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Wavelength-Controlled Dynamic Metathesis: A Light-Driven Exchange Reaction Between Disulfide and Diselenide Bonds

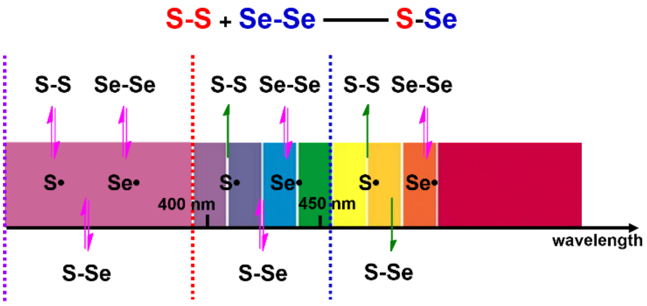
Fuqiang Fan[‡], Shaobo Ji[‡], Chenxing Sun, Cheng Liu, Ying Yu, Yu Fu, and Huaping Xu*

Abstract: Though wavelength-controlled dynamic processes have been well developed, they mostly consist of light-triggered isomerization or the cleavage/formation of molecular connections. Control over dynamic metathesis reactions by different light wavelengths, which would be useful in controllable dynamic chemistry, has rarely been studied. Herein, taking advantage of the different bond energies of disulfide bonds and diselenide bonds, we realized a wavelength-driven exchange reaction between disulfides and diselenides. These molecules underwent metathesis under UV light to produce Se-S bonds. When irradiated by specific visible light, the Se-S bonds were reversed to the original reactants. The conversions of the exchange reaction were found to depend on the wavelength of light, and the exchange mechanism was studied. This light-driven metathesis chemistry was also applied to tune mechanical properties of polymer materials. Furthermore, the visible light-induced reverse reaction was compatible with reductant catalyzed disulfide/diselenide metathesis and provides the potential for a dissipative system using light as the input energy.

Dynamic covalent bonds (DCBs) are capable of being cleaved or formed under certain conditions and have been extensively used in stimuli-responsive systems, dynamic combinatorial chemistry, and dynamic materials[1-6]. The applications in dynamic combinatorial chemistry have provided new methods for drug discovery and simplified the screening of target molecules in various fields[7-10]. Dynamic materials, such as self-healing polymers and vitrimers, can extend the lifetime of polymer materials and enhance their recyclability[11-13]. Thus, DCBs are of significance at both the molecular level and materials level. The dynamic properties of DCBs are triggered by various conditions, such as heating[14,15], pH[16-18], redox conditions and light[19,20].

Among them, light is an outstanding stimulus to trigger or control chemical reactions. This stimulus can be introduced at a distance with high spatial and temporal resolution, which leads to accurate controllability. The parameters of light are highly variable—light can be introduced by different sources in various forms, such as lasers or patterns. In addition, the wavelength, intensity, and polarization are all tunable. On account of these advantages, light-controlled reversible/dynamic processes have also been studied and well established[21-24]. The commonly used processes include trans-cis isomerization of azobenzene[25-28], spiropyran[29] and photoinduced π-electrocyclization of diarylethenes[30-33]. Metathesis reactions, especially olefin metathesis, have had a tremendous impact on scientific research as well as on industrial production[34-36]. In contrast to isomerization (from 1 molecule to 1 molecule), metathesis reactions (from 2 to 2) involve information transformation between different molecules. Manipulation of the dynamic reaction with different wavelengths will provide new opportunities for reversible dynamic chemistry and control over molecular information flow. However, only a few investigators have studied this process with complex design[24, 37].

Disulfide bonds and diselenide bonds are both DCBs[38-50]. Disulfide (~240 kJ/mol)-containing molecules can exchange with each other under UV irradiation, which is realized by photodissociation. The generation of S radicals under different wavelengths of light, is very important in the photostability of materials and atmospheric chemistries[51,52]. Diselenide compounds undergo similar dynamic metathesis reaction. Due to the lower bond energies (~172 kJ/mol)[53], visible light is sufficient for the exchange of diselenide-containing molecules. Considering the different wavelengths requirements for these two DCBs, upon simply mixing, different states can be attained with light of different wavelengths. The transformations between disulfide, diselenide and Se-S bonds are key steps in the catalytic cycles of some enzymes in the human body[54], so control over these transformations is also of significance to understand these enzymatic processes. Therefore, we studied the wavelength-controlled metathesis between disulfides and diselenides. As expected, the reaction showed wavelength dependence (Scheme 1). The exchange between disulfides and diselenides to produce Se-S bonds proceeded under UV light and reversed under visible light without any complicated design.



Scheme 1. Exchange reaction between disulfides and diselenides under light of different wavelengths.

The exchange reaction between di-(1-hydroxylundecyl) diselenide (**DSe1**) and diphenyl disulfide (**DS1**) was tested first (Figure 1). These compounds were mixed and irradiated by 254 nm UV light, which can trigger the metathesis of both diselenide bonds and disulfide bonds. Under this condition, the reactants underwent an exchange reaction, and a product containing a Se-

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S bond was formed. After exchange, the α-proton of selenium shifted from 2.91 ppm to 2.94 ppm in ^1H NMR (Figure 1d). Similar to disulfide/diselenide metathesis, the exchange reached a photostationary state with 50% Se-S, 25% Se-Se and 25% S-S. ^{77}Se NMR spectra also confirmed the exchange reaction. Before UV irradiation, there was only one peak in the spectrum of the mixture (Figure 1c). After the exchange reaction, a new peak belonging to the Se-S bond-containing molecule appeared (Figure 1e). These results revealed metathesis between disulfides and diselenides under UV irradiation.

To trigger the reverse reaction, visible light with wavelength above 410 nm was used to irradiate the exchanged mixture. As expected, the metathesis was reversed, and the content of Se-S product dropped to only ~10% after 2 h (Figure 1f, 1g). Under this condition, disulfide bonds were not fully activated; thus, the exchange between disulfides and diselenides nearly ceased. On the other hand, the Se-S and diselenide bonds were still activated by light above 410 nm, and their dissociation and exchange reaction continued. Once disulfide was formed, it was kinetically trapped, resulting in the observed reverse reaction. Another disulfide with modifiable carboxyl groups, 5,5'-dithiobis-(2-nitrobenzoic acid) (**DS2**) was used in the experiment in place of **DS1** (Figure S1). Because of its electron-withdrawing groups, this disulfide bond can be activated by UV light of higher wavelength. For the metathesis between **DSe1** and **DS2**, 280-390 nm light was sufficient. Similar to the former results, Se-S was produced when the mixture was irradiated by UV light with 50% conversion. Under visible light above 410 nm, the conversion dropped to ~10%. These results provided the evidence and foundation for wavelength-controlled metathesis.

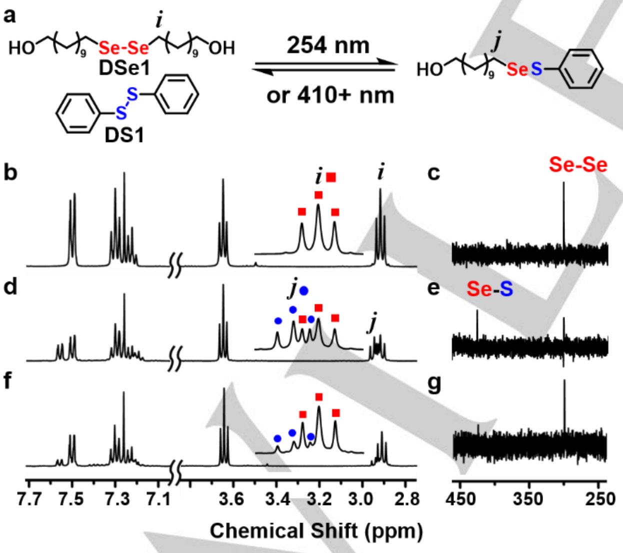

Figure 1. a) Exchange reaction between **DSe1** and **DS1** under light of different wavelengths. ^1H NMR and ^{77}Se NMR spectra of the mixture b), c) before reaction, d), e) after UV irradiation and f), g) after reversal under visible light.

The wavelength-controlled exchange reaction is assumed to proceed via radical mechanism, since UV-triggered disulfide metathesis and visible-light-triggered diselenide metathesis undergo a similar radical mechanism[20]. To directly confirm the radical generation from the diselenide and disulfide compounds, electron spin resonance (ESR) was used in the presence of a radical scavenger 5,5-dimethyl-1-pyrroline N-oxide (DMPO)[55] (Figure S2). As expected, no signal was detected in the darkness, (Figure 2a). When irradiated by visible light (above 410 nm), the signal of the DMPO selenol-radical could be obtained (Figure 2b), which could be simulated by the values for the nitrogen and hydrogen hyperfine coupling constants (A_N=12.94 G, $A_{H\beta}$=10.25 G, $A_{H\gamma}$=1.54 G). However, for the DMPO thiyl-radical, signals could not be detected unless UV light (below 400 nm) was used (Figure 2c). The signal could also be simulated by the values for the similar nitrogen and hydrogen hyperfine coupling constants (A_N= $A_{H\beta}$=13.57 G). Further, when radical scavenger 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) was added in the system, the exchange reaction was greatly hindered (Figure S3), which suggested that radicals are involved in the reaction.

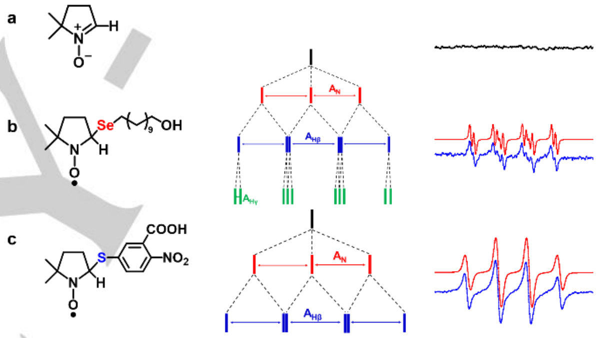

Figure 2. ESR spectra of **DSe1** and **DS2**. 20 mM **DSe1** and **DS2** were dissolved in DMSO in the presence of DMPO (80 mM) a) in darkness, b) **DSe1** under visible light (λ > 410 nm). g = 2.00706. c) **DS2** under UV light (λ < 400 nm). g = 2.00748. The red lines in spectra b, c are computer simulations of the respective spectra using the parameters given in the text. The blue lines are the detected signals.

To better explore the reverse reaction under different wavelengths of light, the Se-S exchange product of **DSe1** and **DS1** was purified (Figure S4). The purified exchange product or the 50% conversion mixture was irradiated by visible light passed through different light filters (Figure S5). When using a wavelength of light above 390 nm, the exchange was reversed, and ~20% conversion was maintained. Above 410 nm or 450 nm, ~10% conversion was maintained (Figure 3b). Similar results were obtained using the purified exchange product (Figure S6). In addition, if light with wavelength above 410 nm was used to directly irradiate the original mixture of **DSe1** and **DS2**, the conversion also reached ~10% (Figure 3c). With the wavelength of the light above 500 nm, the purified exchange product or the 50% conversion mixture did not have any change (Figure 3b, S6). In this way, a brief wavelength range of the reverse reaction was confirmed. If the wavelength was between 390 and 500 nm, the Se-S bond could be activated, and the reverse reaction was achieved. The wavelength dependence of the conversion provides new tunable parameters for controlling the metathesis between disulfides and diselenides.

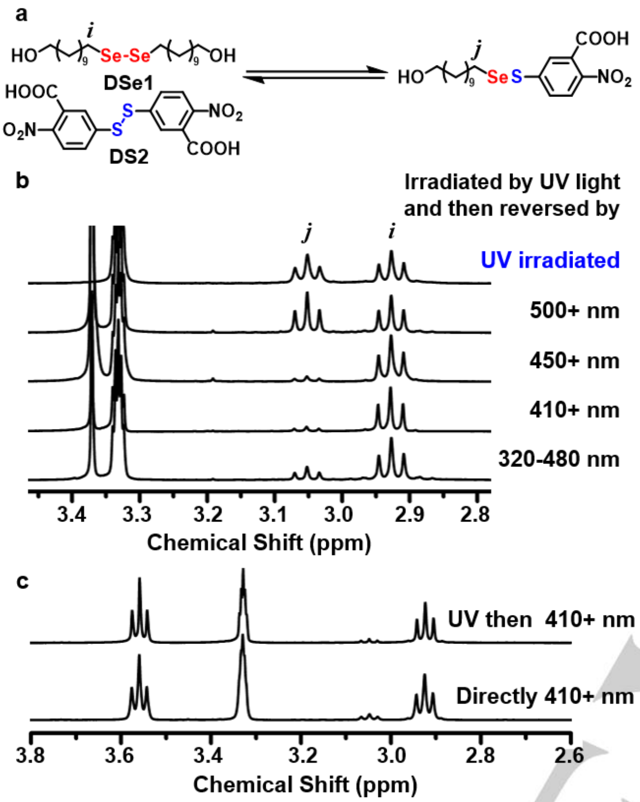

Figure 3. a) Exchange reaction between **DSe1** and **DS2** under light of different wavelengths. b) ^{1}H NMR spectra of the mixture after UV irradiation and reaction reversal under different wavelengths. c) ^{1}H NMR spectra of the mixture after reaction reversal, or direct irradiation by visible light.

Under wavelengths exceeding 500 nm, the Se-S product might still exchange with Se radicals. To confirm this assumption, a second diselenide (**DSe2**) was added to **DSe1** and **DS2** after UV irradiation. With light above 500 nm, a new Se-S product was obtained (Figure 4). Light of wavelength above 500 nm was also used to directly irradiate the original mixture of **DSe1**, **DSe2**, and **DS2**, and no Se-S exchange product was detected (Figure S9). These results showed that under light above 500 nm, though the reverse reaction ceased, the Se radical was still exchanging with Se-S bond. However, under this circumstance, the Se radical could not swap out the S radical from Se-S or S-S bonds due to energy limits. When **DSe2** was added, the **DSe2** radical swapped out the **DSe1** radical from the Se-S product, thus producing the new Se-S product.

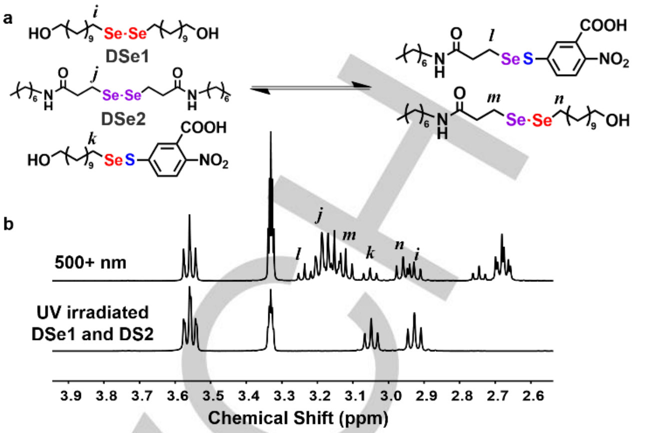

Figure 4. a) Exchange reaction between **DSe2** and exchange mixture of **DSe1** and **DS2** till photostationary state. b) ^{1}H NMR spectra of the mixture after wavelength exceed 500 nm.

For metathesis between disulfides and diselenides, a reductant-catalyzed reaction was also investigated (Figure S10, S11). The catalytic reductants thermodynamically pushed the exchange forward, while visible light irradiation kinetically pushed it backward. By the tuning reaction condition, this process has the potential to become a dissipative system with light as its energy input.

To demonstrate a potential application of wavelength-controlled metathesis, light-triggered cleavage of polymer materials was conducted (Figure 5). Two polyurethane elastomers containing disulfide bonds or diselenide bonds were fabricated (Scheme S2). Samples of each material were attached together and irradiated by UV light. Under this condition, the diselenides and disulfides exchanged with each other, connecting the polymer chains from different samples. After irradiation, the samples were welded together and could be stretched to 75% strain. Then, visible light with a wavelength above 410 nm was directed onto the welded samples, and the Se-S bonds connecting the materials were converted back to disulfides and diselenides, cleaving the samples (Figure 5b). A 457 nm blue light laser could also induce the cleavage of the materials. Without the laser, the samples could sustain a 200 g weight for more than 120 min. With the laser, the materials broke in 5 min (Supplementary video). Thus, a remotely laser-controlled cleavage of polymer materials was realized.

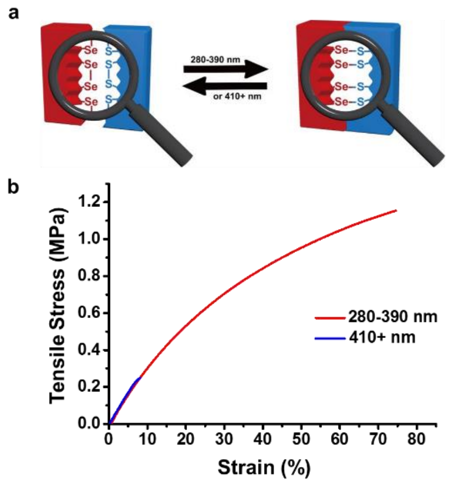

Figure 5. a) Exchange reaction between diselenides and disulfides in different polymer materials. b) Strain-stress curves of samples welded by UV irradiation and broken by visible light irradiation.

In summary, metathesis between disulfide bonds and diselenide bonds was realized under light, and the exchange reaction could be manipulated by the wavelength of the light. When irradiated by UV light, all compounds in the mixture were reactive, and Se-S bonds were produced, while with particular visible light irradiation, the exchange reaction was reversed. Thus, the composition of the mixture was controlled. This chemistry was introduced into polymer materials, and the wavelength-controlled cleavage of the polymers was realized with irradiation from a distance. Furthermore, the metathesis reaction could be catalyzed by reductants such as thiols. By optimizing the reaction rate of the forward reaction catalyzed by thiols and the backward reaction triggered by visible light, a dissipative system is expected to be formed with light as the input energy, instead of the traditionally used chemicals.

Acknowledgements

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Keywords: dynamic covalent bond• metathesis• wavelength controlled reaction • polymeric materials •

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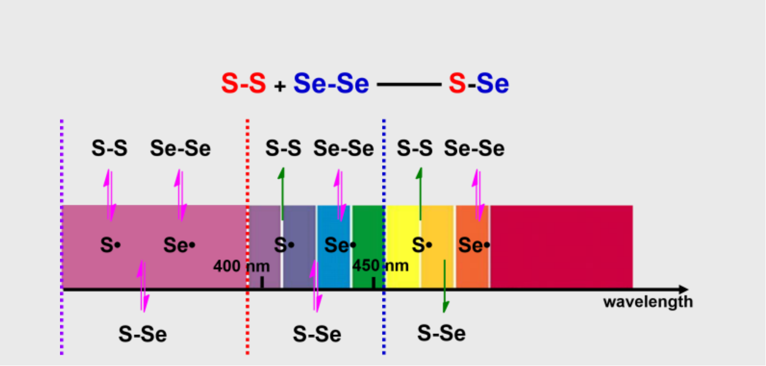

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Controlled Metathesis: metathesis between disulfide bonds and diselenide bonds was realized under light, and the conversion of the exchange reaction could be controlled by the wavelength of the light. This chemistry is induced into polymer materials to control cleavage of the polymers from a distance.