General Introduction : Synthesis of Cyclic Polymers

1. Preamble

Much attention was paid to cyclic polymers and much effort was devoted to their design and synthesis for the last decades because of distinct properties compared to the linear counterparts, such as glass transition temperature, order-disorder transition, hydrodynamic volume, intrinsic viscosity, and enhancement of fluorescene.[1-3] This interest is motivated by the appealing topology of the macrocycles, the stringent restrictions on the backbone conformation, and the absence of chain ends.[4] The discovery of natural DNA ring,[5] where the two strands of the double helix form a high order link, has stimulated the chemists to embark on the macromolecular engineering of cyclic polymers. It must be noted that living organisms produce numerous cyclic compounds, such as oligopeptides, polypeptides, and DNAs, whose the molecular weight and ring size can change extensively. In protozoae, relatively small rings containing approximately 400 base pairs (equivalent to 2400 atoms in the ring) are known that have a molar mass of 1.2×10^5 g/mol. Importantly, it was found recently that cyclic DNA can be prepared in-vitro by using the enzyme ligase.[6] Therefore, synthesis of well-defined macrocycles, extending over a large range of macromolecular characteristic features is of the utmost importance for improving basic knowledge and ultimately mimicking compounds with a specific biological activity.

Synthesis of the cyclic polymers started with the discovery of living anionic polymerization, that made well-defined linear precursors available with functional end-groups well-suited to cyclization reactions. The usual route towards macrocycles relies indeed on the end-to-end coupling of linear precursors. Whenever the end-functionalization is ideal, the

cyclization yield is expressed by eqn. (1), where C is the actual concentration and C_{equal} stands for the concentration at which the probability for the intra- and inter-molecular reactions to occur is the same [eqn. (2)].[1]

$$\text{Cyclization yield} = C_{equal} / (C_{equal} + C) \quad (1)$$

$$C_{equal} = [3 / (2 \pi \langle r^2 \rangle)]^{3/2} M / N_A \quad (2)$$

where $\langle r^2 \rangle$ is the mean square end-to-end distance of the linear precursor, N_A is the Avogadro number, and M is the molar mass.

According to the statistical eqn. 1, the intramolecular cyclization is as effective as the polymer concentration is low ($C < 10^{-5}$ M). The large amount of solvent which is accordingly needed is a severe limitation to the production of reasonable amounts of macrocycles. As a rule, the selective synthesis of high molecular weight cyclic polymers requires an even more diluted medium than the cyclization of oligomers. The improvement of the cyclization efficiency and both the purity and homogeneity of the cyclic polymers is nowadays an urgent requirement for the reliable establishment of macromolecular structure - properties relationships and experimental support to theories about cyclic polymers.[1, 3-4] Therefore, the introduction of the thesis will emphasize the synthesis of cyclic polymers by cyclization of either homo- or hetero-difunctional linear precursors prepared by living or living/controlled polymerization techniques and endowed with well-defined molecular parameters. As a direct consequence of this choice, the studies on contribution of the step-growth polycondensation to synthesis of macrocycles will be out of the scope of this review. The reader is however referred to a paper by H.R. Kricheldorf and G. Schwarz about cyclization by kinetically controlled polycondensation.[7]

2. Synthetic routes towards the main macrocyclic structures

At the time being, cyclic homopolymers, cyclic block copolymers, tadpole-shaped, eight-shaped and sun-shaped (co)polymers, and pluricyclic (co)polymers are the most representative architectures of macrocycles reported in the scientific literature. Their synthesis is discussed hereafter.

2.1 Cyclic homopolymers

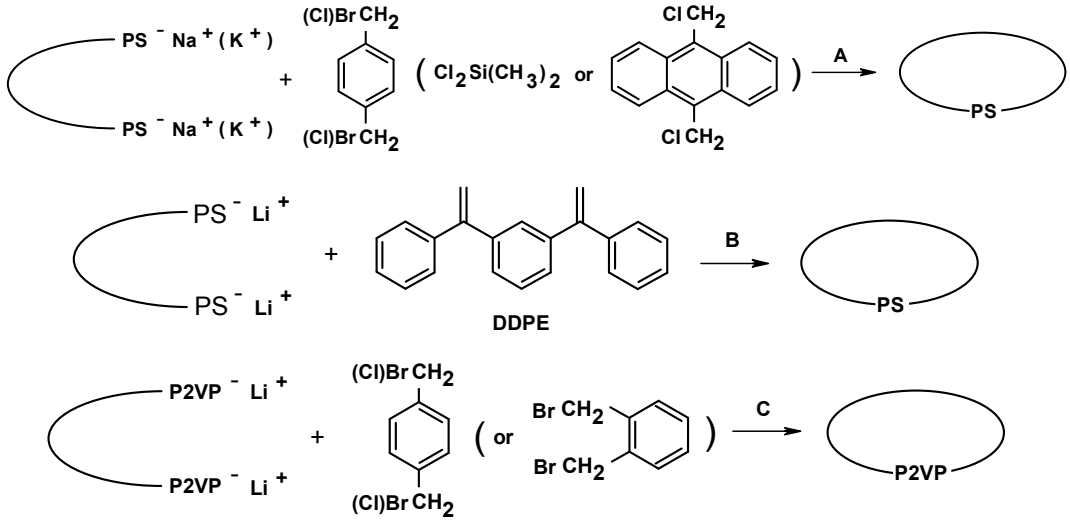
a) Cyclization of symmetric α,ω-functional polymers

The obvious cyclization strategy of this type of precursors consists of the intramolecular coupling of the end-groups by an appropriate agent under extreme dilution. The difunctionality of the polymer, the stoichiometric amount and the dropwise addition of the coupling agent are prerequisites for success. After cyclization, purification of the crude reaction product is also a crucial step because competition between intramolecular cyclization and intermolecular condensation cannot be avoided.

Macrocyclic vinyl aromatic polymers

The living anionic polymerization of styrene was initiated by sodium (or potassium) naphthalenide and terminated by the dropwise addition of, e.g., α,α'-dichloro-p-xylene and

α,α'-dibromo-p-xylene (DBX), under high dilution[8-10] (Scheme 1, A). The raw samples were analyzed by size exclusion chromatography (SEC) and the cyclization yields were calculated from the area of the elution peaks. Cyclization yields in the range of 10 to 45% were found for coupling by DBX in relation to the polystyrene molecular weight and experimental details.



Scheme 1. Synthesis of cyclic aromatic polymers

A major advantage of this strategy has to be found in the synthesis of highly monodisperse and difunctional linear precursors before cyclization into model compounds. An extra benefit is the strong absorption in the UV-Vis region by the carbanionic end-groups of the living precursors, which allows the coupling reaction to be monitored. Nevertheless, the traditional drawback of the high dilution required for limiting the extent of the undesired intermolecular coupling, cannot be avoided. The high dilution is not only a practical limitation on the amount of polymer that can be produced, but also a higher probability of termination of the highly reactive anions. After purification, well-defined cyclic polystyrenes were made available by this technique.

It may be worth recalling here the most common criterion used for assessing the success of cyclization, i.e., cyclic macromolecules are eluted at higher volumes than the linear precursors when analyzed by size exclusion chromatography (SEC). In this respect, the parameter <G>, defined as the ratio of the apparent molecular weights at the cyclic and the linear chains, respectively. <G> thus gives information on the relative hydrodynamic volumes for the cyclic and the parent linear chains. Moreover, the ratio, $g = [\eta]_{cyclic} / [\eta]_{linear}$, of the intrinsic viscosities of the cyclic and linear chains is also commonly reported. It however depends on the molecular weight distribution of the two populations of chains, which explains that it may be perturbed by a fractionation effect on the occasion of the purification of the cyclic chains.

The ratio g was reported for cyclic polystyrene, prepared independently by several research groups. This value is in the 0.56 to 0.76 range in toluene at 25°C (~ 0.65 in cyclohexane at 34.5°C) for samples with a molecular weight lying between 10^4 and $25x10^4$ g mol^{-1}.[11-13]

In an alternative approach (Scheme 1, B), 1,3-bis(1-phenylethylenyl)benzene was used either as an initiator for the anionic polymerization of styrene or as a coupling agent for end-to-end ring closure of α,ω-dianionic polystyryl chains under high dilution. [14-15]

Quite interestingly, anthracene was incorporated into cyclic polystyrene and other vinyl aromatic polymers because of the fluorescent properties of this molecule, which is thus a probe in the study of phenomena, such as energy transfer. In a straightforward approach, 9,10-bis-(chloromethyl)anthracene (Scheme 1, A) was used as coupling agent of linear polystyryldipotassium ($PS-K_2$) or poly(9,9-dimethyl-2-vinylfluorene)yl dipotassium

(PDMVF-K_2) chains in THF at -78°C. [16]

Cyclic poly(2-vinylpyridine) (P2VP) was first reported by T. E. Hogen-Esch et al. (Scheme 1, C).[17-18] They initiated the anionic polymerization of 2-vinylpyridine by a dilithiated compound, 1,4- dilithio-1,1,4,4-tetraphenylbutane, prepared by direct metallation of 1,1-diphenylethylene in THF. The living dianionic chains were cyclized by reaction with 1,4- or 1,2-bis(bromomethyl)benzene (DBX) at ambient temperature because of the higher stability of the living P2VP chains compared to the polystyryl ones.[19] The macrocyclization yield decreased from 70% to 40% upon increasing molecular weight. Accordingly to SEC analysis, the macrocycles contained less than 5% linear precursor, and the hydrodynamic volume of the macrocycles was substantially (~ 30%) lower than the linear precursor. The parameter <G> was found in the 0.88 to 0.75 range when the molecular weight increased from $1.5x10^3$ to $1.1x10^5$. No very significant difference was noted in the SEC hydrodynamic size for the macrocycles formed with 1,2-DBX rather than by 1,4-DBX.[20]

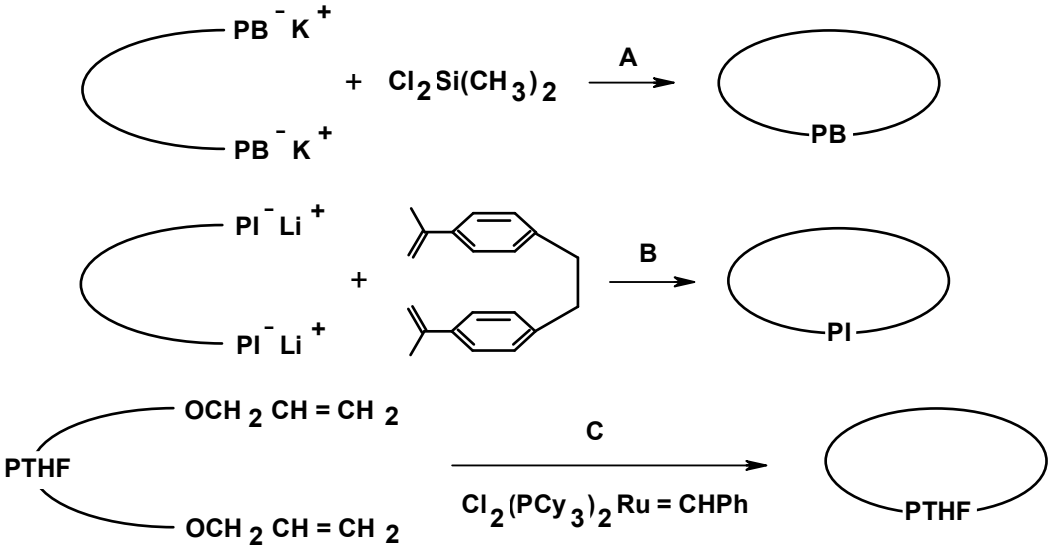
Cyclic P2VP was quaternized by alkyl halides (MeBr or EtBr) in THF at 60°C, with the purpose to prepare macrocyclic polyelectrolytes. Approximately 70% of the pyridine units of P2VP were quaternized by MeBr, compared to 20% in the case of EtBr.[21]

Macrocyclic polydienes

Linear polybutadiene (PB) (62% of 1,2-co-units) was prepared with potassium naphthalenide in a THF/n-hexane (1.3:1) mixture at –1.5°C. The living polybutadienyl chains were slowly added into a large volume of cyclohexane at 0°C, into which

dichlorodimethylsilane was distilled (Scheme 2, A). Discoloration of the living chains (pale yellow color) indicated when the reaction stoichiometry was reached.[22-23] A set of high-resolution SEC columns was used to estimate the cyclization yield (75-80%). The ratio g ($[\eta]_{cyclic}$ / $[\eta]_{linear}$), measured after the purificatin of the cyclic chains, was 0.63 in toluene at 35°C. Cyclic polybutadiene with a predominant 1,4-microstructure (56%), was also synthesized by coupling α,ω-dilithium polybutadiene with 1,3-bis(phenylethenyl) benzene under high dilution, followed by termination with an excess of ethylene oxide[24] in order to have two hydroxyl groups attached to the macrocycles.

Cyclization of α,ω-dilithio polyisoprene was carried out in hexane added with 15 vol% of tetrahydrofuran at -50°C. A non-conjugated diene, 1,2-bis(isopropenyl -4-phenyl)ethane, was used as coupling agent (Scheme 2, B), leading to a cyclization yield of at least 90%, even for molecular weight as high as $3x10^4$ g mol^{-1}.[25] According to the authors, no further purification was required.



Scheme 2. Synthesis of cyclic aliphatic polymers

Macrocyclic polyether

Hydrophilic cyclic PEO was prepared by coupling highly diluted poly(ethylene glycol) with dichloromethane in the presence of solid KOH. An acetal bonding was formed upon cyclization (yield: 80%).[26]

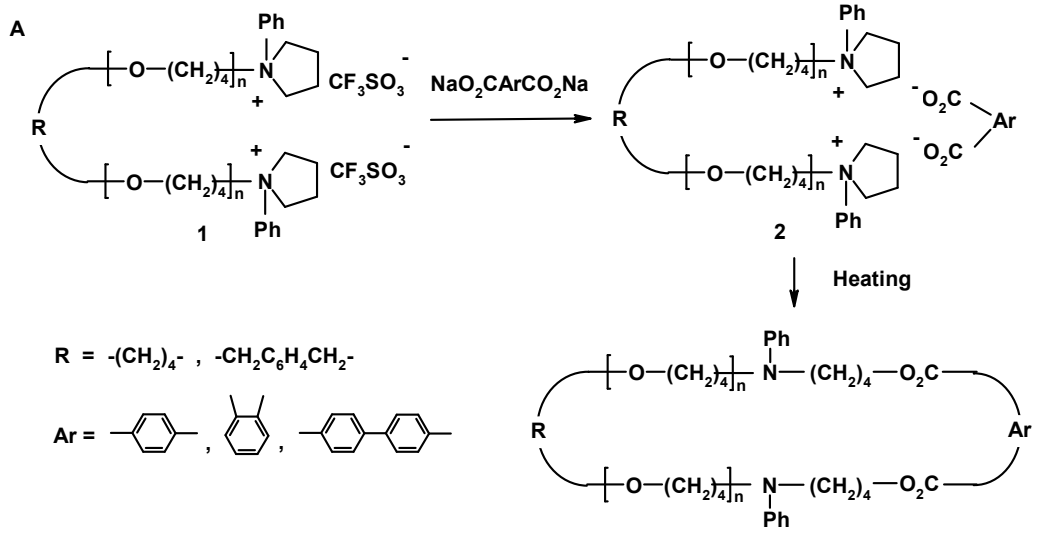
In order to get rid of the coupling agent and, thus, the very demanding requirement of an ideal stoichiometry, macrocycles were synthesized by the direct intramolecular coupling of the two chain-ends of a symmetric α,ω-functional linear precursor. Remarkably, Tezuka et al. succeeded in closing allyl end-capped poly(tetrahydrofuran) by a metathesis reaction mediated by the Grubb's catalyst (Scheme 2, C).[27] Nevertheless, high dilution remains a stringent requirement (~ 10^{-5} mol L^{-1}).

b) Cyclization by interfacial condensation

In order to increase to coupling efficiency of polystyrene, the ring closure was carried out by an interfacial method rather than in a one-phase system. Linear α,ω-dibromobutyl polystyrene was first prepared by reaction of polystyryl dianions with a large excess of 1,4-dibromobutane. This difunctinal polystyrene precursor was dissolved in toluene, whereas the coupling agent (hexamethylene diamine) was dissolved in water. When the concentration of reactants was lower than 6.7×10^{-3} mol L^{-1}, condensation yield was 90 wt% and the cyclization conversion was 100%. [28]

c) Cyclization by electrostatic self-assembly followed by covalent fixation

Y. Tezuka et al. proposed a novel approach towards cyclic polymers. It relies on the pre-cyclization of linear precursors through electrostatic interactions under high dilution, followed by covalent fixation.[29-30,] Pure cyclic polymer was collected by preparative SEC fractionation of the crude reaction product.

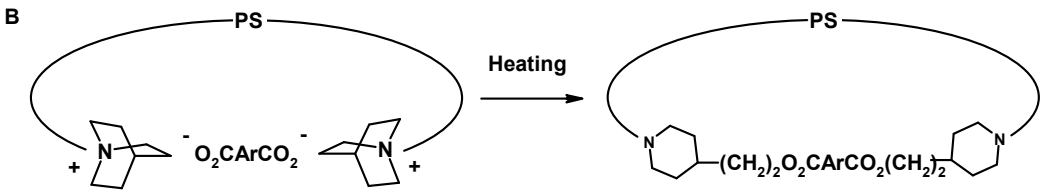


Scheme 3A

For example, living cationic poly(THF) was reacted with N-phenyl(or N-methyl)pyrrolidine with formation of telechelic poly(THF), where N-phenylpyrrolidinium($^{-}OSO_2CF_3$), thus a five-membered ammonium salt, was the end-group (**1** in Scheme 3, A). The trifluoromethanesulfonate counter-anions of the end-groups were readily substituted by a dicarboxylate counter-anion, merely by precipitation of **1** into an aqueous solution of an excess of sodium 4,4'-biphenyldicarboxylate (or terephthalate, o-phthalate). As result of this ion-exchange under high dilution, the linear chains were temporarily stabilized by electrostatic interactions (**2**), the dissociation/association of the ion

pairs depending on the concentration. Upon heating, a covalent bonding was substituted for the ionic bonding, as result of the ring-opening of the pyrrolidine units (yield: 55-75%).[32] The use of a functionalized coupling agent, such as 5-hydroxyisophthalate or 5-allyloxyisophthalate, is a direct way to attach a functional group to cyclic poly(THF).[33]

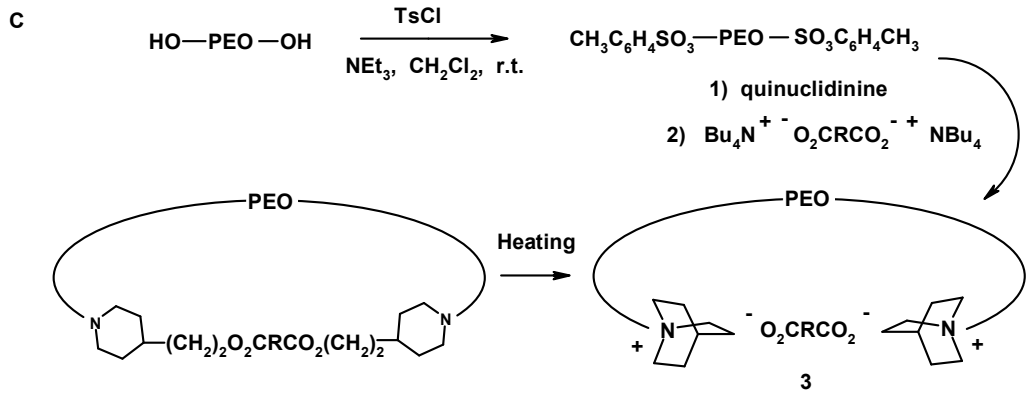
Conversion of the ionic bonds into covalent bonds, thus the ring opening reaction, is a key step. Indeed, three-, four-, five-, and six-membered cyclic ammonium groups, respectively, were attached to the chain-ends of poly(THF) and their impact on the ring-opening reaction was investigated. The ring-opening reaction occurred at room temperature for the highly reactive three- and four-membered ammonium groups, which was not favorable to the macrocycles formation.[34] N-methylpyridinium end-groups had also to be disregarded because the cyclization yield was decreased by a demethylation reaction. Finally, N-phenylpyridinium imparted the best selectivity to the cyclization reaction, as result of the nucleophilic substitution which was inherently suppressed at the phenyl group. Ring-opening then occurred preferentially at the aliphatic *endo*-methylene group.



Scheme 3B

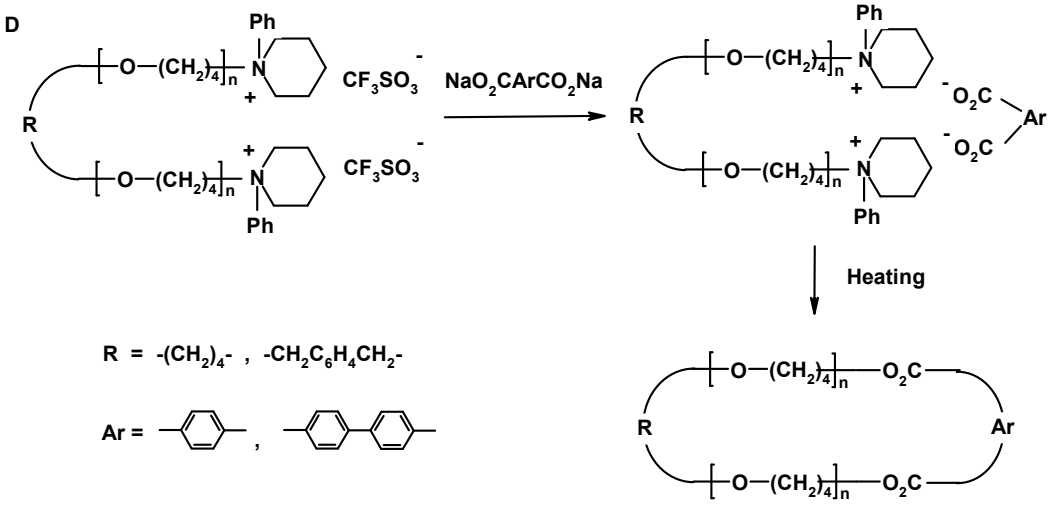
This strategy was extended to cationically prepared polystyrene. However, the propagating cationic species could not be quaternized by N-phenylpyridine. In order to tackle this problem, a six-membered bicyclic quinuclidinium was selected as an end-group (Scheme 3, B). Then, the nucleophilic attack of the quinuclidinium group by the carboxylate counterion

took place selectively at the endo-methylene position with ring-opening of the strained azabicyclo unit.[34]



Scheme 3C

When water-soluble PEO was concerned, the hydroxyl end-groups of poly(ethylene glycol) (M_n = 2.8x10^3) were quantitatively converted into a quinuclidium adipate salt followed by the ion-exchange reaction (Scheme 3, C).[35] Cyclization of **3** was performed in refluxing toluene under high dilution (2.5x10^{-4} mol L^{-1}) (yield: 63%).



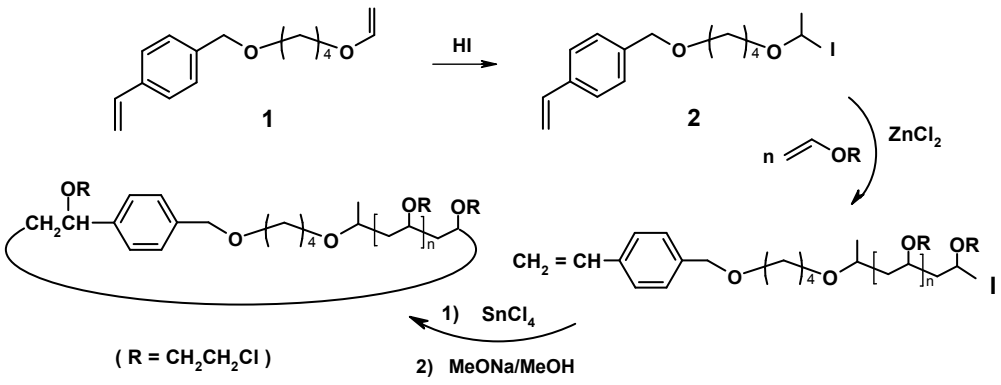
Scheme 3D

It must be noted that the aminoester group, which is formed by ring-opening, can undergo inter- and intramolecular substitution reaction, particularly at high temperature. Very

recently, this drawback was bypassed by end-capping the living poly(THF) chains by an unstrained six-membered ring, i.e., N-phenylpiperidinium, with formation of a more stable linkage. Upon heating, the carboxylate counter-ions selectively attacked the exo position of the cyclic ammonium salt, N-phenylpiperidine was eliminated and a stable ester was formed (Scheme 3, D).[36]

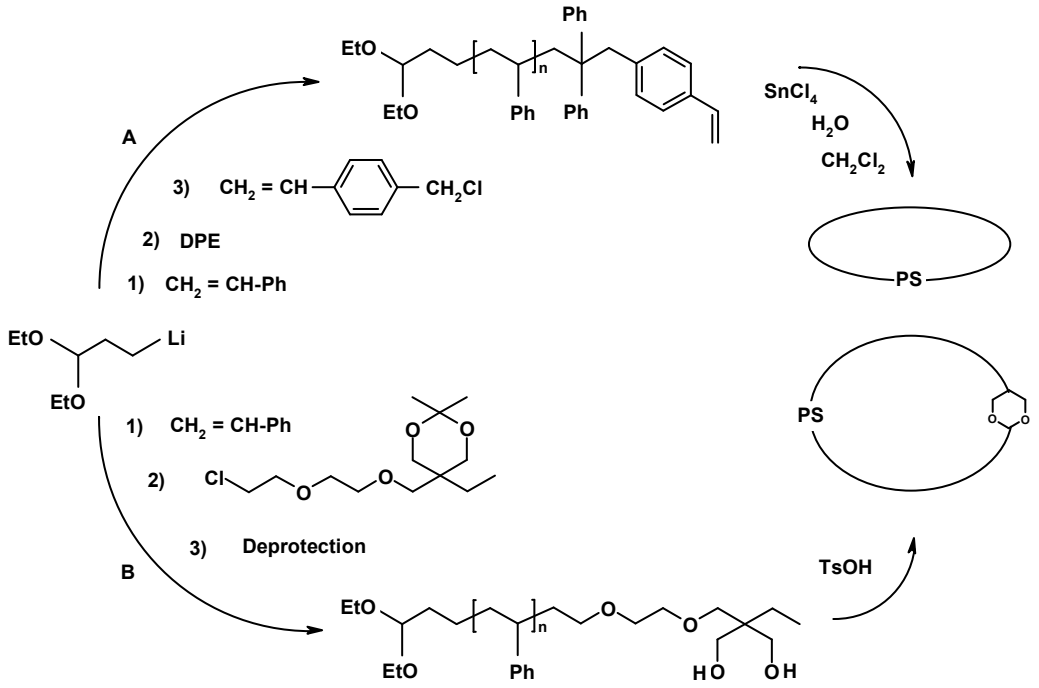
d) Cyclization of asymmetric α,ω-functional polymers in the presence of an activator

An unimolecular cyclization process was first proposed by A. Deffieux et al., who synthesized macrocycles by the direct closure of asymmetric telechelic precursors in the presence of a catalyst under high dilution.[37] The two end-groups were selected for a high mutual reactivity, at least upon activation. The cyclization efficiency was notably improved because the concentration of each type of functional groups was decreased by half compared to the strategies discussed until now, under otherwise identical conditions. The probability of side intermolecular reactions was accordingly decreased. Moreover, no coupling agent was needed, and the inherent stoichiometric balance of the mutually reactive end-groups is an additional advantage.



Scheme 4. Synthesis of cyclic poly(2-chloroethyl vinyl ether)

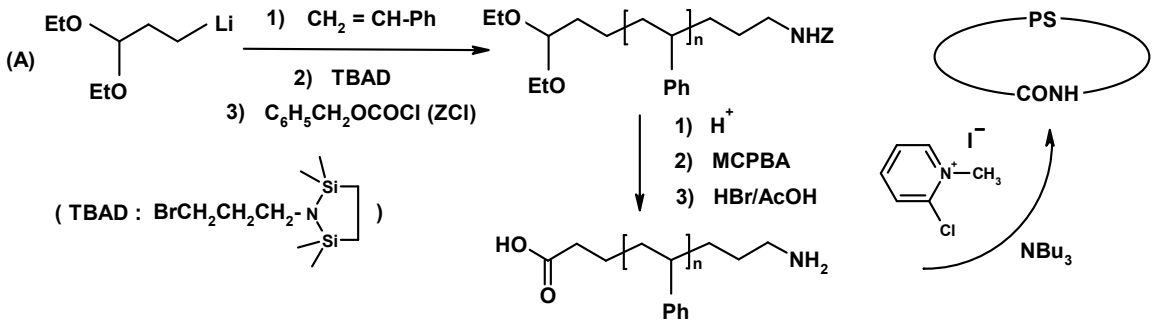
Synthesis of cyclic poly(2-chloroethyl vinyl ether) is illustrated in Scheme 4. Polymerization of 2-chloroethyl vinyl ether was initiated by an iodocompound **2** formed by the selective addition of HI onto the vinyl ether double bond of **1**, in contrast to the styrenic double bond that remained unreacted. Polymerization occurred at -40°C in the presence of $ZnCl_2$. Cyclization was carried out at -10°C by the dropwise addition of the living chains into a toluene solution of $SnCl_4$, used as an activator of the addition reaction of the α-iodoether onto the styrenic double bond. The reaction was terminated by a solution of methoxide in methanol.[37] The cyclization yield was determined by SEC and found in the 72 to 92% range. The <G> parameter was rather constant (0.85-0.88) at least for the low molecular weight chains under consideration ($1.1x10^3$ to $2.8x10^3$ g mol^{-1}).



Scheme 5. Synthesis of cyclic polystyrene from an asymmetric telechelic precursor

This strategy was also implemented for the synthesis of cyclic polystyrene with

controlled molecular weight (M_n = 1.7-12.2x10^3 g mol^{-1}) and molar mass distribution (M_w/M_n = 1.04-1.08).[38-39] The direct cyclization α-diethylacetal, ω-styrenyl polystyrene prepared by living anionic polymerization, was activated by a Lewis acid, such as $SnCl_4$, AlI_3, $AlCl_3$ and $TiCl_4$ (Scheme 5, A). The effect of the Lewis acid on the cyclization yield was investigated in media of increasing dieletric constant. Whatever the Lewis acid, neither cyclization nor polycondensation was observed in pure and anhydrous toluene and dichloromethane. However, the cyclization was quantitative in CH_2Cl_2 containing traces of water or ethanol. Macrocyclic polystyrene was analyzed by liquid chromatography at critical point of adsorption[40] and by mass spectrometry.[41] In an improved version of this strategy,[42] the styrenyl double bond was replaced by a bis(hydroxymethyl) group as shown in Scheme 5, B. Macrocyclic polystyrene (M_n = 1.7-30x10^3) was collected within high yield (>90%) without the need of fractionation.

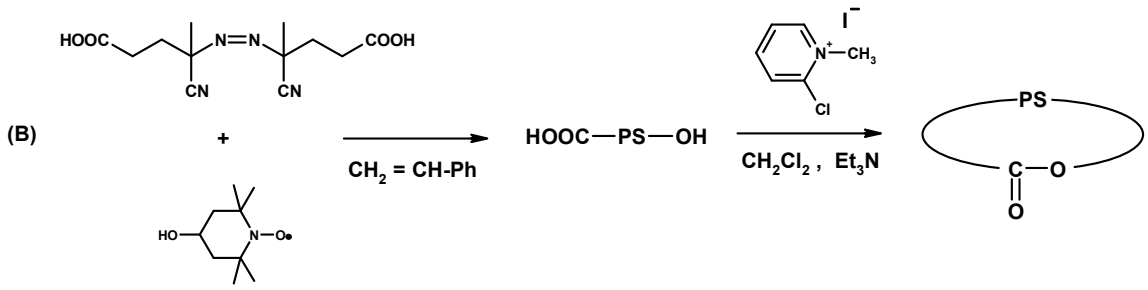


Scheme 6A

Kubo et al. also prepared cyclic polystyrene from asymmetric telechelic chains, i.e., α-carboxyl, ω-amino polystyrene. Actually, the styrene polymerization was initiated by 3-lithiopropionaldehyde diethyl acetal in benzene in the presence of N,N,N',N'-tetramethylethylene diamine (TMEDA) at room temperature. The key point is that the α-acetal is easily converted into a carboxyl group. The ω-amino group was attached by

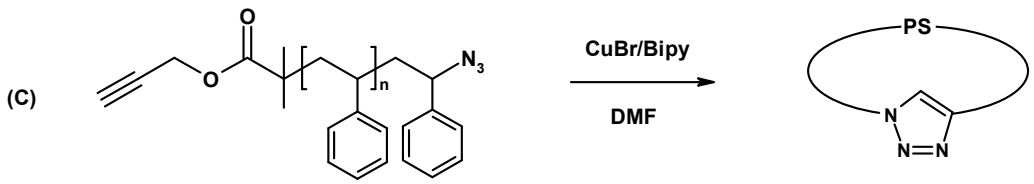
deactivation of the living polystyryllithium chains by an aminating agent, 2,2,5,5-tetramethyl-1-(3-bromopropyl)-1-aza-2,5-disilacyclopentane (TBAD) (Scheme 6, A). The intramolecular cyclization was carried out in dichloromethane under reflux, with 1-methyl-2-chloropyridinium iodide as a catalyst.[43]

Hemery et al. synthesized cyclic polystyrene by closing α-hydroxy-ω-carboxyl polystyrene preformed by nitroxide mediated radical polymerization of styrene (Scheme 6, B).[44]



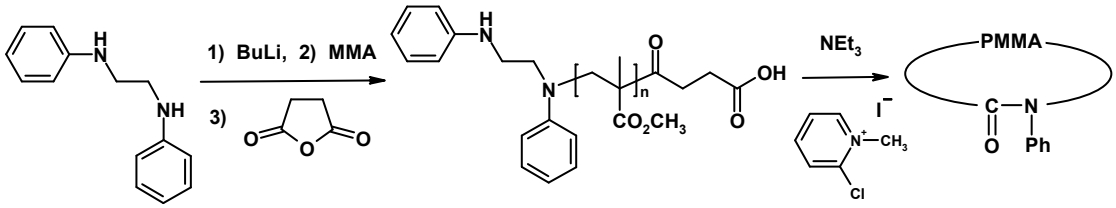
Scheme 6B

Very recently, Grayson et al. used a highly efficient "click" reaction, i.e., the copper-catalyzed Huisgen's dipolar cycloaddition for the synthesis of macrocyclic polystyrene (M_n = 2200 and 4100) (Scheme 6, C). α-Alkyne, ω-azide polystyrene prepared by ATRP was cyclized in DMF at 120°C, in the presence of Cu(I)Br and bipyridine, under high dilution. The intramolecular coupling was nearly quantitative, such that fractionation was not needed for the macrocycles to be isolated.[45]



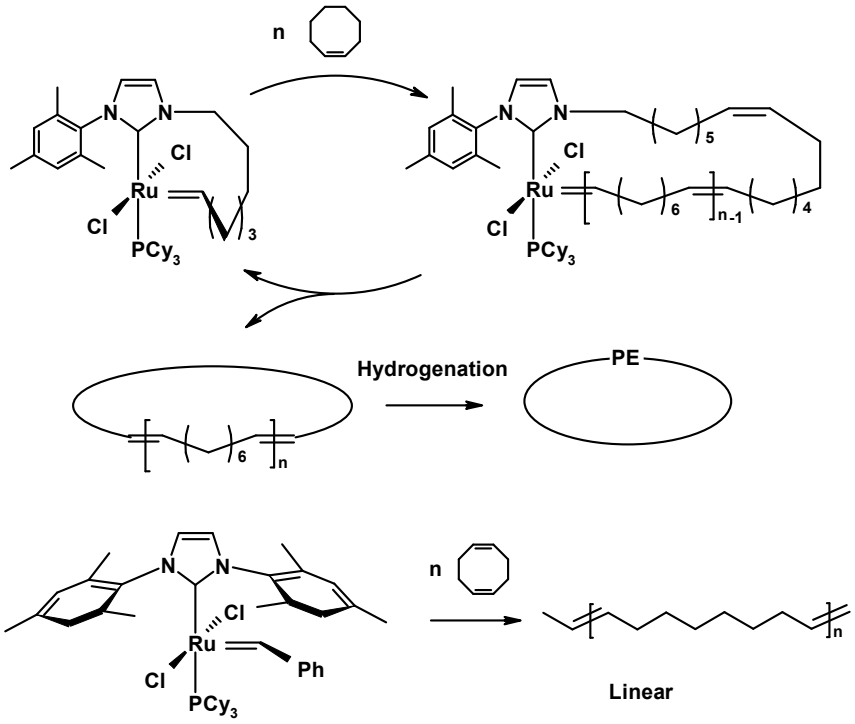
Scheme 6C

The synthesis of cyclic poly(methyl methacrylate) (PMMA) was based on the intramolecular cyclization of α-carboxyl, ω-amino PMMA, prepared by living anionic polymerization of methyl methacrylate initiated by the monolithium derivative of N,N'-diphenylethylenediamine and terminated by succinic anhydride (Scheme 7).[46]



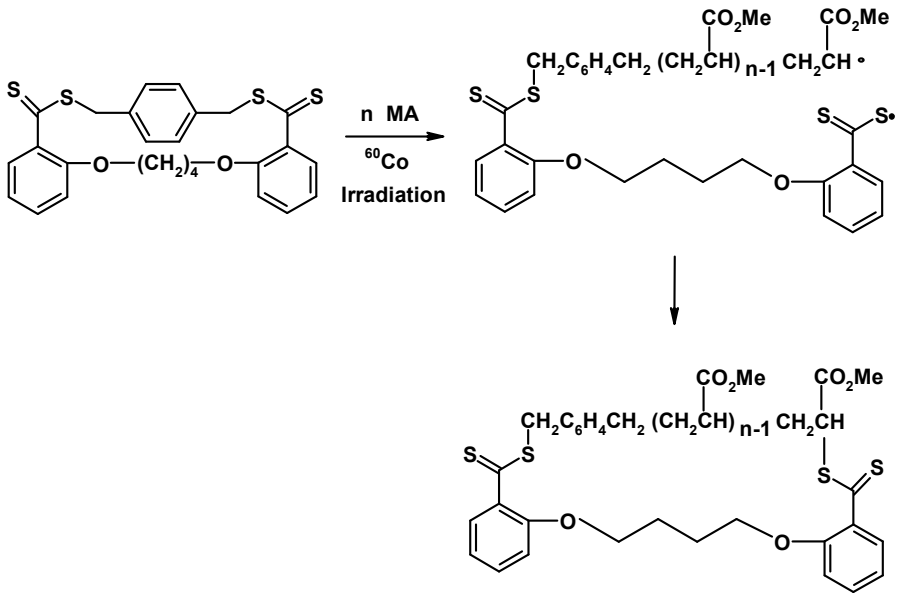
Scheme 7. Synthesis of cyclic PMMA

e) Synthesis of macrocycles initiated by cyclic initiators



Scheme 8. Synthesis of cyclic polymers by ring-opening metathesis polymerization

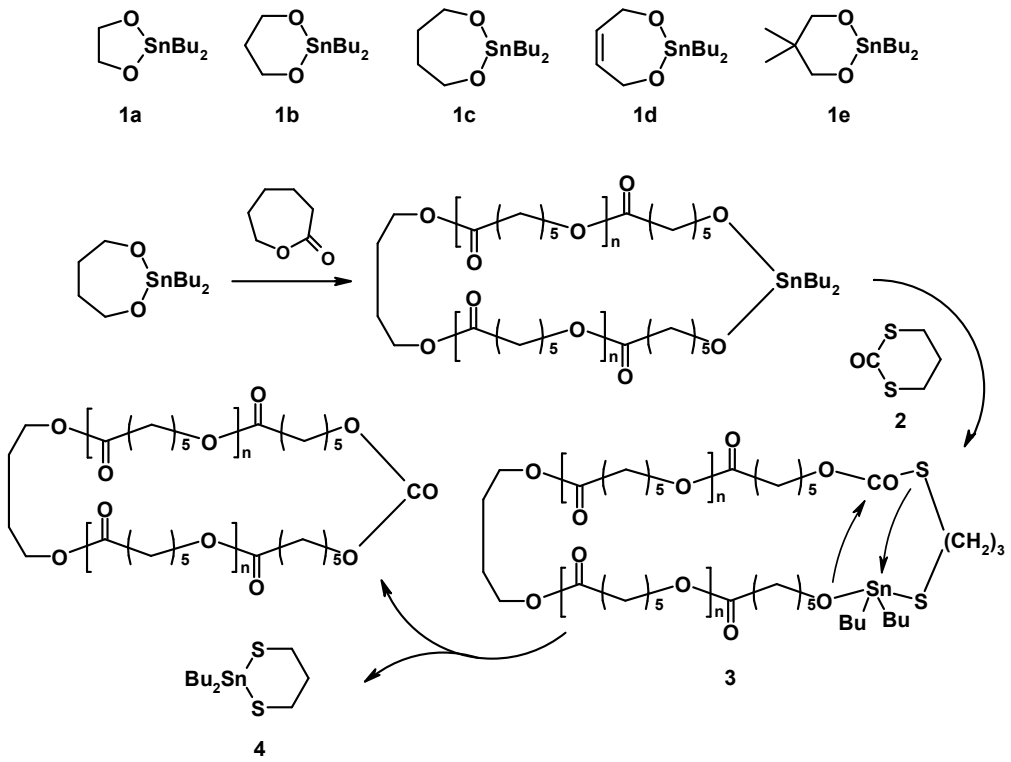
Cyclization by intramolecular chain transfer. In order to bypass the high dilution usually required for the synthesis of macrocycles, R. H. Grubbs initiated the ring-opening metathesis polymerization of cyclooctene by a cyclic ruthenium carbene, such that the growing polymer chains remained attached to the ruthenium complex during the entire polymerization process.[47] Finally, ruthenium-free macrocyclic poly(cyclooctene) (M_n = 6x10^5 – 1.1x10^6) was formed by intramolecular chain transfer. This novel strategy is remarkable because no linear intermediate is involved at any stage of the process. Moreover, the polymerization can be conducted at high concentration, even in the bulk and no purification is necessary. This approach was extended to the synthesis of cyclic polybutadiene with 1,4-regioisomeric backbone, 1,5-cyclooctadiene being then the monomer (Scheme 8).[48]



Scheme 9. Synthesis of cyclic polymers by controlled radical polymerization

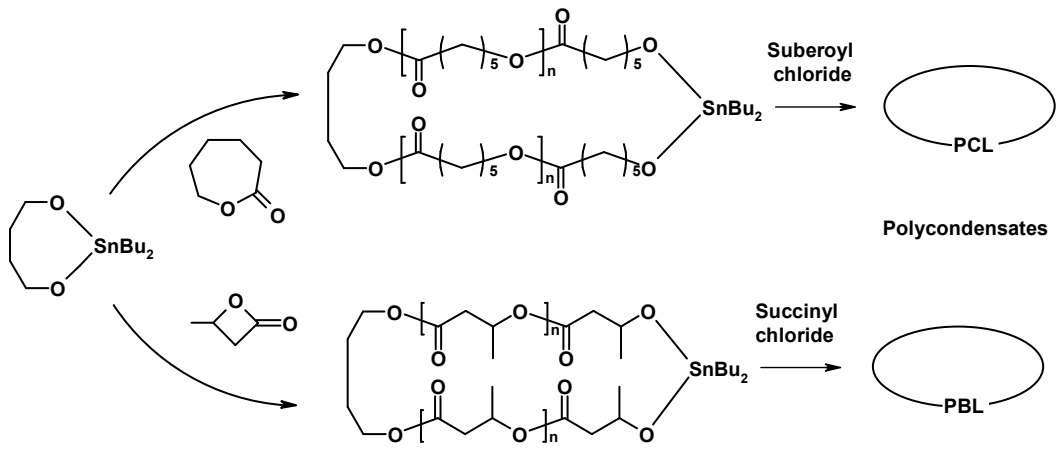
Cyclization by intramolecular chain termination. Another route reported for the synthesis of macrocycles, relies on the controlled radical polymerization of methyl acrylate

(MA) in THF (10 wt%) by using a cyclic initiator with a weak (C-S) bond (Scheme 9).[49] Upon ^{60}Co γ-ray irradiation at -30°C, this C-S bond was cleaved with formation of a benzyl radical and a stable sulfur radical. The benzyl radical initiated the polymerization of MA, that was reversibly terminated by the stable sulfur radical, as it happens in any controlled radical polymerization. However, for the process to be successful, the reversible termination must be fast enough for competing effectively deleterious irreversible termination. In this work, the termination rate constant ($k_t = 0.95x10^7$ for MA) was much higher than the propagation rate constant ($k_p = 2.09x10^3$). Therefore, only few monomers were added before reversible termination occurs. Cyclic poly(methyl acrylate) was accordingly formed with a predetermined molecular weight without high dilution (yield: 77%; $M_n = 8.2x10^3$; M_w/M_n = 1.33).



Scheme 10. Synthesis of cyclic polyester

Kricheldorf et al. initiated ring-opening polymerization of lactones and lactides by a series of cyclic tin dialkoxide **1a-e** (Scheme 10). Typically, the growing chains are macrocyles stabilized by an endocyclic tin dialkoxide.[50] As result of a coordination-insertion polymerization mechanism, no linear oligomer or polymer is formed at any stage of the process. Moreover, polymerization being controlled, the molecular weight can be predicted by the monomer/initiator molar ratio and the monomer conversion.[51-50] Synthesis of tin-free cyclic poly(ε-caprolactone) was also explored. In a representative example, the ring-opening polymerization of ε-caprolactone was initiated by 2,2-dibutyl-2-stanna-1,3-dioxepane (DSDOP) in the bulk at 80°C and terminated by the addition of 1,3-dithian-2-one **2** (slightly excess compared to the initiator) in $CHCl_3$. The reaction mixture was heated at 100°C for 24 h. Cyclization was stabilized by the insertion of **2** into the Sn-O bond with formation of **3**. Finally, the cyclic 2-stanna-1,3-dithiane **4** was selectively eliminated from **3** (Scheme 10). No need for high dilution is a substantial advantage.



Scheme 11. Synthesis of cyclic polyester by combination of ROP and polycondensation

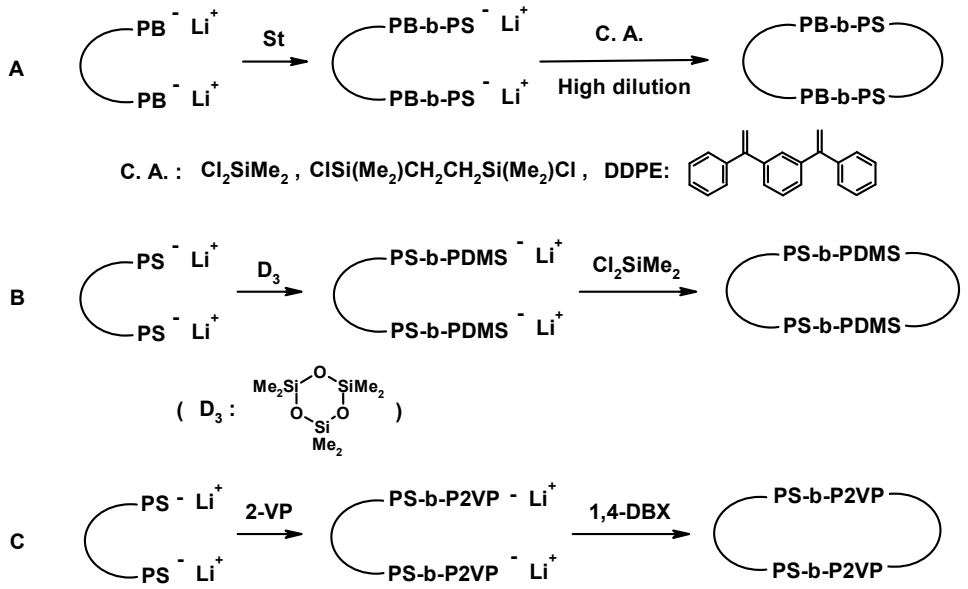
Cyclic aliphatic polyesters were also synthesized by combining ring-opening

polymerization and kinetically controlled polycondensation. For example, cyclic poly(ε-caprolactone) (or poly(β-butyrolactone)) containing an endocyclic tin dialkoxide was synthesized by ring-opening polymerization of ε-caprolactone (ε-CL) (or β-D,L-butyrolactone (β-BL)) initiated by DSDOP. The "living" polyester chains were condensed with either suberoyl chloride (in the case of ε-CL) or succinyl chloride (for β-BL) under optimized conditions (Scheme 11). The isolated tin-free polyester consists of either cyclic polyester ($M_{n,PCL}$ = 10.6x10^3; $M_{n,PBL}$ = 17x10^3) or linear polycondensate. This observation suggests that the chain growth is limited by cyclization and by the incomplete conversion of the functional groups.[52]

2.2 Macrocyclic block copolymers

Block copolymers are known for a long time as precursors of multiphase polymeric materials as result of the nanophase separation of the constitutive immiscible blocks. Much effort was devoted to the dependence of the nanophase morphology on the molecular weight, composition and architecture of the copolymers. In this respect, cyclization of block copolymers deserves interest. As a rule, the strategies proposed for the synthesis of cyclic homopolymers can be extended to block copolymers with well-defined molecular parameters (M_n, M_w/M_n, composition). Because additional steps are involved in the synthesis of block copolymers compared to homopolymers, lower cyclization yields might be expected which would require fractionation for collecting pure macrocycles.

Cyclic polystyrene-b-poly(butadiene) copolymer (~ 40 wt% polystyrene) was prepared by closing living polystyryl(Li^+)-b-polybutadiene-b-polystyryl(Li^+) chains by either 1,3-bis(1-phenylethenyl) benzene (DDPE) or a chlorosilyl derivative, under high dilution (Scheme 12 A).[53-54] The sequential anionic polymerization of butadiene and styrene was initiated by the DDPE/*sec*-BuLi/*sec*-BuOLi system. The microstructure of the polybutadiene block was predominantly of the 1,4-type (86 %). The ratio g $[[\eta]_{cyclic} / [\eta]_{linear}]$ decreased from 0.79 to 0.57 when the molecular weight was increased from $35x10^3$ to $70x10^3$.

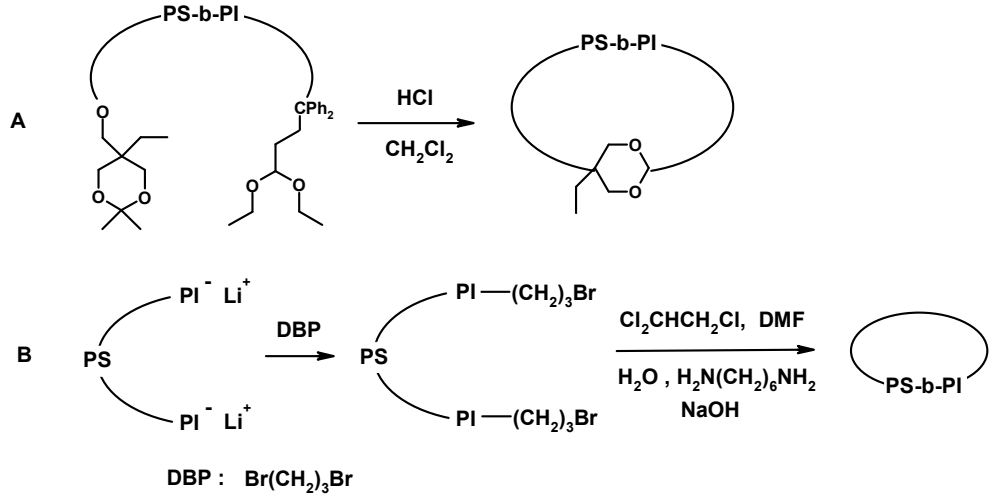


Scheme 12. Synthesis of cyclic diblock copolymers

Polystyrene-b-poly(dimethylsiloxane) copolymers (60-80 mol% of PS) with a narrow molecular weight distribution were prepared by the sequential anionic polymerization of styrene and hexamethylcyclotrisiloxane (D_3) initiated by lithium naphthalenide in THF. The living triblock copolymer chains were cyclized by reaction with dichlorodimethylsilane under high dilution (Scheme 12, B). The <G> parameter was in the 0.69 to 0.87 range, while the

molecular weight was changed from $80x10^3$ to$2.8x10^3$.[55-57]

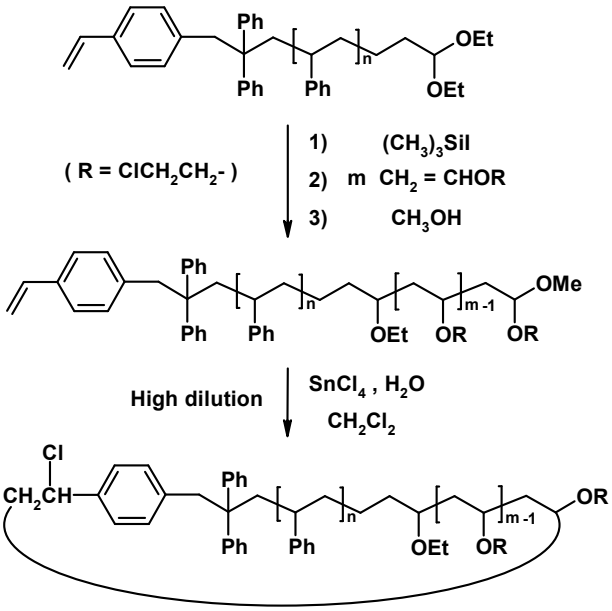
In another example, cyclic polystyrene-b-poly(2-vinylpyridine) block copolymers (50 mol% styrene) were prepared from living Li^+P2VP-b-PS-b-P2VPLi^+ chains initiated by difunctional living polystyryllithium in THF -78°C. The chains were closed by addition of 1,4-bis(bromomenthyl)benzene at -78°C (Scheme 12, C). A characteristic feature of this procedure has to be found in the conversion of the highly reactive polystyryl anion into a much less reactive picolyl anion, which is, however, reactive enough towards the coupling agent. The <G> parameter decreased (from 0.72 to 0.68) with increasing molecular weight (from $6x10^3$ to $6x10^4$).[55, 58]



Scheme 13. Synthesis of cyclic diblock copolymers

A route to cyclic polystyrene-b-poly(isoprene) copolymer with different compositions ($F_{styrene}$ = 0.55 and 0.74) was reported by Deffieux et al., based on the intramolecular coupling of an asymmetric telechelic copolymer, i.e. α-isopropylidene-1,1-dihydroxymethyl -ω-diethylacetal polystyrene-b-poly(isoprene), under high dilution (Scheme 13, A).[59] Ishizu et

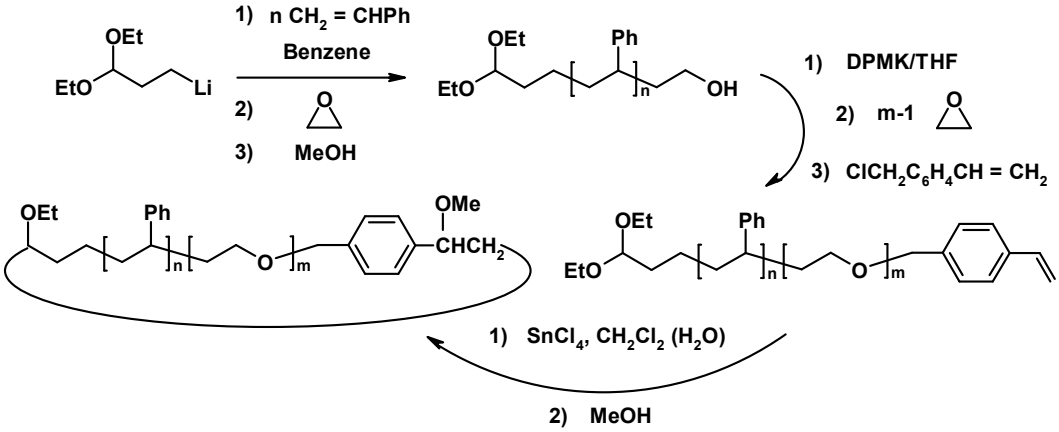
al. prepared the same cyclic diblock copolymer by interfacial condensation.[60] First, an α,ω-dibromopropyl poly(isoprene)-b-polystyrene-b-poly(isoprene) precursor was prepared by end-capping the living dianionic triblock copolymer chains by a large excess of 1,3-dibromopropane. The end-to-end ring closure of the α,ω-difunctional precursor was performed by interfacial condensation, thus at the interface of an aqueous solution of (1,6-diaminohexane) and the organic solution of the diblock copolymer (Scheme 13, B). This strategy proved efficiency with a yield of 83 % for the ring closure.



Scheme 14. Synthesis of cyclic poly(styrene)-b-poly(chloroethyl vinyl ether) copolymer

Cyclic polystyrene-b-poly(vinyl ether) copolymers ($F_{styrene}$ = 0.5; M_n = 4.4x10^3 and 6.4x10^3) were prepared according to Scheme 14. α-Diethylacetal,ω-styrenyl polystyrene was first prepared (scheme 5) and used as a macroinitiator of the chloroethyl vinyl ether polymerization, so leading to an asymmetric telechelic diblock copolymer. Activated by $SnCl_4$ in the presence of traces of water, the α-acetal end-group immediately reacted with the

ω-styrenyl unsatuation under high dilution with formation of cyclic diblock copolymer.[61]



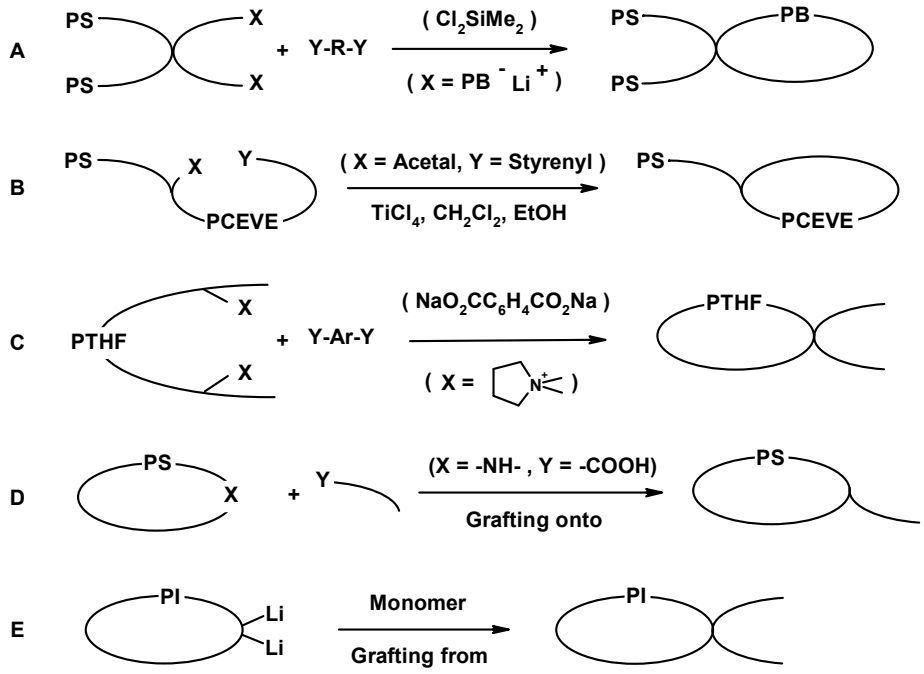
Scheme 15. Synthesis of amphiphilic cyclic diblock copolymer

Synthesis of amphiphilic cyclic polystyrene-b-poly(ethylene oxide) copolymer (M_n: from $1.4x10^3$ to $9.7x10^3$; $F_{styrene}$: from 0.4 to 0.7) was also based on the intramolecular acetal/styrenyl addition (Scheme 15). The α-diethyl acetal-ω-styrenyl polystyrene-b-poly(ethylene oxide) precursor was prepared in two steps.[62] First, α-diethyl acetal polystyryllithium was synthesized by living anionic polymerization of styrene initiated by 3-lithiopropionaldehyde diethyl acetal in benzene, followed by the monoaddition of ethylene oxide to give α-diethyl acetal-ω-hydroxyethyl polystyrene. In the second step, the ω-hydroxyethyl end-group was metallated by diphenyl methyl potassium (DPMK), so making a macroinitiator of the ethylene oxide polymerization available. Ethylene oxide was accordingly polymerized in THF and the propagating polyether block was terminated by *p*-chloromethylstyrene or *p*-iodomethylstyrene (slight excess with respect to the K alkoxide end-group). Finally, cyclization was carried out in methylene dichloride containing traces of water or ethanol and $SnCl_4$. The yield was higher than 90%.[62] No fractionation was needed.

2.3 Tadpole-shaped polymers

At the time being, only a limited effort has been devoted to the synthesis of tadpole-shaped polymers, thus macrocycles substituted by either one[63- 66] or two side chains.[53, 65, 67-68] Most of them were synthesized by cyclization of a linear precursor, according to the aforementioned strategies. A first example relies on the direct cyclization of a duly substituted linear precursor, e.g., a four-arm A_2B_2 star-shaped polymer, whose the arms A are end-capped by a group X reactive towards a difunctional coupling agent (Y-R-Y) (Scheme 16, route A). In a synthesis reported by J. Ma, A was polybutadiene and B polystyrene.[53] A one-tail tadpole-shaped copolymer was also prepared by cyclization of a linear precursor end-capped by a reactive group Y and a mutually reactive group X along the chain (scheme 16, route B). This strategy was implemented by A. Deffieux et al., who synthesized macrocyclic poly(chloroethyl vinyl ether) substituted by one polystyrene tail from linear poly(chloroethyl vinyl ether)-b-polystyrene copolymer.[63] Whenever two reactive groups X are located along a preformed polymer (Scheme 16, route C), a two-tail tadpole-shaped copolymer is formed by coupling with a difunctional compound Y-R-Y. For example, Y. Tezuka et al. prepared a two-arm tadpole-shaped poly(THF) by the previously discussed strategy based on precyclization by electrostatic interactions followed by covalent fixation.[65-66, 69-70] In a less direct two-step strategy, a macrocycle containing a functional group X in the backbone was preformed, followed by the reaction of X with a linear chain end-capped by a complementary functional group Y (Scheme 16, route D). Itoh et al. reported the synthesis of tadpole-shaped polystyrene by grafting a carboxyl end-capped polystyrene onto cyclic polystyrene containing

secondary amine group.[64] This "grafting onto" technique can however be replaced by the "grafting from" technique. P. Hemery et al. synthesized two-arm tadpole-shaped poly(isoprene)[67] by anionic polymerization of isoprene initiated by a dianionic macrocycle, that was prepared by cyclization of dianionic poly(isoprenyl Li) by 1,2-bis(isopropenyl-4-phenyl)ethane (Scheme 16, route E). The same strategy was extended to styrene.[68] Nevertheless, all these strategies require the cyclization of linear precursors under high dilution in order to prevent polycondensation from competing cyclization.



Scheme 16. Synthesis of tadpole-shaped (co)polymers

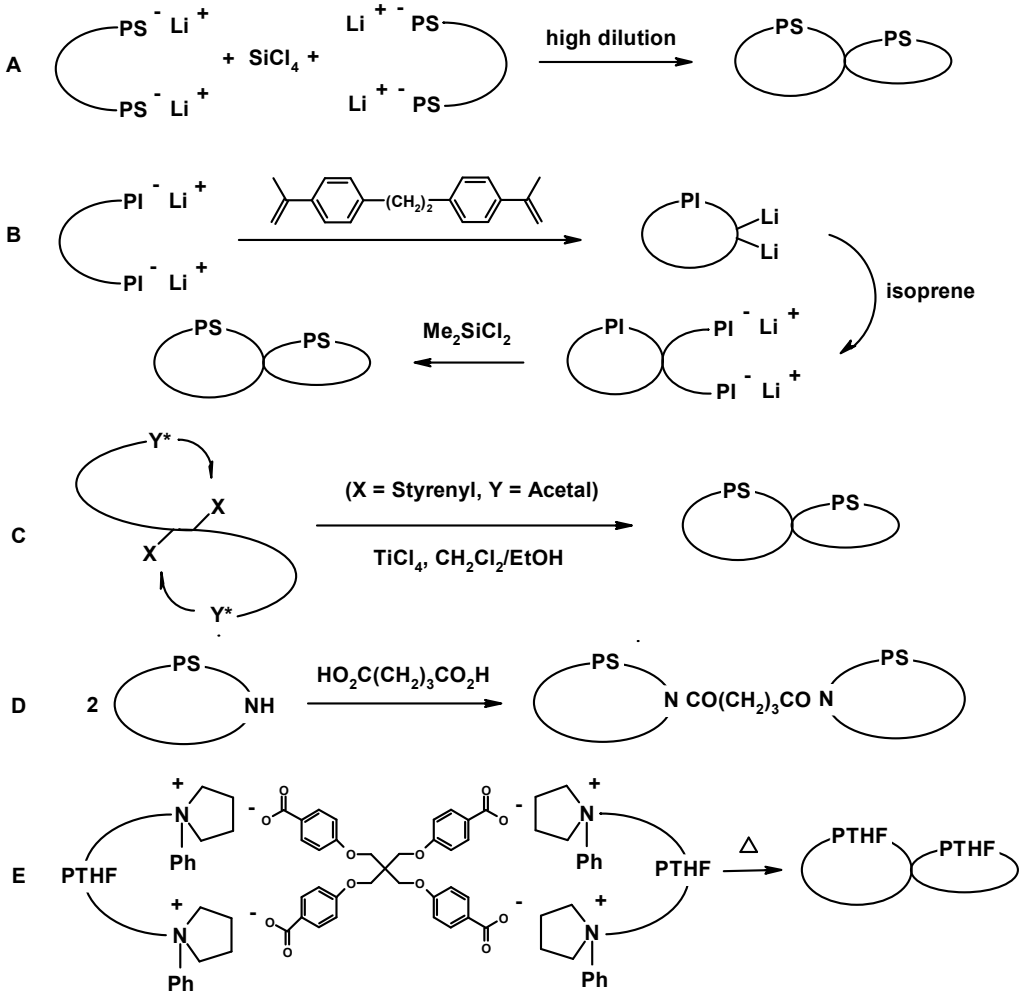
2.4 Pluricyclic polymers

Synthesis of macrocyclic polymers with a complex architecture, e.g., sun-shaped, eight-shaped, θ-shaped and multi-cyclic chain structures, and well-defined molecular

parameters is a very challenging although stimulating task for the polymer chemists.

The first example of synthesis of an eight-shaped polystyrene was based on the coupling of living dianionic polystyrene chains by a tetrafunctional reagent ($SiCl_4$) under high dilution (Scheme 17, A).[71] Although the yield of bicyclic polystyrene was low and the molar mass distribution was multimodal, this pioneering work stimulated further investigation. Indeed, the same route was extended to polyisoprene, and eight-shaped polyisoprene was prepared within a 60% yield.[25] Cyclic polyisoprene also prepared by a three-step strategy illustrated in Scheme 17, B. Dianionic poly(isoprenyl Li) was first cyclized by a stoichiometric amount of 1,2-bis(isopropenyl-4-phenyl) ethane. A dianionic cyclic poly(isoprenyl Li) was accordingly formed and used as a difunctional macroinitiator of the isoprene polymerization with formation of a tadpole-shaped dianionic poly(isoprenyl Li), that was cyclized by reaction with $(CH_3)_2SiCl_2$.[67] The yield in eight-shaped polyisoprene was estimated at 70%. Eight-shaped poly(chloroethyl vinyl ether) (PCEVE) was synthesized from a tetrafunctional linear precursor, i.e., α,α'-distyrenyl-ω,ω'-diacetal-poly(CEVE), that was intramolecularly cyclized under high dilution, in the presence of a Lewis acid and traces of ethanol (Scheme 17, C).[72] The yield in bicyclic PCEVE was higher than 90%, consistent with a highly efficient control of the ring-closure process. In an alternative approach, cyclic polystyrene that contained a secondary amine in the backbone was converted into bicyclic polystyrene by coupling with gluteric acid (Scheme 17, D).[64] Tezuka et al. prepared eight-shaped poly(THF) according to the strategy of pre-cyclization by electrostatic interactions they reported previously. In this case, the self-assembly of linear poly(THF) capped at both ends by an ammonium was triggered by a tetra-carboxylate couteranion under high dilution. Finally, the eight-shaped

architecture was covalently stabilized upon heating (Scheme 17, E).[73-75]

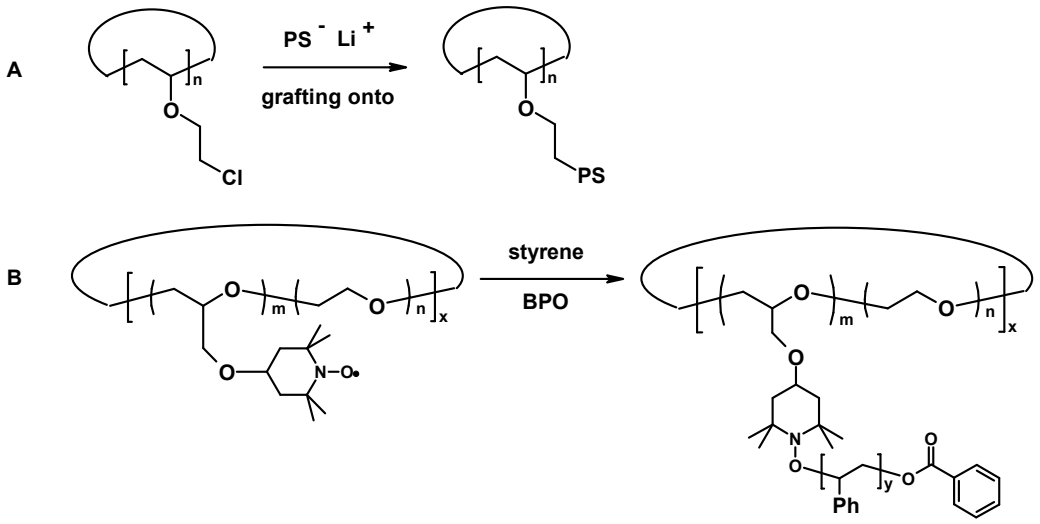


Scheme 17. Synthesis of eight-shaped polymers

Macrotricyclic poly(chloroethyl vinyl ether) of controlled molecular weight and molar mass distribution was synthesized by combining living cationic polymerization and the end-to-end ring closure technique.[76]

At the time being, only two examples of synthesis of sun-shaped macrocycles have been reported. Deffieux et al. grafted living polystyryllithium onto pendant chloroethyl groups of cyclic poly(chloroethyl vinyl ether) (Scheme 18, A).[77] Very recently, an amphiphic sun-shaped copolymer was synthesized by combination of anionic ring-opening

polymerization and nitroxide-mediated radical polymerization. A hydrophilic α,ω-hydroxy-poly(ethylene oxide) with pendant TEMPO groups was prepared by random copolymerization of 4-glycidyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl (GTEMPO) and ethylene oxide. Cyclization of the linear precursor was carried out by end-to-end coupling with CH_2Cl_2 under alkaline conditions and high dilution (< 10^{-5}). The nitroxide mediated polymerization of styrene ("grafting from" technique) was initiated in the presence of benzoyl peroxide, with formation of PS-g-cyclic PEO (Scheme 18, B).[78]



Scheme 18. Synthesis of sun-shaped copolymers

4. Conclusion

This review aimed at highlighting the recent development of progress in the synthetic methods of cyclic polymers, including cyclization of linear precursors capped at both ends by the same functional group or not, by intramolecular chain transfer or intramolecular chain termination. The major problem to be faced, is the competition between intramolecular

cyclization and intermolecular chain extension. For intramolecular cyclization to be predominant, very high dilution is required and the length of the linear precursors must be small enough. Combination of high cyclization yield and mild experimental conditions was reported in few examples in which polymerization and cyclization were carried out without intermediate formation of linear species. These examples are rather "a case in itself" than a general concept extendable to a large variety of cyclic polymer. Therefore, the quest for a general and effective concept of cyclization of high molecular chains under non very demanding conditions remains highly desirable and challenging.

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