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Authors: Shawn Collins, Clémentine Minozzi, Antoine Caron, Jeffrey Santandrea, and Jean-Christophe Grenier-Petel

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# Heteroleptic Copper(I)-Based Complexes for Photocatalysis: Combinatorial Assembly, Discovery, and Optimization.

Clémentine Minozzi, Antoine Caron, Jean-Christophe Grenier-Petel, Jeffrey Santandrea and Shawn K. Collins\*<sup>[a]</sup>

#### Dedication ((optional))

**Abstract:** A library of 50 copper-based complexes derived from bisphosphines and diamines was prepared and evaluated in three mechanistically distinct photocatalytic reactions. In all cases, a copper-based catalyst was identified to afford high yields, where new heteroleptic complexes derived from the bisphosphine **BINAP** displayed high efficiency across all reaction types. Importantly, the evaluation of the library of copper-complexes revealed that even when photophysical data is available, it is not always possible to predict which catalyst structure will be efficient or inefficient in a given process, emphasizing the advantages for catalyst structures with high modularity and structural variability.

Molecular synthesis through the use of light has experienced a renaissance in the past decade.<sup>[1]</sup> In concert, photocatalysis has become increasingly important as a synthetic tool as it offers the possibility to employ a wide variety of wavelengths and the option to exploit different mechanistic pathways. Photocatalysts can be used to promote single electron transfer (SET), to engage in energy transfer (ET), or to participate in protoncoupled electron transfer (PCET) reactions.<sup>[2]</sup> While the utility of Ru- and Ir-based polypyridyl-type complexes as sensitizers has been well demonstrated (Figure 1),<sup>[3]</sup> the development of alternatives based upon more abundant metals has also emerged [4] Despite the rich history of copper-based photochemistry, <sup>[5]</sup> synthetic applications of copper-based photocatalysis have only begun to be revisited<sup>[6,7]</sup> While homoleptic polypyridyl-type complexes of copper can be used as photocatalysts for photoredox-type reactions.<sup>[8]</sup> only recently have heteroleptic Cu(I) complexes been explored. [9,10] Despite the potential of heteroleptic Cu(I)-based photocatalysts, they remain underexplored in comparison to other organometallic complexes who may appear more familiar to synthetic chemists. However, familiarity does not always lead to successful development of a photocatalytic reaction. Even when armed with a suitable background of photophysical data, it is difficult to predict a priori which photocatalyst will be optimal for a given transformation. In addition to redox potentials and excited state lifetimes, stability under the reaction conditions.<sup>[11]</sup> or desired solubility profile can still be critical.<sup>[12]</sup> As such, the ability to prepare catalysts in an efficient and straightforward manner

 [a] Clémentine Minozzi, Antoine Caron, Jean-Christophe Grenier-Petel, Jeffrey Santandrea, and Prof. Dr. Shawn K. Collins Department of Chemistry and Centre for Green Chemistry and Catalysis Université de Montréal CP 6128 Station Downtown, Montréal, Québec, Canada H3C 3J7 E-mail: shawn.collins@umontreal.ca

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becomes highly advantageous, especially if a class of catalysts are effective in three mechanistically distinct processes. Herein, the rapid and facile combinatorial assembly, evaluation and discovery of Cu(I)-complexes for photocatalysis in SET, ET and PCET-based transformations is described.



Figure 1. Metal-based complexes for photocatalysis (top) and. combinatorial assembly of Cu(I)-based photocatalysts (bottom).

An advantage of heteroleptic diamine/bisphosphine Cu(I)-based photocatalysts is their facile synthesis and isolation.[13] Sequential addition of bisphosphine and diamine to Cu(MeCN)<sub>4</sub>BF<sub>4</sub> is followed by isolation by precipitation (Figure 1). To demonstrate the ability to rapidly generate a library of photocatalysts for evaluation, different diamine and bisphosphines were selected. The bisphosphines were chosen to vary the nature of the chromophore and bite angle to influence the photophysical properties and catalytic activity.[14] The selection of diamines included bipyridines, phenanthrolines as well as three triazole-based ligands known to stabilize the LUMOs of photoactive complexes.[15] For comparison, the corresponding homoleptic complexes were also prepared. In summary, 50 different catalysts were prepared on gram scale as crystalline solids. Several homoleptic complexes were found to

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rapidly oxidize and/or have low solubility in common organic solvents and were not included in the subsequent characterization and evaluation. The UV-vis absorption characteristics of the photocatalysts tend to vary very little with respect to the bisphosphine.<sup>[16]</sup> In contrast, change of the diamine ligand can produce significant changes in the UV-vis spectra. None of the complexes explored with the four different bisphosphine ligands exhibited any disproportionation behavior.<sup>[17]</sup> The library of heteroleptic copper complexes was then applied in three mechanistically distinct photocatalytic transformations. As photoredox processes have had a profound impact on molecular synthesis, a representative photoredox process was first selected. The visible-light decarboxylative fragmentation of N-(acyloxy)phthalimides was targeted, as several groups<sup>[18]</sup> have demonstrated the utility of the N-(acyloxy)phthalimides in photochemical carbon-carbon bond forming processes. Chen and co-workers had recently disclosed a reductive decarboxylative  $C_{sp}^{\ 3}$ -C<sub>sp</sub> bond coupling reaction to construct substituted alkynes. The process was optimal when employing N-(acyloxy)phthalimides with  $Ru(bpy)_3(PF_6)_2$  (1 mol %) as photocatalyst and a sulfonyl alkyne. They also reported that simpler bromoalkyne coupling partners were not as effective (1+2 $\rightarrow$ 3, 28% yield).<sup>[19]</sup> Consequently, the C<sub>sp</sub><sup>3</sup>–C<sub>sp</sub> bond coupling was investigated with the library of copper heteroleptic complexes using N-(acvloxy)phthalimide 1 and bromoalkyne 2 as coupling partners (Figure 2). Two controls were performed in the absence of any catalyst at either 394 or 450 nm and no desired coupling product 3 was observed. From the results, the heteroleptic complexes formed from the dq ligand were effective for the C<sub>sp</sub><sup>3</sup>-C<sub>sp</sub> coupling; the Cu(dq)(BINAP)BF<sub>4</sub> complex provided the highest yield of alkyne 3 (87 %, 0 % in absence of light).<sup>[20,21]</sup> The second photocatalytic process investigated was a proton-coupled electron transfer (PCET) reaction. PCETs are regarded as non-classical redox processes in which a proton and electron are exchanged in a concerted manner and have only recently been demonstrated as a viable mode of activation in organic synthesis. As a model transformation, the homolytic activation of ketones to generate neutral ketyl radicals was selected (Figure 2). Knowles and coworkers demonstrated that reductive coupling of ketone 4 and subsequent intramolecular conjugate addition afforded the bicycle 5 in 78 % using Ru(bpy)<sub>3</sub>(BAr<sup>F</sup>)<sub>2</sub> as catalyst.<sup>[22]</sup> When ketone 4 was treated with Ru(bpy)<sub>3</sub>(PF<sub>6</sub>)<sub>2</sub> under the blue LED irradiation experimental set-up and conditions used for the copper complexes, the desired bicycle 5 was obtained in 69% yield. When the transformation was performed in the absence of catalyst, a 40 % yield of bicycle 5 was observed under 394 nm irradiation, however no conversion to the desired bicycle 9 was observed at 450 nm. As such, all PCET reactions were performed with blue LEDs. In examining the results from the screening of the Cu-based photocatalysts, the Cu(dq)(BINAP)BF<sub>4</sub> complex identified from the examination of the photoredox process was again one of the most active complexes (71 % of 5). A second grouping of active photocatalysts triazole-based ligands, with bear Cu(quintri)(Xantphos)BF<sub>4</sub> proving to be optimal (79% of 5). Finally, the library of heteroleptic copper complexes was evaluated in an energy transfer process.[23] A visible light sensitization of vinyl azides recently described by Yoon<sup>[24]</sup> involved energy transfer from  $Ru(dtbbp)_3(PF_6)_2$  to promote decomposition of azide **6** to the pyrrole **7** in excellent yield (99%) in 3 h.



**Figure 2.** Evaluation of the library of copper-based photocatalysts in photoredox processes (top); in proton-coupled electron transfer process: homolytic activation of ketones (middle) and. in an energy transfer process: the visible-light sensitization of vinyl azides (bottom). Reactions irradiated with 394 nm light (charcoal) or 450 nm (light grey). Front entries without an indicated phosphine ligand pertain to homoleptic Cu(diamine)<sub>2</sub>BF<sub>4</sub> complexes.

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In investigating the synthesis of pyrroles  $(6 \rightarrow 7)$  using the library of copper-based photocatalysts, controls revealed that in the absence of catalyst at 394 nm, complete conversion was observed (99% of **7**, Figure 2). Even at 450 nm, some pyrrole was observed (19%), so all further reactions were performed at 450 nm. From the results, the heteroleptic complexes formed from the bisphosphine **Xantphos** ligand tend to display the highest yields regardless of amine ligand. Many of the catalysts were highly effective, six catalysts provided the desired pyrrole **7** in >95% yield, while the complexes Cu(dq)(DPEPhos)BF<sub>4</sub>, Cu(dmbp)(**Xantphos**)BF<sub>4</sub> and Cu(dmp)(**BINAP**)BF<sub>4</sub> all provided the pyrrole **7** quantitatively.

Following the survey of the library of copper photocatalysts in photocatalytic processes (Figure 2), absorption/emission data, excited state lifetime and cyclic voltammetry experiments were conducted for a series of photocatalysts: five complexes of the type Cu(dq)(bisphosphine)BF4, and ten complexes of the type  $Cu(diamine)(BINAP)BF_4^{[16]}$  When examining the photoredox processes  $(1+2\rightarrow 3)$ , the yield obtained for each of the photocatalysts versus their calculated excited state redox potentials and excited state lifetimes was plotted in an effort to discern any trends (Figure 3). When analyzing the influence of the bisphosphine, the excited state redox potentials were shown to vary between approximately -1.3 and -1.9 V (vs. SCE). The Cu-based complexes with Xantphos and BINAP bisphosphines possessed the highest redox potentials, however it was the dppf and **BINAP** catalysts which afforded the highest yields for the process  $(1 \rightarrow 3)$ . The reduction potentials for certain Nhydroxyphthalimides are low enough (-1.28→-1.37 V vs. SCE)<sup>[25]</sup> that most catalysts surveyed should be able to promote the decarboxylation event. When examining the influence of the diamine ligand, again no pattern could be readily identified between the redox potential and the isolated yield in the photoredox transformation. In addition, catalyst types having longer excited state lifetimes did not necessarily afford greater vields of product. In contrast to the photoredox process, the PCET transformation surveyed  $(4 \rightarrow 5, Figure 3)$  did demonstrate trends between the yields and redox potential of the photocatalyst, although again no trend with the excited state lifetime was observed. The Cu(dq)(Xantphos)BF4 and Cu(dg)(BINAP)BF<sub>4</sub> complexes had the highest redox potentials and best yields amongst the different bisphosphine complexes surveyed. Knowles and co-workers had shown that a Ru-based intermediate (Ru<sup>I</sup>(bpy)<sub>3</sub> ( $E_{1/2}^{ox}$  = -1.33 V vs. SCE))<sup>[22]</sup> possessed a redox potential high enough to promote the PCET process. Almost all of the catalysts surveyed possess a similar redox potential capable of promoting the PCET process, but certain classes of catalyst structures were clearly more efficient than others, with the origins of the reactivity still not evident. When examining the energy transfer reaction  $(6 \rightarrow 7, Figure 3)$  the triplet state energy of the corresponding Cu-based complex was highest with the BINAP-based catalyst. The dienyl azide 6 could be estimated to have a triplet energy of approximately 1.9 eV, [24] which would imply that each catalyst should be able to promote the transformation to pyrrole. However, it was the excited state lifetimes which showed a trend with the observed yields: in the Cu(diamine)(BINAP)BF<sub>4</sub> series, the E<sub>T</sub> values remained constant for all catalysts, however the dmp-containing complex having the longest excited state lifetime clearly afforded the highest vield.<sup>[26]</sup>



**Figure 3.** Comparison of yields obtained in using copper-based photocatalysts versus relevant photophysical properties: visible-light decarboxylative fragmentation of *N*-(acyloxy)phthalimides (*top*), a homolytic activation of ketones (*middle*), and visible-light sensitization of vinyl azides (*bottom*). Yields are indicated as bars and are color-coded for reactions irradiated with 394 nm (charcoal) and with 450 nm (grey). Redox potentials and triplet state energies are indicated as discs (black).

Similarly, in the Cu(**dq**)(bisphosphine)BF<sub>4</sub> series, the complex having **DPEPhos** or **XantPhos** ligands had the highest excited state lifetimes and highest overall yields of product.

In summary,  $Cu(diamine)(bisphosphine)BF_4$  complexes possess characteristics that can significantly impact the growing

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area of photocatalysis. Their facile synthesis and modularity is ideally suited to combinatorial synthesis and screening in different photocatalytic processes. Preparation of a 50-complex library was accomplished and evaluated in three mechanistically distinct photocatalytic reactions. In each case, a copper-based catalyst could be identified to provide ≥80 % isolated yield of the desired product. The screening process identified new catalyst structures based upon **BINAP** bisphosphines (for photoredox and energy transfer processes) and triazole-based diamines (for PCET processes). BINAP-based complexes were generally efficient across all reaction types, and possessed higher redox potentials and triplet energies (for photoredox and PCET: Cu(dq)(BINAP)BF<sub>4</sub>,  $\lambda_{abs}$  472 nm,  $\lambda_{em}$  521 nm, E<sup>o</sup> = -1.87 eV, E<sup>1</sup> = 2.38 eV,  $\tau$ =4 ns), although judicious choice of diamine was necessary to extend excited state lifetimes for energy transfer processes (for energy transfer Cu(dmp)(BINAP)BF<sub>4</sub>, λ<sub>abs</sub> 387 nm,  $\lambda_{em}$  445 nm, E<sup>o</sup> = -2.04 eV, E<sup>T</sup> = 2.38 eV,  $\tau$ =2188 ns). The studies also demonstrate the first utility of copper-based photocatalysts in synthetic PCET and energy transfer processes. Efforts to rationalize catalyst efficiency through available photophysical parameters could explain trends seen in a certain transformation, but would not have been able to predict catalyst behavior in another. Importantly, the above study represents a rare evaluation of photocatalyst structure vs. activity in photocatalytic processes, that is surprisingly absent from the literature for other more well-established photocatalyst types. The facile synthesis of heteroleptic Cu(NN)(PP)X, complexes and the ability to vary both physical and photophysical characteristics, should encourage further exploration and new applications of the catalyst-class in photocatalysis.

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A library of 50 copper-based complexes derived from bisphosphines and diamines was prepared and evaluated in three mechanistically distinct photocatalytic reactions. In all cases, a copper-based catalyst was identified to afford high yields/reactivities surpassing other transition-metal based photocatalysts, emphasizing the advantages of using catalyst structures with high degrees of modularity and structural variability.