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Assessment of TEMPO as a Thermally Activatable Base Generator and Its Use in Initiation of Thermally-Triggered Thiol–Michael Addition Polymerizations

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Abstract

We present a thermally initiated thiol-Michael reaction based on initiation via the temperature-dependent thiol-TEMPO oxidation-reduction reaction. In the presence of a thiol, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, $pK_a = 5.5$) is reduced to produce a much stronger base, i.e., tetramethylpiperidine (TMP, $pK_a = 11.4$) in a temperature dependent process. This oxidation-reduction process is dramatically accelerated at elevated temperature, which allows for thermally controlled initiation of the base-catalyzed thiol-Michael addition reaction and potentially other base-catalyzed reaction systems. Several critical factors that affect base generation from TEMPO reduction were investigated *via* systematic variation of reaction conditions including the solvent, temperature, and the thiol type and concentration. The highly temperature-dependent attributes of this redox reaction were demonstrated in various thiol-TEMPO based systems and were further utilized to thermally control thiol-Michael polymerizations under different heating conditions. The strong amine species, TMP, formed at elevated temperatures from the TEMPO-thiol interaction combined with high temperature, enables rapid formation of thiol-Michael-based polymer networks and large scale material preparation without any detrimental effects often associated with highly exothermic polymerizations. This novel approach to develop thermally-initiated thiol-Michael polymer networks is unique, versatile and robust, resulting in wide utility in applications such as facile handling of highly reactive resins, bulk material preparation, pH sensitive materials construction, and composite/macro-particle synthesis.

Graphical Abstract

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Keywords

Thermal-initiated thiol-Michael polymerization; step-growth polymerization; thermal base generator; “click” chemistry

INTRODUCTION

Since being introduced in 2001 by Kolb, Finn and Sharpless, the “click” chemistry concept has gained great attention as one of the most powerful paradigms because of its unique attributes, such as rapid reaction rates, quantitative yields with negligible side product formation and a lack of common synthetic drawbacks such as time-consuming separations or harsh reaction conditions.^{1–3} As representative “click” reactions, the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC),^{4, 5} thiol-ene/thiol-yne coupling,^{6, 7} Diels-Alder reaction,⁸ have all been extensively investigated and implemented in applications, such as polymer and dendrimer synthesis,^{9–11} bio-conjugation,¹² surface functionalization,^{10, 13, 14} and nanoimprinting,¹⁵ to name a few.

Bearing the merits associated with the other “click” reactions, the well-known thiol-Michael addition reaction has also been recognized as a member of the “click” reaction family. Readily initiated by either bases or nucleophiles, the thiol-Michael addition reaction proceeds *via* an alternating addition (or propagation in the case of polymerizations) step, where Michael addition of a thiolate anion to an electron-deficient vinyl group occurs, followed by a chain transfer process from the generated carbonanion to another thiol, which in turn regenerates the thiolate anion and affords a β -thioether as the final addition product.^{16, 17} Compared to conventional radical-mediated polymerization reactions, the anion-mediated thiol-Michael polymerization is a highly orthogonal, robust reaction, which does not suffer from oxygen inhibition or bimolecular recombination. Owing to these prominent qualities, the thiol-Michael addition reaction has seen wide implementation in fundamental biological and chemical research studies as well as in practical applications such as microparticle synthesis,¹⁸ surface modification,^{19, 20} dental restoratives¹¹ and thermoresponsive, rehealable materials²¹. Furthermore, to achieve spatiotemporal control,

external triggers (light or heat) have been introduced to regulate the thiol-Michael addition reaction. For example, photobases have been implemented to photoinitiate thiol-Michael polymerization, which enables high spatiotemporal precision, insignificant sample contamination and highly efficient reactions. With considerable progress in photobase synthesis, the thiol-Michael photoinitiation is readily achieved with improvements in photoefficiency,^{22, 23} visible light sensitivity,^{24–26} and thiol-Michael reaction orthogonality²⁷.

While photoinitiation has significant benefits, it suffers from several inherent shortcomings associated with the use of light such as insufficient penetration depth, inhomogeneous curing (especially in the incident light path), requirements of specific light sources, and limited ability for large scale polymer formation. In contrast, the use of elevated temperature, namely thermal initiation, serves as an alternative curing strategy.²⁸ Consider that in radical polymerizations where both photoinitiation and thermal initiation routes are possible, an overwhelming fraction of commercial processes utilize thermal initiation. Compared with the highly abundant and diversified radical thermal initiator library, implementation of thermal base generators in thiol-Michael addition reactions has been rarely reported. For example, in less reactive thiol-acrylate-based thiol-Michael systems, weak bases, i.e. triethylamine, hexylamine etc., are used to initiate thermal cure but have limited processing time.¹⁶ However, implementation of a weak base in the more reactive thiol-Michael systems (i.e thiol-vinyl sulfone, thiol-maleimide system) leads to rapid, highly exothermic reactions, which then become challenging with respect to handling and material preparation.¹¹ Fmoc-(Fluorenylmethyloxycarbonyl)protected amines have been exploited as a thermal base generator (usually cleaves at 120 °C –160 °C) as well as a base amplifier when co-initiated with a photobase in polymer synthesis and surface patterning.^{29–31} In another case, Ueda and co-workers reported a carbamate linked secondary alicyclic amine (e.g. 2,6-dimethylpiperidine, DMP) as a thermally sensitive base-catalyst for low temperature solid-phase imidation of poly(amic acid) (PAA), which also requires a relatively high induction temperature (around 200 °C).³² However, owing to the tendency of thiol oxidation and the reduced stability of thiol-Michael systems at elevated temperature, these thermal amine generation methods would not be suitable for thermally initiating the thiol-Michael “click” reaction polymerization.

TEMPO was first introduced as a convenient thermal initiation method for forming thiol-Michael-based cross linked networks under mild heating conditions in 2015.^{11, 13} However, many aspects of the thermally-induced process still remain elusive, such as the thermal reaction fate of TEMPO and the mechanism by which TEMPO thermally triggers the thiol-Michael polymerization, including its impacts on the reaction kinetics. Herein, we systematically investigated the TEMPO-mediated redox reactions and the catalytic efficiency of TEMPO in thermally initiated thiol-Michael addition systems. A proposed reaction diagram for the TEMPO initiated thiol-Michael addition reactions is shown in Scheme 1. In previous studies, TEMPO ($pK_a = 5.5$) was reported to be reduced in the presence of a sufficient amount of thiol to generate a much stronger base, 2,2,6,6-tetramethylpiperidine (TMP, $pK_a = 11.4$).^{33–35} This thiol-catalyzed TEMPO oxidation-reduction reaction has been well studied and the reported reaction yield is estimated to be around 20–60%, depending on the type of thiol and the reaction conditions.³⁶ The amine

product continues to deprotonate the thiol and initiates the thiol-Michael addition reaction in the presence of an electron deficient vinyl group. Therefore, the heating conditions not only facilitate the generation of base from TEMPO, which serves as the initiation species for thiol-Michael addition reaction, but also contributes to rapid thiol-Michael addition reaction. In order to gain insight into the base generation process and evaluate the changes during the redox reaction, detailed investigations were performed by electron paramagnetic resonance (EPR), nuclear magnetic resonance spectroscopy (NMR) and mass spectroscopy (MS) experiments. We evaluated several critical factors influencing the TEMPO-thiol oxidation-reduction reaction and also demonstrated its temperature-dependent features *via* systematic variation of reaction conditions such as the temperature, type and concentration of the thiol reactant, as well as the TEMPO concentration. The catalytic ability and efficiency of TEMPO were investigated in two thiol-Michael addition polymerizations, i.e., thiol-acrylate and the more reactive thiol-vinyl sulfone systems, *via* real-time infrared spectroscopy (FT-IR).

EXPERIMENTAL SECTION

1. Materials

2,2,6,6-Tetramethyl piperidine (TMP), divinyl sulfone (DVS), 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical (TEMPO), 1-hexanethiol (HT), butyl 3-mercaptopropionate (BT), butyl acrylate, triethylamine (TEA), (2,2,6,6-Tetramethylpiperidin-1-yl) oxyl (TEMPO), and diethyleneglycol diethyl ether (DEGDE), triethylene glycol diacrylate (TEGDA) were purchased from Sigma-Aldrich. Pentaerythritol tetra(3-mercaptopropionate) (PETMP) was donated by Bruno Bock. All chemicals were used as received. Tetra (2-mercaptopethyl) silane (SiTSH) was synthesized according to a previously reported procedure.³⁷ Molecular structures are depicted in Fig. 1.

2. Methods

Ultraviolet-Visible spectroscopy (UV-Vis)—UV-Vis tests were conducted on a UV-Vis spectrophotometer (Thermo-Fischer Scientific). All samples were tested in PMMA cuvettes with 1 cm light path lengths. Absorbance data was collected in absorbance mode with a bandwidth of 2 nm and a scan speed of 600 nm/min.

Electron paramagnetic resonance (EPR)—EPR experiments of TEMPO radical consumption under heating conditions were performed on a Bruker Elexsys E 500 EPR spectrometer with a Bruker Super-High Sensitivity Resonator (SHQE cavity). Typical EPR parameters for radical generation were a 4 G modulation amplitude with a modulation frequency of 100 kHz, a receiver gain of 60, and an attenuation of 25 dB.

Titration—Titration experiments were conducted with a Fisher Scientific accumet AB15 Basic calibrated by standard buffer systems (pH=4.0, 7.0). A methanol/H₂O mixture (volume ratio of 1:9) was used as a solvent for all titration systems to increase the solubility of TEMPO, the thiol and the amine. By diluting a concentrated HCl solution (12.1 M), an acid solution (0.05 M) was made for titrating the amine generated from thermal TEMPO - thiol oxidation-reduction reaction.

NMR spectra—¹H-NMR spectra were performed on a Bruker Avance-III 400 NMR spectrometer in *d*-chloroform at room temperature. Amine generation (TMP) was determined *via* NMR analysis.

Real-Time Fourier transform infrared spectroscopy (FT-IR)—Polymerization kinetics were analyzed using a Fourier transform infrared spectroscopy (FTIR) instrument (Nicolet 8700) to monitor the real-time functional group conversions in transmission mode. With monomer mixtures sandwiched between two NaCl salt plates, the thermal thiol-Michael polymerization reaction was monitored by the change of the thiol peak (2500–2600 cm⁻¹), the vinyl sulfone peak (3050–3150 cm⁻¹), and the acrylate peak (780–820 cm⁻¹). The IR sample was placed on a heating stage to control accurately the temperature during the thiol-Michael polymerization reactions.

Resin preparation—Stoichiometric mixtures of a thiol and vinyl based on functionality were prepared generally with 2.0 wt % TEMPO as a thermal thiol-Michael initiator. Bulk resins were prepared by injecting monomer mixtures between two glass sides separated by 0.25 mm thickness spacers. Thermally initiated thiol-Michael polymers were post-cured by heating to 80 °C for 8 h.

Dynamic mechanical analysis (DMA)—Mechanical behavior of the crosslinked polymers was evaluated in a DMA Q800 (TA Instruments). Material specimens were measured in multi-frequency strain mode by applying a sinusoidal stress of 1 Hz frequency with the temperature ramping at 3 °C min⁻¹. The T_g was determined as the maximum of the tan δ profile. DMA experiments were thermally cycled and replicated two times to eliminate thermal sample history, and the second heating cycle is reported here as the representative.

RESULTS AND DISCUSSION

TEMPO-thiol redox reaction mechanism and thermal base generation

Previous research has indicated the possible oxidation-reduction reactions between a thiol and TEMPO, describing the possible mechanisms and identifying the generated amine and corresponding side products under different experimental conditions.^{33–35} The redox reaction between TEMPO and a thiol is complicated, and the reaction products vary substantially, being highly dependent on the thiol type, relative concentrations and other reaction conditions such as the solvent and atmosphere. However, the generation of the corresponding amine has been confirmed in almost all thiol-TEMPO redox reaction, along with moderately to highly persistent adducts, including sulfonamides, sulfinamides and sulfenamides.³⁴ The plausible mechanism proposed by previous research is shown in Scheme 2.³⁸ Different nitroxides, with varied structures and oxidation potentials, have great impacts on the yield and reaction rate of this redox reaction. Previous researches illustrated that when reacted with ethyl thiol, 6-membered ring nitroxide (TEMPO) gave much higher amine yield (45 %) than that of the 5-membered ring nitroxides (10–15 %).³³ The reactivity difference probably arises from the greater flexibility of the 6-membered ring, which allows the nitrogen center to planarize more easily during the oxidation/reduction reactions. Here, to evaluate TEMPO as a potential thermal base initiator for thiol-Michael addition

polymerization, the focus is on analyzing the TEMPO degradation kinetics and investigating the amine generation process. ^1H -NMR and MS spectra were used to confirm the generation of the amine product, i.e., 2,2,6,6-tetramethyl piperidine (TMP). After heating a mixture of TEMPO and butyl mercaptopropionate (BT) with a molar ratio of 1:4 at 60 °C for 30 min, both MS spectrum and NMR analysis were performed on the thermal mixture. When compared with the NMR spectrum of acetic acid neutralized TMP salts, the thermal reaction adduct showed similar NMR peaks at 1.15, 1.38, 1.63 ppm, indicative of the generation of TMP (Fig. S1). The amine product was further confirmed with the appearance of a 142.1652 signal in the MS spectrum (Fig. S2). TMP ($pK_a=11.4$) usually appears in its protonated form after the oxidation-reduction reaction in the presence of a thiol reactant.

A phenol red-based colorimetric method was previously found to be a sensitive method in the detection and analysis of base generated from the photo-induced cleavage of a photobase initiator.^{24, 25, 39} Same methodology was adopted here to verify the thermal base generation from the TEMPO-thiol redox reaction (Fig. 2). For the reaction mixture of TEMPO and butyl mercaptopropionate (BT) (molar ratio of 1:4) at 50 °C, UV spectra were gathered at different reaction times (0, 1.5, 4, 10, 20 min) Phenol red (1.0 mM) was then added as a base indicator. According to the collected UV-Vis absorption spectra, a new absorption band emerges around 567 nm with increasing reaction time, which corresponds to the deprotonation of phenol red by the generated base. This result is a clear confirmation of the TMP formation as the base product, as well as the resulting basicity change in the system during the TEMPO-thiol redox reaction. The increase of the medium basicity was also probed by pH measurements (Fig. S3). This pH measurement does not represent the actual pH evolution due to the organic medium, but this method demonstrated the pH change caused by the thermally generated base product (i.e., TMP), and also enables an estimate for the base generation in the redox reaction. A methanol and water mixture (volume ratio of 1:9) was used to increase the solubility of TEMPO, the thiol reactant, butyl mercaptopropionate (BT) and TMP. At 50 °C, the pH of the mixture increased up to 11.3 in 4 minutes, and then the value reached a plateau (Fig. S3a). In further titration experiments (see Fig. S3b and the associated procedures), the acid consumption of TEMPO and the thiol (BT) thermal reaction mixture were compared with that of two control groups (amine TMP and thiol mixture, and pure thiol). Due to the limited yield of TMP in this redox reaction, the titration of the TEMPO/BT mixture used considerably more acid than the pure thiol, but less acid as compared to the TMP/BT mixture. Based on the acid consumption, the TMP yield was roughly estimated to be 60 %.

Optical spectroscopy allows for the study of TEMPO degradation and has been widely used in previous nitroxide-related studies, given that TEMPO exhibits a specific absorption peak at 450 nm.^{38, 40} Here, we also implemented UV-Vis spectrophotometry to evaluate changes in the TEMPO concentration and further demonstrated its highly temperature-dependent decomposition rate. As shown in Fig. 3a, TEMPO and 1-hexanethiol (molar ratio of 1:4) were mixed and kept at ambient temperature (23 °C), UV-Vis measurements were taken every 30 minutes following dilution with methanol to an appropriate concentration for absorption measurements. The decreasing 450 nm peak as a function of increasing reaction time indicates that this redox reaction slowly proceeded without heat and consumed 80% of the TEMPO in 3 hours. In Fig. 3b, another sample with similar components (TEMPO and

HT, molar ratio of 1:4) was heated at 50 °C and the UV-Vis measurements (taken every minute) show much faster TEMPO degradation kinetics, whereby 80% conversion of TEMPO was achieved in 5 minutes. Due to the relatively stable resonance structure provided by the lone pair electrons of the nitrogen atom and steric protection by methyl groups, TEMPO is considered to be a stable radical species. As such, electron paramagnetic resonance (EPR) was implemented as an alternative method to study the TEMPO-thiol redox reaction at elevated temperature. Consistent with the UV-Vis results, a significant decrease in the TEMPO signal was observed within 5–7 minutes in the TEMPO/HT systems heated to 50 °C (Fig. 4). In both the UV-Vis and EPR experiments, it was determined that the reaction rate of this redox reaction is highly dependent on reaction temperature, which opens the possibility for implementing such a reaction as a thermal initiation method for the thiol-Michael addition polymerization.

TEMPO thermal degradation kinetics

It is worth noting that the TEMPO-catalyzed thiol-Michael polymerization required higher temperatures to achieve rapid reaction kinetics (60–90 °C) as compared with the TEMPO-thiol redox reaction (40–50 °C) alone. To investigate critical factors in this redox reaction, the TEMPO degradation kinetics were evaluated *via* systematic variation in factors such as the temperature, thiol type, and species concentrations with all results summarized in Table 1. Firstly, temperature acts as an important factor in both the TEMPO-thiol redox reaction and in the TEMPO-catalyzed thiol-Michael polymerization. The redox reactions between TEMPO and 1-hexanethiol (HT) were performed at 23 °C, 35 °C, 40 °C and 50 °C (Fig. S5–11), and a linear curve fit for the natural logarithm of the TEMPO concentration versus time was observed, indicating a first-order thermal decomposition, which is in accordance with previous reported findings.^{36, 41} The TEMPO/HT reactions at higher temperatures (50 °C) were found to be approximately 60 times faster than those at ambient temperature (23 °C) when comparing the normalized TEMPO degradation rate $k_d(\text{s}^{-1})$, which corresponds to an apparent or overall activation energy for the decomposition of TEMPO of approximately 110 kJ/mol. The pre-exponential factor calculated for this redox reaction is $2.5 \times 10^{16} \text{ s}^{-1}$. (The Arrhenius' plot is shown in Fig. S12) For comparison, a typical radical thermal initiator, 2,2'-azobisisobutyronitrile (AIBN), has a factor of 15 increase in decomposition rate when going from 50 °C ($k_d = 2.2 \times 10^{-6} \text{ s}^{-1}$) to 70 °C ($k_d = 3.2 \times 10^{-5} \text{ s}^{-1}$) in toluene.⁴² As such, this temperature-dependent feature of the TEMPO reduction qualifies it as a promising thermal base generator for the thiol-Michael polymerization as well as other similar base-catalyzed reactions.

Secondly, DEGDE solvent diluted systems were used to mimic the dilute conditions in thiol-vinyl based thiol-Michael polymerization, and the slower oxidation-reduction reaction under these conditions suggests a significant influence of the reactant concentration on the redox reaction rate. In Fig. 5, diluted TEMPO/HT/DEGDE system (molar ratio of 1:4:16) was heated at 50 °C and, a first-order decreasing trend is observed with a much slower reaction rate as compared with the pure TEMPO/HT system (Fig. 3b) at the same condition. This slower reaction kinetics in the diluted TEMPO/thiol reaction was further confirmed with EPR measurements (Fig. S4). These results support that the TEMPO reduction proceeds relatively slowly in less concentrated systems, which explains why the thermally initiated

thiol-Michael polymerization requires a relatively high temperature. Thirdly, owing to the different redox potential and acidity of the reacting thiols, different thiol types exhibited different reactivities in the TEMPO-thiol redox reaction. No obvious TEMPO degradation was observed in the absence of thiol even when heated to 80 °C (in DMSO solution, no NMR spectra change and the generation of the TMP can be observed during heating process), which indicates that the thiol is a necessity in this oxidation-reduction process.

TEMPO-catalyzed thiol-Michael addition polymerization kinetics

Based on the evidence of TMP generation and highly temperature-dependent reaction rate, TEMPO is further implemented to thermally initiate thiol-Michael addition polymerization. After the TMP generation and the thermal degradation kinetics of TEMPO had been demonstrated, difunctional vinyls, i.e., TEGDA and DVS were combined with butyl 3-mercaptopropionate as model substrates to study the catalyzing efficiency of the TEMPO in the thiol-Michael model reactions (Table 2). The TEMPO catalyzed thiol-Michael reaction was monitored by ¹H-NMR and the decreasing vinyl peak (between 5 ppm and 6 ppm) was chosen as an indicative measure of the ultimate yields of the reaction. (Fig. S13). The results in Table 1 indicate that the TEMPO catalyzed thiol-Michael reaction proceeded slowly at ambient conditions, but was accelerated dramatically and achieved high final conversion within 90 minutes at 80 °C. Due to the high reactivity of the vinyl sulfone group, the final conversion of DVS at ambient condition was slightly higher than that of TEGDA.

TEMPO-triggered thiol-Michael polymerizations not only provide an alternative method for developing less reactive thiol-acrylate type polymer networks, which can be also achieved with weak base catalysts, but also acts as a powerful tool to preparing highly reactive thiol-Michael systems thermally, for example through thiol-vinyl sulfone and thiol-maleimide systems. To demonstrate the utility of TEMPO in these types of thiol-Michael addition polymerizations, we formed two thiol-vinyl sulfone networks, i.e., multifunctional PETMP/DVS and SiTSH/DVS resins (Fig. 6). The monomers conversion of the thermal thiol-Michael polymerization reaction was monitored by the change of the thiol peak (2500–2600 cm⁻¹), the vinyl sulfone peak (3050–3150 cm⁻¹). In both the TEMPO-catalyzed PETMP/DVS (Fig. 6a) and the SiTSH/DVS (Fig. 6b) Michael-type addition polymerizations the reaction proceed rapidly at elevated temperatures. However, when compared with the model TEMPO-thiol redox reaction kinetics, the TEMPO-catalyzed thiol-Michael polymerization reactions appear to have relatively slower base generation and require somewhat higher temperatures (usually 60–90 °C) for several reasons. First, when diluted with the vinyl monomers, the thiol concentration is lower as compared to the pure thiol systems (as indicated in Table 1). Also, as the thiol-Michael polymerization progresses, the thiol concentration decreases, which slows down the base generation in later stages of the polymerization. Finally, the increased viscosity, gelation, and ultimately vitrification all limit the mobility of the thiol, TEMPO and base, which negatively influences amine generation and polymerization.

In Fig. 6c, varying amounts of TEMPO were added to stoichiometric PETMP/DVS formulations. As expected, at the same temperature (70 °C), increasing the amount of TEMPO increased the polymerization rate, and the final thiol conversion was limited to 80

90% due to vitrification effects. The samples catalyzed by different TEMPO levels (1, 2, 4 %) showed similar T_g values and modulus behavior, which indicates that the catalytic amount of TEMPO and the corresponding small amount of thiol consumed by the thermal initiation process has a negligible effect on the final properties of the thiol-Michael polymer networks. As compared to conventional thermal-initiated radical polymerizations, thermal thiol-vinyl sulfone Michael-type polymerizations are readily capable of achieving high final functional group conversions in a much shorter reaction period (5–10 minutes) and at relatively mild temperatures, e.g., 70–90 °C. At 25 °C for both of the reactive thiol-vinyl sulfone systems (Fig. 6a and Fig. 6b), the presence of TEMPO leads to stability problems because of the high reactivity of the vinyl sulfone. The less reactive thiol-acrylate system mitigates the problem of limited shelf-life time, which is here demonstrated in a stoichiometric PETMP and TEGDMA system (Fig. S14). However, by sacrificing the monomer system reactivity, these thiol-acrylate systems require higher temperatures (> 90 °C) to achieve rapid thermal polymerization kinetics.

By using the temperature dependent base generation in TEMPO-catalyzed systems, TEMPO was further employed as an efficient initiator catalyst in other base-initiated polymerization reactions. Here, a thiol-isocyanate polymerization was performed with TEMPO initiation in PETMP and HMDI monomer mixtures (Fig. S15). Similar to the thiol-vinyl sulfone polymerization, the thiol-isocyanate system also has a high monomer reactivity that enables fast polymer formation at moderate temperatures.

Thermally-cured TEMPO catalyzed polymer networks: Mechanical Properties

—The thermo-mechanical behavior of thermally polymerized networks was analyzed by dynamic mechanical thermal analysis (DMA) (Fig. 7). Both stoichiometric thiol-acrylate (PETMP/TEGDA) and thiol-vinyl sulfone (PETMP/DVS and SiTSH/DVS) Michael-type addition polymerizations were performed. All thiol-vinyl formulations provided relatively narrow tan delta peaks (T_g 1/2 width around 20–30 °C), which indicates homogenous network formation as a result of the step-growth polymerization mechanism. In Fig. 7a, the TEMPO and TEA (weak base) curing methods were compared in PETMP/TEGDA polymer networks, and no discernible difference was found between these two thermally cured films. DMA analysis was also conducted on networks formed from TEMPO cured thiol-vinyl sulfone resins (PETMP/DVS and SiTSH/DVS). For these systems with high monomer reactivities, facile resin preparation using weak bases is challenging because of the nearly instant gelation that occurs rapidly even during the mixing process. In contrast, it was shown that TEMPO not only extends the sample preparation time extensively, but also exerts its merits of instant dissolution and good solubility in multifunctional bulk monomer systems during sample preparation. Its application has been demonstrated in varied thiol-Michael polymerizations (PETMP/DVS and SiTSH/DVS) yielding materials with different mechanical performance (Fig. 7b). Analogous to the thiol-acrylate resin, TEMPO-cured vinyl sulfone films also form homogeneous polymer networks with sharp and symmetric tan delta peaks.

In this study we elucidated different aspects of the thermally initiated, TEMPO-catalyzed thiol-Michael addition polymerization mechanism and evaluated its catalytic efficiency in both thiol-acrylate and thiol-vinyl sulfone polymerization systems. TEMPO-thiol based

oxidation-reduction reactions lead to TMP at elevated temperatures as a basic species suitable for the initiation of thiol-Michael addition reactions. The TMP species, together with the elevated temperature, contribute to rapid thermal thiol-Michael polymerization at moderate temperatures less than 100°C. The thermal-initiation route provided by TEMPO enables facile preparation of uniform thiol-Michael networks and its application is expected in thermally triggering other base catalyzed polymerizations such as thiol-epoxy and thiol-isocyanate etc. As a whole, its use is expected to diversify the initiation toolbox for thiol-Michael addition polymerizations and extend its application in large scale material preparation, biochemistry, polymer science, and bulk thermoset synthesis under relatively mild thermal conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.
Structures and abbreviations of the chemicals utilized in this study.

Fig. 2.

Absorption spectra changes in phenol red solution upon addition of TEMPO and BT thermal products after different reaction times at the elevated temperature. The TEMPO and butyl mercaptopropionate (BT) mixture (molar ratio of 1:4) was heated at 50 °C, and UV-Vis-analyzed at 0, 1.5, 4, 10, and 20 minutes. Phenol red solution (1.0 mM) was added afterward at ambient temperature as a base indicator, and a new absorption peak is observed with increasing intensity as a function of increasing reaction time.

Fig. 3.

UV-Vis-monitored TEMPO decomposition as a function of the reaction time in TEMPO-thiol redox reactions heated to different temperatures. (a) The TEMPO and 1-hexanethiol (HT) mixture (molar ratio of 1:4) was kept at 23 °C, and UV-Vis samples (0.027 M TEMPO in methanol) were prepared and analyzed every 30 minutes. (b) The TEMPO and HT mixture (molar ratio of 1:4) was heated to 50 °C, and UV-Vis samples (0.027 M TEMPO in methanol) were prepared and analyzed every minute.

Fig. 4.

EPR spectra obtained in TEMPO/BT mixtures with varying heating times. TEMPO was diluted with butyl 3-mercaptopropionate (BT) to 0.96 mM to avoid radical signal saturation in the EPR test. The TEMPO/BT mixture was heated to 50 °C in the EPR tubes and the spectra were collected at 0, 1.5, 4.5, and 8 minutes after heating.

Fig. 5.

(a) UV-Vis spectra of TEMPO/HT redox reaction in DEGDE at 50 °C ([TEMPO]:[HT]:[DEGDE] = 1:4:16). All mixtures were diluted with methanol to appropriate concentrations for the absorption experiments. (b) In TEMPO/HT (molar ratio of 1:4:16) and TEMPO/HT/DEGDE system (molar ratio of 1:4:16), the natural log of the concentration as a function of time used to validate the first order reaction kinetics.

Fig. 6. Thiol conversion as a function of time for (a) PETMP and DVS stoichiometric mixtures heated to 25, 50, 70, and 90 °C supplemented with 2 wt % TEMPO as a thermal initiator; (b) SiTSH and DVS stoichiometric mixtures heated to 25, 50, 70, and 90 °C with 2 wt % TEMPO as a thermal initiator; (c) PETMP and DVS stoichiometric mixtures heated to 70 °C containing 1, 2, and 4 wt % TEMPO as a thermal initiator.

Fig 7. Storage modulus and loss tangent (tan delta) plots for (a) PETMP/TEGDA thiol-acrylate networks triggered with 2 wt % TEMPO and 2 wt% TEA at 70 °C (b) SiTSH/DVS and PETMP/DVS thiol-vinyl sulfone networks.

Scheme 1.

Proposed reaction diagram of TEMPO as a thermal initiator for thiol-Michael addition reactions including polymerizations .

Scheme 2.

The proposed reaction mechanism of the redox reaction between TEMPO and a thiol.

Table 1

Monitored with UV-Vis spectra, the thermal redox reactions were evaluated by varying the reaction temperatures, thiol types and reactant concentrations. k_d (s^{-1}) was calculated from the concentration as a function of time. The corresponding UV-Vis spectra versus reaction time and the fits are provided in Fig. 7 and Fig. S5 to Fig. S11 in the supporting information.

Components	Molar ratio	TEMPO concentration	Temperature ($^{\circ}C$)	k_d (s^{-1})
TEMPO ^a	-	0.064 M	80	-
TEMPO/BT	1:4	6.16 M	50	3.3×10^{-3}
TEMPO/HT	1:4	7.04 M	50	6.5×10^{-3}
TEMPO/HT	1:4	7.04 M	40	2.0×10^{-3}
TEMPO/HT	1:4	7.04 M	35	6.8×10^{-4}
TEMPO/HT	1:4	7.04 M	23	1.4×10^{-4}
TEMPO/HT/DEGDE	1:4:4	2.01 M	40	1.5×10^{-3}
TEMPO/HT/DEGDE	1:4:8	1.16 M	40	1.0×10^{-3}
TEMPO/HT/DEGDE	1:4:16	0.65 M	40	7.5×10^{-4}

^a TEMPO heated without thiol moieties in DMSO solution and determined with NMR.

Table 2

Stoichiometric mixtures of different divinyls and butyl 3-mercaptopropionate thermally initiated with catalytical amount of TEMPO. The model reactions were conducted at 23 °C and 80 °C for 90 minutes without any solvent, and the reaction were monitored by ¹H-NMR (some samples crystallized into solid after reaction).

TEMPO loading	butyl 3-mercaptopropionate and DVS reaction yield (%)		butyl 3-mercaptopropionate and TEGDA reaction yield (%)	
	23 °C	80 °C	23 °C	80 °C
0 wt%	0	0	0	0
1 wt%	10	94	7	90
2 wt%	14	100	10	99
3 wt%	18	100	12	100