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Research Article

Development of a Platform for Near-Infrared Photoredox Catalysis

Benjamin D. Ravetz, Nicholas E. S. Tay, Candice L. Joe,* Melda Sezen-Edmonds, Michael A. Schmidt, Yichen Tan, Jacob M. Janey, Martin D. Eastgate, and Tomislav Rovis*

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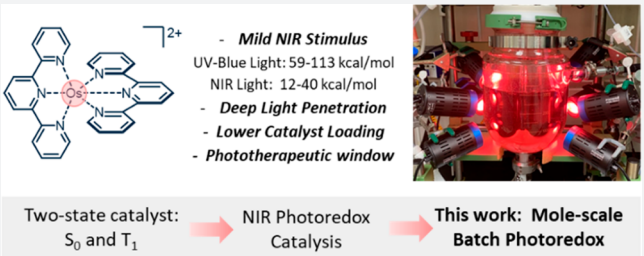
ABSTRACT: Over the past decade, chemists have embraced visible-light photoredox catalysis due to its remarkable ability to activate small molecules. Broadly, these methods employ metal complexes or organic dyes to convert visible light into chemical energy. Unfortunately, the excitation of widely utilized Ru and Ir chromophores is energetically wasteful as ∼25% of light energy is lost thermally before being quenched productively. Hence, photoredox methodologies require high-energy, intense light to accommodate said catalytic inefficiency. Herein, we report photocatalysts which cleanly convert near-infrared (NIR) and deep red (DR) light into chemical energy with minimal energetic waste. We leverage the strong spin−orbit coupling (SOC) of Os(II) photosensitizers to directly access the excited triplet state (T_1) with NIR or DR irradiation from the ground state singlet (S_0). Through strategic catalyst design, we access a wide range of photoredox, photopolymerization, and metallaphotoredox reactions which usually require 15−50% higher excitation energy. Finally, we demonstrate superior light penetration and scalability of NIR photoredox catalysis through a mole-scale arene trifluoromethylation in a batch reactor.



■ INTRODUCTION

The renaissance of synthetic photochemistry in recent years has emerged from major advances in our understanding of the photophysical principles that dictate the interplay between light and matter. While traditional photochemistry relies on the photoexcitation of stoichiometric reagents to overcome challenging thermodynamic barriers, modern photoredox catalysis uses a photon-absorbing molecule—a photocatalyst—to create electronically excited states capable of redox or energy transfer reactions.[1,2] While synthetic photoredox continues to revolutionize organic chemistry and beyond, key weaknesses remain, including reaction scalability, functional group selectivity, and catalyst robustness.[3]

One major advance toward improving the scalability of photocatalytic reactions is flow chemistry, in which parallel microreactors overcome the limitations of photon attenuation as described by the Bouguer−Lambert−Beer (BLB) law.[4] While this strategy is a viable solution from an engineering perspective, it does not address the fundamental inefficiencies inherent to the photocatalysts' photophysical processes.[5] There are two major issues—first, light penetration into reaction medium is limited by large extinction coefficients (ε) associated with the photoexcitation of the photocatalyst's ground state to excited singlet state ($S_0 \rightarrow S_1$ transition) via metal-to-ligand charge transfer (MLCT). For reference, the ε of $[Ru(bpy)_3]^{2+}$ is very large at ∼14 400 M^{-1} cm^{-1} (450 nm). Second, accessing the catalytically relevant MLCT triplet state (T_1) requires spin-forbidden intersystem crossing (ISC) from excited singlet to excited triplet state (S_1 to T_1), which is mediated by spin−orbit coupling (SOC) (Figure 1a). While rapid and efficient ISC is present for many Ru(II) and Ir(III) photocatalysts, it remains a wasteful nonadiabatic process for photoredox with ∼15−25 kcal/mol lost thermally to solvent.[6]

We hypothesize that we could bypass these fundamental issues by leveraging a spin-forbidden $S_0 \rightarrow T_1$ excitation (Figure 1b). $S_0 \rightarrow T_1$ excitation has been reported for Ru(II),[7] Ir(III),[8] and Fe(II),[9] but with inconsequential extinction coefficients for photoredox catalysis. While this concept has been applied to excitation of reagents,[10,11] identifying new photocatalysts with strong SOC will allow direct access to long-lived redox-active T_1 states via $S_0 \rightarrow T_1$ excitation and minimize ISC-specific energy loss. Fundamentally, this creates a two-state system paradigm for transition metal-based photoredox catalysis by direct $S_0 \rightarrow T_1$ excitation, obviating the limitations associated with accessing the T_1 state by initial $S_0 \rightarrow S_1$ excitation.[6]

Os(II) polypyridyl complexes (Figure 1b) display significant $S_0 \rightarrow T_1$ excitation in the DR and NIR regions (660−800 nm)[12] which is typically attributed to strong SOC induced by Os. When compared to Ru(II) tris-bipyridyl species, Os(II) analogues have relatively shorter excited state lifetimes (τ =

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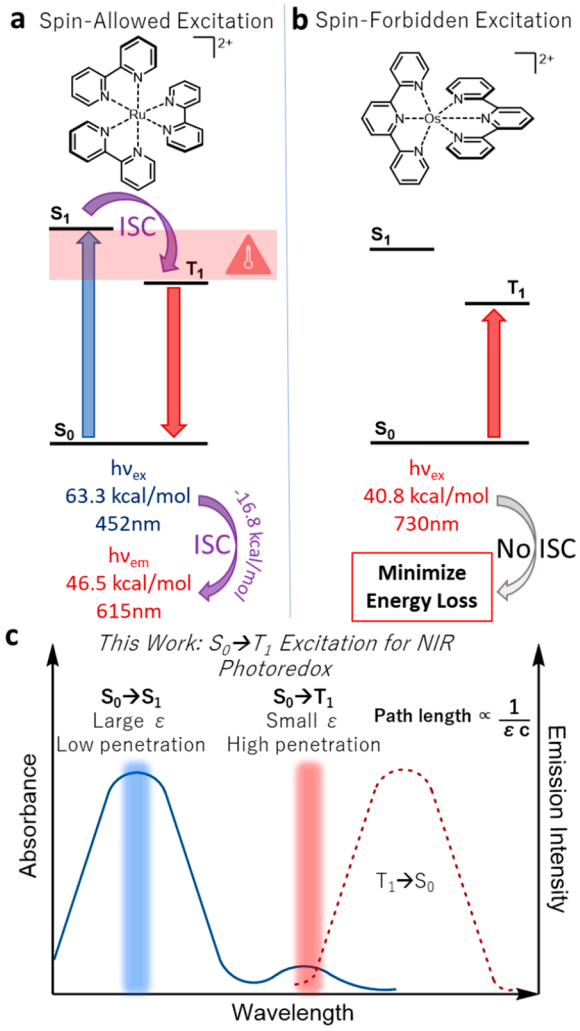

Figure 1. (a) Jablonski schematic for $[Ru(bpy)_3]^{2+}$. (b) Schematic depicting a $S_0 \rightarrow T_1$ excitation. (c) Comparison of blue and NIR light penetration.

600 ns for $Ru(bpy)_3^{2+}$ vs 19 ns for $Os(bpy)_3^{2+}$ in water[13]) due to SOC effects[14] and energy gap considerations.[15] However, Os-based bis-terpyridines have dramatically improved emission lifetimes relative to their Ru congeners (τ = 250 ps for $Ru(tpy)_2^{2+}$ vs 269 ns for $Os(tpy)_2^{2+}$ in MeCN[16]) due to a large energy gap between the ^{3}MLCT and deactivating ^{3}MC (metal centered triplet) states.[17] While the luminescence quantum yield for $Os(tpy)_2^{2+}$ is slightly lower than for $Ru(bpy)_3^{2+}$,[18] these complexes have been used as triplet sensitizers for singlet oxygen generation[19] and for photon upconversion.[20] Their use as photoredox catalysts has yet to be examined and would be interesting due to their red-centered maximum absorption, which enables high solution penetration, as dictated by the BLB law ($\varepsilon \sim 500\ M^{-1}\ cm^{-1}$ (740 nm), which is ~30× lower than $[Ru(bpy)_3]^{2+}$ at 450 nm). Thus, we envisioned that Os(II) chromophores could catalyze photoredox reactions with improved light penetration (Figure 1c) and a broader material penetration profile[21,22]—a particularly attractive tool for the emerging fields of photopolymerization[23] and photoenzymatic catalysis.[24] For instance, NIR light will penetrate up to 200% further than blue light through most tissues with minimal phototoxicity, which lends itself well to materials applications.[22]

■ RESULTS AND DISCUSSION

We began our studies using $Os(bptpy)_2(PF_6)_2$ (**Os3**) as the photocatalyst (Figure 2) and performed reactions under NIR light irradiation (Figure 3a). While there are several examples of NIR photoredox catalysis or NIR-initiated photopolymerization[25−28] using high-powered LEDs, the bulk of photoredox catalysis requires blue or near-UV light. Notably, a recent paper from Gianetti[29] describes a helical carbenium photocatalyst for red light driven photoredox catalysis (640 nm).

To elucidate the disparity of visible vs NIR light driven reactions, we draw comparisons to $Ru(bpy)_3(PF_6)_2$ which absorbs blue light (63.3 kcal/mol) with high efficiency. However, during ISC it loses 16.8 kcal/mol providing T_1 energy of 46.5 kcal/mol, which is similar to the T_1 energy of **Os3** (40.8 kcal/mol) (Figure 1a,b). From a purely energetic standpoint, this rationalizes the wide oxidizing and reducing capabilities of our NIR photoredox platform despite longer-wavelength light stimulus.

We were excited to achieve a variety of photopolymerizations, ranging from cationic polymerization of cyclohexene oxide (CHO) **2**,[30] atom transfer radical polymerization of **5** (ATRP),[31] or reversible addition−fragmentation chain transfer polymerization (RAFT) of methyl methacrylate (MMA) **8**[27]

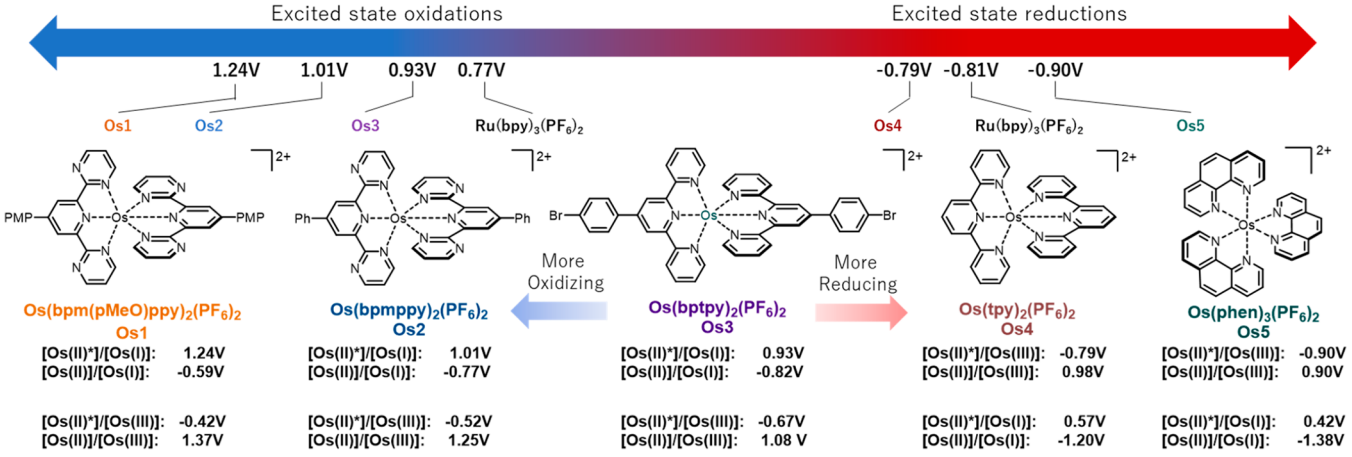

Figure 2. Selected scope of photocatalysts with $S_0 \rightarrow T_1$ transition and their respective redox potentials vs Ag/AgCl in MeCN. Note: The Os(II)*/Os(I) redox couple represents a ligand-centered reduction.

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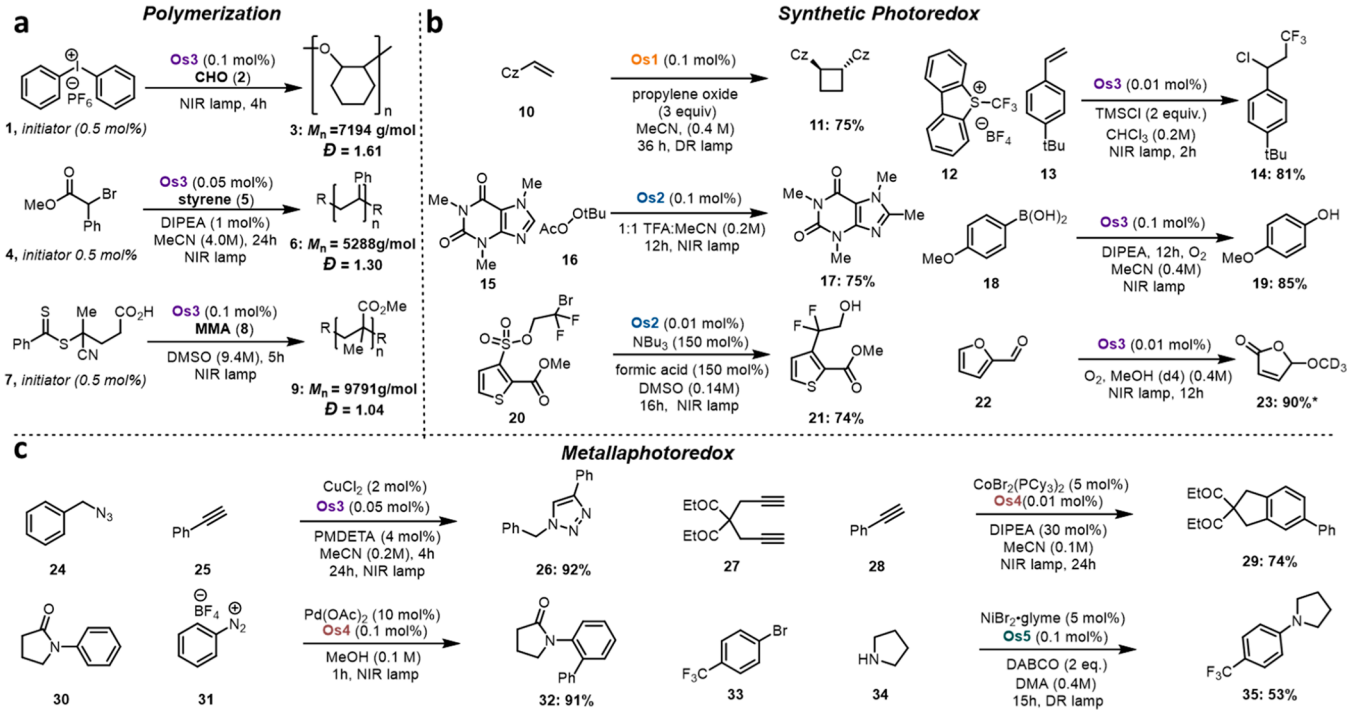

Figure 3. (a) Polymerizations achieved with NIR light. (b) Scope of oxidative and reductive photoredox reactions (yields with * determined by ^{1}H NMR). (c) Scope of metallaphotoredox reactions including Cu, Co, Ni, and Pd. See Figure S7 for a comparison to original published conditions.

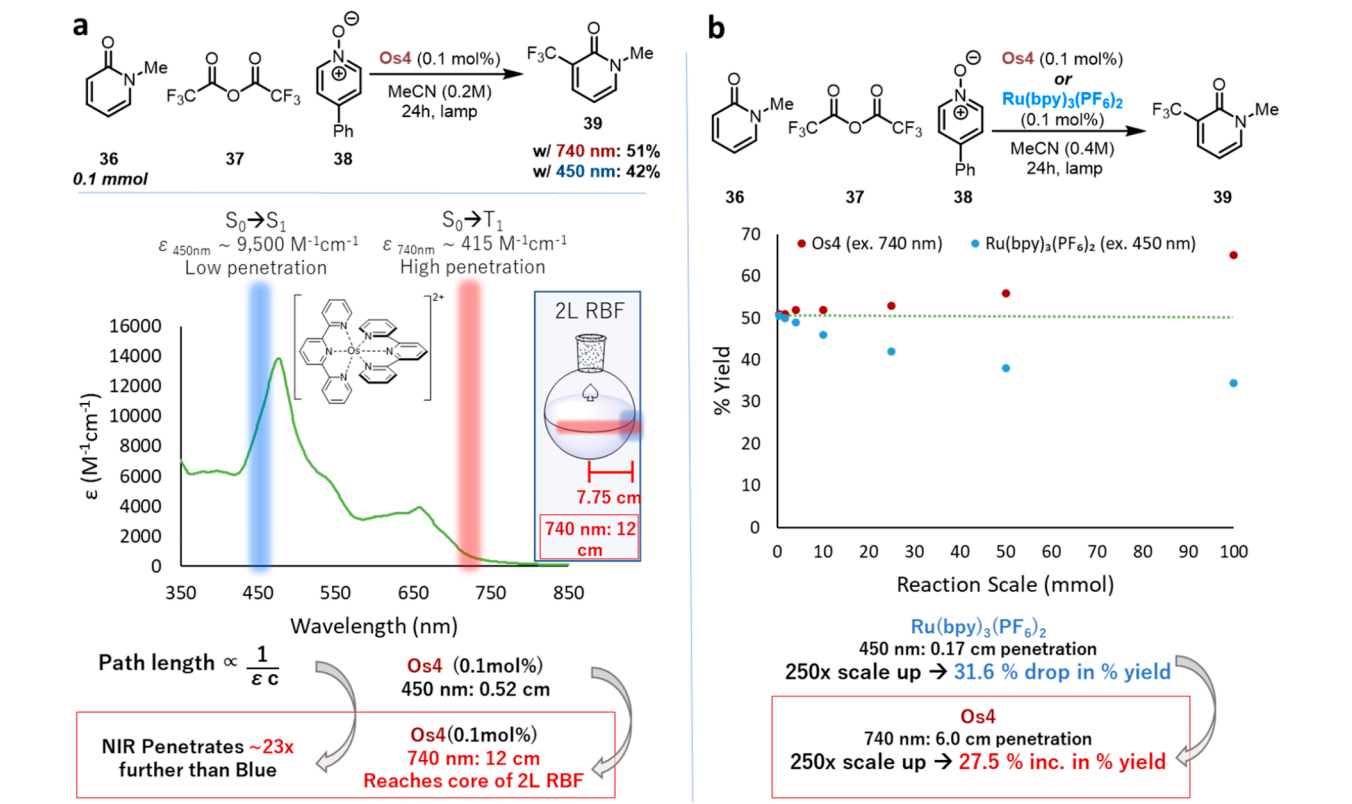

Figure 4. (a) Light penetration comparison of 450 and 740 nm light into reaction mixture. (b) Comparison of 450 nm with $Ru(bpy)_3(PF_6)_2$ and 740 nm light with **Os4** at increasing reaction scale.

(Figure 3a). We next explored transformations that proved challenging with our recently reported method employing triplet fusion upconversion for NIR photoredox catalysis.[32] We found that NIR-irradiated **Os3** is capable of catalyzing alkene chlorotrifluoromethylation[33] of **13** in 81% yield. To test the catalyst's stability (Figure S2) under oxidative conditions, we also performed aryl boronic acid oxidation[34] and oxygen sensitization (Figure 3b).[35] A more oxidizing dipyrimidine

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scaffold (**Os1**) catalyzes a cation radical [2 + 2] cycloaddition,[36] an intramolecular Smiles reaction,[37] and radical methylation.[38] In particular, the Smiles reaction is known to be radical-initiated by direct blue light irradiation.[39] No rearrangement is observed using NIR light in the absence of Os which eliminates the possibility of a light-activated radical initiation pathway.

Next, we directed our attention on achieving NIR-metallaphotoredox to expand our scope to cross-couplings, C−H functionalization, and cycloadditions. We observed that NIR irradiation of **Os3** induces the Cu-click reaction.[28] The lack of azide radical decomposition of **24** to benzyl amine[40] is promising for chemical biology applications[41] as this undesirable pathway is observed under high-energy light irradiation[42] (Figure 3c). While we found **Os3** to be a competent photocatalyst for the Cu-click, it inefficiently activates Co(II) and Pd(II) complexes. Thus, we tuned the terpyridine ligand scaffold to obtain the necessary reduction potentials required to activate Co and Pd (Table S1). We find that $Os(tpy)_2(PF_6)_2$ (**Os4**) is 120 mV more reducing and enables Pd-catalyzed C−H arylation[43] and Co-catalyzed [2 + 2 + 2] cycloaddition of alkynes[44] (Figure 3c). Importantly, diazonium **31**, Pd, and Co intermediates are all competent chromophores for blue light absorption;[45,46] however, using NIR light to selectively activate **Os4** circumvents light-initiated substrate degradation[47] and enables lowering of catalyst loading (see Figure S7).

Ni-metallaphotoredox is particularly impactful,[48] yet we determined that **Os1**−**Os4** are unable to accomplish Ni(II)/Ni(I) reduction. To address this, we turned to trisleptic Os(II) complexes which possess a $S_0 \rightarrow T_1$ excitation in the deep red (DR) region. $Os(phen)_3(PF_6)_2$ (**Os5**) enables Ni-catalyzed Buchwald−Hartwig cross-coupling of aryl bromides and amines[49] under DR irradiation. In light of recent work addressing poor batch scale performance of $Ru(bpy)_3(PF_6)_2$ under blue light conditions, this is a particularly exciting area of potential impact.[50,51] The reactions described above demonstrate novel Os and NIR photoredox catalysis, which are performed with up to 200× lower catalyst loadings compared to the literature precedent (for comparisons, see Figure S7).

To highlight the utility of this platform, we investigated the application of Os(II) photocatalysts to reactions in batch. We used Stephenson's arene trifluoromethylation as the model reaction as it has been studied in batch and flow[52,53] with blue light. Photoredox reactions are typically slower and lower yielding on large scale due to limited light penetration as dictated by the BLB law. As the size of reaction vessels increase, the irradiated surface area to volume ratio decreases such that photon exposure is limiting. While plug flow reactors maximize light penetration and improve reaction rates on kilograms/day scale,[54] their suitability toward commercial manufacturing is still limited.[55] From an industrial application perspective, the ability to use batch reactors is incredibly advantageous as it does not require specialized equipment and can be easily implemented in any multipurpose facility.

Our Os catalysts have lower extinction coefficients in the NIR and DR (~500 and ~3500 M^{-1} cm^{-1}, respectively) (Figure 4a) and bypass the energy losses associated with ISC rendering them more suitable for large-scale reactions in batch reactors. For example, using a catalyst concentration of 0.2 mM and the experimentally determined ε values at 450 and 740 nm, we estimate that NIR light penetrates approximately 23-fold further into reaction solution than blue light (Figure 4a).[56] According to the BLB law, NIR light should penetrate 12 cm into reaction solution before 90% of its power is absorbed by the reaction mixture, whereas blue light can only penetrate 0.52 cm (Figure S5).

We performed Stephenson's trifluoromethylation on various reaction scales (Figure 4b) with $Ru(bpy)_3(PF_6)_2$ excited by 450 nm light and **Os4** excited by 740 nm light. When blue light and $Ru(bpy)_3(PF_6)_2$ are used, we observe the yield decrease with increasing reaction scale, aligning with Stephenson's results. However, when **Os4** and 740 nm light are used, we observe the yield maintain or increase on larger reaction scale. We also see an increase in the yield with higher catalyst loading of Os on small scale (2 mol % **Os4**, 65% yield on 1 mmol scale), in contrast to recent findings in which high-powered laser driven flow chemistry alongside decreased catalyst loading was used to improve blue light harvesting within a CTSR.[55] These findings highlight advantages of **Os4**'s NIR $S_0 \rightarrow T_1$ excitation which allows deeper light penetration into the medium.

To fully demonstrate the scalability of our NIR photoredox platform, we opted to test this system on a 1 mol scale to showcase this technology in batch-mode. Inherently, the vessel required to accommodate the 1 mol scale has a large cross-sectional area (22.5 cm outer diameter) and remains a significant challenge for blue light excitation. As diagrammed in Figure 5, we aligned the lamps in an X-like formation around the reactor, which was affixed with overhead stirring, an

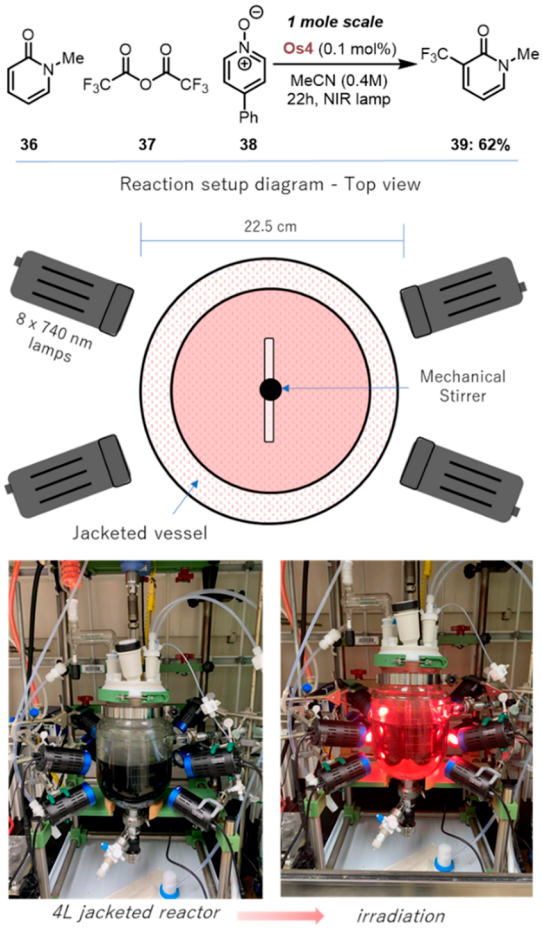

Figure 5. Trifluoromethylation performed on a 1 mol scale in a batch reactor provided 62.6% yield (see the SI).

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internal temperature probe, condenser, N_2 sparge line, and sampling line. Upon performing the scale-up with NIR light, we obtained a 62% yield after 22 h of irradiation with eight 740 nm lamps. The reaction stream is dark in color and is conducted at a high concentration (0.4 M). Surprisingly, the yield surpasses the yield obtained on the 10 mmol scale (∼50%) after just 6 h of irradiation.

We find the successful scale-up result fascinating since the photon flux on large scale is dramatically decreased compared to the 10 mmol scale. As previously reported and described,[52] scaling light irradiance proportionally to reaction volume in a batch reactor is a tremendous challenge. For example, to theoretically maintain the same photon flux on a 1 mol scale from a 10 mmol scale, we would require 200 lamps spaced around the reactor (see Figure S8). However, with just 8 lamps, we observe comparable or increased yields.[57] Taken together, this result demonstrates an excellent proof of concept for scalable photoredox catalysis amenable to batch reactors.

By targeting the NIR $S_0 \rightarrow T_1$ excitation, we demonstrate the photophysical advantages of a two-state photoredox system where direct activation of T_1 from S_0 is made possible by SOC. This is broadly applicable across a variety of oxidative and reductive synthesis, photopolymerization, and metallaphotoredox. Ongoing studies aim to redesign photocatalysts to boost the $S_0 \rightarrow T_1$ transition, which should improve energy efficiency of catalyst excitation, scalability, and excitation selectivity. We believe these findings will lead to the discovery of new reactions and applications of DR/NIR photoredox catalysis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscentsci.0c00948.

Experimental procedures, characterization data, and copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra for all new compounds (PDF)

Crystallographic data for **Os3** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

Candice L. Joe − *Chemical Process Development, Bristol Myers Squibb, New Brunswick, New Jersey 08903, United States;* orcid.org/0000-0002-7167-2416; Email: Candice.joe@bms.com

Tomislav Rovis − *Department of Chemistry, Columbia University, New York, New York 10027, United States;* orcid.org/0000-0001-6287-8669; Email: tr2504@columbia.edu

Authors

Benjamin D. Ravetz − *Department of Chemistry, Columbia University, New York, New York 10027, United States*

Nicholas E. S. Tay − *Department of Chemistry, Columbia University, New York, New York 10027, United States*

Melda Sezen-Edmonds − *Chemical Process Development, Bristol Myers Squibb, New Brunswick, New Jersey 08903, United States;* orcid.org/0000-0003-0476-6815

Michael A. Schmidt − *Chemical Process Development, Bristol Myers Squibb, New Brunswick, New Jersey 08903, United States;* orcid.org/0000-0002-4880-2083

Yichen Tan − *Chemical Process Development, Bristol Myers Squibb, New Brunswick, New Jersey 08903, United States*

Jacob M. Janey − *Chemical Process Development, Bristol Myers Squibb, New Brunswick, New Jersey 08903, United States;* orcid.org/0000-0001-7697-1709

Martin D. Eastgate − *Chemical Process Development, Bristol Myers Squibb, New Brunswick, New Jersey 08903, United States;* orcid.org/0000-0002-6487-3121

Complete contact information is available at: https://pubs.acs.org/10.1021/acscentsci.0c00948

Notes

The authors declare no competing financial interest.

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(57) A reaction quantum yield determination would clearly be of value. However, a consistent and widely accepted chemical standard for NIR actinometry (740 nm) remains to be developed. For a recent development of a universal actinometer applicable up to 700 nm, and a discussion of the state of the art, see: Reinfelds, M.; Hermanns, V.; Halbritter, T.; Wachtveitl, T.; Braun, M.; Slanina, T.; Heckel, A. A robust, broadly absorbing fulgide derivative as a universal chemical actinometer for the UV to NIR region. *ChemPhotoChem.* **2019**, *3*, 441−449.

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