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Mechanism and Origins of Regio- and Enantioselectivities in Rh^I-Catalyzed Hydrogenative Couplings of 1,3-Diynes and Activated Carbonyl Partners: Intervention of a Cumulene Intermediate

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Abstract

The mechanism of the rhodium-catalyzed reductive coupling of 1,3-diynes and vicinal dicarbonyl compounds employing H₂ as reductant was investigated by density functional theory. Oxidative coupling through 1,4-addition of the Rh^I-bound dicarbonyl to the conjugated diyne via a seven-membered cyclic cumulene transition state leads to exclusive formation of linear adducts. Diyne 1,4-addition is much faster than the 1,2-addition to simple alkynes. The 1,2-dicarbonyl compound is bound to rhodium in a bidentate fashion during the oxidative coupling event. The chemo-, regio-, and enantioselectivities of this reaction were investigated and are attributed to this unique 1,4-addition pathway. The close proximity of the ligand and the alkyne substituent distal to the forming C–C bond controls the regio- and enantioselectivity: coupling occurs at the sterically more demanding alkyne terminus, which minimizes nonbonded interaction with the ligand. A stereochemical model is proposed that accounts for preferential formation of the (*R*)-configured coupling product when (*R*)-biaryl phosphine ligands are used.

Keywords

C–C coupling; density functional calculations; enantioselectivity; reaction mechanisms; regioselectivity; rhodium

Introduction

Transition-metal-catalyzed alkyne–carbonyl reductive coupling reactions enable the formation of allylic alcohols, which are important intermediates in synthetic chemistry.^[1] This type of reaction normally requires terminal reductants in the form of stoichiometric organometallic reagents.^[2] In contrast, under hydrogenation conditions, catalytic C–C coupling occurs with complete atom economy.^[1g–k] By using rhodium-based catalysts, hydrogenation of conjugated alkynes (enynes and diynes) in the presence of activated carbonyl compounds and imines delivers C–C coupling products,^[3, 4] and nonconjugated alkynes engage in reductive cyclization with simple unactivated aldehydes.^[5] Rhodium-catalyzed hydrogenation of acetylene in the presence of aldehydes or imines provides

products of (Z)-butadienylation.^[6] Finally, under the conditions of iridium-catalyzed hydrogenation, butyne and other nonconjugated alkynes engage in efficient reductive couplings to activated ketones and *N*-sulfonyl imines.^[7] These studies represent the first systematic efforts toward hydrogen-mediated reductive couplings beyond alkene hydroformylation.^[1g–k] Here, we report DFT studies on the mechanism of rhodium-catalyzed reductive coupling of 1,3-diynes with vicinal dicarbonyl compounds employing H₂ as terminal reductant that reveals a novel pathway for oxidative coupling by 1,4-addition of the Rh^I-bound dicarbonyl to the conjugated diyne through a seven-membered cyclic cumulene transition state (Scheme 1).

Two mechanisms have been proposed for the Rh-catalyzed hydrogenative coupling of 1,3-diynes with carbonyl partners.^[3b] The collective experimental data suggested an oxidative coupling mechanism (Scheme 2 a): oxidative coupling of the 1,3-diyne with an aldehyde furnishes the oxarhodacycle intermediate, followed by hydrogenative cleavage of the oxarhodacycle and reductive elimination. An alternate hydrometallation mechanism involves hydrogen oxidative addition with subsequent alkyne hydrometallation, carbonyl insertion, and, finally, O–H reductive elimination (Scheme 2 b). It was found from the experiment that cationic Rh^I complexes are required for reductive coupling.^[3d] With cationic rhodium catalysts, hydrogenation reactions may occur through heterolytic activation of elemental hydrogen to form neutral rhodium monohydride intermediates^[8] or through homolytic activation of H₂, which only involves cationic rhodium species in the catalytic cycle.

Prior ESI-MS and DFT studies on the Rh-catalyzed reductive coupling of acetylene to aldehydes and imines, corroborate a mechanism involving oxidative coupling of two acetylene molecules to furnish a rhodacyclopentadiene, which engages in carbonyl insertion and subsequent hydrogenolysis to deliver products of carbonyl or imine (Z)-butadienylation.^[6d] In such transformations, it was found that initial acetylene–aldehyde oxidative coupling requires a higher activation energy than the coupling of two acetylenes. In contrast, for conjugated diynes and vicinal dicarbonyl compounds, the present studies corroborate a mechanism in which alkyne–carbonyl oxidative coupling is energetically preferred due to intervention of a cumulene intermediate.

We performed density functional studies to investigate the mechanism as well as the chemo-, regio-, and enantioselectivities of this reaction. Both oxidative coupling and hydrometallation mechanisms involving neutral rhodium monohydride or cationic rhodium complexes as active catalyst were studied. Our theoretical studies suggest that the previously postulated oxidative coupling mechanism via cationic species is preferred.^[9] A unique 1,4-interaction with diynes confers the high reactivity of conjugated alkynes and α -dicarbonyl reactants observed experimentally by way of a cumulene intermediate. The mechanism also accounts for the chemoselectivity of diyne–carbonyl coupling over diyne–diyne coupling and the role of turnover-limiting H₂ addition.

Our theoretical model also explains the high regio- and enantioselectivities observed in the experiment. Previous experimental studies found that the C–C bond formation takes place at the sterically more demanding terminus of 1,3-diynes with complete regioselectivity to furnish linear products in a *cis* addition (Scheme 3 a).^[3h, 10] For example, the coupling of *t*Bu–C $\equiv$ C–C $\equiv$ C–Me with ethyl glyoxylate occurs proximal to the *tert*-butyl moiety with complete levels of regiocontrol. This contrastive regioselectivity is unusual in transition-metal-catalyzed coupling reactions.^[7, 11] Catalytic C–C coupling reactions adjacent to a quaternary propargylic center are rare.^[2g, 12] It is unlikely that the regioselectivity is dominated by electronic effects, because the difference of electronic effects between the two

alkyl termini is too small to completely reverse the steric control to yield coupling products at the more hindered position.

When chiral phosphine ligands such as 2,2'-bis(diphenylphosphino)-5,5'-dichloro-6,6'-dimethoxy-1,1'-biphenyl ((*R*)-Cl,MeO-BIPHEP) and 1-[(*R*^P)-2-{2-[di(3,5-xylyl)phosphino]-phenyl}ferrocenyl]ethyldi(3,5-xylyl)phosphine ((*R*)-xylyl-WALPHOS) are used, the reductive coupling of 1,3-diynes and vicinal dicarbonyl compounds delivers highly optically enriched allylic alcohols (Scheme 3 b).^[3h] Herein, we report that the regioselectivities and enantioselectivities in these reactions are both attributed to the steric repulsions between the ligand and the alkyne substituent distal to the forming C–C bond in the 1,4-addition oxidative coupling transition state.

Results and Discussion

Reaction mechanisms

We performed density functional theory calculations on both oxidative coupling and hydrometallation mechanisms. The 2,4-hexadiyne and glyoxal substrates ($R^1=R^2=Me$, $R^3=H$) were used in the calculations. Two PH_3 ligands were used as a surrogate for the biaryl phosphine ligands used in the experiments. These calculations reveal that the previously postulated oxidative coupling mechanism is preferred.^[6] Cationic rhodium catalysts are far more reactive than the corresponding neutral complexes in the oxidative coupling, which suggests that heterolytic hydrogen activation is not operative. These findings agree with the deuterium labeling experiments and the ESI-MS analysis results, in which hydride intermediates were not observed.^[3d] The calculated free energy profile for the preferred oxidative coupling mechanism is shown in Figure 1.

The catalytic cycle starts from the oxidative coupling of the square-planar, cationic Rh^I -glyoxal η^2 complex **2** with the diyne. A number of pathways are possible in the oxidative coupling step and they have all been investigated. The structures and activation energies of the transition states are shown in Figure 2. In the oxidative coupling, the Rh -glyoxal complex may attack the diyne at the 1,2-positions, leading to a five-membered oxarhodacycle intermediate **4**. In the 1,2-addition, the diyne may adopt two different orientations, leading to linear and branched coupling products (TS1b and TS1c, respectively).^[13] Alternatively, the Rh -glyoxal complex **2** may attack the 1,4-positions of the diyne (TS1a, identical to TS1 in Figure 1). In contrast to the 1,2-addition, the diyne 1,4-addition leads to a seven-membered cumulenyl oxarhodacycle intermediate **3**, which then easily isomerizes to the five-membered oxarhodacycle **4**. Also, the coupling may occur via the η^1 Rh^I -glyoxal complex, in which the α -carbonyl group of the glyoxal is pointing away from the metal. The 1,2- and 1,4-additions involving the η^1 glyoxal complex were also investigated (TS1d–f).

The most stable oxidative coupling transition state is TS1a, which involves 1,4-addition to the diyne with glyoxal bound in a bidentate fashion to the metal in the transition state. The activation Gibbs free energy of TS1a is only 11.3 kcal mol^{−1}. The 1,4-addition of the Rh -glyoxal complex to the diyne is much preferred over the 1,2-addition in the oxidative coupling.^[14] The 1,2-additions to the diyne (TS1b and TS1c) require 9.9 and 16.8 kcal mol^{−1} higher activation energies, respectively, than the 1,4-addition (TS1a). The HOMO of the 16-electron Rh -glyoxal complex **2** is a filled d_{z^2} orbital perpendicular to the plane. It is known that a square-planar Rh^I complex is vulnerable to electrophilic attack from the perpendicular position.^[15] Diyne 1,4-addition (TS1a) maximizes the bonding interaction with the metal d_{z^2} orbital perpendicular to the plane, whereas in the 1,2-addition transition states (TS1b and TS1c), the bonding interaction between the metal and the C-2 carbon atom on the diyne is very small, due to the long distance between these two atoms. The length of

the forming Rh–C bond is 3.52 and 2.58 Å in TS1b and TS1c, respectively, and only 2.19 Å in TS1a. The diyne–glyoxal oxidative coupling transition state TS1a is also stabilized by the coordination of the α -carbonyl group of the glyoxal with the cationic rhodium center. TS1d, in which the α -carbonyl group of the glyoxal does not coordinate with the metal, is 10.0 kcal mol^{−1} less stable than TS1a.

We also investigated the oxidative coupling of two diynes to explain the experimental chemoselectivity in which the cross-coupling of a diyne and a vicinal dicarbonyl compound is observed, whereas homocoupling of two acetylenes is favored over cross-coupling of acetylene with aldehydes. The oxidative coupling transition state of two 2,4-hexadiynes requires an activation energy of 25.3 kcal mol^{−1}, which is 14.0 kcal mol^{−1} higher than the coupling of 2,4-hexadiyne with glyoxal. This is due to two factors: 1) the coupling of 2,4-hexadiyne with glyoxal occurs through a 1,4-addition transition state, whereas the homocoupling of diynes occurs through a 1,2-addition (See the Supporting Information for the 3D structure of the transition state); 2) the coordination of the glyoxal α -carbonyl group with the rhodium in the cross-coupling transition state increases the electrophilicity of rhodium and thus, increases its reactivity. This explains why no homocoupling of diynes is observed in the experiment. When acetylenes and aldehydes are used under similar conditions with rhodium catalysts, the homocoupling of two acetylenes is favored, because the cross-coupling would occur through a 1,2-addition to acetylene, which requires higher activation energy.^[6d]

The oxidative coupling transition state structure also explains the high reactivity of 1,3-diynes and α -carbonyl aldehydes or ketones in this reaction compared to simple alkynes and unactivated carbonyls. Nonconjugated alkynes can only react through a 1,2-addition in the oxidative coupling and thus are much less reactive. The oxidative coupling of 2-butyne and glyoxal requires a 16.3 kcal mol^{−1} higher activation energy than that of 2,4-hexadiyne. The oxidative coupling of 2,4-hexadiyne and simple unactivated formaldehyde requires a 9.4 kcal mol^{−1} higher activation energy than the reaction with glyoxal. For the oxidative coupling of unconjugated 2-butyne and formaldehyde, the activation energy is 15.1 kcal mol^{−1} higher than that for the reaction of 2,4-hexadiyne and glyoxal. The structures and activation energies of the oxidative coupling transition states with these less reactive substrates are shown in the Supporting Information.

The 1,4-additions to conjugated alkynes deliver the seven-membered σ -cumulenyl oxarhodacycle **3**,^[16] which lead to the linear *cis* addition products exclusively. The cyclic cumulene **3** easily isomerizes to form the more stable five-membered oxarhodacycle **4**.^[17] Subsequent σ -bond metathesis with H₂ may cleave the Rh–C bond (Scheme 2 a, path A) or the Rh–O bond (Scheme 2 a, path B) of the metallacycle. Our calculations suggest that cleavage of the Rh–C bond (Scheme 2 a, path A) is favored by 5.6 kcal mol^{−1}. This is presumably due to the more stable product formed after the cleavage of the Rh–C bond. From metallacycle **4**, σ -bond metathesis of H₂ and the Rh–C bond (TS2) requires an activation energy of 25.9 kcal mol^{−1}. This is the turnover-limiting step of the reaction. Cleavage of the metallacycle Rh–C bond affords a square-based pyramidal rhodium monohydride intermediate **6**. Upon reductive elimination, a square-planar product–catalyst complex **7** is formed. The reductive elimination (TS3) requires an activation free energy of 13.9 kcal mol^{−1}, which suggests it is faster than the H₂ activation step (TS2). Complex **7** liberates the product and coordinates with the reactants to enter the next catalytic cycle. The ligand exchange from **7** to regenerate the Rh–glyoxal complex **2** requires 7.2 kcal mol^{−1}.

The free-energy diagram of the first two steps of the hydrometallation mechanism of the coupling of 2,4-hexadiyne and glyoxal is shown in Figure 3. The oxidative addition of H₂ requires an activation energy of 16.9 kcal mol^{−1}, much higher than the oxidative coupling

transition state (TS1, $\Delta G^\ddagger = 11.3 \text{ kcal mol}^{-1}$) and similar to the H_2 σ -bond metathesis transition state (TS2, $\Delta G^\ddagger = 16.8 \text{ kcal mol}^{-1}$) in the oxidative coupling mechanism (see Figure 1). Because a Brønsted acid or a counter ion decreases the barrier of H_2 σ -bond metathesis (see below), the overall barrier of the oxidative coupling mechanism is lower than the hydrometallation.

After formation of the Rh^{III} dihydride intermediate **10**, subsequent hydrometallation of the diyne may occur through two pathways: in TS5a, the hydride is transferred to the terminal carbon of the diyne, leading to branched coupling products, whereas TS5b leads to linear coupling products. TS5a is predicted to be $1.7 \text{ kcal mol}^{-1}$ more stable than TS5b, suggesting that branched products are favored. This contradicts the regioselectivity observed experimentally, in which linear products are formed exclusively. This rules out the hydrometallation mechanism for the reductive coupling of diynes and glyoxals.

Mechanism of Brønsted acid cocatalyst

Experimentally, it is observed that Brønsted acid cocatalysts enhance the rate and the conversion.^[1g] As previously postulated, it is likely that such cocatalysts circumvent highly energetic four-centered transition structures for σ -bond metathesis (TS2), as required for direct hydrogenolysis of metallacyclic intermediates, with six-centered transition structures for hydrogenolysis of rhodium carboxylates derived upon protonolytic cleavage of the metallacycle.^[6d, 18] We have investigated the catalytic cycle in the presence of a Brønsted acid. Acetic acid was used as a surrogate in the calculations. The results are shown in Figure 4.

Acetic acid does not accelerate the oxidative coupling step (TS1). Coordination with acetic acid at the empty site of the Rh of TS1 destabilizes the transition state by $5.2 \text{ kcal mol}^{-1}$ in terms of Gibbs free energy.^[19] In contrast, coordination with acetic acid dramatically stabilizes the metallacycle intermediate **4** and forms a stable Rh–acetic acid complex **12**. The proton in the acetic acid coordinates with the aldehyde oxygen, which becomes more negatively charged in the metallacycle complex. Protonation of the aldehyde oxygen in **12** cleaves the Rh–O bond and forms a rhodium acetate **13**, which is $5.9 \text{ kcal mol}^{-1}$ less stable than **12**. Subsequent H_2 activation occurs through a six-centered transition state (TS6). The six-centered hydrogenolysis transition state (TS6) is much more stable than the four-centered direct hydrogenolysis transition state through σ -bond metathesis (TS2). The overall barrier for the H_2 activation from the stable Rh metallacycle–acetic acid complex **12** is $22.7 \text{ kcal mol}^{-1}$, less than the barrier of $25.9 \text{ kcal mol}^{-1}$ without a Brønsted acid cocatalysts. This suggests that Brønsted acid cocatalysts enhance the rate of the coupling reaction by accelerating the rate-determining H_2 activation step.

The hydrogenolysis (TS6) leads to a Rh–hydride intermediate **15**, which eliminates acetic acid to form intermediate **16**. Reductive elimination via TS7 requires an activation free energy of $12.8 \text{ kcal mol}^{-1}$, faster than the H_2 activation. The same product–catalyst complex **7** is formed as in the catalytic cycle without Brønsted acid cocatalysts, which upon ligand exchange, regenerates the Rh–glyoxal complex **2** to enter the next catalytic cycle.

Origin of regioselectivities

The 1,4-addition pathway of 1,3-diynes delivers unusual regio- and enantiocontrol compared to the 1,2-addition to simple alkynes. In the 1,4-addition, the C–C bond is formed at the terminal position of the diyne to furnish linear coupling products exclusively (see above). In the reactions with unsymmetrical diynes, the coupling may occur at either terminus, leading to two regioisomeric products (Scheme 3 a). To understand the origin of regioselectivities, we need to first identify the regioselectivity-determining step of the coupling reaction.

Our theoretical study on the catalytic cycle indicates that H₂ activation (TS2 or TS6) is the rate-determining step for the coupling reactions with or without Brønsted acid cocatalysts. Under the conditions with Brønsted acid, the regio- and enantioselectivity-determining step is the oxidative coupling (TS1), because the relative free energy of TS6 is much lower than that of TS1, and thus, the formation of the stable Rh metallacycle–Brønsted acid complex **8** is irreversible. Under conditions without Brønsted acid cocatalysts, the counter ion of the catalyst, triflate, could also stabilize the H₂ activation transition state via a similar six-centered mechanism. The relative free energy of the six-centered H₂ activation transition state involving triflate is slightly lower than that of the oxidative coupling transition state bound with triflate (0.3 and 4.1 kcal mol^{−1} in solution and in gas phase, respectively. See the Supporting Information for details). This also suggests that the formation of the metallacycle intermediate is irreversible and that the regio- and enantioselectivity-determining step is the oxidative coupling. We have performed transition-state analysis of the regioisomers of both oxidative coupling and H₂ activation transition states. The regio- and enantioselectivities calculated based on oxidative coupling transition states are in good agreement with the experiments, whereas the selectivities from the H₂ activation step contrast the experimental results. These results suggest that the regio- and enantioselectivity is determined in the oxidative coupling step.

We have performed calculations on the coupling of diyne *t*Bu–C≡C–C≡C–Me with glyoxal to investigate the origin of regioselectivities. To better mimic the effects of ligands on regioselectivities, the larger biaryl ligand, 2,2′-bis(diphenylphosphino) biphenyl (BIPHEP), was used in these calculations. The two regioisomeric oxidative coupling transition states are shown in Figure 5.^[20] Coupling at the *tert*-butyl-substituted propargylic terminus (TS8a) is 13.2 kcal mol^{−1} more stable than coupling at the methyl-substituted terminus (TS8b). This is in agreement with the experiment: only couplings at the more hindered terminus of diynes are observed. The regioselectivity is attributed to the steric repulsions between the biaryl phosphine ligand and the alkyne substituent distal to the forming C–C bond. Both regioisomers involve 1,4-addition to the diyne. In these 1,4-addition transition states, which have strong metal–cumulene co-ordinations, the distal diyne substituent is very close to the bulky ligand, due to the metal–cumulene coordination. When the distal diyne substituent is large, such as *tert*-butyl, significant repulsions with the biaryl phosphine ligand are observed. The steric repulsions in the forming C–C bond are smaller.

This unusual regiocontrol is in contrast to many known metallacycle formations.^[9b, 21] In most alkyne 2π-electron additions to form a metallacycle, including the Rh-catalyzed [5+2] cycloadditions^[21d] and the Ni-catalyzed aldehyde–alkyne reductive couplings,^[9b] the steric repulsions in the forming C–C bond are larger than the repulsions in the forming metal–carbon bond and dominate the regioselectivity (Scheme 4 a). In contrast, in the 1,4-addition involving 1,3-diynes, the regioselectivity is controlled by the steric repulsions between the alkyne substituent and the ligand (Scheme 4 b).

Origin of enantioselectivities

The close contact between the diyne and the chiral phosphine ligand in the oxidative coupling transition state enables high levels of chiral induction in the coupling reactions. We investigated the origin of enantioselectivities in the coupling of diyne *t*Bu–C≡C–C≡C–Me with glyoxal by using the (*R*)-conformer of the BIPHEP ligand as a surrogate. Experimentally, (*R*)-BIPHEP derivatives catalyze the couplings to yield (*R*)-products with more than 80% enantiomeric excess (*ee*).^[3a, h]

The two oxidative coupling transition states leading to the enantiomeric products are shown in Figure 6. In both transition states the coupling occurs at the more hindered *tert*-butyl-substituted propargylic carbon through 1,4-addition to the diyne. The coupling with a diyne

may occur at either the *Re* or *Si* face of the Rh–glyoxal η^2 -complex (TS8a or TS8c, respectively). The repulsions of the diyne with the chiral phosphine ligand are different in the two pathways: in TS8a, the C–C bond is formed at the *Re* face of the Rh–glyoxal η^2 -complex, and the distal methyl group on the diyne is pointing towards the gap between the two phenyl rings in the chiral bisphosphine ligand; whereas in TS8c, the distal methyl group is pointing towards one of the phenyl rings in the ligand. Thus, greater repulsion between the ligand and the diyne is expected in TS8c than in TS8a. When (*R*)-BIPHEP is used, coupling at the *Re* face of the Rh–glyoxal complex is favored, leading to the preferential formation of the (*R*)-products as observed in the experiment. DFT calculations predict that the major transition state TS8a is favored by 1.1 kcal mol^{−1}, corresponding to 73% *ee*. This is in good agreement with the experiment.

Conclusion

Density functional calculations suggest that the reductive couplings of 1,3-diynes and vicinal dicarbonyl compounds occur through an oxidative coupling mechanism involving 1,4-addition to the diyne from a Rh^I-bound dicarbonyl complex to furnish the seven-membered oxarhodacycle intermediate. The seven-membered oxarhodacycle isomerizes to a smaller five-membered oxarhodacycle intermediate, followed by hydrogenative cleavage of the oxarhodacycle and finally reductive elimination to form the allylic alcohol product. The alternative mechanism involving dihydrogen oxidative addition with subsequent alkyne hydrometallation is predicted to have higher activation energies. The catalytic cycle involving cationic rhodium species is far more reactive than corresponding cycle involving neutral complexes, which suggests that heterolytic hydrogen activation is not operative.

The 1,4-addition to the diyne by the Rh–glyoxal complex is much more favorable than the 1,2-addition. The 1,4-addition maximizes the interaction of the LUMO of the diyne with the HOMO of the Rh–glyoxal complex in the oxidative coupling transition state. Furthermore, the oxidative coupling transition state is stabilized by the coordination of the α -carbonyl group of the glyoxal to the metal.

This mechanism establishes the origins of substrate reactivity, as well as chemo-, regio-, and enantioselectivities. The high reactivities of 1,3-diynes and vicinal dicarbonyl compounds are attributed to the stabilization of the oxidative coupling transition state by these substrates. These same effects also lead to exclusive formation of the diyne–aldehyde cross-coupling products. In contrast, under similar conditions, the reductive coupling of acetylene to aldehydes and imines delivers products of carbonyl (*Z*)-butadienylation through oxidative dimerization of acetylenes in the initial step. The presence of a Brønsted acid increases the rate of the diyne–aldehyde coupling reaction by accelerating the turnover-determining H₂ activation step through a six-centered hydrogenolysis transition state instead of a four-centered σ -bond metathesis transition state that takes place under conditions without a Brønsted acid.

The origins of regio- and enantioselectivities are both attributed to the close proximity of the ligand and the diyne substrate in the oxidative coupling transition state. The 1,4-addition to the diyne yields linear coupling product exclusively. When an unsymmetrical diyne is used, the coupling occurs at the sterically more demanding alkyne terminus to avoid repulsions between the large phosphine ligand and the alkyne substituent distal to the forming C–C bond. The most stable oxidative coupling transition state leading to the major enantiomeric product also has less repulsions between the distal alkyne substituent and the phenyl rings on the biaryl phosphine ligand.

Computational Details

All geometry optimizations and frequency calculations were performed with the B3LYP^[22] functional implemented in Gaussian 03.^[23] The LANL2DZ^[24] basis set was used for rhodium, and the 6-31G(d) basis set was used for other atoms. All free energies reported are Gibbs free energies involving zero-point vibrational energy corrections, thermal corrections at 298 K, and single point solvation free energy corrections computed by using the CPCM^[25] polarizable conductor calculation model as implemented in Gaussian 03. The molecular cavities were built up by using the United Atom Topological Model (UAHF), which was reported to be more accurate than cavity models such as UFF, Pauling, or Bondi in calculating solvation free energies by using CPCM.^[26] 1,2-Dichloroethane was specified as solvent. All transition states have been confirmed by intrinsic reaction coordinate (IRC) calculations. Figures of the 3D molecular structures were prepared by using CYLView.^[27]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Free energy diagram of the preferred oxidative coupling mechanism of Rh^I-catalyzed reductive coupling of 2,4-hexadiyne and glyoxal. Calculated at the B3LYP/LANL2DZ+6-31G* level with CPCM(DCE) single point solvation energy correction.

Figure 2.
Possible oxidative coupling transition states for the couplings of 2,4-hexadiyne and glyoxal.

Figure 3.

Free energy diagram of the hydrometallation mechanism of Rh^{I} -catalyzed reductive coupling of 2,4-hexadiyne and glyoxal. One pathway leads to a branched coupling product (**11a**); whereas the other pathway leads to a linear coupling product (**11b**). Both H_2 oxidative addition (TS4) and hydrometallation (TS5) require much higher activation energy than oxidative coupling (TS1 in Figure 1) Calculated at the B3LYP/LANL2DZ+6-31G* level with CPCM(DCE) single point solvation energy correction.

Figure 4. Free energy diagram of Rh^I-catalyzed reductive coupling of 2,4-hexadiyne to glyoxal with acetic acid as cocatalyst. Calculated at the B3LYP/ LANL2DZ+6-31G* level with CPCM(DCE) single point solvation energy correction.

Figure 5. Regioisomeric oxidative coupling transition states. Activation barriers are calculated with respect to the Rh^I-glyoxal η^2 complex.

Figure 6.

Oxidative coupling transition states with the (*R*)-BIPHEP ligand. Activation barriers are calculated with respect to the Rh^{I} -glyoxal η^2 complex.

Scheme 1.

Rh^I-catalyzed reductive coupling reactions of 1,3-diynes with activated carbonyl partners (R^S=small substituent, R^L=large substituent; cod=1,5-cyclooctadiene, OTf=trifluoromethanesulfonyl).

Scheme 2.

Two possible mechanisms of Rh^{I} -catalyzed hydrogenative coupling reactions. The oxidative coupling mechanism is favored.

Scheme 3.

Regio- and enantioselectivities in the Rh^I-catalyzed reductive coupling reactions (DCE=1,2-dichloroethane).^[3h]

Scheme 4.

Origin of regioselectivities of Rh^{I} -catalyzed hydrogenative coupling reactions.^[9b, 21d]