Control of Macromolecular Architectures by Various Polymerization Methods: Advantages and Drawbacks

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SUMMARY: The present work compares the efficiency of various polymerization methods in macromolecular engineering and discusses advantages and drawbacks of different approaches. Anionic polymerization remains the method of choice to synthesize cyclic polymers, functional polymers including macromonomers or functional star-shaped polymers. The controlled radical polymerization is an interesting alternative to anionic polymerization for the controlled homopolymerization of macromonomers yielding well-defined branched species. By combining classic radical polymerization with a heterogeneous reaction, networks were synthesized by homopolymerization of bifunctional poly(ethylene oxide) macromonomers. The resulting hydrogels, obtained directly in water, are new materials for biomedical applications.

Introduction

There has been increasing interest over the years in well-defined macromolecules of various architectures: linear polymers, linear functional polymers, block copolymers, branched polymers, graft copolymers, cyclic polymers and networks with elastic chains of known length$^{1)}$. These species are not only of interest for chemists as macromolecular objects, they are also well suited as models for investigation of relation between molecular structure and properties, in solution as well as in the bulk. Some early attempts to obtain some of these structures by radical polymerization$^{2)}$ have to be mentioned first, but the decisive step in the preparation of these controlled macromolecular structures was the discovery of living anionic polymerization by M. Szwarc$^{3)}$. The purpose of the present work is to compare the performance of anionic polymerization with radical polymerization or with controlled radical polymerization. After a short introduction on basic principles of different polymerization methods, selected examples of recent developments in the field of macromolecular engineering will be discussed. The case of cyclic polymers will be examined first. Various functionalization reactions based on anionic polymerization will be discussed in the next step. The preparation of star-shaped polymers also refers to living polymerization, especially for the synthesis of functional water-soluble star-shaped polymers based on poly(ethylene oxide).

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Two examples of new polyfunctional anionic initiators for the anionic polymerization of oxirane will be given. The case of homopolymerization of monofunctional macromonomers is more complex and the advantages and drawbacks of various polymerization methods to design poly(macromonomer)s will be discussed in detail. Finally, the polymerization of bifunctional macromonomers will be presented with the aim of determining the parameters allowing control of structural parameters of the resulting networks even when radical polymerization is applied.

Comparison of Different Polymerization Methods

Anionic polymerization carried out under proper conditions in aprotic solvents with efficient organometallic initiators was considered until recently the most powerful way to design a large scope of macromolecular architectures[4)]. This reaction involves only two steps: initiation and propagation. No spontaneous transfer or termination should occur. The number of active sites is constant and equal to the number of active sites introduced. In addition, the provided initiation is rapid with respect to propagation, the number-average degree of polymerization being given by the ratio of the monomer converted to the initiator concentration, and the molecular weight distribution is sharp. The growing sites remain living thus enabling further reactions such as functionalization, initiation of the polymerization of a second generation of monomers, and coupling. The polymerization is first-order in monomer concentration and the molecular weight varies linearly with the conversion.

Anionic polymerization is only applicable to a restricted number of monomers. This constitutes a major drawback for an extensive use of that polymerization process. In addition, the reaction cannot be conducted in water although polymerization and reactions in water are of increasing interest.

On the contrary, **radical polymerization** can be used for a much larger number of monomers, the presence of solvent is not always necessary, continuous processes can be envisaged and polymers free of initiator result. This polymerization process has yet strong limitations for macromolecular engineering: molecular weights cannot be chosen at will, the molecular weight distribution is broad and block copolymer synthesis and quantitative functionalization are almost impossible.

The **controlled living radical polymerization process,** recently developed[5)] may become an interesting alternative to design polymers of controlled structure. The underlying idea is to end-cap the macroradical during polymerization. The reversible formation of a σ bond between the growing species and a stable radical can be considered a special case of chemical stabilization, preventing termination and/or transfer side-reactions by maintaining a low instantaneous concentration of radicals in the medium.

Cyclic Polymers

Cyclic macromolecules have been subject of interest for more than four decades. Until the eighties, well-defined cyclic species were not available, most of the work on cyclic polymers being devoted to theoretical aspects concerning the influence of cyclization on solution or solid-state properties. Early attempts to obtain a cyclic structure based on the ring-chain equilibrium have to be mentioned first: the end-standing functions of a polycondensate react under appropriate conditions with any functional link of the polymer chain (Fig. 1a). The development of efficient fractionation methods has thus permitted the separation of the cyclic species from the linear one and, in addition, the fractionation of the cycles according to molecular weights.

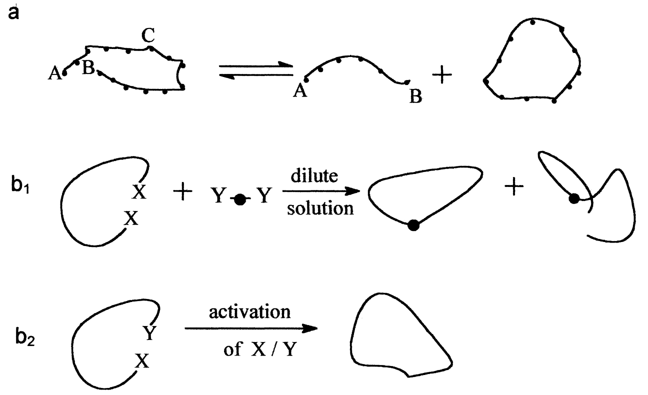

Fig.1: Access to cyclic polymers: (a) backbiting, (b) end-to-end cyclization by anionic polymerization via bimolecular (b_1) or unimolecular (b_2) processes.

Well-defined cyclic poly(dimethylsiloxane)s$^{6)}$ could be obtained in such a way. They have been used to check theoretical predictions concerning solution and solid-state properties of cyclic polymers.

During the past twenty years, it has been shown that anionic polymerization is the method of choice to prepare well-defined cyclic structures of various molecular weights in good yields, characterized by narrow molecular weight distributions$^{7)}$. In addition, their linear equivalents are accessible in the same synthesis. The preparation of cyclic polymers by anionic polymerization is based on the reaction of α,ω-carbanionic polymers with a bifunctional low-molecular-weight deactivating agent, a process where the intramolecular reaction competes with the intermolecular reaction (Fig. 1b$_1$). To favor cyclization, as calculated theoretically by Stockmayer(8), the reaction has to be conducted at a concentration far below the concentration at which cyclization and chain extension occur with the same probability. Combined with appropriate separation procedures, anionic polymerization has had a major impact on the preparation of well-defined homopolymeric or copolymeric cyclic structures(7) of various chemical nature, soluble in organic solvents or in water or potential polyelectrolytes. End-to-end cyclization based on a bimolecular process was developed first. Even when conducted at high dilution, the formation of a chain-extension product besides the cyclic polymer could not be avoided. Using heterofunctional polymers followed by activation of the terminal functional groups, Deffieux(9) succeeded in the preparation of cyclic polymers almost free of chain-extension products (Fig. 1b$_2$).

Functional Polymers Including Macromonomers

Polymers obtained by anionic polymerization are fitted at the chain end with active functions, the carbanions, which can be used in a next step for functionalization reactions. If no deactivation and no side reaction occur, and provided appropriate electrophilic deactivators are used, various functions can be introduced quantitatively. These end-capping reactions have given access to polymers fitted with the hydroxy functions, carboxylic acid functions, etc. Various examples have been described in the literature(10). In addition, the presence of the functions provides opportunities for further reactions such as coupling. The present work discusses in particular the application of anionic polymerization to the preparation of macromonomers. These species will be extensively used for the elaboration of well-defined branched or crosslinked materials. In addition, PEO macromonomers have been shown to be valuable intermediates for the synthesis of a new class of amphiphiles based on silsesquioxane(11)

"Macromolecular" monomers, macromonomers, are defined as polymers, usually of rather low molecular weights, carrying a polymerizable group (double bond, heterocycle) at one or two chain ends(12). Their preparation basically refers to ionic polymerization processes(13) whereby quantitatively functionalized species with narrow molecular weight distributions result. Other attempts based on group transfer polymerization(14) or even radical polymerization processes(15) have to be mentioned with a yet limited efficiency in the latter case. The macromonomers have gained increasing interest over the years as they provide an easy access to graft copolymers by radical copolymerization of the macromonomer with vinyl or acrylic monomers.

Branched Polymers

Branched polymers have been subjects of interest as they exhibit strong differences in properties, in solution as well as in the bulk, compared with their linear equivalents. They allow testing existing theories without changing the basic nature of the polymer chain. The presence of branched structures in polymers obtained by radical polymerization is well established. Their structures are yet complex and their branch length, their functionality or type of branching cannot be predetermined. Anionic polymerization has been shown to be much more powerful to control not only the branch (or arm) length but also the functionality and its distribution. Two cases will be considered: branched polymers based on macromonomers and star-shaped polymers.

Comb polymers derived from macromonomers

Homopolymerization of macromonomers should leads to branched species: comb polymers where each macromonomer unit incorporated constitutes a graft of controlled length. The efficiency of various polymerization methods in producing good yields of well-defined poly(macromonomer)s will be examined.

In radical homopolymerization, characterized by short lifetimes of the active sites, the growing macroradicals have been shown to be reactive enough to induce polymerization. They are yet inherently unstable and susceptible to a number of side reactions, either by termination or transfer reactions. These lead to irreversible termination of the growing species. In addition, their diffusion is slowed down by the high viscosity of the reaction medium. Consequently, branched polymers with broad or even multimodal molecular weight distributions resulted. The homopolymerization yields are not quantitative. Radical homopolymerization of vinyl or acrylic macromonomers is also far beyond the reach of precise chain-growth control. It has yet to be pointed out that in recent years, decisive progress has been made in the domain of radical homopolymerization of various macromonomers16).

The intrinsic characteristics of anionic polymerization methods, in particular the long lifetime of active sites and the absence of transfer reactions provide the best chance for precise control of the different structural parameters just mentioned. Polystyrene macromonomers were subjected to anionic polymerization. Their polymers were obtained in almost quantitative yields and with narrow molecular weight distributions; the homopolymerization degrees (DP) could be controlled in advance[17]. However, the presence of impurities in the macromonomer restricts the applicability of anionic polymerization to rather low DP values.

The "living" controlled radical polymerization process may provide a good alternative for preparation of well-defined poly(macromonomer)s from vinyl macromonomers. Two initiating systems have been compared: 1-(benzoyloxy)-2-phenyl-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)ethane (BPTPE) or a classic initiator, 2,2′-azobis(isobutyronitrile) (AIBN) or dibenzoyl peroxide (BPO), and a stable counter-radical, 1,3,5,5-tetraphenyl-2,5-dihydro-1*H*-1,2,4-triazol-2-yl radical. The kinetics of such homopolymerizations was examined and the almost living character of these reactions could be estabished[18]

Star Polymers

Star polymers are branched species where all the chains of one molecule are linked to a centre, which is called the core. The interest in star polymers arose due to their compactness and enhanced segment density as compared with those of their linear counterparts of the same molecular weight. Again, the synthesis of these species is essentially based on anionic polymerization methods because they allow a good control of structural parameters[19]. Some attempts by cationic polymerization[20] or group transfer polymerization should be mentioned[21]. Recently, the controlled living radical polymerization has been successfully used to obtain well-defined star polymers of controlled arm length and functionality, based on various monomers[22].

There are various ways to obtain star polymers by anionic polymerization. They have been reviewed recently[19] and will be briefly presented here. Either living arms are synthesized first and reacted with appropriate low-molecular-weight compounds to generate the core ("arm-first" methods) or a living core fitted with organometallic sites is used to grow up the arms from the core ("core-first" methods). These approaches have been combined to develop the so-called "in-out" method.

Besides hetero-arm or mikto-arm star polymers[19], major progress in the synthesis of star polymers is based on the development of "core-first" strategies giving access to star species with functionalizable end groups at the outer end of the branches. These functionalizable star polymers, based on poly(divinylbenzene) (DVB) cores, have opened new perspectives in the field of macromolecular engineering.

Much effort has been devoted to further improve these methods to reach a better control of functionality, especially in the field of water-soluble star polymers based on poly(ethylene oxide). The first approach derives directly from the DVB method. A linear poly(1,3-

diisopropenylbenzene) backbone is prepared first by anionic polymerization under conditions leading to soluble polymers having one unsaturation per monomer unit in the chain. These unsaturations are used in a subsequent step after modification for building the living cores. These cores served to grow the PEO branches. A far better control of the functionality resulted in that case[23].

We have also used, after appropriate modification, well defined polyglycidol cores exhibiting up to 58 hydroxy functions as multifunctional initiators for the synthesis of well-defined PEO star polymers[24]. A rapid exchange between alkoxides and hydroxy groups and the addition of a complexing agent ensures fast propagation at all chain ends. Characterization of the materials was carried out by SEC, MALDI-TOF-MS, ^{1}H and ^{13}C NMR. We obtained high-functional PEO multiarm star polymers with molecular weights around 35 000 or higher and rather narrow polydispersities (M_w/M_a around 1.5).

Network Synthesis

Anionic polymerization has extensively contributed to the synthesis of polystyrene or poly(ethylene oxide) model networks, the structure of which is defined rather precisely. These networks are obtained either by anionic block copolymerization of styrene and divinylbenzene or by reacting a PEO precursor chain (resulting or not from anionic polymerization of oxirane) with a stoichiometric amount of a pluriisocyanate to introduce the crosslinks[25]. They exhibit a satisfactory homogeneity and contain only a few structure defects such as pendant chains and double-connected loops. The elastic chains are of known length. Their structure parameters can be controlled by several experimental parameters such as molecular weight of the polymer precursor and polymer concentration. The synthesis of these networks implied the use of organic solvents even for preparation of hydrogels consisting of water-soluble PEO chains. To overcome that problem, we have developed a new way of preparing hydrogels[26] based on the polymerization of bifunctional PEO macromonomers (Fig. 2).

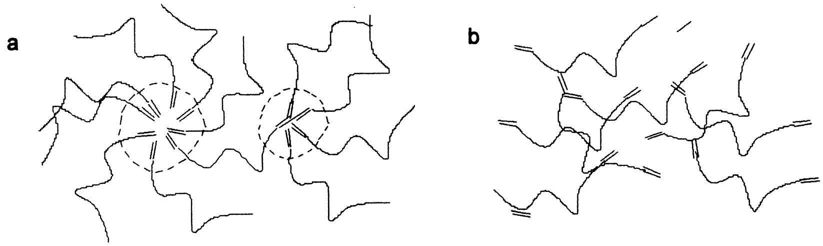

Fig. 2: Homopolymerization of bifunctional PEO macromonomers (a) in water ($K_2S_2O_8$, 24 °C and (b) in organic solvents (benzene, AIBN, 65 °C).

The swelling behavior of these PEO networks and their mechanical response to uniaxial compression were investigated confirming better properties of networks synthesized in water. The method was extended to amphiphilic networks[27)] and to degradable networks[28)]. These PEO hydrogels, well known for their outstanding biocompatible properties, were used as semipermeable membranes for an artificial pancreas[26)]. Growth of central nervous cells on the surface of such PEO hydrogels was possible[29)]. They have now been implanted in rat brain lesions in order to test *in vivo* their neuron regeneration capacities.

Conclusion

In the present work, we have examined the performance of various polymerization methods to design well-defined structures. For cyclic polymers or functional water-soluble star polymers, anionic polymerization remains the method of choice, efficient polyfunctional anionic initiators being now accessible. For other monomers or other structures, the controlled living radical polymerization, less sensitive to impurities, provides an original and efficient approach.

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