

“Living” Free Radical Polymerization: A Unique Technique for the Preparation of Controlled Macromolecular Architectures

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Introduction

The synthesis of well-defined macromolecules with accurately controlled three-dimensional structure is becoming an increasingly important aspect of polymer science due to the continuing desire to prepare materials with new and/or improved physical properties.¹ Our interest in this area was driven by the desire to prepare nanoporous polymeric materials with ultralow dielectric constants for a variety of microelectronic applications.² A novel self-assembling strategy was employed for formation of the nanoscopic structure which ultimately leads to nanoporous materials. In this approach, an ABA block copolymer, containing a thermally stable central B block, typically a polyimide, and a thermally unstable A block undergoes nanoscopic phase separation to give spherical domains of the thermally labile A blocks in the surrounding B matrix. Decomposition of these labile domains under either thermal or combined thermal/photochemical conditions then gives the desired polymeric nanofoam which contain spherical pores of approximately 5–10 nm in diameter (Figure 1).³ The incorporation of significant amounts of air leads to a substantially lower dielectric constant for the polymeric nanofoam than for the parent polyimide or matrix polymer. From a preparative point of view, one of the crucial features of this nanofoam strategy is the structure of the thermally labile A block. For controlled self-assembly to occur, the A block must have a low-polydispersity, defined molecular weight and chain ends. If any of these criteria are not met, the structure and/or purity of the ABA triblock copolymer is compromised and self-assembly does not give spherical nanoscopic domains in a controllable manner.

Craig J. Hawker was born in Toowoomba, Australia, in 1964. He received a B.Sc. in chemistry from the University of Queensland in 1984 and a Ph.D. in bio-organic chemistry from the University of Cambridge in 1988 under the supervision of Prof. Sir Alan Battersby. Jumping into the world of polymer chemistry, he undertook a postdoctoral fellowship with Prof. Jean Fréchet at Cornell University from 1988 to 1990 and then returned to the University of Queensland as a Queen Elizabeth II Fellow from 1991 to 1993. He is currently a Research Staff Member at the IBM Almaden Research Center and is an investigator in the Center for Polymer Interfaces and Macromolecular Assemblies. His research has focused on the interface between organic and polymer chemistry with emphasis on the design, synthesis, and physical properties of unusual macromolecular structures.

When this work was initiated in 1991, the only viable techniques for preparing linear vinyl polymers with the above prerequisites (controlled molecular weight; defined chain ends; low polydispersities) were living polymerization techniques, such as anionic or cationic procedures.^{4–6} Unfortunately, none of these techniques were readily applicable to the rapid synthesis of a wide variety of functionalized vinyl polymers and copolymers for optimization of the thermally labile A blocks. This incompatibility with our requirements is due to the synthetically demanding requirements of living anionic or cationic techniques, which calls for rigorous exclusion of oxygen and water, ultrapure reagents, and solvents and the incompatibility of the growing chain ends (carbanion or carbocation) with many functional groups. To overcome these difficulties, we decided to examine the synthesis of well-defined linear polymers and other complex macromolecular architectures by “living” free radical procedures.

The concept of using stable free radicals, such as nitroxides, to reversibly react with the growing polymer radical chain end can be traced back to the pioneering work of Rizzardo and Moad.⁷ After further refinement by Georges,⁸ the basic blueprint for all subsequent work in the area of “living” free radical polymerization was developed. The key features of nitroxide-mediated “living” free radical polymerizations are that the carbon–oxygen bond of the dormant, or inactive, alkoxyamine **1** is homolytically unstable and undergoes thermal fragmentation to give a stable nitroxide **2** and the polymeric radical **3**. Significantly, the nitroxide free radical **2** does not initiate the growth of any extra polymer chains but it does react at near-diffusion-controlled rates with carbon-centered free radicals. Therefore the polymeric radical **3** can undergo chain extension with monomer to yield a similar polymeric radical (**4**) in which the degree of polymerization has increased. Recombination of **4** with the nitroxide then gives the dormant, unreactive species **5**, and the cycle of homolysis–monomer addition–recombination can be repeated (Scheme 1). Subsequently, the groups of Matyjaszewski,⁹ Sawamoto,¹⁰ and Percec¹¹ and others¹² have replaced the stable nitroxide free radical with transition metal species to obtain a

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- (2) Hedrick, J. L.; Labadie, J. W.; Russell, T.; Wakharker, V. *Polymer* **1993**, *34*, 22.
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- (8) Georges, M. K.; Veregin, R. P. N.; Kazmaier, P. M.; Hamer, G. K. *Macromolecules* **1993**, *26*, 2987.
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- (11) Percec, V.; Barboiu, B. *Macromolecules* **1995**, *28*, 7970.
- (12) Wayland, B. B.; Poszmik, G.; Mukerjee, S. L.; Fryd, M. *J. Am. Chem. Soc.* **1994**, *116*, 7943. Granel, C.; DuBois, P.; Jerome, R.; Teyssie, P. *Macromolecules* **1996**, *29*, 8576.

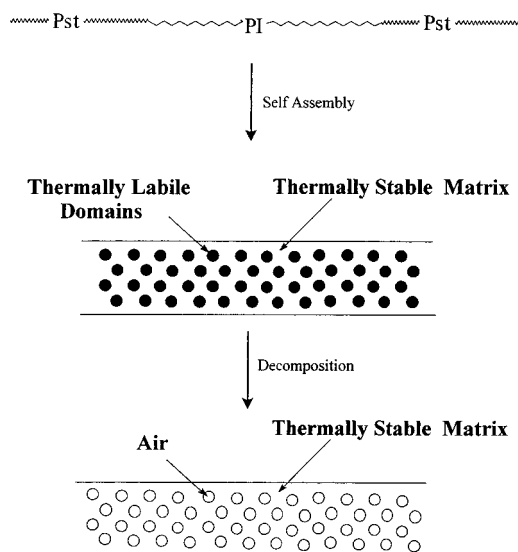
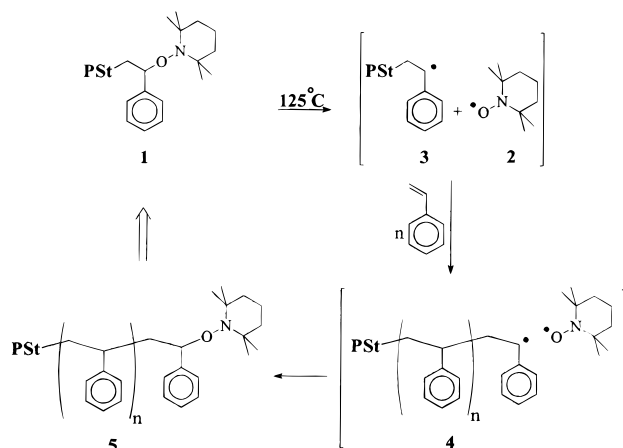


FIGURE 1. Self-assembling block copolymer approach to the generation of polymeric nanofoams.

Scheme 1



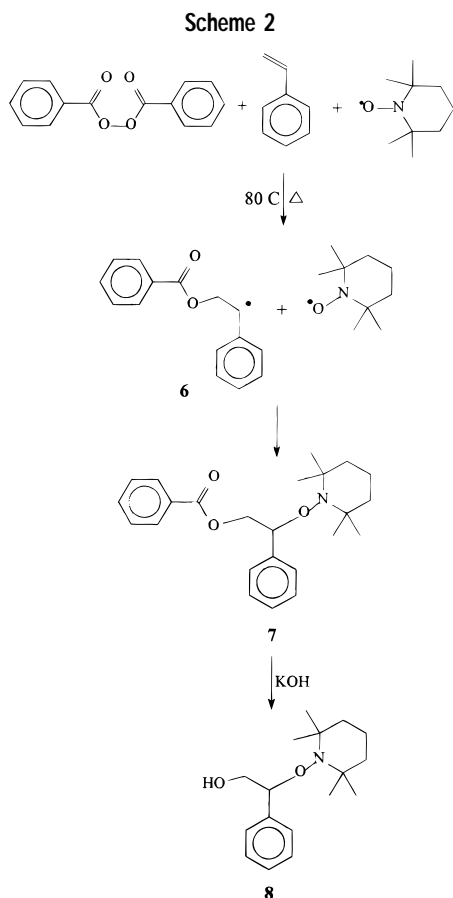
variety of copper-, nickel-, or ruthenium-mediated "living" free radical systems. However, all of these systems have a central theme, reversible homolysis of a covalent, inactive species followed by monomer insertion and reversible recombination. An extremely favorable consequence of the presence of significant amounts of covalent, or inactive, chain ends is that the overall concentration of radical chain ends is decreased substantially, leading to a lower occurrence of unwanted side reactions such as termination, disproportionation, or combination. This enables the polymer chain to grow in a controlled, or pseudo-living, process. It should be noted that the occurrence of these side reactions is not eliminated so, in the strictest sense, the polymerizations are not truly living. The purpose of this Account is to show that nitroxide-mediated free radical polymerizations have many of the attributes of a living system and can be successfully used to prepare a wide range of complex macromolecular architectures, a number of which cannot be prepared by other techniques. While beyond the scope of this Account, many of the synthetic features discussed below are also applicable to transition-metal-mediated "living" free radical procedures such as atom transfer radical polymerization (ATRP).

Unimolecular Initiator Concept

The overriding desire to prepare polymers with controlled structure forced us to consider alternatives to the bimolecular initiating systems that were introduced by Georges.⁸ Borrowing from the concept of well-defined initiating species in anionic polymerizations, a range of unimolecular initiators for "living" free radical systems were developed which offer a number of advantages over the traditional bimolecular mixtures.¹³ The critical feature of these TEMPO (2,2,6,6-tetramethylpiperidinyloxy)-based unimolecular initiators is the presence of a homolytically unstable alkoxyamine (C–ON) bond. As has been shown recently, the strength of this C–ON bond is crucial to the success of the unimolecular initiator, if the bond is too stable to homolytic cleavage, then initiation is slow compared to propagation and broad polydisperse samples are obtained.¹⁴ While the synthesis of alkoxyamines has not been studied extensively in the literature, there are a number of emerging routes for the preparation of these materials based on nucleophilic¹⁵ and radical trapping techniques.¹⁶ For example, reaction of benzoyl peroxide with an excess of styrene leads to the carbon centered radical **6**, and trapping by TEMPO then gives the functionalized alkoxyamine **7**, which is stable under the reaction conditions (Scheme 2). In contrast to initiating species for anionic or cationic polymerizations, such as *n*-butyllithium, alkoxyamine derivatives, such as **7** or its hydrolyzed derivative **8**, proved to be more stable than expected and could be easily purified by a variety of techniques. Prolonged exposure of **7** or **8** to air, light, and moisture resulted in no detectable decomposition, and a variety of chemical transformations can be performed without affecting the critical C–ON bond of the alkoxyamine initiating center.

In analogy with anionic polymerizations, unimolecular initiators, such as **9**, can now be used to accurately control a range of macromolecular features. Typically, "living" free radical polymerizations are conducted under non-demanding reaction conditions, and a mixture of **9** and styrene (used as received) are added to a reaction flask and heated at 125 °C under a nitrogen atmosphere. No purification of any reagents is required, and the reaction setup is exceedingly simple, a round-bottom flask with a nitrogen bubbler. By varying the molar ratio of styrene to **9**, an almost linear relationship is observed between the experimental molecular weight for **10** and the theoretical molecular weight based on the ratio of monomer to initiator (Figure 2). At molecular weights below 30 000, the agreement between experimental and theoretical molecular weights is excellent, and as the molecular weight increases, this difference increases only slightly.

- (13) Hawker, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 11314. Hammouch, S. O.; Catala, J. M. *Macromol. Rapid Commun.* **1996**, *17*, 149. Li, I. Q.; Howell, B. A.; Koster, R. A.; Priddy, D. B. *Macromolecules* **1996**, *29*, 8554.
- (14) Hawker, C. J.; Barclay, G. G.; Orellana, A.; Dao, J.; Devonport, W. *Macromolecules* **1996**, *29*, 5245. Connolly, T. J.; Baldovi, M. V.; Mohtat, N.; Scaiano, J. C. *Tetrahedron Lett.* **1996**, *37*, 4919.
- (15) Hawker, C. J. *Trends Polym. Sci.* **1996**, *4*, 183.
- (16) Li, I.; Howell, B. A.; Ellaboudy, A.; Kastl, P. E.; Priddy, D. B. *Polym. Prepr.* **1995**, *36* (1), 469. Li, I.; Howell, B. A.; Matyjaszewski, K.; Shigemoto, T.; Smith, P. B.; Priddy, D. B. *Macromolecules* **1995**, *28*, 1841. Howell, B. A.; Priddy, D. B.; Li, I. Q.; Smith, P. B.; Kastl, P. E. *Polym. Bull.* **1996**, *37*, 451.



For molecular weights in excess of 100 000, deviations from this relationship become apparent; however, addition of minor amounts of acylating agents, such as acetic anhydride or benzoyl chloride, dramatically improves the relationship between experimental and theoretical molecular weights.¹⁷ In this case, molecular weights can be controlled up to 300 000 while maintaining low polydispersities. Interestingly, the addition of acylating agents also dramatically speeds up the polymerizations and joins a growing list of additives, such as camphorsulfonic acid,¹⁸ which have been successfully used to enhance the viability of nitroxide-mediated "living" polymerizations as a major synthetic tool.

The unique nature of "living" free radical polymerizations can be better appreciated if the polydispersities of the macromolecules obtained are compared with traditional free radical systems. For a variety of styrenic monomers and comonomer mixtures of styrenics with acrylates/methacrylates, the polydispersity of the crude polymerization product is typically 1.1–1.3 with select cases having polydispersities of less than 1.10. When compared to traditional free radical processes, these values are substantially lower than the theoretical limiting polydispersity of 1.5 and the normal experimental value of ca. 2.0. In fact, the polydispersities obtained for "living" free radical polymerizations can approach the values typically obtained for well-behaved living anionic procedures (1.03–1.05).

(17) Malmstrom, E.; Hawker, C. J. *Tetrahedron* **1997**, submitted.
 (18) M. K. Georges, R. P. N. Veregin, P. M. Kazmaier, G. K. Hamer, M. Saban, *Macromolecules* **1994**, *27*, 7228. Odell, P. G.; Veregin, R. P. N.; Michalak, L. M.; Brousmiche, D.; Georges, M. K. *Macromolecules* **1995**, *28*, 8453. Baldovi, M. V.; Mohtat, N.; Scaiano, J. C. *Macromolecules* **1996**, *29*, 5497.

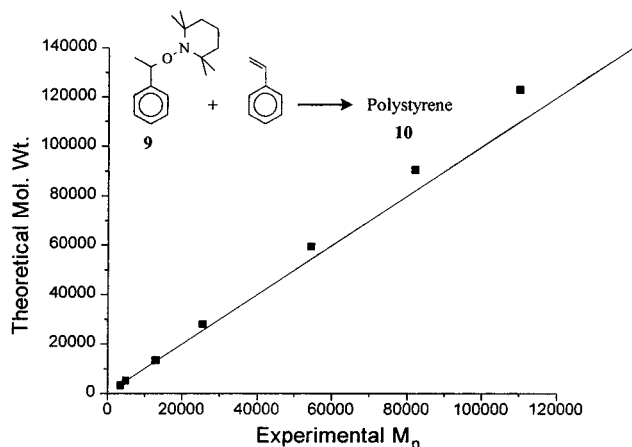


FIGURE 2. Variation in experimentally determined molecular weight, M_n , and the theoretical molecular weights for the polymerization of styrene at 125 °C using varying amounts of the unimolecular initiator 9.

Having demonstrated that low-polydispersity polymers with accurately controlled molecular weights could be obtained by the use of unimolecular initiators, the final aspect that required investigation was control of chain ends. If our proposed reaction sequence is correct for the action of unimolecular initiators, both chain ends should be derived from the initiator structure with one chain end being derived from the nitroxide unit while the other is derived from the substituted benzylic unit. The synthesis of monofunctional linear polymers from functionalized alkoxyamine should therefore be a facile process and permit the introduction of a wide variety of reactive groups. To test this hypothesis, a wide variety of functionalized unimolecular initiators were prepared containing chromophores, (e.g., pyrene, furazan)¹⁹ or reactive groups (e.g., amino) and the degree of functionalization of the resulting polymers (**11**) was determined.²⁰ In each case studied, the incorporation of the functional groups was ca. 95% with no apparent loss in control over molecular weight or polydispersity (Scheme 3).

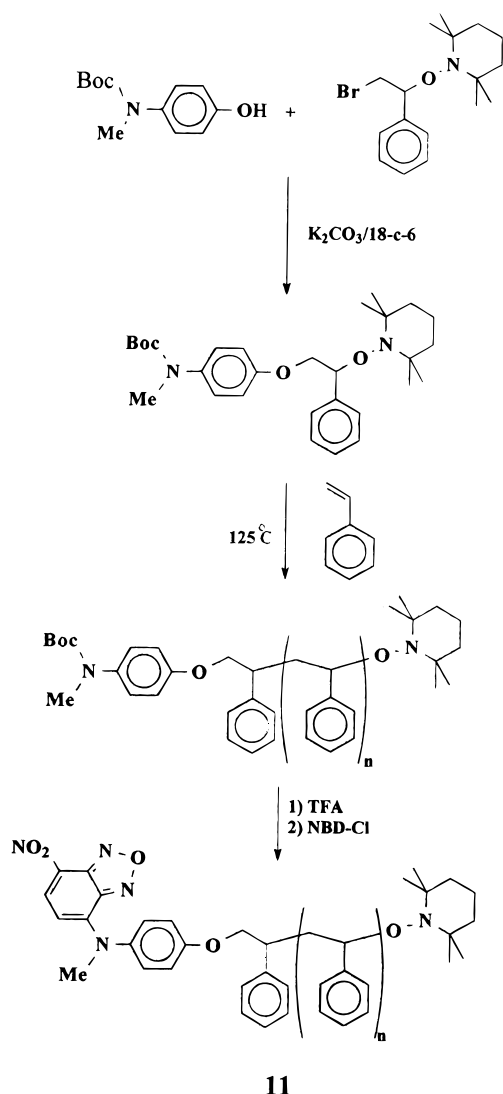
The development of the unimolecular initiator concept in "living" free radical polymerizations therefore permits the rapid synthesis of well-defined vinyl polymers under mild, synthetically nondemanding conditions. A wide variety of functionalized labile blocks have been prepared and successfully used for the fabrication of ultralow dielectric materials using the self-assembling block copolymer approach described above.²¹

Control of Macromolecular Architectures

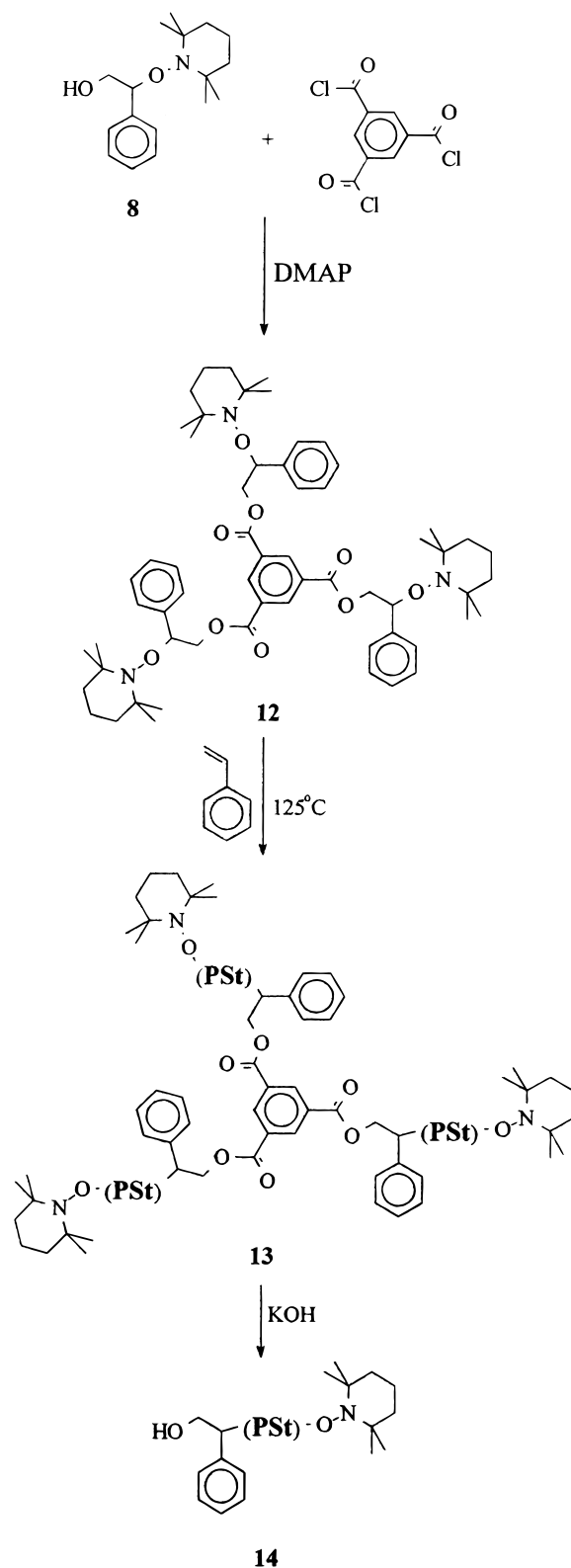
The reduced concentration of growing radical chain ends in "living" free radical polymerizations opens up a wealth of possibilities in the synthesis of complex macromolecular architectures. One of the prime advantages of these "living" systems, when compared to traditional free radical procedures, is the very low occurrence of side reactions such as radical–radical chain coupling. While the use of polyfunctional initiators under normal free radical condi-

(19) Frank, B.; Gast, A. P.; Russell, T. P.; Brown, H. R.; Hawker, C. J. *Macromolecules* **1996**, *29*, 6531.
 (20) Hawker, C. J.; Hedrick, J. L. *Macromolecules* **1995**, *28*, 2993.
 (21) Hedrick, J. L.; Hawker, C. J.; Dipietro, R.; Jerome, R.; Charlier, Y. *Polymer* **1995**, *36*, 4855.

Scheme 3



Scheme 4



tions gives cross-linked networks due to radical coupling reactions, under "living" free radical conditions, a poly-functional initiator may be expected to lead to the desired graft, or star polymer, with little, or no, unwanted coupling products.

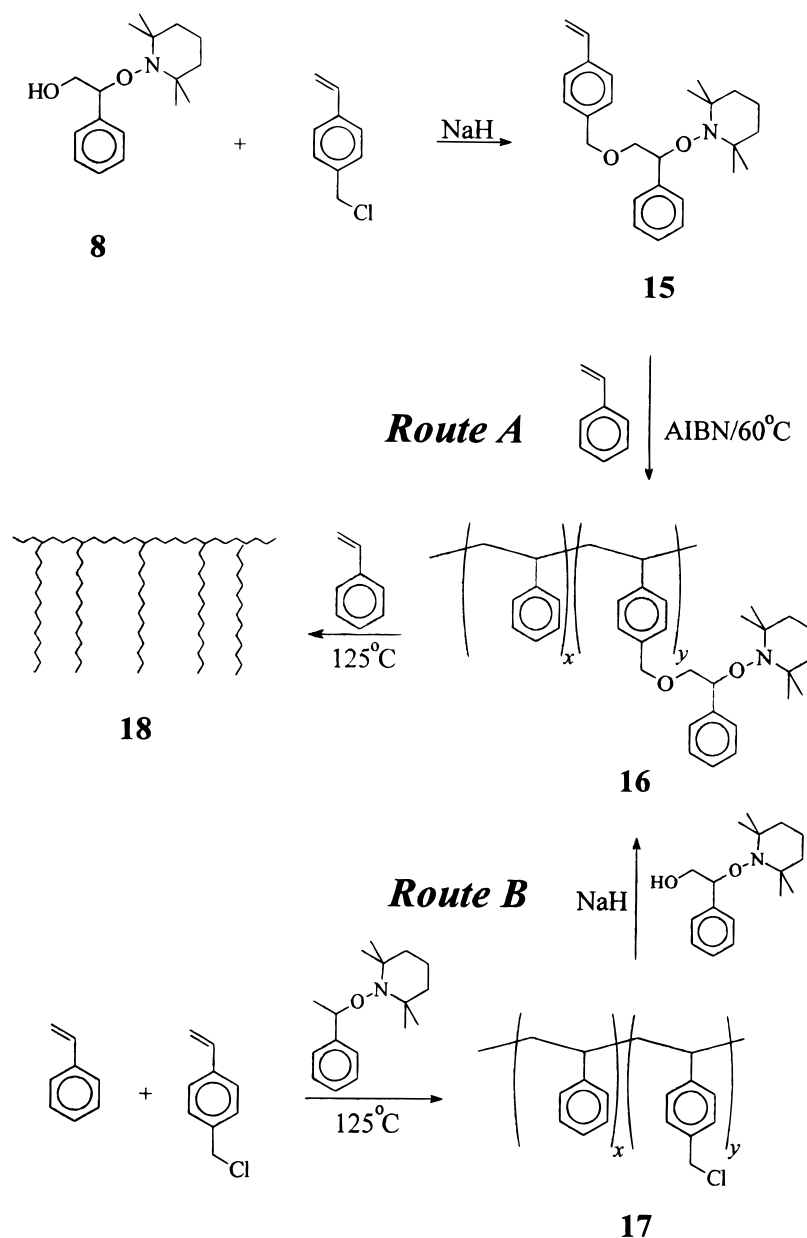
This principal was first tested by the synthesis and polymerization of the trifunctional unimolecular initiator **12**.²² Interestingly, no detectable amounts of cross-linked or insoluble material were observed and degradation of the three-arm polystyrene star **13** by hydrolysis of the ester links was found to give the individual polystyrene arms **14** (Scheme 4). Analysis of **14** revealed a molecular weight comparable to that expected from the initiator to monomer ratio and a narrow polydispersity (ca. 1.10–1.15). These results demonstrate that each of the initiating units in the trialkoxyamine is "active" and the individual polystyrene arms grow at approximately the same rate with little or no cross-linking due to radical coupling reactions.

Subsequently, this concept has been extended to more highly functionalized star-initiators as well as polymeric initiators for the synthesis of graft structures. The versatility of the unimolecular approach to "living" free radical

polymerizations can be better appreciated by examining the range of different approaches that have been developed for the preparation of graft polymers. As shown in Schemes 5 and 6, three different routes have been reported. Route A involves polymerization of a functionalized monomer (**15**) which contains both a vinyl group as well as a latent TEMPO-based initiating group in the same molecule. Polymerization of **15** under standard free radical conditions was shown to give the desired linear

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Scheme 5



polymeric initiator **16** with no decomposition of the initiating centers.²² This result is noteworthy since it demonstrates that the alkoxyamine group is stable to the conditions of normal free radical procedures and suggests that a wide variety of polymers could be grown in the presence of such initiating centers without affecting their reactivity. The polymeric initiators can then be used to prepare a wide variety of block copolymers (**18**) and other complex polymeric structures under mild, synthetically nondemanding reaction conditions. Alternatively, the polymeric initiator (**16**) can be prepared by coupling of a reactive linear polymer with a functionalized unimolecular initiator (route B). For example, a mixture of styrene and *p*-chloromethylstyrene can be polymerized under "living" free radical conditions to give a well-defined linear copolymer (**17**) with controlled molecular weight and low polydispersity (ca. 1.10–1.25). Reaction of **17** with the sodium salt of the hydroxy-functionalized unimolecular initiator then gives the desired polymeric initiator **16**.²³ The advantage of this route is that the molecular weight

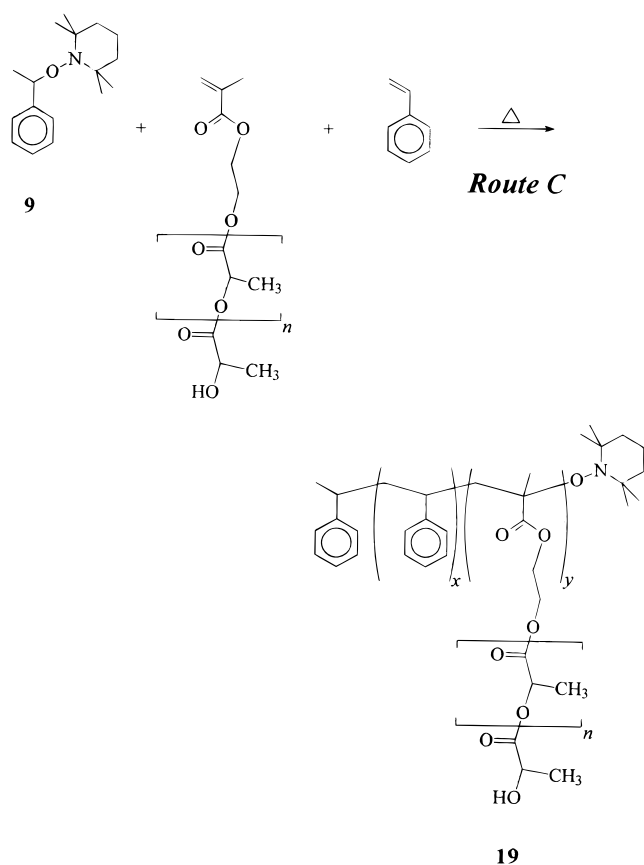
and polydispersity of the linear backbone can be readily controlled during the "living" free radical process leading to well-defined graft copolymers. The compatibility of nitroxide-mediated systems with functional groups also permits the controlled polymerization of a variety of reactive monomer units, ranging from sodium *p*-styrenesulfonate to *p*-vinylbenzoyl chloride and other active ester derivatives.

It has also recently been shown that the bulk polymerization conditions, typically associated with "living" free radical procedures, are compatible with the polymerization of macromonomers to give graft copolymers (route C).²⁴ Using a variety of macromonomers ranging from methacrylate-terminated poly(lactide) to dendritic polyether macromonomers, a series of novel graft copolymers (**19**) were readily prepared under mild conditions

(23) Keoshkerian, B.; Georges, M. K.; Boils-Boissier, D. *Macromolecules* **1995**, *28*, 6381.

(24) Hawker, C. J.; Mecerreyes, D.; Elce, E.; Dao, J.; Hedrick, J. L.; Barakat, I.; Dubois, P.; Jerome, R.; Volksen, W. *Macromol. Chem. Phys.* **1997**, *198*, 155.

Scheme 6

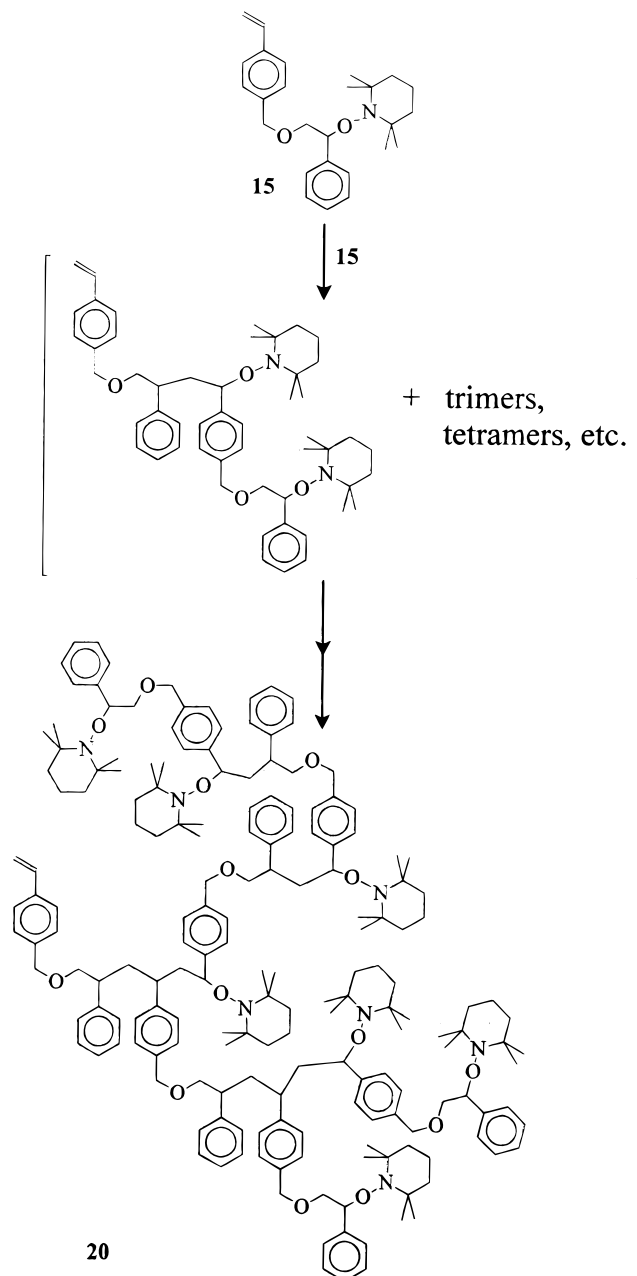


(Scheme 6). The molecular weight of the backbone polymer could again be controlled by the ratio of monomer to initiator, and even at high loading of the macromonomer component, low polydispersities for both the graft structure and the backbone polymer were obtained. It should be noted that attempts to synthesize the same graft copolymers by anionic or cationic procedures would lead to degradation of macromonomers with reactive linkages, such as poly(lactides).

Hyperbranched and Dendritic Structures

The ability to form reactive unimolecular initiators, such as **15**, opens up a number of avenues to unusual macromolecular architectures that are either difficult or impossible to prepare using traditional free radical chemistry or living anionic procedures. In the case of the styrenic derivative, **15**, a propagating center and an initiating center are combined in the same molecule to effectively create a self-condensing monomer which is similar to AB_2 monomers used for the preparation of hyperbranched and dendritic macromolecules by condensation chemistry. Homopolymerization of **15** under "living" free radical conditions was shown to lead to initial formation of dimers, trimers, etc., and eventually hyperbranched macromolecules (**20**) with the kinetics of growth resembling a step-growth polymerization even though the polymerization occurs by a free radical mechanism (Scheme 7).²⁵ One interesting facet of this polymerization is that the hyperbranched polystyrene derivatives contain numerous initiating centers. These numerous initiating centers have

Scheme 7



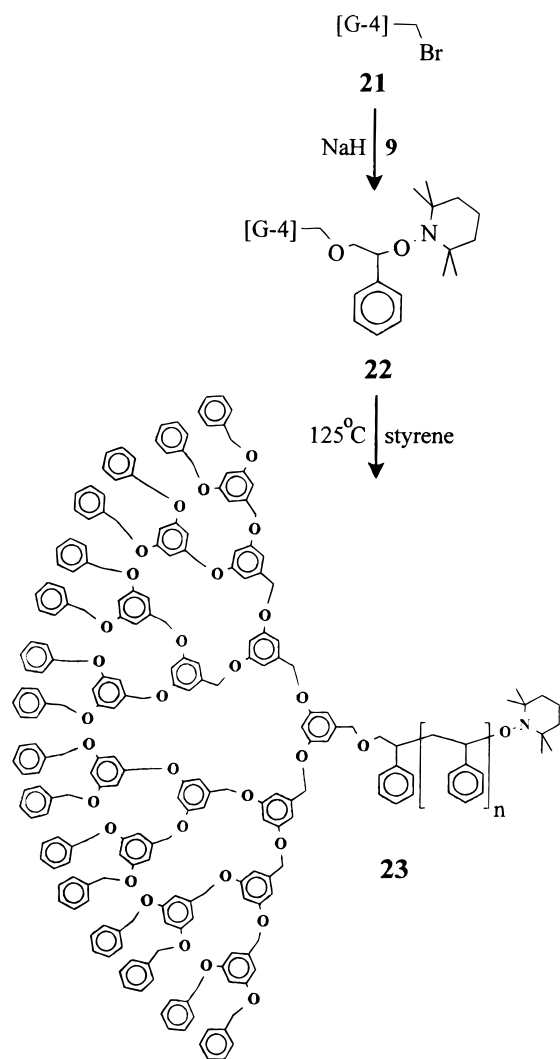
been used to form a unique class of star macromolecules in which the central core is a highly functionalized hyperbranched polymer. Subsequently, Fréchet and Matyjaszewski applied a similar technique to the preparation of hyperbranched polystyrene derivatives by the homopolymerization of *p*-(chloromethyl)styrene using ATRP conditions, though the actual structure of the materials obtained seems to be variable.²⁶

Unusual block copolymers can also be prepared utilizing the compatibility of TEMPO-based unimolecular initiators with a variety of reaction conditions and reagents. This feature permits functionalized initiators to be readily coupled with telechelic or monofunctional oligomers or polymers to give mono- or difunctional polymeric initiators which in turn are ideally suited for the synthesis of AB or ABA block copolymers. A perfect

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(26) Fréchet, J. M. J.; Leduc, M. R.; Weimer, M.; Grubbs, R. B.; Liu, M.; Hawker, C. J. *Polym. Prepr.* **1997**, *38*, 756. Gaynor, S.; Edelman, S.; Matyjaszewski, K. *Macromolecules* **1995**, *28*, 6381.

Scheme 8



example of this involves the use of convergently prepared dendrimers as the monofunctional polymer **21**, which can be readily coupled with the hydroxy-functionalized unimolecular initiators to give the dendritic initiator **22**. Hybrid dendritic-linear block copolymers (**23**) with well-controlled molecular weights and low polydispersities are then obtained by the reaction of **22** with a variety of styrenic monomers or comonomer mixtures under standard "living" free radical polymerization conditions (Scheme 8).²⁷ Similar structures can also be prepared using ATRP chemistry, and in this case, the initiating group is simply a focal point chloromethyl or bromomethyl functionality. A slightly different approach to hybrid dendritic-linear block copolymers has recently been reported by Matyjaszewski.²⁸ In this case, the dendritic block is attached to the nitroxide functionality and typical bimolecular initiating systems are used. The molecular weights and polydispersities obtained were not as well controlled as in the dendritic initiator case, and this difference may be due to the significantly increased steric bulk of the dendritic nitroxide which would be expected to decrease its mobility and hence ability to control the polymerization.

(27) Leduc, M. R.; Hawker, C. J.; Dao, J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1996**, *118*, 11111.
 (28) Matyjaszewski, K.; Shigemoto, T.; Fréchet, J. M. J.; Leduc, M. R. *Macromolecules* **1996**, *29*, 4167.

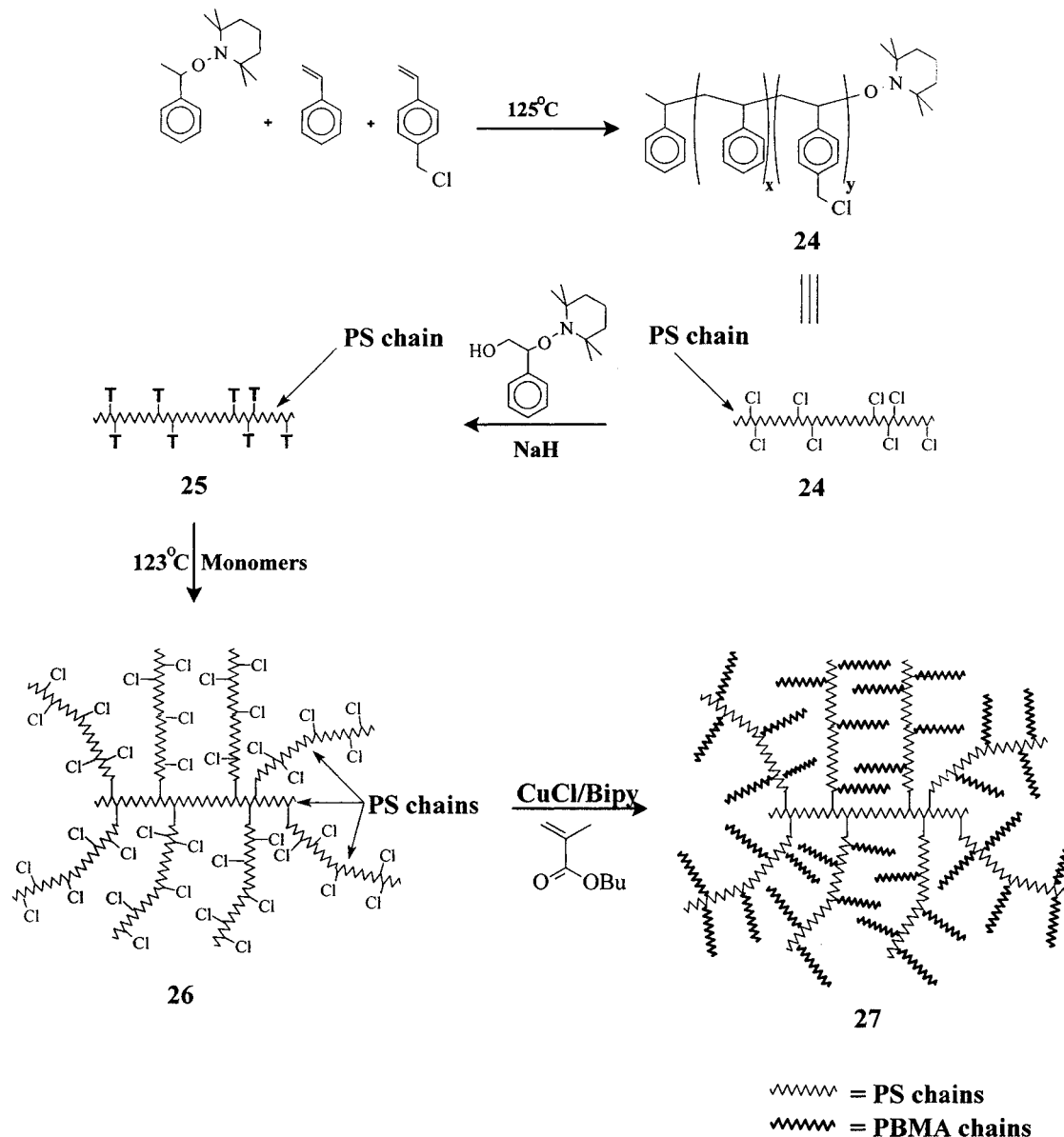
This building block, or modular approach, to the synthesis of complex macromolecular architectures can be taken a step further in the rapid synthesis of combburst or dendritic graft copolymers by a tandem "living" free radical approach. The underlying strategy in this novel approach to highly branched linear polymers is that each layer, or generation, of linear polymers is prepared by "living" free radical procedures and the initiating groups are either present during the polymerization or introduced in a post-polymerization functionalization step. In this way, very large, highly branched combburst copolymers can be prepared in a limited number of steps using mild reaction conditions. As shown in Scheme 9, the initial linear backbone **24** is prepared by nitroxide mediated "living" free radical polymerization of a mixture of styrene and *p*-chloromethyl styrene. At this stage, the polymerization mechanism can be switched from nitroxide-mediated to atom transfer "living" free radical conditions to give graft copolymers or TEMPO-based initiating groups can be introduced by reaction of the numerous chloromethyl groups with the sodium salt of **9** to give the polymeric initiator **25**. A second layer, or generation, of linear chains can then be grown from the linear backbone to give a wide variety of grafted block copolymers. Alternatively, reactive chloromethyl groups can be introduced on the grafted arms (**26**) by a second copolymerization of styrene and *p*-(chloromethyl)styrene. This functionalized graft copolymer can again be used as a complex polymeric initiator for ATRP polymerization which introduces a third layer of linear polymer chains (**27**). In analogy with the divergent growth approach to dendritic macromolecules, this stepwise functionalization/growth strategy can be continued to give larger and larger combburst macromolecules and the mild reaction conditions permit a wide variety of monomer units and functional groups to be used.

Mechanistic Considerations

The dramatic improvement in control over macromolecular structure obtained by using "living" free radical techniques when compared to traditional free radical chemistry suggests that a number of subtle, though important, changes are occurring in the mechanism of these polymerizations. While the majority of this Account has been devoted to the synthetic aspects of nitroxide-mediated "living" free radical polymerizations, a substantial amount of work has been published on the mechanistic aspects of the polymerization process.^{30,31} All of the data obtained so far support the basic scheme discussed earlier, a series of homolytic cleavage/monomer insertion/

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 (30) Greszta, D.; Matyjaszewski, K. *Macromolecules* **1996**, *29*, 7661. Moad, G.; Rizzardo, E. *Macromolecules* **1995**, *28*, 8722. Catala, J. M.; Bubel, F.; Hammouch, S. O. *Macromolecules* **1995**, *28*, 8441. Fukuda, T.; Terauchi, T. *Chem. Lett.* **1996**, 293. Greszta, D.; Matyjaszewski, K. *Macromolecules* **1996**, *29*, 5239. Fukuda, T.; Terauchi, T.; Goto, A.; Ohno, K.; Tsujii, Y.; Miyamoto, T.; Kobatake, S.; Yamada, B. *Macromolecules* **1996**, *29*, 6393.
 (31) Veregin, R. P. N.; Georges, M. K.; Kazmaier, P. M.; Hamer, G. K. *Macromolecules* **1993**, *26*, 5316. Veregin, R. P. N.; Georges, M. K.; Hamer, G. K.; Kazmaier, P. M. *Macromolecules* **1995**, *28*, 4391. Veregin, R. P. N.; Odell, P. G.; Michalak, L. M.; Georges, M. K. *Macromolecules* **1996**, *29*, 2746. Veregin, R. P. N.; Odell, P. G.; Michalak, L. M.; Georges, M. K. *Macromolecules* **1996**, *29*, 3324.

Scheme 9



recombination reactions (Scheme 1). Our own efforts in this area have focused on three main issues: (i) the relationship between the structure and efficiency of the unimolecular initiator, (ii) mobility of the mediating nitroxide radicals during the polymerization, and (iii) understanding the importance and effect of autopolymerization during the "living" free radical polymerization of styrenic monomers.

To guide the synthesis of more efficient unimolecular initiators, we prepared a range of benzylic alkoxyamine initiators and examined their efficiency in the polymerization of styrene.¹⁴ Interestingly, it was found that a variety of functional groups could be substituted on the aromatic ring, nitroxide unit, or β -carbon atom without any deleterious effects on the polymerization process. If the β -carbon atom is however removed, the parent benzyl-TEMPO derivative **28** has little or no control over molecular weight and polydispersity with the polydispersities (ca. 2.5) obtained being actually higher than that obtained under traditional free radical conditions. The crucial initiation step was then studied in detail by following the disappearance of the unimolecular initiator in situ using

deuterated styrene as the monomer unit and high-temperature ¹H NMR spectroscopy. A plot of relative initiator concentration with time for the α -methyl initiator **9** and the benzyl initiator **28** is shown in Figure 3. From this it can be seen that there is a dramatic difference in behavior for the two unimolecular initiators. The α -methyl derivative has a half-life of approximately 5–10 min, and essentially all the initiator is consumed within the first hour. Since the conversion of monomer during this period is less than 5%, the rate of initiation is fast on the polymerization time scale. In contrast, the benzyl initiator **28** has a half-life of ca. 150 min at 123 °C and a substantial amount of **28** remains after 12 h, at which time the polymerization has reached 70% completion. Significant initiation is therefore occurring during the whole course of the polymerization, and this leads to a nonliving system with high polydispersities being obtained. A number of other groups have also investigated the influence of changes in the nitroxide radical on the polymerization process. Significant changes in the reaction rate and compatibility with alternate monomers have been observed on variations in the steric nature and electronic

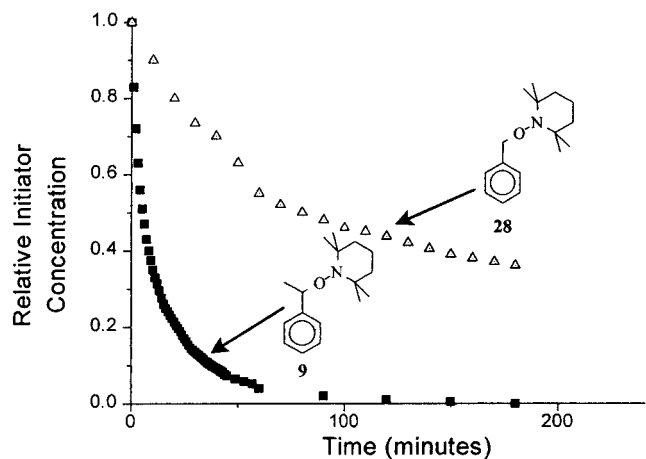
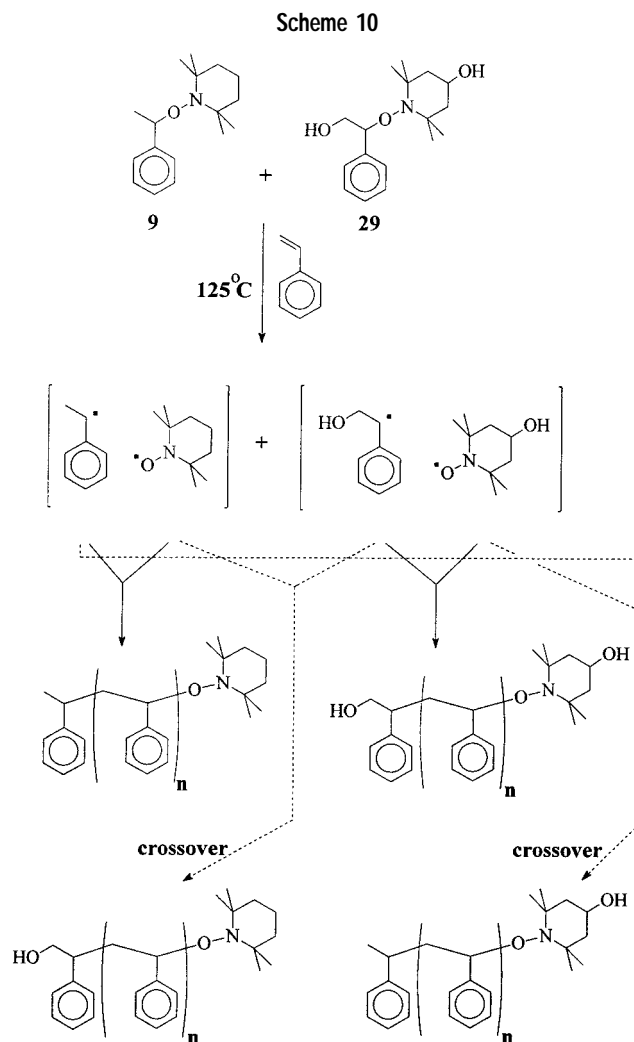


FIGURE 3. Relative concentration of initiators (9 and 28) as a function of time during the polymerization of deuterated styrene at 123 °C.

structure of the nitroxide,³² and advances in this area will no doubt provide fundamentally important results in the future.

The final step in the basic reaction scheme for nitroxide-mediated "living" free radical polymerizations, radical recombination to regenerate the covalent, or dormant, alkoxyamine, is a key feature of the reaction scheme. An intriguing question regarding this critical reaction step, and one which may have important consequences, is the mobility of the mediating nitroxide free radical; *does the nitroxide stay associated with the same growing polymer chain end throughout the polymerization, or is it free to diffuse into the polymerization medium?* To answer this question, we designed a series of radical crossover experiments using a 1:1 combination of two disparate initiators, the unfunctionalized derivative **9** and its corresponding dihydroxy analogue **29**. HPLC analysis of the mixture of polystyrene derivatives obtained from this initiator mixture revealed that all four possible products were obtained in a near statistical ratio, even at low conversions (Scheme 10).³³ This demonstrates that the mediating nitroxide free radicals have a high degree of mobility and undergo facile exchange, or crossover, between growing chain ends at essentially all stages of polymerization.

The question of autopolymerization in "living" free radical polymerizations is an extremely important point due to the relatively high temperatures at which these polymerizations are typically conducted. A number of groups have examined this question in detail,³⁴ and a general consensus that autopolymerization is occurring in these systems, probably via a Mayo-type mechanism, is emerging. To differing degrees, depending on the molecular weight of the polymer chain being grown, the



chains initiated by autopolymerization can be controlled via the mobility of the mediating nitroxide free radicals. At lower molecular weights (< 20 000), the relative proportion of chains formed by autopolymerization is minimal, and therefore, all chains are effectively controlled, leading to low-polydispersity, controlled molecular weight materials. However, at higher molecular weights, the influence of autopolymerization increases significantly and control of the polymerization is gradually lost, leading to the experimentally observed increase in polydispersity and loss of molecular weight control. The addition of additives to speed up the polymerization, or the development of new nitroxides which operate at lower temperatures, should circumvent many of these autopolymerization related problems and lead to an even more controlled process that may be capable of producing low-polydispersity polymers with extremely high molecular weights.

Conclusion

In conclusion, it should be noted that the field of "living" free radical polymerizations is a young, rapidly progressing area of research and many of the difficulties or limitations associated with the general applicability of this technique are steadily, but surely, being overcome. The challenge of polymerizing acrylates is slowly being resolved by new initiators such as those described by Gnanou which

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effectively lower the energy required for homolytic cleavage of the bond to nitroxide while still leading to low-polydispersity materials.³⁵ These advances, coupled with the compatibility with numerous functional groups, wide variety of initiator structures, and mild reaction conditions, suggest that "living" free radical techniques could play a significant future role in the synthesis of controlled macromolecular architectures. When compared to currently available polymer synthesis techniques, "living" free radical procedures may (i) permit the synthesis of known polymers, such as random copolymers, with a significant increase in control over the macromolecular structure, (ii) permit the synthesis of complex macromolecular architectures, such as graft poly(styrene-*g*-methyl methacrylate)

block copolymers, with a significant increase in synthetic ease and mild reaction conditions, (iii) allow the synthesis of unique macromolecular architectures, such as hybrid dendritic-linear block copolymers, which cannot be prepared by other synthetic techniques, and (iv) provide easy implementation due to the simplicity of the syntheses. It is envisaged that the increased synthetic availability of unusual or unique macromolecules via "living" free radical procedures will lead to advanced materials for a range of technological applications. Potential impact areas are surface science,³⁶ adhesion,³⁷ coating technologies, micro-electronic applications,³⁸ biotechnology, etc.

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