Visible-Light Initiated Thiol-Michael Addition Photopolymerization Reactions

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Ⓢ *Supporting Information*

ABSTRACT: A visible-light base generating system was successfully employed in catalyzing the thiol-Michael addition reaction to yield cross-linked polymers from a stoichiometric mixture of model thiol and vinyl monomers. Implementation of the radical inhibitor TEMPO with a combination of a photosensitizer (isopropylthioxanthone, ITX) and a photobase generator (triazabicyclodecene tetraphenylborate, TBD·HBPh₄) resulted in suppression of radical mediated side reactions and provided stoichiometric and complete conversion of both thiol and vinyl functional groups. The new initiating system acts as an efficient visible-light photobase generator that improves the orthogonality of the thiol-Michael addition with respect to off-stoichiometric radical thiol-vinyl addition/vinyl chain reactions. This approach opens up a variety of possibilities for base-catalyzed reactions in multiple applications such as coatings and biomaterials that require biocompatible, environmentally friendly, and low-energy visible-light initiation.
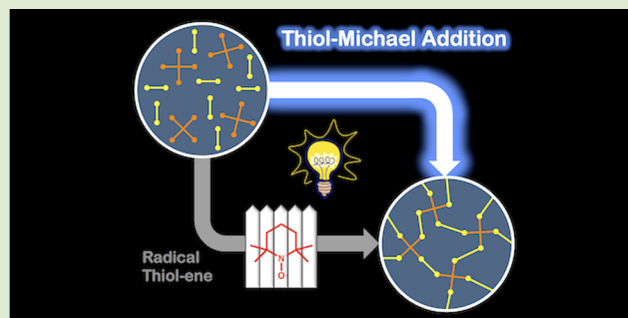
The thiol-Michael addition reaction is a robust, highly efficient "click" reaction that provides high functional group conversion, high reaction rates and orthogonality to other reactions under mild reaction conditions, either in bulk or in environmentally benign solvents.[1−4] It is an addition reaction between thiols and electron deficient vinyls and is often catalyzed by bases or, more recently, by nucleophilic initiators.[5−7] These advantages make this reaction a powerful tool in the area of polymer chemistry, most frequently in polymerization, polymer functionalization, surface modification and bioconjugation.[4] However, unlike other "click" reactions such as the radical-mediated thiol−ene reaction[1−3] and the Cu-catalyzed alkyne−azide reaction,[8−12] this thiol-Michael reaction lacks an efficient photoinitiating system, that is, photobase generator (PBG),[13−15] that could provide spatial and temporal control over its reaction. In addition, visible light initiators are becoming more popular, mainly due to the ability to initiate with lower photon energies, reduced cytotoxicity, compatibility with UV absorbers and greater curing depths.[16] There are a few reports of visible light sensitive PBGs, which are mostly combinations of PBGs (e.g., *O*-acyloximes, ionic complexes of protonated base and tetraphenylborate anion) and sensitizers (e.g., derivatives of isopropylthioxanthone (ITX), ketocoumarin). In general, sensitizers possess longer wavelength absorption (>400 nm) and allow PBGs to perform photochemical reactions via triplet energy transfer from sensitizers to PBGs. In consequence, the base could be generated by light with wavelengths that PBGs originally could not absorb. Shirai and co-workers reported that photolysis of acyloxyimino and

carbamoyloxyimino groups, both of which photoreactions are generally carried out by light with wavelength below 300 nm, could be performed with visible light with wavelength above 400 nm using triplet sensitizers, such as ITX and ketobiscoumarin derivatives.[17] ITX has also been utilized as a sensitizer for tetraphenylborate type ionic complexes to catalyze the thiol-isocyanate reaction[18] and the thiol-Michael addition reaction.[19] However, in these cases, light at 320−390 nm was used to initiate the reactions, and the efficiency of these reactions using light above 400 nm was not discussed. In addition, radical-mediated side reactions such as vinyl−vinyl chain reactions were observed due to the generation of radicals from ITX and tetraphenylborate degradation products, which points out that the photobase generating systems containing only photosensitizers lack reaction control and orthogonality.

In this study, a radical inhibitor 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) was incorporated into a ITX/tetraphenylborate photobase system to promote a stoichiometric reaction between the thiol and vinyl groups (Figure 1) via the traditional base-catalyzed thiol-Michael addition reaction pathway by inhibiting the radicals to avoid any homopolymerization.

As indicated in previous work employing ITX/PBG systems, light irradiation in these systems lead to the simultaneous generation of both bases and radicals.[18,19] Therefore, applying these initiator systems to the thiol-Michael addition reaction
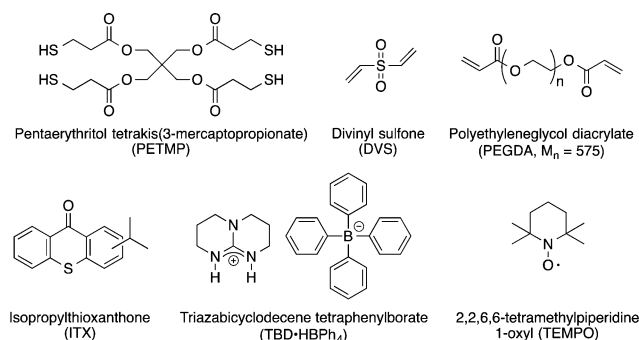
Figure 1. Chemical structures of the compounds used in this study.

Figure 2. Functional group conversion plots as a function of time for stoichiometric (a) PETMP/DVS and (b) PETMP/PEGDA reacted using ITX/TBD·HBPh$_4$ (0.5/1.0 wt %) as an initiator system and reacted with 400−500 nm light. The light intensity was 50 mW/cm^2 and was switched on after 2 min of data acquisition. Thiol conversions were lower than vinyl conversions in both systems, which is in agreement with previous study.[19]

would generally result in the occurrence of both the thiol-Michael addition reaction of thiol to vinyl, and the radical mediated thiol-vinyl addition as well as vinyl−vinyl chain polymerization. In the case of a system that contains a stoichiometric amount of thiol and vinyl functional groups, the former reaction will provide stoichiometric consumption of both functional groups, whereas the latter reaction will predominantly consume vinyls, leaving residual thiols un-reacted. Such a trend was clearly observed in a reaction between PETMP (tetra-thiol) and DVS (divinyl), which was initiated by ITX/TBD·HBPh$_4$ (0.5/1.0 wt %) as an initiator and irradiated by 400−500 nm light with an intensity of 50 mW/cm^2 (Figure 2a). After 1 h of irradiation, the functional group conversions of the thiols and vinyls were measured to be 63 and 73%, respectively. This difference in thiol and vinyl conversions was more pronounced in a second model reaction between PETMP and PEGDA (M_n = 575, diacrylate) using the same initiator system and light intensity, in which thiol and vinyl conversions after 10 min of irradiation reached 54 and 99%, respectively (Figure 2b). This increased difference in final conversions arises from the high reactivity of acrylate−acrylate chain growth reactions via the radical-mediated pathway, which also contributes to the high acrylate conversion being achieved in a relatively short time period. Another factor for reaching high conversion in relatively short times is associated with the high mobility of the PEG-rich network chains as compared to the more cross-linked network structure formed by the reaction of the lower molecular weight DVS.[6] These polymers, reacted by radical and base mixed-mode, are likely lead to be more heterogeneous polymers with a significant amount of unreacted functional groups that would result in reduced thermomechanical properties and long-term property stability.

TEMPO is a molecule that contains a stable radical and is well-known as a highly efficient radical inhibitor or even a radical trap.[20] Therefore, we hypothesized that by adding TEMPO into an ITX/TBD·HBPh$_4$ system, the radical mediated pathway could be eliminated, or at least drastically suppressed so that the reaction could proceed primarily via the base catalyzed, stoichiometric thiol-Michael addition pathway. Figure 3 shows the reaction kinetics of PETMP/DVS and PETMP/PEGDA systems using ITX/TBD·HBPh$_4$/TEMPO (0.5/1.0/0.5 wt %) as an initiator system and irradiated by light at 400−500 nm with an intensity of 50 mW/cm^2. Obviously, inclusion of TEMPO resulted in a significant change in the observed kinetic characteristics of these systems. First of all, thiol and vinyl conversions were almost identical during irradiation at all times in both systems. This outcome is a strong indication that there are minimal radical-mediated reactions occurring throughout the reaction. Second, an
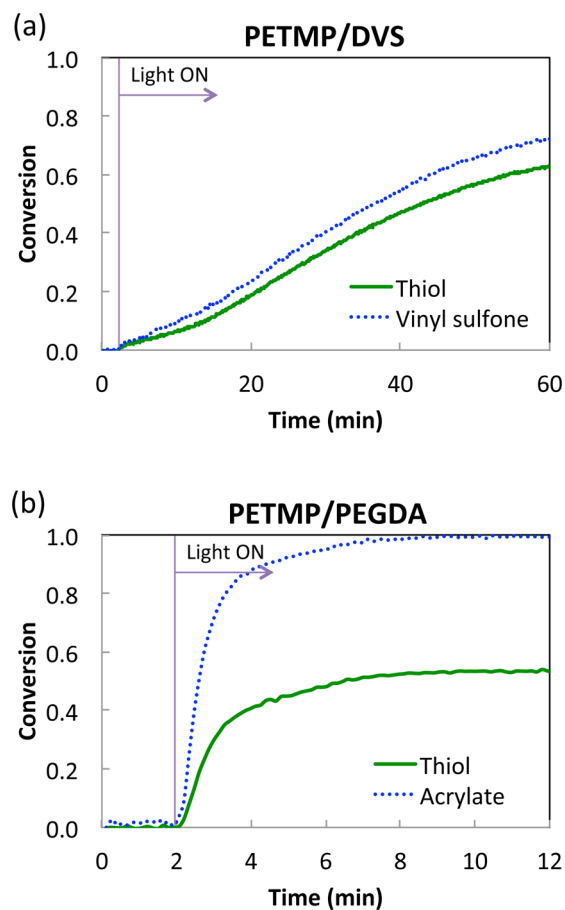
induction time was observed in both systems, which implies that no rapid acrylate homopolymerization occurred and the reaction between the thiol and vinyl was catalyzed only by the photogenerated base. A different ketocoumarin type triplet sensitizer, 7-diethylamino-3-thenoylcoumarin (DEATC, Figure S2), could also be used as a sensitizer instead of ITX to obtain stoichiometric reaction of PETMP/DVS (Figure S2). The reaction rate was slightly lower than in the system with ITX, however, DEATC could be advantageous since its absorption spectrum is shifted to even longer wavelengths (Figure S3) and has a potential to be used with longer wavelength light sources (Figure S4).

Another interesting aspect of this PBG system is that the reactive intermediate is still active after cessation of irradiation (in dark), which assures high conversion and also enhances the cure depths that can be achieved. The reaction was confirmed to progress even after the light was turned off (Figure S1), which strongly indicates that the reaction was catalyzed by the base, as radical lifetimes in the dark are extremely limited in these types of systems. The final conversions are summarized in Table 1 for both thiol and vinyl groups after thermally annealing the samples at 60−70 °C for 1 h after irradiation. Systems with ITX/TBD·HBPh$_4$/TEMPO initiator both lead to nearly complete conversion of both the thiol and vinyl groups.
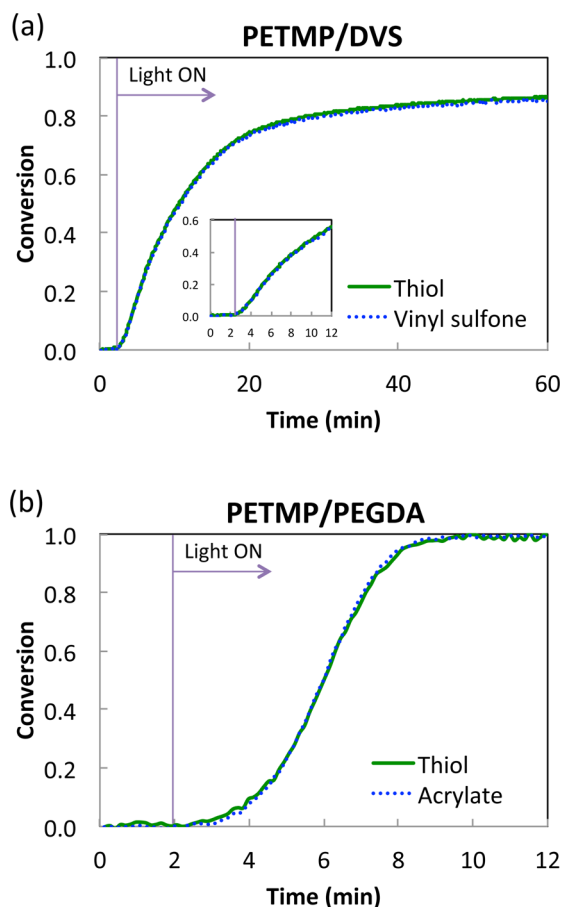
(a)

PETMP/DVS

(b)

PETMP/PEGDA

Figure 3. Functional group conversion plots as a function of time for stoichiometric (a) PETMP/DVS and (b) PETMP/PEGDA containing ITX/TBD·HBPh$_4$/TEMPO (0.5/1.0/0.5 wt %) as an initiator system and reacted with 400−500 nm light. The light intensity was 50 mW/cm^2 and was switched on after 2 min of data acquisition. Inlet of (a) shows magnified view of the initial stage of the reaction. The thiol and vinyl groups reacted stoichiometrically throughout the reaction.

Table 1. Functional Group Conversions after Light Irradiation (50 mW/cm^2, 60 Min Irradiation for PETMP/DVS, and 10 Min Irradiation for PETMP/PEGDA) and Heating 1 h at 60−70 °C[a]

initiator	ITX/TBD·HBPh$_4$		ITX/TBD·HBPh$_4$/TEMPO	
conversion (%)	thiol	vinyl	thiol	vinyl
PETMP/DVS	89 ± 5	100 ± 0	96 ± 3	99 ± 1
PETMP/PEGDA	54 ± 8	100 ± 0	95 ± 4	100 ± 0

[a]The initiator used was either ITX/TBD·HBPh$_4$ (0.5/1.0 wt %) or ITX/TBD·HBPh$_4$/TEMPO (0.5/1.0/0.5 wt %). Conversions were determined by FT-IR.

In contrast, systems without TEMPO resulted in much lower thiol conversion due to the extra vinyl consumption from radical mediated reactions.

Phenol red indicator was used to confirm the generation of bases from the photolysis of TBD·HBPh$_4$.[21] Therefore, this indicator was used to verify and compare the base generating ability of two different systems, ITX/TBD·HBPh$_4$ and ITX/TBD·HBPh$_4$/TEMPO. Initially, directly varying the concentrations of TBD in acetonitrile was tested using the phenol red indicator. These experiments confirmed that the solution color

changes from yellow to orange and eventually to dark purple with increasing TBD concentration (Figure S5) accompanied by the appearance of a new band at 560 nm in the UV−vis absorption spectra. Samples containing 1.2×10^{-3} M ITX and 1.2×10^{-3} M TBD·HBPh$_4$ with (and without) 1.2×10^{-3} M TEMPO were prepared in acetonitrile (total 0.800 mL), followed by irradiation using 13 mW/cm^2 400−500 nm filtered light for 5, 6, 8, and 10 min. Each sample with a different irradiation time was prepared separately, and the phenol red acetonitrile solution (1×10^{-3} M, 0.080 mL) was added after irradiation and used to determine the base concentration from UV−vis spectroscopy. Absorption at 560 nm was increased by longer irradiation times for both ITX/TBD·HBPh$_4$ and ITX/TBD·HBPh$_4$/TEMPO systems; however, interestingly, the absorption at 560 nm was always higher for the ITX/TBD·HBPh$_4$/TEMPO system at a given irradiation time, which indicates that this system generates base at a higher rate and efficiency as compared to the ITX/TBD·HBPh$_4$ system (Figure S6). This result supports the kinetics presented in Figures 2a and 3a, in which the reaction rate was increased by adding TEMPO into the system due to the higher base generation rate. A similar phenomenon was not observed in the PETMP/PEGDA system (Figures 2b and 3b), since the rates of radical mediated reactions of acrylates are much higher than that of the thiol-Michael addition reaction, and the effect of TEMPO addition to the reaction kinetics mainly appeared as the decrease of the initial reaction rate caused by radical inhibition and also in the off-stoichiometric nature of the radical reaction.

Finally, mechanical properties of polymer networks that were synthesized using either ITX/TBD·HBPh$_4$ (0.5/1.0 wt %) or ITX/TBD·HBPh$_4$/TEMPO (0.5/1.0/0.5 wt %) as an initiator were compared. Polymer samples using a stoichiometric mixture of PETMP/DVS were prepared by light irradiation (50 mW/cm^2, 1 h irradiation) and post-heating for 1 h at 60−70 °C. Figure 4 shows tan δ curves for both systems. Polymer networks synthesized with TEMPO (blue) exhibited a higher T_g and narrower tan δ curve, which is in agreement with the FT-IR results, which confirmed nearly complete conversion of both thiol and vinyl functional groups. In comparison, polymer networks without TEMPO (red) showed lower T_g and wider
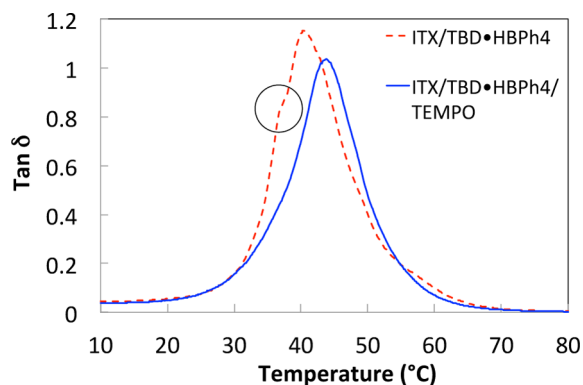

Figure 4. Tan δ plots for (a) ITX/TBD·HBPh$_4$ initiator system (dotted red) and (b) ITX/TBD·HBPh$_4$/TEMPO initiator system (blue). (a) Occurrence of radical mediated side reactions could be recognized from both peak broadening and a shoulder on the peak (circle). (b) In comparison, the existence of a radical inhibitor TEMPO eliminates radical-mediated side reactions to form a homogeneous polymer network, as could be confirmed from a sharp single tan δ peak.

tan δ curve with a shoulder that indicates lower functional group conversion (thiol: 89%, Table 1) and visibly affected network homogeneity due to radical mediated side reactions.

In summary, stoichiometric reaction of thiols and electron deficient vinyls initiated by visible light irradiation was achieved by using ITX/TBD·HBPh$_4$/TEMPO as an initiating system. An addition of TEMPO both facilitates base generation and inhibits radical mediated side reactions. This method is exceptionally useful since it provides controlled stoichiometric reaction between thiols and vinyls via visible light irradiation, which could not be achieved using ITX without TEMPO due to its propensity to cause radical mediated side reactions. This visible-light sensitive photobase generator is one of few recent examples that have the potential for base-catalyzed reactions such as the thiol-Michael addition reaction to be implemented in range of applications, for example, coatings and biomaterials that benefit from a biocompatible, environmentally benign character of visible light initiation.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

Materials and methods and UV−vis and supplemental kinetic data. 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 interest.

■ ACKNOWLEDGMENTS

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