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Molecular Coordination-Switch in a New Role: Controlling Highly Selective Catalytic Hydrogenation with Switchability Function

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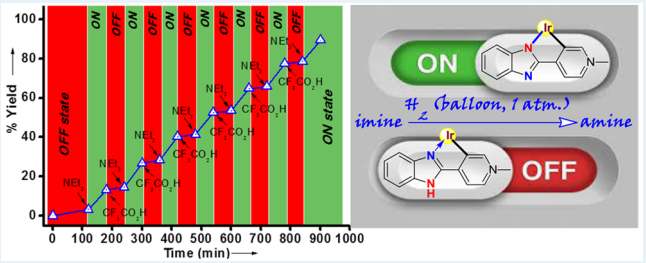
Supporting Information

ABSTRACT: A molecular coordination-switch controlled by acid−base input has been developed and utilized in switchable catalysis. The molecular switch consists of a hybrid pyridylidene−benzimidazole ligand bound to an $Ir^{III}Cp^*$ moiety wherein the benzimidazole functionality has been utilized for acid/base controlled reversible coordination, switching between an Ir^{III}-benzimidazole species (form **I**; neutral imino-type N-coordination) and an Ir^{III}-benzimidazolate species (form **II**; anionic amido-type N−Ir bonding). Owing to the distinctly different nature of the metal−ligand bonding, it has been demonstrated that while the form **I** is almost inactive (TOF 1 h^{-1}) in catalytic hydrogenation of imine under ambient pressure and temperature, the form **II** is greater than an order of magnitude more efficient (TOF 15.8 h^{-1}) in the same catalysis. Moreover, the catalysis could be switched *OFF* and *ON* efficiently for several cycles with the addition of acid and base, respectively. Spectroscopic studies and kinetics have been performed to understand the switching activity.



KEYWORDS: *molecular switch, switchable catalysis, acid−base, iridium(III), hydrogenation*

Molecular property and function depend on the molecular design, which, in turn involves a certain level of sophistication, smartly incorporated into the structure of the molecule concerned. Nature fascinates us with demonstration of several signal-controlled desirable enzymatic activities, from energy harvesting to communication, growth, and reproduction, through a high level of sophisticated trigger-induced features.[1] Inspired by the control mechanisms of the natural systems, it is understood that switching the property, function, and activity of a molecule with simple chemico-physical stimuli (acid/base, metal ion, light, sound, electric potential, mechanical force, etc.) is achievable only through judicious incorporation of a reversibly responsive regulatory feature. Eventually, designing artificial switchable catalysts has become an emerging research area to confer advanced functions with controllable outcome in terms of rate of the reaction and/or chemo-, regio-, stereoselectivity of the product(s), for instance.[2]

An acid/base-controlled molecular coordination-switch involving two interconvertible metal-coordination modes has been known to chemists for a long time (Figure 1).[3] For example, Constable, Wolf, and others demonstrated the reversible switching between the (*Y*,*S*) and (*Y*,*C*) coordination modes of thiophene-derived ligands (Y = a pendant pyridine or phosphine ligand or a metal center) with Ru, Os, or Rh metal centers by reaction with acid or base. However, the phenomenon was used merely to achieve a variable spectroscopic, electrochemical, and/or fluorescence excited state property. No real application, such as switching a chemical catalysis, has been demonstrated so far with this concept. This might be partly due to less efficient switching and/or insufficient stability required to run catalytic turnover in solution. Significantly, the concept of protonation−deprotonation modulated catalysis by utilizing the tunable electronic influence of pH-responsive ligands has been explored previously by the groups of Fujita,[4a] Himeda,[4b] Periana,[4c] Szymczak,[4d,e] and Papish,[4f,g] although a "true" molecular coordination-switch was not involved in these systems. We anticipated that the two interconvertible coordination environments around a metal center, generated by simple acid/base input, might be a prospective platform to design and operate a catalysis-switch. Of course, a delicate balance of electronic characteristics around the metal−ligand core should be able to influence the substrate activation step(s), the most relevant bond-breaking/bond-making processes, and subsequently the reaction kinetics markedly to achieve entirely variable final outcome as required for a prospective switch. Herein we present a molecular design that not only switches its metal-coordination modes reversibly with acid/base input displaying two distinct properties but also operates an efficient switchable-catalysis leading to a great control of *ON*/*OFF* output in terms of catalytic efficiency. The molecular design was based on a hybrid pyridylidene−benzimidazole ligand bound to an $Ir^{III}Cp^*$ moiety wherein the benzimidazole functionality was utilized for acid/base controlled coordination-switch (forms **I** and **II**) while

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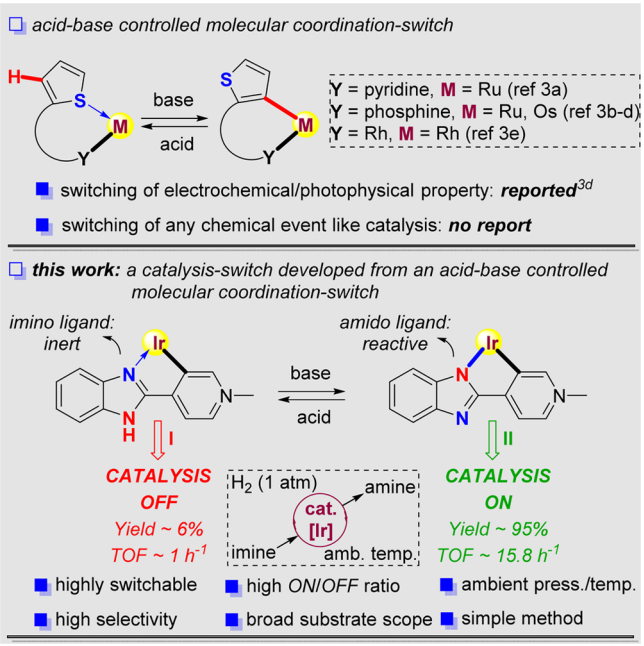
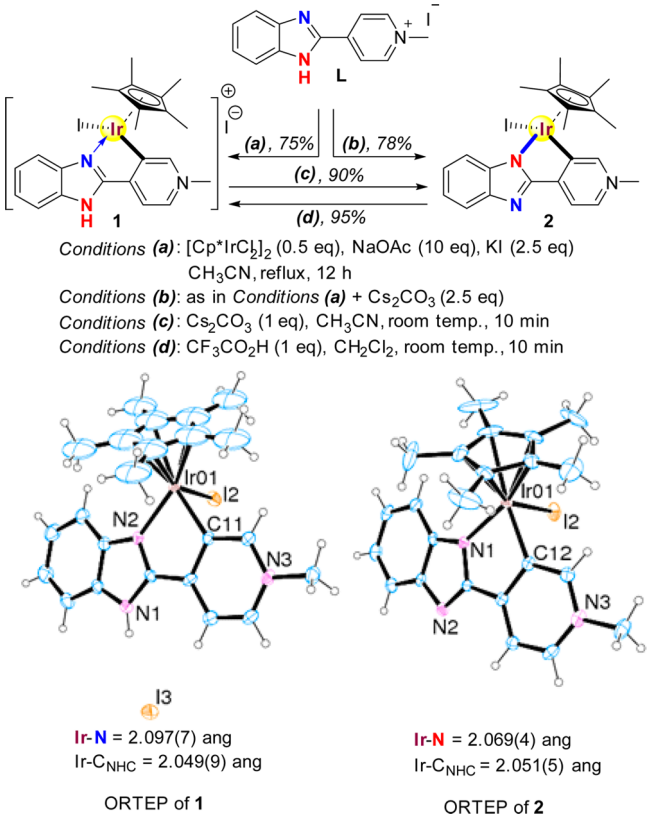


Figure 1. (Top) Example of acid–base controlled molecular coordination-switch and (bottom) a catalysis-switch developed on a molecular coordination-switch platform.

the pyridylidene-based remote NHC ligand was utilized for providing a strong and robust metal–ligand platform to carry out the catalytic reaction (Figure 1). Mayer et al. previously showed that a Ru^{II}-coordinated pendant imidazole ligand could be deprotonated to imidazolate for binding via an anionic fashion to the metal center and with the treatment of an acid the binding mode could be restored as well.[5] We hypothesized that the mode of H_2 activation/cleavage with the Ir^{III}-benzimidazolate species (form **II**; anionic amido-type N–Ir bonding) and the Ir^{III}-benzimidazole species (form **I**; neutral imino-type N-coordination) of the designed bifunctional system would be mechanistically distinct due to distinctly different nature of the metal–ligand bonding which in turn could affect the efficiency of subsequent catalytic hydrogenation of unsaturated organic molecules.[6] For example, the form **II** of the complex may cleave H_2 in a cooperative manner with the help of relatively basic amido-type ligand and an electrophilic Ir^{III} center to generate an Ir–H species quite efficiently and thereby may facilitate catalytic hydrogenation. The proof of concept was realized by performing catalytic hydrogenation of imines[7] at ambient pressure and temperature wherein it was found that the form **II** (TOF of 15.8 h^{-1}) was greater than an order of magnitude more efficient than the form **I** (TOF of 1 h^{-1}) under identical reaction conditions, and the catalysis was switched *OFF* and *ON* efficiently with the addition of acid and base, respectively.

To demonstrate the newly developed proof-of-concept switchable catalyst system, the hybrid pyridylidene–benzimidazole ligand, **L** was designed, synthesized, and metalated with [Cp*Ir^{III}] motif, as shown in Scheme 1, to provide the imino-coordinated Ir(III) complex **1** and the amido-bound Ir(III) complex **2**. The reaction conditions for synthesizing **1** and **2** were essentially identical, but the use of Cs_2CO_3 was necessary for **2**. Successful synthesis of **1** from **2** and **2** from **1** in good yields was also achieved with the use of CF_3CO_2H and Cs_2CO_3, respectively (Scheme 1). The variable coordination environment in the two complexes were characterized by ^1H NMR and $^{13}C\{^1H\}$ NMR spectroscopy and confirmed unambiguously by single-crystal X-ray diffraction studies (Scheme 1 and Supporting Information). Solution-phase interconversion between **1** and **2** with acid–base inputs was studied by ^1H NMR and UV–vis spectroscopic techniques and was established to be highly efficient (Figure 2; see Supporting Information for details). The stability and robustness of the above coordination-switch was also tested in solution with consecutive acid–base switching starting from **2**. The value of the extinction

Scheme 1. Synthesis of the Two Forms (1 and 2) of the Molecular-Switch and the Molecular Structures of 1 and 2



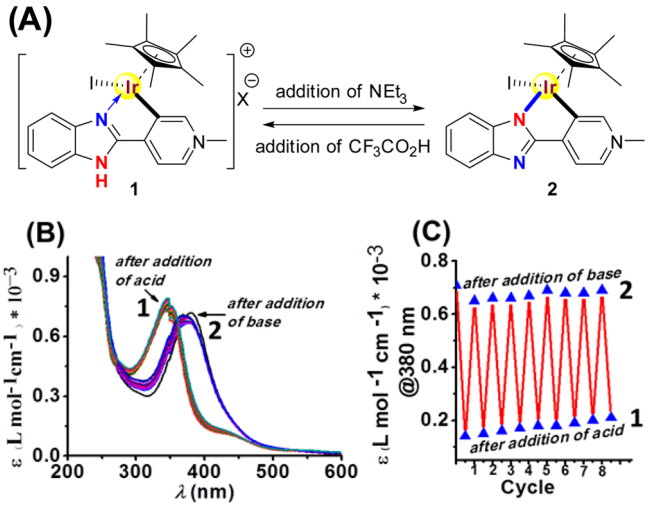


Figure 2. (A) Interconversion of **1** and **2** with base and acid. (B),(C) Consecutive switching between **1** and **2** in solution.

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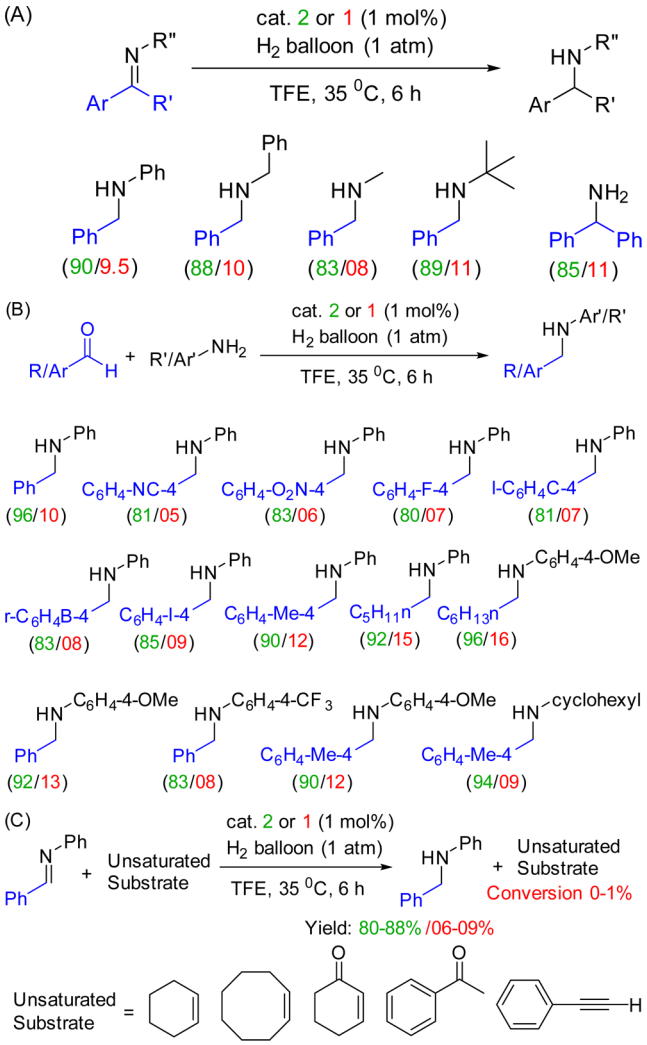
coefficient of the band at 380 nm was found to be almost constant after several regenerative cycles (Figure 2B,C), suggesting the high stability of the switch in solution under operating conditions.

The two complexes **1** and **2** of the switchable catalyst system were utilized for catalytic hydrogenation of imines with molecular hydrogen under ambient conditions (H_2 balloon, 35 °C) in 2,2,2-trifluoroethanol (TFE) (Table 1A). It was observed that for all the substrates, catalyst **2** was active (yield 83−90%), while catalyst **1** was almost inactive (yield 8−11%), indicating the effect of variable coordination platform in **1** and **2**. Notably, in the previously reported pH-responsive catalytic systems, ligand deprotonation by base or at higher pH also led to enhanced activity in CH activation, nitrile hydroboration, and water oxidation catalysis.[4c,d,g] The scope of the present catalysis was further extended successfully via performing the hydrogenation reaction by using an equimolar mixture of various aldehydes and amines as substrates (Table 1B). The trend of the activity of **1** and **2** was again proved to be the same as earlier. Moreover, selectivity toward hydrogenation of imine over other unsaturated organic substrates such as alkene, alkyne, ketone, and enone, were tested via competitive reactions, and it was found to be highly selective with almost no conversion of the competing substrates (Table 1C).

Table 1. Examples of 2 and 1-Catalyzed Hydrogenation of (A) Imines, (B) Equimolar Mixture of Aldehydes and Amines, and (C) Imines in the Presence of Competing Substrates[a]



[a]Conditions: (A) 0.2 mmol of imine, H_2 balloon, 1 mol % catalyst, 2 mL of TFE, 35 °C, 6 h. (B) 0.2 mmol of aldehyde, 0.2 mmol of amine, H_2 balloon, 1 mol % catalyst, 2 mL of TFE, 35 °C, 6 h. (C) 0.2 mmol of *N*-benzylideneaniline, 0.2 mmol of unsaturated substrate, H_2 balloon, 1 mol % catalyst, 2 mL of TFE, 35 °C, 6 h. Yields reported in parentheses represent isolated yields with catalyst **2** and **1**, respectively.

After demonstrating that the imino-bound complex **1** is catalytically inactive (*OFF*; red curve, Figure 3) and the amido-bound complex **2** is active (*ON*; green curve, Figure 3), the potential of switching the catalysis between *ON* and *OFF* during the actual progress of the reaction was explored. Thus, when the hydrogenation catalysis was started with the *OFF* catalyst **1**, there was virtually no yield of the product after 2 h. At this point of time, addition of 1 equiv (with respect to the catalyst) of NEt_3 switched the catalysis *ON*, and after 1 more hour, the yield was found to be 10%. Addition of CF_3CO_2H terminated the ongoing catalysis. However, the *ON* state could be regenerated again by the addition of NEt_3. Seven subsequent cycles were performed without any significant loss of catalytic activity, showing ∼11.4% yield in each *ON* step and ∼1.1% yield in each *OFF* state over the entire course of the reaction (Figure 3, blue curve). Similarly, the reversible switching of *ON*/*OFF* catalysis was also proved efficient when the catalysis was started with the *ON* catalyst **2** and subjected to the addition of acid and base in consecutive steps during the course of the reaction (Figure 3, maroon curve).

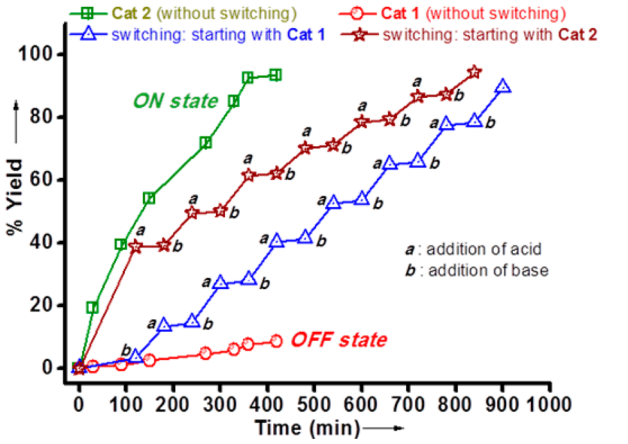


Figure 3. Plot of yield (%) versus time for the hydrogenation of *N*-benzylideneaniline catalyzed by **1** (red curve) and **2** (green curve); blue curve represents the *ON*/*OFF* switching of the catalytic activity when started with catalyst **1** followed by consecutive addition of base (NEt_3) and acid (CF_3CO_2H); maroon curve represents the *ON*/*OFF* switching of the catalytic activity when started with catalyst **2** followed by consecutive addition of acid (CF_3CO_2H) and base (NEt_3).

The dramatic difference in catalytic activity of **1** and **2** might be ascribed to the nature of the ligand sphere and its effect on the key step involving the activation of H_2. Although the imino ligand in **1** is inert in playing any additional role in H_2 activation step, it is reasonable to predict that the basic amido ligand in **2** can facilitate to activate H_2 in a bifunctional manner to generate Ir−H species quite easily, promoting the hydride insertion and subsequent hydrogenation efficiently.[6] The above suggestion for the plausible differential reactivity of

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H_2 with **1** and **2** leading to the formation of σ-Ir(H_2) species from **1** but Ir−H species from **2** was verified by VT ^{1}H NMR (500 MHz) spin−lattice relaxation time (T_1, ms) measurements (Figure 4).[8] A short T_1 (min) of 49 ms at 233 K in case

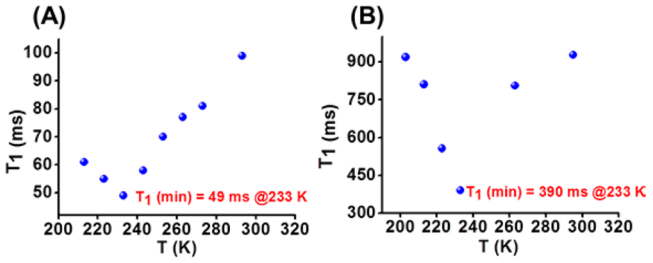

Figure 4. Temperature-dependent spin−lattice relaxation time (T_1, ms) at 500 MHz in CD_2Cl_2, measured for the species generated by the reaction of H_2 with (A) complex **1**, and (B) complex **2**.

of **1** and a long T_1 (min) of 390 ms at 233 K in case of **2** were in good agreement with the proposal, supported by reported values as well.[8] Next, initial-rate analysis was carried out to determine the order of each component and the results suggested the following rate laws: rate = k_{obs}[cat][H_2] with catalyst **2** and rate = k_{obs}[cat][H_2][imine] with catalyst **1**. The rate-laws revealed that for the **2**-catalyzed reaction, the iridium catalyst and H_2 are likely to be involved in the rate-determining step (rds), while for the **1**-catalyzed reaction, the rds involves catalyst, H_2, and imine. To verify the involvement of H_2 in the rds, the kinetic deuterium isotope effect (KDIE) was determined experimentally via conducting the catalytic hydrogenation reaction with H_2 and D_2 under identical conditions. The k_H/k_D value of 3.45 for **2**-catalyzed reaction and 2.45 for **1**-catalyzed reaction supported the involvement of H_2 in the rds. These kinetic data, reactivity with H_2 and the corresponding T_1 (min) values, KDIE, and some additional mechanistic investigation, suggested different catalytic cycles and the nature of the rds for the two catalysts which can be considered as the basis to justify the observed *slow* or *fast* catalysis with **1** or **2**, respectively (see Supporting Information for details).

In summary, two acid/base responsive iridium(III) complexes were used to design a molecular switch which operates on highly reversible variable coordination modes of the ligand backbone. Such a stimuli-responsive molecular coordination-switch was utilized for developing a smart catalyst system to modulate catalytic activity and function on demand on a highly switchable platform. The system was explored in catalytic hydrogenation of a range of imine substrates with molecular dihydrogen gas under ambient pressure and simple conditions featuring a high *ON*/*OFF* ratio, high switchability, and robustness. Controlled studies suggested a difference in the mode of activation of dihydrogen as the probable reason for the dramatic difference in the activity of the *ON* and *OFF* states of the catalyst.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.6b00150.

Experimental details; spectra; additional text and figures (PDF)

CIF file (CIF)

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Notes

The authors declare no competing financial interest.

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