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Formation of β-Ruthenium-Substituted Enones from Propargyl Alcohols†

Charles P. Casey,* Xiangdong Jiao,‡ and Ilia. A. Guzei

Department of Chemistry, University of Wisconsin−Madison, Madison, Wisconsin 53706. ‡Current address: Dalton Pharma Services, 349 Wildcat Rd., Toronto, ON M3J 2S3, Canada.

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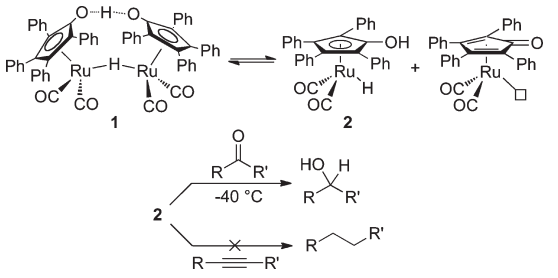
The reaction of the dienone ruthenium dicarbonyl dimer {[2,5-Ph-3,4-Tol(η^5-C_4CO)]$Ru(CO)_2$}$_2$ (**7**) with propargyl alcohol at room temperature gave a high yield of β-ruthenium-enal (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]$Ru(CO)_2$(CH=CHCHO) (**8*E***), which was characterized spectroscopically and by X-ray crystallography. Reaction of **7** with pent-2-yn-1-ol led to the kinetic formation of the *E*-isomer (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]$Ru(CO)_2$[$C(CH_2CH_3)$=CHCHO] (**10*E*-Et**), which isomerized to an equilibrium mixture of *Z*- and *E*-isomers upon heating. The intramolecular nature of the 1,2-hydrogen shifts involved in these reactions was established by the absence of crossover products in the reaction of **7** with a mixture of PhC≡CCH_2OH and PhC≡CCD_2OH. A primary deuterium isotope effect ($k_H/k_D \approx 11$) was seen on the product-forming step in the reaction of **7** with PhC≡CCHDOH. The reaction of PhC≡CCH_3 with **7** produced the alkyne complex [2,5-Ph_2-3,4-Tol_2(η^5-C_4COH)]$Ru(CO)_2$(η^2-PhC≡CCH_3) (**14**). The key step in the mechanism of the reaction of **7** with propargyl alcohols is proposed to be an in-plane 1,2-hydrogen migration to an electrophilic carbon of a complexed alkyne.

Introduction

The Shvo hydrogenation catalyst[1,2] **1** was the first example of a ligand metal bifunctional catalyst.[3] For aldehyde, ketone, and imine hydrogenations, the monoruthenium hydride **2** has been shown to be the active reducing agent in the Shvo system,[1a,4] and detailed mechanistic studies have been performed.[5] In contrast, the mechanism of the hydrogenation of alkenes and alkynes catalyzed by the Shvo catalyst has not been studied extensively. However, it is clear that alkene and alkyne hydrogenations must occur by very different mechanisms from those of aldehyde hydrogenation, since ruthenium hydride **2** does not react with alkenes or alkynes.[1a,4]

Scheme 1



Shvo reported that the hydrogenation of alkynes catalyzed by **1** at 145 °C under 35 atm of H_2 pressure produced fully reduced alkane products.[1a] There are three reports of ruthenium alkyne adducts formed from reactions of alkynes with compounds related to the Shvo catalyst. Shvo reported the isolation of **3** formed during the hydrogenation of diarylalkynes; **3** did not react with H_2 even at 140 °C and was not a catalyst for alkyne hydrogenation (Scheme 2).[6] Shvo isolated **4**, a different kind of alkyne adduct, from the hydrogenation

† Part of the Dietmar Seyferth Festschrift. Dedicated to Dietmar Seyferth, a founding editor of both the Journal of Organometallic Chemistry and Organometallics and an organizer of the first Organometallic Chemistry Gordon Conference held at Wayland Academy in Beaver Dam, Wisconsin, in 1972, and Chair of the second conference. Dietmar's organizational skills, intellectual leadership, contagious enthusiasm, and good humor have helped to develop a real sense of community among organometallic chemists around the world.

*Corresponding author. E-mail: casey@chem.wisc.edu.

(1) (a) Blum, Y.; Czarkie, D.; Rahamim, Y.; Shvo, Y. *Organometallics* **1985**, *4*, 1459. (b) Shvo, Y.; Czarkie, D.; Rahamim, Y.; Chodosh, D. F. *J. Am. Chem. Soc.* **1986**, *108*, 7400. (c) Shvo, Y.; Abed, M.; Blum, Y.; Laine, R. M. *Isr. J. Chem.* **1986**, *27*, 267. (d) Abed, M.; Goldberg, I.; Stein, S.; Shvo, Y. *Organometallics* **1988**, *7*, 2054. (e) Menashe, N.; Shvo, Y. *Organometallics* **1991**, *10*, 3885. (f) Menashe, N.; Salant, E.; Shvo, Y. *J. Organomet. Chem.* **1996**, *514*, 97.

(2) For recent reviews of the Shvo catalyst, see: (a) Karvembu, R.; Prabhakaran, R.; Natarajan, K. *Coord. Chem. Rev.* **2005**, *249*, 911. (b) Samec, J.; Bäckvall, J.; Andersson, P.; Brandt, P. *Chem. Soc. Rev.* **2006**, *35*, 237. (c) Conley, B. L.; Pennington-Boggio, M. K.; Boz, E.; Williams, T. J. *Chem. Rev.*, submitted.

(3) For reviews of ligand−metal bifunctional catalysis, see: (a) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40. (b) Noyori, R.; Kitamura, M.; Ohkuma, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5356. (c) Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2201. (d) Ikariya, T.; Murata, K.; Noyori, R. *Org. Biomol. Chem.* **2006**, *4*, 393.

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(5) (a) Casey, C. P.; Johnson, J. B.; Singer, S. W.; Cui, Q. *J. Am. Chem. Soc.* **2005**, *127*, 3100. (b) Samec, J. S. M.; Éll, A. H.; Åberg, J. B.; Privalov, T.; Eriksson, L.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2006**, *128*, 14293. (c) Casey, C. P.; Clark, T. B.; Guzei, I. A. *J. Am. Chem. Soc.* **2007**, *129*, 11821. (d) Casey, C. P.; Beetner, S. E.; Johnson, J. B. *J. Am. Chem. Soc.* **2008**, *130*, 2285.

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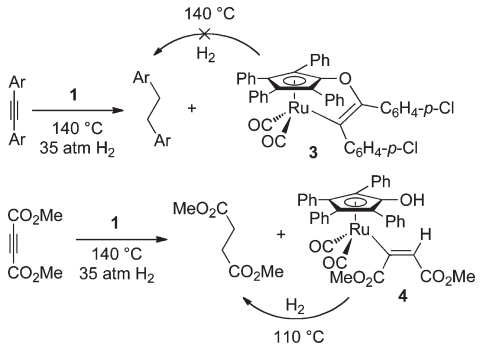
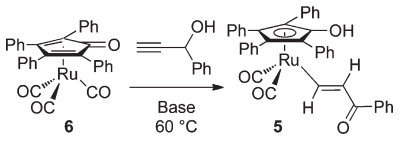
Scheme 2



Scheme 3



of dimethyl acetylenedicarboxylate (DMAD). Vinyl ruthenium complex **4** was stable to 140 °C but reacted with H_2 at 110 °C to give dimethyl succinate; **4** is an active catalyst for the hydrogenation of DMAD.

During studies of ruthenium-catalyzed enamino ketone formation from propargyl alcohols, Haak observed the formation of β-ruthenium-substituted enone **5** from the reaction of dienone ruthenium tricarbonyl complex **6** with 1-phenylprop-2-yn-1-ol (Scheme 3).[7]

Here we report the reaction of ruthenium dienone dimer **7** with propargyl alcohols to give β-ruthenium-substituted enones at room temperature. Mechanistic studies support a mechanistic hypothesis of ruthenium alkyne complex formation followed by an intramolecular 1,2-hydride shift to an electrophilic carbon of the complexed alkyne.

Results

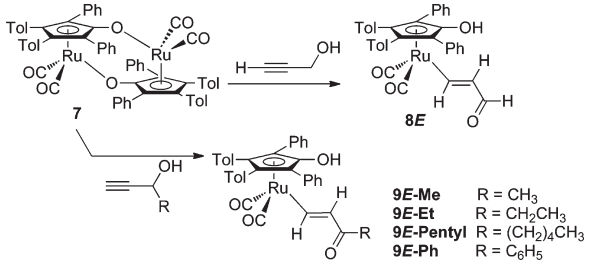
Reaction of Propargyl Alcohols with Ruthenium Dienone Dimer. The addition of excess propargyl alcohol to an orange solution of the ruthenium dicarbonyl dienone dimer **7** in CH_2Cl_2 gave the β-ruthenium-enal compound (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$(CH=CHCHO) (**8*E***) in >90% yield (Scheme 4). **8*E*** was also obtained in high yield by shaking a suspension of **7** in a toluene solution of progargyl alcohol.

The structure of **8*E*** was determined spectroscopically and confirmed by X-ray crystallography. In the ^{1}H NMR spectroscopy of **8*E***, an aldehyde CHO resonance appeared as a doublet (J = 7.4 Hz) at δ 9.18. In addition two strongly coupled vinyl hydrogen resonances were seen at δ 6.73 (dd, J = 15.8, 7.4 Hz) and 8.65 (d, J = 15.6 Hz). This coupling pattern requires trans hydrogens in a β-substituted enal. In the ^{13}C NMR spectrum, the aldehyde carbon resonance appears at δ 190.3 and the vinyl carbon α to the aldehyde was seen at δ 148.0, while that of the vinyl carbon β to the aldehyde appeared at δ 187.0. The X-ray crystal structure of **8*E*·Pentane** confirmed the structural assignment (Figure 1).

Similarly, secondary propargyl alcohols reacted with ruthenium dienone dimer **7** in CH_2Cl_2 to give β-ruthenium-enone

(7) (a) Haak, E. *Synlett* **2006**, 1847. (b) Haak, E. *Eur. J. Org. Chem.* **2007**, 2815.

Scheme 4



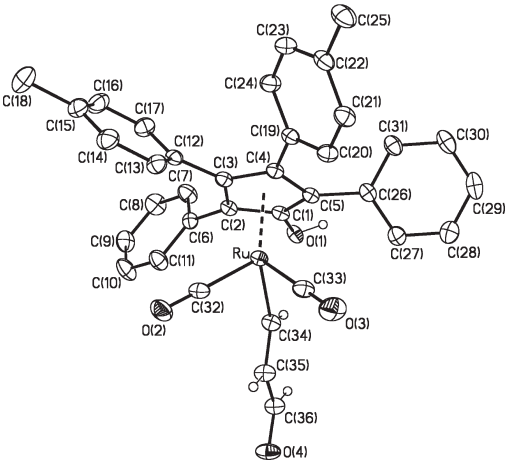


Figure 1. X-ray crystal structure of (*E*)-[2,5-Ph-3,4-Tol-(η^5- C_4COH)]Ru(CO)$_2$(CH=CHCHO) (**8*E*·Pentane**).

compounds. For example, reaction of **7** with oct-1-yn-3-ol gave (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[CH=CHCO(CH$_2$)$_4$-CH$_3$] (**9*E*-Pentyl**). The *E*-configuration of the enone was assigned on the basis of a 16 Hz coupling constant between the vinyl hydrogens in the ^{1}H NMR spectrum. The X-ray crystal structure of **9*E*-Pentyl** confirmed the structural assignment (Figure 2). Similarly, reaction of **7** with but-3-yn-2-ol gave **9*E*-Me**, with pent-1-yn-3-ol gave **9*E*-Et**, and with 1-phenylprop-2-yn-1-ol gave **9*E*-Ph**.

Kinetic Formation of *E*-Isomers of β-Ruthenium-Enones. Propargyl alcohols with an internal triple bond reacted with **7** to initially give *E*-isomers of β-ruthenium-enone compounds that slowly equilibrated with the corresponding *Z*-isomers upon standing at room temperature. Reaction of **7** with pent-2-yn-1-ol gave (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]-Ru(CO)$_2$[C(CH$_2$CH$_3$)=CHCHO] (**10*E*-Et**) (Scheme 5). The assignment of the *E*-enal configuration was first based on the observation of a large 5.1% NOE for the aldehyde CHO resonance at δ 9.53 upon irradiation of the allylic CH_2 resonance at δ 2.96. This assignment was confirmed by an X-ray crystal structure of **10*E*-Et** (Figure 3). Similarly, reaction of **7** with but-2-yn-1-ol initially gave **10*E*-Me**, which isomerized to an equilibrium mixture with **10*Z*-Me**. In contrast, reaction of **7** with 3-phenylprop-2-yn-1-ol gave **10*E*-Ph**, which did not isomerize even upon heating at 65 °C for 5 h.

The kinetics of equilibration of **10*E*-Et** to a 67:33 mixture of **10*E*-Et**:**10*Z*-Et** ($K_{eq} = k_1/k_{-1}$ = 0.49) were measured at 65 °C in THF-d_8. The rate of approach to equilibrium followed clean first-order kinetics ($k_{obs} = k_1 + k_{-1}$ = 2.38×10^{-3} s^{-1}, $t_{1/2}$ = 4.8 min). The rate of isomerization of **10*E*-Et** to **10*Z*-Et** was calculated from K_{eq} and k_{obs} to be $k_1 = 7.84 \times 10^{-4}$ s^{-1} ($\Delta G^{\ddagger}$ = 24.7 kcal mol^{-1}).

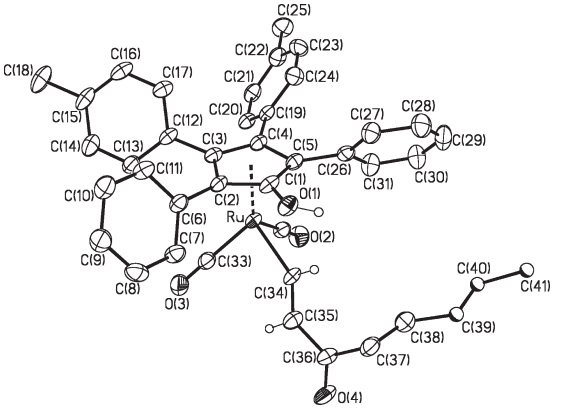


Figure 2. X-ray crystal structure of (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[CH=CHCO(CH$_2$)$_4$CH$_3$] (**9*E*-Pentyl**).

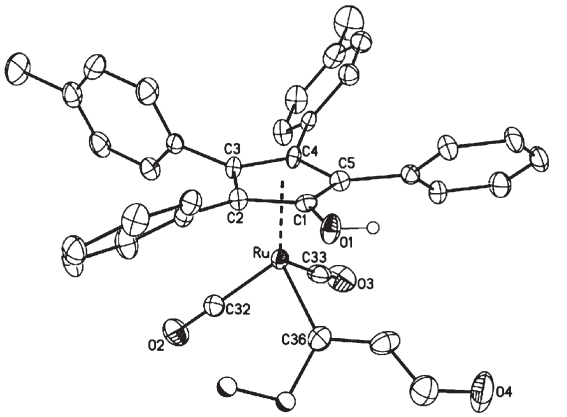
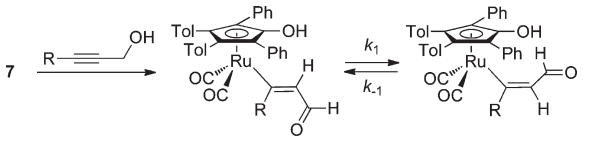


Figure 3. X-ray crystal structure of (*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[C(CH$_2$CH$_3$)=CHCHO] (**10*E*-Et**).

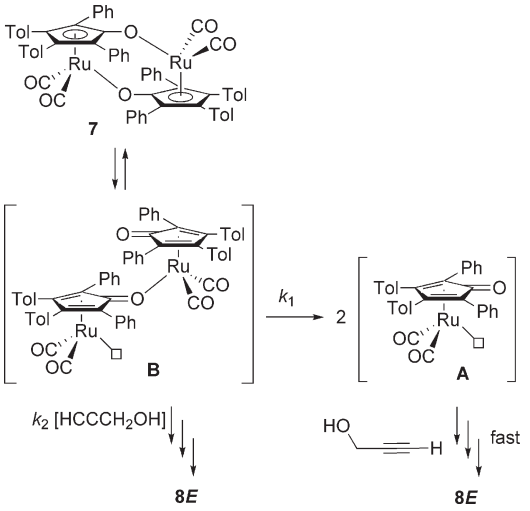
Scheme 5



Kinetics of Reaction of 7 with Propargyl Alcohols. Ruthenium dimer **7** has been used in the synthesis of amine and phosphine ruthenium complexes.[8,4,5b] It can be thought of as a source of the coordinatively unsaturated dienone dicarbonyl ruthenium intermediate **A**, formed by dissociation of **7**. This is probably an oversimplification, since these substitution reactions are normally much faster than crossover between two ruthenium dimers related to **7**. Another possibility is that **7** might sever a single oxygen−ruthenium linkage to give a diruthenium species such as **B**, which has a single unsaturated ruthenium center. The kinetic rate law for reaction of **7** with propargyl alcohols was determined in an effort to narrow the number of possible mechanisms of reaction (Scheme 6).

(8) (a) Mays, M. J.; Morris, M. J.; Raithby, P. R.; Shvo, Y.; Czarkie, D. *Organometallics* **1989**, *8*, 1162. (b) Casey, C. P.; Bikzhanova, G. A.; Cui, Q.; Guzei, I. A. *J. Am. Chem. Soc.* **2005**, *127*, 14062.

Scheme 6



The reaction of **7** with at least a 10-fold excess of propargyl alcohol (pseudo-first-order conditions) in CD_2Cl_2 at −10 °C was monitored by following the disappearance of the tolyl methyl resonance of **7**. Plots of $\ln\{[\mathbf{7}]_t/[\mathbf{7}]_0\}$ vs time were linear to >3 half-lives, indicating a clean first-order dependence on [**7**]. A plot of k_{obs} vs [HC≡CCH$_2$OH] was linear with a slope corresponding to a second-order rate constant of $6.2(3) \times 10^{-4}$ M^{-1} s^{-1} (Figure 4). The intercept of the line corresponds to a first-order reaction of **7** with a rate constant of $1.9(4) \times 10^{-4}$ s^{-1}. Scheme 6 shows a general mechanism for reaction of **7** with propargyl alcohols that is consistent with these kinetics and with the rate law:

$$\text{Rate} = k_2[\mathbf{7}][\text{propargyl alcohol}] + k_1[\mathbf{7}]$$

Similarly, the kinetics of the reaction of **7** with 3-phenylprop-2-yn-1-ol were measured at −10 °C in CD_2Cl_2. A plot of k_{obs} vs [PhC≡CCH$_2$OH] was linear with a slope corresponding to a second-order rate constant of $9.97(2) \times 10^{-4}$ M^{-1} s^{-1}, about 1.5 times faster than HC≡CCH$_2$OH. The intercept corresponds to a first-order reaction of **1** with a rate constant of $1.49(1) \times 10^{-4}$ s^{-1}, which is similar to that seen for HC≡CCH$_2$OH.

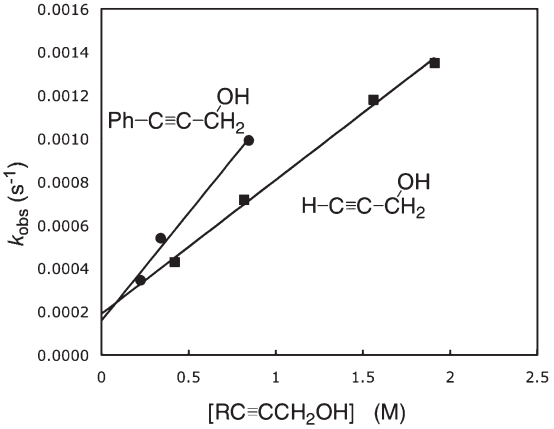
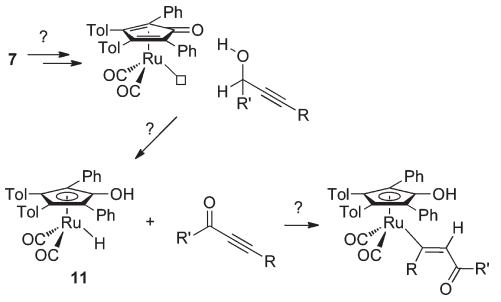


Figure 4. Plot of k_{obs} vs [propargyl alcohols]: (■) HC≡CCH$_2$OH, (●) PhC≡CCH$_2$OH.

A Plausible Mechanism Involving a Ruthenium Hydride Intermediate. One plausible mechanism for the formation

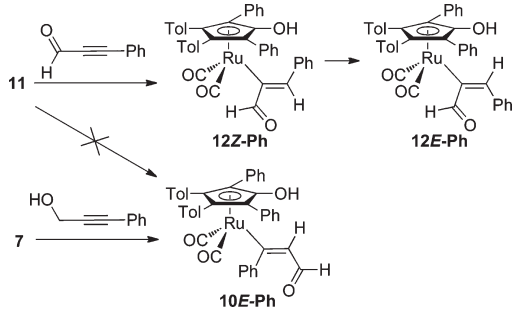
of β-ruthenium enones from the reaction of propargyl alcohols with **1** involves initial dehydrogenation of the propargyl alcohol to an alkynyl aldehyde or ketone and generation of [2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$H (**11**), followed by addition of the RuH intermediate across the triple bond of the alkynyl aldehyde or ketone (Scheme 7). This mechanism requires two readily testable consequences: (1) RuH **11** must react with alkynyl aldehydes or ketones to give the same products as obtained from Ru dimer **7** and propargyl alcohols, and (2) the hydrogen atom that ends up α to the carbonyl group of the β-Ru enone does not have to be derived from the same molecule of propargyl alcohol as the carbon framework of the enone.

Scheme 7



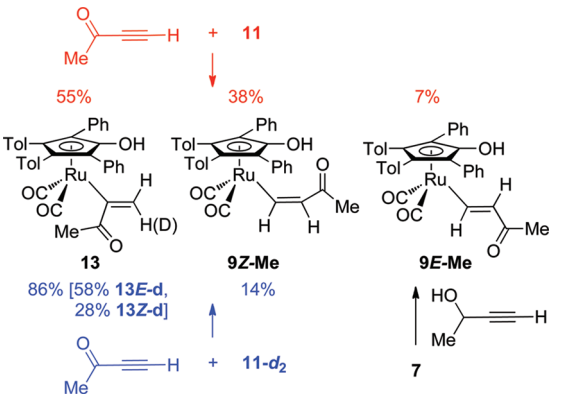
Ruthenium Hydride 11 Does Not React with Alkynyl Ketones to Give β-Ruthenium Enones. Hydroxycyclopentadienyl ruthenium hydride **11** reacted with PhC≡CCHO in toulene-d_8 or THF-d_8 at room temperature in less than 5 min to give α-ruthenium-substituted enone (*Z*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[C(=CHPh)CHO] (**12*Z*-Ph**) in nearly quantitative yield (Scheme 8). Slow isomerization of **12*Z*-Ph** to **12*E*-Ph** occurred at room temperature. No trace of β-ruthenium-substituted enone **10*E*-Ph**, the product of the reaction of **7** with 1-phenylprop-2-yn-1-ol, was observed. The stereochemistry of **12*Z*-Ph** (>9% NOE between aldehyde and vinyl hydrogens) and **12*E*-Ph** (no NOE observed between aldehyde and vinyl hydrogens) was assigned with the aid of NOE experiments and requires a net trans addition of ruthenium hydride across the alkyne triple bond.

Scheme 8



Ruthenium hydride **11** reacted slowly with HC≡CCOMe in THF-d_8 at room temperature to give 55% α-ruthenium-substituted enone [2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[C(=CH_2)COMe] (**13**), 38% (*Z*)-[2,5-Ph_2-3,4-Tol_2(η^5-C_4COH)]Ru(CO)$_2$(CH=CHCOCH$_3$) (**9*Z*-Me**), and only 7% **9*E*-Me** (the product of the reaction of **7** and the propargyl alcohol 3-butyn-2-ol) (Scheme 9). No isomerization of **9*Z*-Me** and **9*E*-Me** was seen over seven days at room temperature. Reaction of ruthenium deuteride **11-*d*$_2$** with HC≡CCOMe gave an 86:14 ratio of **13**:**9*Z*-Me** and no observable **9*E*-Me**. In **13**, the majority (58:28) of the deuterium was located trans to ruthenium. Thus the two major products both result from a net trans addition of ruthenium deuteride across a triple bond. These results show that both cis and trans addition of ruthenium hydride occurs and that there is only moderate regioselectivity favoring α-ruthenium enones over β-ruthenium enones.

Scheme 9

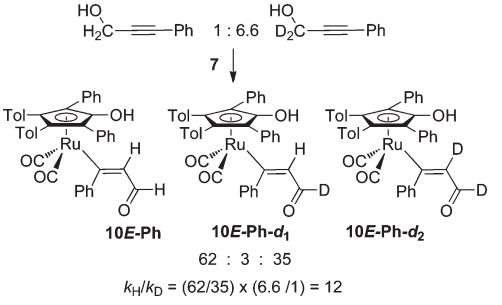


In summary the predominant formation of α- not β-substituted ruthenium enones is not consistent with the mechanism shown in Scheme 7. While helping to clarify the mechanism of reaction of **7** with propargyl alcohols, these experiments raise a difficult and interesting mechanistic problem: how does the very unusual net trans addition of ruthenium hydride across the alkyne triple bond occur?

Crossover Experiment. The mechanism shown in Scheme 7 involves oxidation of the propargyl alcohol by **7** to give ruthenium hydride **11** and an alkynyl aldehyde followed by addition of the ruthenium hydride across the triple bond to give a β-substituted enone. It predicts that crossover of deuterium will occur in the reaction of **7** with a mixture of PhC≡CCH_2OH and PhC≡CCD_2OH to give d_0, d_1, and d_2 β-ruthenium-substituted enones.

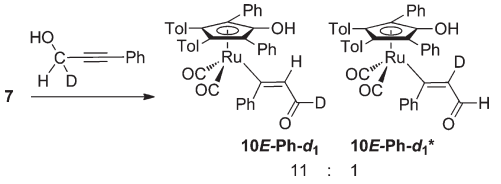
Addition of a large excess of a 6.6:1 mixture of PhC≡CCD_2OH (~95% deuterium) and PhC≡CCH_2OH to a solution of **7** in toluene-d_8 gave **10*E*-Ph** as a white precipitate. The ^{1}H NMR spectrum showed large doublets at δ 8.82 and 6.35 for the =CHCHO fragment of d_0 **10*E*-Ph** and a small signal (~5% of the size of the doublets) at δ 6.35 for the =C*H*CDO fragment of d_1 **10*E*-Ph-*d*$_1$** (Scheme 10). The ratio of **10*E*-Ph**:**10*E*-Ph-*d*$_1$**:**10*E*-Ph-*d*$_2$** was estimated to be 62:3:35. The isotope effect on product formation was estimated to be about 12. This may or may not be an isotope effect on the rate-limiting step.

Scheme 10



Primary Deuterium Isotope Effect on Intramolecular Hydrogen Migration. In the reaction of **7** with PhC≡CCHDOH, 80% of **10*E*-Ph** arose from hydrogen migration to produce Ru[PhC═CHCDO] and only 7% resulted from deuterium migration to give Ru[PhC═CHCDO]; the remaining 13% of material, Ru[PhC═CHCHO], was derived from incompletely deuterated alcohol (Scheme 11). Thus the primary deuterium isotope effect on the step involving hydrogen migration is $k_H/k_D \approx 11$.

Scheme 11

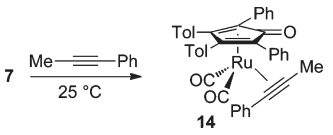


Mechanisms Involving Alkyne Complexes. Some possible mechanisms for reaction of propargyl alcohols with **7** involve ruthenium dienone complexes. The dienone dicarbonyl dimer **7** has been used extensively as the synthetic equivalent of the coordinatively unsaturated ruthenium dienone dicarbonyl intermediate **A** for the synthesis of amine and phosphine complexes. While propargyl alcohol complexes were not observed in reactions with **7** (possibly because of rapid rearrangement), we investigated the possible formation of other alkyne ruthenium complexes.

In addition to simple η^2-alkyne complexes, another structure in which the alkyne unit has been inserted between the dienone carbonyl and ruthenium needs to be considered. Shvo reported that diaryl alkynes react with diruthenium bridging hydrides to give adducts such as **3**, which was characterized by X-ray crystallography (Scheme 2).[6] Significantly, the ^{13}C NMR chemical shifts of the carbons derived from the alkyne appear at δ 147 and 143.

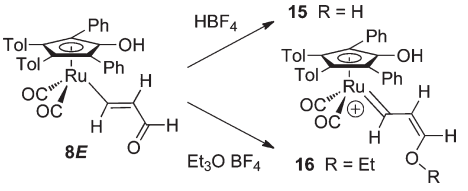
Addition of 1-phenyl-1-propyne to a solution of **7** in CD_2Cl_2 at room temperature led to the formation of [2,5-Ph$_2$-3,4-Tol$_2$(η^5-C$_4$COH)]Ru(CO)$_2$(η^2-PhC≡CCH$_3$) (**14**) within 20 min (Scheme 12). The observation of ^{13}C NMR resonances at δ 71.3 and 66.6 was critical for the structural assignment as an η^2-alkyne complex. The alkyne carbon chemical shifts of (CO)$_4$Ru(η^2-HC≡CH) and (CO)$_4$Ru(η^2-Me$_3$SiC≡CSiMe$_3$) are δ 70 and 89.5, respectively.[9] For Cp*Re(CO)$_2$(η^2-alkyne) complexes, we have observed ^{13}C NMR chemical shifts in the range δ 50−100 for η^2-alkyne carbons.[10]

Scheme 12



Ruthenium Carbene Complexes from Protonation and Alkylation of *β*-Substituted Ruthenium Enal 8*E*. The addition of excess HBF_4 in ether to a yellow CD_2Cl_2 solution of the neutral β-substituted ruthenium enal complex **8*E*** led to protonation of the aldehyde oxygen and formation of a brown solution of the cationic ruthenium carbene complex (*E*)-{[2,5-Ph-3,4-Tol(η^5-C$_4$COH)]Ru(CO)$_2$(═CHCH═CHOH)}-[BF_4] (**15**) (Scheme 13). The presence of a Ru═CH carbene unit in **15** is supported by the observations of a high-frequency ^{1}H NMR resonance for Ru═C*H* at δ 12.46 (d, 15 Hz) and of a high-frequency ^{13}C NMR resonance for Ru═*C*H at δ 277.5 (d, $^1J_{CH}$, 139.9 Hz).

Scheme 13



Similarly, addition of one equivalent of Et_3OBF_4 in CH_2Cl_2 to a yellow CD_2Cl_2 solution of the **8*E*** led to alkylation of the aldehyde oxygen and produced a brown solution of cationic carbene complex (*E*)-{[2,5-Ph-3,4-Tol(η^5-C$_4$COH)]Ru(CO)$_2$(═CHCH═CHOEt)}[BF_4] (**16**). The presence of a Ru═CH unit in **16** is shown by the ^{1}H NMR resonance for Ru═C*H* at δ 11.3 (d, 15 Hz) and by the ^{13}C NMR resonance for Ru═*C*H at δ 252.0 (d, $^1J_{CH}$ 139.9 Hz).

Protonation or alkylation at the aldehyde oxygen has the effect of decreasing the C═C π-bond order of the enal Ru−CH═CH−CH═O by going to Ru═CH−CH═CHOR. Such changes may be involved in the *E*/*Z* isomerization of enone complexes such as **10*E*-Me** to **10*Z*-Me**.

Discussion

Any mechanism for the reaction of ruthenium dienone dimer **7** with propargyl alcohol must explain (1) the kinetic formation of the *E*-isomer of the β-ruthenium-substituted enone even when this is the less thermodynamically stable isomer, (2) the intramolecular nature of the 1,2-hydrogen shift as shown by a crossover experiment, (3) the large deuterium isotope effect on product formation shown in the internal competition experiment with PhC≡CCHDOH, and (4) a kinetic rate law that has a first-order term (dependence on [**7**]) and a second-order term (dependence on both [**7**] and [propargyl alcohol]). Other key experimental findings that constrain mechanistic possibilities include (1) the addition of ruthenium hydride **11** to propargyl aldehydes to give regioisomeric α-ruthenium-substituted enones, (2) the *E* to *Z* isomerization of the kinetically formed *E*-isomer of the β-ruthenium-substituted enone, (3) the protonation and alkylation of the enone oxygen, and (4) the formation of isolable alkyne ruthenium complexes in the absence of an α-hydroxyl function.

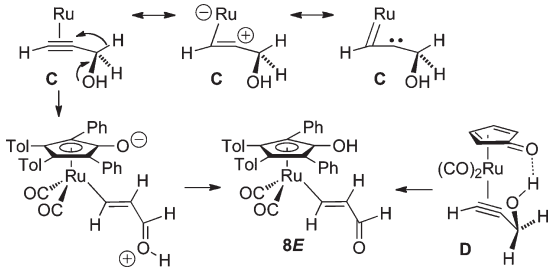
Proposed 1,2-Hydride Migration to an Alkyne Carbon of a Complexed Progargyl Alcohol. The key step in the

(9) (a) Burn, M. J.; Kiel, G.-Y.; Seils, F.; Takats, J.; Washington, J. *J. Am. Chem. Soc.* **1989**, *111*, 6850. (b) Ball, R. G.; Burke, M. R.; Takats, J. *Organometallics* **1987**, *6*, 1918. (c) For (CO)$_4$Os(η^2-MeC≡CMe), δ 69.7: Washington, J.; McDonald, R.; Takats, J.; Menashe, N.; Reshef, D.; Shvo, Y. *Organometallics* **1996**, *14*, 3996. (d) For Cp(PR$_3$)ClOs(η^2-HC≡CCMe$_2$OH), δ 57.5 and 49.6: Carbo, J. J.; Crochet, P.; Esteruelas, M. A.; Jean, Y.; Lledos, A.; Lopez, A. M.; Oñate, E. *Organometallics* **2002**, *21*, 305.

(10) (a) Casey, C. P.; Selmeczy, A. D.; Nash, J. R.; Yi, C. S.; Powell, D. R.; Hayashi, R. K. *J. Am. Chem. Soc.* **1996**, *118*, 6698. (b) Casey, C. P.; Nash, J. R.; Yi, C. S.; Selmeczy, A. D.; Chung, S.; Powell, D. R.; Hayashi, R. K. *J. Am. Chem. Soc.* **1998**, *120*, 722. (c) For Cp complexes: Casey, C. P.; Kraft, S.; Powell, D. R. *J. Am. Chem. Soc.* **2000**, *122*, 3771. (d) For indenyl complexes: Casey, C. P.; Vos, T. E.; Brady, J. T.; Hayashi, R. K. *Organometallics* **2003**, *22*, 1183. (e) For related CpMn(CO)$_2$ complexes: Casey, C. P.; Dzwiniel, T. L.; Kraft, S.; Guzei, I. A. *Organometallics* **2003**, *22*, 3915.

rearrangement is suggested to be an in-plane 1,2-hydrogen migration to an electrophilic carbon of the complexed alkyne in **C** (Scheme 14). Complexation of alkynes to transition metals gives rise to electrophilic carbene- or carbocation-like character of the alkyne carbons. For example, Au(I) and Pt (II) alkyne complexes are readily attacked at carbon by nucleophiles, and in some cases an alkyne carbon reacts with tethered alkenes to produce cyclopropanes.[11] The hydrogen migration is suggested to be assisted by electron donation from the α-hydroxyl oxygen to the developing cationic center. This kind of electron donation is a key to the pinacol rearrangement of 1,2-diols to ketones. Since complexed alkynes are nonlinear and have substituents bent away from the metal, hydrogen migration to give an *E*-isomer involves a least motion process.

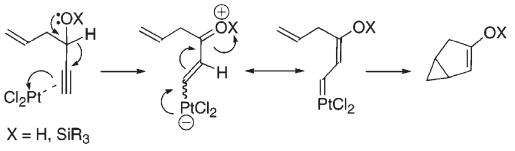
Scheme 14



A proton shift from the alcohol oxygen to the dienone oxygen must take place sometime during the rearrangement. This might occur after the hydride migration or concurrent with it. One interesting possibility is an intramolecular proton shift concerted with the hydrogen migration. Molecular modeling suggests that an appropriate geometry (**D**) with a hydrogen bond between the dienone oxygen and the hydroxyl group of the complexed propargyl alcohol is readily accessible (Scheme 14).

Malacria has proposed a similar 1,2-hydride migration of a complexed propargyl alcohol as a key step in a $PtCl_2$-catalyzed cycloisomerization (Scheme 15).[12]

Scheme 15

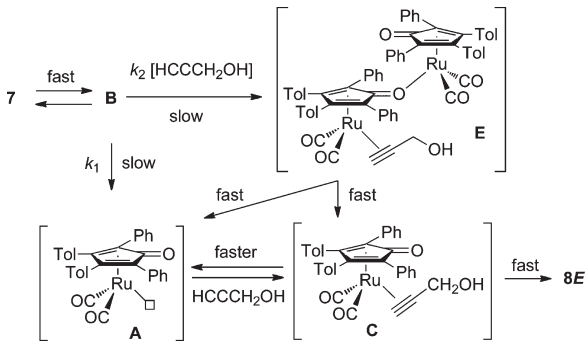


The observation of an intramolecular deuterium isotope effect on hydrogen migration using PhC≡CCHDOH requires that both H and D be available for migration. If the alkyne complexes parallel to the Cp ring, then H and D are in diastereotopic positions. If only one of the diastereotopic hydrogens can migrate (for example, only one of the two diastereomeric hydrogens of **D** is set up for migration), then no isotope effect would be seen unless the hydrogen positions can be interchanged by reversible alkyne coordination or by rapid rotation of the coordinated alkyne. We suggest that both reversible alkyne coordination and rotation of the coordinated alkyne are rapid relative to hydrogen migration.

The large magnitude of the product isotope effect ($k_H/k_D \approx 11$) suggests that tunneling may be involved and is consistent with an early transition state for the hydride migration step. Isotope effects on hydride migration to singlet carbene centers are normally relatively small (for example, k_H/k_D is about 1.5 for MeClC: and about 1.3−2 for $(ROCH_2)R'C:$),[13,14] suggesting an early transition state for hydride migration to a very reactive center. For the pinacol rearrangement of $PhCH(OH)C(OH)Ph_2$, k_H/k_D was inferred to be about 2−3 on the basis of the isotopic dependence of the ratio of phenyl to hydrogen migration.[15] This small isotope effect was attributed to a very early transition state for hydrogen migration to a very reactive carbocation. The larger isotope effects seen in the reactions of **7** with propargyl alcohols possibly involve tunneling and are consistent with a later transition state for migration to the much less electrophilic center of a complexed alkyne.

Proposed Rate-Limiting Generation of Coordinatively Unsaturated Ruthenium Species. The first-order term in the kinetic rate law is interpreted in terms of reversible breaking of one of the Ru−O interactions to generate coordinatively unsaturated diruthenium intermediate **B**, followed by slow breaking of the second Ru−O interaction to generate two equivalents of the monoruthenium unsaturated intermediate **A**, which then reacts rapidly with propargyl alcohol to give alkyne complex **C** and eventually produce β-ruthenium-substituted enone **8*E*** (Scheme 16). The second-order term is proposed to arise from trapping of diruthenium intermediate **B** by propargyl alcohol to give a diruthenium propargyl alcohol complex **E**, which rapidly dissociates to give ruthenium alkyne complex **C** and monoruthenium unsaturated intermediate **A**, which reacts with propargyl alcohol to give **C** and eventually **8*E***. To explain the deuterium isotope effect ($k_H/k_D \approx 12$) on product formation in the competition experiment with $PhC{\equiv}CCH_2OH$ and $PhC{\equiv}CCD_2OH$, we propose that alkyne complex formation is reversible and faster than product-determining hydride migration.

Scheme 16



Mechanism of *E*/*Z* Isomerization of β-Ruthenium Enones. *E* to *Z* isomerization of the kinetically formed *E*-isomer of the β-ruthenium-substituted enones occurred at 65 °C. We suggest that the isomerization is related to the demonstrated

(11) For reviews see: (a) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (b) Jimenez-Nunez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (c) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (d) Abu Sohel, S. M.; Liu, R.-S. *Chem. Soc. Rev.* **2009**, *38*, 2269.

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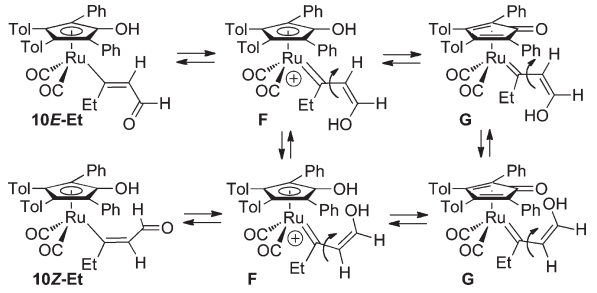
Scheme 17



ability of the aldehyde to be protonated to generate either a cationic carbene complex **F** or a neutral carbene complex **G** (a tautomer of **10*E***) that have greatly reduced barriers to rotation (Scheme 17). It should be pointed out that the CpOH of **10*E*** is likely to be as acidic at that of **11**, which has a pK_a of 17.5 in CH_3CN (for comparison, benzoic acid has a pK_a of 20.7 in CH_3CN).[4]

Untested Risky Predictions of Mechanistic Hypotheses. Since our experimental work in this area was completed before the above mechanistic hypotheses were formulated, there are some predictions based on the proposed mechanism that have not been tested. The mechanism requires that there be no kinetic deuterium isotope effect on the rate of reaction of PhC≡CCD_2OH compared with PhC≡CCH_2OH, in spite of the fact that an isotope effect on the product ratio was seen in a competition experiment to test for crossover. Added alkynes such as PhC≡CMe should speed up the reaction of **7** with propargyl alcohols by intercepting intermediate **B**. Exchange of alkynes with Ru alkyne complexes should be fast relative to reaction of **7** with propargyl alcohols. The *E* to *Z* isomerization of *β*-ruthenium-substituted enones is likely to be acid and/or base catalyzed.

Experimental Section

General Procedures for Reactions of Ruthenium Dienone Dimers with Propargyl Alcohols. A. An excess of a propargyl alcohol (10−16 *μ*L) was added to a CD_2Cl_2 solution (0.4 mL) of a ruthenium dienone dimer (**7**) (15.3 mg, 0.0134 mmol). After ^{1}H NMR spectroscopy indicated complete disappearance of dimer (usually 3−5 min), solvent was partially evaporated and pentane was added to give a precipitate of *β*-ruthenium-substituted enone compounds in >90% yield.

B. A mixture of excess propargyl alcohol (10−16 *μ*L) and yellow solid ruthenium dienone dimer (**7**) (15.3 mg, 0.0134 mmol) in 0.4 mL of toluene-d_8 was shaken for 10−30 min until the solid completely dissolved and the ^{1}H NMR indicated complete disappearance of dimer. Some white precipitate formed and pentane was added to precipitate additional solid. Filtration gave *β*-ruthenium-substituted enone compounds as white or pale yellow solids in >90% yield. In some cases, when no precipitate formed, the solution was concentrated and pentane was added to give *β*-ruthenium-substituted enone compounds in >90% yield. The products were recrystallized by slow diffusion of pentane or hexane into a THF solution.

(*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$(CH=CHCHO) (8*E*). Mp: 190−192 °C (dec). ^{1}H NMR (THF-d_8, 300 MHz): *δ* 2.19 (s, 6H, tol-CH_3), 6.73 (dd, *J* = 15.8 Hz, *J* = 7.4 Hz, 1H, CH=C*H*CHO), 6.85 (d, *J* = 8.4 Hz, 4H, tolyl), 6.92 (d, *J* = 8.4 Hz, 4H, tolyl), 7.24 (m, 6H, phenyl), 7.30 (m, 4H, phenyl), 8.66 (d, *J* = 15.6 Hz, 1H, RuC*H*=CH), 9.18 (d, *J* = 7.2 Hz, 1H, CHO), 9.28 (br s, 1H, OH). ^{13}C{^{1}H} NMR (THF-d_8, 75 MHz): *δ* 21.3 (tolyl CH_3), 90.3 (C3,4 of Cp), 106.0 (C2,5 of Cp), 128.7−138.3 (8 resonances, aromatic), 140.2 (C1 of Cp), 148.0 (C=*C*HCHO), 187.0 (Ru*C*H=CH), 190.3 (CHO), 201.9 (CO). IR (THF): 2024, 1970 cm^{-1}. MS (ESI-TOF) calcd (found) for $C_{36}H_{28}O_4RuNa$: 649.1 (649.1).

(*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[CH=CHCO$(CH_2)_4$-CH_3] (9*E*-pentyl). Mp: 178−180 °C (dec). ^{1}H NMR (THF-d_8, 300 MHz): *δ* 0.86 (t, *J* = 6.9 Hz, 3H, CH_3), 1.24 (m, 4H, CH_2), 1.49 (m, 2H, CH_2), 2.19 (s, 6H, tol-CH_3), 2.38 (t, *J* = 7.4 Hz, 2H, CH_2), 6.68 (d, *J* = 15.9 Hz, 1H, RuCH=C*H*CO), 6.84 (d, *J* = 7.2 Hz, 4H, tolyl), 6.91 (d, *J* = 8.1 Hz, 4H, tolyl), 7.20 (m, 6H, phenyl), 7.31 (m, 4H, phenyl), 8.52 (d, *J* = 16.5 Hz, 1H, RuC*H*=CH), 9.29 (br s, 1H, OH). ^{13}C{^{1}H} NMR (THF-d_8, 126 MHz): *δ* 14.4 (CH_3), 21.1 (tolyl CH_3), 23.5 (CH_2), 25.2 (CH_2), 32.7 (CH_2), 39.3(CH_2), 90.1 (C3,4 of Cp), 105.7 (C2,5 of Cp), 128.4−138.0 (8 resonances, aromatic), 140.0 (C1 of Cp), 144.6 (C=*C*HCO), 170.7 (Ru*C*H=CH), 194.1 (CH*C*OCH_2), 202.1 (CO). Spectral assignments were aided by a DEPT-135 experiment. IR (THF): 2021, 1966 cm^{-1}. MS (ESI-TOF) calcd (found) for $C_{41}H_{38}O_4RuNa$: 719.2 (719.4).

(*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$(CH=CHCOC_2H_5) (9*E*-Et). Mp: 182−184 °C (dec). ^{1}H NMR (THF-d_8, 250 MHz): *δ* 0.94 (t, *J* = 7.5 Hz, 3H, CH_3), 2.19 (s, 6H, tol-CH_3), 2.40(q, *J* = 7.3 Hz, 2H, CH_2), 6.70 (d, *J* = 16.8 Hz, 1H, RuCH=C*H*-CHO), 6.84 (d, *J* = 8.4 Hz, 4H, tolyl), 6.91 (d, *J* = 7.5 Hz, 4H, tolyl), 7.21 (m, 6H, phenyl), 7.30 (m, 4H, phenyl), 8.53 (d, *J* = 15.9 Hz, 1H, RuC*H*=CH), 9.30 (br s, 1H, OH). ^{13}C{^{1}H} NMR (THF-d_8, 126 MHz): *δ* 8.8 (CH_3), 21.1 (tolyl CH_3), 32.3 (CH_2), 89.9 (C3,4 of Cp), 105.6 (C2,5 of Cp), 128.3−137.0 (8 resonances, aromatic), 141.0 (C1 of Cp), 144.2 (C=*C*HCO), 170.9 (Ru*C*H=CH), 194.4 (CHOCH_2), 202.2 (CO). IR (THF): 2021, 1966 cm^{-1}. MS (ESI-TOF) calcd (found) for $C_{38}H_{32}O_4RuNa$: 677.1 (677.3).

(*E*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[C(C_2H_5)=CHCHO] (10*E*-Et). Mp: 172−174 °C (dec). ^{1}H NMR (THF-d_8, 500 MHz): *δ* 1.00 (t, *J* = 7.5 Hz, 3H, CH_3), 2.17 (s, 6H, tol-CH_3), 2.96 (q, *J* = 7.0 Hz, 2H, CH_2), 6.29 (d, *J* = 7.5 Hz, 1H, C=C*H*CHO), 6.83 (d, *J* = 8.5 Hz, 4H, tolyl), 6.95 (d, *J* = 7.5 Hz, 4H, tolyl), 7.24 (m, 6H, phenyl), 7.43 (m, 4H, phenyl), 8.96 (br s, 1H, OH), 9.51 (d, *J* = 7.0 Hz, 1H, CHO). NOE experiments: *δ* (peak irradiated) → *δ* (% NOE); 2.96 → 1.00 (3.0%), 7.40 (0.6%), 9.51 (5.1%); 6.29 → 7.40 (1.1%), 9.51 (0.7%). ^{13}C NMR (THF-d_8, −30 °C, 126 MHz): *δ* 15.7 (q, J_{CH} = 127.0 Hz, CH_3), 21.2 (q, J_{CH} = 126.1 Hz, tolyl CH_3), 37.8 (t, J_{CH} = 130.6 Hz, CH_2), 88.7 (C3,4 of Cp), 105.2 (C2,5 of Cp), 128.3−137.9 (8 resonances, aromatic), 142.9 (dd, $^1J_{CH}$ = 157.5 Hz, $^2J_{CH}$ = 24.8 Hz, C=*C*HCHO), 143.2 (C1 of Cp), 183.0 (d, J_{CH} = 165.9 Hz, CHO), 203.1 (Ru*C*=CH), 203.3 (CO). Spectral assignments were aided by a DEPT-135 experiment. IR (THF): 2014, 1958 cm^{-1}. MS (ESI-TOF) calcd (found) for $C_{38}H_{32}O_4RuNa$: 677.1 (677.3).

(*Z*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[C(C_2H_5)=CHCHO] (10*Z*-Et). Mp: 172−174 °C (dec). ^{1}H NMR (THF-d_8, 500 MHz): *δ* 0.89 (t, *J* = 7.0 Hz, 3H, CH_3), 2.18 (s, 6H, tol-CH_3), 2.56 (q, *J* = 7.5 Hz, 2H, CH_2), 6.38 (d, *J* = 7.0 Hz, 1H, C=C*H*CHO), 6.87 (d, *J* = 8.0 Hz, 4H, tolyl), 7.10 (d, *J* = 8.0 Hz, 4H, tolyl), 7.21 (m, 6H, phenyl), 7.43 (m, 4H, phenyl), 8.80 (br s, 1H, OH), 9.26 (d, *J* = 7.5 Hz, 1H, CHO). NOE experiments: *δ* (peak irradiated) → *δ* (% NOE); 2.56 → 0.89 (1.7%), 6.38 (0.7%), 7.43 (0.5%); 6.38 → 0.89 (4.4%), 2.56 (2.6%). ^{13}C{^{1}H} NMR (THF-d_8, −30 °C, 126 MHz): *δ* 15.0 (CH_3), 21.2 (tolyl CH_3), 46.2 (CH_2), 88.8 (C3,4 of Cp), 105.2 (C2,5 of Cp), 128.3−138.1 (8 resonances, aromatic), 141.5 (C=*C*HCHO), 143.2 (C1 of Cp), 196.3 (Ru*C*=CH), 196.6 (CHO), 203.4 (CO). Spectral assignments were aided by a DEPT-135 experiment. IR (THF): 2014, 1958 cm^{-1}. MS (ESI-TOF) calcd (found) for $C_{38}H_{32}O_4RuNa$: 677.1 (677.3).

Reaction of RuH 11 with PhC≡CCHO. Excess Ph−C≡CCHO (12 *μ*L) was added via syringe to a toluene-d_8 solution of [2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$H (**11**) (0.05 M). After 5 min, the hydride resonance of **11** had disappeared and a single product, (*Z*)-[2,5-Ph-3,4-Tol(η^5-C_4COH)]Ru(CO)$_2$[C(=CHPh)CHO] (**12*Z*-Ph**), was observed with a tolyl resonance at *δ* 1.90. Slow isomerization to **12*E*-Ph** occurred at room temperature.

For 12*Z*-Ph. ^{1}H NMR (toluene-d_8, 500 MHz): δ 1.90 (s, 6H, tol-CH_3), 6.58−7.64 (m, Ph and Tol), 8.00 (s, 1H, RuC=CHPh), 9.23 (s, 1H, CHO). NOE experiments: δ (peak irradiated) → δ (% NOE); 8.00 → 9.23 (10.6%); 9.23 → 8.00 (9.3%).

For 12*E*-Ph. ^{1}H NMR (toluene-d_8, 500 MHz): 1.88 (s, 6H, tol-CH_3), 6.65−7.65 (m, Ph and Tol), 7.64 (s, 1H, RuC=CHPh), 9.64 (s, 1H, CHO). NOE experiments: δ (peak irradiated) → δ (% NOE); 7.64 → none; 9.64 → 6.96 (1.6%).

Reaction of 7 with a Mixture of PhC≡CCD$_2$OH and PhC≡CCH$_2$OH. Addition of a 6.6:1 mixture of PhC≡CCD$_2$OH and PhC≡CCH$_2$OH (15 μL, 0.12 mmol) to a solution of **1** in toluene-d_8 (10 mg, 7.6 μM, in 0.4 mL) gave **10*E*-Ph** as a white precipitate. The ratio of integrals in the ^{1}H NMR spectrum in THF-d_8 was 100 (δ 9.28, s, CpOH) to 62 (δ 8.82, d, CHC*H*O) to 62 (δ 6.35, d, =C*H*CHO) to 3 (s, =C*H*CDO). This ratio is consistent with a mixture of 62% **10*E*-Ph**, 3% **10*E*-Ph-d_1**, and 35% **10*E*-Ph-d_2**.

Reaction of 7 with PhC≡CCHDOH. When a mixture of **7** (19 mg) and PhC≡CCHDOH (18 μL) in toluene-d_8 (0.4 mL) was shaken, **10*E*-Ph** formed as a white precipitate. The vinyl and aldehyde resonances of **10*E*-Ph** in the ^{1}H NMR spectrum (THF-d_8, 300 MHz) were carefully integrated to determine the isotopic distribution in **10*E*-Ph**: 80% was PhC=CHCDO (δ 6.35, s), 7% was PhC=CHCDO (δ 8.822, s), and 13% was PhC=CHCHO (δ 8.825, d, J = 7.5 Hz, and 6.35, d, J = 7.5 Hz).

[2,5-Ph$_2$-3,4-Tol$_2$(η^5-C$_4$COH)]Ru(CO)$_2$(η^2-PhC≡CCH$_3$) (14). Excess 1-phenyl-1-propyne (12 μL) was added to a CD_2Cl_2 solution of **1** (8.6 mg) at room temperature. After 20 min, the tolyl resonance of **1** at δ 2.12 disappeared, and a new single new tolyl resonance at δ 2.22 appeared. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 1.87 (s, 3H, CH_3), 2.22 (s, 6H, tolyl CH_3), 6.8−7.5 (m, phenyl and tolyl-H). ^{13}C{^{1}H} NMR (CD_2Cl_2, 126 Mz): δ 9.1(CH_3), 21.2 (tolyl CH_3), 66.6 (Ph*C*≡C), 71.3 (PhC≡*C*CH$_3$), 84.3 (C3,4 of Cp), 106.1 (C2,5 of Cp), 123.2−138.1 (aromatic), 169.4 (C1 of Cp), 200.8 (CO). IR (CD_2Cl_2): 2025, 1968 cm^{-1}.

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Supporting Information Available: Spectral characterization of **9*E*-Me**, **9*E*-Ph**, **10*E*-Me**, **10*Z*-Me**, **10*E*-Ph**, **15**, and **16**; kinetics of equilibration of **10*E*-Et** and **10*Z*-Et**; reaction of **11** and **11-d_2** with HC≡CCOCH$_3$; synthesis of PhC≡CCD$_2$OH and PhC≡CCHDOH; kinetics of reaction of **7** with propargyl alcohol; X-ray crystal structures of **8*E*-Pentane**, **9*E*-Pentyl**, **9*E*-Et**, and **9*E*-Ph·0.5Pentane**. This material is available free of charge via the Internet at http://pubs.acs.org.