

Visible Light-Gated Cobalt Catalysis for a Spatially and Temporally Resolved [2+2+2] Cycloaddition

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S Supporting Information

ABSTRACT: The ability to exert spatial and temporal control over a transition-metal catalyst offers diverse opportunities for the fabrication of functional materials. Using an external stimulus such as visible light to toggle a catalyst between an active and dormant state has proven to be an effective approach for controlled, radical methodologies. Outside of radical bond formation, there is a dearth of evidence that suggests traditional transition metal catalysis can similarly be controlled with visible light energy. Many cobalt complexes that catalyze the [2+2+2] cycloaddition are assisted by UV photolysis, but strict photocontrolled methods are unattainable due to high levels of thermally driven reactivity. Herein, we disclose the first light-controlled, cobalt-catalyzed [2+2+2] cycloaddition via a dual cobalt and photoredox catalyst manifold. We demonstrate the power of this method with a spatially and temporally resolved technique for arene formation using photolithography.

The need for increased control of catalyst activity for materials and biological applications has underscored the importance of spatially and temporally resolved transformations. This level of control is generally obtained by using an external stimulus to start or stop a catalytic reaction.^{1,2} By far the most ideal external stimulus is visible light, easy to handle and deliver spatially, inexpensive and widely accessible. The use of light to activate or inactivate a catalyst is referred to as light-gated catalysis, and represents a powerful approach to afford exquisite control over several transformations.^{3,4}

Forty years of cobalt catalysis literature has illustrated the synthetic utility of these catalysts in assembling arenes via [2+2+2] cycloadditions. The typical precatalysts used in these transformations such as $\text{Co}_2(\text{CO})_8$ and $\text{CpCo}(\text{CO})_2$, when irradiated with ultraviolet light, catalyze the [2+2+2] cycloaddition reaction at an accelerated rate.⁵ Although photodissociation of the labile CO ligand assists reactivity, thermal ligand dissociation is a competitive pathway which prevents a purely light-controlled reaction. A viable alternative to carbonyl-based precatalysts uses in situ reduction of phosphine-based Co(II) complexes with low-valent metals but affords little opportunity for external regulation.⁶ Indeed, examination of the relevant literature reveals that there are no light-gated catalysts for the vast majority of common organic transformations.^{3,7,8}

Photocaged metal catalysis involves uncaging and irreversible release of an active catalyst (Figure 1a). Light-gated catalysis

utilizes complexes that are active in the presence of light and inactive when the light source is removed (Figure 1b).⁹ This is the situation with photoredox catalysis, with the caveat that recent evidence suggests some extent of initiation behavior with these catalysts but with short lifetimes.¹⁰ Extending this control to new, nonradical bond constructions would greatly expand our ability to use diverse catalyst methods in myriad applications (Figure 1c).¹¹

We began our studies by examining [2+2+2] cycloadditions of three unsaturated coupling partners using earth-abundant Co(II) salts as precatalysts. High oxidation state Co is typically reduced in situ with (super)stoichiometric metal additives in an uncontrolled manner. We speculated that a photoredox catalyst and a sacrificial organic reductant would lead to the controlled formation of a catalytically active species. Voltammetry studies (see SI, Table S1) of phosphine-based cobalt complexes $[\text{CoX}_2(\text{PR}_3)_2]$ indicated many undergo a quasi-reversible reduction event at potentials ranging from -0.60 to -1.04 V versus Ag/AgCl. Measurements also indicate $\text{CoBr}_2(\text{PCy}_3)_2$ displays the highest ability to effectively stabilize low-valent cobalt with reduction events as -1.04 V $[\text{Co}^{\text{II}}/\text{Co}^{\text{I}}]$ and -1.39 V $[\text{Co}^{\text{I}}/\text{Co}^0]$ versus Ag/AgCl. With this knowledge, we envisioned that a reductive quench of the photocatalyst excited state $\text{Ir}^{\text{III}*}$ with sacrificial amine would furnish the reduced Ir^{II} species ($E_{1/2}[\text{Ir}^{\text{III}}/\text{Ir}^{\text{II}}] = -1.30$ V vs Ag/AgCl).¹² Reduction of $\text{CoBr}_2(\text{PCy}_3)_2$ by Ir^{II} would be thermodynamically favored to generate an active low-valent cobalt catalyst.

To test this hypothesis and intercept an active cobalt(II) species for arene formation, we first screened reaction conditions for the [2+2+2] cycloaddition of diyne **1** and phenylacetylene **2**. In the presence of $[\text{Ir}(\text{dF-CF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ and substoichiometric amounts of sacrificial reductant diisopropylethylamine (DIPEA), the complex $\text{CoCl}_2(\text{PCy}_3)_2$ delivers arene product **2** in 74% yield (Figure 2A, entry 1). Exclusion of light or photocatalyst results in little to no conversion (Figure 2A, entries 2, 3) but removal of the amine reductant only diminishes reaction efficiency, still providing **3** in 43% yield. In the absence of sacrificial amine reductant, tricyclohexylphosphine ($E_{1/2} = +0.89$ V vs Ag/AgCl) likely serves as a reductant for $\text{Ir}^{\text{III}*}$ which decreases the effective ligand concentration (Figure 2A, entry 4). Notably, heating the reaction in the absence of light also does not provide product (Figure 2A, entry 5). Although several cobalt precatalysts furnish product (Figure 2A, entry 6, 7), the highest

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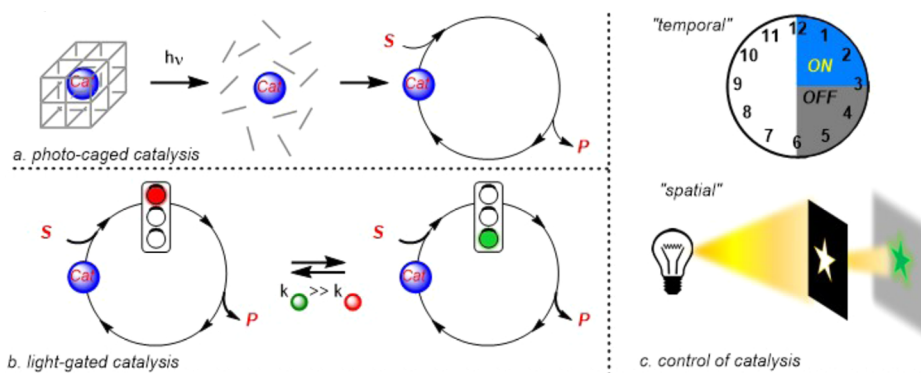
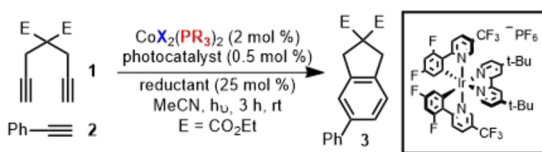


Figure 1. (a) Light initiation of photocaged catalysis typically involves releasing the caged catalyst. (b) Light-gated catalysis leads to a catalyst being on under light irradiation and off once the light source is removed. (c) Light-gated process allows control of catalysis to specific times and spaces.

A. Optimization



Entry	X	PR ₃	Reductant	h _ν (nm)	Yield
1	Cl	PCy ₃	DIPEA	452	74%
2	Cl	PCy ₃	DIPEA	---	<1%
3 ^a	Cl	PCy ₃	DIPEA	452	0%
4	Cl	PCy ₃	---	452	43%
5 ^b	Cl	PCy ₃	DIPEA	---	0%
6 ^c	Br	PEt ₃	DIPEA	452	40%
7	Br	dppp	DIPEA	452	31%
8	Br	PCy ₃	DIPEA	14W CFL	92%

B. Scope

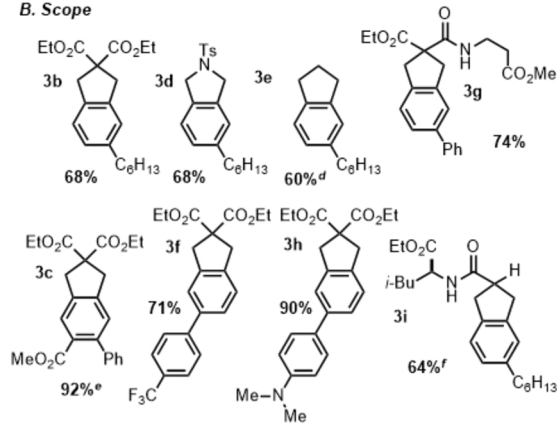
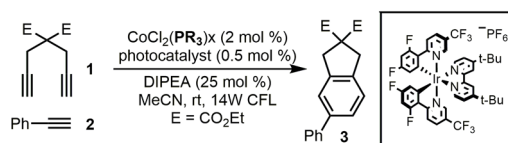


Figure 2. (A) Reaction optimization. Standard conditions: 0.20 mmol diene, 0.35 mmol alkyne, 0.1 M MeCN. Yield determined by HPLC analysis using an internal standard. (B) Reaction scope. Reaction scope under conditions in entry 8, unless otherwise stated. (a) Photocatalyst removed. (b) Reaction heated to 80 °C. (c) 5% CoBr₂(PEt₃)₂, (d) DCE as solvent. (e) 50 °C. (f) 1:1 dr.

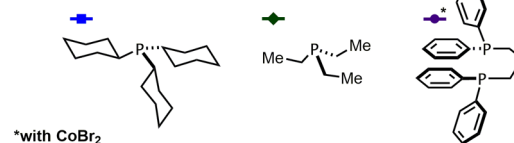
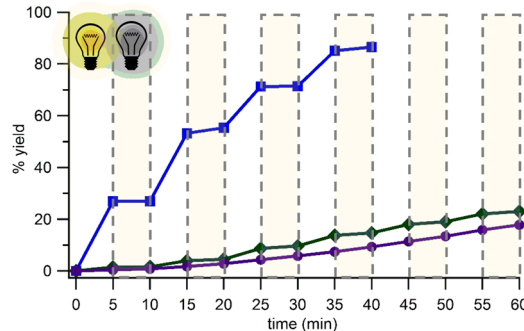
yield of 92% is obtained with CoBr₂·(PCy₃)₂ using a standard 14 W CFL bulb (Figure 2A, entry 8).

To examine further the impact of light we conducted experiments under alternating periods of irradiation and darkness. The parent precatalyst CoBr₂·(PCy₃)₂ shows a distinct response to light (controlled beyond initiation), which allows

precise temporal control over the entire reaction period (Figure 3). Initial irradiation affords product in 27% yield, but removing the light source quickly stops catalysis. Reactivity is easily restored with a second period of irradiation and the reaction proceeds to give a high yield of arene product. Furthermore, the precatalysts CoCl₂·(PEt₃)₂ and CoBr₂·(dppp) both deliver



A. Ligand Effect



*with CoBr₂

B. Attempt at Thermal Restoration of Catalysis (PR₃ = PCy₃)

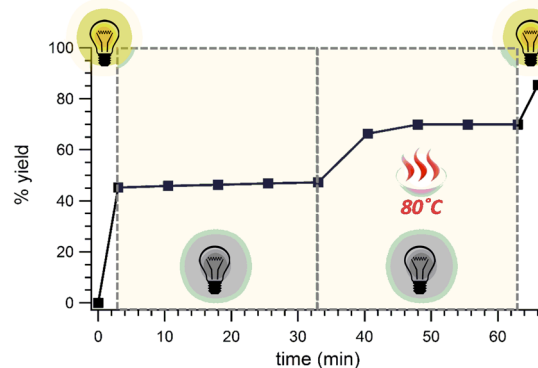


Figure 3. (A) Ligand effect on catalysis. (B) Attempt at thermal restoration of catalysis.

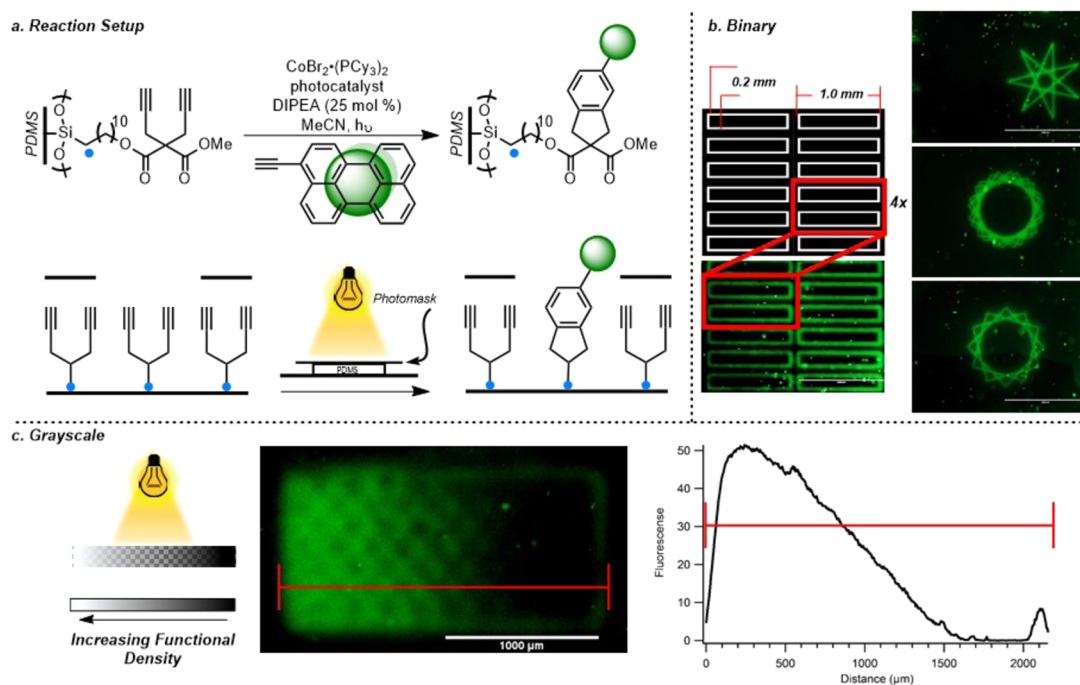


Figure 4. (a) Light-gated spatial control of photolithographic modification of polydimethylsiloxane (PDMS). (b) Magnified fluorescence images of functionalized material with binary masks. (c) Gradient scale photomasks suggest increased light exposure gives rise to increased level of functional density on the PDMS surface. Plot shows average fluorescence as a function of distance, left to right.

product albeit in low yield. In contrast to $\text{CoBr}_2 \cdot (\text{PCy}_3)_2$, the precatalysts form arene product during periods of darkness which offers no external regulation beyond initiation.

Elevated temperatures are inefficient at restoring active catalyst in the absence of light. Subjecting an arrested reaction to 80°C results in a modest increase in reactivity but the reaction stalls.¹³ Exposure of a cooled solution to ambient light results in complete restoration of reactivity (Figure 3B). After finding this unique ligand effect and its impact on reaction control, we began to explore the utility of light-gated arene formation.

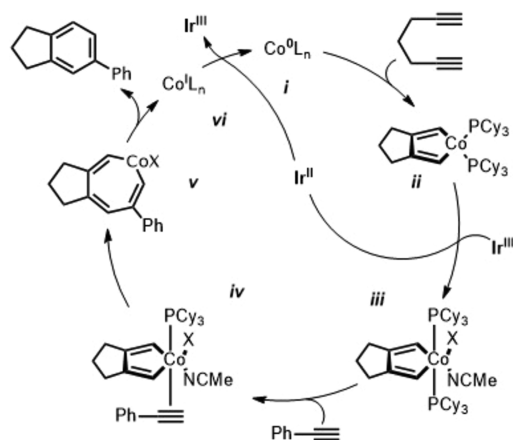
One leading method to construct arene-rich materials uses arene radicals generated by the reduction of aryl diazonium salts.¹⁴ Although the high reactivity of arene radicals offers many opportunities for bond formation, it consequently leads to undesired side reactions. In most examples, diazonium salt reduction lacks spatial resolution and requires specialized equipment.¹⁵ Similarly, etching material from a uniform self-assembled monolayer can also be done with AFM or X-ray technology.¹⁶ We envisioned using photolithographic techniques to control arene formation spatially via light-controlled cobalt catalysis.

We chose polydimethylsiloxane (PDMS)¹⁷ as a support and began our studies with the installation of a diene-bearing trichlorosilane to provide an alkyne-rich PDMS substrate. This functionalized PDMS is then treated with a solution containing precatalyst, photocatalyst, alkyne and reductant. The solution is liberally pipetted onto the PDMS substrate and a photomask is placed in direct contact. A blue LED is then used to irradiate the solution (Figure 4A). After irradiation, the PDMS is transferred to a solution of THF where excess reagents are removed from the PDMS with successive washes. Imaging the PDMS surface with a fluorescence microscope reveals the [2+2+2] cycloaddition occurs with excellent spatial resolution (Figure 4B). Control experiments in the absence of alkyne functionalization or cobalt precatalyst indicate little to no background fluorescence (see

Supporting Information, Figure S2). In addition to binary photolithography, we wanted to further explore the reaction control at the surface through grayscale printing. Reports from Hawker and co-workers demonstrate that the functional density of ATRP is directly proportional to the amount of light exposure.^{18a-c} Indeed, conducting the spatially resolved [2+2+2] cycloaddition with a grayscale mask suggests the extent of arene functionalization on the surface correlates with the amount of light exposure (Figure 4C).

The most surprising aspect is the role that light and photocatalyst play in regulating catalysis. We propose, thus, that the Ir photocatalyst plays two distinct roles. Confirmed by electrochemical measurements, the photocatalyst acts as a reductant to deliver a catalytically active low valent cobalt species (*i*, Scheme 1).¹⁹⁻²¹ Cyclic voltammetry (CV) studies in the presence of diene substrate suggest oxidative cyclization occurs favorably at $\text{Co}(0)$ to deliver a cobaltacyclopentadiene

Scheme 1. Proposed Mechanism



observed by CV (*ii*, Scheme 1). After an oxidation²² of *ii* by the photocatalyst excited state to the octahedral intermediate *iii*, alkyne coordination provides intermediate *iv*.²³ Insertion and subsequent reductive elimination from *v* generates a Co(I) species which is reduced to the active cobalt(0) species by the Ir^{III} reduced state.²⁴ Thus, the unique features inherent to photo-redox catalysis allow the mechanism to access every oxidation step at Co between 0 and 3.

In conclusion, we have identified a cobalt catalyst that enables light-controlled arene assembly using visible light as the external stimulus. This photochemically gated process provides unique opportunities for external regulation of catalysis, illustrated with the photolithographic patterning of PDMS.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b08792.

Procedures and compound characterization (PDF)

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Notes

The authors declare the following competing financial interest(s): A provisional patent has been filed on this technology.

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