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A Theoretical Study on the *trans*-Addition Intramolecular Hydroacylation of 4-Alkynals Catalyzed by Cationic Rhodium Complexes

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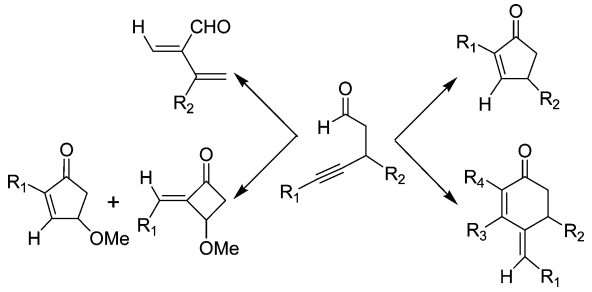

The mechanism of the intramolecular hydroacylation reaction of 4-alkynals is studied for a 4-pentynal-$[Rh(PH_2CH_2CH_2PH_2)]^+$ model system using MP2 calculations. The *endo*-cyclization to form a rhodacyclohexenone intermediate is kinetically less favorable than the *exo*-cyclization to form a rhodacyclopentanone intermediate. The kinetic preference toward the *endo*-cyclization is found to be enhanced by complexation of donor ligands (H_2CO, NCH, and HCCH). The formation of cyclopentenone product proceeds via reductive elimination from one of the two rhodacyclohexenone intermediates, whereas the formation of cyclobutanone product from the two rhodacyclopentanone intermediates requires high activation energy. Addition of an acetylene stabilizes the highly electron-poor rhodacyclopentanone intermediate generated from *exo*-cyclization and leads to an insertion to give [4 + 2] annulation product, cyclohexenone. The role of a coordinating acetone solvent in the formation of cyclopentenone product is also discussed.

Introduction

Cyclopentanones and cyclopentenones are important structural elements and synthetic intermediates for a wide variety of biologically active compounds and natural products. Consequently, a wide range of synthetic methods for the construction of cyclopentenone have been developed.[1] Although the intramolecular hydroacylation reactions of 4-alkenals catalyzed by transition-metal complexes is one of the most commonly used methods to afford cyclopentanones,[2,3] the synthesis of cyclopentenone through hydroacylation of 4-alkynals to give cyclopentenones has not been realized until more recently.[4−6]

Nicolaou's group obtained 78% yield of the unexpected intramolecular hydroacylation product cyclohexenone based on

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(1) See for example (a) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (b) Giese, S.; Kastrup, L.; Stiens, D.; West, F. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1970. (c) Morimoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Am. Chem. Soc.* **2002**, *124*, 3806. (d) Evans, P. A.; Robinson, J. E. *J. Am. Chem. Soc.* **2001**, *123*, 4609. (e) Sturla, S. J.; Buchwald, S. L. *Organometallics* **2002**, *21*, 739 and references therein.

(2) For example, see: (a) Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, 1287. (b) Fairlie, D. P.; Bosnich, B. *Organometallics* **1988**, *7*, 946. (c) Fujio, M.; Tanaka, M.; Wu, X.; Funakoshi, F.; Sakai, K.; Suemune, H. *Chem. Lett*. **1998**, 881. (d) Tanaka, M.; Imai, M.; Fujio, M.; Sakamoto, E.; Takahashi, M.; Eto-Kato, Y.; Wu, X.; Funakoshi, K.; Sakai, K.; Suemune, H. *J. Org. Chem.* **2000**, *65*, 5806. (e) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1997**, *119*, 3165.

(3) (a) Fairlie, D. P.; Bosnich, B. *Organometallics* **1988**, *7*, 936. (b) Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821. (c) Bosnich, B. *Acc. Chem. Res.* **1998**, *31*, 667 and references therein.

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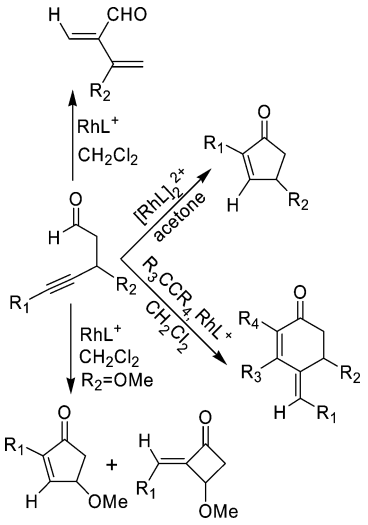
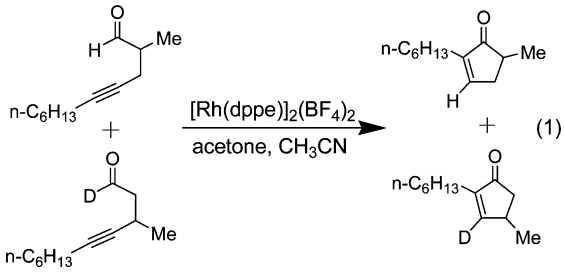


50% conversion when they attempted decarbonylation by a stoichiometric amount of Wilkinson's catalyst.[7] In 2001, Tanaka and Fu successfully developed the first catalytic intramolecular hydroacylation of 4-alkynals mediated by a cationic rhodium complex. A variety of interesting products can be obtained by changing the bisphosphine ligand, substrate, and reaction conditions (Scheme 1).[8−10] Besides the cyclopentenones, the method allows the synthesis of cyclobutanones that are difficult to access through other transition-metal-catalyzed reactions, as well as the formation of cyclohexenones in the presence of alkynes. They elegantly extended this reaction to simple kinetic resolution, desymmetrization, and parallel kinetic resolution.[8b,c] The versatility of the reaction indicates an unusual variability of the pathways depending on the exact reaction conditions that could be exploited to great effect if properly understood.

Tanaka and Fu conducted several experiments to elucidate the mechanism of the intramolecular hydroacylation of 4-alkynals.[8a,c,11] Crossover experiments showed that the hydroacylation reaction is intramolecular and the transferred hydrogen originates from the aldehyde (Scheme 2).[8a] Good

SCHEME 2



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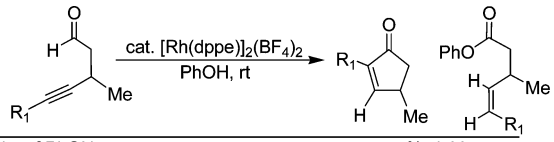

	Equiv. of PhOH	Solvent & conditions	% yield	
R_1 = *n*-C_6H_{13}	0	acetone, 24hr	36	0
	0	acetone, 100°C, 10 equiv. MeCN, 72hr	75	0
	5	acetone, 24hr	34	58
	5	CH_2Cl_2, 24hr	0	87
R_1 = Ph	0	acetone, 48hr	88	
	0	CH_2Cl_2	31[a]	

a. Major product is [4+2] annuluation/dimerization product cyclohexenones

coordinating solvents such as acetone were shown to be essential for the reaction. This was also emphasized by the fact that the addition of acetonitrile was necessary if R_1 is an alkyl group.[8a,11] Conversely, the formation of cyclopentenones was suppressed when a poorly coordinating solvent such as CH_2Cl_2 was used (Scheme 3), and only acyclic products were isolated in the presence of phenol in these cases. The transient rhodacyclopentanone intermediates could also be trapped by alcohols or electron-poor alkynes (Schemes 3).[11,12] Remarkably, when a methoxyl group was incorporated at the 3 position, the reaction proceeded well in CH_2Cl_2 and gave a mixture of cyclopentenones and cyclobutanones (Scheme 1).[8c] Finally, some amount of dienal was obtained when R_2 was an alkyl group (Scheme 1).[13]

For the intramolecular hydroacylation reaction of alkenals, the generally accepted mechanism is oxidative addition of the aldehydic C−H bond onto the metal center, which is supported by isolation and characterization of rhodium hydrido acyl intermediates.[14] The resulting hydrido acyl transition-metal complex then undergoes hydrometallation to give a metallacyclohexanone intermediate, followed by reductive elimination to afford the cyclopentanone product. Isotope studies shows that the mechanism of intramolecular hydroacylation catalyzed by $[Rh(diphos)]^+$ is unusually complicated: all of the steps occur rapidly and reversibly prior to the irreversible C−C reductive elimination step to form cyclopentanones.[15] An analogous mechanistic pathway for the intramolecular hydroacylation of 4-alkynals was proposed by Fu's group (Scheme 4). However, the proposed intermediates have not been observed for the case of the 4-alkynals, and the mechanistic origin of the versatility of the reactions with 4-alkynals leading to the different products shown in Scheme 1 is not completely understood.

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(10) The intramolecular hydroacylation of alkynals catalyzed by Wilkinson's catalyst to produce *syn*-addition of 7-m-r and 8-m-r *exo*-cyclization products by means of a chelating sulfur tether atom have been reported: Bendorf, H. D.; Colella, C. M.; Dixon, E. C.; Marchetti, M.; Matukonis, A. N.; Musselman, J. D.; Tiley, T. A. *Tetrahedron Lett.* **2002**, *43*, 7031.

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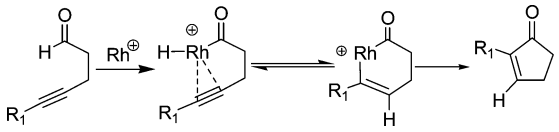
SCHEME 4



Recently, two of us reported a theoretical study on intermolecular hydroacylation of alkynes[16] These studies pointed out some of the challenges to be overcome in the intermolecular hydroacylation due to decarbonylation. However, the apparent mechanistic diversity observed by Fu and Tanaka does not appear to play a role in these systems. In the present study, we report our theoretical investigation of the mechanism of the intramolecular hydroacylation reaction of 4-pentynal[17] catalyzed by the cationic model catalyst $[Rh(PH_2CH_2CH_2PH_2)]^+$. Specifically, the present study will focus on (1) the energetics of the overall catalytic pathways in the intramolecular hydroacylation and the rearrangement processes, (2) the structural features of the intermediates and transition structures involved, (3) the origin of *trans*-addition hydroacylation,[18−21] and (4) the intriguing role of a coordinating ligand in the reaction mechanism.

Computational Methods

All calculations were performed with the GAUSSIAN 98 and 03 series of programs.[22] All reactants, transition structures, and intermediates were optimized by the MP2 method. This method is considered more appropriate for reactions involving hydrogen shift reactions because of the systematic overestimation of the activation energies for hydrogen shifts obtained by DFT calculations such as the popular B3LYP functional.[23] The 6-31G* basis set was used for the hydrogen, carbon, nitrogen, and oxygen atoms. The Hay and Wadt effective core potentials and basis sets were used for phosphorus and rhodium atoms.[24] The phosphorus atoms were augmented with d-polarization functions[25] as specified in Supporting Information. Harmonic vibration frequency calculations were then performed to derive the free energy and verify the stationary points as local minima or transition structures. The implicit solvent effect for CH_2Cl_2 ($\epsilon = 8.93$) and acetone ($\epsilon = 20.7$) was evaluated by the CPCM model[26] using the default parameters for these solvents. For these single-point energy evaluations, the basis set 6-31+G* was adopted for the hydrogen, carbon, nitrogen, and oxygen atoms. The explicit effects of coordinating ligands and reaction of alkyne insertion were also carried out on the key intermediates and transition structures, in which simple formaldehyde and acetylene were used. All relative energies presented in the text are Gibbs free energies in kcal/mol at standard 1 atm and 298 K relative to $[Rh(PH_2CH_2CH_2PH_2)(4\text{-pentynal})]^+$ **1**[27] and all bond lengths are given in angstroms.

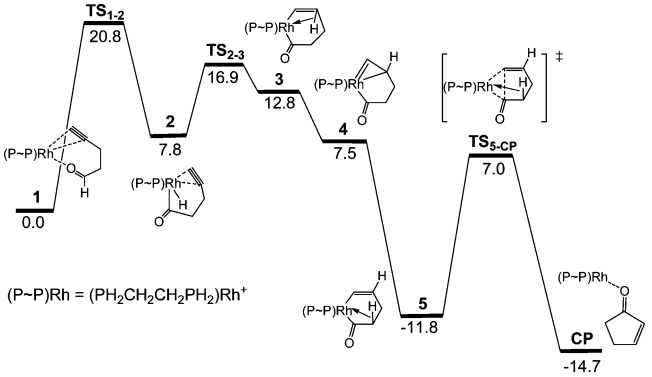


FIGURE 1. Free energy profile for the proposed pathway of forming a Rh-cyclopentenone adduct **CP**.

Results and Discussion

Precursor Complex. Bosnich et al. showed that the 18 e$^-$, catalytically inactive rhodium catalyst dimer, $[Rh(dppe)]_2^{2+}$, dissociates into the 16 e$^-$ catalytically active disolvento monomer, $[Rh(dppe)(S)_2]^+$, where S stands for the coordinating solvent.[3a] They also proposed that $[Rh(dppe)(4\text{-alkenal})]^+$ is a precursor complex for intramolecular hydroacylation, in which both the carbonyl oxygen atom and the carbon−carbon double bond of the 4-alkenal coordinate with the metal. Analogously, the square planar $[Rh(PH_2CH_2CH_2PH_2)(4\text{-pentynal})]^+$, **1**, is adopted as a precursor complex for intramolecular hydroacylation of alkynals with the aldehydic hydrogen *anti* to the rhodium center ($HC_{acyl}ORh$) (Figure 1). The ligand exchange process from $[Rh(PH_2CH_2CH_2PH_2)(H_2CO)_2]^+$ to give $[Rh(PH_2CH_2CH_2PH_2)(4\text{-pentynal})]^+$ **1** is calculated to be exergonic by 13.2 kcal/mol, showing that the precursor complex is easily generated. Based on the findings by Bosnich, all further discussions will be referenced to the energy of this precursor complex **1**.

Formation of the Cyclopentenone. We will start our discussion of the reaction with the pathway leading to the formation of the cyclopentenone product **CP**. Figure 1 shows the potential energy hypersurface for this pathway. The C−H

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(17) In most experimentally studied systems, the C5 position is substituted by an alkyl group. Preliminary calculations at the B3LYP level of theory show that the substituent effect of these groups is negligible.

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(27) For the explicit solvent calculations and the addition of acetylene, the energies of **1** and the separated species were used as reference because no stable complexes are formed with 18 e$^-$ species **1**. Similarly, complexes of other 18 e$^-$ species as well as the η3 complexes of $\mathbf{TS_{8-CB}}$ and $\mathbf{TS_{11-CP}}$ could not be located. The basis set superposition error introduced by this approach is expected to be small compared to the energy differences discussed here.

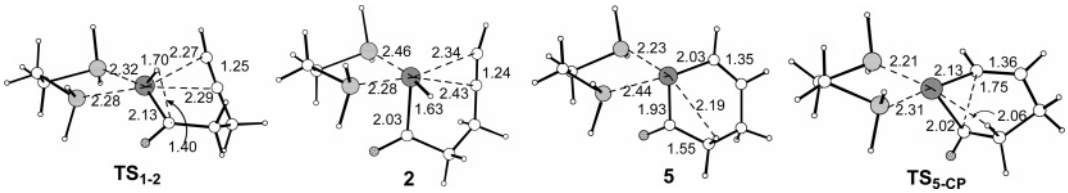

FIGURE 2. Selected calculated structures for the formation of **CP**.

activation transition structure $\mathbf{TS_{1-2}}$ leading to the hydrido complex **2** is the rate-determining step and, with a free energy of 20.8 kcal/mol, the highest stationary point in the process of the formation of **CP**. Intermediate **2** then undergoes a *cis*-addition to the alkyne (intramolecular hydrometallation) via $\mathbf{TS_{2-3}}$ with a free energy of activation of 16.9 kcal/mol to give **3**. This adduct is unstable and undergoes isomerization to metallacyclopropene **4**. We were not able to locate a transition structure for this step, but relaxed potential energy scans of the reaction coordinate indicate that the activation energy for this step will be approximately 1 kcal/mol, rendering the isomerization effectively barrierless on the free energy surface. Similarly, we were unable to locate a transition structure for the opening of **4** to **5**, which is exergonic by 19.3 kcal/mol. It is, however, noteworthy that the apparent *trans*-addition from **2** to **5** proceeds in fact through a series of unstable intermediates that involve a more common *cis*-addition, followed by a rearrangement to give the apparent *trans*-addition product **5**.[28] The intermediates and presumably the transition structures involved are lower in energy than the rate-determining C−H insertion transition structure $\mathbf{TS_{1-2}}$. The metallacyclohexenone **5** finally undergoes reductive elimination to form the final product complex **CP** in a step that is exergonic by 2.9 kcal/mol, bringing the overall driving force for the reaction to 14.7 kcal/mol. The free energy of activation for the reductive elimination is calculated to be 18.8 kcal/mol, which is relatively close to the calculated free energy of activation for the C−H insertion step. It is therefore conceivable that appropriate ligands and reaction conditions might be able to change the rate-determining step of the reaction toward the reductive elimination step. For example, more basic phosphine ligands will lower the activation for the oxidative addition step but increase the barrier for the reductive elimination.[21b] Considering the similar free energies of activation, these effects might be large enough to change the rate-determining step and thus the selectivity of the reaction. As will be shown in a later section, there is also another pathway leading to the formation of **CP** that is very similar in activation energy.

Figure 2 shows the structures of the key intermediates and transition structures along the reaction pathway. The computed bond lengths of 1.70 and 2.31 Å for the H−Rh and Rh−C bond formations, respectively, suggests that $\mathbf{TS_{1-2}}$ is a late transition structure. This is consistent with the calculated reaction energy for the formation of **2**, which adopts a distorted square pyramidal geometry with a H−Rh bond length of 1.63 Å and a C−Rh bond length of 2.03 Å.[29] Compound **2** can be considered as a 16 e^- intermediate from an oxidative addition when the acetylene is regarded as a two-electron donor ligand. Alternatively, it can be considered as an 18 e^- species if the acetylene donates four electrons. The presumed four-coordinated, 14 e^- intermediate **5** adopts a "seesaw" or "*cis*-divacant octahedron" geometry, in which the acyl group is *trans* to one vacant site.[30] **5** is found to be stabilized by an agostic interaction with hydrogen at the C2 position that is 2.19 Å away,[31] which weakens the C1−C2 bond in **5** and helps decarbonylation, as will be discussed later. This interaction gets stronger in the transition structure $\mathbf{TS_{5-CP}}$ with a H−Rh distance of 2.06 Å, presumably lowering the activation energy for the reductive elimination by donation of electrons to the 14 e^- species. $\mathbf{TS_{5-CP}}$ has a number of other interesting characteristics in that carbon−carbon bond formation is with a bond lengths of 1.75 Å fairly advanced, whereas the other two C−Rh bonds are only lengthened by ∼0.1 Å compared to **5** as a result of the electron deficiency of the rhodium. This raises the possibility that additional high-energy species might occur along the reaction pathway. However, these will be lower in energy than $\mathbf{TS_{5-CP}}$ and were therefore not investigated further.

Formation of the Cyclobutanone. One of the most surprising and synthetically useful features of the reaction is the formation of the cyclobutanone **CB** first described by Fu et al.[8c] We therefore investigated the pathway leading to the formation of this very interesting product. Starting from the same intermediate **2**, $\mathbf{TS_{2-6}}$ leads to the formation of the metallacyclopentanone **6** in a step that is exothermic by 15.6 kcal/mol. Formation of **CB** via transition structure $\mathbf{TS_{6-CB}}$ has a very high free energy of activation of 31.8 kcal/mol, rendering this step unlikely for the unsubstituted system. This is in line with the experimental finding that for the parent system **6** can be trapped by using alcohols and alkynes to form other products, as will be discussed in more detail later. Furthermore, the formation of **CB** is only observed for donor substituted systems and BINAP-type ligands (Scheme 1).[8c]

The two key structures for this pathway, **6** and $\mathbf{TS_{6-CB}}$, are shown in Figure 4. The metallacyclopentanone **6** has an essentially planar structure, preventing the agostic interaction that stabilizes **5**, accounting for at least some of the 4 kcal/mol energy difference between **5** and **6**. Distortion of the ring in $\mathbf{TS_{6-CB}}$ allows a weak H−Rh interaction with a distance of 2.30 Å but also leads to a highly strained [2.1.0] system, accounting for the high free energy of activation computed for this step.

(28) The possibility of the formation of *trans*-addition product **CP** via α-acyl migration from the less stable d^6 metallacyclopropene intermediate **4** can be ruled out, since **4** is higher in energy than $\mathbf{TS_{5-CP}}$ and $\mathbf{TS_{11-CP}}$ (c.f. ref 20a).

(29) It should be mentioned that there is a second conformation of **2** with the hydride in the apical position that is essentially isoenergetic for the small model system discussed here. However, this conformation will be destabilized for more highly substituted systems as a result of steric repulsion and is therefore not considered further.

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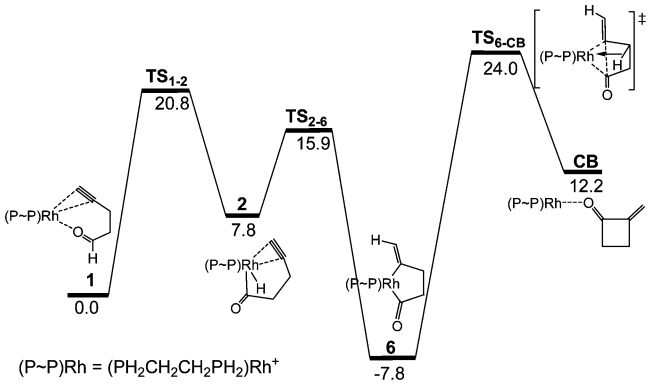

FIGURE 3. Free energy profile for the proposed pathway of forming a Rh-cyclobutanone adduct **CB**.

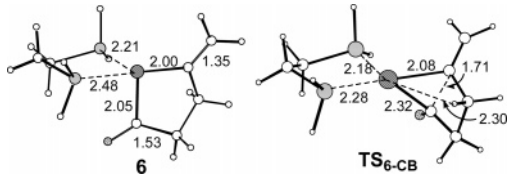

FIGURE 4. Calculated structures of metallacyclopentanone **6** and reductive elimination transition structure $\mathbf{TS_{6-CB}}$.

Nevertheless, the interaction in $\mathbf{TS_{6-CB}}$ is important to note because it opens the possibility for the selective stabilization of this transition structure by stronger donor substituents and could rationalize the experimentally observed formation of **CB** in the case of donor-substituted substrates.[8c] The unprecedented observation that one diastereomeric ligand/substrate combination leads to the cyclopentenone product, whereas the other leads to the formation of the cyclobutanone,[8c] implies that the donor substituent and the chiral center on the ligand are in close contact, in agreement with the structure of the [2.1.0] bicyclic system calculated for $\mathbf{TS_{6-CB}}$. Details of this intriguing reaction controlled by a substituent will be the topic of separate study.

Formation of the Dienal. Experimental studies by the Fu group show that under certain reaction conditions, 1,3-butadiene-2-carboxaldehydes **DE2**, but not the 1,3-butadiene-1-carboxaldehydes **DE1**, are formed.[13] While it is clear that the formation of this product has to proceed via a decarbonylation step, it is not obvious why only one of the two possible products is formed. We therefore calculated the two pathways leading to **DE1** and **DE2** and the results are shown in Figures 5 and 6, respectively.

The results show that **DE1** is formed for the metallacyclohexenone **5** via a decarbonylation to form **10** and a series of rearrangements to form **12.** Although the formation of **12** from **5** is exergonic by 6.6 kcal/mol, the barrier for the formation of **DE1** is at 27.1 kcal/mol prohibitively high. Nevertheless, this pathway is also interesting because of an alternative route for the formation of **CP** with a free energy of activation of 18.4 kcal/mol, slightly less than the two alternative pathways discussed previously. It is therefore clear the **DE1** will not be formed because there is an energetically more favorable pathway for the formation of **CP**.

These results contrast with the ones starting from the metallacyclopentanone **6**, summarized in Figure 6. The corresponding decarbonylation and reinsertion of the CO group leads to the isomer **8**, which is about 3.6 kcal/mol higher in energy than **6**. However, **8** can be further stabilized by 12.3 kcal/mol through the formation of the intramolecular η^2 complex with the olefin, which is not possible in **6**. This complex, **8′**, has two pathways available for further reaction. β-Elimination leads to **9** with a free energy of activation of 17.1 kcal/mol, which after reductive elimination with a free energy barrier of 22.1 kcal/mol, relative to **8′**, leads to **DE2**. The computed relative free energy of $\mathbf{TS_{9-DE2}}$ is quite similar to those of the two hydrometallation transition structures ($\mathbf{TS_{2-5}}$ and $\mathbf{TS_{2-6}}$). Again, the ligands, substrates, and reaction conditions might be able to finely tune the relative energies of these three transition structures, which in turn determines the nature of products. The formation of **DE2** becomes favorable when $\mathbf{TS_{9-DE2}}$ becomes lower in energy than $\mathbf{TS_{2-5}}$ and $\mathbf{TS_{2-6}}$. In contrast, the amount of **CP** can be increased, rather than the dienal adduct **DE2**, by raising the relative energy of $\mathbf{TS_{9-DE2}}$ or lowering the relative energy of $\mathbf{TS_{2-5}}$ and $\mathbf{TS_{2-6}}$. The second pathway, which is analogous to the formation of **CP** in Figure 5 and leads to **CB**, is with a free energy of activation of 37.4 kcal/mol prohibitively high in energy. The origin of the experimental observation that only **DE2**, but not **DE1**, is formed can therefore be traced to the relative energies of the reductive elimination versus β-elimination-reductive elimination pathways leading to the cyclic versus acyclic products, respectively.

The relevant transition structures for the two pathways shown in Figures 5 and 6 are shown in Figure 7. The carbon−carbon bond in the decarbonylation transition structure $\mathbf{TS_{6-7}}$ is with a length of 2.29 Å substantially lengthened, and the two Rh−C bonds are almost completely formed. It can therefore be considered a fairly late transition structure even though the reaction is only slightly endothermic. This is most likely due to the fact that the formation of the strained metallacyclobutane is offset by the coordination of the CO ligand to the rhodium. In $\mathbf{TS_{12-DE1}}$, the transition structure for the reductive elimination to form **DE1**, the rhodium cation is stabilized through coordination to the olefin. The H−Rh is lengthened by ∼0.1 Å to 1.81 Å, while the C−H bond is with a calculated bond length of 1.24 Å almost completely formed. In comparison, the transition structure for the formation of **DE2**, $\mathbf{TS_{9-DE2}}$, is a slightly earlier transition structure with a H−C bond of 1.33 Å, a H−Rh bond of 1.77 Å, and a C−Rh bond of 2.16 Å. The η^2 coordination is relatively similar in the two structures. It should be noted that $\mathbf{TS_{9-DE2}}$, the transition structure leading to the experimentally observed **DE2**, is 6.7 kcal/mol *higher* in energy than $\mathbf{TS_{12-DE1}}$. The origin of the much higher free energy of activation for the formation of **DE1** is therefore not significant energy or structural differences in the transition structures, but rather the relative energies of the starting materials in these steps, which are determined by the favorable η^2 coordination in **12**.

The dominant pathway in Figure 5 is therefore the formation of **CP** through transition structure $\mathbf{TS_{11-CP}}$ shown on the right in Figure 7. Interestingly, $\mathbf{TS_{11-CP}}$ shares more geometrical features with $\mathbf{TS_{6-CB}}$ than with the other transition structure for the formation of **CP**, $\mathbf{TS_{5-CP}}$, in that the structure is highly puckered and does not show the agostic interaction that was considered important in $\mathbf{TS_{5-CP}}$. Instead, the η^2 coordination to the olefin saturates the electron demand of the rhodium and leads to the puckered structure, which is less strained than in the case of $\mathbf{TS_{6-CB}}$ because of the formation of a five-membered rather than a four-membered ring.

Other Reactions. The reaction pathways outlined above also allow the explanation of several other experimental observations, namely, the importance of the acetone solvent for the reaction

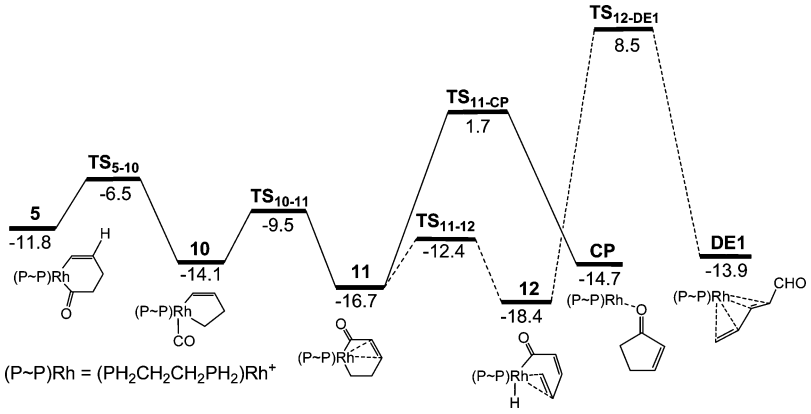

FIGURE 5. Free energy profile for the alternative pathway for the formation of **CP** and of dienal **DE1**.

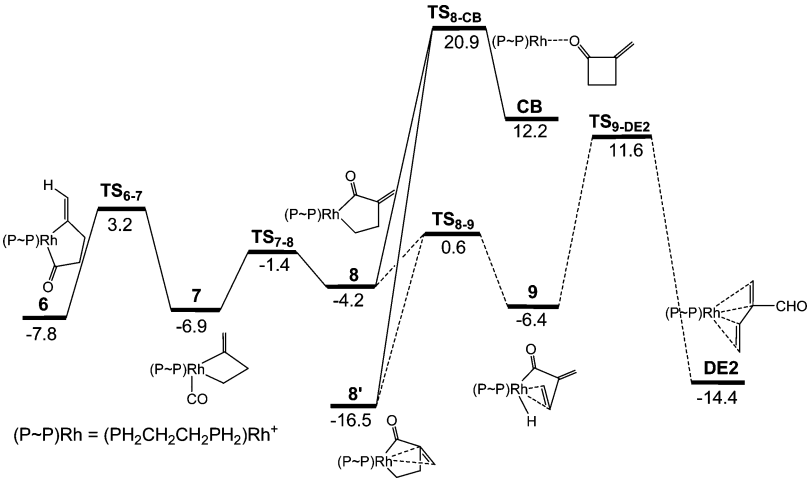

FIGURE 6. Free energy profile for the alternative pathway for the formation of **CB** and of dienal **DE2**.

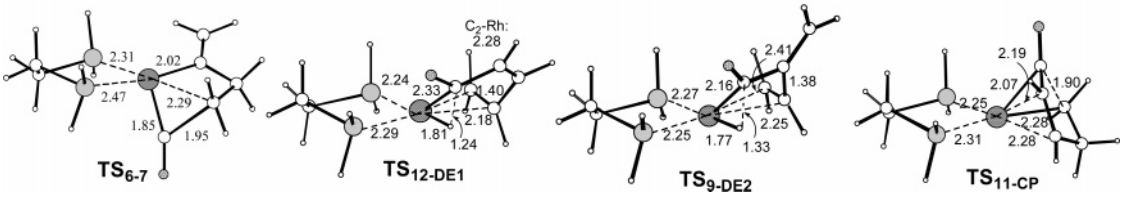

FIGURE 7. Selected structures of the pathways for dienal formation and alternative pathways for formation of **CP** and **CB**.

and the formation of cyclohexenones in the presence of acetylene. We will now discuss the structural and electronic origins of these findings.

To understand the solvent effect on the reaction courses, both implicit and explicit solvent calculations were performed. From the implicit solvent model calculations, CH_2Cl_2 and acetone solutions exert very similar effects on the catalytic cycles (compare Table S1 in Supporting Information). Thus, the implicit solvent model calculations cannot elucidate the role of a good coordinating solvent such as acetone on different reaction pathways. Therefore, we used a formaldehyde molecule to model the coordination of acetone solvent molecule onto the metal. Table 1 summarizes the energetic effects of the coordination of a formaldehyde molecule to the key intermediates and transition structures along the reaction pathways.

Several interesting results due to the coordination of formaldehyde molecule are summarized as follows: (1) The somewhat later transition structure $\mathbf{TS_{2-3}}$ has a stronger binding affinity than $\mathbf{TS_{2-6}}$, and the formation of the 6-m-r rhodacyclohexenone intermediate via the endo-cyclization can thus be promoted by a donor ligand, such as acetone and acetonitrile. (2) The formaldehyde molecule stabilizes the 14 e^- intermediates **5** and **6** much more than it stabilizes the transition structures $\mathbf{TS_{2-3}}$ and $\mathbf{TS_{2-6}}$. As a result, the conversion from intermediate **6** into intermediate **5** through transition structure $\mathbf{TS_{2-6}}$ becomes more difficult in a highly coordinating solvent. (3) The activation energies for reductive elimination ($\mathbf{TS_{5-CP}}$ and $\mathbf{TS_{6-CB}}$) and decarbonylation ($\mathbf{TS_{6-7}}$) from intermediate **6** are increased under the coordination of formaldehyde. However, the decarbonylation/carbonylation reactions are still faster than the C−C reductive elimination. For the case of the solvated species, the η^1-reductive elimination transition structures $\mathbf{TS_{11-CP}}$ and $\mathbf{TS_{8-CB}}$ are calculated to be less favorable than $\mathbf{TS_{5-CP}}$ and $\mathbf{TS_{6-CB}}$. (4) The formation of the **CB** product through the corresponding solvated $\mathbf{TS_{6-CB}}$ has an activation energy of about 34.9 kcal/mol, indicating that in a good coordinating solvent,

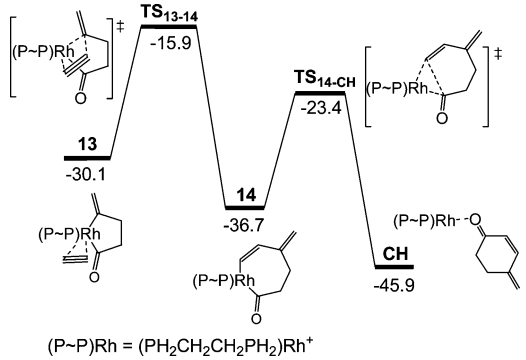

FIGURE 8. Free energy profile for the acetylene insertion from intermediate **13** to form **CH**.

TABLE 1. Relative Free Energies (ΔG_{H_2CO}) of Intermediates and Transition Structures in the Absence and Presence of One Explicit H_2CO Molecule in the Gas Phase (kcal/mol)

	ΔG_{gas}	ΔG_{H_2CO}
2	7.8	0.6
TS$_{2-3}$	16.9	13.0
TS$_{2-6}$	15.9	13.1
5	−11.8	−20.4
TS$_{5-CP}$	7.0	−0.1
6	−7.8	−21.3
TS$_{6-CB}$	24.0	13.5
TS$_{6-7}$	3.2	−3.6
7	−6.9	−19.0
TS$_{7-8}$	−1.4	−8.5
8	−4.2	−17.2
8′	−16.5	−21.6
TS$_{8-CB}$	20.9	20.3
TS$_{8-9}$	0.6	−3.7
9	−6.4	−11.1
10	−14.1	−25.8
11	−16.7	−18.9
TS$_{11-CP}$	1.7	6.6
TS$_{11-12}$	−12.4	−17.0
12	−18.4	−23.4
CP	−14.7	−28.7
CB	12.2	−2.8

the **CB** product cannot be formed from simple alkynals. Nevertheless, **TS$_{6-CB}$** gains a considerable stabilization from the coordination of formaldehyde compared with **TS$_{2-6}$**. Hence, **TS$_{6-CB}$** upon coordination of the formaldehyde becomes close in energy to **TS$_{2-6}$** and lower in energy than **TS$_{9-DE1}$**. This implies an important role of a chelating methoxyl group at the C3 position (agostic interaction at the C3 position involved in **TS$_{6-CB}$**) in the formation of cyclobutanone in experiments that will have to be explored further.[8c] (5) **TS$_{9-DE1}$**, **TS$_{12-DE2}$**, **DE1**, and **DE2** do not favor coordination of formaldehyde molecule because they are coordinatively saturated. To afford dienal adducts (**DE1** and **DE2**), intermediates **9** and **12** are required to dissociate the solvent molecule prior to **TS$_{9-DE1}$** and **TS$_{12-DE2}$**. Thus, a coordinating solvent does not favor the formation of dienal adducts.[8,11,13]

In experiments, transient intermediate **6** can be trapped by an additional alkyne or 4-alkynal itself to form cyclohexenones.[12] To investigate this process, one acetylene is added to intermediate **6**. Figure 8 shows the calculated potential energy surface obtained from these calculations.

Starting from **13**, which is equivalent to **6** with an additional acetylene molecule, the [2 + 2] cycloaddition via **TS$_{13-14}$** is with a free energy of activation of 14.2 kcal/mol facile. This leads to formation of the metalla-cycloheptenone **14** with an overall reaction energy of 4.2 kcal/mol. Structurally, **14** resembles **5** in that it is stabilized by an agostic interaction that becomes stronger in the transition structure for the reductive elimination **TS$_{14-CH}$**, resulting in a relatively low free energy of activation of 13.3 kcal/mol that leads to the formation of the experimentally observed cyclohexenone product with an overall reaction energy of −45.9 kcal/mol. As to be expected for the reaction of the high-energy acetylene to the unstrained cyclohexenone, this is the most exothermic part of the reactions described here. This facile, highly exothemic pathway for the trapping of **6** lends further support to the involvement of this structure.

Conclusions

The computations on the intramolecular hydroacylation reaction of 4-pentynal promoted by a $[Rh(PH_2CH_2CH_2PH_2)]^+$ model catalyst have revealed the complex reaction pathways leading to the variety of experimentally observed products as well as the geometric and electronic structure of the transition structures and intermediates involved. In the absence of a good coordinating solvent, the activation of the aldehydic C−H bond is the rate-determining step. Hydrometallation to form a rhodacyclopentanone intermediate **6** is kinetically more favorable than the formation of the rhodacyclohexenone intermediate **5**. Intermediate **6** does not lead to the formation of a cyclobutanone product for the systems studied here because of a prohibitively high activation energy, which is in line with the experimentally observed trapping of **6** by alcohols. Thus, the formation of **CP** via two different possible pathways via **5** is favored. Alternatively, alkynes can coordinate to intermediate **6**, which can then readily undergo insertion and lead to the formation of cyclohexenone product. The experimentally observed formation of the 2-substituted dienals, but not the 1-substituted isomer, is found to be due to the competition between rearrangement steps and, particularly, the C−H reductive elimination step to give **DE2**, which are lower than the activation energy for the reductive elimination in the case of **6**, but the C−H reductive elimination step to give **DE1** is higher in the case of **5**.

A good coordinating solvent is shown (1) to promote the *endo*-cyclization kinetically, (2) to displace alkyne coordination to the metal by excess acetone to inhibit [4 + 2] annulation, (3) to narrow the kinetic preference toward decarbonylation over C−C reductive elimination, and (4) to enhance the stability of the cyclopentenone adduct but suppress the formation of rearranged dienals.

The current study has established a foundation for a detailed understanding of the reaction mechanism and stereochemistry of intramolecular hydroacylation catalyzed by cationic rhodium complexes. Further studies are designed to understand the critical role of a 3-methoxy substituent on the formation of the cyclobutanone product and various observed kinetic resolutions and stereoselectivities.

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Supporting Information Available: Full citation for ref 22, basis set used, Cartesian coordinates and free energies of all structures obtained by the MP2 method. This material is available free of charge via the Internet at http://pubs.acs.org.

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