A Practical Approach to the Living Polymerization of Functionalized Monomers: Application to Block Copolymers and 3-Dimensional Macromolecular Architectures

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SUMMARY: The tolerance of living free radical procedures to reactive functional groups, coupled with their ability to prepare well-defined random and block copolymers is demonstrated by the use of novel α-hydrogen alkoxyamine derivatives instead of the traditional TEMPO-based systems. This refinement in the nitroxide structure overcomes many limitations typically associated with TEMPO and has permitted a dramatic increase in the range of monomers, which can be polymerized under controlled conditions. The ability to prepare well-defined multi-arm star polymers from a variety of alkoxyamine terminated vinyl and non-vinyl linear polymers are major benefits when compared to traditional living procedures, such as anionic polymerizations.

Introduction

The desire to prepare advanced materials with new and/or improved properties is a continuing focus in many academic and industrial laboratories. The driving force is the belief that these materials will offer substantial benefits in areas ranging from microelectronic fabrication, to catalyst design, to biotechnology. In the macromolecular arena, a common feature of many of these new materials is their well defined nature with the number of functional groups, molecular weight, polydispersity, and the presence or absence of branching being precisely controlled1). Traditionally, such well-defined macromolecules were only available from living procedures, such as anionic polymerization, which are synthetically challenging and not amenable to significant changes in the structure of the macromolecule, or the presence of functional groups.

To address these difficulties, the field of 'living' free radical polymerization2) has expanded rapidly in recent years with major advances occurring in both nitroxide mediated processes3),

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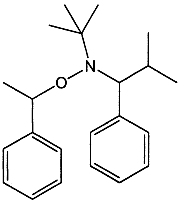
as well as atom transfer radical procedures (ATRP)[4], and more recently radical addition fragmentation transfer (RAFT) strategies[5].

Results and Discussion

We have explored a range of different nitroxides and their associated alkoxyamines in an effort to develop a universal system suitable for the controlled polymerization of vinyl monomers[6,7]. The family of nitroxides, which proved to be the most successful, were the α-hydrido derivatives such as **1** and **2**.



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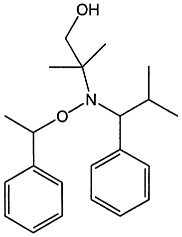

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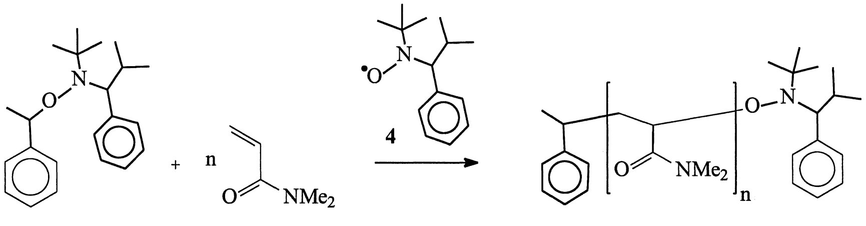
To investigate the synthetic versatility of **1** and **2**, the polymerization of commercially important monomer families such as acrylamides or 1,3–dienes was performed under standard conditions. In the case of the acrylamide derivatives, extremely fast, uncontrolled polymerization was observed for the reaction of **1** and 200 equivalents of N,N-dimethylacrylamide at 120 °C. This result is similar to that observed for acrylate derivatives[6] and, in analogy with the acrylate case, 0.05 equivalents of free nitroxide was added to the reaction mixture in an effort to control the polymerization. This strategy proved to be successful and a variety of functionalized acrylamide derivatives, such as N-isopropylacrylamide (NIPAM) could be homo and copolymerized with accurate control accurate control of molecular weights and polydipersities as low as 1.06 (Scheme 1).



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Scheme 1

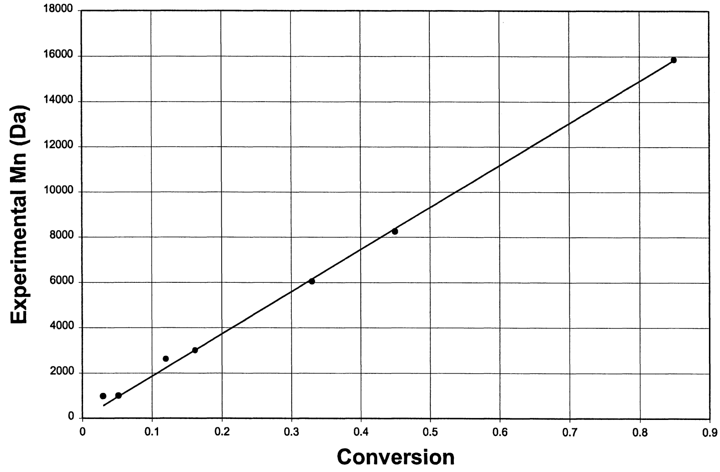
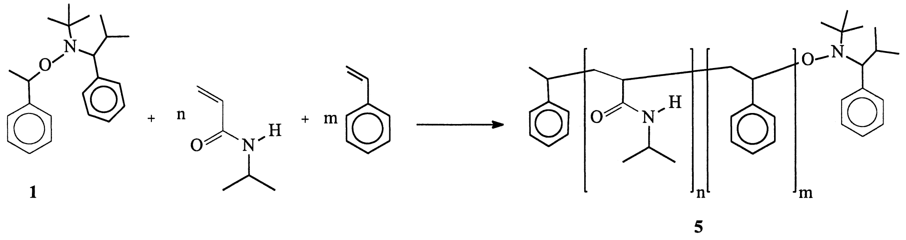


Fig. 1: Dependence of molecular weight, M_n, SEC, on monomer conversion for the polymerization of DMA with alkoxyamine **1** and 0.05 equivalents of the corresponding nitroxide, **4**, at 120°C.

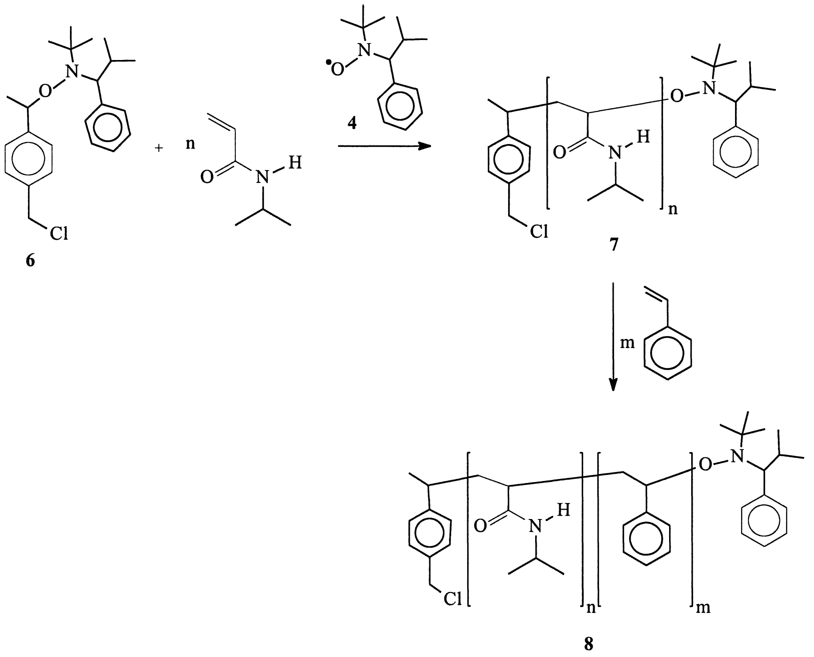
Figure 1 shows a kinetic study for the homopolymerisation of *N,N*-dimethylacrylamide in the presence of **1** and 5mol% of the corresponding nitroxide. Significantly, the linear relationship between both, ln([Mo]/[M]) vs. time, and molecular weight vs. conversion further demonstrates the living nature of the polymerization and suggests that the preparation of functionalized acrylamide block copolymers by this new procedure should be a facile reaction. It should also be noted that attempts to control the polymerization of acrylamides derivatives by TEMPO or ATRP procedures is problematic due to interaction of the acrylamide units with the mediating metal complex in the latter case$^{8)}$.

Significantly, block and random copolymers based on combinations of functionalized acrylamides with a variety of vinyl monomers, such as styrene, acrylate, or methacrylate derivatives and non-vinyl polymers, such as poly(ethylene glycol) could be synthesized with similar control. For styrene, well-defined random copolymers, **5**, could be prepared over the whole comonomer range from 95% NIPAM to 5% NIPAM with no change in molecular weight control and polydispersity (PD.= 1.1 – 1.2) (Scheme 2).



Scheme 2

The synthesis of block copolymers was equally facile and is best demonstrated by the synthesis of analogous NIPAM based block copolymers, though it should be noted that the acrylamide block should be polymerized first, followed by the styrenic block. For example, the chloromethyl substituted alkoxyamine, **6**, was used to initiate the polymerization of NIPAM to give the starting block, **7** (M_n = 9 100, PD. = 1.07), containing a dormant alkoxyamine chain end which could be purified and characterized before growth of the second block. Dissolution of **7** in styrene and DMF followed by heating to 120 °C for 6 hours then gave the desired diblock copolymer, **8**, with accurate control over molecular weight and polydispersity (Scheme 3). The essentially quantitative formation of the block copolymer, **8**, was determined by a combination of GPC, NMR and MALDI-TOF spectroscopy.



Scheme 3

Significantly, block copolymers such as **8** represent an interesting class of materials in which the 2^{nd} block can ensures water or organic solubility, while the LCST behavior of the PNIPAM block can be used to switch the polarity of the second block from water-soluble to water insoluble. This thermally responsive switch can be used for a number of advanced applications, such as drug delivery, thermal sensors, etc.

Highly Branched Polymers

To investigate the influence of functionality and architecture on the use of polymeric materials in nanoscale applications we have recently developed a versatile, one-step approach to highly branched star polymers based on nitroxide mediated living free radical procedures. The key to initial development of this chemistry was the preferential and controlled polymerization of maleic anhydride derivatives in the presence of **1**[9)]. In exploiting this last feature it should be noted that random copolymers prepared from monomers with different reactivity ratios by either traditional or living free radical procedures, while similar on a macroscopic level (i.e. comparable tacticity and triad ratios) may be significantly different on a molecular level. For traditional free radical systems, there will be a distribution of chain structures, with chains initiated at low conversion having a different monomer composition than those initiated later in the process. In direct contrast, all chains prepared by living free radical procedures should be approximately the same with each chain growing at the same rate and experiencing the same change in monomer feed ratios. Therefore, if a living free radical system can be developed for monomer combinations with dramatically different reactivity ratios, such as maleic anhydride and styrene, the alternating nature of this copolymerization may be exploited and a new one-step strategy for novel functionalized block copolymers developed or hyper-star architectures with a densely crosslinked core.

To demonstrate a novel approach to functionalized block copolymers the living free radical polymerization of a 9:1 mixture of styrene and maleic anhydride was studied at 120 °C in the presence of the recently reported α-hydrido based alkoxyamine, **1**. It was found that a small excess (5 mole%) of free nitroxide, **4**, necessary to control the rate of polymerization to give well defined materials. Examining the monomer conversion as a function of time by ^{1}H NMR spectroscopy provided insight into the compositional nature of the chains. As can be seen in Figure 2, the polymerization is initially fast with preferential consumption of maleic anhydride. After 1.5 hours, no detectable amounts of maleic anhydride could be observed in the reaction mixture, while the conversion of styrene was ca 25-30%.

At this point, the monomer feed is pure styrene and so further polymerization involves growth of a pure polystyrene block leading to a block copolymer. Application of similar chemistry to the copolymerization of styrene and a bis(maleimide) derivative also results in preferential reaction of the bis(maleimide), which undergoes crosslinking to give a soluble, highly branched initiating nodule from which linear arms can then grow. Under specific conditions this chemistry has been shown to be extremely versatile resulting in the one-step synthesis of

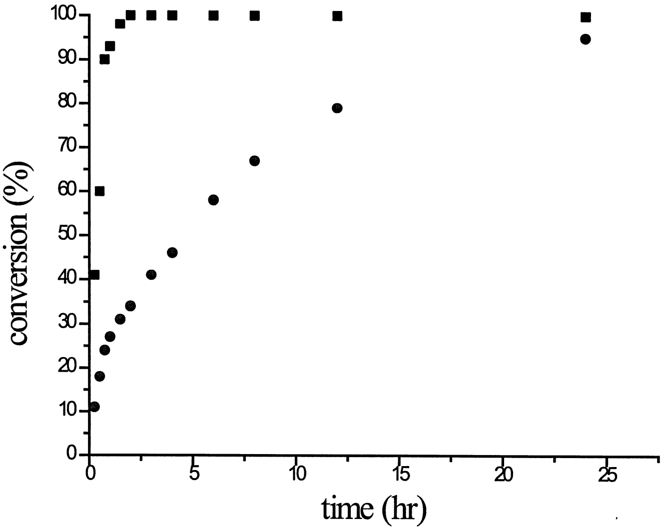
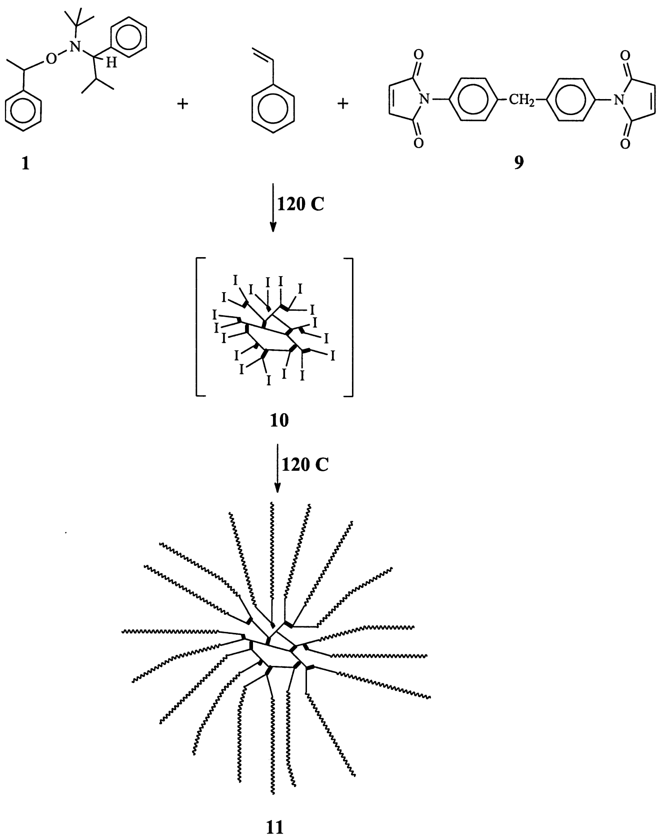


Fig. 2: Monomer conversion with time for the 9:1 copolymerization of styrene (●) and maleic anhydride (■) at 120 °C under argon.

highly branched star polymers from a wide range of functionalized monomers. For example, reaction of **1** with a 99:1 mixture of styrene and the bis(maleimide), **9**, at 120 °C for 8 hours gives a highly branched polystyrene derivative, **11** (Mn = 1 250 000; PD. = 2.10) (Scheme 4). Examination of the rate of conversion of each monomer with time showed that the bis(maleimide), 9, was rapidly consumed within the first 30 minutes of reaction. At this stage the styrene had reached only ca. 5-10% conversion which is not only in agreement with the earlier maleic anhydride polymerizations but suggests that a highly branched polymer, **10**, is initially formed which has numerous alkoxyamine initiating groups at the chain ends. Since all of the bis(maleimide), **9**, has been consumed these initiating centers then lead to the growth of linear polystyrene arms to give the final highly branched structure, **11**. This reaction pathway was further confirmed by cleavage of the bis(maleimide) crosslinks to give the linear polystyrene arms which were shown to have very low polydispersities (PD. = 1.1-1.2) and molecular weights that correlate with the initial ratio of **1** and styrene.



Scheme 4

Conclusions

The recent introduction of novel α-hydrogen alkoxyamine derivatives instead of the traditional TEMPO-based systems has permitted a significant increase in the range of monomer units that can be polymerized under controlled conditions by nitroxide mediated living free radical procedures. This permits one of the main advantages of nitroxide systems, Their tolerance to reactive functional groups to be fully exploited. This feature is demonstrated by the preparation of acrylamide, maleic anhydride and isoprene based random and block copolymers, monomers that are difficult to polymerize by other techniques. The ability to prepare well-defined multi-arm star polymers from a variety of alkoxyamine terminated vinyl and non-vinyl linear polymers has also been demonstrated and offers a number of advantages when compared to traditional living procedures, such as anionic polymerizations.

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