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A Nitroxide for Effecting Controlled Nitroxide-Mediated Radical Polymerization at Temperatures ≤90 °C

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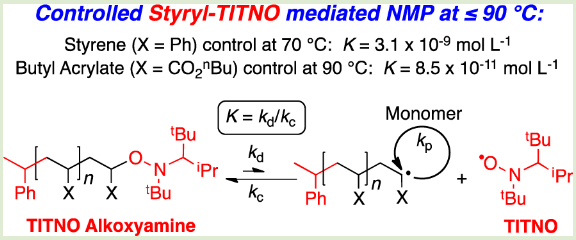
Supporting Information

ABSTRACT: Factors underlying design of a new nitroxide, 2,2,5-trimethyl-4-*tert*-butyl-3-azahexane-3-oxyl (TITNO), and its styrene alkoxyamine (Styryl-TITNO) for effecting nitroxide-mediated polymerization (NMP) at temperatures ≤90 °C are described. The rate coefficient, k_d, for thermal dissociation of Styryl-TITNO was determined in the range 70−100 °C, giving Arrhenius parameters $A_d = 2.9 \times 10^{12}$ s^{-1} and $E_d = 104.1$ kJ mol^{-1}. Due to the low value of E_d, values of k_d and the activation−deactivation equilibrium constant for NMP of *n*-butyl acrylate (BA) and styrene are much lower at any given temperature than for alkoxyamines of more established nitroxides. Good control of molecular weight and dispersity, with negligible contributions from termination, is achieved at 90 °C for BA and at 70 °C for styrene, thus, eliminating the complicating contributions from styrene thermal initiation. Hence, TITNO and Styryl-TITNO offer new opportunities for controlled NMP at temperatures much lower than has previously been attainable.



Nitroxide-mediated radical polymerization (NMP) is an important method for synthesis of polymers of predefined molecular weight with low dispersity and, in the case of block copolymers, well-defined architecture. Control depends upon the alkoxyamine dissociation equilibrium constant $K = k_d/k_c$, where k_d and k_c are the rate coefficients for alkoxyamine dissociation and for combination of the chain radical with the nitroxide, respectively. For a given nitroxide/monomer system, K depends principally on the polymerization temperature, and there is an optimum temperature for control in each system. Early studies used 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) as mediator, but it requires a high temperature (typically 125−135 °C) and is largely limited to NMP of styrenic monomers. Hence, the discovery that acyclic nitroxides with a C−H bond α to the nitroxide nitrogen are capable of controlling NMP of styrenic monomers and acrylates at lower temperatures (typically 110−125 °C) was an important development; the most important of these nitroxides are *N*-(*tert*-butyl)-*N*-(1-diethylphosphono-2,2-dimethylpropyl)nitroxide (SG1)[1] and 2,2,5-trimethyl-4-phenyl-3-azahexane-3-oxyl (TIPNO).[2] The principal objective of our work has been to design, synthesize, and evaluate new nitroxides with the aim of controlling NMP at temperatures below 100 °C, facilitating use in aqueous media under atmospheric pressure and which have greater hydrophobicity in order to reduce nitroxide partitioning into the aqueous phase during heterogeneous polymerizations in aqueous media (e.g., minemulsion). In the first phase of this work,[3] a range of nitroxides and their styryl alkoxyamines were developed based on the skeleton of TIPNO, most of which replaced the TIPNO α-phenyl substituent by larger aromatic groups (biphenyl, phenanthryl, and *tert*-butylphenyl), but their effects in reducing the activation energy, E_d, and/or increasing the frequency factor, A_d, for alkoxyamine dissociation and increasing k_d were insufficient to reduce the optimum polymerization temperature below 100 °C. Similarly, replacing the TIPNO α'-*tert*-butyl substituent by an adamantyl group did not reduce E_d sufficiently to provide the required increase in k_d.

In seeking to design nitroxides that give suitable values of K at lower temperatures, it must be recognized that the balance between the values of k_d and k_c is subtle. Nevertheless, it is clear that the alkoxyamine C−O bond strength is a key parameter. For successful NMP, the value of k_d should be around 10^{-3} s^{-1}.[3,4] The alkoxyamine C−O bond strength is known to depend strongly on steric hindrance and polarity in the alkoxyamine, as well as on the stability of both the nitroxide and the leaving carbon-centered radical.[4,5] Steric effects result from C−O bond strain and commonly are quantified in terms of a steric constant, r_s, which indicates greater steric crowding as it becomes more negative. Bearing in mind ease of nitroxide and alkoxyamine synthesis, a *tert*-butyl group ($r_s = -2.46$)[6] is attractive and should be significantly more effective than a phenyl group ($r_s = -1.40$)[6b] in reducing E_d. Electron-withdrawing groups in the nitroxide moiety appear to destabilize the nitroxide radical and strengthen the alkoxyamine C−O bond.[4,7] These polarity effects normally are quantified in terms of a polar constant, σ_L, positive values of which indicate electron withdrawing and negative values electron donating

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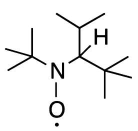
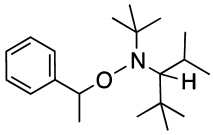
effects. The values of σ_L for phenyl and *tert*-butyl groups are +0.12 and −0.01,[8] respectively, indicating a relatively small difference between these groups compared to the difference in r_s. Hence, overall, replacement of the TIPNO α-phenyl substituent by a *tert*-butyl group was expected to provide a significant increase in k_d. We also performed gas phase molecular modeling using an MM3 force field to determine minimum energy 3D structures for a wide range of nitroxides. This yielded theoretical values of equilibrium CNC bond angle and ONCH dihedral angle for each nitroxide (presented in Table S1). It is significant that the ONCH dihedral angle for 2,2,5-trimethyl-4-*tert*-butyl-3-azahexane-3-oxyl (TITNO) is quite low (162.1°) compared to many other nitroxides, much lower than TIPNO (175.6°) and all the other new hydrophobic nitroxides we reported previously, but much closer to that of SG1 (159.2°). TITNO also has a relatively low CNC bond angle (122.0°), which is unusual because very few nitroxides have relatively low values of CNC bond angle and ONCH dihedral angle. When combined with the anticipated steric effects of the *tert*-butyl groups, these observations provided the motivation for evaluating TITNO as a mediator of NMP at lower temperatures. The route for synthesis of TITNO and its styrene alkoxyamine (Styryl-TITNO), and microanalysis, NMR and MS data confirming their structure and purity, are described in the Supporting Information.


TITNO


Styryl-TITNO

Evaluation of k_d for thermal dissociation of Styryl-TITNO was achieved using a well-established EPR method[4,9] that involves monitoring the increase in nitroxide concentration on heating of an alkoxyamine in the presence of excess oxygen, which acts as a highly efficient scavenger of the organic radical released but does not trap the nitroxide radical. Styryl-TITNO dissociation was studied in this way at 70, 80, 90, and 100 °C and gave the concentration−time profiles presented in Figure S2, which show that dissociation of Styryl-TITNO is very rapid at 100 °C (essentially complete within 10 min) and also proceeds at a significant rate at 70 °C. Assuming the dissociation to be first-order with oxygen acting as a sink for the styryl radical, as described by Fischer and co-workers,[4,7] the data can be fitted to the following equation

$$\ln\{1 - ([\mathrm{TITNO}]_t/[\mathrm{Styryl\text{-}TITNO}]_0)\} = -k_d t \qquad (1)$$

where $[\mathrm{Styryl\text{-}TITNO}]_0$ is the initial concentration of Styryl-TITNO and $[\mathrm{TITNO}]_t$ is the concentration of TITNO at time t. The data are plotted in Figure 1; linear least-square fits give the values of k_d summarized in Table 1.

An Arrhenius plot of the Styryl-TITNO k_d data is shown in Figure S3 and fits to the following equation with a correlation coefficient of 0.997.

$$k_d = 2.9 \times 10^{12} \exp(-104.1\ \mathrm{kJ\,mol^{-1}}/RT)\ \mathrm{s^{-1}} \qquad (2)$$

Literature values of activation energy, E_d, for thermolysis of styryl alkoxyamines typically fall in the range 116−133 kJ mol^{-1}, as summarized in Table S2. Hence, by comparison, the magnitude of E_d for Styryl-TITNO (104.1 kJ mol^{-1}) is very much lower than observed for the established alkoxyamines.

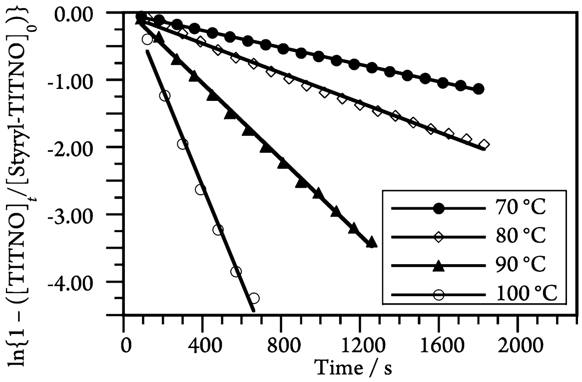


Figure 1. First order plot of $[\mathrm{TITNO}]_t$ vs time in accord with eq 1 for 0.1 mM solutions of Styryl-TITNO in xylene heated at 70, 80, 90, and 100 °C.

Table 1. Styryl-TITNO Thermal Dissociation Rate Coefficient, k_d, Values Determined by Fitting the Plots in Figure 1 to Eq 1

temperature (°C)	k_d (s^{-1})
70	4.5×10^{-4} (0.999)[a]
80	1.0×10^{-3} (0.998)
90	3.0×10^{-3} (0.999)
100	8.2×10^{-3} (0.996)

[a] Correlation coefficients from linear least-squares fits.

The pre-exponential factor, A_d, for Styryl-TITNO (2.9×10^{12} s^{-1}) also is lower than the reported[4] average value for styryl alkoxyamines (2.6×10^{14} s^{-1}), which moderates the effect of the lower value of E_d, but is consistent with the observation of Bacon et al.[10] who reported that A_d tends to be lower for alkoxyamines with lower values of E_d. Nevertheless, it is the much lower value of E_d that is most important in providing higher values of k_d at lower temperatures. Given that our aim was to design a hydrophobic alkoxyamine that would be effective at temperatures below 100 °C, it is pertinent to compare values of k_d at 90 °C, which were calculated for various styryl alkoxyamines from literature values of E_d and A_d and are shown in Table 2. It is clear that k_d (90 °C) for Styryl-TITNO is far higher than for the other styryl alkoxyamines and comparable to the values of k_d (120 °C) for Styryl-TIPNO and Styryl-SG1 (3.3×10^{-3} s^{-1} and 5.5×10^{-3} s^{-1}, respectively, calculated from the data in Table S2), which indicates that Styryl-TITNO should be effective in NMP at 90 °C. Solution polymerizations of *n*-butyl acrylate (BA) and styrene in anisole (selected for its low chain transfer activity) have been used to evaluate control of NMP with Styryl-TITNO as initiator.

Table 2. Values of Dissociation Rate Coefficient, k_d, at 90 °C Calculated from Experimental E_d and A_d Data (see Table S2)

alkoxyamines	k_d (90 °C; s^{-1})	ref
Styryl-TEMPO	1.8×10^{-6}	4
Styryl-TIPNO	1.2×10^{-4}	4
Styryl-SG1	2.3×10^{-4}	4
Styryl-DBNO	6.5×10^{-4}	4
Styryl-(*N*-β-sulfinyl)	3.3×10^{-4}	11
Styryl-TITNO	3.0×10^{-3}	this work

Controlled growth of poly(*n*-butyl acrylate) (PBA) chains at 90 °C is evident from Figure 2a, which shows a clear shift of the

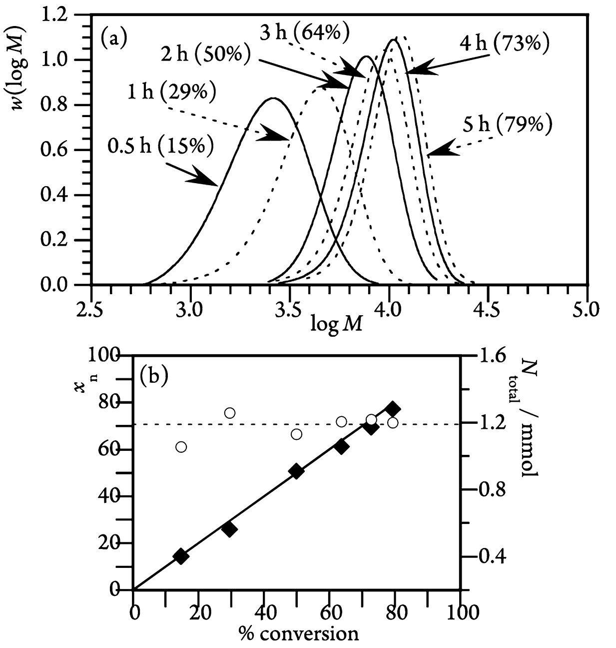


Figure 2. Data showing (a) evolution of MWD with reaction time (% conversion) and (b) measured x_{n} (◆), theoretical x_{n} (solid line), measured N_{total} (○), and theoretical N_{total} (dashed line), with conversion for solution polymerization of BA in anisole at 90 °C mediated by Styryl-TITNO with $[\mathrm{BA}]_0/[\text{Styryl-TITNO}]_0 = 101.0$.

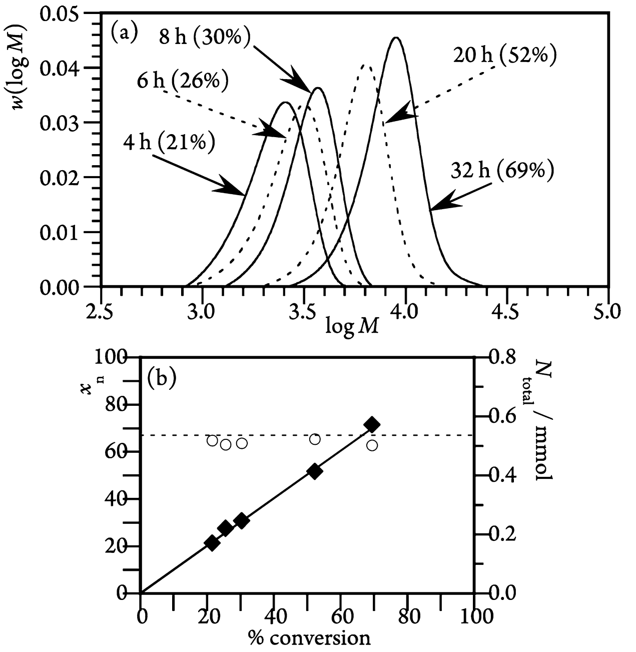


Figure 3. Data showing (a) evolution of MWD with reaction time (% conversion) and (b) measured x_{n} (◆), theoretical x_{n} (solid line), measured N_{total} (○), and theoretical N_{total} (dashed line), with conversion for solution polymerization of styrene in anisole at 70 °C mediated by Styryl-TITNO, with $[\mathrm{BA}]_0/[\text{Styryl-TITNO}]_0 = 96.6$ in the presence of 16.4 mol % TITNO (smaller scale reaction, so N_{total} is lower than for BA).

unimodal molecular weight distribution (MWD) to higher molecular weight as conversion increases and is confirmed by the change in number-average degree of polymerization, x_{n}, with conversion shown in Figure 2b (x_{n} was calculated from number-average molecular weight, M_{n}, determined by GPC). PBA with molecular weight dispersity $Đ_{\mathrm{M}} = 1.22$ was obtained at low conversion (15%), indicating that initiation was relatively fast and mostly complete early in the polymerization. There was then a steady slight decrease in $Đ_{\mathrm{M}}$ with conversion, with a low final $Đ_{\mathrm{M}}$ of 1.12, observations that are consistent with living-like conditions. Furthermore, x_{n} increases linearly with conversion and in good agreement with the theoretical x_{n} for living polymerization. A more robust test of "livingness" is to establish how the total number of moles of polymer chains, N_{total}, varies with conversion, because it should not change under true living conditions and should be equal to the initial number of moles of Styryl-TITNO used in the polymerization. The value of N_{total} was calculated from the experimental data as $N_{\mathrm{total}} = m{\cdot}f_{\mathrm{c}}/M_{\mathrm{n}}$ where m is the initial mass of monomer, f_{c} is the fractional monomer conversion, and M_{n} is the measured value at the corresponding monomer conversion. The data are shown in Figure 2b and reveal that, within experimental error, N_{total} does not deviate from the initial number of moles of Styryl-TITNO. While it is important to recognize that the molecular weights used in the calculations were determined by GPC with a polystyrene calibration, the data provide irrefutable evidence of a high degree of chain livingness and control in Styryl-TITNO mediated BA polymerization at 90 °C.

Similar observations are evident in polymerization of styrene using Styryl-TITNO, but at the lower temperature of 70 °C (see Figure 3). The polymerization is significantly slower than for BA (cf. conversion−time data in Figures 2a and 3a), as expected due to the lower temperature and much lower propagation rate coefficient.[12] More importantly, MWDs shift along the molecular weight axis as conversion increases with no evidence of a low molecular weight tail (with $1.15 \leq Đ_{\mathrm{M}} \leq 1.20$ throughout) and the x_{n} data are close to theoretical prediction. Furthermore, the much lower temperature provides additional benefits for styrene polymerization resulting from the much smaller (negligible) complicating contribution from styrene thermal initiation.

Analysis of conversion−time data by a standard, first order kinetics method (see the Supporting Information) facilitates evaluation of K. In Styryl-TITNO-mediated NMP of styrene at 70 °C, $K = 3.1 \times 10^{-9}$ mol L^{-1}, and of BA at 90 °C, $K = 8.5 \times 10^{-11}$ mol L^{-1}. With the exception of Styryl-TEMPO-mediated NMP of styrene (which has a very low value[13] of $K = 2.1 \times 10^{-11}$ mol L^{-1}), these values are comparable to values of K for established acylic nitroxide alkoxyamines at their normal *higher* optimum polymerization temperature ranges (typically $K \sim 2$–8×10^{-9} mol L^{-1} for styrene at 110–125 °C[11,14] and $K \sim 10^{-10}$ mol L^{-1} for BA at 115–125 °C[14a,15]). Hence, values of K for NMP mediated using Styryl-TITNO are entirely consistent with the values known to be needed for good control, but are achieved at much lower temperatures.

In summary, TITNO and Styryl-TITNO offer new opportunities for controlled NMP of acrylate and styrenic monomers at temperatures ≤90 °C, which is much lower than previously attainable. This facilitates NMP in aqueous media (such as miniemulsion polymerization) under atmospheric pressure. The lower temperatures also eliminate the complicating contribution from thermal initiation in NMP of styrene and, for acrylates, the complicating effects of β-scission of midchain radicals that occurs at higher temperatures, thus, enabling much cleaner syntheses of well-defined polymers. Furthermore, the lower temperatures will be an advantage in the use of NMP for acrylic or styrenic monomers that have more temperature-sensitive moieties in side groups, such as for synthesis of well-defined block copolymers for life sciences and other functional applications, including block copolymer self-assembly into higher-order structures.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

MM3 modeling data; synthesis and characterization of TITNO and Styryl-TITNO; evaluation of k_d, E_d, and A_d, and comparison with other alkoxyamines; details of polymerizations; evaluation of K. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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