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Awakening Rhodium Catalysis for C–H Activation with an In-Metalloligand

Ryosuke Yamada^[a], Nobuharu Iwasawa^[a], and Jun Takaya*^{[a][b]}

Abstract: Rhodium complexes having an In-metalloligand are successfully synthesized utilizing a pyridine-tethered cyclopentadienyl ligand as a support for an In–Rh bond. The In-metalloligand dramatically changes the electronic and redox properties of the rhodium metal, awakening its catalysis for an sp²C– H bond activation reaction.

Z-type ligands have recently emerged as a new tool for tuning reactivity of transition metal complexes.^[1] They are usually main group Lewis acids and serve as a σ -acceptor via dative bonding from a transition metal, which is in sharp contrast to the case of commonly employed σ -donor, L-type ligands such as phosphines. Such a reverse electronic perturbation is highly promising for unique reactivity and catalysis. In particular, rationally designed supported Z-type ligands are beneficial to stabilize the M-Z bond (Z = Z-type ligand), thus enabling systematic synthesis of the M-Z complexes and their use as a catalyst in synthetic reactions.^[2,3] For examples, an orthophosphinophenyl-linker has been widely utilized for Z-type ligands of group 13 elements and antimony, and the catalysis of their metal complexes were often demonstrated in electrophilic activation of alkynes utilizing the electron-accepting nature of the Z-type ligands (Figure 1-a).^[1c,4,5] Lu, Tauchert, and our group developed N,P-multidentate ligands as suitable supports for M-Z bonds (Z = group 13 metals, Li, Cu, Zn), in which the Z-type ligands substantially affect the reactivity of group 10 metals for hydrogenation and hydrosilylation reactions.^[6-8] However, previous reports mostly focused on phosphine-based supports for M-Z bonds to give metal complexes having PZP-pincer type or ZP3-tetradentate tripodal ligands, and their catalysis were rather limited to activation of alkynes and E-H bonds (E = H, Si).^[9] Therefore, development of novel M-Z complexes that enable new modes of catalysis control by Z-type ligands is necessary in order to extend its usage in synthetic chemistry.

Herein we report the first synthesis and catalysis of cyclopentadienylrhodium (CpRh) complexes having a Z-type Inmetalloligand supported by a pyridine-tethered Cp ligand. The In-metalloligand dramatically changes the electronic and redox

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properties of the rhodium metal, awakening its catalysis for an ${\rm sp^2C-H}$ bond activation reaction.





by changing electronic and redox properties

Figure 1. Z-type metalloligands in organic synthesis

Cp-metal complexes are one of the most important classes of transition metal catalysts in synthetic chemistry because of their various reactivity and utility. However, tuning their catalysis with Z-type ligands has rarely been investigated partly due to the difficulty of designing a multidentate support with the Cp structure.^[10,11] We chose a tetramethyl(2-pyridyl)cyclopentadienyl ligand as a suitable support for an M-Z bond and examined synthesis of the corresponding rhodium complexes. The reaction of potassium tetramethyl(2-pyridyl)cyclopentadienylide with [RhCl(cod)]₂ afforded a rhodium complex 1 having a pyridinetethered Cp ligand in good yield (Scheme 1). Four alkenyl protons on the cod moiety were observed equivalently as a broad singlet in ¹H NMR, thus suggesting the pyridine side arm does not coordinate to rhodium.^[12] Screening of various Lewis acidic metals as an additive to 1 revealed that some metal halides, in particular InCl₃, can efficiently work as a Z-type metalloligand for the rhodium.^[13] The reaction of 2 equivalents of InCl₃ with 1 in toluene at 80 °C afforded a cationic In-Rh bimetallic complex [2][InCl₄] having an -InCl₄ as a counter anion in 64% isolated yield.^[14] Treatment of [2][InCl₄] with sodium tetra(3,5-bis(trifluoromethyl)phenyl)borate gave the corresponding BAr^F complex [2][BAr^F]. ¹H NMR of both complexes displayed two sets of alkenyl protons of the cod moiety, indicating the coordinated cod became asymmetric due to the formation of an In-Rh bond. No decomposition of [2][InCl4] was observed even in coordinating solvent CD₃CN at 80 °C, indicating sufficient stability of the supported In-Rh bond. The structures of [2][InCl4] and [2][BArF] were fully characterized by

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X-ray analyses, and the ORTEP of [2][BAr^F] was depicted in Figure 2. The In–Rh bond length is 2.6170(7) Å, which is shorter than the sum of the covalent radii of In and Rh (2.84 Å).^[15] The covalent ratio (r = 0.92) is in a range of typical M–Z distances,^[1b] thus supporting Z-type ligation of the InCl₂ moiety. The geometry around In is trigonal bipyramidal with a vacancy and pyridine at apical and Cl and Rh at equatorial positions. The average distance between Rh and alkenyl carbons of cod is 2.220 Å, which is longer compared to that of the reported CpRh^I(cod) complex (2.115 Å).^[16] This reflects weaker π -back donation of Rh in [2][BAr^F] caused by strong electron-accepting nature of the In-metalloligand.



Scheme 1. Synthesis of In-Rh complexes



Figure 2. ORTEP drawing of [2][BAr^F] at 50% probability level. The counter anion BAr^F and hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): In–Rh = 2.6170(7), In–Cl1 = 2.376(2), In–Cl2 = 2.357(2), Rh–C6 = 2.246(6), Rh–C7 = 2.196(6), Rh–C8 = 2.241(7), Rh–C9 = 2.197(8), Cl1–In–Cl2 = 107.29(7), Cl2–In–Rh = 122.71(5), Rh–In–Cl1 = 121.42(5).

We performed theoretical calculations to gain further insights into bonding situation and electronic nature of [2]+. The Z-type ligation of the In-metalloligand to Rh is clearly supported by the natural bond orbital (NBO) analyses. The In–Rh bond mainly consists of two donor-acceptor interactions between occupied *d* orbitals on Rh and a vacant orbital on In; one is a donation from LP2(Rh) and the other is from LP4(Rh) to LV1(In), which resulted in 31.2 and 20.7 kcal/mol stabilization, respectively

(Figure 3). Molecular orbital analysis also demonstrated that MOs of [2]+ are composed of those of a neutral CpRh^I and a cationic In^{III}Cl₂ via Z-type ligation (see Figure S6). The orbital energy of LUMO was calculated to be -0.094 a.u. by DFT, which is lower than that of Cp*Rh(cod) and comparable to that of Cp*RhCl₂ (Figure 4).^[17] The lowered LUMO level of [2]+ was further confirmed by cyclic voltammetry (Figure 5). Monovalent rhodium complexes, 1 and Cp*Rh(cod), were electrochemically inert in a range from -1.0 to -1.7 V. On the other hand, the In-Rh complex [2][InCl₄] exhibited an irreversible reduction peak at $E_{\rm pc}$ = -1.41 V vs. Fc⁺/Fc, which was a similar value to that of $[Cp^*RhCl_2]_2$ ($E_{pc} = -1.38$ V vs. Fc⁺/Fc). These results strongly support that the In-Rh complex [2]+ has similar electronic and redox properties to those of trivalent Cp*Rh^{III} complexes rather than the original monovalent Rh^I complex 1 through complexation with the Z-type In-metalloligand.



LV1(In, s 95%, p 5%), occ = 0.79

Figure 3. NBO analysis of [2]+. a) Donor and acceptor orbitals of [2]+ for the In–Rh bond. LP denotes a lone pair orbital, LV denotes a lone vacancy (unoccupied valence orbital), and occ denotes the electron occupancy. b) Stabilization energies by the Donor-Acceptor interaction.



Figure 4. Energy levels of frontier molecular orbitals of [2]+ and standard Cp*Rh complexes.



Figure 5. Cyclic voltammetry of 1, [2][InCl₄], Cp*Rh(cod), and [Cp*RhCl₂]₂ in CH_2Cl_2 (0.1 M NBu₄PF₆, 1 mM substrate, 100 mV/sec).

The unique electronic and redox properties of the In-Rh complex invoked us to test its catalytic reactivity for the chelation-assisted oxidative sp²C-H bond functionalization reactions of arenes, which are usually catalyzed by Cp*Rh^{III} complexes.^[18] After extensive screening, the In-Rh complex [2][InCl₄] was found to catalyze the sp²C–H amidation reaction of benzo[h]quinoline with 1.5 equiv. of TsN₃ to afford an N-aryl tosylamide derivative 3 in good yield (Entries 1, Table 1).[19] Counter anions did not affect the reactivity (Entry 2). CpRh^I complexes have rarely been reported to be active for this type of reactions,^[20] and indeed, the In-free, pyridine-tethered 1 and Cp*Rh(cod) did not catalyze the reaction at all (Entries 3 and 4). Importantly, in situ formation of the In-Rh complex by mixing 1 and InCl₃ was also effective (Entry 7), and the catalytic activity was on the same level with that of the standard catalyst system for this reaction, Cp*RhCl₂/AgSbF₆ (Entry 6).^[19a]. This method enables easy screening of Z-type metalloligands for optimization reaction conditions. Addition of AICI3, GaCI3, or of trifluoromethanesulfonic acid (TfOH) resulted in low yield of 3 or no reaction, thus demonstrating crucial role of InCl₂⁺ as a metalloligand (Entries 8-10). The combination of Cp*Rh(cod) and InCl₃ was also not effective, giving the amidation product 3 in poor yield (Entry 11). These results clearly demonstrated that both InCl2⁺ and the pyridine-tethered cyclopentadienyl ligand were necessary to turn on the C-H activation catalysis of the rhodium metal in 1.

Preliminary investigation on substrate generality disclosed that the In-Rh catalyst system was also applicable to the reaction of various 2-arylpyridines (**5a-c**, Table 2). Not only TsN₃, but also 3-phenyl-1,4,2-dioxazole-5-one **4** was employable as a nitrene source to give *N*-aryl benzamide derivatives **6a-c** in moderate to good yield. Furthermore, pyrimidine was also effective as a directing group for this reaction. *N*-tosyl amidation of *N*-pyrimidyl indole proceeded selectively at 2-position to afford **7a**. Selective double amidation at both *ortho*-positions of 2-arylpyrimidine was also achieved using 3 equiv. of TsN₃ to give **7b** in good yield. Although the reaction mechanism is not clear yet (see the SI for some preliminary investigations), this is the

first example of tuning transition metal catalysis for C–H activation by a Z-type metalloligand. Detailed mechanistic studies are ongoing in our group and will be reported in due course.

Table 1. C-H amidation catalyzed by In-Rh 2



[a] NMR yield. [b] Isolated yield. [c] 2.5 mol%. [d] 2.5 mol% $[Cp^{*}RhCl_{2}]_{2}$ and 10 mol% AgSbF_6. [e] 10 mol%.

Table 2. Generality of substrates



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[a] TsN₃ as a nitrene source. [b] **4** as a nitrene source. [c] 20 mol% of THF was added. [d] NMR yield. [e] 3.0 equiv. of TsN₃ was used.

In conclusion, we have developed new CpRh complexes having a supported Z-type In-metalloligand that turns on rhodium catalysis for sp²C–H bond activation. This study demonstrated powerful utility of the Z-type metalloligand for tuning transition metal catalysis by seemingly changing the oxidation state of the transition metal. Application of this strategy to other reactions and Cp metal complexes is in progress toward further development of organometallic and synthetic chemistry.

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Rhodium complexes having an In-metalloligand are successfully synthesized utilizing a pyridine-tethered cyclopentadienyl ligand as a support for an In–Rh bond. The In-metalloligand dramatically changes the electronic and redox properties of the rhodium metal, awakening its catalysis for an sp²C–H bond activation reaction.

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