cyclic diblock copolymers prepared from telechelic PMA-PS-PMA triblocks, with yields of cyclic product up to 80% for pseudo high dilute RTA-ATRC cyclization reactions.

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53. Model reactions of unpurified monobrominated PMA chains underwent dimerization in the presence of the radical trap MNP, while analogous trials lacking the radical trap continued to undergo ATRP. **RTA-ATRC reaction:** Precursor PMABr $M_n = 3500$ Da, $M_p = 3800$ Da, $\bar{D} = 1.08$; RTA-ATRC product: $M_n = 6000$ Da, $M_p = 8000$ Da, $\bar{D} = 1.17$. **ATRC reaction:** Precursor PMABr $M_n = 3200$ Da, $M_p = 3400$ Da, $\bar{D} = 1.08$; RTA-ATRC product: $M_n = 4100$ Da, $M_p = 4500$ Da, $\bar{D} = 1.15$.
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