A Versatile Approach for In Situ Monitoring of Photoswitches and Photopolymerizations

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A simple, inexpensive, and modular method to directly illuminate NMR samples for in situ analysis of photochemical transformations is reported. The versatility of this technique is demonstrated by analyzing the light-induced propagating front for small-molecule photoswitches and the kinetics of photocontrolled living radical polymerizations. In situ measurements allow oxygen-sensitive and rapid photoevents to be studied in detail, leading to reliable determination of photoswitching quantum yields and polymerization rates. By systematically tuning light intensity, a direct relationship between propagation rate and intensity is revealed. Of particular note is the facile translation of the conditions identified through this NMR analysis to analogous benchtop experiments with insight into the nature of the photoreactive species.

1. Introduction

Photochemical transformations encompass a wide variety of reactions, including deprotection, acid/base generation, dehalogenation, isomerization, and polymerization, where the absorption and conversion of photon energy is central.[1,2] Over the past decade, the design of new photochemical switches[2−16] and photopolymerization processes[17−25] has led to functional platforms with applications in actuators, sensing, biology, catalysis, and electronics. A key to these advances has been insight into the mechanism and pathway of the photochemical processes with the most commonly utilized techniques to probe these reactions being ultraviolet-visible (UV/vis) absorption,[10,26] real-time Fourier transform (near) infrared (RT-FT(N)IR) absorption,[25,27,28] and nuclear magnetic resonance (NMR)[16,22,23,29,30] spectroscopies. Although operating effectively at different concentrations, important criteria to consider for each technique include: 1) utilization of probe radiation outside the active range of the system under observation, 2) modularity of external stimuli (for example temperature and light intensity), 3) technical simplicity and low cost, and 4) high resolution with fast acquisition times (on the order of seconds).

UV/vis-based strategies utilize ultraviolet and visible light as a probe, which is often within the active energy window for stimulating the photochemical process under study, making it undesirable as a monitoring method (especially for sensitive systems). Similarly, RT-FT(N)IR absorption does not provide a high degree of detailed structural information and the desired signals may be diluted by those from overlapping solvent absorption. In contrast, NMR spectroscopy is a common, versatile, and rapid technique, which provides detailed information about molecular structure and composition and uses non-invasive radio frequencies as a probe. Although successful for conventional thermal reactions, a number of issues still persist with employing NMR procedures for the study of photochemical processes. These include relatively high concentrations of NMR experiments (mm range) as compared to UV/vis absorption spectroscopy (μm range), along with manual transfer of a photochemical reaction mixture, or an aliquot thereof, to an NMR tube. As for FT(N)IR approaches, this is time consuming and provides a dataset limited by transfer rate as opposed to measurement acquisition. Moreover, removing aliquots from a reaction can lead to contamination (e.g., oxygen) and continually decreases the volume of the system. Alternatively, direct illumination and monitoring has been accomplished within an NMR spectrometer, either by installing a light source inside the instrument or using an optical fiber, which typically requires probe modification or a coaxial glass insert, respectively.[31−43] The use of light-coupled optical fibers with NMR spectroscopy has distinct advantages from the standpoint of technical simplicity, compatibility with a wide radiation range (UV–IR), and relatively low cost (compared to probe modifications). Apart from traditional coaxial capillary inserts, “pencil tip” inserts[34,39] and fiber-tip etching procedures[31,33] have been utilized to pro-

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vide uniform light distribution within the NMR measurement zone, but does not lead to the formation of a propagating reaction front needed to determine photoswitch isomerization quantum yield ($\Phi$; see below). However, etching of delicate optical fibers requires harsh conditions, such as the use of hydrofluoric acid, and can be difficult to reproduce, while coaxial capillary inserts often lead to reduced sensitivity.

Herein we report a simple NMR-based technique to monitor photochemical transformations in situ using inexpensive and universal optical-fiber inserts, coupled with modular, computer-controlled LED irradiation. To illustrate the utility of this strategy, the $\Phi$ of two photochromic small molecules, a donor–acceptor Stenhouse adduct (DASA) \cite{ref1, ref2, ref3, ref4, ref5} as well as a diarylethene (DAE) \cite{ref6} were determined from optically dense propagating fronts. Complementing the small-molecule studies, this new technique was also used to analyze several light-driven controlled polymerizations, leading to kinetic insights and a detailed understanding of molecular weight, structure, and dispersity evolution with conversion \cite{ref7, ref8, ref9}. These examples showcase the versatility and potential impact of our method on the broad field of photochemistry.

2. Results and Discussion

2.1. NMR Illumination Setup

In this work, a length of optical fiber connected to modular LEDs (Thorlabs) with controllable intensity, is centered over an NMR sample and used to collect real-time data on photochemical transformations. Initial attempts to irradiate samples without centering the fiber tip gave irreproducible results due to non-uniform illumination. To remedy this, a small universal Teflon insert, designed to fit standard 5 mm NMR tubes, allowed for the tip of the optical fiber to be centered directly above the sample, thereby ensuring uniform lateral irradiation during measurement (an engineering drawing of the Teflon insert is provided in Figure S1 in the Supporting Information). As compared to typical glass coaxial inserts, the reusable Teflon inserts can be fabricated with simple machinery to keep cost to a minimum, and have the added benefit of being both mechanically and chemically robust. Additionally, the LEDs used to illuminate the samples are modular, having tunable light intensities for wavelengths spanning from the deep-UV to far-IR regions, suitable for a wide range of photochemical processes (Figure 1). The light intensity of the LEDs was controlled by modulating the current output of a commercial LED driver and provided an intensity range from 4 to 66 mWcm$^{-2}$, 4 to 114 mWcm$^{-2}$, 8 to 140 mWcm$^{-2}$, and 6 to 68 mWcm$^{-2}$ for the warm-white (4000 K, $\lambda$ = 400–800 nm), violet (405 nm), blue (470 nm), and green (530 nm) LEDs used in these studies, respectively (see Figure S2 for LED profiles and intensities). Additionally, a LabVIEW program was written to control the light intensity of the LED as well as control light “on” and “off” times for cycling experiments.

2.2. Photoswitch Front Propagation

Donor–acceptor Stenhouse adducts (DASAs) represent a new class of “negative” or “reverse” photochromes and were selected for initial study due to their high molar absorptivity ($\epsilon \approx 100,000 \text{ M}^{-1} \text{ cm}^{-1}$) in the visible range of the spectrum and characteristic $^1$H NMR signal shifts upon photosomerization (Figure 2). \cite{ref1, ref2, ref3, ref4, ref5} These features allow the two forms of the DASA switches, that is, the colored “open” triene 1 and the colorless “closed” cyclopentenone 2, to be identified and tracked throughout the process. Importantly, during the measurement employing irradiation with visible light, it is only the colored form 1, but not its colorless valence tautomer 2, which absorbs and thus only ring closure is taking place. Briefly, a 10 mM tolune solution of the open tetrahydroquinoline (THQ) barbituric acid derivative 1 was irradiated using a white LED (46 mWcm$^{-2}$) through the optical fiber/Teflon insert with a circa 2 mm gap between the tip of the fiber and the top of the DASA solution (Figure 2B; absorption profile Figure S3; thermal equilibration Figure S4). Due to the high optical density of 1, 99.9% of the white light coming from the optical fiber tip is absorbed within the first 10 $\mu$m of the solution, with photosomerization to colorless 2 allowing for the light to progressively penetrate deeper into the solution, generating a front that propagates in a linear fashion over time. This regular propagation rate suggests that the solvent and tube act as an efficient “waveguide” (Figure S5), retaining uniform light intensity throughout the measurement. The samples were measured in the dark for two scans (30 s scan$^{-1}$), followed by illumination, with the resulting photochemical transformation being
tracked over time by integrating the N-methyl protons of the barbituric acid, which shift from $\delta = 3.22$ and $3.08$ ppm ($H_d$) in 1 to $2.99$ and $2.76$ ppm ($H_b$) in 2 (Figure 2C; the full $^1$H NMR spectrum is given in Figure S6). Plotting the relative fraction of 1 revealed three distinct regions: 1) buffering, where the front has not entered into the measurement window; 2) active, where photoswitching occurs in the measurement window; and 3) post-active, where the front has passed through the measurement window. Notably, a linear front is observed as it moves through the measurement window, in good agreement with video analysis (represented as $X$'s in Figure 3B and showed as still images in Figure 2B). The utility of this method was also demonstrated by analyzing front-propagation kinetics with respect to the effective power (considering only light absorbed by 1). Simple tuning of the LED provided a comprehensive range of irradiation powers to be effectively studied, resulting in a linear relationship from about 4 to $54$ mW/cm$^2$.

Given the complete disappearance of absorption bands in the visible region, these materials follow the equation developed by Pearlstein and Terrones$^{[59]}$ describing idealized photoinitiation fronts from perfectly bleaching molecules [Eq. (1)]:

$$S(z, t) = [1 - e^{-\omega z}e^{-\Phi t} (1 - e^{-\Phi t})]^{-1}$$  \hspace{1cm} (1)$$

where $\alpha$ is the molar extinction coefficient, $C_0$ is the initial concentration, $z$ is the position, $I_o$ is the incident photon flux at the surface, $\Phi$ is the quantum yield, and $t$ is time. Though diffusion is not accounted for in Equation (1), numerical solutions for the governing equations yield nearly identical results to those expected for typical small-molecule diffusion coefficients.$^{[60]}$ For solutions where $\alpha$ and $C_0$ are sufficiently large, as is the case for the DASA samples measured here, the front velocity ($V$) simplifies to the following form [Eq. (2)]:

$$V = \frac{\Phi I_o}{C_0}$$  \hspace{1cm} (2)$$

This behavior is independent of the exact $\alpha$ value, which is advantageous given the difficulty associated with measuring $\alpha$ for transient photoswitches (e.g., thermodynamic state not in the colored form). As seen in Figure 3, the front speed is linear with intensity as predicted by Equation (2). Therefore, the slope of this line can be used to estimate the $\Phi$ value of the switch, which for 1 was found to be 0.15, and opens up interesting questions regarding the associated consequences of DASA structure, solvent polarity, and surrounding temperature on $\Phi$.$^{[26]}$ To the best of our knowledge, this is the first reported use of the above equations for the determination of $\Phi$ for a photoswitchable molecule. To affirm the accuracy of this technique, a classic diarylethene photoswitch (DAE), 1,2-bis[2-methylbenzo[7]thiophen-3-yl]-3,3,4,4,5,5-hexafluoro-1-cyclopentene, with a known $\Phi$ (about 0.3)$^{[61-63]}$ was measured (the structure, absorption profile, and $^1$H NMR spectra given in Figures S3 and S7). The previously used white LED was exchanged with a 530 nm LED and photoisomerization of the colored closed form to the colorless open form of DAE in toluene at different light intensities was monitored inside the NMR spectrometer to determine a series of front velocities. A $\Phi$ value of 0.30 for the ring-opening reaction was obtained, which is consistent with literature reports.$^{[61-63]}$ Given the simplicity of the governing equation, Equation (2), this NMR-based method offers significant potential for the rapid screening of otherwise difficult-to-analyze photochromic compounds.$^{[64]}$ In addition, the method is particularly useful for negative photochromic systems, also known as T-type, since NMR allows for convenient measurements at low temperatures, at which the thermal back reaction of the colorless metastable form is slow/negligible.

2.3. Controlled Photopolymerizations

To further demonstrate the versatility of this technique, several light-driven controlled polymerization systems were subsequently studied (Figure 4A; NMR spectra provided for all sys-
which would be difficult to translate these measurements to a typical benchtop-scale, batch reaction, a constant light intensity (140 mW cm\(^{-2}\)) was used with the scale of the polymerization ranging from 0.1 to 3.0 g of MA (Figure S12). Significantly, similar \(k_p\) values and monomer conversion were observed between the in situ NMR experiments and the benchtop polymerizations with both systems showing a correlation between reaction scale and light intensity. This suggests facile transfer of \(k_p\) values determined in a small-scale NMR experiment to large-scale batch processes under known irradiation intensities.

Temporal control is a particularly sought-after feature that has been achieved with living photopolymerizations, where aliquots are again traditionally used to monitor chain growth during cycles of light “on” and “off”. Two PET-RAFT systems and one photo-atom transfer radical polymerization (photo-ATRP) system were therefore monitored using this in situ NMR strategy and rich kinetic data was acquired during automated “on”/“off” cycling (Figure 4C). Systems examined were: i) MA, [Ru(bpy)\(_3\)]\(Cl_2\) (87 ppm relative to the monomer), and BTPA with 470 nm illumination at 35 mW cm\(^{-2}\); ii) N,N-dimethylacrylamide (DMA), tris(2-phenylpyridinato-C\(^2-\))Ir(III) [Ir(ppy)\(_3\)] (66 ppm relative to monomer), and BTPA with 405 nm illumination at 23 mW cm\(^{-2}\); and iii) methyl methacrylate (MMA), [Ir(ppy)\(_3\)] (66 ppm relative to the monomer), and ethyl \(N\)-bromophenylacetate (EBPA) with 405 nm illumination at 114 mW cm\(^{-2}\) (Figure 4C). Impressive temporal control is observed for all three systems, where rapid polymerizations halt when the light is turned “off” and begin again within 18 sec of the light being turned “on”; notably, with the same \(k_p\) values for each “on” cycle (\(k_p\) = 2.04, 2.92, and 0.13 h\(^{-1}\) for MA, DMA, and MMA, respectively).

For “living” polymerizations, DP versus conversion is a linear relationship, and as a final measure of “control” this was deter-
mined for PET-RAFT of MA using 1D and 2D NMR spectroscopy (Figure 4D). 1H NMR spectroscopy was used to determine both DP and conversion by comparing the integration of polymer backbone protons and either the polymer chain-end proton located α to the carboxylic acid (for DP) or vinyl monomer protons (for conversion; see Figures S9-S11). Six time points were taken and a plot of DP versus conversion revealed a linear relationship, indicative of a “living” polymerization (Figure 4D). Moreover, diffusion-ordered spectroscopy (DOSY) was used to determine DP relative to poly(methyl methacrylate) (PMMA) standards and show the compatibility of this technique with 2D NMR spectroscopy. Diffusion coefficients (D) were measured during six “off” cycles and interpolated in a PMMA calibration curve to determine DP (corresponding details are given in the Supporting Information, see Table S1 and Figures S14 and S15). The results again show a linear relationship, with the data being consistent with that obtained from 1D NMR spectroscopy. The ability to monitor photopolymerizations in real time using 1D and 2D NMR spectroscopy is a powerful combination, and can be used to provide additional information from a single photopolymerization sample, including intrinsic viscosity (η), weight average molecular weight (Mw), and D.15,56

One of the unique advantages of NMR analysis is the ability to identify and monitor specific molecular entities in reaction mixtures. In this case, the 1H NMR signals from the CTA were visible and on insertion of one or more acrylate units, a distinct change in the chemical shift (δ), in particular for the proton located α to the trithiocarbonate group (Hc to Hδ), is observed (Figure 5). Complete reaction of the CTA leading to the trithiocarbonate chain ends of the growing polymers (that is, initiation) is an important aspect for RAFT, as the rate of initiation must greatly exceed propagation for a controlled/living polymerization. Fast consumption of the CTA leads to narrower D and a more controlled process. Upon examination of the NMR spectra for the polymerization, described in Figure 4B, the conversion at which all CTA was incorporated into the monomer chain ends increased with catalyst loading from 13, to 16, to 20% for 44, 87 and 175 ppm (relative to monomer), respective-

![Figure 4](image1.png)

**Figure 4.** Monitoring controlled photopolymerization kinetics. A) Reaction scheme for polymerization of i) MA by PET-RAFT, ii) DMA by PET-RAFT, and iii) MMA by photo-ATRP. Kinetic traces of all three polymerization systems are shown in Figure S13. B) Kinetic plot of MA conversion over time at three light intensities, where X symbols represent aliquots from representative benchtop reactions at three different scales of monomer, using the highest light intensity. The X’s have been shifted to account for the inhibition time present in the NMR samples due to oxygen contamination. C) A series of “on”/“off” plots showing detailed temporal control of (i), (ii), and (iii) where the light intensity and cycles were digitally controlled. D) Degree of polymerization versus conversion determined by 1H (blue circles) and DOSY (orange squares) NMR, as well as a theoretical line for (i) targeting a DP of 200.

![Figure 5](image2.png)

**Figure 5.** Monitoring CTA incorporation at different catalyst loadings relative to monomer. A) Reaction scheme denoting the observable chemical shift when going from the intact small molecule (Hc) to the fully incorporated CTA (Hδ). B) Plots of conversion versus time, with the point of full CTA incorporation marked with an X. Inset: NMR signals used to determine CTA conversion.
Table 1. Results from the CTA study shown in Figure 5. Polymerizations were carried out to 70% monomer conversion in all cases and molecular weights and dispersities were measured using GPC in chloroform relative to polystyrenes standards.

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[a] Mₙ = number average molecular weight; Mₚ = peak molecular weight.

ly (marked by X symbols in Figure 5B). Table 1 shows the molecular weight and D value obtained from gel permeation chromatography (GPC). As predicted, the increased catalyst loadings, which had higher conversion for complete CTA incorporation, have a larger D value, increasing from 1.14 to 1.24, and 1.30 for 44, 87, and 175 ppm catalyst loadings, respectively (Figure S16). The ability to simply measure these trends with high-molecular-weight precision is made possible by this technique and is the first time a photomediated controlled polymerization process has been monitored in real time using NMR spectroscopy.

3. Conclusions

In summary, a method to monitor photochemical transformations with in situ NMR spectroscopy using fiber-coupled LEDs and reusable Teflon inserts was presented. Observing the front propagation of optically dense DASA and DAES photoswitch solutions led to a unique way of determining reaction quantum yields, while rich kinetic data on PET-RAFT of MA revealed different levels of polymerization "control" as well as a relative prediction for dispersity of the growing polymer chains. By removing the requirement for obtaining aliquots to monitor reactions in a rather invasive manner, our direct and non-invasive technique serves to streamline researchers' efforts to analyze new photochemical processes. As shown here, basic one-dimensional NMR spectroscopy can be insightful with this novel illumination technique being easily used in combination with two-dimensional NMR spectroscopy to provide more complex structural, compositional, and dynamic information. It is anticipated that this method will be beneficial for future developments in both small molecule and polymer photochemistry.

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