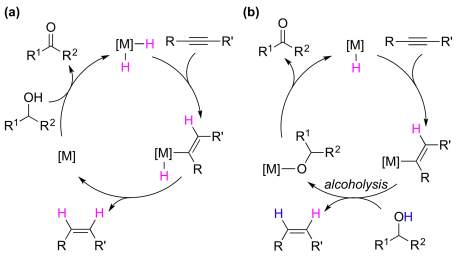
An Amine-Assisted Ionic Monohydride Mechanism Enables Selective Alkyne *cis*-Semihydrogenation with Ethanol: From Elementary Steps to Catalysis

J. Am. Chem. Soc. **2021**, *143*, 4824.

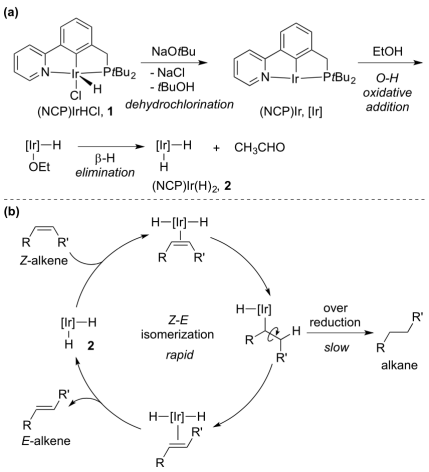
Introduction

A selective Semihydrogenation of alkynes to afford *Z*-alkenes is reported. An EtOH coordination-driven Cl^- dissociation from pincer-type (NCP)IrHCl complex will form a cationic Ir (III) monohydride complex to react with alkynes to give *Z*-alkenes selectively. The use of amine is the key to promote the alcoholysis, instead of direct protonolysis of the Ir–C(vinyl) bond.

Scheme 1. Schematic Illustration of Two Inner-Sphere Mechanisms Proposed for TH of Alkyne with Alcohol: (a) Dihydride Mechanism; (b) Monohydride Mechanism



Scheme 2. Possible Pathway for *Z*–*E* Alkene Isomerization and Overreduction by an NCP Pincer Ir(III) Dihydride Complex



Previous Work

Catalytic syntheses of *Z*-alkenes have been achieved by numerous strategies including direct hydrogenation of alkenes with H_2, or transfer hydrogenation (TH) with various hydrogen donors. Despite efforts above, the chemo-, regio- and stereoselectivity remain insufficient in producing pure target *Z*-alkenes. Particularly, *Z*-*E* alkene stereoisomerization and overreduction are two common side-reactions in most catalytic systems. On the other hand, despite TH of C–O and C–N double bond with alcohols has been full-realized, the same transformation of unactivated C–C multiple bonds is less studied.

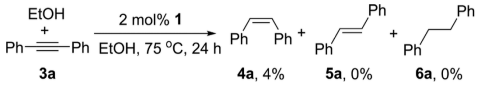
Two proposed pathways of inner-sphere TH for *Z*-alkenes using alcohol were shown in **Scheme 1**, in which a dihydride and a monohydride mechanism were shown respectively.

In **Scheme 2a** shown a (NCP)IrHCl-*t*-BuONa-EtOH system which forms a dihydride complex **2** to catalyze semihydrogenation of alkynes. However, competitive coordination from formed *Z*-alkene will generate an alkyl species to give *E*-alkenes (**via beta-hydride elimination**) or alkane (**via reductive elimination**) (**Scheme 2b**).

This Work

> Initial Attempt:

2 mol% of (NCP)IrHCl (**1**) was added to reduce diphenylacetylene (**3a**) in MeOH. *Z*-diphenylethylene (**4a**) was obtained only 4% but neither *E*-isomer (**5a**) or overreduction product **6a** was observed.



> 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**). This difference indicated an EtOH-Ir coordinating complex (**7**) and subsequent XRD structure proved this assumption (**Figure 1a, 7**). Stoichiometric addition (50 equiv) of **3a** gave a vinyl iridium chloride complex with XRD structure (**Figure 1a, 8**). However, treatment with *cis*-stilbene did not give a ethyl iridium chloride complex (**Figure 1a, 9**).

Alkyne **3a** coordination at the open site of **1** is not reasonable since the coordinating alkyne will be *trans* to hydride and difficult to allow insertion (**Figure 1c, upper path**). A possible **path A** shown a migration of Cl^- followed by coordination of **3a** to form **8**. Another possible **path B** proposed an EtOH coordination to form **7**, followed by dissociation of Cl^- 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** and EtOH (**Figure 1c**).

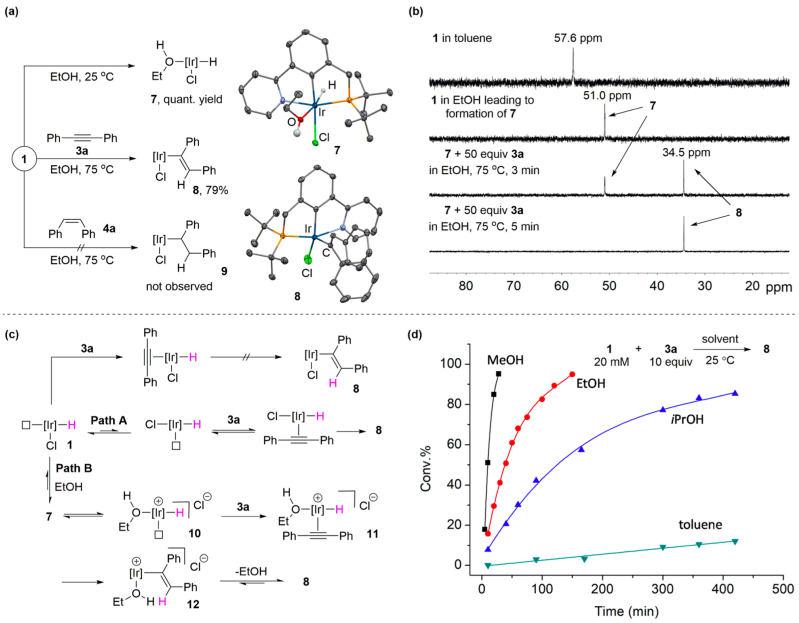


Figure 1. Alkyne hydrometalation by Ir(III) monohydride chloride complex **1**. (a) Synthesis and crystallographic characterization of Ir(III) complexes **7** and **8**. (b) ^{31}P NMR spectra for conversion of complex **1** to **7** and **8**. (c) Possible pathways for alkyne hydrometalation. (d) Time-course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

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 (H_2O/EtOH performs best , see **SI**)to demonstrated the size effect of alcohol solvents to the rate.

These results indicated the alcohol-coordination-driven Cl^- dissociation **path B**.

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

Cationic complex **13** was successfully synthesized from **1** and bpy ligand but failed to gain single crystal due to poor solubility. However, electrical conductivity of **13** indicated a cationic complex (**Figure 2a**).

By mixing 0.5 equiv. of bpy ligand with **1**, another complex **14** is obtained with a conductivity of 17.2 Ω^{-1} cm^2 mol^{-1}. XRD analysis revealed a structure bearing Ir-containing anion & cation. This result indicated the dissociation of Cl$^-$ (**Figure 2b**).

By mixing dtbpy ligand with **1**, a soluble complex **15** was synthesized. XRD analysis revealed a structure clearly with dissociating Cl$^-$ ion (**Figure 2c**).

These results provided evidence for supporting the alcohol-coordination-driven Cl$^-$ dissociation path in **Figure 1c, path A**.

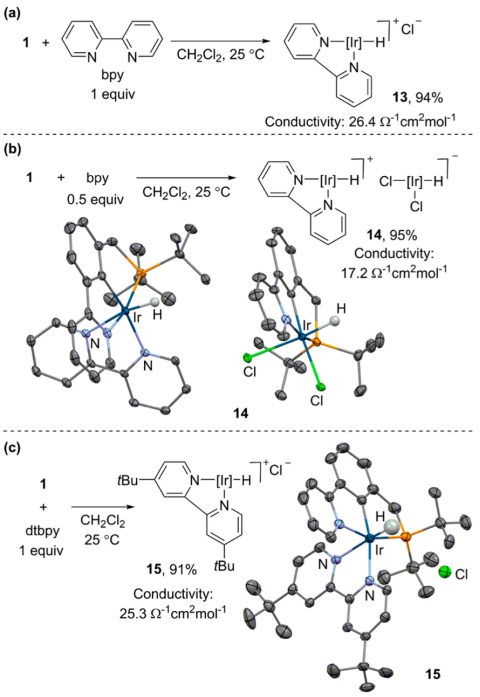
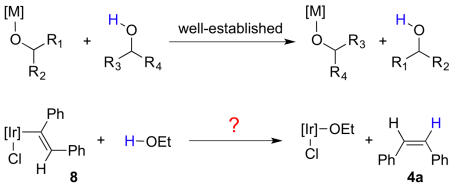


Figure 2. Synthesis and crystallographic characterization of cationic monohydride complexes bearing a Cl$^-$ ion.

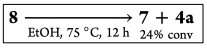
> Alcoholysis & Amine Assistance

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

Scheme 3. Direct Alcoholysis Pathway



Subsequent investigation indicated the difficulty of the direct alcoholysis of **8**, wherein by heating **8** in EtOH for 12 h afforded **7** and **4a** with only 24% conversion (see the **formula** at right).



A proposed alcoholysis is shown in **Figure 3a**. In which cationic species **12** was generated via EtOH coordination and Cl$^-$ anion dissociation. Subsequently via deprotonation to form **16** and then β-H elimination to form **17**, followed by reductive elimination to afford *cis*-alkene **4a** and aldehyde. EtOH-Ir complex **7** is regenerated via oxidative addition of HCl in EtOH.

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

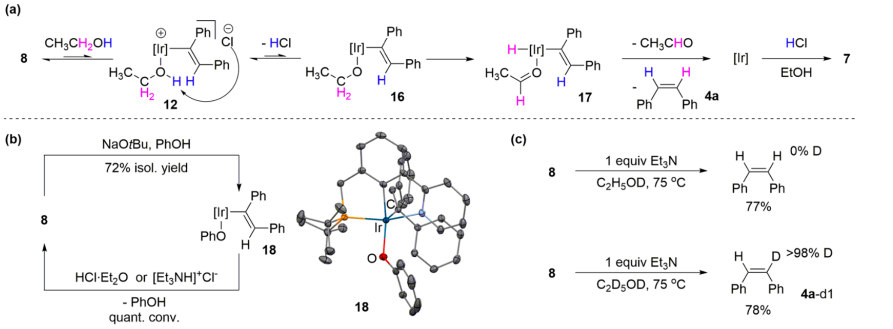
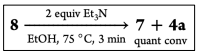
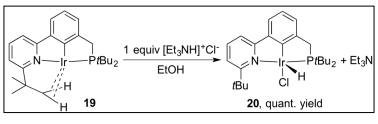


Figure 3. Alcoholysis of an Ir(III) vinyl chloride **8** with EtOH. (a) Proposed mechanism for ethanolysis of **8**. (b) Interconversion between **8** and a phenoxide vinyl complex **18**. (c) Deuterium-labeling experiments.

Since the deprotonation (**Figure 3a, 12** to **16**) step is reversible, addition of a suitable base might promote it. Because strong base might occur dehydrochlorination of (NCP)IrHCl complex **1**, amine was selected as the candidate due to its weak basicity. As their prediction, addition of 2 equiv of Et$_3$N increased the conversion of **8** to **7** and **4a** (see the **formula** at right).

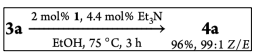


Deuterium labeling experiments were then performed. By treating **8** with C_2H_5OD and C_2D_5OD respectively, formed *cis*-alkene was deuterated only when employing C_2D_5OD, indicated the β-H elimination of ethoxy moiety rather that direct alcoholysis (**Figure 3c**). Notably, *Z*-alkene was deuterated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



A stable complex **19** bearing *t*-Bu group was prepared, to react with [Et$_3$NH]$^+$Cl$^-$ then successfully regenerate ($^{t\text{-Bu}}$NCP)IrHCl (see the right **Formula**).

Knowing that Et$_3$N could accelerate alcoholysis, and resulted [Et$_3$NH]$^+$Cl$^-$ could regenerate (NCP)IrHCl complex **7**, alkyne **3a** was treated with **1** and Et$_3$N 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.



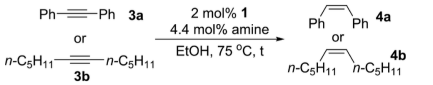
> Catalytic Transfer Hydrogenation of Alkynes under Amine Cocatalysis

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 , 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 formation of overreduced product (linear alkane) or isomers were observed, which demonstrated that this iridium monohydride catalyst could overcome alkene isomerization and overreduction of alkynes.

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



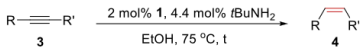
entry	alkyne	amine	*t* (h)	conv (%)	*Z*/*E*
1	**3a**	Et_3N	3	96	99:1
2	**3a**	Et_3N	6	>99	98:2
3	**3a**	Et_2NH	3	96	>99:1
4	**3a**	*n*$BuNH_2$	3	91	98:2
5	**3a**	*t*$BuNH_2$	3	95	>99:1
6	**3a**	*t*$BuNH_2$	6	>99	99:1
7	**3a**	*t*$BuNH_2$	10	>99	99:1
8	**3a**	pyridine	6	<2	
9	**3b**	Et_3N	15	21	>99:1
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

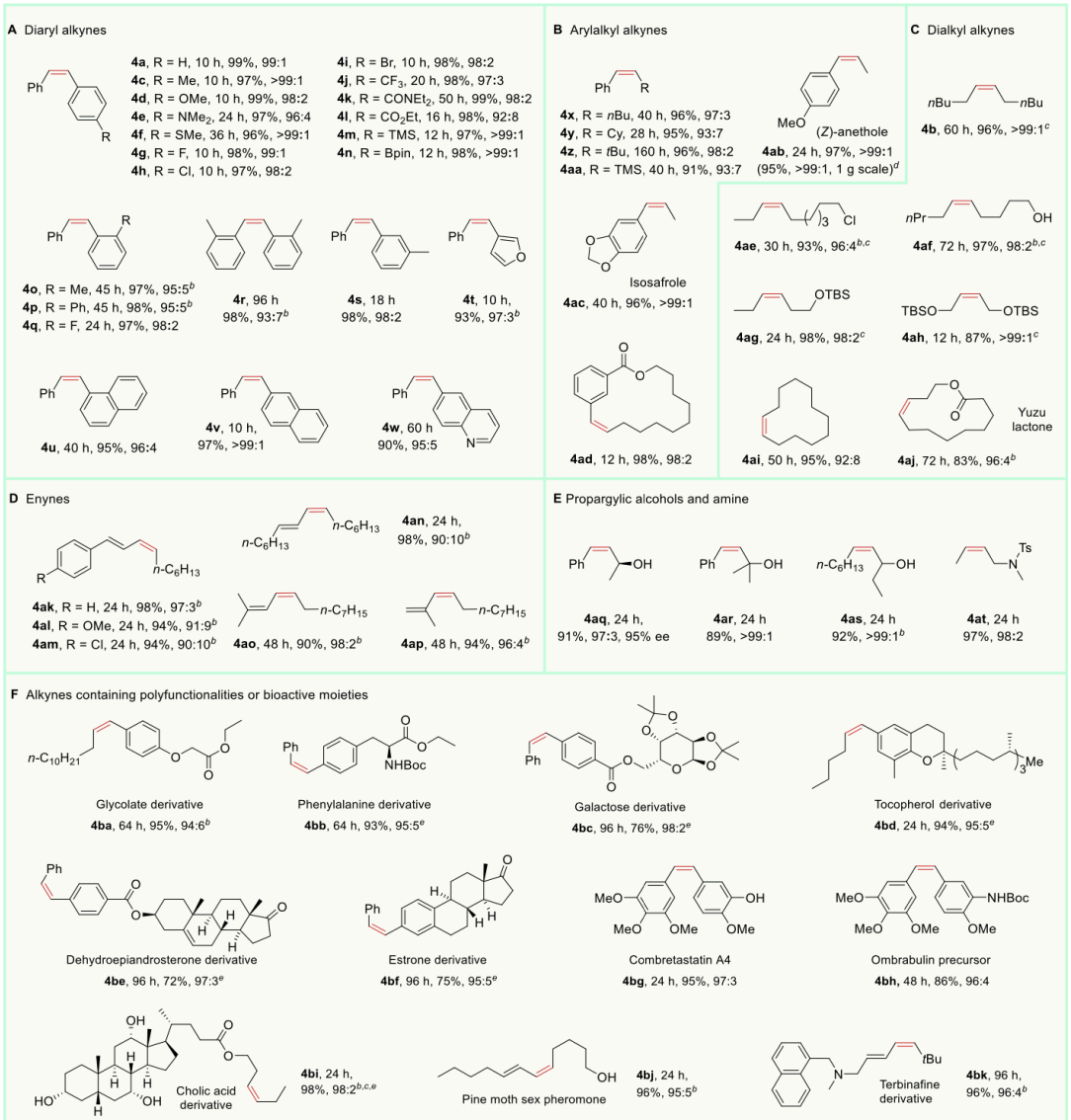
[a]Conditions: **3a** or **3b** (0.5 mmol), **1** (2 mol %), amine (4.4 mol %), and EtOH (2 mL) at 75 °C. The conversion and *Z*/*E* ratios were determined by GC. [b]Using 10% *t*$BuNH_2$.

> Substrate Scope

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**).

Table 2. Scope of Catalytic TH of Alkynes to *Z*-Alkenes with EtOH[a]





[a]Conditions: **3** (0.5 mmol), **1** (2 mol %), *t*$BuNH_2$ (4.4 mol %) in EtOH (2 mL) at 75 °C. Yields shown are of isolated products. The *Z*/*E* ratios were determined by GC or ^{1}H NMR. [b]85 °C. [c]*t*$BuNH_2$ (10 mol %). [d]**3ab** (1.0 g, 6.8 mmol), **1** (0.5 mol %), *t*$BuNH_2$ (10 mol %) in EtOH (10 mL) at 100 °C, 18 h. [e]Substrate (0.2 mmol), EtOH (1 mL), toluene (1 mL).

> Monohydride Mechanism

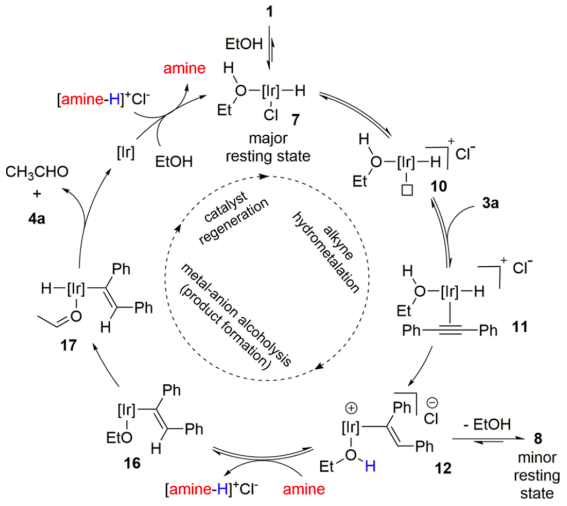
Based on various mechanistic studies and investigations above, an ionic monohydride mechanism was proposed in **Scheme 4.**

Wherein, the monohydride complex (NCP)IrHCl **1** is coordinated by EtOH to form coordinating species **7** 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 iridium vinyl complex **12**.

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

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 $BArF^-$

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 an **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 iridium vinyl complex **22**.

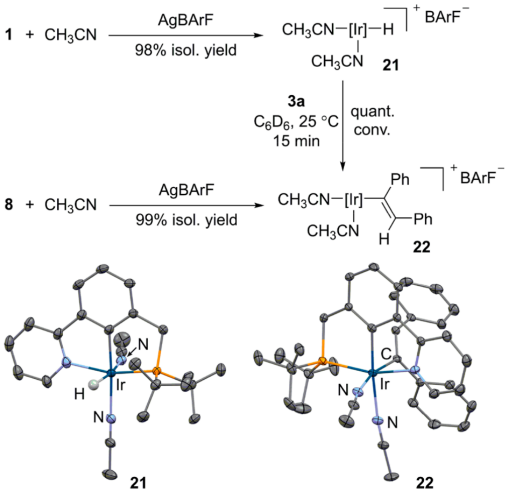
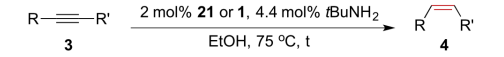


Figure 4. Synthesis of cationic complexes **21** and **22** with a $BArF^-$ ion and crystallographic characterization ($BArF^-$ anion omitted for clarity).

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



4a	**4g**	**4w**
21: 0.5 h, 99%, 95:5 **1**: 10 h, 99%, 99:1	**21**: 40 min, 97%, 96:4 **1**: 10 h, 98%, 99:1	**21**: 6 h, 88%, 81:19 **1**: 60 h, 90%, 95:5
4x	**4ag**	**4al**
21: 2 h, 95% 95:5 **1**: 40 h, 96%, 97:3	**21**: 2 h, 95%, 96:4 **1**: 24 h, 98%, 98:2[b]	**21**: 6 h, 95%, 67:33 **1**: 24 h, 94%, 91:9[c]
4ao	**4aq**	**4ar**
21: 6 h, 92%, 90:10 **1**: 48 h, 90%, 98:2[c]	**21**: 2 h, 94%, 91:9 **1**: 24 h, 91%, 97:3	**21**: 2 h, 95%, >99:1 **1**: 24 h, 89%, >99:1

[a]Conditions: **3** (0.5 mmol), **21** or **1** (2 mol %), $tBuNH_2$ (4.4 mol %) in EtOH (2 mL) at 75 °C. Yields shown are of isolated products. [b]$tBuNH_2$ (10 mol %). [c]85 °C.

As a control experiment for the anion effect, (NCP)IrHCl complex **1** and $BArF^-$ complex **21** were next respectively examined to the *Z*-semihydrogenation of alkyne (**Table 3**). Generally, using **21** will maintain high efficiency but within shorter reaction time than using **1**. However, the selectivity of product decreased (see **blue** and **green** results in **Table 3**). These results best describe a

Conclusion

An ionic monohydride mechanism for the *Z*-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, an 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.