# An (NCP)IrHCl Complex-Catalyzed Semihydrogenation of Alkynes: Different Base-Directed *cis-* /*trans-* Selectivity and Reaction Mechanism

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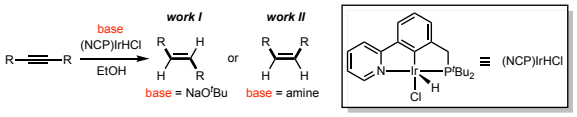
## Introduction




Catalytic transfer hydrogenation (TH) is recognized as a $H_2$ surrogate method for the hydrogenation of compounds bearing unsaturated bond. Over decades, numerous transition metal-catalyzed THs have been developed using HCOOH or $NH_3BH_3$ as H donor but less on alcohols, especially when using Ir catalyst.

Herein, the semihydrogenation of alkynes for *E*- and *Z*-alkenes is reported by the same group using an (NCP)IrHCl complex with ethanol as the H donor, but with different base. In the *trans*-hydrogenation (**work I**), *Z*-alkene formation followed by *E*/*Z* isomerization assisted by a (NCP)$IrH_2$ species is proposed. In the *cis*-hydrogenation (**work II**) by using amine as base, a different route involved a monohydrido species is proposed which gives *Z*-alkenes.

## Work I

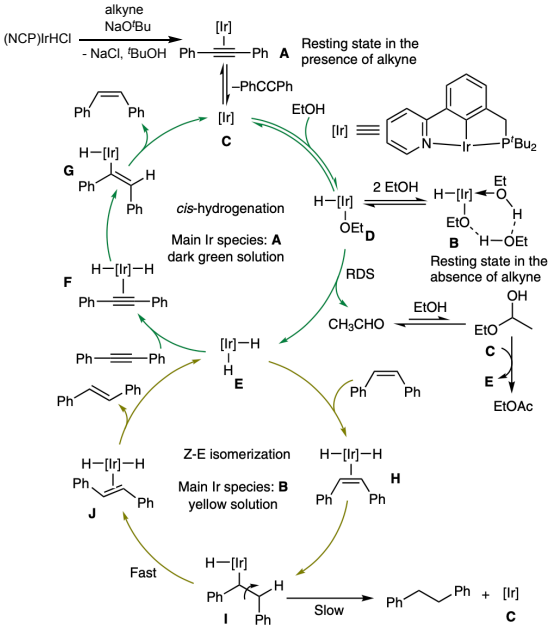
**Work I** report the semihydrogenation for *E*-alkenes. As shown in **Fig**, to treat (NCP)IrHCl with NaO$^t$Bu and alkyne, Ir alkyne species **A** is formed. Alkyne-dissociation followed by EtOH addition generates Ir hydrido ethoxy species **D**. After $\beta$-H elimination releasing aldehyde, an Ir dihydrido complex **E** is obtained.

Importantly, in the presence of alkyne, formation of **F** is faster than **H**. Hence the *E*/*Z* isomerization (yellow round) is slower than semihydrogenation (green round) in the presence of alkyne.

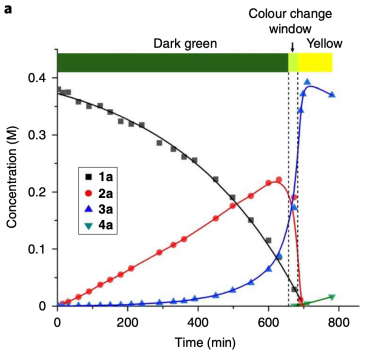
Finally, *Z*-alkene product is obtained via alkyne insertion from **F** and reductive elimination of **G**.

With the most conversion of alkyne, formation of **H** from **E** will be dominant. Then by alkene insertion, alkyl species **I** will form. Faster C–C rotation & $\beta$-H elimination at **I** will form **J** instead of alkane and **C**, which is product of reductive elimination.

Notably, in *E*/*Z* isomerization round, a six-membered species **B** is the resting state which derives from **D** and two additional EtOH molecules. Preparation of **B** indicated a yellow color.




In this report, various Ir species act not only as catalysts, but also as color indicators. Since Ir-alkyne species **A** has a green color, which is the resting state in the presence of alkyne, and species **B** has a yellow color, which is the resting state in the absence of alkyne. To observe the color of reaction mixture will provide a direct signal for monitoring.




As shown in the **time table**, when alkyne exists (even as small amount), **A** is the resting state to make solution dark green. Initially, semihydrogenation of alkyne (**1a**) for *Z*-alkene (**2a**) is the dominant step, while *E*/*Z* isomerization for *E*-alkene (**3a**) is still slow.

When conversion of alkyne almost complete, yellow colored six-membered **B** will be the resting state to make solution change the color. However, even the semihydrogenation for **2a** ends, the *E*/*Z* isomerization (for **3a**) is still faster than reductive elimination (for alkane **4a**).

When *E*/*Z* isomerization completely finished, the solution will change to full yellow color, which is the signal to end the reaction. If not, the formation of alkane **4a** will occur as side reaction to decrease the yield of **3a**.

In **work I**, *E*-selective semihydrogenation is achieved by *E*/*Z* isomerization of *Z*-alkene into *E*-alkene to avoid *Z*-product, and by color indication to avoid alkane as over-reduction product. In which, an **Ir dihydrido complex** is the key to undergo desired transformation, which is a well-established mechanism.

However, in **work II**, the authors proposed a totally different **Ir monohydrido complex** to fulfill the semihydrogenation (**see right Fig**). In which, a key alcoholysis step is expected to undergo *Z*-alkene formation from the Ir vinyl species.

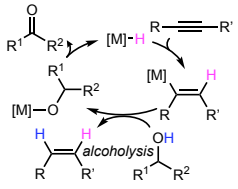



**Fig. Monohydride Mechanism**

## Work II

**> Initial Attempt**:

2 mol% of (NCP)IrHCl (**1**) and diphenylacetylene (**3a**) in MeOH without base under conditions shown in right **Fig**, *Z*-diphenylethylene (**4a**) was obtained only 4%, but neither *E*-isomer (**5a**) nor overreduction product **6a** was observed, which is a good signal.

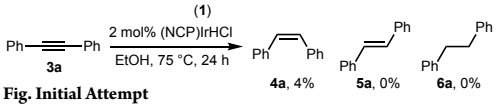



**Fig. Initial Attempt**

**> Alkyne Hydrometalation:**

$^{31}$P NMR measurement of (NCP)IrHCl (**1**) in toluene (57.6 ppm) and in EtOH (51.0 ppm) shown different chemical shift (**Figure 1b**), indicated an EtOH-Ir coordinating complex (**7**) with XRD structure (**Figure 1a, 7**). Addition of **3a** gave an Ir vinyl chloride species with XRD structure (**Figure 1a, 8**). But such species shown no activity towards *cis*-stilbene (**Figure 1a, 9**).

**3a** coordination at the open site of **1** is not reasonable since the **3a** will be ***trans*** to hydride then difficult to allow insertion (**Figure 1c, upper path**). **path A** shown a $Cl^-$ migration followed by coordination of **3a** to form **8**. **path B** proposed an EtOH coordination to form **7**, followed by $Cl^-$ dissociation and coordination of **3a** to form intermediate **11**, then occur migratory insertion of **3a** to form **12**. Upon rebinding of $Cl^-$ to **12** form **8** (**Figure 1c**).

Solvent effect was also investigated in **Figure 1d** wherein shown a faster rate of reaction in EtOH than toluene. This result is contrast to **path A** which assuming EtOH will abandon coordination of **3a**. Toluene and different alcohols were tested to demonstrated the size effect of alcohol solvents to the rate, and these results indicated the alcohol-coordination-driven $Cl^-$ dissociation **path B**.

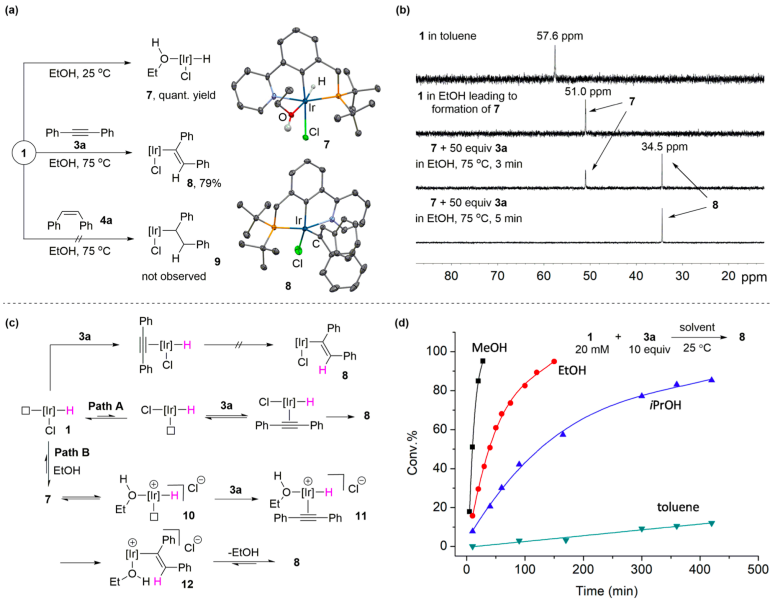



**Figure 1.** Alkyne hydrometalation by Ir(III) monohydride chloride complex **1**. (a) Synthesis and crystallographic characterization of Ir(III) complexes **7** and **8**. (b) $^{31}$P NMR spectra for conversion of complex **1** to **7** and **8**. (c) Possible pathways for alkyne hydrometalation. (d) Time-course of reactions of **1** with **3a** in different solvents.

**> Synthesis & Characterization of $[(EtOH)IrH]^+Cl^-$:**

Cationic complex **13** but failed to gain single crystal due to poor solubility. However, electrical conductivity of **13** indicated **14** is a cationic complex (**Figure 2a**).

Using 0.5 equiv of bpy gave another complex **14** with a conductivity of 17.2 $\Omega^{-1}$ cm$^2$ mol$^{-1}$. XRD analysis revealed a structure bearing Ir-containing anion & cation. This result indicated the dissociation of $Cl^-$ in EtOH (**Figure 2b**).

Using dtbpy gave a soluble complex **15**. XRD analysis revealed a structure clearly showing dissociating $Cl^-$ ion (**Figure 2c**). These results provided evidence for supporting the alcohol-coordination-driven $Cl^-$ dissociation path in **Figure 1c, path A**.

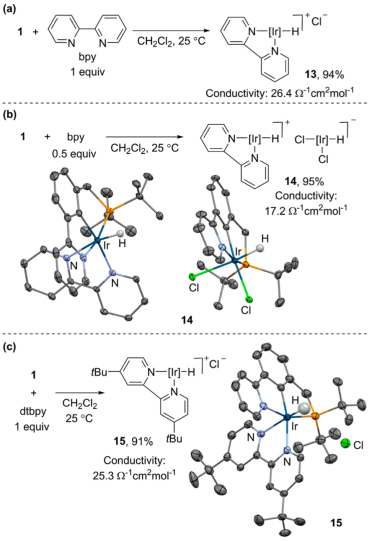
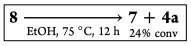



**Figure 2.** Synthesis and crystallographic characterization of cationic monohydride complexes bearing a $Cl^-$ ion.

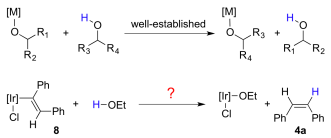
**> Alcoholysis & Amine Assistance**

Up to date, direct alcoholysis of metal alkoxide with alcohol has been well-established (**Scheme 3, top**). But analogous alcoholysis of vinyl Ir chloride **8** with alcohol is likely difficult due to the strength and polarity of the Ir–C(vinyl) bond (**Scheme 3, btm.**).

The direct alcoholysis of **8** is likely difficult. By heating **8** in EtOH for 12 h afforded **7** and **4a** with only 24% conversion (see the **formula** at right).




**Scheme 3. Direct Alcoholysis Pathway**




A proposed alcoholysis is shown in **Figure 3a**. Cationic species **12** was generated via EtOH coordination and $Cl^-$ dissociation. Deprotonation by $Cl^-$ to form **16** and then $\beta$-H elimination to form **17**, followed by reductive elimination to afford *Z*-alkene **4a** and aldehyde. EtOH-Ir complex **7** is regenerated via oxidative addition of HCl in EtOH.

This proposal is hard to be determined since **16** could not be detected probably due to the facile $\beta$-H elimination. Thus, **8** was reacted with PhOH to afforded species **18** with XRD structure (**Figure 3b**) as a **16**-like species. At **18**, the phenoxide and vinyl group are *cis*-configuration. Moreover, treatment with $Cl^-$ anion regenerate **8**. These results revealed the hypothesis in **Figure 3a**.

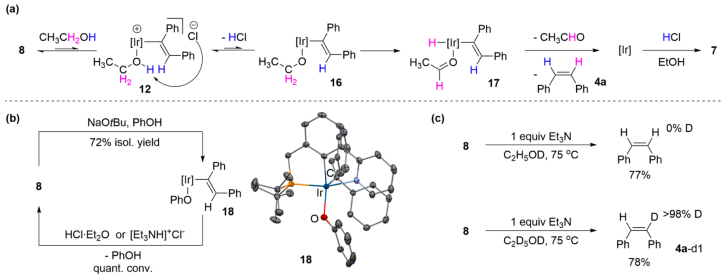
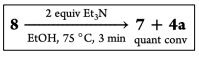


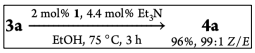

**Figure 3.** Alcoholysis of an Ir(III) vinyl chloride **8** with EtOH. (a) Proposed mechanism for ethanolysis of **8**. (b) Interconversion between **8** and a phenoxide vinyl complex **18**. (c) Deuterium-labeling experiments.

Since the deprotonation (**Figure 3a, 12-16;18-8**) step is reversible, addition of a suitable base might promote it. Because strong base might occur dehydrochlorination of (NCP)IrHCl like **work I**, amine was selected as the candidate due to its weak basicity. As their prediction, addition of 2 equiv of $Et_3N$ increased the conversion of **8** to **7** and **4a** (see the **formula** at right).



By treating **8** with $C_2H_5OD$ and $C_2D_5OD$ respectively, formed *cis*-alkene was deuterated only when employing $C_2D_5OD$, indicated *β*-H elimination of ethoxy moiety rather that direct alcoholysis (**Figure 3c**). Notably, *Z*-alkene was deuterated at only one side, indicated that coordination insertion of *Z*-alkene probably does not occur, otherwise the H/D exchange of both sides will proceed.

Knowing that $Et_3N$ could accelerate alcoholysis, and resulted $[Et_3NH]^+Cl^-$ could regenerate (NCP)IrHCl complex **7**, alkyne **3a** was treated with **1** and $Et_3N$ in EtOH under 75 for 3 h, resulted 96% yield of **4a** with 99:1 *Z/E* selectivity (see the right **Formula**), indicated the importance of adding amine in this methodology.




**> Catalytic Transfer Hydrogenation of Alkynes under Amine Cocatalysis**

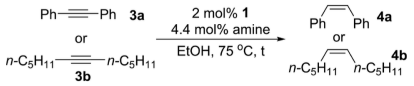
Two different alkynes **3a** (diaryl) and **3b** (dialkyl), were respectively treated with 2 mol% of **1** and 4.4 mol% of amine in EtOH under 75 °C to afford corresponding *Z*-alkenes **4a** and **4b** (**Table 1**).

**We see**:

$Et_3N$, $Et_2NH$, *n*-$BuNH_2$ and *t*-$BuNH_2$ all serve as suitable base giving high yields with good selectivity (**entries 1-7**). However, pyridine was not applicable in this method (**entry 8**). In cases of alkyne **3b**, the efficiency greatly dropped, and *t*-$BuNH_2$ emerged as the best base (**entries 9-11**). A longer time improved the yield (**entry 12**). By adding excess amount (10 mol%) of *t*-$BuNH_2$, the best yield and selectivity were obtained (**entry 13**).

Notably, no overreduced product (linear alkane) and almost no *E/Z* isomers formed, which demonstrated that this Ir monohydrido catalyst could overcome alkene isomerization and overreduction of alkynes.

**Table 1. Evaluation of Amine Cocatalysts for Catalytic TH of Diphenylacetylene and 6-Dodecyne**[a]




| entry | alkyne | amine | *t* (h) | conv (%) | *Z/E* |
|---|---|---|---|---|---|
| 1 | **3a** | $Et_3N$ | 3 | 96 | 99:1 |
| 2 | **3a** | $Et_3N$ | 6 | >99 | 98:2 |
| 3 | **3a** | $Et_2NH$ | 3 | 96 | >99:1 |
| 4 | **3a** | *n*$BuNH_2$ | 3 | 91 | 98:2 |
| 5 | **3a** | *t*$BuNH_2$ | 3 | 95 | >99:1 |
| 6 | **3a** | *t*$BuNH_2$ | 6 | >99 | 99:1 |
| 7 | **3a** | *t*$BuNH_2$ | 10 | >99 | 99:1 |
| 8 | **3a** | pyridine | 6 | <2 | |
| 9 | **3b** | $Et_3N$ | 15 | 21 | >99:1 |
| 10 | **3b** | *n*$BuNH_2$ | 15 | 52 | >99:1 |
| 11 | **3b** | *t*$BuNH_2$ | 15 | 57 | >99:1 |
| 12 | **3b** | *t*$BuNH_2$ | 60 | 93 | >99:1 |
| 13[b] | **3b** | *t*$BuNH_2$ | 60 | >99 | >99:1 |

[a]Conditions: **3a** or **3b** (0.5 mmol), **1** (2 mol %), amine (4.4 mol %), and EtOH (2 mL) at 75 °C. The conversion and *Z/E* ratios were determined by GC. [b]Using 10% *t*$BuNH_2$.

**> Substrate Scope (Please see attached file in Google Drive)**

With optimized conditions in hand, substrate scope investigation was then conducted. Various diaryl alkynes, dialkyl alkynes, enynes, propargylic alcohols and propargylic amines were investigated (**Table 2, A-E**). Pleasingly, all substrates were tolerated well to give corresponding products in good yield and selectivity after reasonable time, demonstrated the extraordinary tolerance and compatibility of this methodology. Notably, alkynes containing polyfunctionalities or bioactive moieties also react smoothly under standard conditions and afford corresponding products efficiently (**Table 2, F**).

**> Monohydrido Mechanism**

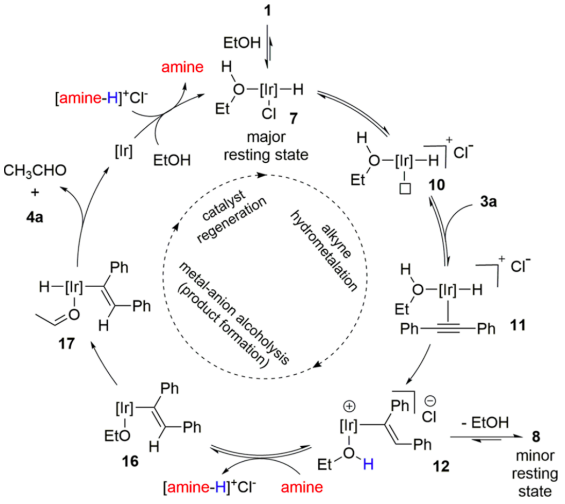
Based on various mechanistic studies and investigations above, an ionic monohydrido mechanism was proposed in **Scheme 4.**

Wherein, the monohydrido complex (NCP)IrHCl **1** is coordinated by EtOH to form coordinating species **7**, which is the major resting state. Then to give cationic species **10** via $Cl^-$ dissociation. Next, alkyne **3a** coordinates to the open site of **10** to allow migratory insertion of alkyne **3a** to form cationic Ir vinyl complex **12**.

(Notably, reversible $Cl^-$ rebinding upon EtOH dissociation on cationic complex **12** will form the neutral vinyl iridium chloride complex **8**, which is the minor resting state).

Amine-assisted $Cl^-$-driven deprotonation generated vinyl iridium ethoxide complex **16** and $[amine\text{-}H]^+Cl^-$ species. *β*-H elimination of **16** followed by reductive elimination release formaldehyde and target *Z*-alkene **4a** with (NCP)Ir complex. EtOH-Ir complex **7** will be regenerated from (NCP)Ir complex upon rebinding of EtOH and $Cl^-$ from $[amine\text{-}H]^+Cl^-$ species.

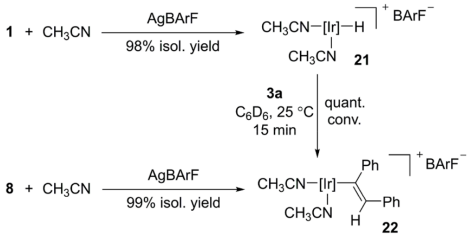
**Scheme 4. Proposed Ionic Monohydride Mechanism**




**> Anion Effect: $Cl^-$ vs $BArF^-$ I: Preparation**

$Cl^-$ anion serves as many roles in this catalysis. For example, its dissociation (**7** to **10**) will form an open site to allow the coordination of alkyne. And its rebinding to metal center (**12** to **8**), will affect the catalytic efficiency. Thus, the anion effect was investigated to clarify its exact role.

$BArF^-$ was chosen as a **non-coordinating** anion for the control experiment. (NCP)IrHCl complex **1** is treated with AgBArF in $CH_3CN$ to form 98% yield of cationic iridium complex **21**. **21** was then reacted with alkyne **3a** in $C_6D_6$ to afford cationic Ir vinyl complex **22**.



On the other hand, **22** could also been obtained by directly treating **8** with AgBArF in $CH_3CN$. XRD structure of cationic complexes **21** and **22** are also shown (**see right Figure 4**).

Furthermore, EtOH coordination instead of $CH_3CN$ will occur *in-situ* when react these species in EtOH as solvent.

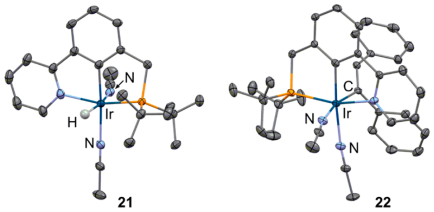



**Figure 4.** Synthesis of cationic complexes **21** and **22** with a $BArF^-$ ion and crystallographic characterization ($BArF^-$ anion omitted for clarity).

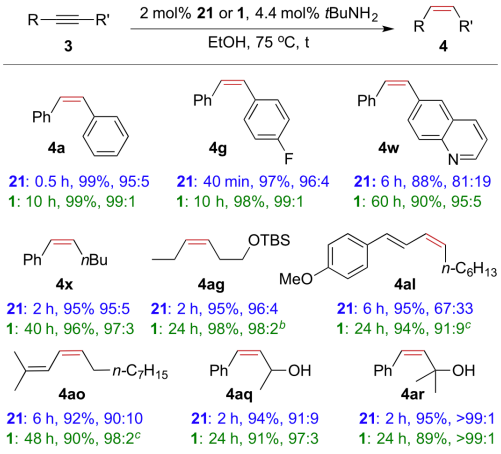
**> Anion Effect: $Cl^-$ vs $BArF^-$ II: Reactivity Investigation**

As a control experiment for the anion effect, (NCP)IrHCl complex **1** and $BArF^-$ complex **21** were next respectively examined to the *cis*-semihydrogenation of alkyne (**Table 3**).

Generally, using **21** will dramatically fulfill the reaction with very short time but high efficiency comparing to using **1**.

However, the selectivity of product when using **21** decreased (see **blue** and **green** results in **Table 3**). These results best describe the Cl-to-BArF substitution generates a more efficient catalyst, but at the expense of selectivity.

**Table 3. Comparison of Catalytic Performance between Complexes 1 and 21**[a]



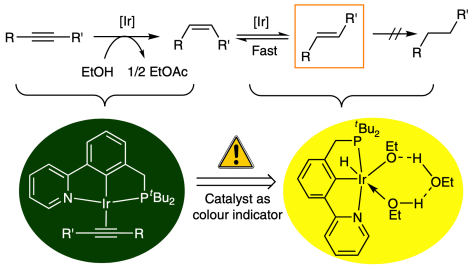

[a]Conditions: **3** (0.5 mmol), **21** or **1** (2 mol %), $t$BuNH$_2$ (4.4 mol %) in EtOH (2 mL) at 75 °C. Yields shown are of isolated products. [b]$t$BuNH$_2$ (10 mol %). [c]85 °C.

## Conclusion

A semihydrogenation using a (NCP)IrHCl complex has been reported for both *E*- and *Z*- selective version.

In **work I**, a dihydride species-involved mechanism is proposed. The *trans*-semihydrogenation of alkyne is achieved following a route of *cis*-semihydrogenation followed by *E/Z* isomerization.

By using "color indicator", ---two major resting state compound shown dark green and bright yellow respectively, in the step of semihydrogenation and *E/Z* isomerization, which will be the signal to end the reaction in a timely way to avoid overreduction.




In **work II**, a totally different mechanism is reported, in which an ionic monohydride mechanism for the *cis*-semihydrogenation of alkyne has been established.

The EtOH coordination-driven dissociation of $Cl^-$ anion forms an open coordinating site, which selectively allows the addition of alkyne rather than *Z*-alkene, avoid the overreduction of alkyne to alkane, to furnish the *cis*-alkenes selectively and efficiently.

Meanwhile, a significant assistance of amine during the alcoholysis step has also been established in this research, which is essential for the formation of *Z*-alkene as product.

Since the difference of these two reports is the use of different base, it is called a base-directed selectivity.