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Acceleration in nitroxide mediated 'living' free radical polymerizations

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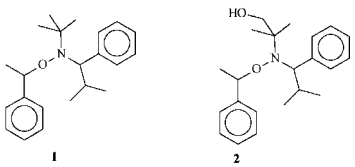
Intramolecular H-bonding has been shown to be a powerful tool in increasing the performance of alkoxyamine initiators for nitroxide mediated living free radical polymerizations.

The continued evolution of nanoscale science as a major research area has attracted significant attention in recent years.[1–3] In concert with this evolution, the field of polymer synthesis has witnessed an increase in sophistication with a wide range of new synthetic techniques being developed for the preparation of well defined, functionalized macromolecules. Prime examples are the preparation of dendritic macromolecules,[4,5] single site catalysts,[6–8] and the elucidation of a variety of different living free radical polymerization strategies.[9,10] These include nitroxide mediated,[11,12] atom transfer radical polymerization (ATRP),[13,14] and radical addition fragmentation/transfer procedures (RAFT).[15,16] While there are advantages and disadvantages to each procedure, our recent work has concentrated on nitroxide mediated processes since it has the potential to be the simplest of the three procedures.

A major recent advance in nitroxide mediated polymerizations has been the development of α-hydrido nitroxides, in which the presence of a hydrogen atom on the α-carbon leads to a significant increase in the range of vinyl monomers that undergo controlled polymerization.[17,18] While these new nitroxides, or their corresponding alkoxyamines such as **1**, can now be used to prepare poly(acrylates) with polydispersities in the range 1.05–1.10, the typical reaction times and temperatures (48 h at 125 °C) are still unacceptable for reactive monomers that may undergo unwanted side reactions. Also from an industrial point of view, reaction times of less than 6 h and temperatures of *ca.* 100 °C are more economically desirable.

In developing new nitroxides for living free radical polymerizations we were drawn to an observation from our initial work[19] in which the hydroxy-substituted alkoxyamine **2** was observed



1 **2**

to yield slightly faster rates of polymerization when compared to the parent alkoxyamine **1**. While the effect was not dramatic it did correlate with the tendency of nitroxides to act as H-bond acceptors, thereby modifying their reactivity.[20] These observations, coupled with a seminal report by Studer[21] of enhanced dissociation rates for hydroxy-substituted alkoxyamines prompted an investigation into the influence of H-bonding on nitroxide mediated living free radical polymerizations. Since dissociation of **2** leads to the nitroxide **3** which is able to form a favored six-membered intramolecular H-bond (Fig. 1), it was decided to maximize the potential of this intramolecular H-bonding effect by examining the initiating ability of the tris-hydroxy derivative, **4**.

The synthesis of **4** starts from the cheap and readily available 2,2,2-tris(hydroxymethyl)nitromethane **5** which was protected

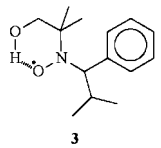


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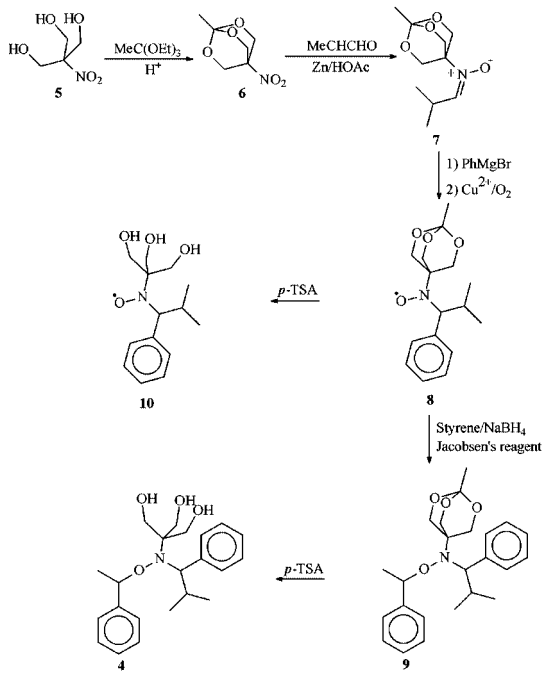
Fig. 1 Structure of proposed intramolecular H-bonding in nitroxide **3**.

as its ortho ester **6** before reductive coupling with isobutyryl aldehyde in the presence of zinc/HOAc to give the nitrone **7**. Reaction with phenyl magnesium bromide at reduced temperatures affords the protected nitroxide **8** which can then be coupled with styrene under catalytic Jacobsen's conditions[22] yielding the protected alkoxyamine **9**. Deprotection of either **8** or **9** could be accomplished under mild conditions with *p*-toluenesulfonic acid to give the corresponding tris(hydroxymethyl) derivatives, **10** and **4**, in essentially quantitative yields (Scheme 1).

The ability of **4** to mediate living free radical polymerization was initially examined using styrene as the monomer. Under identical conditions, the alkoxyamine initiator, **1** or **4**, was dissolved in 200 equivalents of styrene and heated at 125 °C under argon with samples being removed at various intervals. Comparison of the results showed an increase in the rate of polymerization for **4** of *ca.* 50% with high conversion being obtained in 3–4 h (*cf.* 5–6 h for **1**). More importantly, the increased rate of polymerization was accompanied by a decrease in polydispersity with values of between 1.07 and 1.09 typically being obtained (*cf.* 1.10–1.12 for **1**). This increased reactivity for **4** also allowed the polymerization temperature to



5 **6** **7** **8** **9** **10** **4**

Scheme 1

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be reduced while still maintaining acceptable polymerization times. For example, the polymerization of styrene at 85 °C for 48 h resulted in moderate conversions (50–55%) and low polydispersities (1.15–1.20). Extension of this work to 1,3-dienes such as isoprene also showed a similar trend, increased rate of polymerization and a reduction in polydispersity.[23]

A more significant result was observed when the polymerization of polar monomers was examined. For acrylates, the polymerization rate was increased by at least an order of magnitude by the use of the tris(hydroxymethyl) derivative, **4**. As can be seen in Fig. 2, the polymerization of *n*-butyl acrylate initiated by **4** in the presence of 5 mol% of the corresponding nitroxide **10** reaches 80% conversion after only 2 h at 120 °C, in direct contrast to **1** and 5 mol% of **12**, for which a conversion of only 6% is obtained. It should also be noted a loss of control did not accompany this increased rate of polymerization, narrow polydispersities in the region of 1.1 and controlled molecular weights were obtained with **4**. This improvement now permits acrylate monomers to be polymerized to high conversion under controlled living free radical conditions in only 2–3 h compared to 36–48 h for **1**. Attempts to perform the polymerization of acrylate monomers at lower temperatures were also successful with moderate conversions (*ca*. 40–50%) being obtained after heating at 100 °C for 24 h. At these lower temperatures, the unfunctionalized initiator **1** did not result in any detectable polymerization.

This anomalous behavior of acrylate monomers, when compared to styrene and 1,3-dienes, suggested that the increased efficiency of **4** was monomer dependent and to address this question the polymerization of acrylamides was examined. Interestingly, an increase in the rate of polymerization was again observed with **4** and high conversions were obtained after 7–8 h.[23] While not as dramatic an increase as for acrylates, it is significantly greater than the rate increase observed for styrene or isoprene.

The unique ability of the tris(hydroxymethyl) substitution pattern to facilitate nitroxide mediated polymerizations suggested that H-bonding might be a key feature. To elucidate the effect of H-bonding, similar experiments to those described above were performed with the protected alkoxyamine **9** which is not capable of forming H-bonds. Surprisingly, **9** proved to be a poor initiator for all the monomer families studied with high polydispersities and low polymerization rates being obtained in each case. For example, polymerization of 200 equivalents of styrene in the presence of **9** for 2 h at 125 °C resulted in only 19% conversion with high conversions requiring 16 h (*cf*. 3–4 h for **4** and 5–6 h for **1**). The polymers obtained were also poorly defined with polydispersities typically in the range of 1.4–1.5. Similar decreased rates of polymerization and levels of control were observed for other monomer families suggesting that the protected initiator **9** is a poor initiator for nitroxide mediated living free radical polymerizations. Since the substitution pattern in **4** is similar to **9**, the substantially improved performance of **4** is most likely a result of intramolecular H-bonding and not steric or electronic effects. Additional support for the importance of H-bonding comes from the kinetic observations of Marque[24] coupled with preliminary work from Matyjaszewski[25] using phosphonic acid derivatives of 2,2,6,6-tetramethylpiperidinyloxy, TEMPO.

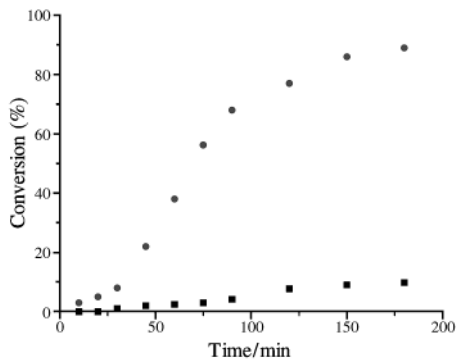

Fig. 2 Plot of percent monomer conversion *vs*. time for the polymerization of *n*-butyl acrylate (200 equivalents) in the presence of **4** (1.0 equivalent) and **10** (0.05 equivalents) (●) and **1** (1.0 equivalents) and **12** (0.05 equivalents) (■) at 125 °C.

In conclusion, intramolecular H-bonding has been shown to be a powerful tool in increasing the performance of alkoxyamine initiators for nitroxide mediated living free radical polymerizations. Increases in the rate of polymerization were observed for polar monomers such as acrylamides and especially acrylates, while only moderate improvements were obtained for non-polar monomers, such as styrene and isoprene. In each case, the degree of control during the polymerization was improved which led to lower polydispersities and a better correlation between experimental and theoretical molecular weights.

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