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Conjugate Addition vs Heck Reaction: A Theoretical Study on Competitive Coupling Catalyzed by Isoelectronic Metal (Pd(II) and Rh(I))

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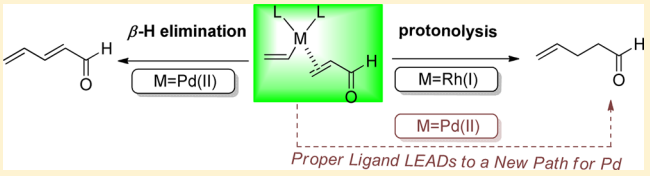
Supporting Information

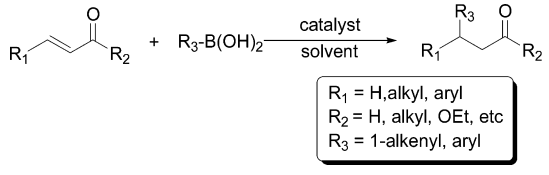
ABSTRACT: Density functional theory studies have been carried out to investigate the mechanism of the Pd(II)(bpy)- and Rh(I)(bpy)-catalyzed conjugate additions and their competitive Heck reactions involving α,β-unsaturated carbonyl compounds. The critical steps of the mechanism are insertion and termination. The insertion step favors 1,2-addition of the vinyl-coordinated species to generate a stable *C*-bound enolate intermediate, which then may isomerize to either an oxa-π-allyl species or an *O*-bound enolate. The termination step involves a competition between β-hydride elimination, leading to a Heck reaction product, and protonolysis reaction that gives a conjugate addition product. These two pathways are competitive in the Pd(II)-catalyzed reaction, while a preference for protonolysis has been found in the Rh(I)-catalyzed reaction. The calculations are in good agreement with the experimental observations. The potential energy surface and the rate-determining step of the β-hydride elimination are similar for both Pd(II)- and Rh(I)-catalyzed processes. The rate-determining steps of the Pd(II)- and Rh(I)-catalyzed protonolysis are different. Introduction of an N- or P-ligand significantly stabilizes the protonolysis transition state via the O-bound enolate or oxa-π-allyl complex intermediate, resulting in a reduced free energy of activation. However, the barrier of the β-hydride elimination is less sensitive to ligands. For the Rh(I)-catalyzed reaction, protonolysis is calculated to be more favorable than the β-hydride elimination for all investigated N and P ligands due to the significant ligand stabilization to the protonolysis transition state. For the Pd(II)-catalyzed reaction, the complex with monodentate pyridine ligands prefers the Heck-type product through β-hydride elimination, while the complex with bidentate N and P ligands favors the protonolysis. The theoretical finding suggests the possibility to control the selectivity between the conjugate addition and the Heck reaction by using proper ligands.



INTRODUCTION

Among the powerful tools for carbon−carbon bond formation, the conjugate addition of organoboron reagents to α,β-unsaturated carbonyl compounds (Scheme 1) has attracted considerable attention for the stability of the substrates in aqueous solvents, tolerance of a broad range of functional groups, and prospects for asymmetric syntheses.[1] Catalysis of the conjugate addition has been mainly focused on rhodium(I)-based complexes since 1997,[2] when Miyaura reported the first asymmetric 1,4-addition of aryl- and alkenylboronic acids to α,β-unsaturated ketones catalyzed by a phosphine−rhodium complex.[3] In recent years, the Rh-catalyzed conjugate addition has been extended to a wide variety of Michael acceptors, such as α,β-unsaturated ketones,[4] esters,[5] and aldehydes.[6]

Scheme 1. Catalyzed conjugate Addition of Aryl- or Alkenylboronic Acids to α,β-Unsaturated Carbonyl Compounds



By contrast, the use of Pd(II) complexes in conjugate additions has been less developed. This is in part due to the propensity of palladium catalysts to promote a competitive formation of Heck-type products.[7] Given the lower cost and diversity of Pd, Pd(II)-catalyzed conjugate additions have attracted more attention, and many successful cases have been discovered in the last two decades.[8−10] Lu et al. were the first to develop $Pd(OAc)_2$/bipyridine(bpy) as an efficient catalyst for the

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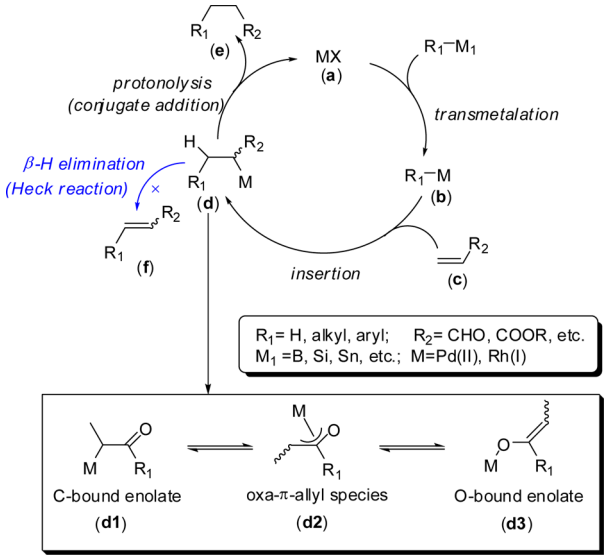
addition of vinylpalladium intermediates, generated by the acetoxypalladation of alkynes, to α,β-unsaturated aldehydes and ketones.[10a,b] Miyaura[9] and Lu[10c−e] reported the addition of arylboronic acids to enones catalyzed by Pd(II)−phosphine and Pd(II)−bpy complexes, respectively.

Recently, several groups reported competitive reactions between Rh(I)-catalyzed Heck reaction and conjugate addition at different reaction conditions, e.g., solvents,[11a,c,d] substrates,[11b] ligands,[11e,h,i] pH,[11f] and reaction sites.[11g] These findings suggest that by adjusting the reaction conditions, especially tuning the ligands, it is possible to control the selectivity between conjugate addition and Heck reaction in the Pd(II)- or Rh(I)-catalyzed reactions. However, the mechanisms of the reaction are not well enough understood to rationally predict which ligands will prefer what reaction pathway.

As shown in Scheme 2, the general catalytic cycle of a Pd(II)/Rh(I)-catalyzed conjugate addition involves transmetalation,

Scheme 2. Catalytic Cycle for Pd(II)/Rh(I)-Catalyzed Conjugate Addition



insertion, and protonolysis.[2b] The cycle is initiated by a Pd(II)/Rh(I) complex (**a**), which undergoes transmetalation to yield an aryl or 1-alkenyl Pd(II)/Rh(I) intermediate (**b**). The insertion of an α,β-unsaturated substrate into (**b**) leads to a *C*-bound enolate (**d**, **d1**), which is in equilibrium with both an oxa-π-allyl species (**d2**) or an *O*-enolate (**d3**). The resulting enolate is then protonated to give addition product (**e**) and regenerate the Pd(II)/Rh(I) complex (**a**). It is also possible to obtain a Heck-type product (**f**) from the enolate by a competitive β-hydride elimination reaction, which is a side reaction and should be suppressed. It is generally accepted that a rhodium catalyst predominantly forms *O*-bound enolates that can readily undergo protonolysis to generate conjugate addition products.[12,13a,b] The mechanism of the Rh(I)-catalyzed conjugate addition of aryl boronic acids to enones has been well established by Hayashi et al. (Scheme 2).[2b,13a] Intermediates such as phenylrhodium (**b**), oxa-π-allylrhodium (**d2**), and hydroxorhodium complexes were observed in NMR spectroscopic studies.[13] The *O*-bound and oxa-π-rhodium enolates (**d3**, **d2**) were also detected in other stoichiometric transformations.[12,14] As for the Rh(I)-catalyzed Heck reaction, though the mechanism has been hypothesized to be analogous to that of the Pd(II)-catalyzed one in few reports, there is no experimental evidence of the relevant intermediates yet.[11b,e−i]

Different from the Rh(I) catalyst, a palladium catalyst is believed to form *C*-bound enolates in the insertion step that can easily undergo β-hydride elimination to give Heck-type products.[9a,10c] In contrast to the Pd(II)-catalyzed Heck reaction and the Pd(0)-catalyzed oxidative addition reaction,[7,15−17] mechanistic studies of the Pd(II)-catalyzed conjugate addition are relatively rare. Miyaura characterized the transmetalation intermediate (**b**) in the 1,4-addition of arylboronic acids or arylsiloxanes to enones by X-ray analysis and proposed a catalytic cycle analogous to that of the Rh(I)-catalyzed reaction (Scheme 2).[9b] Nevertheless, since key intermediates in the latter two steps (insertion and protonolysis) have not yet been determined experimentally, the mechanism of Pd(II)-catalyzed conjugate addition is still unclear, especially regarding the form of Pd(II) enolates. Unlike the Rh(I)-catalyzed cycloaddition, enolates prefer to coordinate to palladium either through the carbon atom or in the chelating oxa-π-allyl fashion,[18−21] even though the Pd(II) *O*-bound enolates are supposed to play a fundamental role in protonolysis. It is therefore speculated that the addition to the enones generates the Pd(II) *C*-bound enolate (**d1**), which would be in equilibrium with *O*-bound enolate (**d3**) and oxa-π-allyl species (**d2**) in solution.[9,10]

Recently, a number of computational mechanistic studies focused on the Pd(II)-catalyzed Heck reaction[22] and the Pd(II)- or Pd(0)-catalyzed oxidative addition.[23,24] In the case of the Pd(II)/Rh(I)-catalyzed conjugate reaction, theoretical studies are rare.[25,26] Mauleon et al. reported a density functional theory (DFT) study of the insertion step of Rh(I)-catalyzed asymmetric addition of boronic acids to sulfones.[25] Miyaura reported a DFT study of the Pd(II)-catalyzed substrate coordination in enantioselective 1,4-additions of Ar_3Bi, $[ArBF_3]K$, and $ArSiF_3$ to enones.[26a] Baba et al. calculated two transition states for the Rh(I)-catalyzed β-elimination step in the reaction of borylporphyrins with esters using DFT methods to study site selectivity.[11g] Very recently, Houk investigated the Pd(II)-catalyzed addition of arylboronic acids to enones and reported the details of the three steps involved in the mechanism, i.e., transmetalation, alkene insertion, and protonolysis.[26b] However, there are few systematic comparisons between Pd(II) and Rh(I) catalyzed conjugate addition. Moreover, metal- or ligand-directed selectivity on protonolysis and β-hydride elimination require a comprehensive computational study as well, but such studies have not been reported yet.

In the present work, a DFT study of the reaction mechanism has been carried out to (1) obtain detailed structural and energetic information about the insertion and termination steps of the Pd(II) and Rh(I)-catalyzed conjugate addition, (2) elucidate the differences between Pd(II)- and Rh(I)-mediated β-hydride eliminations and protonolysis in the termination process of the catalytic cycle, (3) characterize the key enolate intermediates to facilitate termination steps, and (4) understand the effect of metal and ligand on the competition between β-hydride elimination and protonolysis.

■ COMPUTATIONAL DETAILS

Since the previous experimental mechanistic studies of Pd(II)-catalyzed conjugate addition confirmed the transmetalation process by the X-ray crystal structures of the aryl-Pd(II) intermediates (b),[9b] we focused on the insertion step and the termination reactions (including β-hydride elimination and protonolysis, Scheme 2), which determine chemo- and regioselectivity. As shown in Scheme 3, the models for the reagents were

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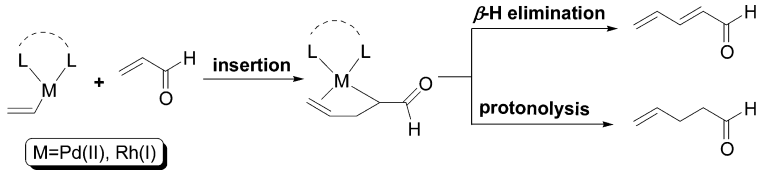
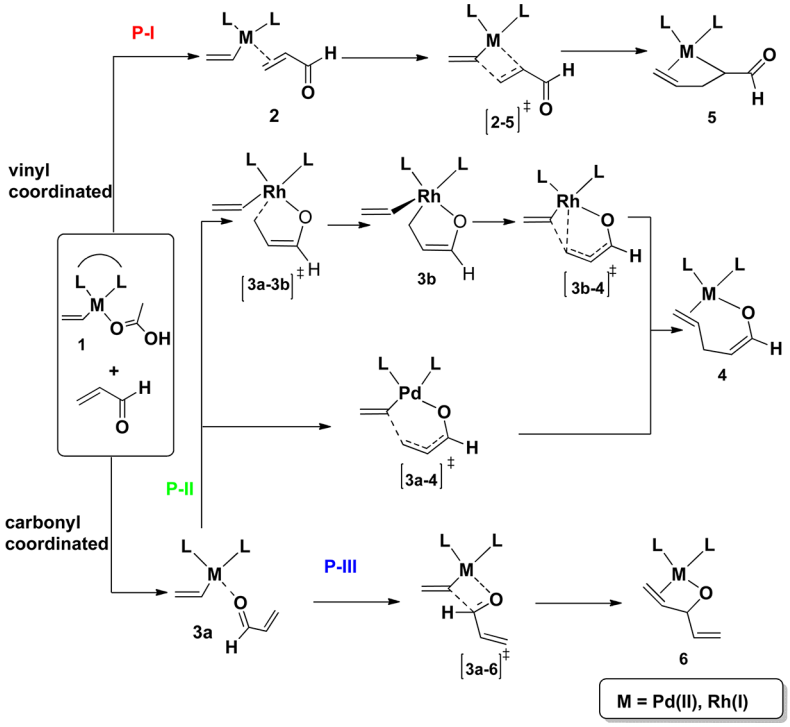
Scheme 3. Simplified Models for the Computational Study of the Pd(II)- and Rh(I)-Catalyzed Conjugate Addition



Scheme 4. Plausible Insertion Pathways of Vinyl Coordinated 1,2-Addition, Carbonyl Coordinated 1,4-Addition, and Nucleophilic 1,2-Addition Initiated from the HOAc-Solvated Species (Charges Are Omitted for Clarity)



simplified as the vinyl-Pd(II)/Rh(I) complex and acrolein, which contain the key functional parts of the reaction with a smaller computational cost. 2,2-Bipyridine (bpy) was used as the ligand for M according to Lu's previous experiment.[10] Other N and P ligands, which have also been reported in Pd(II)-catalyzed addition,[9,10] were calculated to illustrate ligand effect on the termination reactions. Rh(I) is ligated to the same ligands for comparison.

All calculations were carried out with the Gaussian 03 program package.[27] Molecular geometries were fully optimized with the B3LYP method.[28] The LanL2DZ basis sets with effective core potentials (ECPs) were employed for Pd and Rh,[29] and the 6-31G* basis set[30] was used for H, C, N, O, and P. Harmonic vibrational frequency calculations at the same level of theory were performed to obtain thermal corrections and confirm whether an optimized structure as a minimum or transition state. Single-point energies were calculated using larger basis sets (6-311+G** basis set for H, C, N, O, and P) for Pd(II)(bpy) complexes in order to examine the effect of basis sets. Solvent effects were estimated by the integral equation formulation of the polarized continuum model (IEFPCM),[31] using simple united atom topological model radii with the default parameters for THF. The energies given throughout the paper are Gibbs free energy and enthalpy values computed at 298 K in kcal/mol

RESULTS AND DISCUSSION

Insertion Step: 1,2-Addition versus 1,4-Addition. *a. Vinyl-Coordinated Pathway and Carbonyl-Coordinated Pathway in Pd(II)-Catalyzed Reaction.* α,β-unsaturated carbonyl compounds may coordinate to the vinyl−Pd(II) complex with either the vinyl or the carbonyl moiety. Thus, the insertion reaction can proceed via three plausible pathways, namely, P−I for 1,2-addition (**2** → **5**) of the vinyl coordinated species, P−II for 1,4-addition of the carbonyl coordinated speices (**3a** → **4**), and P−III for 1,2-addition of the carbonyl coordinated species (**3a** → **6**) (Scheme 4).

Figure 1 displays the relative free energy profiles for the Pd(II)-catalyzed insertion step with bpy as ligand. Pd(II) prefers to coordinate with the carbonyl oxygen (**3a**) over the alkene C═C double bond (**2**) by 10.0 kcal/mol. Nevertheless, **2** is much more reactive than **3a**. Transition state [**2**−**5**]‡ was calculated to be more stable than [**3a**−**4**]‡ and [**3a**−**6**]‡ by 10.3 and 5.4 kcal/mol, respectively. Thus, the vinyl-coordinated P−I pathway is much more favorable than the carbonyl-coordinated pathways.

Geometries of the key transition states and intermediates in the Pd(II)-catalyzed insertion reaction are illustrated in Figure 2. [**2**−**5**]‡ with the M−C3−C4−C5 four-membered ring is an early transition state with a C4−C5 bond length of 2.14 Å. Such a long distance does not lead to a significant strain for the four-membered ring. As a result, this transition structure is relatively stable. In comparison, the six-membered-ring state [**3a**−**4**]‡ is a relatively late transition state with a shorter C4−C5 bond length of 1.90 Å. Since the C2−C3 bond length (1.39 Å) is of double-bond character, the O1−C2−C3−C4 dihedral angle is −15.0°, indicating that the conjugation of acroleine has been weakened. This is induced by the strain of the forming the six-membered-ring.

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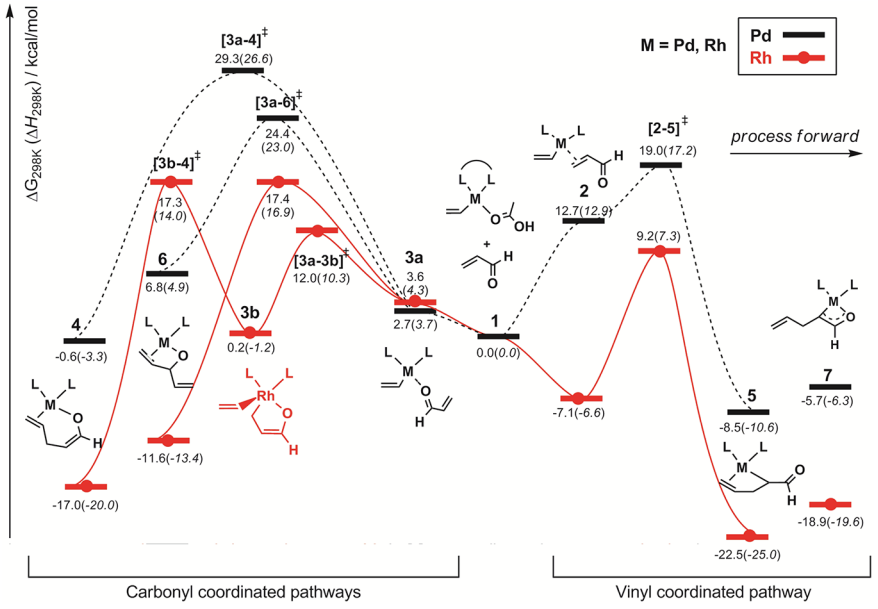

Figure 1. Relative free energies (enthalpies) of the structures included in the insertion part shown in Scheme 4 for both Pd(II)(bpy)- and Rh(I)(bpy)-catalyzed processes; charges are omitted for clarity.

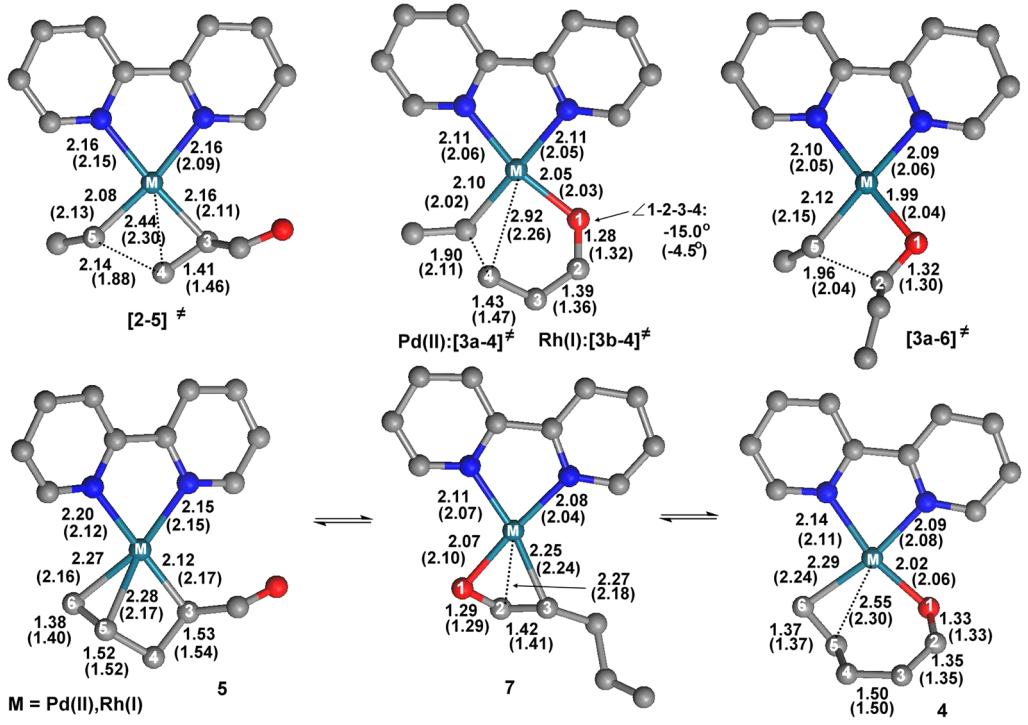

Figure 2. Optimized geometries of key structures of transition states and intermediates in the Pd(II)(bpy)- and Rh(I)(bpy)-catalyzed insertion reaction. Distances are in angstroms, and those related to Rh(I) catalysis are shown in brackets; hydrogen atoms are omitted for clarity.

In [**3a**−**6**]‡, the C2−C5 distance is shorter than the C4−C5 distance of [**2**−**5**]‡ but longer than C4−C5 of [**3a**−**4**]‡. The higher energy of [**3a**−**4**]‡ or [**3a**−**6**]‡ with respect to [**2**−**5**]‡ is also partially attributed to the relative stabilities of the corresponding products according to Hammond's postulate. It is noted that the free energy of activation (24.4 kcal/mol) for the formation of **6** is also accessible under the reaction conditions, implying that nucleophilic addition to a carbonyl may occur in the absence of a conjugated C═C bond, where no competition with (**2** → **5**) reaction is possible. This hypothesis is supported by Lu's experimental findings that Pd(II)(bpy) and Pd(II)(BINAP) complexes can catalyze symmetric and asymmetric intermolecular nucleophilic additions to carbonyl and nitrile groups.[32,33]

b. Differences between the Pd(II)- and Rh(I)-Catalyzed Reactions in Insertion Pathways. Similar to Pd(II), there are also three possible pathways for Rh(I)-catalyzed reaction (Scheme 4). The pathways P−I (**2** → **5**) and P−III (**3a** → **6**, **3a** is the Rh(I)-intermediate) are analogous to that of Pd(II)-catalyzed insertion step. However, there are some differences in pathway P−II (**3a** → **4**), where a five-coordinated intermediate

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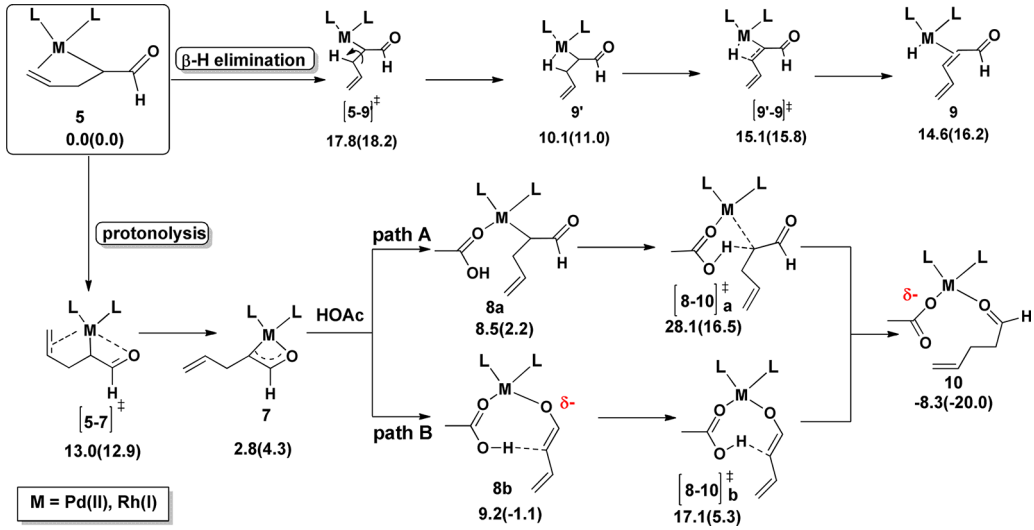
Scheme 5. Plausible M-Catalyzed (M = Pd(II) and Rh(I)) Termination Pathways, Along with the Relative Gibbs Free Energies (Enthalpies) in kcal/mol of the Relevant Structures in Pd(II)-Catalyzed Reactions[a]



[a]Pathways C and D have been omitted for clarity; see Scheme S1 in the Supporting Information for details.

3b was located (the lowest energy in three isomers of **3b** was shown in Figure 1). Since the oxidation state of Rh(I) is lower than that of Pd(II), it is easy to generate the Rh(III)-intermediate (**3b**) via a transition state [**3a**−**3b**]‡, which then undergoes reductive elimination to form the Rh(I)-intermediate (**4**). The pathway P−I (**2** → **5**) is also the most favorable pathway for the Rh(I)-catalyzed insertion (Figure 1).

As shown in Figure 1, complex **1** of Pd(II) and Rh(I) preferrs different binding modes with acroleine by ligand exchange. Rh(I) prefers to coordinate with electron-deficient vinyl to form **2**, while Pd(II) favors coordination with carbonyl in the first step to form **3a** due to the different electronic nature of Pd(II) and Rh(I). Although the electron configuration of both is 4d,[8] the charge of Pd(II) is higher. The Pd(II) *d* orbitals are stabilized by the higher nuclear charge; thus, Pd(II) is a better Lewis acid than Rh(I) with the latter being better for π back-donation to vinyl.[1c] Pd(II) more easily coordinates with the O of C═O, which is a better Lewis base than C═C. The barrier of the pathway P−I (**2** → **5**) for Rh(I) catalysis is lower than Pd(II) catalysis by 2.7 kcal/mol, suggesting that Rh(I) can stabilize the insertion reaction of the 1,2-Michael addition.

As shown in Figure 2, the coordination of C3═C4 to Rh(I) (Rh−C3: 2.11 Å, Rh−C4: 2.30 Å) has shorter bond lengths than in the case of Pd(II) (Pd−C3: 2.16 Å, Pd−C4:2.44 Å) for [**2**−**5**]‡ (Figure 2). This might lead to the asymmetric coordination between Rh and N atoms of bpy (Rh−N: 2.15 and 2.09 Å). In the case of [**3b**−**4**]‡, the O1−C2−C3−C4 dihedral angle of Rh(I) complex is smaller (−4.5°) than that of Pd(II) one (−15.0° in [**3a**−**4**]‡). The conjugation effect of O1−C2−C3−C4 stabilizes this six-membered-ring transition state of Rh(I)−catalyzed P−II (**3b** → **4**) compared to Pd(II)-catalyzed one, leading the lower activation energy for Rh(I). As for the pathway P−III (**3a** → **6**), the Rh(I)-catalyzed reaction shows longer M−O1, M−C5, and C4−C5 bond lengths in [**3a**−**6**]‡, which decreases the strain of the four-membered-ring and stabilizes the transition state. Therefore, the barriers of both (**3a** → **4**) and (**3a** → **6**) of Rh(I)-catalyzed process are also lower than those of Pd(II) one.

*c. Stablities of Enolate Intermediates **5**, **4**, and **7** between the Pd(II)- and Rh(I)-Catalyzed Reactions.* The intermediates **5** and **4** shown in Figure 2 are the *C*- and *O*-bound enolates formed in the insertion reaction, respectively. The intermediate **7** represents the oxa-π-allyl species. In case of the *O*-bound enolate (**4**), the Rh(I) complex is more stable than that of Pd(II) due to the stronger coordination between Rh(I) and C5═C6 than that of Pd(II), which stabilizes the seven-membered-ring structure. As for the oxa-π-allyl species **7**, the Rh(I) complex has shorter M−C2 bonds than that of Pd(II), indicating Rh(I) favors the metal-π species. In the *C*-bound enolate **5**, the Pd−C3 bond is shorter than that of Rh−C3 (Pd−C3: 2.12 Å; Rh−C3: 2.17 Å), but the coordination between C5═C6 and Rh(I) (Rh−C5/C6: 2.16/2.17 Å) is shorter than that of Pd(II) (Pd−C5/C6: 2.27/2.28 Å). As shown in Figure 1, the free energy of formation for the Rh(I) *C*-bound enolate **5** (31.7 kcal/mol) is also higher than in the case of Pd(II) (27.5 kcal/mol).

Among **5**, **7**, and **4**, the *C*-bound enolate **5** is the most stable enolate intermediate for Pd(II). This result is in line with the experimental finding that Pd(II) *C*-bound enolate structure is more favorable.[18−21] Similarly, a stable *C*-bound enolate intermediate is also obtained as the relative stable product for the Rh(I)bpy-catalyzed insertion. Therefore, both Pd(II) and Rh(I)-catalyzed insertion step converged to a *C*-bound enolate intermediate for the following termination steps, which will involve a transfer from *C*-bound enolate to oxa-π-allyl species and *O*-bound enolate (see following discussion of protonolysis pathways for details). This process is in agreement with the detectable oxa-π-allyl species and *O*-bound enolate in Rh(I)-catalyzed reaction.[12−14] From the most stable insertion product **5**, the reaction may proceed forward to the termination step.

Termination Step: β-Hydride Elimination versus Protonolysis. *a. β-Hydride Elimination Pathway in the Pd(II)-Catalyzed Reaction.* The possible pathways for the competitive β-hydride elimination and protonolysis are shown in Scheme 5, along with the relative Gibbs free energies of the relevant structures in Pd(II)-catalyzed reactions. Based on previous reports regarding the mechanism of β-hydride elimination,[34] a traditional four-membered-ring transition state [**9′**−**9**]‡ was proposed, but it was not found to be the rate-determining step in some calculations. To achieve such a transition structure, the β-hydrogen in *C*-bound enolate **5** needs to reorient toward the Pd(II) center via an isomerization step [**5**−**9′**]‡, in which

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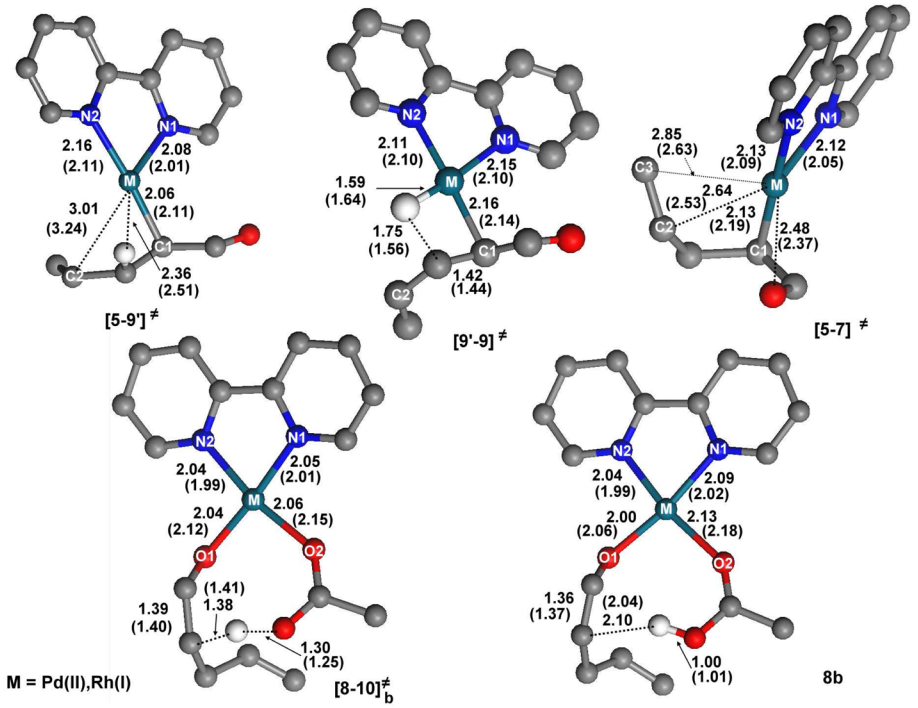

Figure 3. Calculated geometries of important transition states and intermediates of the Pd(II)(bpy)- and Rh(I)(bpy)-catalyzed termination reactions. Distances are in angstroms, and those related to Rh(I) catalysis are shown in brackets; hydrogen atoms in the backbones are omitted, charges have been omitted for clarity.

C5−C6 Pd coordination is replaced by a β-H agostic interaction. The activation energy of the Pd−H agostic bond formation ([**5**−**9′**]‡) is calculated to be 2.7 kcal/mol higher than that of the β-H elimination step ([**9′**−**9**]‡). Therefore, [**5**−**9′**]‡ becomes the rate-determining step for this β-hydride elimination pathway. This result indicates that it is important to provide a vacant site to the β-hydrogen atom in β-hydride elimination providing an experimentaly verifyable hypothesis how to inhibit or facilitate this reaction.

As depicted in Figure 3, in the transition state [**9′**−**9**]‡, the Pd−H bond length (1.59 Å) is close to that of product **9** (1.56 Å), showing that [**9′**−**9**]‡ is a late transition state.

b. Protonolysis Pathways in the Pd(II)-Catalyzed Reaction. We used HOAc, the proton source for the protonolysis used experimentally,[10] in our calculations. Four possible pathways initiated from the intermediate **5** were considered. All of them initiate from the isomerization of **5** to **7**, which is an oxa-π-allyl complex and ready for incorporating HOAc with different fashions. These different orientations determined the following protonation as shown in Schemes 5 and S1 (Supporting Information).

Pathway A is not a plausible mechanism due to the high activation energy (28.1 kcal/mol). The stable intermediate, aldehyde **10** in pathway B, is generated from the enolate aided by HOAc. In addition, the activation energy (17.1 kcal/mol) is accessible. This pathway B is consistent with Houk's work using methanol as proton donor.[26b] As shown in Scheme S1 (Supporting Information), pathways C and D involve the formation of related enol as intermediates. However, their enol-coordinated products **10c** and **10d** are much less stable (by 11.9 and 18.1 kcal/mol, respectively) than **10** and can eventually transform to the thermochemically stable aldehyde-coordinated product **10** via rate determination [**8**−**10**]$_b^{‡}$ of pathway B. Therefore, [**8**−**10**]$_b^{‡}$ of pathway B can be chosen as a key transition state in the following discussions regardless of uncertain pathways from B, C, or D.

The key transition states and intermediates in Scheme 5 are shown in Figure 3. The transition state [**5**−**7**]‡ is relatively stable compared to [**5**−**9**]‡, in line with the relative stability of oxa-π-allyl complex **7** and agostic complex **9**. During the transformation from the *O*-bound enolate intermediate **8b** to aldehyde **10b**, the Pd−O1 and Pd−O2 bond lengths are changed from 2.00 and 2.13 Å in **8b** to 2.04 and 2.06 Å in the transition state [**8**−**10**]$_b^{‡}$, respectively. At the same time, the *trans* coordination between Pd and bpy is strengthened with the Pd−N1 bond being shorter from 2.09 to 2.05 Å. Thus, the introduction of the bpy ligand increases the stability of this transition state.

On the basis of the above discussion, we can conclude that the termination involves two competitive steps, the β-hydride elimination and protonolysis. The β-hydride elimination leads to the Heck-type product through a traditional four-membered-ring transition state, whereas the protonolysis is a process where the proton transfer results in the conjugate addition product via an *O*-enolate intermediate. The barrier of the protonolysis of Pd(II)-catalyzed reaction is lower than that of the β-hydride elimination by 0.7 kcal/mol (2.8 kcal/mol in solution, see details in Table 1) and 12.9 kcal/mol in free energy and enthalpy, respectively. The protonolysis is thus relatively more favorable than β-hydride elimination with bpy as ligand, agreeing well with the experimental findings.[10]

c. Differences between the Pd(II)- and Rh(I)-Catalyzed Competitive Reactions in Termination Pathways. In the classic view of organometallic chemistry, Pd(II) species is an electrophilic species that favors the well-known C−C bond forming reactions such as the Heck reaction, the Suzuki reaction, the carbonylation, and the Sonogashira coupling.[35,36] In contrast, the Rh(I) species is generally considered to be nucleophilic, which prefers the conjugate addition, the carbonyl addition, or the

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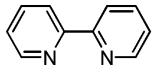
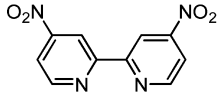
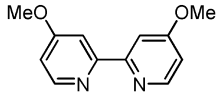
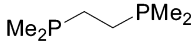
Table 1. Energy Barriers for the Pd(II)- and Rh(I)-Catalyzed Competitive β-Hydride Elimination and Protonolysis Process with Different Ligands (ΔG/kcal/mol)

Entry	Ligand	β-hydride elimination				Protonolysis			
		Pd(II)[c]		Rh(I)[c]		Pd(II)[d]		Rh(I)[e]	
		ΔG_g[a]	ΔG_s[b]	ΔG_g[a]	ΔG_s[b]	ΔG_g[a]	ΔG_s[b]	ΔG_g[a]	ΔG_s[b]
1	2 HOAc	23.4	25.9	21.9[b]	23.9	31.3	32.4	38.1	38.8
2		17.8	20.2	22.2	24.0	17.1	17.4	15.9	18.5
3		18.7	21.4	20.8	21.4	17.9	19.3	12.0	12.8
4		16.6	18.9	23.5	22.7	16.8	16.7	18.3	20.7
5		18.8	21.6	24.0	25.2	21.9	22.0	18.3	19.1
6		14.4[f]	18.0[f]	15.0	17.1	14.1	15.3	10.3	12.1
7	2 PMe_3	9.1[f]	12.1[f]	-	-	11.9	13.7	-	-

[a]Relative Gibbs free energies in gas phase. [b]Relative Gibbs free energies corrected in solvent phase, see Table S3 for details. [c]$[\mathbf{5-9'}]^{\ddagger}$ as a rate-determining transition state. [d]$[\mathbf{8-10}]_b^{\ddagger}$ as a rate-determining transition state. [e]$[\mathbf{5-7}]^{\ddagger}$ as a rate-determining transition state. [f]$[\mathbf{9-9'}]^{\ddagger}$ as a rate-determining transition state.

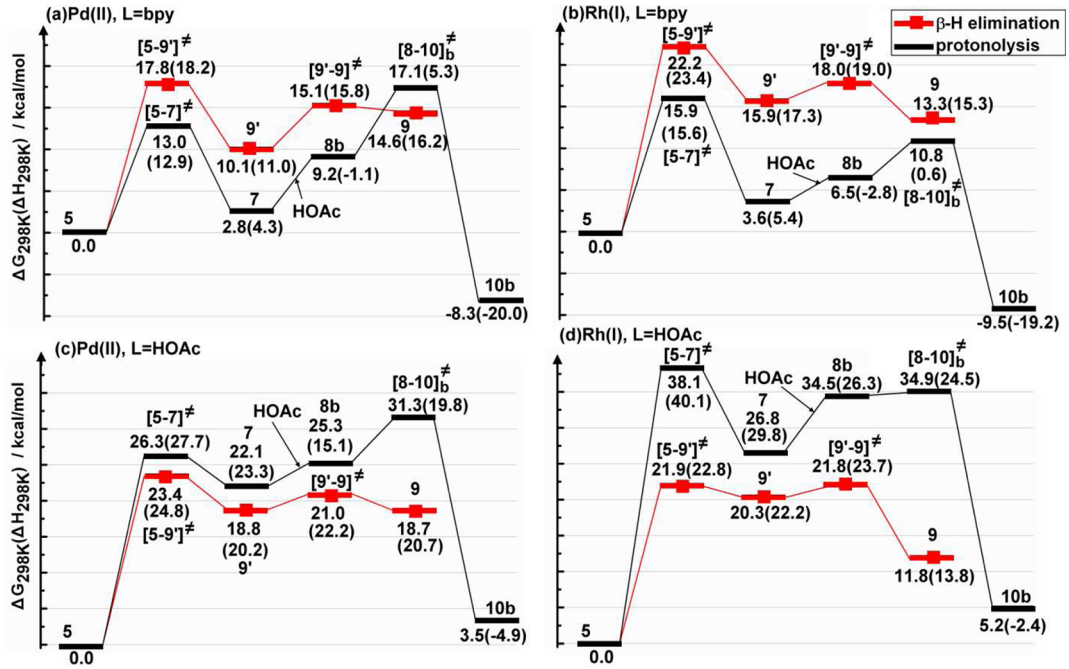


Figure 4. Relative free energy profiles of termination steps for Pd(II)- and Rh(I)-catalyzed reactions in gas phase with ligands bpy and HOAc, respectively; structural number shown as Scheme 5.

Mannich reaction.[2] Our computional results suggest that it is possible to switch the preference of Pd(II)- and Rh(I)-catalyzed reactions by adjusting ligands. To further study the competition between the Heck reaction and the conjugate addition, we calculated the termination pathways of the Rh(I)(bpy)-catalyzed reactions. Similar to those of the Pd(II)-catalyzed reaction, both β-hydride elimination ($\mathbf{5} \rightarrow \mathbf{9}$) and protonolysis ($\mathbf{5} \rightarrow \mathbf{10}$) were studied, as shown in Scheme 5.

The relative free energy profiles of the termination steps for the Rh(I)(bpy)-catalyzed reaction are shown in Figure 4b. The barrier for the rate-determining step for the protonolysis of the Rh(I) catalyzed reaction ($[\mathbf{5-7}]^{\ddagger}$) is lower than that for the β-hydride elimination ($[\mathbf{5-9}]^{\ddagger}$) by 6.3 kcal/mol, indicating that protonolysis is much more favorable for the Rh(I) system. This is also consistent with the experimental observation that the conjugate addition reaction is predominant in Rh(I)-catalyzed reactions.[2] As depicted in Figure 4a,b, the *O*-bound enolate $[\mathbf{8-10}]_b^{\ddagger}$ is the rate-determining transition state in the Pd(II)-catalyzed protonolysis. However, for Rh(I), $[\mathbf{8-10}]_b^{\ddagger}$ is a relatively early transition state with shorter O−H and longer H−C distances than in the case of Pd(II) (Figure 3). This difference reduces the energy barrier of the step ($\mathbf{8b} \rightarrow \mathbf{10}$) for Rh(I)-catalyzed reaction. Thus, $[\mathbf{8-10}]_b^{\ddagger}$ is no longer the rate-determining transition state in the Rh(I)-catalyzed protonolysis. The late transition

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state $[\mathbf{5}-\mathbf{9}']^{\ddagger}$ is the rate-determining transition state of the β-hydride elimination for both Pd(II)- and Rh(I)-catalyzed reaction. In $[\mathbf{5}-\mathbf{9}']^{\ddagger}$, the bond length of Pd−H is 2.36 Å, shorter than Rh−H (2.51 Å) (Figure 3). With respect to the electronic properties, Pd(II) prefers accepting electrons, thus it will coordinate with the hydride and undergo the β-hydride elimination more easily. Rh(I) prefers to donate electrons and coordinate strongly with the C═C bond in **5** via back-donation. As a result, complex **5** does not isomerize to **9′** by exchanging the C−C π bond to a hydride coordination and consequently disfavors the pathway for β-hydride elimination.

d. Ligand Effect on the Pd(II)- and Rh(I)-Catalyzed Termination Competitive Reactions. The discussion above suggests that bpy may play an important role in the Pd(II)-catalyzed conjugation addition. To study the ligand effect, further calculations were carried out to investigate the competition of between protonolysis and β-hydride elimination for the termination step. First, HOAc is set as the reference ligand when there is no other ligand since the reaction is conducted in HOAc.[10a,b,e]

As shown in Figure 4c,d, when Pd(II) or Rh(I) is ligated with two HOAc instead of bpy, the barriers of the β-hydride eliminations do not change significantly (5.6 kcal/mol increase for Pd(II); 0.3 kcal/mol decrease for Rh(I)). However, the barriers of protonolysis rise significantly (14.2 kcal/mol increase for Pd(II); 22.2 kcal/mol increase for Rh(I)). The β-hydride elimination thus becomes more favorable, and this tendency is difficult to be reversed due to the significant difference between the energy barriers of these two competitive steps. These findings suggest that the introduction of the bpy ligand plays a significant role in reducing the barrier of the protonolysis, but the β-hydride elimination is not that sensitive to the ligand, especially for Rh(I)-catalysis. In addition, the bpy ligand stabilizes the precursor of the conjugate addition product (**10**), which leads to the pathway (**5** → **10**) turning into a thermodynamically favored exergonic process. As a result, bpy is a ligand that favors the protonolysis reaction. The results are in good agreement with the experimental observations that bpy is crucial in suppressing the Pd(II)-catalyzed β-hydride elimination and promoting protonolysis.[10]

When other N or P ligands were chosen to replace bpy, it was found that the structural features of all species and the shape of the potential energy surface along the two competitive pathways do not change significantly (Tables S3 and S4, Supporting Information). The β-hydride elimination involves the hydride transfer from C to M, and the protonolysis includes the proton transfer between two oxygen atoms (Scheme 5). Since these processes may be influenced by solvents, the solvent effect was taken into account in our calculation (Table 1).

Table 1 lists the activation free energies for the Pd(II)- and Rh(I)-catalyzed competitive β-hydride elimination and protonolysis with different ligands. When the favored N or P ligands are coordinated to the metal, both of the β-hydride elimination and protonolysis are accelerated for both Pd(II)- and Rh(I)-catalyzed reactions. Such acceleration is more marked for the protonolysis, which may be due to the sensitivity of the *trans*-effect of ligands in the protonolysis process because the concerted charge transfer occurs on the two carbonyl oxygen (shown in Scheme 5, path B). For the same ligand, in most cases of Rh(I)-catalyzed reaction, the barrier of β-hydride elimination is higher than that of protonolysis process, while for Pd(II)-catalyzed reaction, comparable barriers are found for β-hydride elimination and protonolysis. Therefore, no matter what N or P ligand is studied in the calculations, the Rh(I)-catalyzed reaction prefers the protonolysis over the β-hydride elimination with marked barrier differences (4.0−9.0 kcal/mol) between the two competitive processes. The selectivity of the termination step for Rh(I)-catalyzed reaction is thus hard to change by the calculated N and P ligand. However, for the Pd(II)-catalyzed reactions, that is not the case. When the monodentate pyridine and PMe_3 ligands are used (entries 5 and 7), the barrier of the Pd(II)-catalyzed β-hydride elimination decreases and Heck-type product is slightly favored. This might be attributed to the flexibility of the monodentate ligand that can easily provide a vacant site to the β-hydrogen atom, which assists the hydride transfer. For the bidentate N ligands (entry 2−4), the energy barriers of the protonolysis are lower than that of the β-hydride elimination to give conjugate adducts. The same preference and a much lower barrier of the protonolysis were found for the bisphosphine ligand (entry 6), suggesting that the protonolysis may benefit more from such bisphosphine ligand due to its weak π acidity. These findings indicate that the bidentate ligands play an important role in stabilizing the transition states of the Pd(II)-catalyzed protonolysis. These above results agree well with the experimental findings that the Heck products were obtained in the Pd(II)-catalyzed process with pyridine ligands, while the conjugate adducts were isolated with the bpy or bisphosphine ligands.[9,10,32a,c] Also, the reported Rh(I)-catalyzed Heck products with P-ligands rather than the conjugate adducts were obtained by controlling reaction conditions such as solvents and substrates.[11]

The trend of substituent effects on the bipyridine ring are different in the Rh(I)- and Pd(II)-catalyzed reactions. Electron-donating groups such a methoxy reduce the barriers for the Pd(II)-catalyzed β-hydride elimination and protonolysis. In contrast, the electron-withdrawing nitro group reduces the barriers for Rh(I)-catalyzed reactions. These results are consistent with the different electronic nature of Pd(II) and Rh(I).[1b] The *d* orbital of metals are stabilized by the nuclear charge. Thus, Pd(II) favors electron-rich ligands to accept electrons and Rh(I) is more easily to coordinate with electron-deficient ligands for back-donation. This indicates that the tendency of the competitive reactions is not only affected by the property of the ligands, but also affected by the property of the metal cations.

Comparing the energy profiles and the change of the energy barriers with different ligands for both the Pd(II)- and Rh(I)-catalyzed reaction (Figure 4 and Table 1), it is noted that the significant effect in adjusting the selectivity of the β-hydride elimination vs protonolysis is the relative energy decrease of transition states $[\mathbf{8}-\mathbf{10}]_b^{\ddagger}$ and $[\mathbf{5}-\mathbf{7}]^{\ddagger}$ (Scheme 5, Figure 3), which decreased the barriers of the protonolysis in the Pd(II)- and Rh(I)-catalyzed reactions dramatically, especially for the Rh(I)-catalyzed reactions. These results also agree with the experimental findings that Rh(I) prefers to form *O*-bound enolate and oxa-π-allyl species, thus favoring the conjugate addition.[2] This suggests that the balance of protonolysis and β-hydride elimination can be altered by the introduction of different ligands, especially in the Pd(II)-catalyzed reactions. In other words, the computational findings imply that it is feasible to tuning the selectivity of the terminal competitive processes by selecting proper ligands.

■ CONCLUSIONS

The mechanism for Pd(II)/Rh(I)-catalyzed conjugate addition reaction and its competitive Heck reaction between organometallic reagents and α,β-unsaturated carbonyl compounds with

bpy as ligand was investigated through the DFT calculations. The insertion step prefers the 1,2- addition to the vinyl coordinated species to generate the *C*-bound enolate intermediate. The following termination step involves the competitive β-hydride elimination and protonolysis reactions. The rate-determining transition states of the β-hydride eliminations for both the Pd(II)- and Rh(I)-catalyzed reactions are isomerizations of *C*-bound enolate $[\mathbf{5}-\mathbf{9}']^{\ddagger}$, but the rate-determining transition state of the protonolysis are the *O*-bound enolate $[\mathbf{8}-\mathbf{10}]_b^{\ddagger}$ and oxa-π-allyl complex $[\mathbf{5}-\mathbf{7}]^{\ddagger}$ for the Pd(II)- and Rh(I)-catalyzed reactions, respectively. The introduction of ligands plays a significant role in decreasing the barrier of protonolysis but not that of the β-hydride elimination for both the Pd(II)- and Rh(I)-catalyzed reactions. The stability of the *O*-bound enolate and the oxa-π-allyl species is very important for promoting the protonolysis and inhibiting the competitive β-hydride elimination. It is therefore possible to adjust the selectivity of the terminal competitive processes by selecting proper ligands, especially for the Pd(II)-catalyzed reactions. The findings agree well with the experimental observations. The results provide insights into the detailed mechanism and origins of the competitive β-hydride elimination vs protonolysis. The mechanistic understanding may contribute to the further development of highly controllable catalyst, not only for conjugate addition and Heck reaction but also for other reactions involving β-hydride elimination or protonolysis processes.

■ ASSOCIATED CONTENT

Supporting Information

Total energies, free energies, enthalpies, and negative frequencies of the optimized structures including Pd(II) and Rh(I) with bpy and HOAc as ligand (Table S1, S2); free energies, relative free energies in the gas phase, and solvation free energy and relative free energies in THF of the optimized structures for calculating the barriers of the Pd(II)- and Rh(I)-catalyzed termination reactions with different ligands (Table S3); Cartesian coordinates of all the optimized complexes (Table S4). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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