



CBZ6 as a Recyclable Organic Photoreductant for Pinacol Coupling

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potential enables the reductive coupling of carbonyl compounds and their derivatives. **CBZ6** can be prepared in gram scale and is acid/base- or air-stable. It could be applied in large-scale photoreductive synthesis and recovered in high yield after the reaction.

 R^{1}

pinacol coupling is a powerful reaction for constructing vicinal diols or diamines directly from the reductive coupling of aldehydes, ketones, and imines, especially for coupling in a highly sterically hindered manner.¹ Vicinal diols or diamines are common scaffolds in pharmaceuticals, agrochemicals, and natural products, such as taxols, protease inhibitors, inositols, and so on.² The traditional pinacol coupling involves stoichiometric metal reducing agents, such as Ti, Mg, Mn, Zn, Sm, In, and other metals (Scheme 1a).^{1a} However, these methods have to face excessive metals as reducing agents, which is inconvenient for pretreatment, unfriendly to the environment, and generates a large amount of metal waste. Visible-light-induced organic photoredox catalysis has bloomed in organic synthesis.³ Several photoinduced pinacol couplings have been developed, using metal complexes (Ir, Pt, Cu, etc.),⁴ GaN nanowires,⁵ supramolecules,⁶ coumarin dves^{7a} or pervlene^{7b} as photocatalysts (Scheme 1b,c). Actually, the high cost of noble metal⁸ photocatalysts and the low efficiency of the photocatalytic ability of organic dyes limit the practical application of such photocatalysis. In addition, most aforementioned photocatalysts are not recyclable or are unstable to strong acids or bases. The exploration of easily available low-cost, acid/basestable, and metal-free photocatalysts for pinacol coupling is thus required.

Diphenyldibenzocarbazole **CBZ6** is an organic photoreductant,⁹ which is readily available from the hydroisoxazole rearrangement and cyclization.¹⁰ The oxidation potential of the excited state of **CBZ6** is established as -1.92 V (vs SCE). It could be envisioned that **CBZ6** is a photosensitizer for the visible-light-induced pinacol coupling (Scheme 1d). This noble- or transition-metal-free method not using toxic reagents or catalysts provides practical and convenient access to vicinal diols and diamines under very mild reaction conditions. In this work, we report the results in detail.

Scheme 1. Pinacol Coupling of Aldehydes, Ketones, and Imines

a) Metals as electron donor for pinacol coupling

$$\begin{array}{c} O \\ R^{1} \\ R^{2} \\ R^{3} \\ R^{4} \\ R^{$$

b) Metal-containing PCs-promoted pinacol coupling

$$\begin{array}{c} \begin{array}{c} \text{metal complex PCs (Ir, Pt, Cu, etc)} \\ 0 \\ R^2 \\ R^3 \\ R^4 \end{array} \xrightarrow[\text{Reductant: } R_3N, \text{ Hantzsch ester, etc} \\ \text{xenon lamp or LEDs (> 420 \text{ pm})} \end{array} \xrightarrow[\text{OH}]{} \begin{array}{c} \text{OH} \\ R^2 \\ R^2 \\ \text{OH} \end{array}$$

c) Organic dyes promoted pinacol coupling

$$\begin{array}{c} O \\ R^{1} \\ R^{2} \\ R^{2} \\ R^{3} \\ R^{4} \end{array} \xrightarrow{\begin{subarray}{c} \text{organic dyes (5-12 mol \%)} \\ \hline Reductant: R_{3}N \\ \hline White or blue LEDs \end{array} \xrightarrow{\begin{subarray}{c} OH \\ R^{1} \\ R^{2} \\ OH \\ \hline R^{2} \\ OH \end{array} \xrightarrow{\begin{subarray}{c} OH \\ R^{2} \\ OH \\ \hline R^{2} \\ OH \\ \hline H \\ \hline R^{2} \\ OH \\ \hline R$$

coumarin dyes: 5 mol %, \leq 55% for ketones perylene: 12 mol %, \leq 38% for ketones

d) CBZ6 as recyclable redox neutral organic photoreductant for pinacol coupling



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Scheme 2. Scope of Pinacol Coupling^a



^aReaction conditions: **CBZ6** (1 mol %), **1** (0.5 mmol), Et₃N (1.0 equiv), CH₃CN (2 mL), 9 W LEDs (407 nm), argon, about 32 °C, 2.5 h, isolated yields, diastereomeric ratio (d.r.) 1.8:1 to 1:1.2. See the SI for details. ^bWith 2.0 equiv Et₃N, 18 W LEDs (407 nm), 12 h. ^cLEDs (18 W, 407 nm).

Initially, the reaction conditions are investigated using benzaldehyde **1a** as a model substrate. The reductive coupling of **1a** using 1 mol % **CBZ6** and 1.0 equiv Et₃N in MeCN under the irradiation of 9 W LEDs ($\lambda_{max} = 407$ nm) affords the desired product **2a** in 75% yield (Table 1, entries 1 and 2). This set of conditions was established as the "standard conditions". The changes to the standard conditions do not result in better yields (Table 1, entries 2–10). The coupling without **CBZ6** or light or Et₃N gives no **2a** (entries 11–13). Molecular oxygen inhibits the reaction (entry 14).

With the standard conditions in hand, the scope of aldehydes and ketones was investigated. Various aldehydes have been subjected to the standard conditions, and the desired pinacol coupling products 2 were obtained in up to 99% yield (Scheme 2, 2a to 2n from aldehydes, 2o to 2y from ketones). Carbonyl compounds 1 usually completed in 2.5 or 12 h. Either electron-rich or electron-deficient carbonyl compounds are suitable, whereas the aldehydes bearing strong electron-withdrawing groups such as $-CF_3$, $-CO_2Me$, or -CN need a longer reaction time (2j–2l, 2n). Compared to aldehydes, despite higher steric hindrance, ketones could also be converted to tertiary 1,2-diols in up to 99% yields (2o–2x). Besides the aromatic ketones, the coupling of the derivate of

pyruvic acid affords the corresponding product 2y in 58% yield. Reactions of aliphatic aldehydes, enals, and propynals were also investigated, but no desired products were observed.

The competing reduction of aldehydes or ketones to alcohols can be observed. Alcohols were normally obtained in 2-14% yields. For example, in the coupling of **11** and **10**, the corresponding alcohols were determined by ¹H NMR in 4 and 2% yields, respectively (eqs 1 and 2).



In further study, imines were also tested under the pinacol coupling conditions (Scheme 3). Various *N*-Bn imines were subjected to the photoreduction conditions, and the

Table 1. Reaction Conditions

O H 1a	standard conditions CBZ6 (1 mol %)	
	Et ₃ N (1.0 equiv), MeCN argon, ~ 32 °C, 407 nm 9 W LEDs	ОН 2а
entry	changes to standard conditions ^a	2a (%)
1	none	75
2	ⁱ Pr ₂ NEt instead of Et ₃ N	75
3	Ir(ppy) ₃ instead of CBZ6	25
4	Ru(bpy) ₃ Cl ₂ ·6H ₂ O instead of CBZ6	0
5	eosin Y instead of CBZ6	0
6	rhodamine B instead of CBZ6	0
7	DMSO instead of MeCN as solvent	70
8	DMF instead of MeCN as solvent	45
9	DCM instead of MeCN as solvent	10
10	MeOH instead of MeCN as solvent	0
11	no CBZ6	0
12	no light	0
13	no Et ₃ N	0
14	under O ₂	0

^aStandard conditions: **1a** (0.2 mmol), **CBZ6** (1 mol %), MeCN (2 mL), 9 W (3 W × 3) LEDs (407 nm), under argon atmosphere, about 32 °C, 2.5 h. Yields were determined by ¹H NMR using CH_3NO_2 and *tert*-butyl methyl ether as internal standards.



4g, 12 h, 82%, meso:dl 1:1

^{*a*}Reaction conditions: CBZ6 (1 mol %), 3 (0.5 mmol), Et₃N (2.0 equiv), CH₃CN (2 mL), 18 W LEDs (407 nm), argon atmosphere, about 32 $^{\circ}$ C, isolated yields, d.r. 1.3:1 to 1:1.8.

4h, 12 h, 86%, meso:dl 1.3:1

corresponding 1,2-diamines were obtained in 68 to 94% yields (4a-4f). N-Aryl imines gave comparable results (4g and 4h).

The recyclability of most photocatalysts still remains challenging. One remarkable advantage of **CBZ6** is its low catalyst loading as an organic photoreductant as well as its recyclability. In the gram-scale synthesis, **2r** was obtained in 76% yield (Scheme 4). After reaction, **CBZ6** was recovered in 92% yield by silica gel chromatography.

Scheme 4. Gram-Scale Synthesis and Catalyst Recovery Experiment



The imine/aldehyde cross-coupling was also investigated affording the corresponding cross-coupling product 5 in 34% together with the homocoupling product 2a (40%) and 4h (41%) (eq 3).

The on/off experiments show that light is necessary in this reductive coupling reaction (Figure 1). Fluorescence quench-



Figure 1. Light on/off control experiments for pinacol coupling of 1a to 2a under standard conditions. Yields of 2a were determined by 1 H NMR analysis using ethyl benzoate as an internal standard.

ing experiments of CBZ6 suggest the quenching effect with 1a (Figure 2a). The Stern–Volmer plot indicates that the excited state of CBZ6 was quenched by 1a, and the quenching effect increased with the concentration of 1a (Figure 2b).



Figure 2. Fluorescence quenching effect (a) and Stern–Volmer plot (b).

A radical anion intermediate could be trapped by TEMPO, and the trapping adduct 11-TEMPO was detected by HRMS (Scheme 5). The benzaldehydes bearing *para*-electron-with-drawing groups get electrons easier. For example, the 1:1 mixture of 1d and 1k was subjected to the standard conditions, and only 2k was obtained (Scheme 5).

The proposed reaction mechanism is shown in Scheme 6. The excited **CBZ6*** by purple light (407 nm) gives an electron to the carbonyl group of **1**, consequently generating radical







Scheme 6. Proposed Mechanism



anion A. CBZ6 is regenerated by a single-electron transfer (SET) reduction with Et_3N . The coupling of radical B affords the target product diol 2. Analogously, the imino-pinacol coupling passes through the same pathway.

In conclusion, we have developed CBZ6-catalyzed visible light photoreductive pinacol coupling of aldehydes, ketones, and imines. The relatively high potential of the excited state of CBZ6 (-1.92 V vs SCE) enables this reaction. CBZ6 is stable to strong acid/base or air and can be prepared in more than gram scale. The high recyclability ensures its application in large-scale synthesis.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00537.

Reaction procedures and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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