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An Electron-Deficient Cp^E Iridium(III) Catalyst: Synthesis, Characterization, and Application to Ether-Directed C–H Amidation

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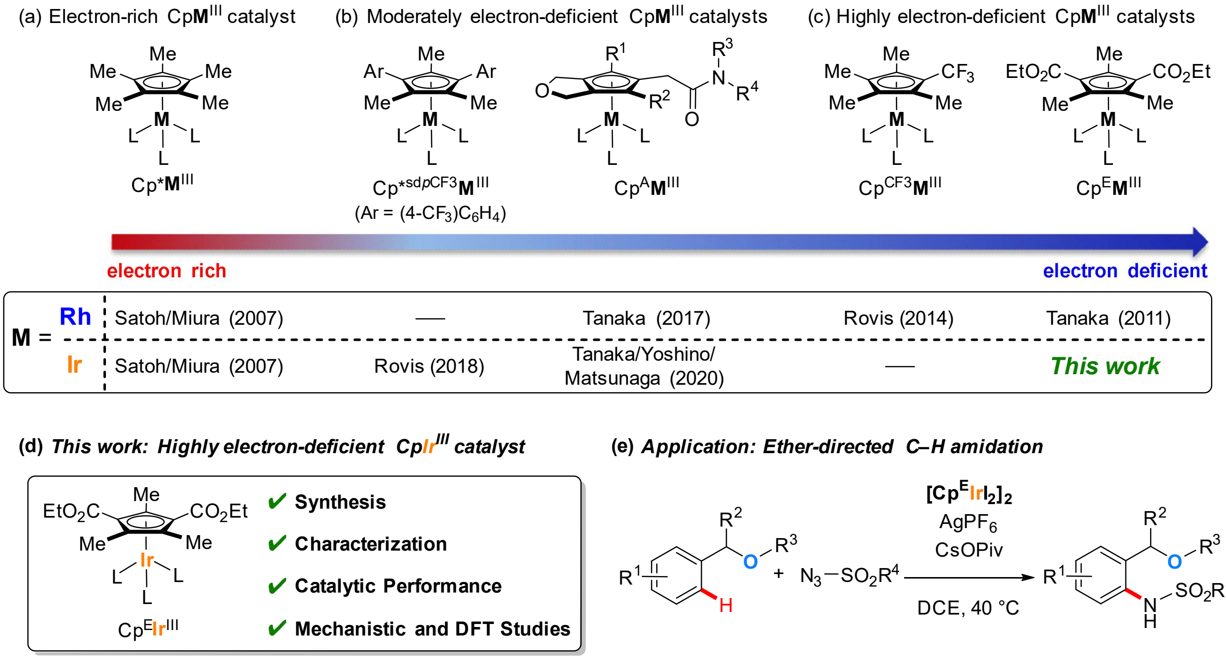
Abstract: The synthesis, characterization, and catalytic performance of an iridium(III) catalyst with an electron-deficient cyclopentadienyl ligand ($[Cp^EIrI_2]_2$) are reported. The $[Cp^EIrI_2]_2$ catalyst was synthesized by complexation of a precursor of the Cp^E ligand with $[Ir(cod)OAc]_2$, followed by oxidation, desilylation, and removal of the COD ligand. The electron-deficient $[Cp^EIrI_2]_2$ catalyst enabled C–H amidation reactions assisted by a weakly coordinating ether directing group. Experimental mechanistic studies and DFT calculations suggested that the high catalytic performance of $[Cp^EIrI_2]_2$ is due to its electron-deficient nature, which accelerates both C–H activation and Ir(V)-nitrenoid formation.

Introduction

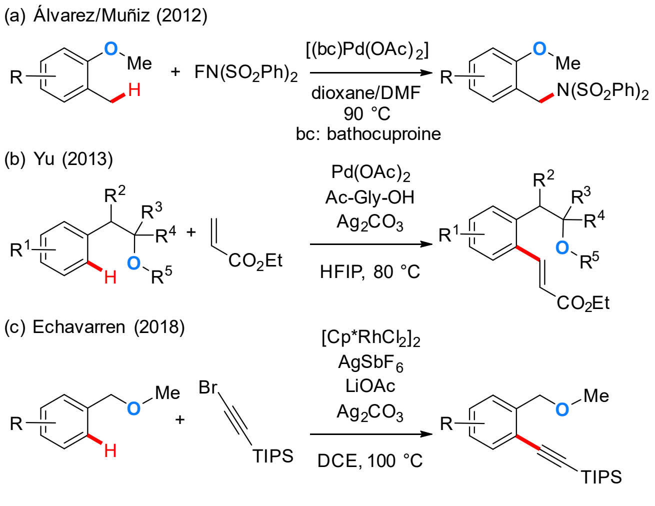
Catalytic C–H functionalization reactions, which can directly transform inert C–H bonds into targeted functional groups, are versatile and environmentally benign synthetic methods due to their atom- and step-economy.[1] Group 9 transition-metal complexes with cyclopentadienyl ligands (CpM^{III}; M = Co, Rh, Ir) have been widely used as catalysts for these reactions.[2] The pentamethylcyclopentadienyl (Cp*) ligand is one of the most frequently used ancillary ligands for these complexes because its steric bulkiness and strong electron-donating ability enhance their stability (Scheme 1a).[3] Additionally, appropriate steric and electronic modifications of the Cp ligand can dramatically improve the selectivity and reactivity of the catalysts.[4-10] Steric modifications of Cp ligands generally influence the regio-,[4] diastereo-,[5] site-,[6] chemo-,[7] and enantio-selectivity.[8,9] In contrast, electronic modifications of Cp ligands can influence the reactivity of the catalyst[10] and sometimes change the reaction



Scheme 1. Modified CpM^{III} catalysts with different electronic properties.

mechanism.[11,12] Electronic tuning by introducing electron-withdrawing groups on the Cp ring to render the metal catalyst electron-deficient and impart unique reactivity has attracted great attention. For example, Rovis and co-workers reported that a CF$_3$-substituted cyclopentadienyl rhodium (Cp^{*CF3}Rh^{III}) catalyst exhibits higher catalytic activity than a standard Cp*Rh^{III} catalyst in the synthesis of pyridines and dihydropyridines as well as in the cyclopropanation of allylic alcohols (Scheme 1c).[13] One of the authors of this study (K.T.) has developed amide-pendant cyclopentadienyl rhodium (Cp^{A}Rh^{III}) catalysts[11b,d,14] and a bis(ethoxycarbonyl)-substituted cyclopentadienyl rhodium (Cp^{E}Rh^{III}) catalyst (Scheme 1b, c).[11a,c,15] These rhodium catalysts also exhibit high and/or unique reactivity for several C–H functionalization reactions.[14,15]

Despite the success of these electron-deficient modified CpRh^{III} catalysts, limited attention has been paid to the corresponding electron-deficient CpIr^{III} catalysts, which are homologous to the rhodium catalysts but often exhibit complementary catalytic activity.[16] As notable examples, Rovis and co-workers have disclosed that a series of aryl-substituted moderately electron-deficient CpIr^{III} catalysts, such as Cp^{*sdpCF3}Ir^{III}, successfully catalyze the non-directed C–H carbocarbation of anisole derivatives (Scheme 1b).[17,18] In addition, we have developed amide-pendant cyclopentadienyl iridium catalysts (Cp^{A}Ir^{III}) that exhibit high catalytic activity for double aromatic homologation reactions of benzamides by fourfold C–H activation (Scheme 1b).[19] However, the Cp ligands of these catalysts possess only relatively weak electron-withdrawing groups and are thus expected to exhibit merely moderate electron-deficiency. In contrast, the Cp^{E} ligand, which contains two ester groups directly on the cyclopentadienyl ring, should make the corresponding metal catalysts highly electron-deficient.[20] However, this Cp^{E} ligand has only been introduced to rhodium catalysis.[11a,c,15] We speculated that the combination of the Cp^{E} ligand and iridium, which has strong Lewis acidity due to relativistic effects,[21] would afford a novel catalyst with strong Lewis acidity and a highly electrophilic metal center (Cp^{E}Ir^{III}; Scheme 1d). We also envisioned that the Cp^{E}Ir^{III} complex could effectively catalyze weakly directed C–H functionalization reactions,[22] by compensating the weak coordinating ability of the substrates with its high Lewis acidity and electrophilicity.



Scheme 2. Examples of ether-directed C–H functionalization reactions catalyzed by high-valent transition-metal catalysts.

Herein, we report the synthesis, characterization, and catalytic performance of a [Cp^{E}IrI$_2$]$_2$ catalyst, which was obtained from the complexation of a precursor of the Cp^{E} ligand with [Ir(cod)OAc]$_2$, followed by oxidation, desilylation, and removal of the COD ligand. We used the [Cp^{E}IrI$_2$]$_2$ complex for ether-directed C–H amidation reactions (Scheme 1e). Compared to nitrogen functional groups or carbonyl groups,[23] the ether group has the much weaker coordinating ability.[24] Therefore, only limited examples of ether-directed C–H functionalization reactions have been reported, and these methods still suffer from moderate yields, limited substrate scopes, and relatively harsh reaction conditions (Scheme 2).[25-28] The $[Cp^EIrI_2]_2$ catalyst facilitated the benzyl-ether-directed C–H amidation under mild reaction conditions (40 °C in DCE) with a broad substrate scope. We also conducted experimental mechanistic studies and DFT calculations, which revealed that the $[Cp^EIrI_2]_2$ catalyst accelerates both C–H activation and Ir(V)-nitrenoid formation.

Results and Discussion

The $[Cp^ERhCl_2]_2$ complex **2** was previously synthesized by the reductive complexation of fulvene $Cp^{E\text{-}TIPS}$ ligand **1a** with $RhCl_3{\cdot}nH_2O$ (Scheme 3a).[15] However, the same protocol using $IrCl_3{\cdot}nH_2O$ failed to afford $[Cp^EIrCl_2]_2$ **3**, and only a complex mixture was obtained (Scheme 3b). Based on our previous report on Cp^AIr complexes,[19] we then tried to synthesize the $[Cp^EIrI_2]_2$ complex via the complexation of $[Ir(cod)OAc]_2$ and the corresponding cyclopentadiene ligand. Although the reduction of **1a** by $NaBH_4$ proceeded smoothly and afforded $Cp^{E\text{-}TIPS}H$ ligand in quantitative yield, the subsequent complexation of $Cp^{E\text{-}TIPS}H$ ligand with $[Ir(cod)OAc]_2$ according to the protocol developed by Cramer and co-workers[29] was unsuccessful, probably due to the steric hindrance of the bulky TIPS group (for details, see Scheme S1). On the other hand, a sterically less hindered $Cp^{E\text{-}TBS}H$ ligand **4**, which was obtained in 95% yield via the reduction of fulvene **1c** using $NaBH_4$, reacted smoothly with $[Ir(cod)OAc]_2$ to give the corresponding iridium complex **5** in 95% yield (Scheme 3c). Oxidation of **5** with two equivalents of I_2 at –78 °C resulted in the formation of COD-coordinated complex **6**.[19,30] Unlike in our previous synthesis of Cp^AIr complexes,[19] the dissociation of the COD ligand and the subsequent dimerization of **6** to directly afford the μ-iodo dimeric complex did not proceed spontaneously in CH_2Cl_2, probably due to the strong coordination of the COD ligand to the highly electron-deficient iridium center. Hence, an alternative synthetic route based on reports by Rheingold and co-workers was investigated;[31] we planned to replace the COD ligand with a CO ligand, which could then be removed via oxidation using NMO. During the investigation of this route, we surprisingly found that the TBS group of **6** was removed under a CO atmosphere to afford desilylated **7** when an appropriate solvent and temperature were selected; it should be noted here that the details of the reaction mechanism of this desilylation process remain unclear at present. After intensive optimization,

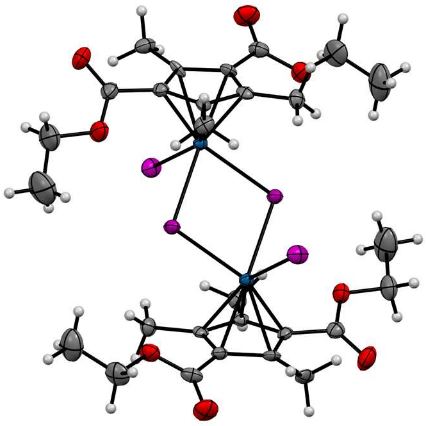
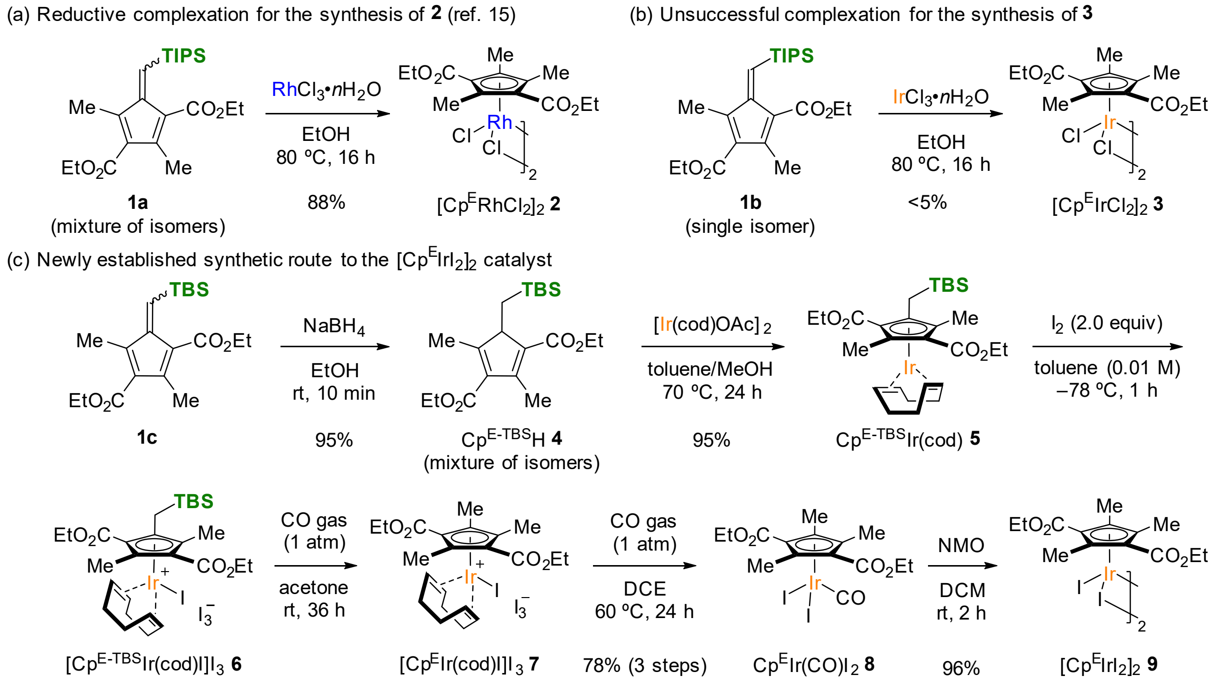


Figure 1. X-ray structure of $[Cp^EIrI_2]_2$ complex **9** with 50% thermal probability.

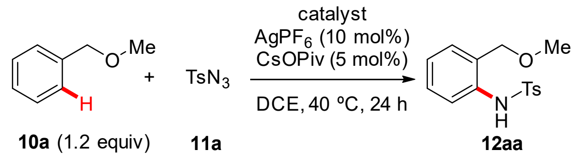


Scheme 3. Synthesis of $[Cp^EIrI_2]_2$ catalyst.

the desilylation reaction was found to proceed effectively under a 1 atm CO atmosphere in acetone at room temperature. The resulting **7** was carbonylated under a 1 atm CO atmosphere in DCE at 60 °C to afford **8**. After purification by silica gel column chromatography, **8** was obtained in 78% yield (3 steps from **5**). Finally, the oxidation of the CO ligand to CO_2 by NMO afforded the desired $[Cp^{E}IrI_2]_2$ complex **9** in 96% yield. The structure of **9** was unambiguously determined by single crystal X-ray diffraction analysis (Figure 1).[32]

With $[Cp^{E}IrI_2]_2$ catalyst **9** in hand, we turned our attention to its application in weakly directed C–H functionalization reactions. After several investigations, we found that the C–H amidation reaction of benzyl methyl ether **10a** with TsN_3 **11a** proceeded in almost quantitative yield at 40 °C in DCE when catalytic amounts of **9**, $AgPF_6$, and CsOPiv were used (Table 1, entry 1).[33] As control experiments, we examined the reactivity of other CpM^{III} catalysts under the same conditions (entries 2–9, Figure 2). A standard $[Cp^{*}IrCl_2]_2$, a moderately electron-deficient $[Cp^{A1}IrI_2]_2$, and $[Cp^{*sdpCF3}IrI_2]_2$ catalyst exhibited inferior reactivity (entries 2–5), highlighting the importance of the highly electron-deficient nature of **9**. Moreover, $[Cp^{*}RhCl_2]_2$, $[Cp^{E}RhCl_2]_2$, $[Cp^{A1}RhCl_2]_2$, and $Cp^{*}Co(CO)I_2$[34] did not give the desired product, and **11a** was recovered quantitatively (entries 6–9). The result with $[Cp^{E}RhCl_2]_2$ showed that the combination of a Cp^{E} ligand and iridium is indispensable for this transformation. We also confirmed that the reaction did not proceed in the absence of a catalyst (entry 10).

Table 1. Optimized reaction conditions and control experiments for the ether-directed C–H amidation reaction of **10a** with **11a**.[a]



Entry	Catalyst	Yield (%)[b]
1	$[Cp^{E}IrI_2]_2$ **9** (2.5 mol%)	>95
2	$[Cp^{*}IrCl_2]_2$ (2.5 mol%)	9
3	$[Cp^{A1}IrI_2]_2$ (2.5 mol%)	<5
4	$[Cp^{*sdpCF3}IrCl_2]_2$ (2.5 mol%)	31
5	$[Cp^{*sdpCF3}IrI_2]_2$ (2.5 mol%)	33
6	$[Cp^{E}RhCl_2]_2$ (2.5 mol%)	N.R.
7	$[Cp^{A1}RhCl_2]_2$ (2.5 mol%)	N.R.
8	$[Cp^{*}RhCl_2]_2$ (2.5 mol%)	N.R.
9	$Cp^{*}Co(CO)I_2$ (5 mol%)	N.R.
10	none	N.R.

[a] Reaction conditions: **10a** (0.060 mmol), **11a** (0.050 mmol), catalyst (0.00125 mmol), $AgPF_6$ (0.0050 mmol), and CsOPiv (0.0025 mmol) in DCE (0.50 mL) at 40 °C for 24 h under an argon atmosphere. [b] The yields were determined via ^1H NMR analysis of the crude mixture using 1,1,2,2-tetrachloroethane as an internal standard.

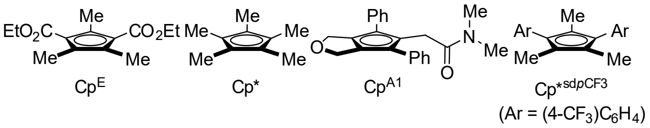
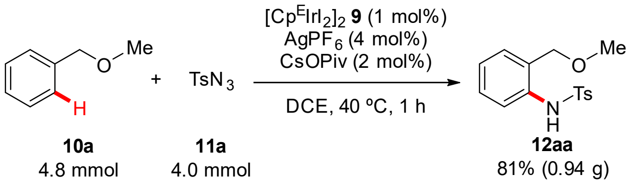


Figure 2. Structures of Cp ligands applied for this study.

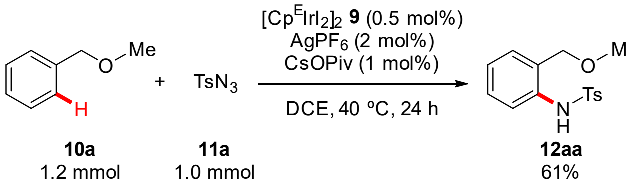
The substrate scope and limitations of the ether-directed C–H amidation reactions are summarized in Scheme 4. Model substrate **10a** gave **12aa** in 91% isolated yield. Substituents at the *para* position were well tolerated; alkyl- (**12ba**–**12da**), phenyl- (**12ea**), halogen- (**12fa**–**11ia**), Bpin- (**12ja**), and OCF_3-substituted (**12ka**) ethers afforded the corresponding amidated products in moderate to good yield, and *meta*-halogen-substituted ethers were also compatible (**12la**–**12na**). We also investigated substrates bearing various *ortho*-substituents, including halogen (**12oa**–**12ra**), methyl (**12sa**), and CF_3 (**12ta**) groups, which afforded the products in 50–91% yields. In addition, a methyl substituent at the benzylic position was tolerated in this reaction, and **12ua** was obtained in 77% yield. Furthermore, six- and five-membered cyclic ethers also successfully acted as directing groups, furnishing the corresponding products in 99% (**12va**) and 63% yield (**12wa**). With ethyl and *n*-butyl ethers, the reactivity was somewhat decreased as the steric hindrance increased (**12xa**, **12ya**). Ethers with additional coordinating functional groups were also investigated (**12za**–**12aca**). When an ester-substituted ether was used, the C–H amidation reactions directed by the ether and by the ester competed without selectivity, but doubly amidated **12za** was obtained in 71% yield in the presence of 2.5 equivalents of **11a**. On the other hand, a ketone-substituted ether was amidated selectively at the *ortho*-position to the ketone moiety, affording**12aaa** in 97% yield. Substrates containing a pyridine ring and a cyano group were not applicable with this reaction probably due to the strong coordination of these groups to the Ir metal center (**12aba**, **12aca**). Other unsuccessful substrates were summarized in Figure S1.

The scope of sulfonyl azides **11** was subsequently investigated (Scheme 4, bottom). Phenyl sulfonyl azide and 1-naphthyl sulfonyl azide furnished the expected products in good yields (**12ab**, **12ag**). Aryl sulfonyl azides with electron-donating or -withdrawing substituents reacted smoothly to give the corresponding amidated products in moderate to good yields (**12ac**–**12af**). Alkyl sulfonyl azides were also applicable without difficulty (**12ah**, **12ai**). In addition, sulfonyl azide with bulky mesityl group aforrded **12aj** in 67% yield. Notably, the difunctionalization of *ortho*-C–H bonds, which was problematic in previously reported ether-directed C–H functionalization reactions,[26,27] was not observed for any of the investigated substrates in Scheme 4. Other amidating/aminating reagents, such as dioxazolone, aryl- or alkylazides, did not furnish the desired products under the current reaction conditions (for details, see Figure S1).

To confirm the scalability of this reaction, a gram-scale reaction was conducted using model substrate **10a**, which



(1)



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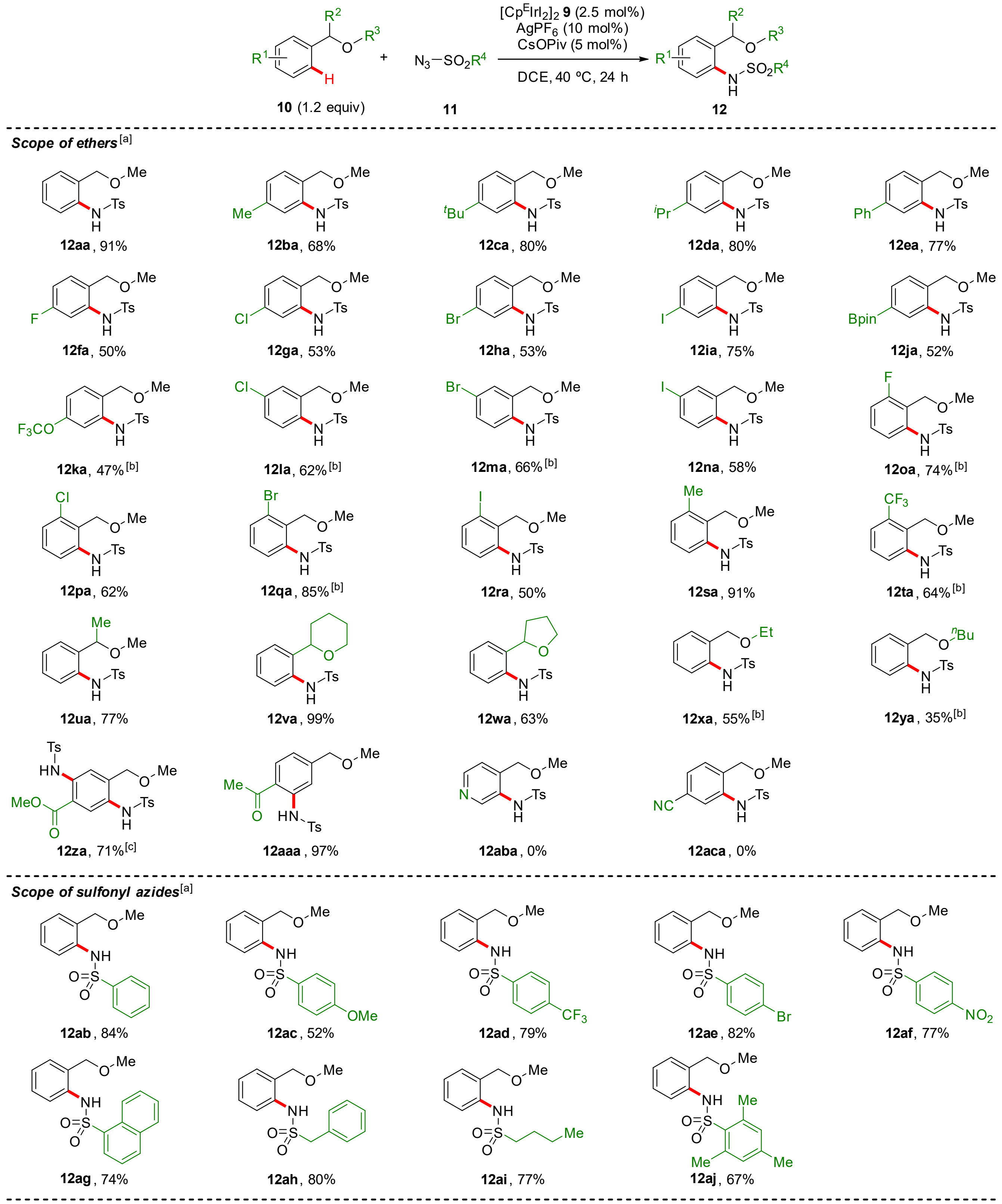


Scheme 4. Substrate scope and limitations of the ether-directed C–H amidation reaction between **10** and **11**. [a] Reaction conditions: **10** (0.24 mmol), **11** (0.20 mmol), **9** (0.0050 mmol), $AgPF_6$ (0.020 mmol) and CsOPiv (0.010 mmol) in DCE (2 mL) at 40 °C for 24 h. [b] **9** (0.010 mmol, 5 mol%), $AgPF_6$ (0.040 mmol, 20 mol%), and CsOPiv (0.020 mmol, 10 mol%). [c] **10z** (0.20 mmol), **11a** (0.50 mmol, 2.5 equiv), **9** (0.010 mmol, 5 mol%), $AgPF_6$ (0.040 mmol, 20 mol%) and CsOPiv (0.020 mmol, 10 mol%).

furnished **12aa** in 81% yield (0.94 g) with a low catalyst loading of **9** (1 mol%) in a short reaction time (1 h; eq 1). When the catalyst loading was further reduced to 0.5 mol%, **12aa** was obtained in 61% yield (eq 2).

The distinctive reactivity of **9** in the ether-directed C–H amidation prompted us to clarify the difference among **9**, $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}$Ir, and Cp*Ir complexes. To evaluate the electronic nature of the Ir center of the catalyst, we synthesized triethylphosphite-coordinated complexes $\mathrm{Cp^EIr(P(OEt)_3)I_2}$ **13**, $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}\mathrm{Ir(P(OEt)_3)I_2}$ **14**, and $\mathrm{Cp^*Ir(P(OEt)_3)I_2}$ **15** (for details, see the Supporting Information), which we used in Gutmann–Beckett-type experiments.[35] The chemical shift of the ^{31}P NMR signal of **13** exhibited a large upfield shift relative to that of **15** (70.18 ppm to 56.50 ppm; Figure 3a), which demonstrates the higher electron-deficiency of **13** compared to that of **15**. The ^{31}P NMR signal of **14** (57.32 ppm) was between those of **13** and **15,** albeit closer to that of **13**. This behavior is similar to that observed in previous studies of modified CpRh complexes.[10b,20] We also measured the CO stretching frequencies of the complexes $\mathrm{Cp^EIr(CO)I_2}$ **8**, $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}\mathrm{Ir(CO)I_2}$ **16**, and $\mathrm{Cp^*Ir(CO)I_2}$ **17** using IR spectroscopy (Figure 3b).[10b,20] Much higher CO stretching frequencies were observed for **8** (2050.9 cm^{-1}) and **16** (2050.9 cm^{-1}) compared to that of **17** (2016.2 cm^{-1}). These values reflect the weaker π-back donation in the $\mathrm{Cp^E}$Ir and $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}$Ir complexes compared to that in the Cp*Ir complex, which supports the electron-deficient nature of these complexes. The cyclic voltammogram of $\mathrm{[Cp^*IrI_2]_2}$ **19** exhibited an irreversible anodic peak current at +0.15 V vs. Fc/Fc$^+$, which probably corresponds to the oxidation of Ir$^{\mathrm{III}}$ to Ir$^{\mathrm{IV}}$ (Figure 3c). The cyclic voltammogram of **9** also showed an irreversible oxidation, albeit at a much higher potential (+0.81 V vs. Fc/Fc$^+$), while that of $[\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}\mathrm{IrI_2}]_2$ **18** showed an intermediate oxidation potential (+0.70 V vs. Fc/Fc$^+$). The higher oxidation potential of **9** compared to those of **18** and **19** was also attributed to its highly electron-deficient nature. All these experimental observations supported the highly electron-deficient nature of **9**.

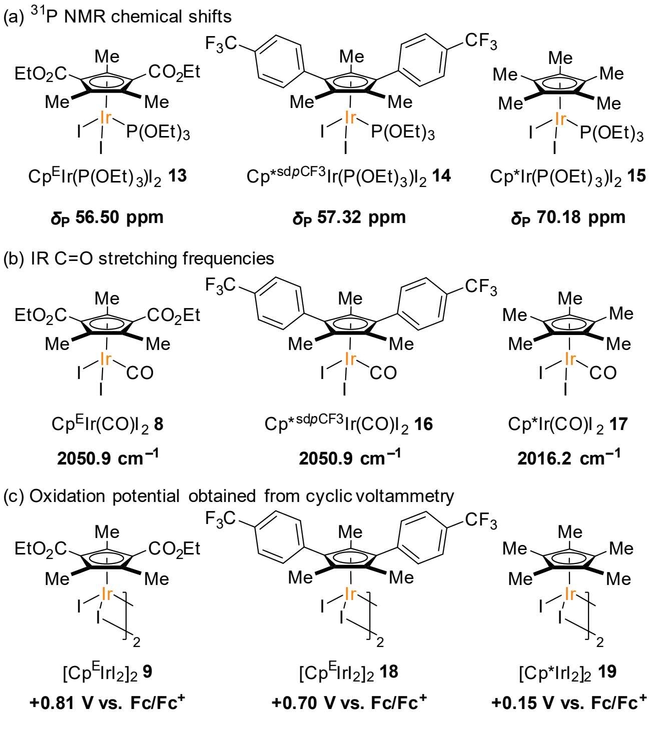
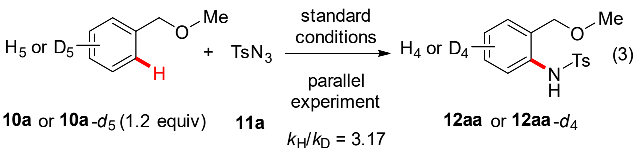


Figure 3. Evaluation of the electronic nature of the Ir center.

To shed light on the mechanistic aspects of the present ether-directed C–H amidation reaction, kinetic isotope effect (KIE) experiments were performed. In parallel experiments using undeuterated **10a** and deuterated **10a**-d_4, a primary KIE was observed (k_H/k_D = 3.17; eq 3), which implied that C–H bond cleavage may be involved in the rate-determining step.[36]



We also performed kinetic studies to reveal the dependence of the reaction rate on the concentrations of ether **10a**, azide **11a**, and the catalyst (for details, see the Supporting Information). While a near first-order dependence (1.19) was observed for the catalyst, Michaelis–Menten type saturation kinetics were observed for **10a** and **11a**.[37] These results indicated that both C–H activation and Ir(V)-nitrenoid formation would be similarly slow, and both steps could be rate-determining depending on the reaction conditions. In addition, the product inhibition was not observed for this reaction.

We conducted DFT calculations of the mechanism of the ether-directed C–H amidation reaction to gain further insight into the reason for the high reactivity of **9**. A full catalytic cycle was calculated at the B3LYP-D3/6-311++G**, SDD =Ir, CPCM(DCE)//B3LYP-D3/6-31G**, LanL2DZ=Ir, CPCM(DCE) level of theory for a highly electron-deficient $\mathrm{Cp^E}$Ir catalyst as well as for a moderately electron-deficient $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}$Ir catalyst and an electron-rich Cp*Ir catalysts for comparison. The plausible catalytic cycle for these catalysts and the activation energies of each step are summarized in Figure 4 (for full energy diagrams, see Scheme S2). The catalytic cycle begins with the generation of the active cationic complex from $\mathrm{[Cp^xIrX_2]_2}$ (X = Cl or I), $\mathrm{AgPF_6}$, and CsOPiv. The subsequent C–H activation occurs via a pivalate-assisted concerted-metalation deprotonation (CMD) mechanism,[38] and the activation barrier for this step is 17.7 kcal/mol for $\mathrm{Cp^E}$Ir, 17.6 kcal/mol for $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}$Ir, and 21.4 kcal/mol for Cp*Ir. Although there is no clear energy difference between $\mathrm{Cp^E}$Ir and $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}$Ir for this step, a high activation energy is required with the Cp*Ir catalyst, suggesting that the electron-deficient catalysts facilitate the C–H activation. After the C–H activation, ligand exchange with $\mathrm{TsN_3}$, followed by $\mathrm{N_2}$ extrusion gives an Ir(V)-nitrenoid intermediate.[39] The overall activation energy for the Ir(V)-nitrenoid formation is significantly lower with $\mathrm{Cp^E}$Ir (18.4 kcal/mol) than with $\mathrm{Cp}^{*\mathrm{sd}p\mathrm{CF3}}$Ir (20.7 kcal/mol) or Cp*Ir (22.5 kcal/mol). The subsequent C–N bond formation exhibits similar barriers regardless of the ligands, and the final protodemetalation step is an almost-barrierless process. In the case of the $\mathrm{Cp^E}$Ir-catalyzed reaction, the difference between the activation energies for the C–H activation (17.6 kcal/mol) and the formation of the Ir(V)-nitrenoid (18.3 kcal/mol) is small (<1 kcal/mol). The calculated energy profile, as well as the experimental mechanistic studies, suggest that both C–H activation and the formation of the Ir(V)-nitrenoid are kinetically relevant. The results of several additional computational studies suggest that the electron-deficient $\mathrm{Cp^E}$ ligand can strengthen the interaction between the ether substrate and metal catalyst, which leads to stabilization of the transition state for the C–H activation as well as the metallacycle intermediate.[40] The stabilization of the metallacycle intermediate would then eventually lower the activation energy for the subsequent Ir(V)-nitrenoid formation (for details, see the Supporting Information).

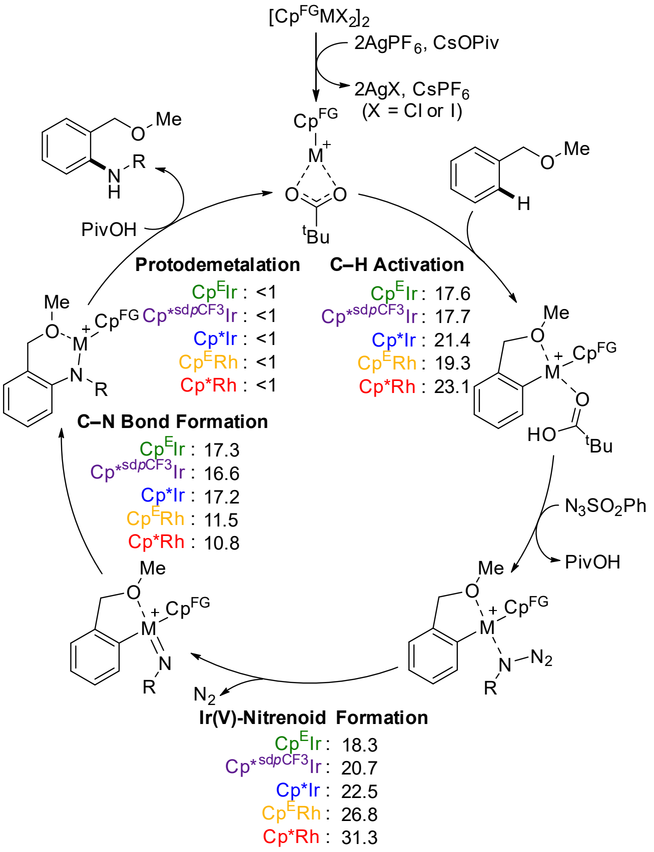


Figure 4. Plausible catalytic cycle and calculated activation energies $\Delta G^\ddagger$ (kca/mol). Gibbs free energies were obtained at the B3LYP-D3/6-311++G**, SDD=Ir, CPCM(DCE)//B3LYP-D3/6-31G**, LanL2DZ=Ir, CPCM(DCE) level of theory.

The full catalytic cycle with Cp*Rh or Cp^{E}Rh catalysts was also calculated at the same level (for details, see Scheme S3). The activation barriers for the cleavage of the C–H bond (Cp^{E}Rh: 19.3 kcal/mol; Cp*Rh: 23.1 kcal/mol) are slightly higher than those with the Ir catalysts, albeit still feasible. In contrast, the activation energies required for the formation of the Rh(V)-nitrenoid are considerably higher than those for the formation of the Ir(V)-nitrenoid (Cp^{E}Rh: 26.8 kcal/mol; Cp*Rh: 31.3 kcal/mol). The Rh(V)-nitrenoid formation is by ca. 15 kcal/mol less exergonic than the Ir(V)-nitrenoid formation. The higher activation barrier and lower exergonicity for the Rh(V)-nitrenoid formation can be attributed to the weaker Rh=N bond compared to the Ir=N bond.[21c,d,41] The subsequent insertion and protonation steps exhibit reasonably low activation barriers. Overall, the Rh catalysts are unsuitable for the present reaction due to the difficulty of Rh(V)-nitrenoid formation, and thus, the use of the electron-deficient Cp^{E}Ir catalyst is crucial to the successful ether-directed C–H amidation reaction under mild conditions.

Conclusion

In conclusion, we have synthesized and characterized an iridium(III) catalyst with a highly electron-deficient cyclopentadienyl ligand ([Cp^{E}IrI$_2$]$_2$), which catalyzes ether-directed C–H amidation reactions under mild reaction conditions. The catalytic activity of other related group 9 metal catalysts, such as the Cp*Ir, Cp*Rh, and Cp^{E}Rh catalysts, is greatly inferior to that of Cp^{E}Ir. Experimental and computational mechanistic studies revealed that the high reactivity of the Cp^{E}Ir complex is due to its high electron-deficiency, which accelerate both the activation of the C–H bond and the formation of the Ir(V)-nitrenoid, while the corresponding Cp^{E}Rh catalyst is not suitable for the formation of the nitrenoid species under such mild conditions. Our results demonstrate the importance of the combination of the highly electron-deficient Cp^E ligand with an iridium center to achieve high reactivity in challenging ether-directed C–H amidation reactions. Based on its distinct properties, the Cp^{E}Ir catalyst may find further applications in C–H functionalization reactions and other synthetic organic transformations in which other related metal catalysts show insufficient reactivity.

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Keywords: iridium • Cp^E ligand • C–H activation • ether directing group • amidation

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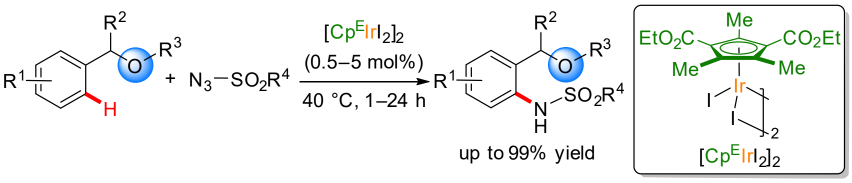

A highly electron-deficient cyclopentadienyl iridium(III) complex was developed ([Cp^{E}IrI$_2$]$_2$). This complex effectively catalyzed weakly coordinating ether-directed C–H amidation reactions under mild reaction conditions. Mechanistic experiments and DFT calculations indicated that the high catalytic activity of the [Cp^{E}IrI$_2$]$_2$ complex is attributed to its highly electron-deficient nature.

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