Photocatalysis by Phenothiazine Dyes: Visible-Light-Driven Oxidative Coupling of Primary Amines at Ambient Temperature
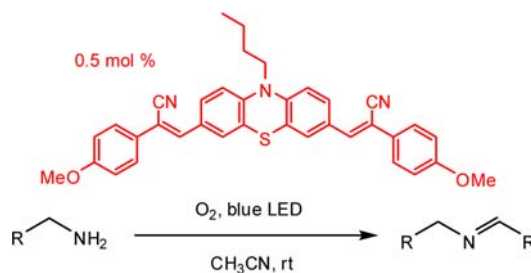
Ji Hoon Park,[†] Kyoung Chul Ko,[†] Eunchul Kim,[‡] Nojin Park,[‡] Ju Hong Ko,[†]
Do Hyun Ryu,[†] Tae Kyu Ahn,*[‡] Jin Yong Lee,*[†] and Seung Uk Son*[†,‡]

*Department of Chemistry and Department of Energy Science,
Sungkyunkwan University, Suwon 440-746, Korea*

sson@skku.edu

Received September 20, 2012

ABSTRACT

New phenothiazine based organic dyes were prepared for visible-light-driven organic transformations. The 3,7-disubstituted phenothiazine derivatives showed visible light absorption and reversible one-electron oxidation behavior. In the presence of 0.5 mol % of 3,7-disubstituted phenothiazines, primary benzylamines showed oxidative coupling under visible light irradiation from a blue LED. The electronic effect of substituents in phenothiazine dyes was observed in catalytic activities. The mechanistic pathway of oxidative coupling was discussed based on the detection of H_2O_2 after the reaction.

As energy issues become more and more important in modern life, many scientific studies have sought the development of new sustainable energy resources.[1] Among them, solar energy is one of the most attractive resources.[2] It is well-known that solar light contains 43% visible light.[2] Thus, chemical transformations triggered by visible light are energetically beneficial.[3]

Recently, photoredox catalysis using visible light harvesting dyes has shown successful results in a variety of chemical transformations.[4] Usually, ruthenium or iridium complexes have been used as dyes in these reactions. In addition to efforts for expansion of the range of organic reactions, further studies are definitely required for more diverse dyes including organic dyes.

Imines are versatile building blocks in various organic transformations such as nucleophilic addition and cyclo-addition.[5] Besides the conventional preparation methods such as condensation of carbonyl and amines, imines can be prepared from secondary amines by visible-light-driven aerobic oxidation.[6] Furthermore, imines can be prepared by intriguing oxidative coupling of primary amines.[7] It is noteworthy that studies on the oxidative coupling of primary amines to imines were relatively less explored than simple oxidation of secondary amines. The oxidative coupling of primary amines can be catalyzed by transition

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[†] Department of Chemistry.

[‡] Department of Energy Science.

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metal complexes, and others, without visible light.[7a–c] However, the reaction temperatures were around 100 °C.

Very recently, several reports appeared on the *photocatalytic* conversion of *primary* amines to imines.[8] For example, Zhao and co-workers reported a TiO$_2$-based photocatalytic system for aerobic oxidative coupling of primary amines with a 100 W Hg lamp (wavelength > 300 nm).[8a] Nitta's group reported a metal-free photocatalytic system with an ~84 turnover number (TON) using a 350 nm lamp.[8b,c] Wang and Blechert group reported metal-free carbon nitride photocatalysts with visible light (wavelength > 420 nm) at 80 °C.[8d] Although catalytic systems operated by visible light have appeared in recent literatures,[8d] more exploration is definitely required for more efficient photocatalytic systems which can conduct reactions *with higher TONs at ambient temperature*. In this work, we report highly efficient phenothiazine dyes for the photocatalytic oxidative coupling of primary amine at ambient temperature. As far as we are aware, this is the most active visible-light-driven photocatalytic system for the oxidative coupling of primary amines.

In the literature, there have been several mechanistic suggestions on the photocatalytic oxidative coupling of primary amines to imines.[7,8] For example, the photoinduced generation of aldehyde and successive imination were suggested for coupled imine formation. In addition, alternative intermediates such as benzenemethanimine were suggested. In these catalytic photoredox mechanisms, electron transfer to oxygen by the photoexcited dyes and abstraction of electrons from amines were generally described (Scheme 1). Nontheless, the photoinduced singlet oxygen pathway by dyes without electron transfer to oxygen cannot be excluded.[6a,9]

Scheme 1. Photoredox Catalysis between Oxygen and Amines Induced by Light Harvesting Dyes
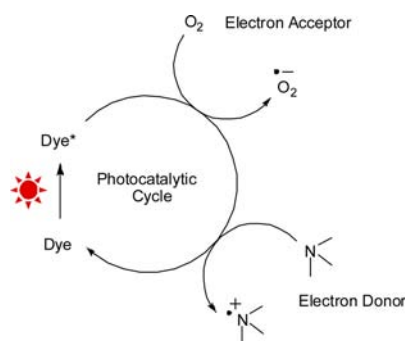

Scheme 2 shows synthetic routes for phenothiazine dyes used in this study. *N*-Butylphenothiazine with 3-carboxaldehyde or 3,7-dicarboxaldehyde groups were prepared

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(9) See the Figure S1 in the SI for more detailed discussion.

by Vilsmeier reaction of *N*-butylphenothiazine.[5] Arylcyano groups were then introduced by nucleophilic condensation with aldehyde groups.[5] The prepared dyes (**D1**−**D6**) were fully characterized by ^{1}H NMR, ^{13}C NMR, and high resolution mass spectroscopy (refer to the Supporting Information (SI)).

Scheme 2. Synthesis of Phenothiazine Dyes (**D1**−**D6**)
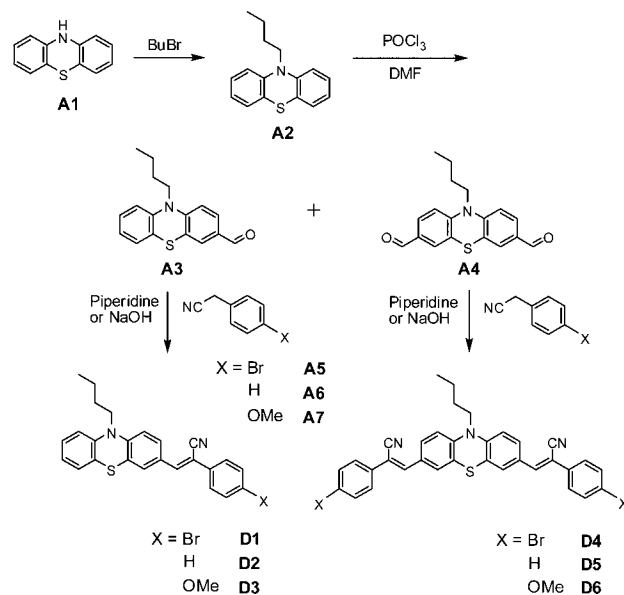
The optical and electrochemical properties of the prepared dyes (**D1**−**D6**) were studied by UV−vis absorption spectroscopy and cyclic voltammetry (Figure 1 and Table 1). The dyes showed maximum absorption peaks in the 402−447 nm range. As more electron-donating groups were attached at the 4-position of the side phenyl groups, the locations of the maximum absorption peak were gradually blue-shifted. At the same time, reversible one-electron oxidation potentials were gradually shifted to less positive values, indicating a more facile oxidation
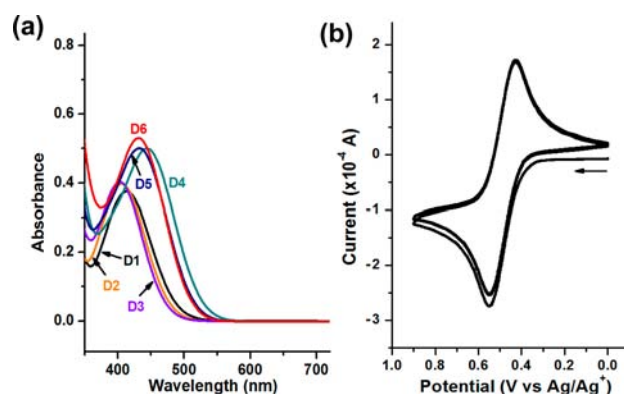
Figure 1. UV−vis absorption spectra of dyes (**D1**−**D6**) (a) and representative cyclic voltammogram with five scans (b) of **D6**.

(Figure S2 in the SI). Using onset UV−vis absorption peaks and oxidation potentials of the dyes, the locations of the HOMO and LUMO were calculated (Table 1). As the electronic surrounding of the dyes became more electron-rich, the HOMO and LUMO were moved to higher energy levels.

Table 1. Optical and Electrochemical Properties of Phenothiazine Dyes (**D1−D6**)[a]

dyes	$\lambda_{max}, \varepsilon$ (nm, $M^{-1} cm^{-1}$)	ox. potential[b] (V)	E_{0-0}[c] (eV)	HOMO[d] (eV)	LUMO[e] (eV)
D1	416, 14800	0.48 (rev)[f]	2.54	−5.23	−2.69
D2	406, 16000	0.47 (rev)	2.59	−5.23	−2.64
D3	402, 16400	0.45 (rev)	2.62	−5.22	−2.60
D4	447, 20000	0.53 (rev)	2.36	−5.26	−2.88
D5	434, 20400	0.51 (rev)	2.41	−5.25	−2.83
D6	433, 21200	0.48 (rev)	2.43	−5.22	−2.78

[a] Acetonitrile was used as solvent. [b] Potentials vs Ag/Ag$^+$ (reference electrode) determined in a conventional three electrode cell by using 0.10 M tetrabutylammonium hexafluorophosphate (TBAPF$_6$) in acetonitrile as the supporting electrolyte, indium tin oxide (ITO) glass as the working electrode, and platinum as the counter electrode. [c] 0−0 transition energies measured using the onset of UV−vis absorption spectra. [d] HOMO values calculated using potentials of oxidative waves. [e] LUMO values obtained from HOMO + E_{0-0}. [f] Reversible peaks.

Considering the visible light absorption behavior and reversible one-electron oxidation properties, we applied the dyes **D1−D6** to the photocatalytic oxidative coupling of primary amines. The benzylamine was irradiated with blue LED in the presence of 0.25 mol % dyes and 1 atm of oxygen. Acetonitrile (80% conversion with **D5**, entry 5 in Table 2) was selected as the best solvent after DMSO (69%) and toluene (4%) were also considered. The temperature of the reaction mixture was maintained below 30 °C using a circulated water bath. As shown in entries 1−6 in Table 2, the dyes (**D4−D6**) with two side groups at the 3,7-positions showed better activities than those (**D1−D3**) with one side group. Among **D4−D6**, the more electron-rich dyes showed better reactivities. The 0.25 mol % **D6** showed 83% conversion of benzylamine to the coupled imine. As far as we are aware, this is one of the most active photocatalytic systems for oxidative coupling of primary amines.[8]

As shown in Scheme 1, cationic radical dye species would be formed in photocatalytic processes by electron transfer to oxygen. The instability of this cationic radical species results in low TONs of the catalytic cycle. The highly catalytic performances of the dyes in this work might originate from the unique stability of the cationic radical of phenothiazines. As shown in Figure 1b, the oxidized species of **D6** underwent reversible redox conversion. It is noteworthy that the unique reversible redox process of phenothiazines has been applied to display devices.[10]

In a control experiment (entry 7), when glassware covered with aluminum foil was used, no conversion was

observed. In the absence of **D6**, the catalytic system showed no conversion (entry 8). These observations clearly support that oxidative couplings proceeded by a photo-catalytic process. In optimized conditions, the catalytic system with 0.50 mol % **D6** showed 100% conversion at room temperature after 20 h (entry 9).

Table 2. Photocatalytic Oxidative Coupling of Benzylamine Induced by Phenothiazine Dyes (**D1−D6**)[a]

Ph—NH$_2$ **R1** $\xrightarrow[\text{CH}_3\text{CN, rt, 20 h}]{\substack{\text{O}_2,\text{ blue LED}\\ \text{cat. dye}}}$ Ph—N=Ph **P1**

entry	dye	amount of dye (mol %)[b]	yield (%)[c]
1	**D1**	0.25	22
2	**D2**	0.25	24
3	**D3**	0.25	46
4	**D4**	0.25	51
5	**D5**	0.25	80
6	**D6**	0.25	83
7[d]	**D6**	0.25	0
8	–	0	0
9	**D6**	0.50	100

[a] Reaction conditions: 1 mmol of benzylamine, 1 atm of oxygen, 3 mL of acetonitrile, blue LED, rt, and 20 h. [b] Mol % to benzylamine. [c] Conversion yield based on ^{1}H NMR spectroscopy. [d] The glassware was completely coated with Al foil before LED irradiation.
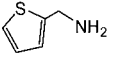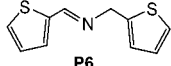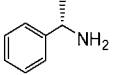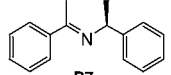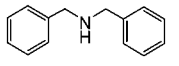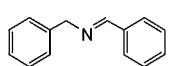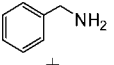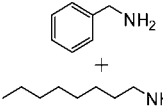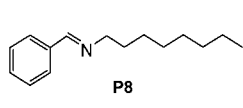
To rationalize the photoredox process, the energy levels of the used materials were considered. As expected, the LUMO of oxygen was lower than that of **D6**. However, the HOMO of benzylamine was lower than that of **D6** (Figures S3−S5 in the SI). Interestingly, the SOMO of oxidized **D6** was lower than the HOMO of benzylamine, indicating that the photoredox process in this work follows the oxidative quenching pathway.[4] The more electron-rich dye showed a higher LUMO, facilitating the electron transfer from dyes to oxygen (Table 1). Moreover, the higher fluoresence quantum yield was observed in more electron-rich dyes (Figure S6 in the SI). Thus, it can be speculated that the increase of catalytic activities from **D4** to **D6** resulted from the more efficient electron transfer of excited states to oxygen.

The photocatalytic system using **D6** was applied to various amines (Table 3). The electronic effect of substituents on arenes of benzyl amines was insignificant in conversion (entries 1−4). 2-Thiophenmethylamine showed 88% conversion (entry 5). The methyl group in the α-carbon of benzylamine dramatically retarded the conversion (entry 6). The photocatalytic system showed good activity in the simple oxidation of the secondary amine (entry 7). However, alkylamines were not converted to the coupled imines. Instead, octylamine could be used as a coupling partner of benzylamine (entry 8).

Several mechanisms of oxidative coupling of primary amines in the literature[7,8] are summarized in Figure 2a.

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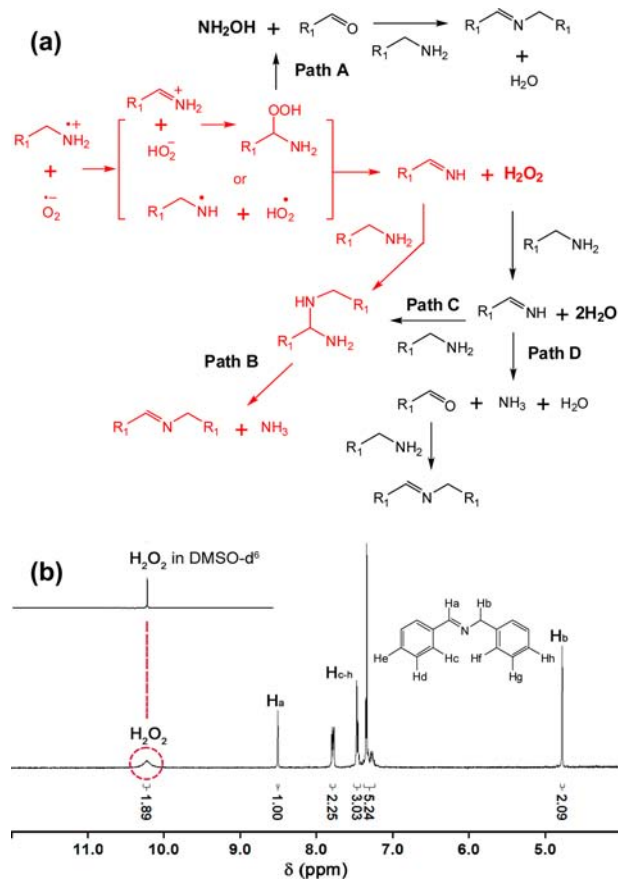
Table 3. Photocatalytic Oxidative Coupling of Amines by **D6**[a]

entry	amine	product	yield (%)[b]
1	X = CH₃ (**R2**)		96(94)
2	X = F (**R3**)		97(93)
3	X = Cl (**R4**)		98(94)
4	X = OMe (**R5**)	**P2-P5**	92(88)
5	**R6**	**P6**	88(84)
6	**R7**	**P7**	35(30)
7	**R8**	**P1**	100(95)
8	**R1** + **R9**	**P8**	62(49)

[a] Reaction conditions: 1 mmol of amine, 1 atm of oxygen, 0.5 mol % **D6**, 3 mL of acetonitrile, blue LED, rt, and 20 h. [b] Conversion yield based on ¹H NMR spectroscopy. The values in parentheses indicate isolated yields. [c] Additional 3 mmol of octylamine was used.

In path A, the formation of benzaldehyde and successive condensation resulted in the coupled imine. In path B, the formation of benzenemethanimine and successive addition of amine resulted in the coupled imine and H_2O_2. In paths C and D, the generated H_2O_2 acts as an additional oxidant. In paths A, C, and D, the H_2O_2 will not be detected. Interestingly, after reaction using **D6**, a quantitative amount of H_2O_2 was detected at 10.2 ppm in ¹H NMR spectrosocpy (Figure 2b). Considering the integration of peaks, the amount of H_2O_2 was very close to a 1:1 ratio to the product, which strongly indicates that the oxidative coupling in this work follows path B in Figure 2a.

In conclusion, new photocatalytic systems were developed using 3,7-disubstituted phenothiazine dyes which showed reversible one-electron oxidation behaviors. The photocatalytic systems with 0.5 mol % dye **D6** showed complete conversion of benzylamine at room temperature. The reaction mechanism was suggested by detection of H_2O_2 as a byproduct. We believe that the prepared phenothiazine dyes can be further applied to more diverse photochemical transformations.

Figure 2. (a) Suggested reaction pathways of oxidative coupling of primary amines to imines through photocatalysis. (b) The detection of H_2O_2 by ¹H NMR spectroscopy after reaction using **D6**.

Supporting Information Available. Experimental procedure for preparation of new compounds and their characterization data, additional optical and electrochemical characterization data, DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.