

Hybrid Catalysis Enabling Room-Temperature Hydrogen Gas Release from *N*-Heterocycles and Tetrahydronaphthalenes

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Supporting Information

ABSTRACT: Hybrid catalyst systems to achieve acceptorless dehydrogenation of *N*-heterocycles and tetrahydronaphthalenes—model substrates for liquid organic hydrogen carriers—were developed. A binary hybrid catalysis comprising an acridinium photoredox catalyst and a Pd metal catalyst was effective for the dehydrogenation of *N*-heterocycles, whereas a ternary hybrid catalysis comprising an acridinium photoredox catalyst, a Pd metal catalyst, and a thiophosphoric imide organocatalyst achieved dehydrogenation of tetrahydronaphthalenes. These hybrid catalyst systems allowed for 2 molar equiv of H₂ gas release from six-membered *N*-heterocycles and tetrahydronaphthalenes under mild conditions, i.e., visible light irradiation at rt. The combined use of two or three different catalyst types was essential for the catalytic activity.

Catalytic acceptorless dehydrogenation (CAD) from saturated organic compounds, such as *N*-heterocycles and hydrocarbons, to produce unsaturated molecules and hydrogen gas is a fundamentally important chemical process with numerous applications in organic synthesis¹ as well as for a potential future “hydrogen society”.² This process is generally very difficult, however, because desaturation of organic compounds is generally unfavorable in terms of the enthalpy factor. Iridium complexes are prevalent catalysts for dehydrogenation of *N*-heterocycles.³ Crabtree and Jones independently reported base metal (nickel,^{4a} iron,^{4b} and cobalt^{4c})-catalyzed dehydrogenation of *N*-heterocycles.⁴ Further, Grimme and Paradies^{5a} and our group^{5b} recently achieved organocatalyzed dehydrogenation of *N*-heterocycles by a Lewis acidic borane.⁵ Despite the significant progress, forcing conditions with a reaction temperature higher than 100 °C are often required, except for Crabtree’s electrocatalytic example.^{4a} For CAD from hydrocarbons, iridium–pincer complexes provide a privileged catalyst platform.⁶ Beller recently reported that Vaska-type rhodium complexes [Rh(PR₃)₂(CO)Cl] exhibit improved reactivity.⁷ Nevertheless, CAD from hydrocarbons generally requires even harsher conditions than *N*-heterocycles, such as high temperature (up to 200 °C) or UV light irradiation. This is partly due to the great energy barrier for initiating the

catalytic cycle, i.e., C(sp³)–H metalation through oxidative addition to iridium or rhodium complexes. Sorensen reported the first example of room-temperature CAD from alkanes by combining two sequential hydrogen atom-transfer steps mediated by tetrabutylammonium decatungstate and cobaloxime pyridine chloride catalysts, respectively, under near-UV irradiation conditions.⁸ This pioneering base metal CAD from hydrocarbons has room for improvement, however, especially with regard to its efficiency (up to 19% yield based on substrates). Here we developed binary and ternary hybrid catalyst systems, enabling CAD from *N*-heterocycles and tetrahydronaphthalenes, respectively, at rt under visible light irradiation conditions.

Our approach for realizing room-temperature CAD is based on facilitating the initiation step in the overall catalytic cycle, i.e., formation of metal amide or organometallic species from *N*-heterocycles or hydrocarbons. This is possible through one-electron oxidation of the substrates directly or indirectly mediated by a photoredox catalyst,⁹ followed by capture of the resulting radical with a metal catalyst.^{10,11} Based on this idea, we first studied CAD from *N*-heterocycles using 1-phenyltetrahydroisoquinoline (**1a**) as a model substrate.

Our working hypothesis to achieve CAD from **1a** is illustrated in Figure 1. First, single electron transfer (SET) from **1a** to an excited photoredox catalyst (*PC⁺) would produce aminyl radical

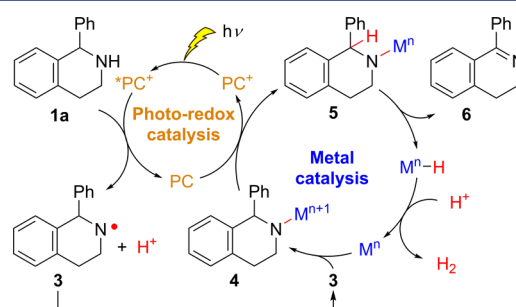


Figure 1. Working hypothesis for CAD of 1-phenyltetrahydroisoquinoline (**1a**) by binary hybrid catalysis.

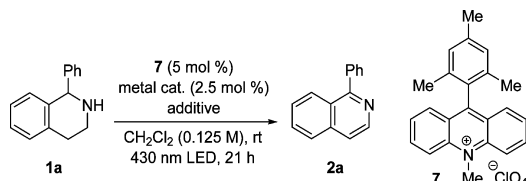
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3. Then, **3** would be intercepted by a metal catalyst (M^n) to generate oxidized metal amide **4** bearing a metal with an $n + 1$ oxidation state (M^{n+1}), which in turn would be reduced by a photoredox catalyst acting as a reductant (PC), affording metal amide **5**.^{12,13} β -Hydride elimination from **5** would produce unsaturated 1-phenyldihydroisoquinoline (**6**) and metal hydride species M^n-H , which would evolve hydrogen gas through reacting with the proton¹⁴ generated in the photo-oxidation step of **1a**. Further dehydrogenation from **6** would produce **2a** with a net generation of 2 molar equiv of hydrogen gas from **1a**.

Based on this scenario, we optimized CAD from **1a** using combinations of photoredox catalysts (5 mol %) and metal catalysts (2.5 mol %) under 430 nm visible light irradiation at room temperature (Table 1).¹³ Although first-row transition

Table 1. Optimization for CAD from **1a**



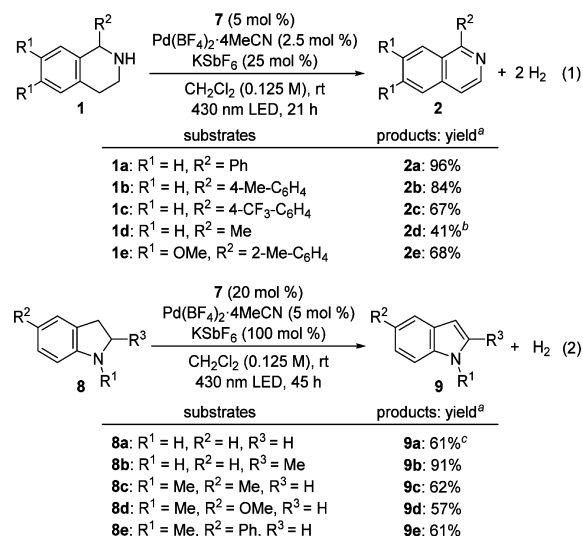
entry	metal cat.	additive (mol %)	2a (%) ^a	6 (%) ^a
1	FeCl ₂	-	<1	6
2	NiCl ₂	-	6	20
3 ^b	NiCl ₂	-	<1	4
4 ^b	CuCl	-	<1	4
5	Pd(OAc) ₂	-	18	20
6	PdCl ₂ ·2MeCN	-	19	19
7	Pd(BF ₄) ₂ ·4MeCN	-	37	7
8	Pd(BF ₄) ₂ ·4MeCN	KSbF ₆ (5)	60	<1
9	Pd(BF ₄) ₂ ·4MeCN	KSbF ₆ (25)	96 (96) ^c	<1
10	-	KSbF ₆ (25)	11	<1
11 ^d	Pd(BF ₄) ₂ ·4MeCN	KSbF ₆ (25)	<1	9
12 ^e	Pd(BF ₄) ₂ ·4MeCN	KSbF ₆ (25)	5	<1

^aNMR yield using 1,1,2,2-tetrachloroethane as an internal standard. ^bIn the presence of 1,10-phenanthroline as a ligand for the metal catalyst. ^cIsolated yield in the parentheses. ^dThe reaction was run without **7**. ^eThe reaction was run without photoirradiation.

metal catalysts were ineffective (entries 1–4), palladium catalysts afforded promising results (entries 5–7); specifically, combining acridinium photoredox catalyst **7**¹⁵ and the Pd(BF₄)₂·4MeCN catalyst produced a moderate yield of isoquinoline **2a** (37%; entry 7). A survey of several photoredox catalysts revealed that **7** produced the highest yield.¹³ To further improve the reactivity, we studied the effects of additives.¹³ The addition of 5 mol % KSbF₆ significantly accelerated the reaction, affording **2a** in 60% yield (entry 8). Finally, in the presence of 5 mol % **7**, 2.5 mol % Pd(BF₄)₂·4MeCN, and 25 mol % KSbF₆, **2a** was obtained in 96% yield (entry 9).¹⁶ The binary hybrid catalyst system was essential for the CAD process (entries 10–12). The yield of **2a** decreased dramatically when either of the two catalyst components was absent (11% without the palladium catalyst, entry 10; <1% without the photoredox catalyst, entry 11), or without photoirradiation (5%, entry 12).

We examined the substrate scope of the binary catalysis for CAD from *N*-heterocycles under the optimized conditions (Scheme 1). Various tetrahydroisoquinolines **1a**–**1e** containing an electron-donating or -withdrawing group were converted to the corresponding isoquinolines **2a**–**2e** in generally high yield (Scheme 1, reaction 1). 1-Methyltetrahydroisoquinoline (**1d**) bearing higher hydrogen density was also a good substrate, giving **2d** in 41% yield. In addition, indolines **8**, either NH-free (**8a**–**8b**)

Scheme 1. Substrate Scope of CAD from *N*-Heterocycles Using Binary Hybrid Catalysis



^aIsolated yield. ^bReaction run for 70 h. ^cReaction run for 21 h.

or *N*-methylated (**8c**–**8e**), were competent substrates for the binary catalysis, affording indoles **9** in moderate to high yield (Scheme 1, reaction 2).

We next examined CAD from a more difficult substrate, tetrahydronaphthalene (**10a**). It was previously reported that rhodium^{7c,d} and iron^{4b} catalysts were applied to the dehydrogenation of **10a**, but only trace amounts of naphthalene (**11a**) were produced. We examined the binary hybrid catalysis conditions optimized for *N*-heterocycles with **10a**, but **11a** was not obtained at all.¹³ The lack of reactivity using the binary hybrid catalysis was likely due to the inability to generate a benzyl radical species (see **12** in Figure 2) from **10a**. Therefore, we attempted to further

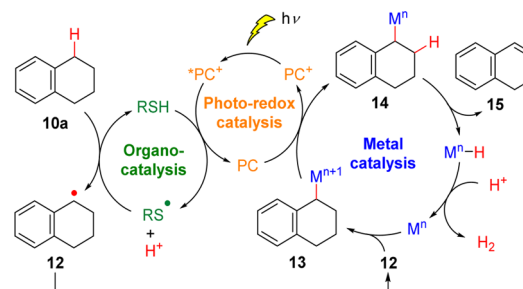


Figure 2. Working hypothesis for CAD of tetrahydronaphthalene (**10a**) by ternary hybrid catalysis.

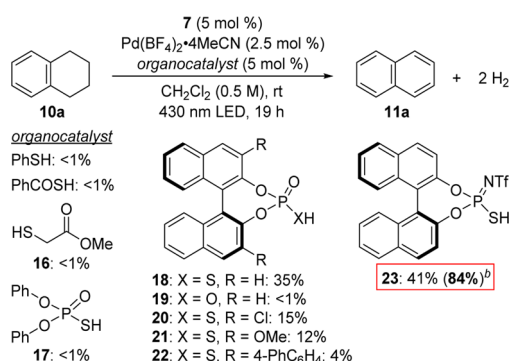
hybridize a third catalysis, an organocatalysis that would abstract a hydrogen atom from the benzylic C(sp³)–H bond (**10a** to **12**).¹⁷ For this purpose, we selected a sulfur-centered radical RS•, which would be generated from a sulfur-containing organocatalyst (RSH) by photoredox catalyzed one-electron oxidation. RSH bears a bond dissociation energy high enough to cleave the benzylic C(sp³)–H bond of **10a**.¹⁸

Our hypothesis for CAD from a hydrocarbon substrate **10a** is illustrated in Figure 2. The sulfur-centered radical RS•, generated by SET from RSH to an oxidizing excited photoredox catalyst (*PC⁺), would abstract the benzylic hydrogen atom of **10a**, producing benzyl radical **12**. Radical **12** would combine with a metal catalyst (Mⁿ) to generate organometallic species **13** bearing

a metal with an $n + 1$ oxidation state (M^{n+1}), which in turn would be reduced by the photoredox catalyst acting as a reductant (PC), affording organometallic species **14**.¹⁰ β -Hydride elimination from **14** would produce unsaturated dihydronaphthalene (**15**) and metal hydride species $M^{n-1}-H$, which would evolve hydrogen gas through a reaction with the proton¹⁴ generated in the photo-oxidation step of the organocatalyst RSH. Repeating this cycle from **15** would produce **11a** with a net generation of 2 molar equiv of hydrogen gas from **10a**.

Based on this hypothesis, we surveyed organocatalysts (5 mol %) in the presence of **7** (5 mol %) and $Pd(BF_4)_2 \cdot 4MeCN$ (2.5 mol %) upon 430 nm LED irradiation at room temperature (Scheme 2).^{13,19} The CAD reaction from **10a** did not proceed using

Scheme 2. Effects of Organocatalyst in CAD of **10a**^a



^aYield was determined by GC analysis because the product is volatile.

^bThe yield in parentheses is for the reaction performed using 5 mol % **7**, 2.5 mol % **23**, and 2.5 mol % $Pd(BF_4)_2 \cdot 4MeCN$ for 60 h under temperature control (ca. 27–29 °C) with 0.125 M **10a**.

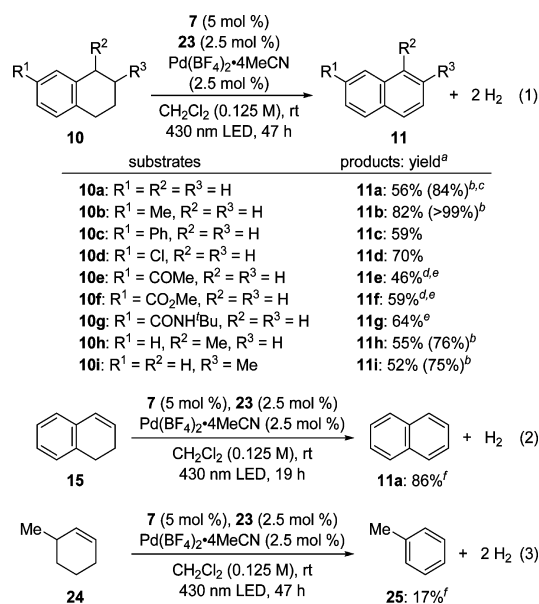
benzenethiol, thiobenzoic acid, or methyl 2-mercaptoacetate (**16**), whose thiyl radical generated via SET oxidation under photoredox conditions was previously reported to generate a benzyl radical from benzyl ether substrates through $C(sp^3)-H$ abstraction.^{18a} In contrast, thiophosphoric acid organocatalyst **18** exhibited moderate reactivity (35% yield). The observed reactivity of **18** was likely due to the high hydrogen atom abstraction ability of the electron-deficient sulfur-centered radical generated from **18**.²⁰ The binaphthyl backbone and SH functionality proved to be critical elements for the catalytic activity of **18**; almost no reaction proceeded using thiophosphoric acid **17** or phosphoric acid **19**. We studied the effects of substituents at the 2-positions of the binaphthyl backbone of **18**; reactivity was significantly decreased by introducing an electron-withdrawing group (**20**: 15%), an electron-donating group (**21**: 12%), or a sterically demanding group (**22**: 4%). Finally, we found that thiophosphoric imide **23** was a better organocatalyst than **18**, producing **11a** in 41% yield. After the catalyst loading, reaction temperature, time, and concentration were optimized, **11a** was obtained in 84% yield.¹⁶

To confirm that the ternary hybrid catalysis manifold is essential for the CAD process, we also conducted several control experiments.¹³ Almost no reactions occurred when any one of the three catalyst components was absent: the photoredox catalyst, the metal catalyst, or the organocatalyst. Furthermore, exciting the photoredox catalyst **7** with visible light was also indispensable: no reaction proceeded under thermal conditions without light irradiation. These results indicate that the three different types of catalysis cooperatively played critical roles. Moreover, in contrast to Beller's result using a rhodium catalyst,^{7c} intermediate

dihydronaphthalene (**15**) was not detected at any point during the reaction course, indicating that the initial dehydrogenation from **10a** to **15** is more difficult than the second dehydrogenation from **15** to **11a**.

Under the optimized conditions, we investigated the substrate scope of this ternary hybrid catalysis (Scheme 3).²¹ Various

Scheme 3. Substrate Scope of CAD from Tetrahydronaphthalene Derivatives and 3-Methylcyclohexene Using Ternary Hybrid Catalysis



^aIsolated yield is shown unless otherwise noted. ^bGC yield in the parentheses. ^cThe reaction was run for 60 h. ^d5 mol % **23** was used. ^eThe reaction was run for 72 h. ^fGC yield.

substituents on the phenyl ring of tetrahydronaphthalenes were tolerated, including a methyl group (**10b**), an aryl group (**10c**), a halogen atom (**10d**), a keto group (**10e**), an ester group (**10f**), and an amide group (**10g**). The reactions of tetrahydronaphthalenes **10h** and **10i** bearing a methyl group at a saturated carbon also proceeded in high yield. Dihydronaphthalene **15** was a suitable substrate, giving **11a** in 86% yield in a shorter reaction time (19 h) than starting from **10a**. The results support our hypothesis that the 2 molar equiv hydrogen evolution proceeds in a stepwise manner through the intermediate **15** (Figure 2). Dehydrogenation of 3-methylcyclohexene (**24**), albeit in moderate yield (17%), is a current limitation of this method. The result is still noteworthy, however, and demonstrates the potential of this ternary hybrid catalyst system for application in room-temperature CAD from aliphatic liquid organic hydrogen carriers containing higher hydrogen-per-molecular weight ratios.

In summary, we developed a binary hybrid catalyst system comprising an acridinium photoredox catalyst and a palladium metal catalyst for CAD from *N*-heterocycles. Moreover, we achieved CAD from tetrahydronaphthalenes, devising a ternary hybrid catalyst system by combined use of an acridinium photoredox catalyst, a palladium metal catalyst, and a thiophosphoric imide organocatalyst. These are the first molecular catalysts for acceptorless dehydrogenation of *N*-heterocycles and hydrocarbons at room temperature and under visible light irradiation conditions. The complete release of 2 molar equiv of hydrogen gas from tetrahydroisoquinolines and tetrahydronaphthalenes is also unique in these processes. This

study demonstrates that proper hybridization of different catalyst types enables CAD from *N*-heterocycles and hydrocarbons under mild conditions. Detailed studies to elucidate the reaction mechanism are ongoing in our laboratories.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b00253.

Experimental details and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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- (16) Generation of 2 molar equiv of hydrogen gas was confirmed by a two-pot transfer hydrogenation experiment, connecting the reaction atmosphere of the dehydrogenation reaction to a rhodium-catalyzed hydrogenation reaction of cyclododecene performed in another vessel. For detailed experiments, see [SI](#).
- (17) During preparation of this manuscript, MacMillan and coworkers reported a cross-coupling reaction between aliphatic substrates and aryl bromides by developing a triple catalysis involving an iridium photoredox catalyst, a quinuclidine hydrogen atom transfer organocatalyst, and a nickel catalyst. See: Shaw, M. H.; Shurtleff, V. W.; Terrett, J. A.; Cuthbertson, J. D.; MacMillan, D. W. C. *Science* **2016**, *352*, 1304.
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- (19) A combination of **7** and Pd(BF₄)₂·4MeCN was also optimum in the case of CAD from **10a**. See [SI](#).
- (20) Electrochemical and photochemical studies indicated that sulfur-centered radical species RS[•] would be generated from thiophosphate **18** via a single electron oxidation of **18** by the excited state of photoredox catalyst **7**. SET from **18** to photoexcited **7** is also thermodynamically feasible, based on their oxidation potential values. See [SI](#) for details.
- (21) The ternary hybrid catalyst system produced less satisfactory results than the binary system in CAD from *N*-heterocycles (see [Scheme 1](#)): CAD from **1a** using **7** (5 mol %), **18** (2.5 mol %), and Pd(BF₄)₂·4MeCN (2.5 mol %) for 20 h afforded products **2a** and **6** in 15% and 12% yields, respectively.