Photooxidative Coupling of Thiophenol Derivatives to Disulfides

Hyung Jun Kim, Jun Hee Yoon, and Sangwoon Yoon*

Department of Chemistry, Dankook University, 126 Jukjeon-dong, Suji-gu, Yongin, Gyeonggi 448-701, Korea

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Disulfide bonds play an important role in determining the structure and stability of proteins and nanoparticles. Despite extensive studies on the oxidation of thiols for the synthesis of disulfides, little is known about the photooxidation of thiols, which may be a clean, safe, and economical alternative to the use of harmful and expensive metal-containing oxidants and catalysts. In this paper, we report the photooxidative coupling of thiophenol derivatives to disulfides. Para-substituted thiophenol derivatives, p-SHC_6H_4X ($X = NO_2$, COOH, Cl, and OCH_3), are irradiated, and disulfides, $X_2(C_6H_4)_2S_2$, are identified as the major photoproducts using Raman, UV−vis, IR, and NMR spectroscopies. For p-nitrothiophenol (pNTP), 4,4′-dinitrodiphenyldisulfide (DNDPDS) is produced in 81% yield. The product yield changes with pH, being the highest at pH $\approx$ 5, suggesting that both neutral thiol and anionic thiolate forms of pNTP are required for the photoreaction to occur. Excitation at 455 nm, at which the thiolate form of pNTP absorbs strongly, leads to the largest yield of DNDPDS, whereas very little DNDPDS is formed by excitation of the thiol form of pNTP at 325 nm. Our observations suggest that the photooxidation occurs via collisions of the electronically excited thiolate form of pNTP with the surrounding neutral thiol forms of pNTP. The photooxidation reaction happens regardless of the electron-withdrawing or electron-donating properties of the substituents if the pH and excitation wavelengths are properly chosen. The versatility of light and generality of the photooxidative coupling reaction of thiophenol derivatives may open new possibilities for selective and site-specific photocontrol of disulfide bond formation in biology and nanomaterial science as well as in synthetic chemistry.

1. Introduction

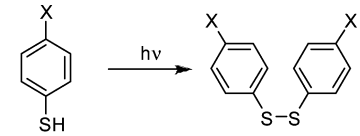
The formation of disulfide bonds is an important reaction because these bonds play a key role in determining the structure and stability of proteins and nanoparticles. Reversible disulfide linkages between cysteine residues determine the structure and biological functions of many proteins.[1] Thiol is also one of the most commonly used surface-stabilizing agents for nanoparticles, and the formation or cleavage of disulfide bonds on their surfaces significantly influences nanoparticle stability.[2,3] The formation of new disulfide bridges by breaking original disulfide bonds with thiols is the basis of the important thiol−disulfide exchange reactions used to detect thiols in solution and in biological samples such as blood.[4–7]

The most common approach for the synthesis of disulfides is the oxidation of thiols. Various oxidants with catalysts have been used, including K_3PO_4,[8] halogens,[9–12] NH_4OH,[13] and H_2O_2.[14] Although these conventional methods produce disulfide products in high yields, they often involve complicated purification processes, hazardous chemicals, and expensive metal-containing reagents or catalysts. Therefore, developing new strategies to prepare disulfides in a cost-effective and an environmentally-friendly fashion is a quest worth pursuing.

One clean, safe, and economical way of driving chemical reactions is through the use of light. In addition to its many other useful properties, light has the unique capability of spatial control. By delivering light to a specific area of interest, one can induce reactions locally, an ability that has applications in biomedicine, surface sciences, and nanomaterial sciences.[15–17]

In this article, we report the photooxidative coupling of thiols to disulfides (Scheme 1). Thiophenols, with their para positions substituted by $-NO_2$ (p-nitrothiophenol, pNTP), $-COOH$ (p-mercaptobenzoic acid, pMBA), $-Cl$ (p-chlorothiophenol, pCTP), and $-OCH_3$ (p-methoxythiophenol, pMTP), are irradiated, and the photoproducts are identified by Raman, IR, UV−vis, and NMR spectroscopies. Raman spectroscopy is particularly advantageous in many respects. As a vibrational spectroscopy, it provides fingerprints of the products. It also allows for the monitoring of the formation of photoproducts in situ and in real time as the reaction progresses. Further investigation into the effects of pH, excitation wavelength, and substituents provides clues to the reaction mechanism.

SCHEME 1: Photooxidation of Thiophenol Derivatives



(X = NO_2, COOH, Cl, OCH_3)

2. Experimental Section

Samples. All reagents were purchased and used without further purification. For the photooxidation of pNTP, 10 mM pNTP was prepared in 10 mL of tetrahydrofuran (THF)/water. To dissolve both the reactant and the possible disulfide photoproduct, a 1:1 mixture of THF and water was used as the solvent. The concentrations of the other thiophenol derivatives were 50 mM for pMBA and pCTP and 100 mM for pMTP in ethanol/water. A 4 mL volume of solution was transferred to a quartz cuvette (10 mm ×10 mm) for irradiation. The pH of the solution was adjusted by adding HCl or NaOH.

Irradiation. A wide range of wavelengths from various light sources was used to drive the photoreaction. Hg−Xe lamps

* To whom correspondence should be addressed. Phone: +82-31-8005-3152. Fax: +82-31-8005-3148. E-mail: sangwoon@dankook.ac.kr.

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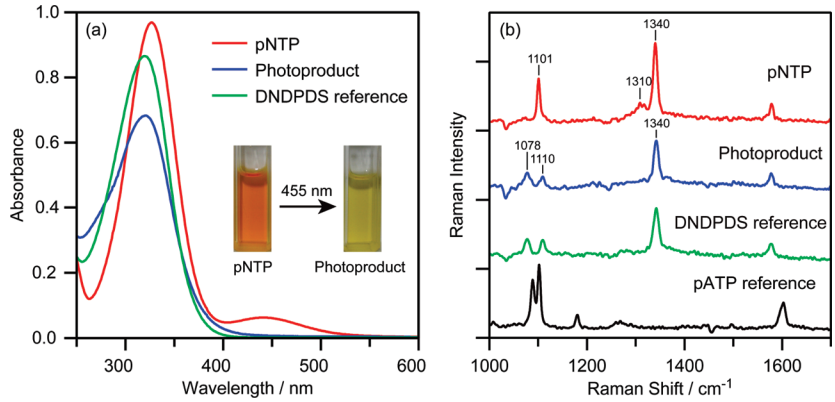


Figure 1. (a) UV−vis absorption spectra of pNTP in THF/H_2O (80 μM) and the photoproduct formed by irradiation of the pNTP solution at 455 nm and 150 mW for 1 h. The UV−vis absorption spectrum of DNDPDS is included for comparison. The inset shows the visual color change of pNTP upon irradiation. (b) Raman spectra of pNTP in THF/H_2O (10 mM) and photoproduct. Raman spectra of DNDPDS (5 mM) and pATP (100 mM) are included to identify the photoproduct. Spectra are displayed with offset for clarity.

(Vilber Lourmat and Hamamatsu) provided 254 and 365 nm wavelengths. Light-emitting diodes (Thorlabs) were used to irradiate the samples at 455, 530, and 660 nm. A He−Cd laser (Kimmon) provided continuous wave (cw) light with a wavelength of 325 nm. An Nd:YAG laser with KDP crystals (Spectra Physics) provided pulsed light (8 ns, 10 Hz) at 532, 355, and 266 nm.

Spectroscopy. Raman spectra were acquired using a Raman microscope system (Kaiser). A diode laser at 785 nm was focused onto the sample by a 10× objective. Raman scattering from the sample was collected at 180° by the same objective and directed to a spectrometer equipped with a holographic grating (*f*/1.8, focal length 85 mm) and a Peltier-cooled CCD. All presented Raman spectra were acquired for a total exposure time of 60 s with a spectral resolution of 4 cm^{-1}. The photoproducts were further characterized using UV−vis absorption spectroscopy (Perkin-Elmer, Lambda 25), NMR spectroscopy (Bruker, Avance 600, 600 MHz), and IR spectroscopy (Perkin-Elmer, Spectrum 100).

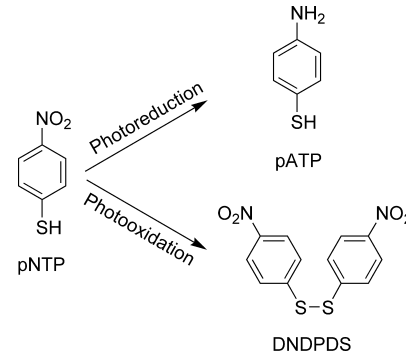
3. Results and Discussion

3.1. Observation of the Photoreaction of pNTP and Characterization of the Photoproduct. We first investigated the photoreaction of pNTP. A 10 mM solution of pNTP in a mixture of THF and H_2O was irradiated at 455 nm and 150 mW for 1 h. Upon irradiation, the color of the solution changed from orange to yellow, as shown in the inset of Figure 1a. The UV−vis absorption spectrum of the pNTP solution, also presented in Figure 1a, exhibits two absorption bands at 326 and 441 nm, attributed to absorption by a thiol form and a thiolate form of pNTP, respectively, as discussed later. Irradiation results in a new absorption spectrum with a single absorption band at 320 nm.

The changes observed in the Raman spectra are more pronounced. Figure 1b shows that upon irradiation, the Raman peaks at 1101 and 1310 cm^{-1} of pNTP disappear and new peaks arise at 1078 and 1110 cm^{-1}. Furthermore, these changes are induced by light only, strongly indicating that a photoreaction does take place. When we left the sample in the dark or under fluorescent light bulbs for the same period of time as irradiation or when we heated the sample to 55 °C to see if the reaction was possibly driven by the heat generated by irradiation, the Raman spectrum of the pNTP solution remained unchanged (Supporting Information, Figure S1).

Because pNTP has two functional groups, two photoreaction pathways are possible, as shown in Scheme 2. One is the photoreduction of the nitro group to an amine group, forming *p*-aminothiophenol (pATP). The other is the photooxidation of the thiol group, yielding 4,4′-dinitrodiphenyldisulfide (DNDPDS). To identify the actual reaction product, we acquired Raman spectra of the commercially available pATP and DNDPDS as references. Figure 1b shows that the Raman spectrum of the photoproduct produced by irradiation of pNTP at 455 nm is exactly identical to that of the reference DNDPDS. The UV−vis absorption spectrum of DNDPDS also matches that of the photoproduct (Figure 1a).

SCHEME 2: Two Possible Photoreaction Pathways for pNTP



Because the vibrational spectra of DNDPDS are not well known,[18,19] we assigned the Raman spectrum using density functional theory calculations (B3LYP/6-31(d,p)).[20] Figure 2 presents the optimized structures of pNTP and DNDPDS, along with the calculated Raman spectra, in which the Raman intensities at scaled harmonic frequencies are convoluted with the Lorentzian function with a full-width at half-maximum (fwhm) of 4 cm^{-1}. The optimized structure of DNDPDS shows that the length of the S−S bond is 2.07 Å and the dihedral angle 90°. The vibrational mode analysis shows that the C−S stretching mode is sensitively influenced by the formation of a disulfide linkage. The C−S stretching vibration of pNTP at 1101 cm^{-1} red shifts to 1078 cm^{-1} as the adjacent S−H bond is replaced by the S−S bond, indicating that the C−S bond is slightly weakened by the disulfide bond. The peak at 1110 cm^{-1} in the DNDPDS spectrum is assigned to the C−N stretch, which is invisible in the spectrum of pNTP. Because of the clear distinction in the peak position and the peak intensity between pNTP and DNDPDS, these two peaks at 1078 and 1110 cm^{-1} are used to monitor the formation of DNDPDS. The 1310 cm^{-1}

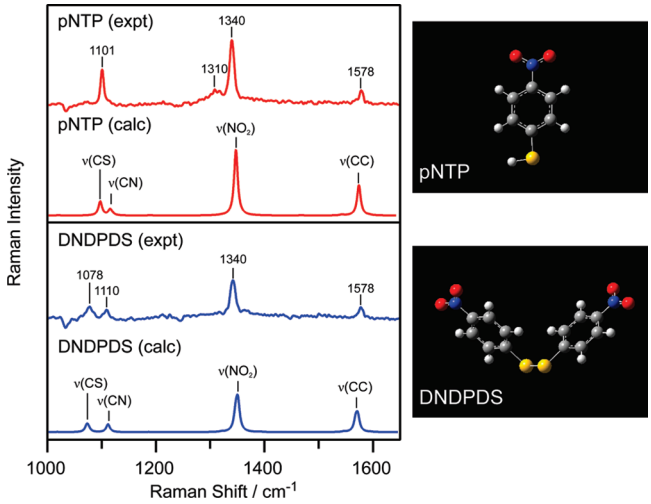


Figure 2. Assignment of the vibrational Raman spectra (left) and optimized structures (right) of pNTP and DNDPDS as calculated by density functional theory.

peak, present only in pNTP, is attributed to the N−O stretch of pNTP in the anionic thiolate form.

In addition to the UV−vis and Raman spectroscopic measurements, we further confirmed the formation of DNDPDS as a major photoproduct from pNTP using IR and NMR spectroscopies (Supporting Information, Figures S2 and S3). The prominent S−H stretching band at 2545 cm^{-1} in the IR spectrum of pNTP is not observed in the IR spectrum of the photoproduct, indicating the formation of a disulfide product. The ^1H NMR spectrum of the photoproduct is in excellent agreement with that of the reference DNDPDS. The NMR peak originating from the proton in S−H (δ 3.77) is absent in the NMR spectrum of DNDPDS. Protons on the benzene ring are deshielded by the nearby disulfide bond.

Quantitative analysis of the Raman and NMR spectra provides the yield of the disulfide photoproduct. Comparison of the Raman peak intensity of the photoproduct from 10 mM of pNTP with that of the 5 mM reference DNDPDS results in a yield of 81%, which is also consistent with the value obtained from the peak areas of the NMR spectrum.

The different solubilities of pNTP and DNDPDS allow easy separation of the photoproduct. Disulfides are generally strongly hydrophobic, whereas thiols form hydrogen bonds with water. As we irradiated pNTP dissolved in ethanol/water, the photoproducts were recovered as solids because of their poor solubility

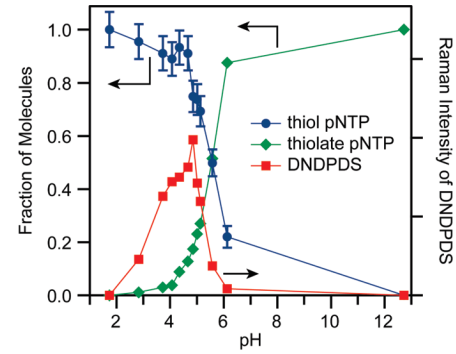


Figure 4. Relative populations of the neutral thiol and anionic thiolate form of pNTP as a function of pH. The relative yield of photooxidation of pNTP at each pH was measured by the Raman intensity of the photoproduct DNDPDS at 1110 cm^{-1}.

in the solvent. The Raman spectrum of the precipitate matches that of solid DNDPDS (Supporting Information, Figure S4).

3.2. Effect of pH. For a better understanding of the photooxidative coupling reaction of thiophenol derivatives and to unravel the reaction mechanism, we explored the effects of three experimental parameters: pH, photoexcitation wavelength, and substituents of reactants. First, we examined the effect of pH on the reactivity. We found that pNTP, analogously to *p*-nitrophenol,[21] exists either in the neutral or the anionic thiol form, depending on pH. These two forms exhibit distinctively different spectroscopic features. Figure 3 shows the UV−vis absorption spectra and Raman spectra of pNTP over a wide range of pH. In acidic conditions, pNTP in the thiol form has a maximum absorbance at 326 nm. As pH increases, the absorption band at 326 nm decreases and is replaced by a new band at 441 nm. The UV−vis absorption spectrum is dominated by the 441 nm band at high pH. Figure 3b shows the color changes of pNTP solution in THF/H_2O in response to pH changes. The thiolate form of pNTP is red, reflecting the absorption at 441 nm. The neutral pNTP species is colorless because it absorbs in the UV region. A main feature of the Raman spectra of the neutral thiol forms of pNTP is the N−O stretching mode at 1340 cm^{-1}. As pNTP becomes deprotonated at higher pH, the N−O stretching mode shifts to 1310 cm^{-1}, and the overall Raman intensity increases, presumably because of the preresonance effect (Figure 3c).[21] Therefore, the ratio between the 1310 and the 1340 cm^{-1} peak intensities gives the relative population of the two forms of pNTP in the solution.

In Figure 4, we plotted the relative population of the thiol and the thiolate forms of pNTP as a function of pH. The fraction

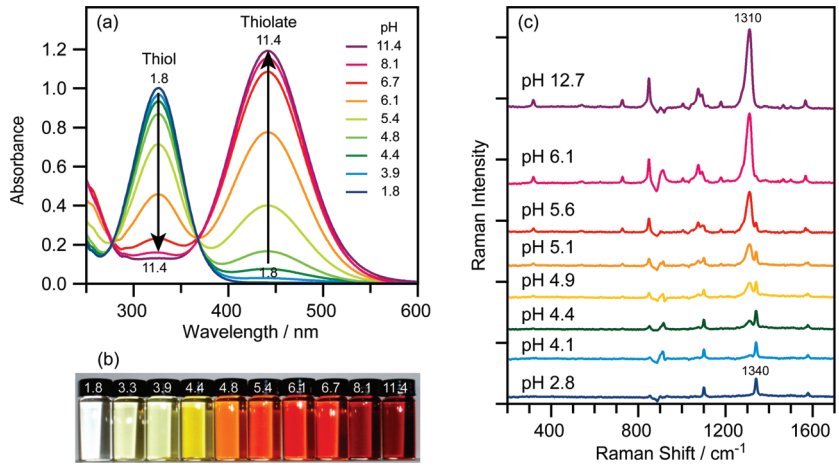


Figure 3. (a) UV−vis absorption spectra, (b) color, and (c) Raman spectra of pNTP at pH levels indicated in the figure.

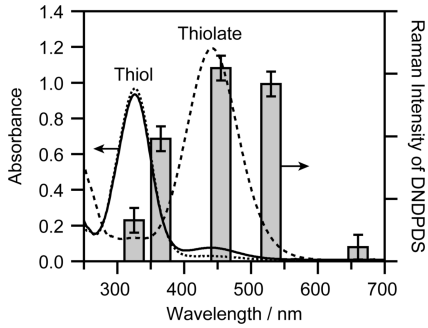


Figure 5. Dependence of the photooxidation reaction yield of pNTP on excitation wavelength. The pNTP solution at pH 4.3 was irradiated at 325, 365, 455, 530, and 660 nm at 25 mW for 2 h. The yield was measured by the Raman intensity of the photoproduct DNDPDS at 1078 cm^{-1}. The absorption spectrum of the solution used in the experiment (solid line) is included to indicate which species, the thiol or the thiolate form of pNTP, is excited to yield the product. Absorption spectra of the thiol (dotted line) and thiolate (dashed line) forms of pNTP are adopted from Figure 3 to show the absorption region of each species.

of the thiol form of pNTP is calculated from the Raman peak intensity at 1340 cm^{-1} at each pH divided by the Raman intensity at pH 1.7, where pNTP exists exclusively in the thiol form. The 1310 cm^{-1} Raman peak intensity was used for calculation of the fraction of the thiolate form of pNTP. Calculation of the fraction using the UV−vis absorption bands at 326 and 441 nm produced the same results. Plotted together is the relative amount of the photoproduct by irradiation of pNTP at each pH, measured by the Raman intensity of DNDPDS at 1110 cm^{-1}. Figure 4 shows that the formation of DNDPDS reaches a maximum at pH $\approx$ 5. In other words, photooxidation occurs most efficiently in the pH range between 4 and 5 and does not occur at pH lower than 2 or higher than 6. This suggests that the reaction requires both thiol and thiolate forms of pNTP.

The requirement for the presence of both forms of pNTP is further corroborated by the observation that DNDPDS was not produced in pure organic solvents such as THF and dichloromethane (DCM), where only the thiol form of pNTP exists (Supporting Information, Figure S5). Quantitative analysis of the fraction of molecules in Figure 4 indicates that photooxidation occurs best when the neutral form is about three times more abundant than the anion form. As discussed in the following section, photooxidation of pNTP occurs via electronic excitation of the anionic thiolate form of pNTP. Therefore, a higher population of the thiol form of pNTP surrounding the electronically excited thiolate form may increase the chance of reactive collisions between the two species, leading to the best yield.

3.3. Effect of Excitation Wavelength. To find which form of pNTP is excited by irradiation, leading to the photoreaction, we varied the excitation wavelengths and measured the product yield using Raman spectroscopy. Figure 5 presents the Raman intensity of the DNDPDS photoproduct at 1078 cm^{-1}, acquired after irradiation of pNTP at 325, 365, 455, 530, and 660 nm (25 mW, 2 h). Overlaid are the absorption spectra of pNTP at pH 4.3 (solid line), where the experiments were performed, together with the absorption spectra of the thiol (dotted line) and the thiolate (dashed line) forms of pNTP, with λ_{max} at 326 and 441 nm, respectively. DNDPDS is best produced by irradiation at 455 nm, which is where the thiolate form of pNTP absorbs strongly. Excitation of neutral pNTP at 325 nm does not yield significant amounts of the photoproduct. Therefore, the photooxidation of pNTP occurs via electronic excitation of the thiolate form rather than the thiol form of pNTP.

It is not clear yet how electronic excitation of thiolate leads to the formation of disulfide. We performed time-dependent density functional theory calculations (TD DFT) to find the nature of the electronic excited state of the thiolate form of pNTP and to gain insights into the reaction mechanism. The calculations revealed that the only transition with a nonzero oscillator strength (f) is to the excited singlet state at 435 nm ($f = 0.54$), in good agreement with the measured absorption at 441 nm (Supporting Information, Figure S6). The molecular orbitals involved in the transition show that the electron density moves from the anionic sulfur atom to the nitro group upon transition from the ground state to the excited singlet state. We also note that thiyl radicals ($RS^{\bullet}$) have been proposed as intermediates in the formation of disulfide in previous catalytic oxidation studies.[8,13] Therefore, it is possible that photoexcitation of thiolate may facilitate the production of the thiyl radicals by removing the electron density from the anionic sulfur atom, leading to the formation of disulfide. Further experimental and theoretical investigations are required to unravel the reaction mechanism.

3.4. Effect of the Substituents. Because the electron-withdrawing/donating properties of substituents often influences the reactivity of aryl compounds, it is possible that the photooxidative coupling reaction we observed is limited to the strong electron-withdrawing group, namely, $-NO_2$. Thus, we explored the photooxidation of other functional-group-substituted thiophenols. We selected pMBA for its moderate electron-withdrawing functional group (−COOH), pCTP for its weak electron-withdrawing functional group (−Cl), and pMTP for its strong electron-donating functional group ($-OCH_3$). The samples were prepared in ethanol/water and irradiated at selected wavelengths. Because the excitation of the thiolate form is key to driving the photooxidation reaction as discussed above, we measured the UV−vis absorption spectra of the thiolate form of each molecule and selected the excitation wavelengths accordingly. Figure 6 shows the UV−vis absorption spectra of pMBA, pCTP, and pMTP in ethanol/water (red lines) and of the corresponding thiolate forms in the basic condition (gray lines) to identify the absorption band of the thiolate. The wavelengths used for photoexcitation are marked by the arrows in the figure. Upon irradiation, photoproducts were formed and measured by Raman spectroscopy.

Figure 6d−f presents Raman spectra of pMBA, pCTP, pMTP, and their photoproducts. The Raman spectra of the photoproducts are characterized by the absence of the S−H stretching peak near 2560 cm^{-1} and the appearance of a new peak at ~500 cm^{-1}, assigned to the S−S stretching mode.[22] This observation strongly suggests that disulfide bonds are formed by irradiation. In addition, the red shift of the C−S stretching mode from ~1100 to ~1080 cm^{-1} is observed, as is the case for pNTP. Furthermore, comparison between the Raman spectrum of the product from irradiation of pCTP and that of the reference, 4,4′-dichlorodiphenyldisulfide (DCDPDS), confirms that the photooxidative coupling reaction has indeed occurred (Supporting Information, Figure S7). Therefore, the photooxidative coupling of thiophenol derivatives occurs regardless of the electron-donating/withdrawing properties of the substituents.

Our observations imply that photooxidative coupling may be generally applicable to a variety of thiophenol molecules if the excitation wavelength and pH conditions are properly selected. The synthesis of disulfides via photooxidation is easy, safe, clean, and thus well suited to green chemistry. The separation of the products is also straightforward. Furthermore, the photooxidative coupling reaction enables the synthesis of asymmetric

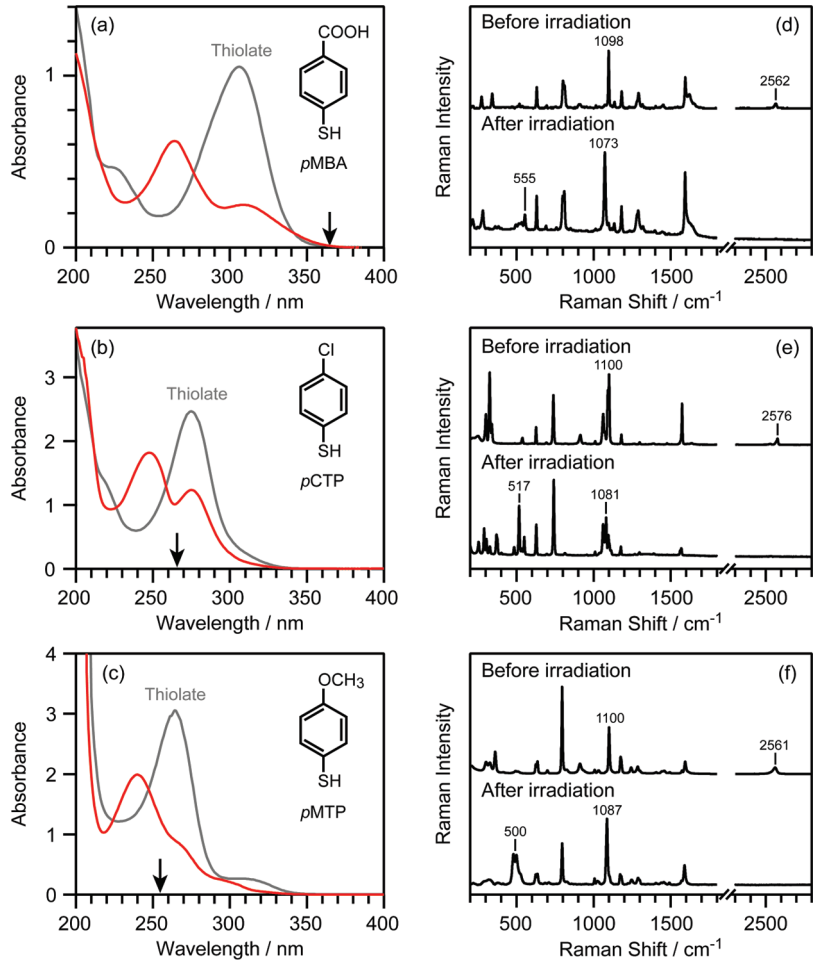


Figure 6. (a−c) UV−vis absorption spectra of (a) pMBA, (b) pCTP, and (c) pMTP solutions in ethanol/water (red lines). The absorption spectra of the thiolate form of each molecule obtained in basic conditions are also included to identify the absorption band of the thiolate (gray lines). The arrows mark the excitation wavelength used in the photooxidation experiments. (d−f) Raman spectra of (d) pMBA, (e) pCTP, and (f) pMTP before and after irradiation at the wavelengths indicated by the arrows.

disulfides by choosing appropriate wavelengths and pH levels, which is difficult to achieve in a conventional synthetic approach. Photooxidation also opens the possibilities of the modification of the local structures of proteins and nanomaterials by forming disulfide bonds in specific areas. Therefore, the observation of the photooxidative coupling of thiophenol derivatives to disulfides and the understanding of the reaction mechanism that this study provides will contribute to advancing biology and nanomaterial sciences as well as synthetic chemistry.

4. Conclusions

We observed photooxidative coupling of thiophenol derivatives to disulfides. Irradiation of pNTP at 455 nm produces the disulfide product, DNDPDS, in 81% yield, as identified by UV−vis, Raman, IR, and NMR spectroscopies. Density functional theory calculations revealed that the characteristic vibrational frequencies of DNDPDS at 1078 and 1110 cm^{-1} can be assigned to the C−S and C−N stretching modes, respectively. The yield of the product changed with pH, being the highest at pH ≈ 5, at which the thiol and thiolate forms of pNTP exist in a 3:1 ratio. The disulfides are not formed at very low or high pH, suggesting that the photooxidative coupling reaction requires the presence of both thiol and thiolate forms. In the presence of both forms of pNTP, irradiation at 455 nm, at which the thiolate form strongly absorbs, leads to the best yield of DNDPDS, whereas excitation of the thiol form at 325 nm yields much less product. The effects of pH and excitation wavelengths on the reactivity suggest that the photooxidative coupling of thiophenol derivatives occurs via reactive collisions of the electronically excited thiolate form of pNTP with the neutral thiol form of pNTP. Replacement of $-NO_2$ with less electron-withdrawing groups such as −COOH and −Cl or a strong electron-donating group such as $-OCH_3$ leads to the same results, yielding the disulfides by excitation of the thiolate forms. Although more molecules should be investigated, it seems that the photooxidative coupling reaction is universal for thiophenol derivatives if pH and excitation wavelengths are properly chosen. The generality of the reaction and versatility of light may open new possibilities for selective and site-specific photocontrol of disulfide bond formation in biology and nanomaterial science as well as synthetic chemistry.

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Supporting Information Available: Control experiments confirming the photoreaction of pNTP; IR, NMR, and solid Raman data for identification of photoproducts; photooxidation of pNTP in various organic solvents; time-dependent density functional theory calculations of the excited thiolate state. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Nelson, D. L.; Cox, M. M. *Lehninger Principles of Biochemistry*, 3rd ed.; Worth Publishers: New York, 2000.
(2) Aldana, J.; Wang, Y. A.; Peng, X. *J. Am. Chem. Soc.* **2001**, *123*, 8844.
(3) Billone, P. S.; Maretti, L.; Maurel, V.; Scaiano, J. C. *J. Am. Chem. Soc.* **2007**, *129*, 14150.
(4) Gilbert, H. F. *Adv. Enzymol.* **1990**, *63*, 69.
(5) Gilbert, H. F. *Methods Enzymol.* **1995**, *251*, 8.
(6) Chaudhuri, A. R.; Khan, I. A.; Luduena, R. F. *Biochemistry* **2001**, *40*, 8834.
(7) Ates, B.; Ercal, B. C.; Manda, K.; Abrahama, L.; Ercala, N. *Biomed. Chromatogr.* **2009**, *23*, 119.
(8) Joshi, A. V.; Bhusare, S.; Baidossi, M.; Qafisheh, N.; Sasson, Y. *Tetrahedron Lett.* **2005**, *46*, 3583.
(9) Abele, E.; Abele, R.; Lukevics, E. *J. Chem. Res., Synop.* **1999**, *10*, 624.
(10) Ali, M. H.; McDermott, M. *Tetrahedron Lett.* **2002**, *43*, 6271.
(11) Drabowicz, J.; Mikołajczyk, M. *Synthesis* **1980**, *1*, 32.
(12) Wu, X.; Rieke, R. D.; Zhu, L. *Synth. Commun.* **1996**, *26*, 191.
(13) Carril, M.; SanMartin, R.; Domínguez, E.; Tellitu, I. *Green Chem.* **2007**, *9*, 315.
(14) Kesavan, V.; Bonnet-Delpon, D.; Bégué, J.-P. *Synthesis* **2000**, *2*, 223.
(15) O'Neal, D. P.; Hirsch, L. R.; Halas, N. J.; Payne, J. D.; West, J. L. *Cancer Lett.* **2004**, *209*, 171.
(16) Duffus, C.; Camp, P. J.; Alexander, A. J. *J. Am. Chem. Soc.* **2009**, *131*, 11676.
(17) Klajn, R.; Wesson, P. J.; Bishop, K. J. M.; Grzybowski, B. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 7035.
(18) Kross, R. D.; Fassel, V. A. *J. Am. Chem. Soc.* **1956**, *78*, 4225.
(19) Merklin, G. T.; He, L.-T.; Griffiths, P. R. *Appl. Spectrosc.* **1999**, *53*, 1448.
(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.;and Pople, J. A. *Gaussian 03*, Revision C02; Gaussian: Wallingford, CT, 2004.
(21) Ando, R. A.; Borin, A. C.; Santos, P. S. *J. Phys. Chem. A* **2007**, *111*, 7194.
(22) Sandroff, C. J.; Herschbach, D. R. *J. Phys. Chem.* **1982**, *86*, 3277.

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