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Switchable hydrogenation with a betaine-derived bifunctional Ir–NHC catalyst†

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A bifunctional iridium catalyst based on the 'uracil–abnormal NHC' hybrid ligand platform was developed for switchable hydrogenation of quinoxalines. Control studies suggested heterolytic H_2 activation *via* a metal–ligand bifunctional operation to generate Ir–H and an adjacent protic O–H group for facile H^+/H^- transfer to quinoxaline. The presence of a base blocked the most essential H^+-transfer step thus switching off the catalysis, while an acid stimulus reversed the action to switch on the reaction again.

Investigating the influence of external chemical or physical stimuli on the function of suitably designed homogeneous and heterogeneous catalysts creates knowledge that may contribute to developing new artificial switchable catalysts.[1] However, as far as catalyst design is concerned, it is always a challenging task to create a harmonious combination of stimuli-triggered property switching and an application-worthy smart catalytic response. Nevertheless, the field of artificial switchable catalysis has blossomed exciting developments over the past few years with notable applications in several areas ranging from polymerization and organic synthesis and energy research to material science.[1] Alongside the most popular stimuli such as light, redox potential, pH, and metal-coordination, recently reversible alteration of the reaction conditions was also utilized as a stimulus to regulate the rate and/or selectivity of catalytic reactions.[1,2] To control such regulation, while the former stimuli modulate the structural and/or stereoelectronic property of the catalyst itself, the later generally affects the reaction path and/or intermediates.

Our recent success on reversible and switchable hydrogenation/dehydrogenation catalysis was based on a strategy of applying acid/base-stimulated switchable metal–ligand coordination modes within the catalyst backbone to toggle the stereoelectronic property and thereby the activity of the catalysts.[3] Striving towards a new switching strategy and pathway, herein we present a base-switchable hydrogenation reaction with a bifunctional Ir–N-heterocyclic carbene (NHC) catalyst. In the present work, atmospheric-pressure hydrogenation of quinoxalines was selected to demonstrate the switchable action of the catalyst. It is noteworthy to mention here that, at the forefront of alternative energy research, catalytic hydrogenation of liquid N-heteroarenes (such as quinolines, quinoxalines, naphthyridines *etc.*) has received a renewed attention.[4] This is because hydrogenated N-heterocycles are proposed as suitable hydrogen storage/carrier systems, and interestingly fuel cells and flow batteries using such liquid organic hydrogen carriers (LOHCs) are being investigated as promising energy technology.[4,5]

The design of the new catalyst involved the use of a 'uracil–abnormal NHC' hybrid bidentate ligand bound to the Cp^*Ir^{III} catalytic center (Fig. 1A). The uracilate motif within the resulting Ir-betaine architecture present in the catalyst backbone is prone to lactam–lactim tautomerization[6] resulting in a pendant base (Ir–N=C–$\boldsymbol{O}^-$) which can render metal–ligand bifunctionality[7] favorable for heterolytic H_2 activation (Fig. 1B). We hypothesize that such heterolytic H_2 activation would generate a coordinatively saturated catalytic intermediate consisting of **Ir–*H*** and Ir–N=C–***OH*** units (structure **IV**, (Fig. 1B)), susceptible for consecutive H^+/H^- transfer to the quinoxaline (**Q**) substrate *via* the outer-sphere mechanism (Fig. 1C). It was reported earlier in several studies that hydride (H^-) transfer to protonated quinolines rather than to the free neutral quinolines is a feasible path in their hydrogenation.[4] Considering a similar pathway for quinoxalines as well, we observed facile hydrogenation catalysis by using 1 mol% **Ir-U$_{NH}$** as a catalyst under a H_2 balloon atmosphere resulting in 90–96% yield of 1,2,3,4-tetrahydroquinoxalines in just 1.5 h at 50 °C in 2,2,2-trifluoroethanol (TFE)/H_2O (3 : 1, v/v) mixed solvent (Fig. 1C). Notably, a catalyst loading of 0.5 mol% or the reaction temperature of 30 °C were also effective albeit with a slightly lower rate. The hydrogenation protocol with this catalyst was also found to be applied effectively for quinolines (see ESI†). It is known that TFE helps effective solvation and dissociation of the chloride ligand attached to the Ir^{III} center of the catalyst,[4f] thus creating the vacant site required for facile H_2-coordination, followed by

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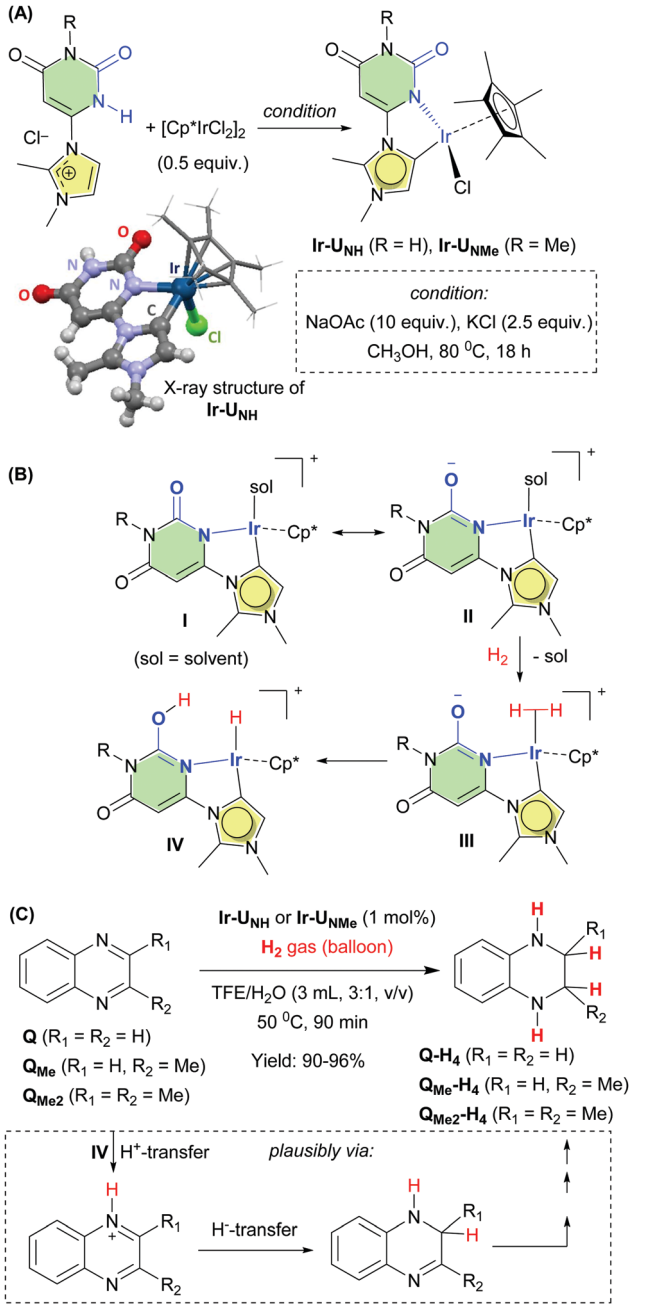

Fig. 1 (A) Synthetic scheme of the complexes **Ir-U$_{NH}$** and **Ir-U$_{NMe}$**, and crystal structure of **Ir-U$_{NH}$**; (B) plausible lactam–lactim tautomerization for the complex backbone, and proposed bifunctional heterolytic H_2-activation. The possible second –N(H)–C(=O)– ↔ –N=C(OH)– tautomerization for the complex **Ir-U$_{NH}$** is not shown; (C) general scheme for catalytic hydrogenation of quinoxalines, and the proposed H^+/H^- transfer pathway.

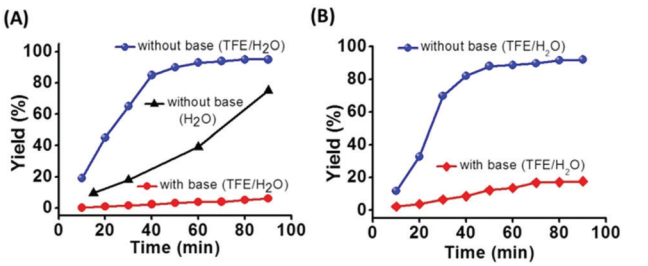

Fig. 2 Catalytic hydrogenation of quinoxaline (**Q**) with (A) **Ir-U$_{NH}$** and (B) **Ir-U$_{NMe}$** as a catalyst in the absence (blue trace) and presence (red trace) of base (K_2CO_3).

subsequent catalytic steps. Next, a time profile of the catalysis with quinoxaline as the substrate and **Ir-U$_{NH}$** (1 mol%) as the catalyst in a TFE/H_2O solvent mixture was derived, showing the smooth formation of the hydrogenated product during the course of the reaction (Fig. 2A). Even the catalysis in the absence of TFE, *i.e.*, only in H_2O as a solvent, was successful. Interestingly, the catalysis was found to be almost switched off (product yield of only 6% in 1.5 h) when the reaction was performed in the presence of 40 mol% K_2CO_3 under otherwise identical conditions (Fig. 2A). This result was remarkable and to verify if this was due to the presence of the acidic N–H group within the uracilate backbone of the catalyst **Ir-U$_{NH}$**, control catalytic reactions were performed with the N–Me version **Ir-U$_{NMe}$**. The results were found to be similar; *i.e.*, the highly efficient reaction observed with **Ir-U$_{NMe}$** was almost switched off (product yield of 17% in 1.5 h) in the presence of a base (K_2CO_3) (Fig. 2B).

Next, the feasibility of the most vital switchable action of the catalyst **Ir-U$_{NH}$** (1 mol%) for the hydrogenation of quinoxaline was tested by applying the base (K_2CO_3) to switch it off and the reverse stimulus, *i.e.*, an acid (HCl), to switch it on again. Thus, an ongoing catalytic reaction could be consecutively switched off and on for multiple times with these stimuli (Fig. 3A). Although the probable buffering effect due to the salt formation during consecutive addition of K_2CO_3 and HCl did not hamper the activity much at the later stage of the catalysis, the switching experiment was performed using KOH and HCl as stimuli. Delightedly, the resulting OFF/ON switching kinetics was found to be improved (Fig. 3B). Based on these results, a working mechanism has been proposed to explain the observed switchability in this case (Fig. 3C). Of course, other proposals can also be put forth which can not be ruled out at this moment without extensive mechanistic investigation including computational studies. However, to gain insight into the hypothesis on bifunctional H_2 activation and switchable hydrogenation as shown in Fig. 1B and C and 3C, a few control ^{1}H NMR spectroscopic studies were performed. The results of these investigations have been described below.

First of all, a solution of the complex **Ir-U$_{NH}$** (5.2 μmol) was made in 0.5 mL of CD_3CN containing 50 μL of TFE and 20 μL of H_2O. The ambient temperature ^{1}H NMR spectrum of this light yellow-colored solution was consistent with the characteristic resonances of all the Hs of **Ir-U$_{NH}$** (Fig. 4A-a and ESI†). However, the N–***H*** (or the O–***H***) resonance was not observed, probably due to fast tautomerization in the present solvent mixture. When this solution was exposed to H_2 gas for a few minutes, the color changed to red, and in the ^{1}H NMR spectrum, the characteristic iridium-hydride (Ir–***H***) peak was observed at −14.65 ppm (Fig. 4A-b). This was associated with the appearance of an additional new set of peaks (with an expected integration ratio corresponding to the ligand backbone), plausibly due to the intermediate **IV** generated by the heterolytic cleavage of H_2.

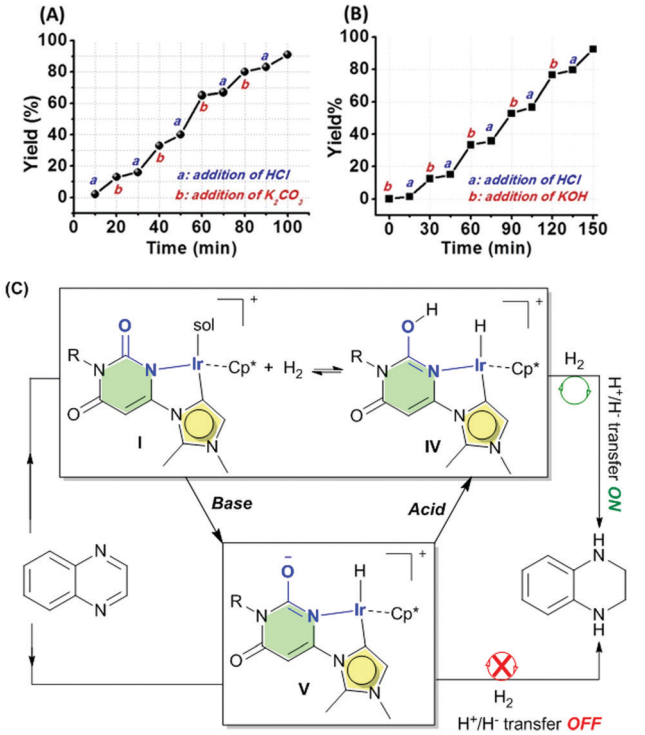

Fig. 3 (A) and (B) Switchable hydrogenation of quinoxaline (**Q**) with **Ir-U_{NH}** as a catalyst; (C) the working proposal for the switchable action of the catalyst.

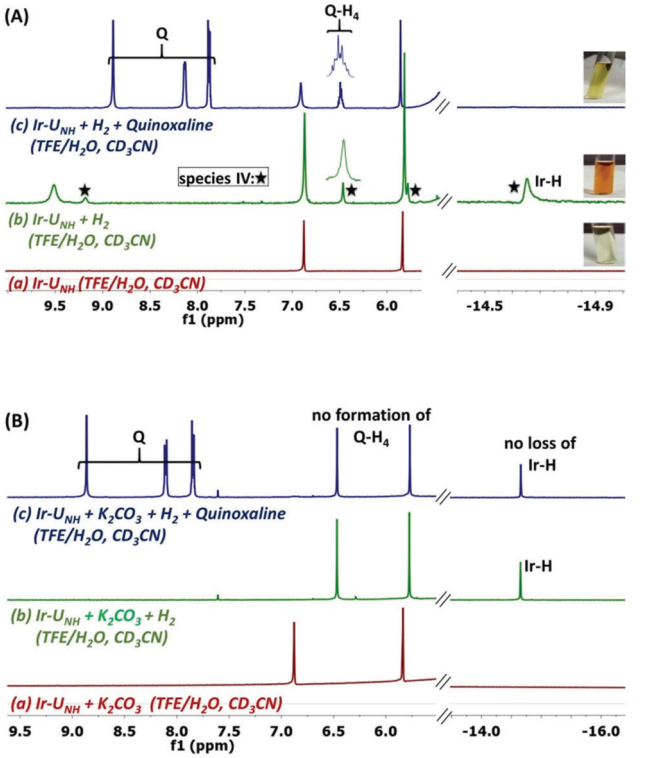

Fig. 4 (A) The ^{1}H NMR spectroscopic monitoring for the reaction of the **Ir-U_{NH}** catalyst with H_2 gas followed by the addition of quinoxaline (**Q**) leading to the formation of hydrogenated quinoxaline (**Q-H_4**); the images of the corresponding solutions are shown alongside; (B) The ^{1}H NMR spectroscopic monitoring for the reaction of the **Ir-U_{NH}** catalyst with H_2 gas in the presence of base (K_2CO_3) followed by addition of quinoxaline (**Q**) showing no consumption of iridium hydride and no product formation.

Interestingly, the evolution of a broad singlet peak at ~9.17 ppm (having integration of one H to the abovementioned backbone protons) was suggestive and indicative toward the presence of an Ir–N=C–***OH*** proton. Similar NHC–Ir^{III}(Cp*)–pyridinol complexes, reported by Papish and co-workers exhibited the O–***H*** resonances at 10.3 ppm in CD_3CN.[8] Notably, the conversion to this hydride intermediate complex from the parent **Ir-U_{NH}** was found to be ~15%. The rest of the complex **Ir-U_{NH}** was also present in the same solution as evident from the spectrum with the corresponding backbone protons having the desired integration ratio, along with the appearance of the earlier-obscured lactim O–***H*** at ~9.51 ppm. The reason for this unexpected behaviour is not clear to us at this moment and needs more extensive investigation. Nevertheless, when quinoxaline (**Q**) (5.1 μmol) was added to this mixture in the presence of H_2 gas, the proposed hydride species disappeared along with its resonances including the peaks at −14.65 ppm (for hydride Ir–***H***) and at ~9.17 ppm (for proton O–***H***) (Fig. 4A-c). The color of the solution also changed back to yellow. Additionally, ~15% of the hydrogenated product 1,2,3,4-tetrahydroquinoxaline (**Q-H_4**) was formed as evident from its characteristic multiplet peaks at ~6.46–6.49 ppm. This fact suggested that only ~15% quinoxaline reacted with the available ~15% hydride species *via* the H^+/H^- transfer twice in the presence of H_2 gas to produce the hydrogenated product in ~15% yield. On the contrary, a similar ^{1}H NMR spectroscopic study, as discussed above, with the catalyst **Ir-U_{NH}** but now in the presence of a base (K_2CO_3) showed the generation of Ir–***H*** but no Ir–N=C–***OH*** upon reaction with H_2 gas (Fig. 4B-b). The base would have captured the acidic H^+ available from the heterolytic cleavage of H_2. Under such circumstances, when quinoxaline was added to the reaction mixture, the characteristic Ir–***H*** peak at −14.65 ppm did not disappear and no hydrogenation occurred (Fig. 4B-c). This switching off of the reaction could be due to the lack of the initial H^+ transfer to quinoxaline to produce protonated quinoxaline which could accept the available hydride from the Ir–H species. Hydride transfer was not feasible to the free neutral quinoxaline, thus disfavoring hydrogenation. This off condition could be switched on again by adding acid (HCl) to the reaction mixture leading to the formation of the hydrogenated product 1,2,3,4-tetrahydroquinoxaline (**Q-H_4**). Finally, the catalytic hydrogenation of quinoxaline with **Ir-U_{NH}** as a catalyst using D_2 gas led to the incorporation of the D atoms into the product, thus confirming that hydrogen gas was the source of hydrogen atoms in this reaction (see ESI†).

In summary, a switchable hydrogenation protocol was demonstrated with a new bifunctional Ir–NHC catalyst. Under ambient H_2 pressure, the catalyst was highly active toward hydrogenation of quinoxalines to load two molecules of H_2 per molecule of the N-heteroarene. The action of a base stimulus to this catalysis led to switching off of the hydrogenation, while a reverse stimulus, an acid, switched it on again. The mechanistic hypothesis for the switching phenomenon was examined with some control *in situ* NMR experiments, which suggested a bifunctional pendant base-assisted heterolytic H_2 activation to generate iridium hydride and

an adjacent protic O–H functionality for the facile H^+/H^- transfer to the substrate quinoxalines during hydrogenation. The presence of base modulated the mechanism and plausibly did not allow the ready availability of any protic O–H or proton to be transferred to quinoxaline, which itself was a bad substrate for accepting hydride from Ir–H. Interestingly, subsequent acid addition reverses the situation and triggered hydrogenation by protonating the neutral quinoxaline molecule to make it now susceptible for hydride transfer from Ir–H generated from H_2. These results exemplified the possibility of devising a new switchable hydrogenation catalysis protocol by intercepting the mechanistic paths with a harmonious combination of suitable stimuli and an appropriately designed catalyst. As the present catalyst was also found to be effective in the dehydrogenation of the tetrahydroquinoxaline products (ESI†), switchable and reversible dehydrogenation/hydrogenation catalysis will be the subject of future study.

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Conflicts of interest

There are no conflicts to declare.

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