



CHEMISTRY & SUSTAINABILITY

CHEM **SUS** CHEM

ENERGY & MATERIALS

Accepted Article

Title: Iridium Catalyzed Hydrogenation and Dehydrogenation of N-Heterocycles in Water under Mild Conditions

Authors: Shengdong Wang, Haiyun Huang, Christian Bruneau, and Cedric Fischmeister

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: *ChemSusChem* 10.1002/cssc.201900626

Link to VoR: <http://dx.doi.org/10.1002/cssc.201900626>

WILEY-VCH

www.chemsuschem.org

A Journal of



Iridium Catalyzed Hydrogenation and Dehydrogenation of *N*-Heterocycles in Water under Mild Conditions

Shengdong Wang,^{[a],#} Haiyun Huang,^{[a], #} Christian Bruneau,^[a] and Cédric Fischmeister*^[a]

Dedication ((optional))

Abstract: In this communication is presented an efficient catalytic method for the hydrogenation of *N*-heterocycles. The iridium-based catalyst operates under mild conditions in water without any co-catalyst or stoichiometric additives. The catalyst is also promoting the reverse reaction of dehydrogenation of *N*-heterocycles hence displaying appropriate characteristics for hydrogen-based energy economy based on liquid hydrogen carriers.

The hydrogenation of *N*-heterocycles is of current interest as many of these heterocycles are important building blocks in organic synthesis with applications in drugs and agrochemicals.¹ Recently, the hydrogenation and dehydrogenation of *N*-heterocycles has been considered as a method for hydrogen storage. Liquid organic hydrogen carrier's (LOHC) have been indeed proposed as convenient and safe solutions for hydrogen storage.² Several heterogeneous³ and homogeneous⁴ catalysts have been reported for either hydrogenation or dehydrogenation of *N*-heterocycles. Heterogeneous catalytic systems can in general be recovered and reused but they require rather high temperatures as compared to homogeneous catalysts. Recently, Corma reported a nanolayered cobalt-molybdenum sulfide catalyst able to hydrogenate a broad range of substituted quinolines at 120 °C under 12 bar of hydrogen pressure in toluene with high chemo- and regioselectivity.⁵ In 2017, Toste reported dendrimer-stabilized metal nanoparticles operating the dehydrogenation of quinoline derivatives at 130 °C in toluene. The reverse reaction was possible under milder conditions (60 °C, 1 bar H₂).⁶ Only very few homogeneous catalytic systems are able to operate both hydrogenation/dehydrogenation of *N*-heterocycles. The first example of homogeneous catalysts capable of carrying out both hydrogenation and dehydrogenation of *N*-heterocycles was reported by Yamaguchi and Fujita⁷ in 2009. A Cp*Ir complex containing a pyridonate ligand could perform the dehydrogenation of 1,2,3,4-tetrahydroquinolines in refluxing *p*-xylene for 20 h. In 2014, the same group reported Cp*Ir complexes bearing functional bipyridonate ligands for the efficient perdehydrogenation and perhydrogenation of fused bicyclic *N*-heterocycles.⁸ However, harsh conditions (130 °C, 70 bar H₂) and 20 h in refluxing toluene were necessary. Other iridium catalysts were reported by Crabtree⁹ and Albrecht,¹⁰ the

latter performing the hydrogenation of quinoline under 5 bar of hydrogen pressure at 90 °C in water and the reverse reaction at 100 °C in water. As revealed by these examples and despite their higher cost as compared to other transition metals, iridium-based complexes are predominant catalysts for the hydrogenation/dehydrogenation of *N*-heterocycles. Of note, reversible dehydrogenation/hydrogenation of *N*-heterocycles can be performed using non-noble cobalt^{11a} and iron^{11b} pincer complexes. However, these catalysts' performances still need to be improved as they require expensive pincer ligands, high catalyst loadings and high temperatures to reach high efficiency.

Recently, we have been investigating the catalytic properties of ruthenium and iridium complexes bearing underutilized dipyrindylamine ligands (dpa)¹² in the valorization of the biosourced levulinic acid (Figure 1).¹³ During these studies we disclosed that the electron-rich complex **Ir3** was very efficient for the dehydrogenation of formic acid,¹⁴ another potential LOHC.¹⁵ In particular, **Ir3** could perform the dehydrogenation of aqueous and neat formic acid at low pH. This result prompted us to investigate the catalytic performance of these complexes in the hydrogenation/dehydrogenation of *N*-heterocycles.

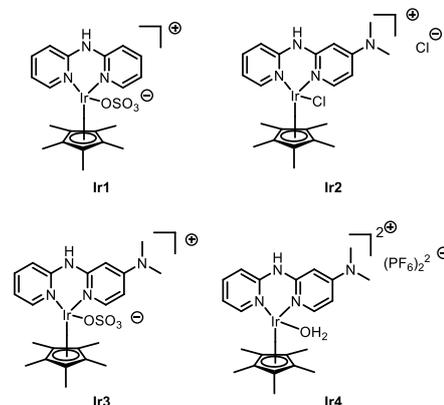


Figure 1. DPA-based iridium complexes.

We initiated our investigations using quinoline **1a** as a model substrate. Several experimental parameters were screened and optimized. As shown in Table 1, entry 1, the hydrogenation of **1a** was carried out with 0.5 mol% of **Ir3** under 1 bar of dihydrogen pressure at 90 °C in water for 17 h. Under these conditions, 1,2,3,4-tetrahydroquinoline **2a** was cleanly obtained with almost full conversion of **1a**. Upon decreasing the temperature from 90 °C to room temperature, the conversions decreased from 99% to less than 5% (Table 1, entry 2-5). 80 °C was selected as the temperature to further investigate the catalyst loading (Table 1, entry 6-9). Interestingly, the catalyst loading could be reduced to 0.2 mol% without decreasing the reaction conversion (Table 1, entry 8). Other catalysts **Ir1**, **Ir2**, **Ir4** (Table 1, entry 10-12) have

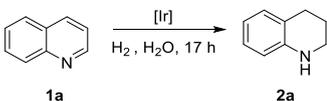
[a] S. Wang, H. Huang, Dr. C. Fischmeister, Dr. C. Bruneau
Institut des Sciences Chimiques de Rennes
Organometallics: Materials and Catalysis
UMR 6226 CNRS, Université de Rennes 1, Campus de Beaulieu, F-
35042 Rennes Cedex, France
E-mail: cedric.fischmeister@univ-rennes1.fr

*These two authors contributed equally to this work [b] Title(s),

Supporting information for this article is given via a link at the end of the document. ((Please delete this text if not appropriate))

been evaluated but none of them led to higher performances than **Ir3**.

Table 1. Ir-catalyzed hydrogenation of quinoline **1a**: Investigation of Iridium complexes and Temperature. ^[a]



Entry	[Ir](mol%)	T (°C)	Conv.(%) ^[b]
1	Ir3 (0.5)	90	99
2	Ir3 (0.5)	80	99
3	Ir3 (0.5)	70	93
4	Ir3 (0.5)	60	81
5	Ir3 (0.5)	25	<5
6	Ir3 (0.4)	80	99
7	Ir3 (0.3)	80	99
8	Ir3 (0.2)	80	99
9	Ir3 (0.1)	80	96
10	Ir1 (0.2)	80	60
11	Ir2 (0.2)	80	25
12	Ir4 (0.2)	80	83

[a] Reaction conditions: quinoline (0.4 mmol), [Ir] (0.1-0.5 mol%), H₂ (1 bar), H₂O (2 mL), 17 h. [b] Determined by ¹H NMR analysis.

With the optimal conditions in hand, the scope of the iridium catalyzed hydrogenation of *N*-heterocycles was investigated as described in Table 2. Numerous substituted quinoline derivatives were subjected to hydrogenation. The hydrogenation of quinoline derivatives substituted at the aryl ring i.e. 8-methyl **1b**, 8-hydroxy- **1c** and 8-bromo **1d** (Table 2, entry 1-4) proceeded smoothly giving the product in good to excellent yields (71-98%). 2-Alkyl **1e-1f** and 2-aryl quinolines **1g-1m** also led to the corresponding products in good to excellent yields. Hence, neither the steric hindrance nor the electronic properties of the substituents had an impact on the reaction outcome. It must be noted that dehalogenation of aryl-halide bonds was not observed hence making the product valuable for further cross-coupling reactions. 2-Heterocycle-substituted quinolines such as 2-(pyridin-2-yl) **1n**, 2-(thiophen-2-yl) **1o** and 2-(benzofuran-2-yl) **1p** were also efficiently and selectively hydrogenated in good to high yields. Interestingly, the polycyclic *N*-heterocycles **1q-1t** were also hydrogenated successfully leading to the corresponding products **2q-2t** in 53–94% yields. Very interestingly, the 1,10-phenanthroline **1t** can be selectively reduced to 1,2,3,4-tetrahydro-1,10-phenanthroline **2t** in 98% yield. Finally, **Ir3** could be further applied to the hydrogenation of other types of *N*-heterocycles such as quinoxaline **1u**, indole **1v** and isoquinoline **1s**. However, the reaction temperature was raised to 120 ° C in order to achieve good yields of **2u** and **2v**.

Table 2. Iridium catalyzed hydrogenation of *N*-heterocycles^[a]

Entry	Substrate	Product	Yield ^[b]
1	1a	2a	98
2	1b	2b	93
3	1c	2c	98
4	1d	2d	71
5	1e	2e	97
6	1f	2f	95
7	1g	2g	98
8	1h	2h	98
9	1i	2i	79
10	1j	2j	87
11	1k	2k	76
12	1l	2l	83
13	1m	2m	95
14	1n	2n	93
15	1o	2o	96
16	1p	2p	71

17		1q		2q	79
18		1r		2r	75
19		1s		2s	60
20		1t		2t	98
21		1u		2u	95 ^[c]
22		1v		2v	97 ^[c]
23		1w		2w	53

[a] Reaction conditions: Substrate (0.4 mmol), **Ir3** (0.2 mol%), H₂ (1 bar), H₂O (2 mL), 80 °C, 17 h. [b] Isolated yield. [c] 120 °C.

Only very few studies on the mechanism of the hydrogenation of quinoline have been reported.^[4b,4e] These proposed mechanisms depend on both the nature of the catalyst and the reaction conditions. In order to get information on the mechanism at play with our catalyst we have carried out two experiments. First, we have monitored the activation of hydrogen by **Ir3** by ¹H NMR. As depicted in Figure 2, when **Ir3** was submitted to a hydrogen atmosphere, the clean formation of a mono-hydride iridium complex was observed ($\delta = -9.87$ ppm). We have then carried out the hydrogenation of quinoline in D₂O. This reaction led to the reduced product with 100% incorporation of deuterium at C3 (Figure 3). This result is in line with the proposed mechanisms, which involve hydride transfer at C2 and C4 and protonation at C3 as described in Figure 3.

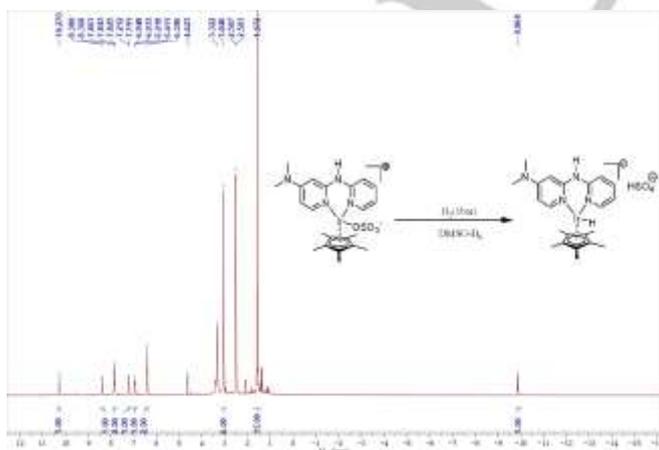


Figure 2. ¹H NMR monitoring of the hydride intermediate.

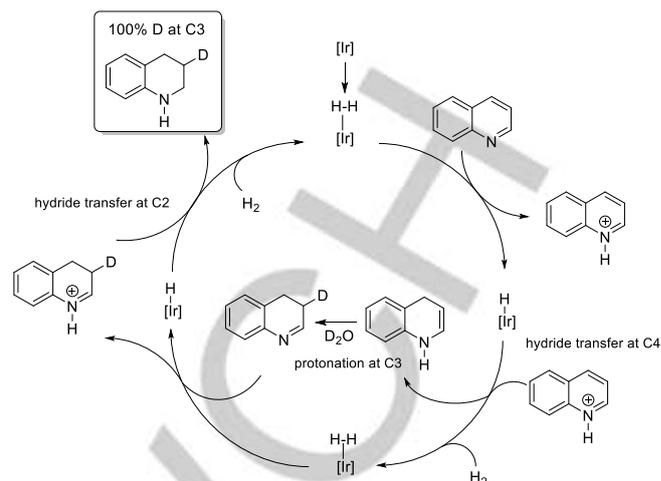


Figure 3. Deuterium-labelling studies and proposed mechanism

Following these studies on the hydrogenation of quinolines, we turned our attention to the reverse reaction using the same catalyst **Ir3**. We were pleased to observe that the acceptorless dehydrogenation of a number of tetrahydroquinolines took place providing the corresponding quinolines in good to excellent yields (Table 3). As generally required, higher temperature and longer reaction time were required but **Ir3** appeared to be among the most active catalysts for this reaction. The release of dihydrogen was confirmed using a vessel consisting of two connected Schlenk tubes, as previously reported for the dehydrogenation of formic acid.^[13b] Using this experimental setup, levulinic acid was quantitatively converted into γ -valerolactone (see ESI).

Table 3. Iridium catalyzed dehydrogenation of *N*-heterocycles^[a]

Entry	Substrate	Substrate	Yield ^[b]		
1		2a		1a	98
2		2b		1b	83
3		2e		1e	79
4		2g		1g	82
5		2u		1u	73

6



2w



1w

67

[a] Reaction conditions: Substrate (0.4 mmol), Ir3 (2 mol%), H₂O (2 mL), reflux, 30 h. [b] Isolated yield.

In conclusion, we have developed an iridium-based catalyst bearing an electron-enriched dipyridylamine ligand for the reversible hydrogenation of quinoline derivatives. The catalyst operates under mild reaction conditions in water without any additive hence meeting the requirements for clean and sustainable process. This catalyst is one of the few able to promote both the hydrogenation and dehydrogenation of *N*-heterocycles hence offering promising developments for the reversible storage of hydrogen. Further efforts aiming at improving the catalyst performances are in progress.

Experimental Section

General procedure for the hydrogenation reactions

Quinolines (0.4 mmol), Ir3 (0.5-0.1 mol%), water (2 ml) were placed in a 20 ml thick wall Schlenk tube equipped with a Teflon screw cap. The reaction mixture was degassed by 2 freeze-thaw cycles in liquid nitrogen. After warming to r.t. the Schlenk tube was placed under 1 bar of hydrogen and left upon stirring for 2 minutes before closing. The mixture was stirred at the appropriate temperature for the desired time. After the reaction, the vessel was cooled down and carefully depressurized. The product mixture was analysed by ¹H NMR. The mixture was purified by flash column chromatography using petroleum ether and ethyl acetate as eluent.

Acknowledgements

The authors acknowledge the China Scholarship Council for a grant to SW and M. Duo Wei for providing some reagents.

Keywords: homogeneous catalysis • Iridium • hydrogenation • dehydrogenation • quinolines

- [1] a) E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257-10274; b) J. D. Scott, R. M. Williams, *Chem. Rev.* **2002**, *102*, 1669-1730.
 [2] a) R. H. Crabtree, *Energy Environ. Sci.* **2008**, *1*, 134-138; (b) U. Eberle, M. Felderhoff, F. Schuth, *Angew. Chem. Int. Ed.* **2009**, *48*, 6608-6630; c) D. Teichmann, W. Arlt, P. Wasserscheid, R. Freymann, *Energy Environ. Sci.* **2011**, *4*, 2767-2773; d) N. Armaroli, V. Balzani, *ChemSusChem* **2011**, *4*, 21-36.
 [3] a) H. Adkins, L. G. Lundsted, *J. Am. Chem. Soc.* **1949**, *71*, 2964-2965; b) F. Sotoodeh, K. J. Smith, *J. Catal.* **2011**, *279*, 36-47; b) K. Mikami, K. Ebata, T. Mitsudome, T. Mizugaki, K. Jitsukawa, K. Kaneda, *Heterocycles* **2011**, *82*, 1371-1377; c) F. Sotoodeh, B. J. M. Huber, K. Smith, *Appl. Catal. A* **2012**, *420*, 67-72; d) M. Yang, C. Han, G. Ni, J. Wu, H. Cheng, *Int. J. Hydrogen Energy* **2012**, *37*, 12839-12845; e) D. Ren, L. He, L. Yu, R.-S.

- Ding, Y.-M. Liu, Y. Cao, H.-Y. He, K.-N. Fan, *J. Am. Chem. Soc.* **2012**, *134*, 17592-17598; f) M. M. Dell'Anna, V. F. Capodiferno, M. Mali, D. Manno, P. Cotugno, A. Monopoli, P. Mastroianni, *Appl. Catal. A* **2014**, *481*, 89-95; g) D. Zhu, H. Jiang, L. Zhang, X. Zheng, H. Fu, M. Yuan, H. Chen, R. Li, *ChemCatChem* **2014**, *6*, 2954-2960; h) Y. Zhang, J. Zhu, Y.-T. Xia, X.-T. Sun, L. Wu, *Adv. Synth. Catal.* **2016**, *358*, 3039-3045; i) M. Tang, J. Deng, M. Li, X. Li, H. Li, Z. Chen, Y. Wang, *Green Chem.* **2016**, *18*, 6082-6090; j) X. Cui, Y. Li, S. Bachmann, M. Scalone, A.-E. Surkus, K. Junge, C. Topf, M. Beller, *J. Am. Chem. Soc.* **2015**, *137*, 10652-10658; k) X.-T. Sun, Y. Zhu, Y.-T. Xia, L. Wu, *ChemCatChem* **2017**, *9*, 2463-2466; l) B. Vilhanova, J. A. van Bokhoven, M. Ranocchiaric, *Adv. Synth. Catal.* **2017**, *359*, 677-686; m) Y.-G. Ji, K. Wei, T. Liu, L. Wu, W.-H. Zhang, *Adv. Synth. Catal.* **2017**, *359*, 933-940; n) F. Chen, B. Sahoo, C. Kreyenschulte, H. Lund, M. Zeng, L. He, K. Junge, M. Beller, *Chem. Sci.* **2017**, *8*, 6239-6246; o) X. Xue, M. Zeng, Y. Wang, *Appl. Catal. A*, **2018**, *560*, 37-4; p) S. Zhang, Z. Xia, T. Ni, Z. Zhang, Y. Ma, Y. Qu, *J. Catal.* **2018**, *359*, 101-111.
 [4] a) W. B. Wang, S. M. Lu, P. Y. Yang, X. W. Han, Y. G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536-10537; b) H. Zhou, Z. Li, Z. Wang, T. Wang, L. Xu, Y. He, Q.-H. Fan, J. Pan, L. Gu, A. S. C. Chan, *Angew. Chem., Int. Ed.* **2008**, *47*, 8464-8467; c) Z. Wang, I. Tonks, J. Belli, C. M. Jensen, *J. Organomet. Chem.* **2009**, *694*, 2854-2857; d) H. Li, J. Jiang, G. Lu, F. Huang, Z.-X. Wang, *Organometallics* **2011**, *30*, 3131-3141; e) G. E. Dobreiner, A. Nova, N. D. Schley, N. Hazari, S. J. Miller, O. Eisenstein, R. H. Crabtree, *J. Am. Chem. Soc.* **2011**, *133*, 7547-7562; f) O. Luca, D. L. Huang, M. K. Takase, R. H. Crabtree, *New J. Chem.* **2013**, *37*, 3402-3405; g) X.-F. Cai, W.-X. Huang, Z.-P. Chen, Y.-G. Zhou, *Chem. Commun.* **2014**, *50*, 9588-9590; j) A. E. Wendlandt, S. S. Stahl, *J. Am. Chem. Soc.* **2014**, *136*, 11910-11913; i) R. Adam, J. R. Cabrero-Antonino, A. Spannenberg, K. Junge, R. Jackstell, M. Beller, *Angew. Chem., Int. Ed.* **2017**, *56*, 3216-3220; j) J. R. Cabrero-Antonino, R. Adam, K. Junge, R. Jackstell, M. Beller, *Catal. Sci. Technol.* **2017**, *7*, 1981-1985; k) Y. Wang, Z. Huang, X. Leng, H. Zhu, G. Liu, Z. Huang, *J. Am. Chem. Soc.* **2018**, *140*, 4417-4429; l) J. Wu, D. Talwar, S. Johnston, M. Yan, J. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 6983-6987; m) J. Wu, J. H. Barnard, Y. Zhang, D. Talwar, C. M. Robertson, J. Xiao, *Chem. Commun.* **2013**, *49*, 7052-7054.
 [5] I. Sorribes, L. Liu, A. Doménech-Carbó, A. Corma, *ACS Catal.*, **2018**, *8*, 4545-4557
 [6] C. Deraedt, R. Ye, W. T. Ralston, F. D. Toste, G. A. Somorjai, *J. Am. Chem. Soc.* **2017**, *139*, 18084-18092
 [7] R. Yamaguchi, C. Ikeda, T. Takahashi, K. Fujita, *J. Am. Chem. Soc.* **2009**, *131*, 8410-8412;
 [8] K. Fujita, Y. Tanaka, M. Kobayashi, R. Yamaguchi, *J. Am. Chem. Soc.* **2014**, *136*, 4829-4832;
 [9] M. G. Manas, L. S. Sharninghausen, E. Lin, R. H. Crabtree, *J. Organomet. Chem.* **2015**, *792*, 184-189
 [10] A. Vivancos, M. Beller, M. Albrecht, *ACS Catal.* **2018**, *8*, 17-21.
 [11] a) R. Xu, S. Chakraborty, H. Yuan, W. D. Jones, *ACS Catal.* **2015**, *5*, 6350-6354. b) S. Chakraborty, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2014**, *136*, 8564-8565.
 [12] a) C. Romain, S. Gaillard, M. K. Elmekdem, L. Toupet, C. Fischmeister, C. M. Thomas, J.-L. Renaud, *Organometallics* **2010**, *29*, 1992-1995; b) C. Bolm, J.-C. Frison, J. Le Paih, C. Moessner, G. Raabe, *J. Organomet. Chem.* **2004**, *689*, 3767; c) A. J. Swarts, S. F. Mapolie, *Dalton Trans.* **2014**, *43*, 9892-9900; d) B. Wozniak, A. Spannenberg, Y. Li, S. Hinze, J. G. de Vries, *ChemSusChem*, **2018**, *11*, 356-359.

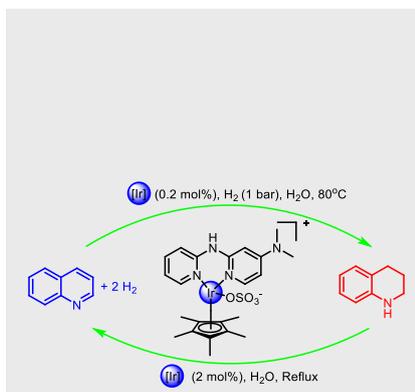
- [13] a) S. Wang, V. Dorcet, T. Roisnel, C. Bruneau, C. Fischmeister, *Organometallics* **2017**, *36*, 708-713; b) S. Wang, H. Huang, V. Dorcet, T. Roisnel, C. Bruneau, C. Fischmeister, *Organometallics* **2017**, *36*, 3152-3162; c) S. Wang, H. Huang, C. Bruneau, C. Fischmeister, *ChemSusChem* **2017**, *10*, 4150-4154.
- [14] S. Wang, H. Huang, T. Roisnel, C. Bruneau, C. Fischmeister, *ChemSusChem* **2019**, *12*, 179-184
- [15] a) N. Onishi, G. Laurency, M. Beller, Y. Himeda, *Coord. Chem. Rev.* **2018**, *373*, 317-332; b) J. F. Hull, Y. Himeda, W.-H. Wang, B. Hashiguchi, R. Periana, D. J. Szalda, J. T. Muckerman, E. Fujita, *Nat. Chem.* **2012**, *4*, 383-388; c) K. Sordakis, C. Tang, L. K. Vogt, H. Junge, P. J. Dyson, M. Beller, G. Laurency, *Chem. Rev.* **2018**, *118*, 372-433

Entry for the Table of Contents (Please choose one layout)

Layout 1:

COMMUNICATION

The reversible hydrogenation/dehydrogenation of *N*-heterocycles with an electron-enriched iridium catalyst bearing a dimethylamino-substituted dipyridylamine ligand is reported.



Author(s), Corresponding Author(s)*

Page No. – Page No.

Title

Accepted Manuscript