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Metal–Organic Capsules with NADH Mimics as Switchable Selectivity Regulators for Photocatalytic Transfer Hydrogenation

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Supporting Information

ABSTRACT: Switchable selective hydrogenation among the groups in multifunctional compounds is challenging because selective hydrogenation is of great interest in the synthesis of fine chemicals and pharmaceuticals as a result of the importance of key intermediates. Herein, we report a new approach to highly selectively (>99%) reducing C–X (X = O, N) over the thermodynamically more favorable nitro groups locating the substrate in a metal–organic capsule containing NADH active sites. Within the capsule, the NADH active sites reduce the double bonds via a typical 2e− hydride transfer hydrogenation, and the formed excited-state NAD+ mimics oxidize the reductant via two consecutive 1e− processes to regenerate the NADH active sites under illumination. Outside the capsule, nitro groups are highly selectively reduced through a typical 1e− hydrogenation. By combining photoinduced 1e− transfer regeneration outside the cage, both 1e− and 2e− hydrogenation can be switched controllably by varying the concentrations of the substrates and the redox potential of electron donors. This promising alternative approach, which could proceed under mild reaction conditions and use easy-to-handle hydrogen donors with enhanced high selectivity toward different groups, is based on the localization and differentiation of the 2e− and 1e− hydrogenation pathways inside and outside the capsules, provides a deep comprehension of photocatalytic microscopic reaction processes, and will allow the design and optimization of catalysts. We demonstrate the advantage of this method over typical hydrogenation that involves specific activation via well-modified catalytic sites and present results on the high, well-controlled, and switchable selectivity for the hydrogenation of a variety of substituted and bifunctional aldehydes, ketones, and imines.

INTRODUCTION

Transfer hydrogenation reactions that proceed under mild reaction conditions with easy-to-handle hydrogen donors instead of hydrogen gas are a rapidly growing field because they facilitate the practical synthesis of fine chemicals using complicated compounds with multiple functional groups.1–9 Recent breakthroughs in transfer hydrogenation have enabled the selective transformations of ketones6,6 and aldehydes7,8 into their corresponding alcohols in the presence of other functional groups, including thermodynamically more favorable hydrogenation groups such as nitroarenes and olefins. However, the direct activation of specific groups using well-modified catalytic sites precludes practically inventing and switching the selectivity of the hydrogenation in bifunctional compounds in a single catalytic process. A strategy for selective hydrogenation was proposed, which involves the differentiation of 2e− (hydride) and 1e− hydrogenation pathways. The hydride 2e− transfer hydrogenation of ketones and aldehydes over substrates typically hydrogenated via 1e− transfer pathways.9 Of particular interest is the 2e− hydride transfer hydrogenation using redox cofactor NADH (reduced nicotinamide adenine nucleotide) and its mimics10 based on its central role as a cosubstrate in biosynthetic pathways and the potential of NADH to serve as a hydride source while being a weak single-electron reductant.11,12 Therefore, new synthetic platforms in which the selectivity in the transformations of bifunctional compounds could be strictly controlled and readily tuned by regulating the reaction kinetics of the hydrogenation pathways involving NADH, such as those involving natural enzymes, may facilitate the selective preparation of fine chemicals and pharmaceuticals bearing multiple functional groups.

To mimic the remarkable abilities of enzymes to achieve efficient chemical conversions, researchers have used various molecular capsules, including symmetric metal–organic capsules with defined hydrophobic cavities that are spontaneously generated through preorganized ligands and functionalized metalloccorers, as promising hosts to catalyze unique chemical transformations.13–16 Reactions performed in such molecular capsules could be enhanced by proximity effects allowing unusual selectivity and unique dynamics owing to the...
restricted motion of the substrates. Recently, it was demonstrated that capsules can be used to separate redox events, exploiting the difference between the inner and outer spaces of a host to combine photocatalytic proton reduction and substrate oxidation in a one-pot transformation.17,18 Artificial enzymatic systems that combine photocatalytic chemical transformations, including proton reduction, to regenerate the active sites in NADH mimics and biomimetic hydrogenation reactions have also been postulated as a new synthetic platform.19−21 The localization of a 2e− hydride transfer hydrogenation pathway inside the reaction vessel containing the NADH mimics thus allows the design and optimization of catalysts, which could proceed under mild reaction conditions and use easy-to-handle hydrogen donors with enhanced high selectivity.

We herein report a molecular flask with NADH-type cofactors that allows us to control the selectivity of a photocatalytic transfer hydrogenation reaction, toggling between a carbonyl or nitro group reduction in bifunctionalized compounds under mild reaction conditions (Scheme 1).

Scheme 1. Schematic of Switching the Transfer Hydrogenation Selectivity inside and outside the Pocket of the Capsule

Substrate binding in the molecular flask results in preorganization and thus facilitates typical 2e− hydride transfer hydrogenation, which is highly selective for the carbonyl, whereas the 1e− transfer hydrogenation events takes place when the substrate is outside the molecular flask. We envisioned that with this approach, aldehyde and ketone groups could be highly selectively hydrogenated in the presence of nitro groups that are thermodynamically more favorable to convert. These active NADH mimics could be regenerated from the formed NAD+ mimics via oxidation of the reductant through two consecutive 1e− reduction processes under illumination. Outside the pocket, a typical 1e− transfer hydrogenation environment was modified by the presence of a reductant or photosensitizer to highly selectively reduce the nitro group over the carbonyl group. Notably, both hydrogenation processes are well controlled by strictly limiting the different electron transfer pathways to inside and outside the molecular host. The selectivity of the hydrogenation of bifunctional compounds could be inverted by simply regulating the reaction kinetics of the two hydrogenation pathways (i.e., varying the concentrations of the substrate and electron donor) because the kinetics inside the pocket are controlled only by the concentration of the host−guest complex and not directly by the concentration of the substrate.

RESULTS AND DISCUSSION

Preparation and Characterization of Macrocycles and the Host−Guest Complex. Ligand H2FPB was synthesized by a Schiff-base reaction of 2-pyridylaldehyde and 1-(furan-2-ylmethyl)-4-phenyl-1,4-dihydropyridine-3,5-dicarboxhydrazide in an ethanol solution. The M4L4 metal−organic macrocycles were prepared by reacting ligand H2FPB with the appropriate metal salts in acetonitrile solution. Diffraction-grade single crystals of the macrocycles including Zn−FPB, Fe−FPB, Co−FPB, and Ni−FPB were obtained by the vapor diffusion of diethyl ether into the corresponding CH3CN solutions of the macrocycles (Figures 1a,b and S1−S4).

Figure 1. Crystal structures of macrocycle Zn−FPB (a) with NADH-mimicking ligands showing the coordination geometry of the zinc ions and top view (b) of the macrocycle showing the resulting confined space. Crystal structures of host−guest complex Zn−FPB ⊃ 1 (c) and macrocycle Ni−FMB (d) without NADH-mimicking ligands. Anions and solvent molecules are omitted for clarity. Zn, cyan; Ni, green; O red; N, blue; C, gray; and H, white.

Single-crystal structure analyses revealed that the four macrocycles are isostructural and exhibit S4 symmetry via the connection of four ligands with the dihydropyridine amido (DHPA) fragments and four metal ions in an alternating fashion.22 The four DHPA moieties are positioned on parallel edges of the molecular square with the phenyl ring outside of the cavity and the four active H atoms in the pocket interior.23 Given the van der Waals radii (3.6 Å) of the guest molecules and the edges of the square, the average Zn−⋯Zn separation of approximately 8.62 Å suggests that the cavity of the square is sufficiently large to encapsulate a planar aromatic substrate. Each zinc ion was coordinated in a mer position with a pair of extensively delocalized N2O chelators to ensure the mobility of electrons along the whole backbone of the ligands. Such electrons have the potential to migrate from the metal centers to the active sites of the NAD+ models, enabling the regeneration of the active sites from the photoreduced redox reaction involving the metal ions. The four furan rings are positioned above and below the molecular square to form a pocket for guest inclusion. Importantly, host−guest complex Zn−FPB ⊃ 1 (4-nitrobenzaldehyde) was obtained by the same method, which provided unambiguous evidence for complex formation (Figures 1c and S5). Single-crystal structure analysis shows that one guest molecule, 1, binds in the pocket.24 The main structure of the molecular square is maintained with the furan rings twisting in the lateral direction. The shortest
interatomic distance between 1 and the host structure is 3.52 Å.25 Moreover, the molecular structures of both Zn–FPB and host–guest complex Zn–FPB ⊇ 1 determined from DFT calculation were consistent with their single-crystal structures (Figure S19).26 There is close proximity between the active hydrides of the host and 1, providing the possibility to stabilize the structurally confined intermediate for potential size- and shape-selective hydrogenation.27

The structural stability of Zn–FPB in solution was further characterized by ESI–MS spectra that exhibited two sharp peaks at m/z = 793.83 and 1190.23 with the exact distribution fingerprint of the [H2Zn(FPB)]4+ and [H2Zn(FPB)]6+ species, respectively (Figure 2a). Guest binding in the pocket of the host is evident by ESI-MS analysis of a mixture of Zn–FPB stoichiometric species, Zn2+, and Zn2+ with the exact distribution fingerprint of the [H2Zn(FPB)]4+ and [H2Zn(FPB)]6+ species, respectively (Figure S19).26 There is close proximity between the active hydrides of the host and 1, providing the possibility to stabilize the structurally confined intermediate for potential size- and shape-selective hydrogenation.27

Figure 2. ESI-MS spectra of Zn–FPB (a), Zn–FPB (b) following the addition of 5 equiv of substrate 1, and Zn–FPB (c) following the addition of 5 equiv of inhibitor ATP in CH3CN. The insets show the measured and simulated isotopic patterns at m/z = 793.83, 844.16, 1190.23, 1265.73, and 1444.74.

Further characterization of the host–guest complex comes from isothermal titration calorimetry (ITC) experiments, of which the spectrum fit well to a 1:1 binding model, providing both the enthalpy (ΔH = 0.03) and entropy (ΔS = 24.83 kJ mol⁻¹) of formation of complex Zn–FPB ⊇ 1 with association constant 2.21 × 10⁴ M⁻¹ (Figures 3a and S11).28 The formation of the host–guest complex is also evident from the fluorescence titration (Figure S21) and the change in chemical shifts in the ¹H NMR spectra of both the substrate and molecular square (Figure S14). In addition, NOE contacts between the benzene rings of 1 and the NADH mimics of the molecular macrocycle were observed in the NOESY spectrum of the host–guest complex Zn–FPB ⊇ 1 (Figure S15), which suggests that 1 is in close contact with the host when bound in the macrocycle.29 These results indicate that the formation of the host–guest complex was preorganized for efficient substrate activation.30,31

Highly Selective Photocatalytic Transfer Hydrogenation. The activity of macrocycle catalyst Zn–FPB was first studied by chemical reduction of the different types of double bonds (carbonyl, imine, olefin, and nitro). The substrates containing double bonds C=O and C=C can be stoichiometrically reduced by Zn–FPB through the 2e⁻ hydride transfer hydrogenation in the presence of NaBH₃CN52 and yield increases with the increase in substance potential (Table 1). In the presence of an electron-withdrawing group, the conversion of the transfer hydrogenation significantly increased, whereas an electron-donating group significantly decreased the benzaldehyde conversion. However, neither an electron-withdrawing nor electron-donating group changed the reactivity of nitrobenzene as it stayed inert for the 2e⁻ transfer hydrogenation, even though the reduction of the nitro group is thermodynamically more favorable than the reduction of the carbonyl group.

In the model reaction of substrate 1 (5.0 mM) containing both nitro and aldehyde groups, Zn–FPB stoichiometrically yielded product 1a (4-nitrophenylmethanol, 91%) with over 99% selectivity. Localizing the electron donors (i.e., HCOOH/Et₃N) outside the capsules to isomerize the active sites of the NADH mimics allowed Zn–FPB to operate as an efficient catalyst and achieve highly selective hydrogenation under light illumination. While the ground-state NAD⁺ mimic is a weak single-electron oxidant, the excited-state NAD⁺ mimic is a strong oxidant that is able to extract two electrons consecutively from the substrate in the solution, quickly regenerating the active NADH mimic. The loading of Zn–FPB (0.1 mM) resulted in 82% conversion of 1a with a selectivity of 98% after 6 h under 420 nm LED light illumination, and the conversion of thermodynamically favored hydrogenation product 1b (4-aminobenzaldehyde) is less than 1% (Figure 3b). The results indicate that our approach of localizing the NADH cofactor-derived biomimetic 2e⁻ hydride transfer hydrogenation pathway to control the selectivity is feasible.

Control experiments using the related salts and ligands yielded a trace of the product under the same conditions, confirming that the supramolecular host used to preorganize the substrate is essential. When the concentrations of HCOOH/Et₃N and 1 are fixed, the initial rate constant for hydrogenation exhibited a linear relationship with the concentration of Zn–FPB (Figure 4a). When the concentrations of 1 and Zn–FPB are fixed, the initial turnover frequency of hydrogenation did not vary with the concentration of HCOOH/Et₃N, but the conversion of 1 increased
result shows a 1:1 encapsulation of ATP within the pocket of Zn.

Electronic Pushing and Drawing Substituents with Zn

Importantly, two negative charges and multiple hydrogen donors and acceptors present in ATP contribute to a more efficient hydrogenation process. The association constant for ATP to Zn was determined to be 1.58 × 10^4 M\(^{-1}\), which is significantly larger than the association constant for neutral substrates. This indicates a stronger binding affinity of ATP compared to neutral substrates.

We wondered if we could also switch the catalyst properties by binding a competing guest in the host. Adenosine triphosphate (ATP) has a similar width to that of Zn−FPB and can competitively replace the substrate. The association constant of ATP to Zn was determined to be 25.0 mM, which is much smaller than the association constant for neutral substrates. This suggests that ATP effectively competes with the substrate in the pocket.

From a mechanistic viewpoint, the encapsulation of a substrate in a pocket forces the active sites to be in close proximity to the substrate, enabling efficient hydrogenation in the pocket. This is consistent with previous data that showed a significant increase in the yield of a substrate in the presence of ATP.

Table 1. Evaluation of Hydrogenation for Different Types of Unsaturated Groups and Unsaturated Groups Containing NAD+ Mimics with Zn−FPB

<table>
<thead>
<tr>
<th>No.</th>
<th>Substrates</th>
<th>Potential (eV)</th>
<th>Yield (%)</th>
<th>No.</th>
<th>Substrates</th>
<th>Potential (eV)</th>
<th>Yield (%)</th>
<th>No.</th>
<th>Substrates</th>
<th>Potential (eV)</th>
<th>Yield (%)</th>
</tr>
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<td>NO₂</td>
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<td>Trace</td>
<td>7</td>
<td></td>
<td>-1.29</td>
<td>87</td>
<td>12</td>
<td>NO₂</td>
<td>-1.06</td>
<td>Trace</td>
</tr>
<tr>
<td>3</td>
<td>N₃</td>
<td>-1.42</td>
<td>86</td>
<td>8</td>
<td></td>
<td>-1.61</td>
<td>75</td>
<td>13</td>
<td></td>
<td>-1.19</td>
<td>Trace</td>
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<td>-1.75</td>
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<td>-1.88</td>
<td>28</td>
<td>16</td>
<td></td>
<td>-1.49</td>
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</tbody>
</table>

*Reaction conditions: Substrate (10.0 mM), Zn−FPB (10.0 mM), and NaBH₃CN (10.0 mM) in CH₃CN/H₂O solution (1:1, 5 mL), 6 h. The conversions were determined by ¹H NMR spectroscopy of the crude products. The redox potentials of substrates were determined by cyclic voltammetry of the 1.0 mM CH₃CN/H₂O solution containing 0.1 M KCl. Scan rate: 100 mV/s.*
situ regeneration of the NADH mimic active sites. The superiority of such combined systems that promote the highly selective hydrogenation reaction by controlling the electron-transfer pathway using clean energy could be extended to several types of different functional groups (Table 2, 18a–28a). This selective hydrogenation reaction system was not only available for the aromatic compounds but also had better catalytic activity with respect to the aliphatic compounds containing alkyl or alkenyl groups (29a–32a). Simultaneously, the different types of alkenyl groups did not affect the selective catalytic hydrogenation (33a–36a).

The widespread demand of the flavoring, perfume, and pharmaceutical industries for unsaturated alcohols, which are key intermediates in the preparation of cinnarizine, fluoxazine, flunarizine, and naftifine,47,48 is met by producing these alcohols from α,β-unsaturated aldehydes via highly selective hydrogenation of the carbonyl group. Benzhydrylpiperazine or 1-naphthalenemethanamine were added to the aforementioned reaction system to directly prepare drug molecules by a one-pot synthesis. Under typical conditions, benzhydrylpiperazine and 1-naphthalenemethanamine (12.0 mM), Zn−FPB (0.2 mM), and cinnamaldehyde (4.0 mM) yielded 71 and 55% cinnarizine and naftifine with 94 and 97% selectivities, respectively, in 12 h under 420 nm LED light illumination (Table 3).

Switchable Selectivity of Photocatalytic Transfer Hydrogenation. While changing the redox potential of the electron donors changed the product conversion, the hydrogenation selectivity could not be influenced, except in the presence of Na2S2O4 (Figure 6a). The highly negative potential of Na2S2O4 reduced the nitro group outside the pocket to give 1b while simultaneously donating electrons to the NAD+ mimics to in situ regenerate the active sites for hydrogenation of the aldehyde group.59,60 Clearly, the modification of the electron-donating ability can tune the selectivity of hydrogenation toward 1a and 1b.

Ir(ppy)2(phen)+ is a well-known photosensitizer that drives several photocatalytic reactions51 and exhibits a similar absorption band52 compared to that of the NAD+ mimics with a negative redox potential in its reduced state, Ir(ppy)2(phen). The luminescent titration of Ir(ppy)2(phen)+

Table 2. Evaluation of the Scope in Hydrogenation Catalysis along with the Highly Selective Hydrogenation of Different Types of Substrates with Functional Groups

Table 3. Evaluation of the Scope of Hydrogenation Catalysis along with the Synthesis of Drug Molecules Cinnarizine and Naftifine

References:

1Reaction conditions: Substrate (5.0 mM), Zn−FPB (0.1 mM), HCOOH/Et3N (0.1 M/0.05 M), and NaBH3CN (1.0 mM) in a CH3CN/H2O solution (1:1, pH 8.50) for 6 h under 420 nm illumination. Yields were determined by 1H NMR spectroscopy of crude products, and the selectivities are labeled in parentheses.

2Reaction conditions: Cinnamaldehyde (4.0 mM), Zn−FPB (0.2 mM), benzhydrylpiperazine or 1-naphthalenemethanamine (12.0 mM), HCOOH/Et3N (0.1 M/0.05 M), and NaBH3CN (1.0 mM) in a CH3CN/H2O solution (1:1, pH 8.50) for 12 h under 420 nm illumination. Yields were determined by 1H NMR spectroscopy of crude products, and the selectivities are labeled in parentheses.
upon the addition of 1 and electron donors HCOOH/Et₃N and Zn−FPB at the same concentrations used in the reaction suggested that a photoinduced electron transfer from Ir(ppy)₂(phen)+ to 1 dominated the excited quenching processes (Figures S24−S27). The addition of Ir−(ppy)₂(phen)+ (1.0 mM) in the aforementioned reaction mixture gave the major product as 1b in 64% yield with a 22% yield of minor product 1a. When decreasing the reaction concentration of 1 (2.5 μmol/time, 10 times), the photoinduced electron transfer from electron donors HCOOH/Et₃N to Ir(ppy)₂(phen)+ dominated the excited quenching processes to give reduced Ir(ppy)₂(phen)+, which further reduced catalyst Zn−FPB and 1.⁵¹ The major product was 1b in a decreased yield of 54%, and the yield of minor product 1a increased to 33% (Figure 7a).

Ni−FPB (Figures 7c and S7) as a catalyst yielded 81% 1a with a high selectivity greater than 99% in the presence of HCOOH/Et₃N as a reductant, and the addition of Ir−(ppy)₂(phen)+ (1.0 mM) to the reaction mixture decreased the yield of 1a to 18% with a 1b yield of 70% (Table S14). We lowered the reaction concentration of 1 (2.5 μmol/time, 10 times) to decrease the quenching process of 1 on the photosensitizer (Figures S27 and S28) and the reaction rate outside the molecular flask, and reduced Ir(ppy)₂(phen)+ reduced the redox-active metal ions in the host, which further enhanced the regeneration of NADH mimics. The major product was switched to 1a with a yield of 71% and a selectivity of more than 85% (Figure 6b) by the carefully regulation of the reaction kinetics inside and outside the host with respect to the influence of the thermodynamically favored hydrogenation groups. The results indicated that this simple approach to localizing and differentiating 2e− and 1e− hydrogenation pathways inside and outside the pocket could...
comfortably tune the selectivity of the two functional groups in bifunctional chemicals. Clearly, the selectivity of the hydrogenation product toward 1a and 1b can be directly switched via varying the substrate concentration (Figure S29). A control experiment based on molecular flasks Ni=FMb (Figures 1d, 56, and 58) that resembles both the coordination geometry of the nickel(II) ion and the molecular square but with a central benzene ring replacing the center ring of the NADH mimics gave >80% selectivity of 1b under the same conditions in the presence of Ir(ppy)2(phen)+ (1.0 mM), even when lowering the reaction concentration of 1 (Figure S30 and Table S14). The absence of NADH mimics prevents any switchable possibility of selectivity. Such a switching approach could also be extended to the redox-active hosts containing Co(II) and Fe(II) ions (Figures 7d,e, S9, and S10). The differences in the selectivity for 1a over 1b even in the presence of a photosensitizer suggested that the electron-donating ability to the redox-active metal ions, in addition to the NADH mimics, is an important factor influencing the in situ regeneration of the active sites, the conversion, and the hydrogenation selectivity (Figures S31, S33, and 1b and Table S14). A simple comparison of the selectivity of 1a with the redox potentials of these molecular squares further confirmed that the direct electron transfer from the redox state of the photosensitizer outside the pocket to the catalyst hosts dominates the in situ generation of the active sites (Figure S17).

39 (p-(nitro)nitrobenzene), which contains two reducing groups with different electron transfer pathways, was selected as another typical substrate to demonstrate the broader applicability of the approach (Figure S33). Generally, the reduction of a nitro group to a nitroso group with hydroxylamine in solution, the switchable and S34). The reduction of a nitro group to a nitroso group and a hydroxylamine to an amino were through a 1e− transfer hydrogenation process, whereas the reduction of nitro to hydroxylamine occurs through a 2e− hydride transfer hydrogenation.53 In the absence of the photosensitizer, 1,2-bis(4-nitrophenyl)diazene (39a)54 was obtained with a selectivity of >99% (Table S15). Substrate 39 (5.0 mM) was added to the solution containing Ir(ppy)2(phen)+ (1.0 mM), and urso (39b) was obtained in an 80% yield. By lowering the reaction concentration of 39 (2.5 μmol/time, 10 times), an 89% yield of 39a with a 90% selectivity was achieved after 6 h (Figure 7b). Because 39a was formed by mixing a nitro group with hydroxylamine in solution, the switchable selectivity should be attributed to the selective reduction of the nitro group through a 1e− electron transfer process outside the flask, whereas the reduction of the nitroso group is through a 2e− hydride transfer hydrogenation inside the flask (Figures 8 and S34).

In summary, by incorporating NADH active sites into metal–organic hosts to localize the hydrogenation events inside and outside the pocket, we establish a new approach for modifying 2e− hydride transfer hydrogenation and 1e− transfer hydrogenation pathways to control and switch the selectivity between C=X (X = O, N) groups and nitro groups in bifunctional compounds. Inside the molecular flask, the NADH active sites highly selectively reduce the C=X (X = O, N) groups in the pocket via a typical 2e− hydride transfer hydrogenation, and the formed excited-state NAD+ mimics oxidize the reductant via two consecutive 1e− processes to regenerate the NADH active sites under illumination. Outside the molecular flask, electron donors in the ground state or in the excited state highly selectively reduce nitro groups through a typical 1e− hydrogenation process. Notably, the selectivity of hydrogenation of bifunctional compounds could be switched by simply regulating the reaction kinetics of the two hydrogenation pathways (i.e., by varying the concentrations of the substrate and electron donor) because the kinetics inside the pocket are controlled only by the concentration of the host–guest complex and not directly by the concentration of the substrate. Thus, this method represents a new synthetic platform for the designation of a novel photocatalysis. Compared to other reported transfer hydrogenation approaches, our approach of localizing the NADH-cofactor-derived biomimetic 2e− hydride transfer hydrogenation pathway inside a molecular flask to control the electron transfer pathway and the high selectivity of the product are quite significant, representing an unexplored intersection of group-selective syntheses, catalysis with earth-abundant metals, photoinduced processes, and transfer hydrogenation, each of which represents an important current theme in chemical synthesis.

## EXPERIMENTAL SECTION

### Synthetic of H2FPB

Compound 1-(furan-2-ylmethyl)-4-phenyl-1,4-di(hydrydropyridine-3,5-dicarboxyhydrazide (3.53 g, 10 mmol) was added to an ethanol solution (50 mL) containing 2-pyrydylaldehyde (2.35 g, 22 mmol). After 5 drops of acetic acid was added, the mixture was held at 85 °C under magnetic stirring for 12 h according to the reference. The yellow solid was collected by filtration, washed with methanol, and dried in vacuum. Yield: 3.29 g, 65.6%. 1H NMR (400 MHz, DMSO-d6 ppm): δ 13.38 (s, 2H), 8.57 (d, J = 4.4 Hz, 2H), 8.24 (s, 2H), 7.84 (m, 4H), 7.75 (s, 1H), 7.47 (s, 2H), 7.37 (m, 2H), 7.24 (m, 4H), 7.11 (t, J = 7.2 Hz, 1H), 6.52 (s, 2H), 5.33 (s, 1H), 4.76 (s, 2H). 13C NMR (101 MHz, DMSO-d6 ppm): δ 163.9, 153.5, 150.6, 149.4, 146.4, 145.3, 136.7, 135.2, 128.1, 127.6, 126.2, 124.0, 119.6, 110.7, 109.3, 108.8, 50.1, 36.1. Elemental analysis calcd for C25H20N6O3: H 4.74, C 67.79, N 18.44%. Found: H 4.82, C 67.01, N 18.21%. ESI-MS calcd for C30H25N7O3: [M + Na]+ (100%), 554.1927 [M + Na]+ (8%).

### Synthesis of H2FMB

Compound 5-(furan-2-ylmethyl)isophthaloylhydrazide (2.84 g, 10 mmol) was added to an ethanol solution (50 mL) containing 2-pyrydylaldehyde (2.35 g, 22 mmol). After 5 drops of acetic acid was added, the mixture was held at 85 °C under magnetic stirring for 12 h according to the reference. The yellow solid was collected by filtration, washed with methanol, and dried in vacuum. Yield: 3.82 g, 83%. 1H NMR (400 MHz, DMSO-d6 ppm): δ 12.24 (s, 2H), 8.64 (d, J = 4.4 Hz, 2H), 8.51 (s, 2H), 8.37 (s, 1H), 8.02 (m, 4H), 7.90 (t, J = 7.6 Hz, 2H), 7.58 (s, 1H), 7.44 (t, J = 6.4 Hz, 2H), 6.41 (s, 1H), 6.24 (s, 1H), 4.18 (s, 2H), 15C NMR (101 MHz, DMSO-d6 ppm): δ 162.7, 153.2, 153.1, 149.5, 148.5, 142.2, 139.4, 136.9, 138.7, 131.3, 128.1, 124.5, 120.0, 110.6, 106.8, 163.5. Elemental analysis calcd for C125H125N9O12: H 4.46, C 66.36%, N 18.57%. Found: H 4.56, C 66.57, N 18.41%. ESI-MS calcd for C125H125N9O12: 452.1517, found 453.1681 [M + H]+ (100%), 475.1476 [M + Na]+ (9%).

**Figure 8.**(a) Normalized fluorescence of Ir(ppy)2(phen)+ (1.0 mM, black line) and of the aforementioned solution upon addition of 39 (0.5 mM, red line), 39 (5.0 mM, blue line), or HCOOH/Et,N (0.1/0.05 M, green line). (b) Selective hydrogenation pathways of the p-(nitro)nitrobenzene.
Preparation of Zn–FPB. Zn(BF₄)₂·6H₂O (34.7 mg, 0.10 mmol) and H₂FPB (53.2 mg, 0.10 mmol) were dissolved in CH₂CN to give a yellow solution. The solution was diffused with ether for several days at room temperature to give X-ray-quality yellow block crystals. Yield: 68%. ¹H NMR (400 MHz, DMSO-d₆, ppm): δ 12.00 (s, 2H), 8.53 (s, 2H), 8.33 (s, 2H), 7.93 (m, 4H), 7.76 (s, 1H), 7.61 (s, 2H), 7.51 (s, 2H), 7.22 (m, 4H), 7.12 (m, 1H), 6.53 (s, 2H), 5.29 (s, 1H), 4.84 (s, 2H). Elemental analysis calculated for Zn₄(C₂₅H₁₉.₅N₆O₃)₄·8CF₃SO₃·7CH₂CN·H₂O: C 39.78, H 3.47, N 11.39%. Found: C 39.73, H 3.47, N 11.39%. ESI–MS: m/z: 793.8252 [H₂[Zn₄(FPB)₄]⁺] (100%), 1190.2319 [H₃[Zn₄(FPB)₃]⁺] (78%).

Preparation of Zn–FPB ⊂ 1. Zn(C₂₅H₁₈.₅N₆O₃)₂·76H₂O (36.1 mg, 0.10 mmol) and H₂FPB (53.2 mg, 0.10 mmol), and 4-nitrobenzaldehyde (37.8 mg, 0.25 mmol) were dissolved in CH₂CN to give a yellow solution. The solution was diffused with ether for several days at room temperature to give X-ray-quality yellow block crystals. Yield: 54%. Elemental analysis calculated for Fe₄(C₂₅H₁₈.₅N₆O₃)₄·6H₂O·1.5CH₂CN·H₂O: C 44.80, H 3.58, N 12.81%. Found: C 44.87, H 3.59, N 12.85%. ESI–MS: m/z: 865.5142 [H₂[Fe₄(FPB)₄]⁺] (100%), 1231.5265 [H₂[Fe₄(FPB)₃]⁺BF₄] (50%).

Preparation of Fe–FPB. Fe(C₂₅H₁₈.₅N₆O₃)₂·76H₂O (36.3 mg, 0.10 mmol) and H₂FPB (53.2 mg, 0.10 mmol) were dissolved in CH₂CN to give a yellow solution. The solution was diffused with ether for several days at room temperature to give X-ray-quality purple block crystals. Yield: 54%. Elemental analysis calculated for Fe₄(C₂₅H₁₈.₅N₆O₃)₄·6H₂O·1.5CH₂CN·H₂O: C 44.80, H 3.58, N 12.81%. Found: C 44.87, H 3.59, N 12.85%. ESI–MS: m/z: 865.5142 [H₂[Fe₄(FPB)₄]⁺] (100%), 1231.5265 [H₂[Fe₄(FPB)₃]⁺BF₄] (50%).

Preparation of Ni–FPB. Ni(C₂₅H₁₈.₅N₆O₃)₂·76H₂O (36.5 mg, 0.10 mmol) and H₂FPB (54.2 mg, 0.10 mmol) were dissolved in CH₂CN to give a yellow solution. The solution was diffused with ether for several days at room temperature to give X-ray-quality yellow block crystals. Yield: 56%. Elemental analysis calculated for Ni₄(C₂₅H₁₈.₅N₆O₃)₄·5CH₂CN·H₂O: C 44.80, H 3.58, N 12.81%. Found: C 44.87, H 3.59, N 12.85%. ESI–MS: m/z: 857.1639 [H₃[Ni₄(FPB)₄]⁺] (100%), 1177.4292 [H₄[Ni₄(FPB)₄]⁺] (53%).

Preparation of Ni–FMB. Ni(C₂₅H₁₈.₅N₆O₃)₂·76H₂O (36.5 mg, 0.10 mmol) and H₂FMB (46.3 mg, 0.10 mmol) were dissolved in CH₂CN·C₂H₅OH (ν/ν = 9:1) to give a yellow solution. The solution was diffused with ether for several days at room temperature to give X-ray-quality light-yellow block crystals. Yield: 21%. Elemental analysis calculated for Ni₄(C₂₅H₁₈.₅N₆O₃)₂·6C₂H₅OH·CH₂CN·3H₂O·4BF₄: C 39.48, H 4.40, N 12.81%. Found: C 39.46, H 4.40, N 12.77%. ESI–MS: m/z: 879.7817 [H₃[Ni₄(FMB)₄]⁺] (100%), 1091.1665 [H₄[Ni₄(FMB)₄]⁺] (76%).

Single-Crystal X-ray Crystallography. The intensities were collected on a Bruker SMART APEX II diffractometer equipped with a graphite-monochromated Mo Kα (λ = 0.71073 Å) radiation source; the data were acquired using the SMART and SAINT programs. The structures were solved by direct methods and refined on F² by full-matrix least-squares methods using the SHELXTL version 5.1 software.

In the structural refinement of Zn–FPB, except for one partially occupied solvent CH₂CN molecule and all of the fluorine atoms in a disordered BF₄⁻ anion, all of the non-hydrogen atoms were refined anisotropically. Hydrogen atoms within the ligand backbones and the solvent CH₂CN molecule were fixed geometrically at calculated distances and allowed to ride on the parent non-hydrogen atoms. To assist the stability of refinements, the furan and benzene rings in the ligand, BF₄⁻ anions, and solvent CH₂CN molecule were restrained as idealized regular polygons, and thermal parameters on adjacent atoms in furan and benzene rings were restrained to be similar. All of the oxygen atoms of a ClO₄⁻ anion were disordered into two parts, with the s.o.f. of each part being fixed at free values. The SQUEEZE subroutine in PLATON was used.

In the structural refinement of Fe–FPB, except for one partly occupied solvent CH₂CN molecule and all of the oxygen atoms of a disordered ClO₄⁻ anion, all of the non-hydrogen atoms were refined anisotropically. Hydrogen atoms within the ligand backbones and the solvent CH₂CN molecule were fixed geometrically at calculated distances and allowed to ride on the parent non-hydrogen atoms. To assist the stability of refinements, the furan and benzene rings in the ligand, BF₄⁻ anions, and solvent CH₂CN molecule were restrained as idealized regular polygons, and thermal parameters on adjacent atoms in furan and benzene rings were restrained to be similar. All of the oxygen atoms of a ClO₄⁻ anion were disordered into two parts, with the s.o.f. of each part being fixed at free values. The SQUEEZE subroutine in PLATON was used.

In the structural refinement of Ni–FPB, except for two partly occupied solvent CH₂CN molecules and all of the oxygen atoms of a disordered ClO₄⁻ anion, all of the non-hydrogen atoms were refined anisotropically. Hydrogen atoms within the ligand backbones and the solvent CH₂CN molecule were fixed geometrically at calculated distances and allowed to ride on the parent non-hydrogen atoms. To assist the stability of refinements, the furan and benzene rings in the ligand, BF₄⁻ anions, and solvent CH₂CN molecule were restrained as idealized regular polygons, and thermal parameters on adjacent atoms in furan and benzene rings were restrained to be similar. All of the oxygen atoms of a ClO₄⁻ anion were disordered into two parts, with the s.o.f. of each part being fixed at free values. The SQUEEZE subroutine in PLATON was used.

In the structural refinement of Ni–FMB, except for some solvent water molecules, all of the non-hydrogen atoms were refined anisotropically. Hydrogen atoms within the ligand backbones, the solvent CH₂CN, ether, and ethanol molecule were fixed geometrically at calculated distances and allowed to ride on the parent non-hydrogen atoms. To assist the stability of refinements, two furan rings and one benzene ring in the ligand, ClO₄⁻ anions, and solvent CH₂CN, ether, and ethanol molecules were restrained as idealized regular polygons, and thermal parameters on adjacent atoms in furan rings were restrained to be similar. The furan and benzene rings in one ligand were disordered into two parts, with the s.o.f. of each part being fixed at free values. All the oxygen atoms of three ClO₄⁻ anions
were disordered into two parts, with the s.o.f. of each part being fixed at free values.

**Photocatalytic Transfer Hydrogenation Protocol.** The catalyst (0.1 mM, 0.5 μmol), substrates (5.0 mM, 25.0 μmol), NaBH₃CN (1.0 mM, 5.0 μmol), and HCOOH/Et₃N (0.1/0.05 M, 0.5/0.25 mmol) in CH₃CN/H₂O (1:1 in volume) were added to a 20 mL flask. The flask was degassed by bubbling argon for 15 min under atmospheric pressure at room temperature. The pH (8.5) of this solution was adjusted to a specific pH by adding H₃SO₄ or NaOH and measured with a pH meter. After that, the samples were irradiated with a 100 W LED lamp at 420 nm, and the reaction temperature was held at 298 K by using a water filter to absorb heat. The yields were determined by ¹H NMR analysis of the crude products.

**ASSOCIATED CONTENT**

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b05351.

Complete experimental details and supporting figures; X-ray data for Zn−FPB (CCDC 1891712), Zn−FPB ⊃ 1 (CCDC 1891711), Fe−FPB (CCDC 1891710), Co−FPB (CCDC 1891708), Ni−FPB (CCDC 1891709), and Ni−FMB (CCDC 1906243) (PDF)

C124 H102 B4 F16 N30 O12 Zn4 (CIF)
C145 H122 F24 N34 O40 S8 Zn4 (CIF)
C120 H96 B4 C40 F16 N28 O12 (CIF)
C124 H104 Cl6 Fe4 N30 O36 (CIF)
C128 H110 Cl6 N32 Ni4 O36 (CIF)
C116 H130 Cl6 N26 Ni4 O47 (CIF)

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**Notes**
The authors declare no competing financial interest.

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(54) SAINT Data Reduction Software, version 6.54; Bruker AXS Inc.: Madison, WI, 2003.