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E-Selective Semi-hydrogenation of Alkynes with Dinuclear Iridium Complexes under Atmospheric Pressure of Hydrogen

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Semi-hydrogenation of alkynes was catalyzed by halide-bridged dinuclear iridium complexes, yielding (*E*)-alkenes with high selectivity. Mechanistic studies conducted with monohydride dinuclear species, dihydride mononuclear species, and trihydride dinuclear species led us to propose a mechanism involving dual cycles.

Keywords: Dinuclear iridium complex | Stereoselective semi-hydrogenation | Alkyne

Stereoselective semi-hydrogenation of alkynes is one of the most straightforward and atom-economical synthetic protocols for preparing configurationally defined alkenes,[1] which are often found in natural products[2] as well as in various organic materials,[3] and a much advantageous synthetic protocol than semi-transfer-hydrogenation[4] and Birch-type reduction.[5] Semi-hydrogenation of alkynes by heterogeneous catalyst systems such as the Lindlar catalyst produces (*Z*)-alkenes as the main product.[6,7] The unique combination of two heterogeneous catalyst systems was recently reported to catalyze the semi-hydrogenation of alkynes under atmospheric pressure of H_2 to (*E*)-alkenes, where Pd_3Pb/SiO_2 catalyzed the hydrogenation of alkynes to (*Z*)-alkenes, and $RhSb/SiO_2$ facilitated the isomerization of (*Z*)-alkenes to (*E*)-alkenes.[8] On the other hand, some homogeneous catalyst systems effectively achieve (*E*)-selective semi-hydrogenation as the best solution for (*E*)-selective semi-hydrogenation of alkynes. Fürstner and his collaborators reported that a cationic ruthenium complex bearing a Cp* ligand serves as a catalyst for (*E*)-selective semi-hydrogenation of alkynes with high selectivity and wide functional group tolerance.[9] Milstein et al. demonstrated that an iron complex with a PNP tridentate ligand acts as a catalyst for highly (*E*)-selective semi-hydrogenation,[10] and, quite recently, Mankad et al. demonstrated that a unique bimetallic catalyst of Ag and Ru hydrogenates alkynes under atmospheric pressure to give the corresponding (*E*)-alkenes, and proposed a mechanism involving heterolytic cleavage of a H–H bond by Ag–Ru complexes.[11] Moreover, a boron system of $HB(C_6F_5)_2$ combined with vinylpentafluorobenzene was reported to act as a moderately active catalyst for (*E*)-selective semi-hydrogenation of alkynes.[12]

We recently found that triply-halide-bridged dinuclear iridium complexes bearing suitable chiral and achiral diphosphine ligands **1** catalyzed the hydrogenation of imine, *N*-heteroaromatic compounds, and others, and maintained the carbonyl and olefinic groups (Figure 1 and SI).[13] As part of our continuing efforts to expand the catalytic scope of the iridium system of **1**, we applied **1** to the catalytic hydrogenation of alkynes, which led to semi-hydrogenation of alkynes under atmospheric pressure of H_2 to give the corresponding alkenes with high (*E*)-selectivity.

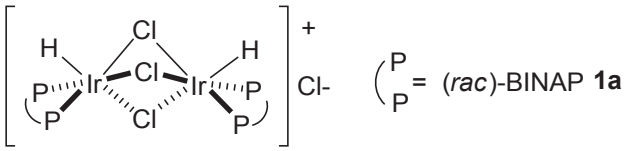
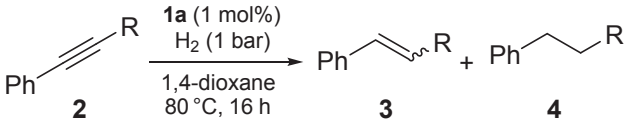


Figure 1. The structure of dinuclear iridium complexes.

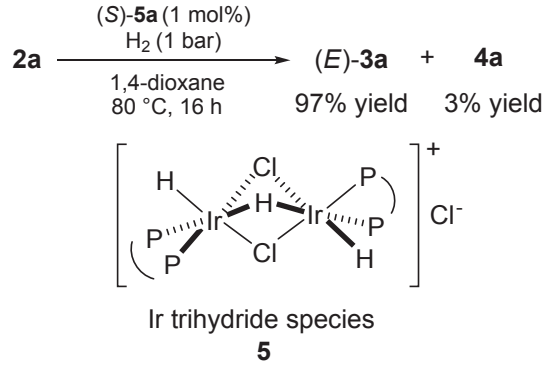
Table 1. Scope and limitation



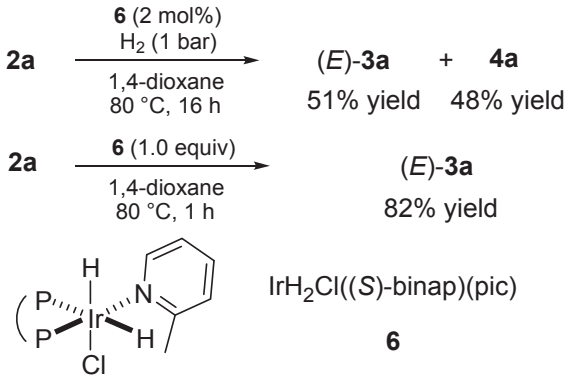
Entry	R		(*E*)-**3**/%[a]	(*Z*)-**3**/%[a]	**4**/%[a]
1	C_6H_5	**2a**	97	n.d.[b]	3
2	*p*-$MeOC_6H_4$	**2b**	94	n.d.[b]	5
3	*p*-$(CH_2OH)C_6H_4$	**2c**	96	n.d.[b]	4
4	*p*-BrC_6H_4	**2d**	92	n.d.[b]	8
5	*p*-$BpinC_6H_4$	**2e**	95	n.d.[b]	4
6	*p*-$AcNHC_6H_4$	**2f**	98	n.d.[b]	2
7[c]	*p*-AcC_6H_4	**2g**	91	n.d.[b]	4
8[c]	*p*-NCC_6H_4	**2h**	95	n.d.[b]	5
9[d]	*p*-$NO_2C_6H_4$	**2i**	93	n.d.[b]	6
10	TMS	**2j**	79	n.d.[b]	7
11	^{n}Bu	**2k**	90	n.d.[b]	10
12	$C(CH_3)_2OH$	**2l**	87	5	6

[a]Yields were determined by ^{1}H NMR analysis using phenanthrene as an internal standard. [b]n.d.: not detected. [c]The reaction was performed at 65 °C. [d]The reaction was performed at 50 °C.

We conducted catalyst screening to select **1a** as the best catalyst (see SI). Next, we examined the substrate scope of this reaction (Table 1). 1-Methoxy-4-(phenylethynyl)benzene (**2b**) was hydrogenated to give the corresponding (*E*)-alkene **3b** in 94% yield along with the formation of alkane **4b** in 5% yield. Alkyne **2c** with the other electron-donating substituent resulted in a similarly high (*E*)-selectivity of **3c** in 96% yield. Alkynes containing bromo and boronic ester groups were applicable for this semi-hydrogenation to give the corresponding (*E*)-alkenes without the loss of these functional groups, making them available for further coupling reactions. Amide, acetyl, nitrile, and nitro groups in **2f**–**2i**, which are functional groups capable of being hydrogenated,[14] were tolerated under the hydrogenation conditions, although a lower reaction temperature was required for **2g**–**2i** to avoid generating the corresponding alkanes **4g**–**4i**. The semi-hydrogenation of trimethylsilyl derivative **2j** and *n*-butyl derivative **2k** afforded the corresponding (*E*)-alkenes with high selectivity and moderate yields, whereas hydrogenation of 2-methyl-4-phenylbut-3-yn-2-ol (**2l**) was contaminated with a significant amount of (*Z*)-alkene (5%).



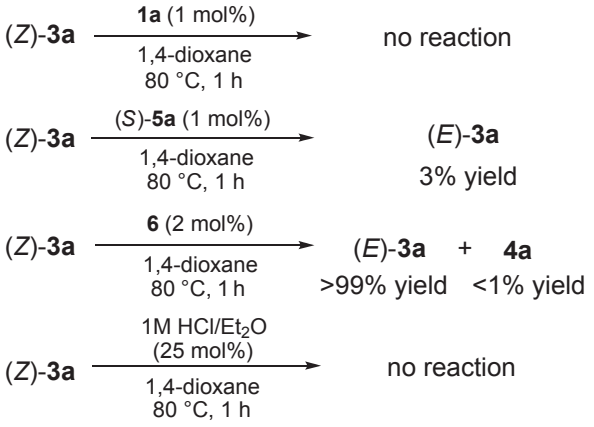
Scheme 1. Semi-hydrogenation with iridium trihydride species.



Scheme 2. Control experiments by iridium dihydride complex **6**.

We conducted a time-course experiment of hydrogenating **2a** under the optimized conditions, and each yield of (*E*)-**3a**, (*Z*)-**3a**, and **4a** was plotted over the reaction time. At the beginning, (*Z*)-**3a** was formed, and the amount of (*E*)-**3a** gradually increased with a decrease of (*Z*)-**3a**, indicating the isomerization of (*Z*)-**3a** to (*E*)-**3a**. During the reaction, the yield of **4a** was suppressed and, after 16 h, only 3% of **4a** was detected. Additionally, under the optimized conditions, (*Z*)-**3a** was fully converted to (*E*)-**3a** (95%) and a small amount of **4a** (5% yield).

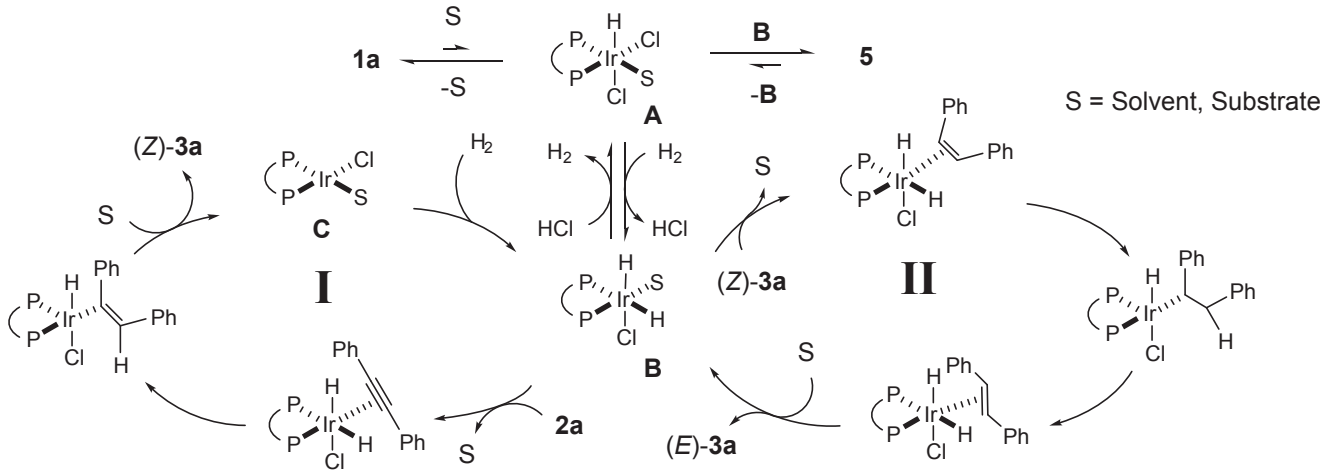
Measurement of the ^{1}H NMR spectrum of the crude reaction mixture after the hydrogenation of **2a** revealed an iridium trihydride complex **5a**.[13b] Thus, we alternatively prepared the corresponding iridium trihydride complex of (*S*)-BINAP [(*S*)-**5a**], and examined its catalytic performance for the hydrogenation of **2a**, giving (*E*)-**3a** (97%) and **4a** (3%) in almost the same distribution as that of **1a** (Scheme 1). Because complex **5a** was a product of recombination between a mononuclear iridium dihydride species and a mononuclear iridium monohydride species, both the dihydride species and monohydride species were expected to be candidate active species. To investigate the reaction mechanism, we performed some controlled experiments using an isolated dihydride complex **6**, whose monomeric structure was supported by the coordination of α-picoline (Scheme 2).[13f] We carried out the catalytic semi-hydrogenation of **2a** using **6** to afford (*E*)-**3a** in 51% yield along with the over-reduction product **4a** in 48% yield, and performed the stoichiometric reaction of **6** with **2a** under the conditions without hydrogen gas to produce (*E*)-**3a** in 82% yield, indicating that



Scheme 3. Catalytic activity for the isomerization of (*Z*)-**3a**.

insertion of **2a** into an Ir–H bond of **6** gave (*E*)-alkenyl-iridium species, whose reductive elimination resulted in the formation of (*Z*)-**3a**, and **6** also worked as a catalyst for the isomerization of (*Z*)-**3a** to (*E*)-**3a**. With respect to the isomerization, we tested the catalytic performance of various iridium precursors, **1a**, (*S*)-**5**, and **6** along with HCl, which was expected to be formed in situ from precursor **1a**. Among them, **6** exhibited high catalytic activity, whereas **1a**, (*S*)-**5a**, and HCl exhibited almost no activity for the isomerization (Scheme 3), suggesting that a dihydride species catalyzed the isomerization, while monohydride species had very low activity.

Based on these experimental results, the plausible mechanism can be divided into two cycles that involve the hydrogenation of alkyne to (*Z*)-alkene (cycle **I**) and isomerization of the (*Z*)-isomer to an (*E*)-isomer (cycle **II**) (Scheme 4). Under optimal conditions, the dinuclear iridium complex **1a** dissociates to a monohydride iridium complex **A**, which reacts with H_2 to give a dihydride iridium complex **B** with the elimination of HCl. Dihydride complex **B** works as a catalyst for both reaction cycles. In cycle **I**, alkyne inserts into the Ir–H bond of **B** followed by a reductive elimination to afford (*Z*)-alkene and mononuclear Ir(I) complex **C**, whose exposure to hydrogen gas regenerates **B**, although we cannot exclude another possible mechanism of σ-bond metathesis-type direct cleavage of the Ir–C(alkenyl) bond by H_2 to regenerate **B**,[15] as well as direct semi-hydrogenation of alkyne to give (*E*)-alkene.[9,16] In cycle **II**, in situ-generated (*Z*)-alkene inserts into the Ir–H bond of **B**, followed by rotation of the C–C bond and β-hydride elimination to give the corresponding (*E*)-alkene and regenerate **B** as a consequence of faster β-hydride elimination than reductive elimination. The Ir(I) precursor (Table S2, Entry 9) and the mononuclear iridium dihydride species **6** (Scheme 2) produced more of the over-reduced product **4**, and therefore, we propose the potent scenario that the dinuclear iridium(III) species **1a** and **5** were dormant species in equilibrium with **B**, and consumption of alkynes shifted the equilibrium to dominant **5** together with **1a** because of the different coordination abilities of alkynes and alkenes to **B**. In fact, we conducted a semi-hydrogenation of alkynes using a catalyst system of **6** treated with HCl (25 mol %), which spontaneously generated the dinuclear iridium(III) complex **1a**, to significantly suppress the formation of alkane **4a** (less than 1%) while maintaining (*E*)-selectivity.



Scheme 4. Proposed mechanism including dual cycles by dihydride species.

In summary, we developed (*E*)-selective semi-hydrogenation of alkynes using dinuclear iridium complex **1a** under mild conditions (H_2 1 bar, 80 °C) through a dual mechanism where a dihydride iridium species acted to catalyze both the hydrogenation of alkynes to (*Z*)-alkenes and the isomerization of (*Z*)-alkenes into (*E*)-alkenes based on the catalytic performance of a dihydride complex such as **6**.

Supporting Information is available on http://dx.doi.org/10.1246/cl.160410.

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