# On the Mechanism of the Ruthenium-Catalyzed Reconstitutive Condensation of Allylic Alcohols and Terminal Alkynes

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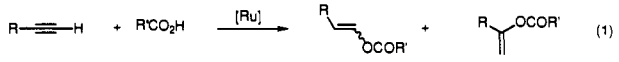
**Abstract:** The ruthenium complex ($\eta^5$-$C_5H_5$)($PPh_3$)$_2$RuCl (**1**) catalyzes the addition of allylic alcohols to terminal alkynes, yielding $\beta,\gamma$-unsaturated ketones. The intermediacy of a ruthenium vinylidene complex is indicated by the synthesis of this proposed intermediate and the demonstration of the same reaction profile as with catalyst **1**. Loss of terminal deuterium in labeled alkynes supports this conclusion. Ligand substitution studies demonstrate the necessity of phosphine loss and precoordination of the allylic alcohol. Deuterium labeling of allyl alcohol demonstrates that the two allylic termini do not become equivalent and that the olefin geometry does not scramble. In contrast to these observations, 3-buten-2-ol shows complete regioselectivity in the condensation but randomization of olefin geometry as determined by deuterium labeling. A cohesive mechanistic rationale accommodates these seemingly disparate observations.

## Introduction

Transition metal vinylidene complexes (M=C=CHR)[1] have attracted a great deal of attention in recent years as a new type of organometallic intermediate that may have unusual reactivity. Indeed, many such complexes form spontaneously from terminal alkynes and coordinatively unsaturated metal species by a metal-promoted C-H insertion followed by a tautomerization. This observation, combined with the increased susceptibility of the $\alpha$-carbon of the vinylidene ligand toward nucleophilic attack, suggests that such complexes might find application in organic synthesis. A number of recent reports have in fact described the addition of oxygen nucleophiles to alkynes (eqs 1 and 2), catalyzed by a wide range of ruthenium complexes.[2a-3] In the first case



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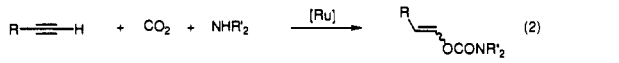
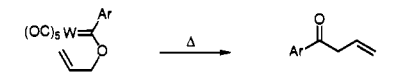


(2)

(eq 1), the lack of regioselectivity and the comparable reactivity with internal alkynes[2a] argue against a vinylidene intermediate. In the latter example (eq 2),[2b] addition occurs only to the unsubstituted carbon of terminal alkynes. Although vinylidene intermediates were not proven in this case, the most active catalysts for carbamate synthesis (e.g., ($\eta^6$-arene)($PR_3$)$RuCl_2$) have been demonstrated to form unstable but observable vinylidene complexes (although under different conditions),[3] which react rapidly with alcohols to form alkoxycarbene complexes.

In a program directed toward developing reactions which are simple additions to enhance synthetic efficiency,[4] we proposed a working hypothesis as outlined in Scheme I whereby allyl alcohols condense with terminal acetylenes to form $\beta,\gamma$-unsaturated ketones. Precedent for the latter stages of this scheme derives from formation of a $\beta,\gamma$-unsaturated ketone by the thermolysis of a tungsten (allyloxy)carbene complex (eq 3).[5] Some observations



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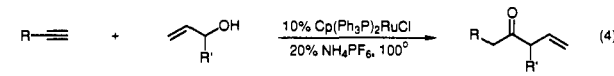
of the palladium-catalyzed reactions of terminal acetylenes[6] initially led us to explore various palladium complexes for this reaction but with no success. Greater literature precedent for the formation of vinylidene complexes from ruthenium[1,7] led to our development of a reconstitutive condensation according to eq 4.[8] The success of this reaction, the surprising regioselectivity with $\alpha$-substituted allyl alcohols, and the absence of authenticated examples of catalytic reactions involving vinylideneruthenium intermediates led us to more closely examine the mechanism of eq 4. We report evidence supporting a multistep mechanism involving a vinylidene complex in the catalytic cycle.



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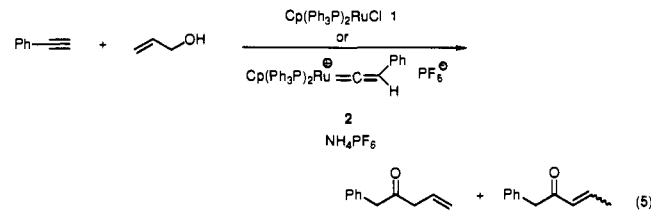
## Results and Discussion

**A. Vinylidene Formation.** The feasibility that a vinylideneruthenium complex is a reactive intermediate in the catalytic cycle is suggested by the following: (1) the known formation of such a complex under similar conditions but in the absence of allyl alcohol[1] and (2) our observation that in a stoichiometric reaction allyl alcohol adds to a vinylidene complex to form $\beta,\gamma$- and $\alpha,\beta$-unsaturated ketones.[9] To validate its presence in a catalytic cycle, we tested both the ruthenium chloride complex **1** and the preformed vinylidene complex **2**[10] as catalysts for the condensation of phenylacetylene with allyl alcohol (eq 5). In both cases, *the*



(5)

*rates of reaction and yields of enones were identical*, within experimental error. This observation strongly suggests the intermediacy of vinylidene complex **2** in the catalytic cycle. The reasonableness of this proposal also derives from the known rapid

(1) For reviews, see: Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. Bruce, M. I.; Swincer, G. A. *Adv. Organomet. Chem.* **1983**, *22*, 59. Nugent, W. A.; Mayer, J. M. *Metal-Ligand Multiple Bonds*; John Wiley & Sons: New York, 1988.

(2) (a) Ruppin, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1986**, *27*, 6323. (b) Mahé, R.; Dixneuf, P. H.; LeColier, S. *Tetrahedron Lett.* **1986**, *27*, 6333. (c) Bruneau, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1987**, *28*, 2005. (d) Mahé, R.; Sasaki, Y.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1989**, *54*, 1518. (e) Deranne, O.; Ruppin, C.; Dixneuf, P. H. *J. Org. Chem.* **1988**, *53*, 925.

(3) Ouzzine, K.; LeBozec, H.; Dixneuf, P. H. *J. Organomet. Chem.* **1986**, *317*, C25. LeBozec, H.; Ouzzine, K.; Dixneuf, P. H. *Organometallics* **1991**, *10*, 2768.

(4) Trost, B. M. *Science* **1991**, *254*, 1471. For recent examples, see: Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1991**, *113*, 701. Trost, B. M.; Kottirsch, G. *J. Am. Chem. Soc.* **1990**, *112*, 2816.

(5) Shusterman, A. J.; Casey, C. P. *Organometallics* **1985**, *4*, 736.

(6) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34. Trost, B. M.; Tanoury, G. *J. Am. Chem. Soc.* **1985**, *110*, 1636. Trost, B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850.

(7) Davies, S. G.; McNally, J. P.; Smallridge, A. J. *Adv. Organomet. Chem.* **1990**, *30*, 1.

(8) Trost, B. M.; Dyker, G.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 7809.

(9) G. Dyker, unpublished results in these laboratories, 1989.

(10) Bruce, M. I.; Hameister, C.; Swincer, A. G.; Wallis, R. C. *Inorg. Synth.* **1982**, *78*, 21.

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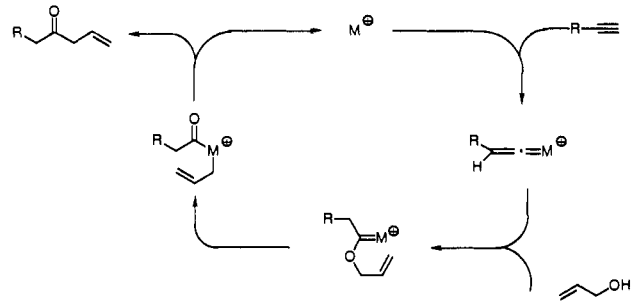
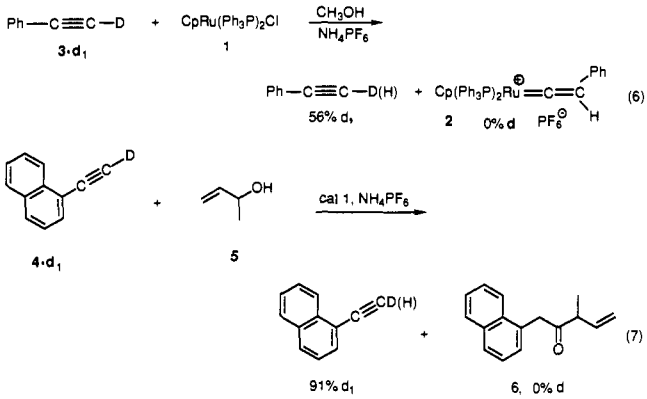
**Scheme I.** A Proposal for Addition of Allyl Alcohols to Terminal Acetylenes

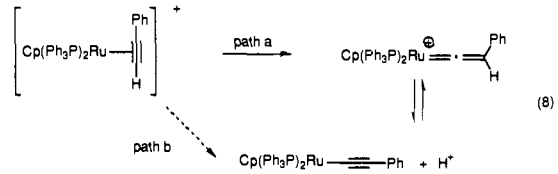


formation of **2** in simple alcohol solvents.[1] Further, the absence of an induction period in the reaction with catalyst **1** shows that vinylidene complex formation is not the turnover-limiting step.

Deuterium labeling results also proved interesting. Under stoichiometric conditions, reaction of excess (deuterioethynyl)-benzene (**3**-$d_1$, >98% $d_1$) with **1** yields the vinylidene complex **2** (eq 6), in which all of the deuterium is lost. The recovered alkyne shows only 56% of the deuterium remaining. Similarly, catalytic condensation of a neat mixture of 1-(deuterioethynyl)naphthalene (**4**-$d_1$, >98% $d_1$) with excess 3-buten-2-ol (**5**) to partial completion yields the $\beta,\gamma$-enone **6** (19% yield), with no deuterium remaining (eq 7). The unreacted alkyne (46% recovery) showed only 9% loss of deuterium.



The mechanism of formation of a ruthenium vinylidene has been discussed in terms of initial formation of a $\pi$-alkyne complex followed by direct rearrangement (eq 8, path a).[7] Silvestre and Hoffmann have performed EHMO calculations[11] demonstrating the feasibility of vinylidene formation via such a cationic $\pi$-alkyne complex followed by a concerted 1,2-hydride migration.



The deuterium labeling studies are consistent with this mechanistic proposal. The known high acidity of the $\beta$-hydrogen of the vinylidene ligand[1] suggests rapid proton exchange with solvent and thus complete loss of the label in the product. To demonstrate this point, the NMR spectrum of **2** was observed in $CD_3OD$ containing $ND_4PF_6$ and showed the absence of the vinylic hydrogen. In addition, the $^{13}C$ signal for the vinylidene carbon ($\delta$ 120.75 in the all-protio compound under identical conditions but in a protonic medium) disappeared although all the other $^{13}C$ signals for the complex remained unchanged from the protio case. The loss of the $^{13}C$ signal reflects the effect of deuterium on the relaxation time of this carbon, further demonstrating the rapid incorporation of deuterium at this carbon. The exchange occurs upon simple mixing in an alcoholic solvent. Clearly, the vinylidene complex does lead to rapid hydrogen exchange. A process as illustrated in eq 8 most directly accounts for this exchange.

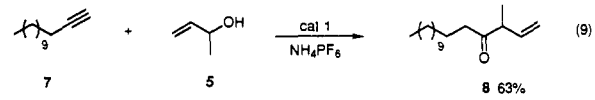
The fate of the unreacted deuterioalkyne in these experiments demonstrates the variable reversibility of vinylidene formation. In eq 6, substantial deuterium exchange shows vinylidene formation to be easily reversible in the presence of the moderately coordinating solvent. (In a separate experiment, it has been observed that benzonitrile completely displaces the vinylidene ligand to produce alkyne and the benzonitrile complex.)[12] Under catalytic conditions, however, little deuterium loss occurs, presumably because subsequent reactions of the vinylidene ligand are faster than decomplexation.

An alternative involving initial formation of a $\sigma$-acetylide complex from the $\pi$-complex either by C–H insertion followed by deprotonation or by direct deprotonation (eq 8, path b) cannot be ruled out. In this event, solvent protonation of the $\sigma$-acetylide complex accounts for the absence of deuterium in the product. The low exchange of starting acetylide under catalytic conditions would indicate that $\beta$-protonation of the $\sigma$-acetylide must be much faster than reversal to the $\pi$-alkyne complex. The main conclusion to be drawn from these labeling studies is that equilibration of the vinylidene complex with starting alkyne is slow compared to its further reaction with the allyl alcohol.

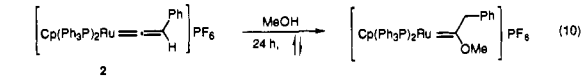
**B. Addition of Allylic Alcohols.** The next step of the reaction must involve addition of allylic alcohol to the vinylidene complex. We propose that this step occurs via loss of triphenylphosphine and precoordination of the olefinic moiety of the allylic alcohol to the ruthenium. Several pieces of evidence support this proposal:

(1) Loss of triphenylphosphine from **1** is well-known to be extremely facile,[7] presumably for steric reasons. Such phosphine loss has been widely exploited for the preparation of a range of mixed-ligand complexes of the type $Cp(PPh_3)(L)RuCl$ (L = N, P, isocyanide, or olefin donor ligand).[13]

(2) Addition of triphenylphosphine significantly retards the rate of the condensation reaction. Specifically, the condensation of 1-tridecyne (**7**) with 3-buten-2-ol (**5**) to give 3-methyl-1-hexadecen-4-one (**8**) proceeds to completion within 1 h under standard conditions (eq 9). However, under identical conditions *except* in the presence of excess triphenylphosphine (1 equiv/Ru), the reaction requires 4 h to reach completion.



(3) Methanol adds to complex **2** only slowly, to generate the methoxycarbene complex (eq 10), which does not reverse under the reaction conditions, but neither ethanol nor 2-propanol adds at all, presumably for steric reasons.[1] Sterically, 3-buten-2-ol (**5**) is about equivalent to 2-propanol, yet **5** condenses quite rapidly since the catalytic reaction is complete within 1 h. A reasonable source of the facilitation of the addition of allylic alcohols is precoordination of the olefinic group, making the nucleophilic addition *intra*molecular rather than *inter*molecular.



(4) Placing methyl substituents directly on the double bond of the allylic alcohols shuts down the reaction. For example, neither methallyl nor crotyl alcohol reacts to give condensation products, presumably because of steric inhibition of olefin coordination.

(5) Replacing triphenylphosphine with the chelating ligands dppe (1,2-bis(diphenylphosphino)ethane) and dppb (1,4-bis(di-

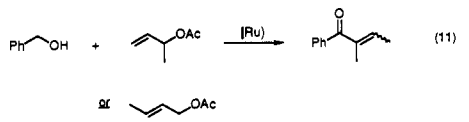
(11) Silvestre, J.; Hoffmann, R. *Helv. Chim. Acta* **1985**, *68*, 1461.

(12) Bullock, R. M. *J. Chem. Soc., Chem. Commun.* **1989**, 165. Flygare, J. A. Unpublished observations in these laboratories.

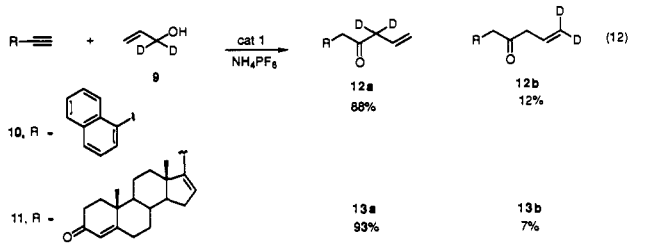
(13) For examples, see: Bruce, M. I.; Wong, F. S.; Shelton, B. W.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1983**, 2293. Bruce, M. I.; Hambley, T. W.; Snow, M. R.; Swincer, A. G. *J. Organomet. Chem.* **1984**, *273*, 361. Bruce, M. I.; Wallis, R. C. *Aust. J. Chem.* **1981**, *34*, 209.

phenylphosphino)butane) completely inhibits the condensation reaction. The lack of reaction does not derive from failure to form a vinylidene complex since cyclopentadienylruthenium complexes with chelating bis(phosphine) ligands are known to form vinylidene complexes with alkynes under the same conditions as for triphenylphosphine.[14] It appears reasonable to attribute the lack of reaction to the reluctance of the dppe to dissociate a phosphine, which precludes precoordination of the olefinic group of the allylic alcohol, thus preventing condensation.

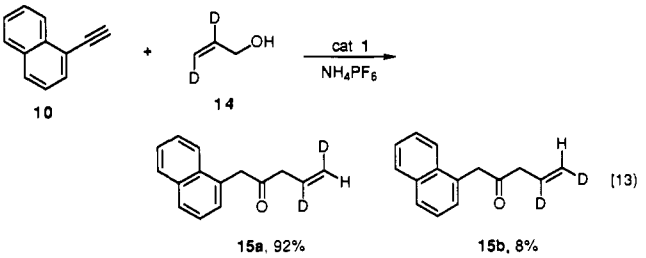
**C. The Nature of the Allyl Intermediate.** Rupture of the C–O bond most likely occurs following addition of the allyl alcohol to generate two ruthenium-bound organic fragments, one of which is an allyl unit. In condensation reactions with 1-substituted allylic alcohols, we observe *only* coupling at the substituted carbon (as in eq 4). Similarly, Watanabe and co-workers have observed $\alpha$-branched products in the ruthenium-catalyzed coupling of benzyl alcohols and allylic acetates (eq 11)[15] independent of which regioisomeric allylic acetate was employed. These results argue



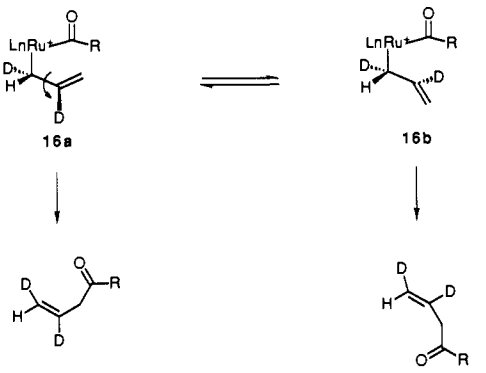

for an intrinsic preference for C–C bond formation to the more substituted allyl terminus. Since we were unable to examine crotyl alcohol, we decided to explore the regiochemical outcome in a sterically and electronically unbiased example. 1,1-Dideuterio-2-propen-1-ol (**9**) condenses with terminal alkynes **10** and **11** to form isomeric $\beta,\gamma$-enones **12a,b** and **13a,b**, repsectively, in addition to the isomerized $\alpha,\beta$-unsaturated derivatives in 51% yield (eq 12). Analyses were performed on the isomeric mixture of enones. Repetitively integrating the $^1$H NMR signals for the allylic methylene group (**12**, $\delta$ 3.17; **13**, $\delta$ 3.23) vs the olefinic methylene group (**12**, $\delta$ 5.16 and 5.07; **13**, $\delta$ 5.17 and 5.14) establishes that **12a** and **13a** strongly dominate and, therefore, the majority of the $\beta,\gamma$-unsaturated ketone retains the positional identity of the allyl alcohol.



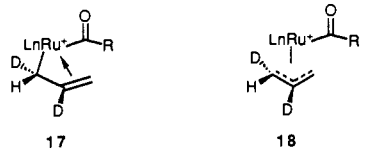

To obtain evidence regarding the role of $\sigma$- vs $\pi$-allyl complexes, we probed the influence upon the reaction of olefin geometry by condensing (*E*)-2,3-dideuterio-2-propen-1-ol (**14**) with alkyne **10** (eq 13). Analyses were performed on the mixture of enones



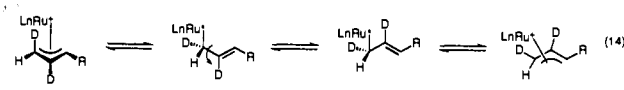

formed in 28% yield. The $^1$H NMR spectrum of this product showed the signal at $\delta$ 5.15 (in all protio dd, $J$ = 10.2, 1.4 Hz) to strongly dominate that at $\delta$ 5.05 (in all protio dd, $J$ = 17.2, 1.5 Hz) and thus establish the dominance of the (*E*)-dideuterio ketone **15a** over the (*Z*)-dideuterio ketone **15b**. For a $\sigma$-complex to be considered as the intermediate, the interconversion between the putative kinetic $\sigma$-complex **16a** and its conformer **16b**, which arises by rotation about the C–C single bond, must be slow relative to reductive elimination. Furthermore, reductive elimination must proceed with clean allyl inversion. Neither of these requirements is precedented. Considering the very low barriers to rotation about




such single bonds, it does not appear reasonable to require that such a process be slow relative to reductive elimination. In fact, loss of olefin geometry is normally a diagnostic test for the intervention of $\sigma$-complexes.[16] It can be argued that $\pi$-coordination in the $\sigma$-complex as in **17** accounts for enhancing the barrier to rotation; however, the latter is, in reality, an equivalent of the $\pi$-allyl complex. In both **17** and **18** the allyl fragment serves as a four-electron donor to ruthenium in which they become functionally equivalent. In fact, **17** has been described as a resonance form of the $\pi$-allyl **18**.[17] Thus, trying to differentiate between such entities almost becomes a semantic problem.




Invoking the $\pi$-complex does not demand the two unlikely requirements outlined above. Furthermore, the retention of olefin geometry demonstrates that, in such a $\pi$-complex, $\eta^3$ to $\eta^1$ allyl slippage must be slower than reductive elimination. Otherwise, the facile rotation about the C–C single bond in the intermediate $\sigma$-allyl complex would scramble the olefin geometry (eq 14, R = H).




Other considerations make the suggestion of a $\sigma$-allyl complex less appealing as well. There is no obvious reason why a cationic Ru(IV) complex with the strongly electron-withdrawing acyl ligand would exist as a coordinatively unsaturated 16-electron complex ($\eta^1$-allyl) when there appears to be no steric barrier to formation of the 18-electron $\eta^3$-allyl complex. All cyclopentadienylruthenium(IV) complexes characterized to date are 18-electron complexes.[18] While the latter does not rule out a reactive 16-electron complex, it does suggest that such a species

(14) Consiglio, G.; Morandini, F.; Ciani, G. F.; Sironi, A. *Organometallics* **1986**, *5*, 1976.

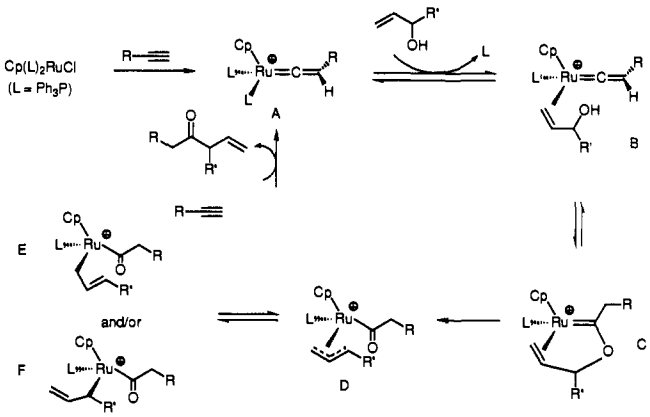
(15) Tsuji, Y.; Mukai, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1989**, *369*, C51. Kondo, T.; Mukai, T.; Watanabe, Y. *J. Org. Chem.* **1991**, *56*, 487.

(16) Vrieze, K. In *Dynamic Nuclear Magnetic Resonance Spectroscopy*; Jackman, L. M., Cotton, F. A., Eds.; Academic: New York, 1975; p 44. Faller, J. W.; Thomsen, M. E.; Mattina, M. J. *J. Am. Chem. Soc.* **1971**, *93*, 2643.

(17) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; John Wiley & Sons: New York, 1988; p 24.

(18) For representative examples of 18e-ruthenium(IV) complexes, see: Albers, M. O.; Liles, D. C.; Robinson, D. J.; Shaver, A.; Singleton, E. *Organometallics* **1987**, *6*, 2347. Chinn, M. S.; Heinekey, D. M. *J. Am. Chem. Soc.* **1987**, *109*, 5865. Chang, J.; Bergman, R. G. *J. Am. Chem. Soc.* **1987**, *109*, 1444. Bruce, M. I.; Tomkins, I. B.; Wong, F. S.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1982**, 687. Nowell, I. W.; Tabatabaian, K.; White, C. *J. Chem. Soc., Chem. Commun.* **1979**, 547.

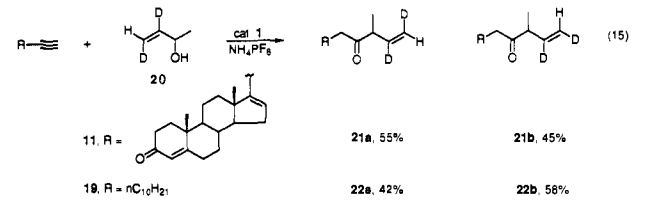
**Scheme II.** A Mechanistic Rationale for Ru-Catalyzed Reconstitutive Condensation



should not be invoked unless there is direct evidence requiring it. The opposite is the case here.

**D. A Mechanistic Proposal.** Scheme II depicts a mechanistic rationale which accommodates all of the preceding observations. Invoking the $\eta^3$-$\pi$-allyl structure in D requires that reductive elimination of the allyl and acyl fragments, while retaining the positional identity of the $CH_2CHCD_2$ moiety, be faster than allyl rotation. Lehmkuhl et al. have studied the dynamics of allyl rotation in $Cp(PPh_3)Ru(\eta^3\text{-}CH_2CHCH_2)$[19] and have demonstrated that the isomerization of the cisoid rotamer (central C syn to $PPh_3$) to the transoid rotamer (central C syn to Cp) requires several hours at 80 °C. In intermediate D, the presence of the strongly electron-withdrawing acyl group on an already electron-poor Ru(IV) species should sufficiently destabilize the intermediate to ensure rapid reductive elimination. Some leakage to a $\sigma$-complex like E or F may occur to a small extent, accounting for the slight isotopic scrambling of eqs 12 and 13.

A dramatic difference emerges with a substituted allylic alcohol like 3-buten-2-ol (**5**). The high regioselectivity for formation of the new C–C bond to the allyl terminus that originally bore the alcohol might indicate a direct correlation to the case of allyl alcohol itself. However, examination of olefin geometry revealed a profound difference. Reacting terminal alkyne **11** or **19** with (*E*)-3,4-dideuterio-3-buten-2-ol (**20**) gave nearly a 1:1 mixture of *E* (**21a** and **22a**, respectively) and *Z* (**21b** and **22b**, respectively) deuterated products (eq 15). The $^1H$ NMR spectra clearly revealed the olefin geometry [**21a**, $\delta$ 5.01 (in protio case d, $J$ = 9.4 Hz), vs **21b**, $\delta$ 5.06 (in protio case d, $J$ = 18.5 Hz); **22a**, $\delta$ 5.15 (in protio case dm, $J$ = 9.4 Hz), vs **22b**, $\delta$ 5.23 (in protio case dd, $J$ = 17.1, 1.4 Hz)].



At first glance, the high regioselectivity seems at odds with the loss of olefin geometry. However, the bias introduced by the presence of the alkyl substituent may be responsible for the regioselectivity of reductive elimination, as has been noted for other reactions involving allylruthenium intermediates (cf. eq 11).[15] Unfortunately, the lack of reactivity of 2-buten-1-ol does not allow us to explore the question further. Scrambling of olefin geometry with alcohol **20** strongly implicates the $\sigma$-complex E either as an obligatory intermediate or as a species in dynamic equilibrium with $\pi$-complex D. The regioselectivity is reminiscent of the highly regioselective addition of monosubstituted allyl organometallics to the more substituted carbon in their additions to carbonyl groups.[20] Such reactions invoke the $\sigma$-allyl species bearing the metal at the less substituted allyl terminus and a six-centered cyclic array invoking allyl inversion to account for this regioselectivity. Perhaps similar factors are involved in reductive elimination of the substituted ruthenium complex.

The contrast between the parent allyl and methallyl systems arises from the competition between the rate for reductive elimination and slippage from a $\eta^3$ to $\eta^1$ coordination. The very small amount of olefin isomerization accompanying the parent allyl coupling likely reflects the fact that while the relative rates of these two processes favor reductive elimination, they must not be too far apart in energy. Introduction of the electron-releasing alkyl group facilitates the slippage both electronically and sterically and thereby inverts the relative rates.

## Conclusion

Ligand substitution, kinetic and deuterium labeling experiments, and the identity of the reactivity profile of a proposed intermediate to the catalytic process provide strong support for the proposed mechanistic rationale for the novel ruthenium-catalyzed alkyne–allylic alcohol condensation in which a vinylideneruthenium complex is a reactive intermediate in a catalytic cycle. Although the complexity of the reaction precludes either observation or isolation of proposed intermediates under the exact conditions of the catalytic cycle, several features of the mechanism are clear: (1) The ruthenium catalyst activates terminal alkynes toward condensation by formation of a vinylidene complex; (2) nucleophilic addition of allylic alcohols is facilitated by phosphine loss from ruthenium and precoordination of the olefinic moiety; (3) the enone arises from rapid reductive elimination from an allylruthenium intermediate, in which the hapticity of the allyl ligand depends upon its substitution: $\eta^3$ for an unsubstituted allyl, resulting in retention of olefin geometry, but interconversion between $\eta^3$ and $\eta^1$ for the methyl-substituted allyl, resulting in scrambled olefin geometry.

The sharp distinction between the unsubstituted and substituted allyl alcohol substrates highlights the difficulty of general conclusions in transition metal catalyzed reactions derived from studies of single substrates. In the current case, a small structural variation changes the relative rates of two competing steps with major implications regarding the stereochemistry and prospects for asymmetric induction. The increased importance of the $\sigma$-complex upon alkyl substitution may derive from both steric and electronic effects. The above data combined with our earlier observations provide strong support for the mechanistic scheme as outlined. We are currently utilizing the insights gained from this study for the design of more selective catalysts.

## Experimental Section

**General.** All reactions were performed in oven-dried glassware under an atmosphere of dry $N_2$, using one or both of syringe–septum and Schlenk techniques. Solvents and chemicals were obtained commercially and purified by standard procedures. $^1H$ NMR spectra were measured in $CDCl_3$ (unless otherwise noted), with chemical shifts referenced to TMS, on a Varian Gemini-300 or XL-400 instrument. Infrared spectra were measured as neat films (unless otherwise noted) on a Nicolet 205 FTIR instrument. Gas chromatography was performed on a Varian Model 3700 instrument using a SE-30, OV-1 25 m × 0.25 mm poly(methylsiloxane) capillary column and a Hewlett-Packard 3390A integrator. High-resolution mass spectra were measured by the Mass Spectrometry Facility of the School of Pharmacy, University of California, San Francisco. The compounds $Cp(PPh_3)_2RuCl$ (**1**),[10] $[Cp(PPh_3)_2Ru{=}C{=}CHPh](PF_6)$ (**2**),[10] Cp(dppe)RuCl,[21] Cp(dppb)RuCl,[22] 1,1-dideuterio-2-propen-1-ol (**9**),[23] and 1-ethynylnaphthalene (**10**)[24] were prepared by literature methods.

**Comparison of Catalytic Activities of 1 and 2.** Into each of two test tubes were added ethynylbenzene (88 $\mu$L, 0.80 mmol), $NH_4PF_6$ (26 mg,

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(20) For a review, see: Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555.

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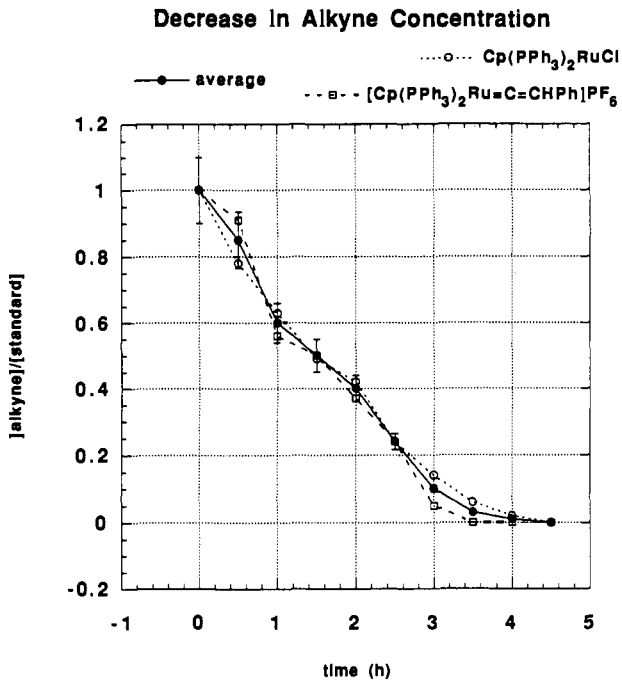


Figure 1.

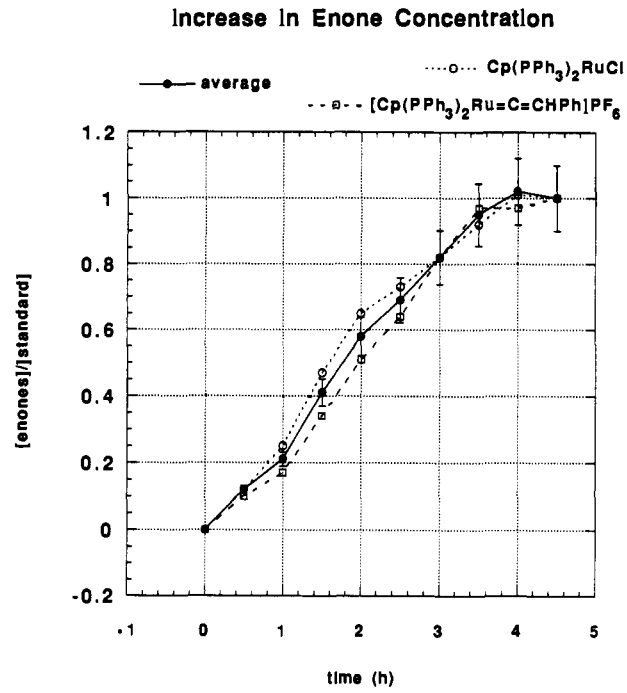


Figure 2.

0.16 mmol), pentadecane (0.5 mL, 1.81 mmol), and deoxygenated allyl alcohol (2.0 mL). To the first was added **1** (58 mg, 80 μmol), and to the second was added **2** (75 mg, 80 μmol). The tubes were sealed with rubber septa, purged with $N_2$, and heated at 100 °C under $N_2$. The progress of the reactions was monitored by capillary GC, and the ratios of alkyne and products to the internal standard were determined by integration. The results are depicted in Figures 1 and 2.

**Synthesis of 1-(Deuterioethynyl)naphthalene (4-$d_1$).** A solution of 1-ethynylnaphthalene (307 mg, 2.02 mmol) in THF (10 mL) was cooled to −78 °C, treated with $^n$BuLi (2.0 mL, 2.77 mmol, 1.35 M in hexane, 1.3 equiv), and stirred at −78 °C for 10 min. The deep burgundy solution was warmed to room temperature for 20 min, recooled to −78 °C, and quenched with $D_2O$ (1.0 mL). The solution was diluted with ether and aqueous $NaHSO_4$ (5 mL each) and separated; the organic layer was washed with brine (3 × 5 mL), dried, and chromatographed (hexane, $R_f$ = 0.36) to give the product (274 mg, 89%). $^1$H NMR (300 MHz): δ 8.370 (d, $J$ = 8.2 Hz, 1 H), 7.864 (d, $J$ = 8.3 Hz, 2 H), 7.749 (d, $J$ = 7.1 Hz, 1 H), 7.620–7505 (m, 2 H), 7.435 (t, $J$ = 7.8 Hz, 1 H). The singlet at 3.470 seen in the starting material was not detectable. IR: 3059, 2583, 1587, 1508, 1392, 1336, 1265.

**Synthesis of 1-(3-Methyl-2-oxo-4-penten-1-yl)naphthalene (6) from 4-$d_1$.** A solution of 4-$d_1$ (99.5 mg, 0.653 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 47.4 mg, 65.3 μmol, 0.1 equiv), and $NH_4PF_6$ (21.3 mg, 131 μmol, 0.2 equiv) in deoxygenated 3-buten-2-ol (**5**, 1.0 mL, 11.7 mmol) was heated at 100 °C under $N_2$. After 1.5 h, GC showed the reaction to be partially complete. The mixture was chromatographed (4:1 hexane–ether), allowing isolation of unreacted 4-$d_1$ (45.6 mg, 46%; $R_f$ = 0.73) and **6** (27.4 mg, 19%; $R_f$ = 0.51; full characterization of this compound is described in the supplementary material of ref 8). $^1$H NMR (4-$d_1$, 400 MHz): as described above, with a resonance at δ 3.470 (s) integrating as 0.09 H. $^1$H NMR (**6**, 400 MHz): 7.869–7.779 (m, 3 H), 7.522–7.331 (m, 4 H), 5.842 (m, 1 H), 5.173 (d, $J$ = 10.4 Hz, 1 H), 5.167 (dd, $J$ = 1.6, 1.1 Hz, 1 H), 4.208 (s, 1 H), 4.197 (s, 1 H), 3.383 (quint, $J$ = 7.6 Hz, 1 H), 1.148 (d, $J$ = 6.8 Hz, 3 H).

**Synthesis of (Deuterioethynyl)benzene (3-$d_1$).** This compound was prepared by the method described above for 4-$d_1$, using ethynylbenzene (0.5 mL, 4.55 mmol), $^n$BuLi (3.8 mL, 5.00 mmol, 1.35 M in hexane), and $D_2O$ (0.5 mL). After workup, passage through a short plug of silica and evaporation gave the compound, 476 mg, contaminated with a trace of hexane. $^1$H NMR (300 MHz): 7.528–7.487 (m, 2 H), 7.359–7.291 (m, 3 H). IR: 3082, 3059, 3034, 3022, 2587, 1973, 1884, 1807, 1757, 1598, 1574.

**Synthesis of ($\eta^5$-Cyclopentadienyl)($\eta^1$-phenylvinylidene)bis(triphenylphosphine)ruthenium(II) Hexafluorophosphate (2) from 3-$d_1$.** This compound was prepared by the literature procedure[10] using $Cp(PPh_3)_2RuCl$ (**1**, 80 mg, 110 μmol), 3-$d_1$ (100 μL, ca. 0.91 mmol), $NH_4PF_6$ (19 mg, 116 μmol), and methanol (8 mL). After precipitation of the solid complex (77 mg, 74%), the combined filtrates were evaporated to an orange oil, which was extracted with pentane (3 × 2 mL), and the extracts were filtered through a short plug of silica. Evaporation gave 38 mg of a colorless oil, containing unreacted 3-$d_1$. $^1$H NMR (**2**, 300 MHz): 7.426–7.378 (m, 6 H), 7.269–7.155 (m, 16 H), 7.130–6.896 (m, 13 H), 5.374 (t, $J$ = 2.3 Hz, 1 H; C=C*H*Ph), 5.277 (s, 5 H, $C_5H_5$). $^1$H NMR (**3**, 300 MHz): 7.529–7.487 (m, 2 H), 7.366–7.292 (m, 3 H), 3.076 (s, 0.44 H). The integrated area ratio of the aryl to alkynyl resonances was 290.5:25.6, corresponding to 44% H incorporation.

**Synthesis of 3-Methyl-1-hexadecen-4-one (8).** A solution of 1-tridecyne (**7**, 72.4 mg, 0.401 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 29.1 mg, 40.1 μmol), and $NH_4PF_6$ (13.1 mg, 80.3 μmol) in deoxygenated 3-buten-2-ol (1.0 mL) was heated at 100 °C under $N_2$ for 1 h, at which point the alkyne was completely consumed (determined by GC). The compound was isolated by flash chromatography (silica, 19:1 pentane–ether) to yield 64.2 mg (63%). Under identical conditions, except for the addition of 1 equiv of $PPh_3$/ruthenium, the reaction required 4 h to afford the compound in 61% yield. Full characterization of this compound is given in the supplementary material of ref 8.

**Synthesis of Pregna-4,16-dien-20-yn-3-one (11).** A slurry of α-ethynyltestosterone (2.60 g, 8.32 mmol) and anhydrous $CuSO_4$ (6.64 g, 41.6 mmol) in light mineral oil (15 g) was heated under $N_2$ at 160–180 °C for 1 h. After cooling, the mixture was diluted with hexane (25 mL) and chromatographed on a column of silica gel (4 × 16 cm). The mineral oil was eluted with hexane (ca. 500 mL), and the product was eluted with 1:1 hexane–ether. Those fractions showing a spot at $R_f$ = 0.72 were combined, evaporated, and recrystallized (1:1 hexane–ethyl acetate) to give 0.69 g of the compound as white crystals, mp = 170 °C (28%). IR ($CDCl_3$): 3420, 2960, 2870, 2100, 1670, 1620, 1600, 1460, 1380, 1240 cm$^{-1}$. $^1$H NMR (300 MHz, selected signals): 6.09 (t, $J$ = 2.9 Hz, 1 H), 5.72 (s, 1 H), 3.06 (s, 1 H), 1.20 (s, 3 H), 0.88 (s, 3 H). $^{13}$C NMR (75 MHz): 199.90, 171.25, 137.71, 136.29, 124.17, 80.52, 79.25, 55.29, 54.01, 47.54, 38.59, 35.40, 34.14, 33.93, 33.75, 32.55, 31.76, 20.56, 16.97, 15.75.

**Reaction of Alkyne 10 and Deuterated Alcohol 9.** A solution of 1-ethynylnaphthalene (**10**, 52.1 mg, 0.342 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 24.9 mg, 34.3 μmol), and $NH_4PF_6$ (11.2 mg, 68.7 μmol) in 1,1-dideuterio-2-propen-1-ol (**9**, 400 μL) was heated at 100 °C for 14 h. The reaction mixture was stirred overnight with $p$-$TsOH{\cdot}H_2O$ (10 mg) in 15 mL of 2:1 acetone–water, saturated with NaCl, and extracted with ether. The organic extracts were dried, evaporated, and subjected to flash chromatography (silica, 4:1 pentane–ether) to yield β,γ-enone; $R_f$ = 0.50. $^1$H NMR ($CDCl_3$): δ 7.898–7.763 (m, 3 H), 7.532–7.384 (m, 4 H), 5.929–5.839 (m, 1 H), 5.163 (d, $J$ = 10.3 Hz, 1 H), 5.068 (d, $J$ = 17.2 Hz, 1 H), 4.159 (s, 2 H). Integration of the methylidene vs the α-methylene (d δ 3.17 (m)) resonances showed 88.3 (±1.7%) deuteration in the α-position (average of three integrations). IR: 3061, 3047, 3012, 2931, 2854, 2180, 2077, 1712, 1672, 1638, 1597, 1510, 1398. HRMS: calcd for $C_{15}H_{12}D_2O$ $M^+$ = 212.1171, found 212.1168.

**Reaction of Alkyne 11 and Deuterated Alcohol 9.** A solution of **11** (50.0 mg, 0.170 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 12.4 mg, 17.1 μmol, 0.1

equiv), and $NH_4PF_6$ (5.6 mg, 34.4 μmol, 0.2 equiv) in deoxygenated 1,1-dideuterio-2-propen-1-ol (**9**, 310 mg, 5.16 mmol) was heated at 100 °C under $N_2$. After 13 h, TLC showed the starting material to have been consumed. The mixture was chromatographed (2:1 hexane–ethyl acetate; $R_f$ = 0.39–0.20) to give 30.1 mg (50% yield) of a mixture of α,β- and β,γ-enones (~1:1), which was analyzed by $^1$H NMR. Integration of the methylidene (5.174 (dd, $J$ = 1.5, 11.1 Hz), 5.138 (dd, $J$ = 1.5, 18.0 Hz)) vs α-methylene (3.231 (m)) resonances of the β,γ-enone showed 92.4% (±1.2%) deuteration in the α-position (average of three integrations).

**Synthesis of (*E*)-2,3-Dideuterio-2-propen-1-ol (14).** A suspension of $LiAlD_4$ (5.14 g, 122 mmol) in ether (90 mL) was cooled to 0 °C and treated with 2-propyn-1-ol (5.5 mL, 94.2 mmol) dropwise over 10 min. The suspension was stirred at 0 °C for 15 min, warmed to room temperature, and subsequently refluxed under $N_2$ for 20 h. The mixture was cooled to 0 °C and quenched with $D_2O$ (5 mL); after 30 min at room temperature, 15% NaOH (3.6 mL), water (12 mL), and $MgSO_4$ were added. After cooling, the suspension was filtered through Celite, and the residue and filter cake were washed with several small portions of ether. The filtrate was distilled through a 20-cm vacuum-jacketed, helix-packed column; most of the solvent was removed at ≤70 °C; the remaining liquid was distilled at 92–100 °C, to yield 4.39 g of product. $^1$H NMR analysis showed the mixture to contain 2,3-dideuterio-2-propen-1-ol (**14**, 71%; 92.1 ± 1.0% (*E*)-$d_2$, average of three integrations), deuterated *n*-propanol (17%), 2-propyn-1-ol (4%), and ether (3%). $^1$H NMR (300 MHz): 5.144 (m, 0.56 H), 4.167 (d, $J$ = 5.8 Hz, 2 H), 1.594 (m, 1 H).

**Reaction of Alkyne 10 and Deuterated Alcohol 14.** A solution of 1-ethynylnaphthalene (**10**, 137.7 mg, 0.905 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 65.7 mg, 90.5 μmol, 0.1 equiv), and $NH_4PF_6$ (29.5 mg, 181 μmol, 0.2 equiv) in deoxygenated 2,3-dideuterio-2-propen-1-ol (**14**, 1.2 mL) was heated at 100 °C under $N_2$. After 13 h, the mixture was chromatographed (4:1 hexane–ether, $R_f$ = 0.47–0.27) to give 52.1 mg (27% yield) of a mixture of α,β- and β,γ-enones, which was rechromatographed to give 11.6 mg of nearly pure β,γ-isomer **15** ($R_f$ = 0.40), which was analyzed by $^1$H NMR. Integration of the methylene resonances at δ 5.145 (s, *trans*-$d_2$) (compared to δ 5.157 (dd, $J$ = 10.2, 1.4 Hz) in the protio compound) and 5.048 (s, *cis*-$d_2$) (compared to δ 5.061 (dd, $J$ = 17.2, 1.5 Hz) in the protio compound) shows the *trans*-$d_2$ compound to be present in 84.9 (±0.7)% (average of three integrations). Since the starting allyl alcohol was 92.1 (±1.0)% *trans*-$d_2$, this result corresponds to 92.2 (±1.7)% retention of olefin geometry. HRMS: calcd for $C_{15}H_{12}D_2O$ 212.1171, found 212.1151.

**Synthesis of (*E*)-3,4-Dideuterio-3-buten-2-ol (20).** To a cooled (0 °C) suspension of $LiAlD_4$ (2.98 g, 71.0 mmol) in ether (90 mL) was added 3-butyn-2-ol (4.0 mL, 51.0 mmol), dropwise over 15 min. The suspension was stirred at 0 °C for 90 min and then refluxed for 21 h. The suspension was cooled to 0 °C and quenched carefully first with $D_2O$ (3.0 mL) and then with NaOH (15% aq, 2.5 mL) and water (8 mL). After drying ($MgSO_4$), the suspension was filtered through Celite and the residue thoroughly extracted with ether. Removal of ether via a 20-cm, vacuum-jacketed, helix-packed column, followed by distillation through a 15-cm Vigreux column, gave 3.139 g of product, bp 92–96 °C. $^1$H NMR analysis showed the mixture to contain a mixture of (*E*)- and (*Z*)-$d_2$ allylic alcohol (81%), deuterated 2-butanol (14%), and ether (5%). Integration of the olefinic region showed the allylic alcohol to consist of 85.8 (±1.5)% (*E*)-3,4-$d_2$-3-buten-2-ol (average of three integrations).

**Reaction of Alkyne 19 and Deuterated Alcohol 20.** A solution of 1-dodecyne (**19**, 150 μL, 0.702 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 51.0 mg, 70.2 μmol, 0.1 equiv), $NH_4PF_6$ (22.8 mg, 140 μmol, 0.2 equiv), and (*E*)-3,4-dideuterio-3-buten-2-ol (**20**, 1.0 mL) was heated at 100 °C under $N_2$. After 4 h, GC indicated complete consumption of the alkyne, and the mixture was chromatographed (19:1 hexane–ether, $R_f$ = 0.29) to give 58.5 mg of the desired product as a pure compound (35%). $^1$H NMR analysis ($d_6$-acetone, 400 MHz) indicated at 58.4:41.6 (±0.6) ratio of *cis*-$d_2$ to *trans*-$d_2$ enones, based on integration of the olefinic resonances at δ 5.23 (m, *cis*-$d_2$) and 5.15 (m, *trans*-$d_2$). The assignments are based on the resonances of the protio compound (400 MHz, $d_6$-acetone): δ 5.245 (dt, $J$ = 17.1, 1.4 Hz, 1 H, trans to C*H*=$CH_2$), 5.163 (d of m, $J$ = 9.4 Hz, 1 H, cis to C*H*=$CH_2$). $^1$H NMR ($C_6D_6$, 400 MHz): 4.927–4.902 (m, 1 H), 4.834 (q, $J$ = 6.9 Hz, 1 H), 2.222 (dt, $J$ = 17.2, 7.4 Hz, 1 H), 2.062 (dt, $J$ = 17.2, 7.2 Hz, 1 H), 1.567 (quint, $J$ = 7.2 Hz, 2 H), 1.270 (br s, $J$ = 16 Hz), 1.071 (d, $J$ = 6.9 Hz, 3 H), 0.910 (t, $J$ = 6.9 Hz, 3 H). $^{13}$C NMR (75 MHz): 212.22, 116.36 (t, $J$ = 24 Hz), 51.05, 40.59, 31.72, 29.41 (2 C), 29.29, 29.23, 29.14, 29.03, 23.48, 22.46, 15.51, 13.85 (resonance seen in protio compound at δ 138 not observed). IR: 2926, 2855, 2320, 1717, 1596, 1457, 1408, 1373, 1133, 1026, 884. HRMS: calcd for $C_{16}H_{28}D_2O$ 240.2423, found 240.2408.

**Reaction of Alkyne 11 and Deuterated Alcohol 20.** A solution of **11** (45.6 mg, 0.155 mmol), $Cp(PPh_3)_2RuCl$ (**1**, 11.2 mg, 15.5 μmol, 0.1 equiv), and $NH_4PF_6$ (5.0 mg, 3.10 μmol, 0.2 equiv) in (*E*)-3,4-dideuterio-3-buten-2-ol (**20**, 0.5 mL) was heated at 100 °C under $N_2$. After 5 h, TLC indicated complete consumption of the alkyne, and the mixture was chromatographed (2:1 ether–hexane, $R_f$ = 0.43) to give 35.5 mg of the desired product as a pure compound (62%). $^1$H NMR analysis ($C_6D_6$, 400 MHz) indicated at 54.8:45.2 (±0.4) ratio of *trans*-$d_2$ to *cis*-$d_2$ enones, based on integration of the olefinic resonances at δ 5.062 (m, *cis*-$d_2$) and 5.006 (br s, *trans*-$d_2$). The assignments are based on the resonances of the protio compound (400 MHz, $C_6D_6$): δ 5.081 (d, $J$ = 18.5 Hz, 1 H, trans to C*H*=$CH_2$), 5.021 (d, $J$ = 9.4 Hz, 1 H, cis to C*H*=$CH_2$). $^1$H NMR ($C_6D_6$, 400 MHz): 6.048 (t, $J$ = 2.4 Hz, 0.5 H), 6.017 (t, $J$ = 2.4 Hz, 0.5 H), 5.808 (s, 1 H), 5.062 (m), 5.006 (br, 1 H), 3.06–3.18 (m, 1 H), 3.026 (m, 2 H), 2.31–2.11 (m, 3 H), 1.92–0.42 (c, 14 H), 1.247 (d, $J$ = 6.9 Hz, 1.5 H), 1.242 (d, $J$ = 6.8 Hz, 1.5 H), 0.678 (s, 1.5 H), 0.670 (s, 1.5 H), 0.599 (s, 1.5 H), 0.573 (s, 1.5 H). IR: 3026, 2940, 2854, 1712, 1675, 1617, 1452, 1373, 1353, 1271, 1233, 1189, 1060, 865. HRMS: calcd for $C_{25}H_{32}D_2O_2$ 368.2686, found 368.2672.

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