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Ruthenium-Catalyzed Hydration of 1-Alkynes to Give Aldehydes: Insight into *anti*-Markovnikov Regiochemistry

Makoto Tokunaga,[‡] Toshiaki Suzuki,[†] Nobuaki Koga,[§] Tomoaki Fukushima,[¶] Akira Horiuchi,[¶] and Yasuo Wakatsuki*,[†]

*Contribution from RIKEN (The Institute of Physical and Chemical Research),
Wako-shi, Saitama 351-0198, Japan, PRESTO (Japan Science and Technology Corporation), Kawaguchi,
Saitama 332-0012, Japan, Graduate School of Human Informatics, Nagoya University, Chikusa,
Nagoya 464-8601, Japan, and Faculty of Science, Rikkyo University, Toshima, Tokyo 171-8501, Japan*

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Abstract: The mechanism of the selective conversion of 1-alkynes to aldehydes by hydration was investigated by isolating organic and organometallic byproducts, deuterium-labeling experiments, and DFT calculations. The D-labeled acetylenic hydrogen of 1-alkyne was found exclusively in the formyl group of the resulting aldehydes. After the reaction, the presence of metal-coordinated CO was confirmed. All of the experimental results strongly suggest the involvement of a metal−acyl intermediate with the original acetylenic hydrogen also bound to the metal center as a hydride, with the next step being release of aldehyde by reductive elimination. Theoretical analyses suggest that the first step of the catalytic cycle is not oxidative addition of acetylene C−H or tautomerization of η^2-alkyne to a vinylidene complex, but rather protonation of the coordinated 1-alkyne at the substituted carbon to form a metal−vinyl intermediate. This cationic intermediate then isomerizes to Ru(IV)−hydride−vinylidene via α-hydride migration of the vinyl group to the metal center, followed by attack of the vinylidene α-carbon by OH^- to give the metal−hydride−acyl intermediate.

Previously reported addition reactions of water to 1-alkynes catalyzed by acids, mercuric salt,[1] $NaAuCl_4$,[2] Ru(III),[3] $RhCl_3$,[4] $[PtCl_2(CH_2{=}CH_2)]_2$,[5] $PtCl_4$,[6] and other metals[7] have all followed Markovnikov's rule and furnished ketones, until we reported the first *anti*-Markovnikov hydration in 1998. This hydration was catalyzed by a $RuCl_2$/phosphine mixture (system-1), where the phosphine had to be rather special, although they are commercially available, i.e., $P(C_6H_5)_2(C_6F_5)$ or $P(C_6H_4\text{-}3\text{-}SO_3Na)_3$ (TPPTS).[8a] The activity of system-1 was not very high, since ca. 10 mol % of catalyst was required and a small amount of the conventional Markovnikov product, i.e., ketone, was always present in the reaction products. However, we later found that complexes of the type $RuCpCl(PR_3)_2$ (system-2) are excellent catalysts that show both high activity and perfect selectivity for the *anti*-Markovnikov hydration of 1-alkynes.[8b] Our next goal has been to clarify the mechanism and to elucidate the controlling factor of this completely reversed regioselectivity. Closely related *stoichiometric* reactions of 1-alkynes and water assisted by iron-group metal complexes have been reported to result in C−C triple bond cleavage.[9] Reactions of metal−vinylidene complexes, tautomers of metal−(1-alkyne) complexes, with water have been known to lead to a similar C−C bond cleavage.[10] Summarizing these 1-alkyne/water/metal or metal−vinylidene/water reactions, Bianchini et al. reported their detailed "final chapter" study on the *stoichiometric* Ru(II)-assisted C−C fission of phenylacetylene by water into toluene and a Ru(II)−CO complex, which demonstrated the participation of a Ru(II)−vinylidene intermediate and successive generation of a metal−acyl intermediate (Scheme 1).[11] Therefore, it seemed likely that our *catalytic* reaction also involves isomerization of η^2-coordinated 1-alkyne to a vinylidene form prior to attack by water. Unlike the known cases based on coordination chemistry as described above, the resulting metal−acyl intermediate formed in our catalytic cycle was thought to take up a proton to release an aldehyde rather than undergo competitive decarbonylation to carbonyl−metal complex (C−C fission type reaction). Unexpectedly, deuterium-labeling experiments in our systems have clearly indicated that the reaction mechanism in water solvent is not so straightforward, i.e., not the catalytic version of modified Bianchini-type reactions shown in lower part of Scheme 2. We report here the full details of a mechanistic

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[†] RIKEN

[‡] PRESTO

[§] Nagoya University

[¶] Rikkyo University

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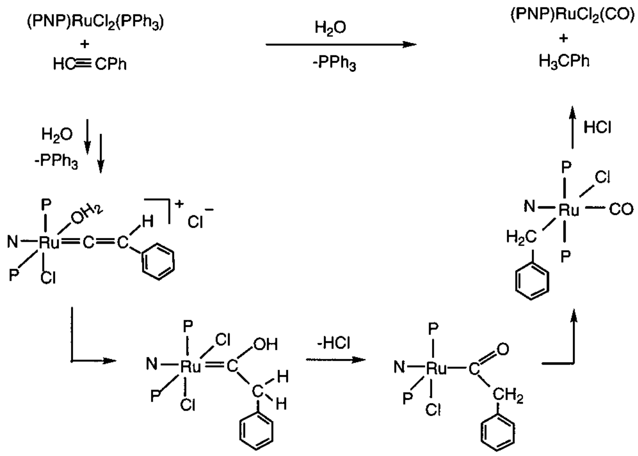
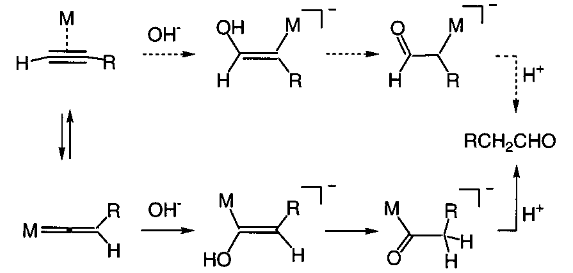
Scheme 1



Scheme 2



study involving both experiments and theoretical simulations of the catalytic *anti*-Markovnikov hydration of 1-alkynes.

Results and Discussion

A wide variety of 1-alkynes can be hydrated to the corresponding aldehydes by two catalytic systems. System-1 consists of $[RuCl_2(C_6H_6)]_2$ or $RuCl_2(C_6H_6)(PR_3)$ with added excess PR_3 ($PR_3 = P(C_6H_5)_2(C_6F_5)$ or $P(C_6H_4\text{-}3\text{-}SO_3Na)_3$) as the catalyst mixture.[8a] This combination should, under the applied reaction conditions (65−100 °C, in 2-propanol/H_2O), release benzene and form $RuCl_2(PR_3)_x$, the ruthenium version of the Wilkinson complex, as monitored by NMR spectra. System-2 employs a family of discrete complexes, $RuCpCl(PR_3)_2$ or its cationic form $[RuCp(MeCN)(PR_3)_2]PF_6$, where $(PR_3)_2$ is either a bidentate phosphine, typically dppm, or two monodentate phosphines such as $(PMe_3)_2$, and operates in 2-propanol/H_2O at 100 °C in most cases.[8b] Both catalyst systems are considered here.

(1) Hydration of 1-Octyne in $H_2{}^{18}O$. The hydration reactions were carried out under argon, but the vigorous exclusion of air was not necessary. While this is convenient from a preparative point of view, we should clarify that the oxygen of the resulting aldehyde does not come from atmospheric O_2. In fact, some vinylidene complexes, including $[RuCp({=}C{=}CHR)(PPh_3)_2]^+$, are known to react with O_2 although in all cases cleavage of the C−C bond is observed.[12] The reaction of 1-octyne with system-2 under standard conditions (RuCpCl(dppm) catalyst, 100 °C, 12 h) with $H_2{}^{18}O$ and successive isolation of octanal was performed. The IR ν(CO) band of the resulting aldehyde obtained in almost quantitative yield consists of a single band at 1695 cm^{-1}, which is 34 cm^{-1} lower than the corresponding peak of usual octanal, 1729 cm^{-1}, indicating unambiguously that the oxygen originates from water.

(2) Hydration of 1-Octyne Catalyzed by $RuCpCl(PPh_3)_2$ (1). The catalytic activity of system-2 is in general quite satisfactory, e.g. addition of water to 1-hexyne catalyzed by 1 mol % of RuCpCl(dppm) gives hexanal in 95% isolated yield. Virtually no appreciable amount of ketone or other byproduct is formed. Although this is excellent from the viewpoint of practical aldehyde synthesis, the lack of byproducts does not give any hints regarding the reaction pathways, which can often be obtained from the information on side products. Fortunately, the activity of the triphenylphosphine analogue, $RuCpCl(PPh_3)_2$ (**1**), turned out to be very low and a large amount of **1** is needed to get a reasonable amount of aldehyde. While hydration catalyzed by **1** also gave some byproducts, the selectivity to aldehyde was still very high and the formation of ketone was not observed at all. Thus, a mixture of 1-octyne and 30 mol % of **1** in H_2O/2-propanol gave, after heating at 100 °C for 15 h, octanal in only 35% yield without any detectable amount of 2-octanone. The major byproduct was *n*-heptane, which was formed in 18% GC yield based on 1-octyne. By column chromatography of the reaction mixture, $RuCpCl(CO)(PPh_3)$ was isolated in 65% yield based on **1**. When a similar reaction of 1-octyne was carried out with initial addition of 100 mol % of NH_4PF_6 to the starting mixture, which should help to generate cationic species from **1**, aldehyde was obtained in 74% yield, heptane was obtained in 21% yield, and the complexes obtained were mixtures of $RuCpCl(CO)(PPh_3)$ and $[RuCp(CO)(PPh_3)_2]PF_6$[13] in respective yields of 41 and 26% yield, as determined by NMR spectra.

Similarly, the hydration of benzylacetylene catalyzed by system-1 (10 mol % of $RuCl_2(C_6H_6)(PPh_2C_6F_5)$ + 3 equiv of $PPh_2C_6F_5$) gave 3-phenylpropanal, 1-phenyl-2-propanone, and styrene in 65, 7, and 17% yield, respectively. The formation of styrene is best explained by β-elimination from an intermediate $RuCl_2(PPh_2C_6F_5)_x(CO)(CH_2CH_2Ph)$. Further, the ruthenium-containing solid recovered after reactions with system-1 always showed multiple but clear IR absorption bands at 1970−2070 cm^{-1} that were assignable to coordinated CO.

To examine the possibility that this metal-coordinated CO might result from the decarbonylation of aldehyde already produced in the reaction mixture, the hydration of 1-octyne catalyzed by system-1 (10 mol % of $RuCl_2(C_6H_6)(PPh_2C_6F_5)$ + 3 equiv of $PPh_2C_6F_5$) was carried out in the presence of 20 mol % of 3-phenylpropanal. After 3 h at 80 °C, octanal was formed in 61% yield, but the 3-phenylpropanal remained intact. In addition, the assumed decarbonylation product from the aldehyde, ethylbenzene or styrene, was not detected at all.

All of these observations, including the formation of a one-carbon-shorter byproduct and isolation of CO-coordinated complexes, clearly indicate that *a metal−acyl complex is an intermediate* in the catalytic cycle. The direct attack of the η^2-coordinated acetylene by OH^-, or formal insertion of the triple bond into a metal−OH bond, which has often been suggested to be the mechanism for metal-catalyzed hydration of alkynes to ketones,[3c,4−6] is not applicable to the present *anti*-Markovnikov reaction because the path does not contain a metal−acyl intermediate (Scheme 2, the upper part). In contrast, the water addition to vinylidene complexes, a well-established reaction in coordination chemistry,[11] is compatible with our observation so far described in this section, in that it proceeds via a metal−acyl intermediate.

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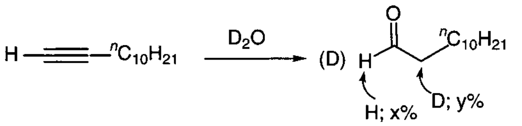
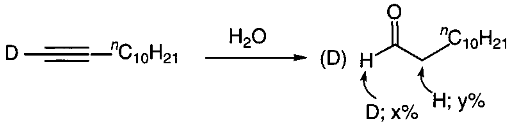
Scheme 3



cat.	aldehyde yield (%)	Incorporation of	
		H; x (%)	D; y(%)
$RuCl_2(C_6H_6)(PPh_2C_6F_5)$ + 3 $PPh_2C_6F_5$)	15	> 95	92
$[RuCl(C_6H_6)(TPPTS)_2]Cl$ + 2 TPPTS	15	> 95	88
$RuCpCl(PPh_3)_2$ (**1**)	30	90	92



cat.	aldehyde yield (%)	Incorporation of	
		D; x (%)	H; y(%)
$RuCl_2(C_6H_6)(PPh_2C_6F_5)$ + 3 $PPh_2C_6F_5$)	27	94	> 95
$[RuCl(C_6H_6)(TPPTS)_2]Cl$ + 2 TPPTS	30	90	> 95
$RuCpCl(PPh_3)_2$ (**1**)	30	93	> 95

(3) Hydration Reactions with D_2O or DC≡CR as a Reactant. Under the typical reaction conditions used with both system-1 and system-2, the terminal hydrogen of free 1-alkynes was exchangeable with a water proton, as easily monitored in the NMR spectra of the reaction with D_2O/HCCR/Ru(II) or H_2O/DCCR/Ru(II). Fortunately, this exchange rate was slower than the hydration of 1-alkyne; hence at the early stage of the hydration reaction (conversion $\leq$30% under the standard conditions), we could omit the exchange of acetylenic hydrogen with water hydrogen.

The hydration reactions of 1-dodecyne and D-labeled 1-dodecene were carried out in $(CH_3)_2COD/D_2O$ and $(CH_3)_2COH/H_2O$, respectively, at 100 °C for 18 h (system-1) or at 100 °C for 15 h (system-2). The pattern of H and D found in the resulting aldehyde was determined by NMR as illustrated in Scheme 3. The results clearly show that the formyl hydrogen exclusively originates from acetylenic hydrogen while the two hydrogen atoms of the methylene group next to the carbonyl carbon are from water. This observation was at first completely unexpected since the assumed interconversion of η^2-alkyne to vinylidene (Scheme 2) should bring acetylenic hydrogen on the carbon substituted with group R, and eventually should give RCH(D)−CHO in the addition of H_2O to RC≡CD and RCH(D)−CDO in the addition of D_2O to RC≡CH. If, on the other hand, a rapid intermolecular exchange of vinylidene hydrogen with water takes place as in the case of Bianchini's system (Scheme 1),[11] the addition of H_2O to RC≡CD should yield RCH_2−CHO and the addition of D_2O to RC≡CH would result in the formation of RCD_2−CDO.

(4) Examination of the Hydration Reaction of PhC≡CH Using RuCp(C≡CPh)(dppm) or [RuCp(=C=CHPh)(dppm)]PF_6 as the Catalyst Precursor. Our previous work showed that RuCpCl(dppm) (**2**) is a good catalyst (system-2) in the *anti*-Markovnikov hydration of phenylacetylene: in the presence of 5 mol % of **2**, PhC≡CH reacted with water at 100 °C for 12 h to give $PhCH_2CHO$ in 90% isolated yield.[8b] To examine the possibility that a Ru(II)−acetylide or cationic Ru(II)−vinylidene complex could be an intermediate in the catalytic cycle, we prepared the corresponding complexes and checked their reactivity.

Under the same reaction conditions as above (100 °C, 12 h), both RuCp(C≡CPh)(dppm) and [RuCp(=C=CHPh)(dppm)]PF_6 were unreactive: in the presence of 10 mol % of these complexes, the hydration of PhC≡CH did not take place and the complex was recovered unchanged in both cases. When the phosphine ligand was changed to PPh_3, [RuCp(=C=CHPh)(PPh_3)$_2$]PF_6 reacted with water to give a stoichiometric amount of toluene, in agreement with previous reports,[10a,b] but no further catalytic reaction was observed. Concerning the initial attack of the α-carbon of the Ru(II)−vinylidene species by OH^-, dppm complex is thus less reactive probably because of stronger back-donation from Ru to Cα, compared to the PPh_3 analogue, which makes the carbon less electrophilic. The unreactive nature of [RuCp(=C=CHPh)(dppm)]PF_6 provides, together with the observation shown in section (3), evidence that Ru(II)−vinylidene is not an intermediate in the present *anti*-Markovnikov hydration. Alternatively, theoretical calculation (vide infra) suggests that Ru(IV)−vinylidene is likely to be the true intermediate.

(5) Summary of Experimental Observations. The results we have discussed so far may be summarized as follows: (a) The catalytic cycle involves an acyl intermediate, (b) an acetylenic hydrogen of the terminal alkyne is selectively transformed to a formyl hydrogen of the resulting aldehydes, and (c) Ru(II)−acetylide and Ru(II)−vinylidene complexes presumably are not involved in the present hydration reaction.

(6) DFT Calculations. Calculations based on B3LYP hybrid density functional methods[14−16] were performed with the Gaussian 98 program.[17] All of the geometry optimizations were carried out by using the [2s2p2d]/(3s3p4d) basis set with the corresponding effective core potential of Hay and Wadt[18] for the metal, the 6-31G* basis set[19] for C and H atoms of methylacetylene and fragments derived thereof, as well as for P atoms, and the 6-31G basis set[20] for other atoms in the molecule. Vibrational frequencies for all the optimized structures were carried out to confirm the nature of stationary points. The energetics of the optimized structures were refined at the MP4SDQ level with use of the [2s2p2d1f]/(3s3p4d1f) basis set and the same effective core potential as above for the metal,

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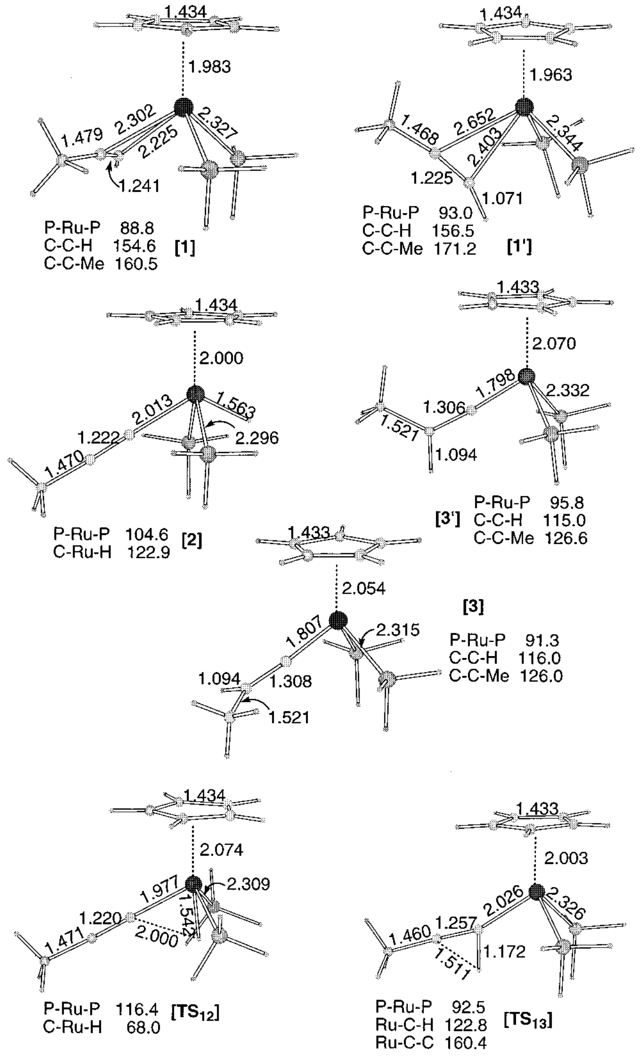

Figure 1. Calculated structures (in Å and deg) for **[1]**−**[3]**, rotational isomers, and related transition states.

the 6-31G** basis set[21] for C and H atoms in methylacetylene and fragments derived thereof, the 6-31G* set for P atoms, and C and H atoms in the Cp-ring and PH_3.

(6-1) η^2-Alkyne, Vinylidene, and Hydride−Alkynyl Complexes. The species that is formed first from **2** and 1-alkyne must be a cationic complex $[RuCp(\eta^2\text{-alkyne})(dppm)]^+$. Alkyne complex $[RuCp(C_2H_2)(PMe_2Ph)_2]^+$ was prepared and structurally characterized by Selegue et al. from $RuCpCl(PMe_2Ph)_2$ and HC≡CH.[22] As a model for calculations, we chose $[RuCp(\eta^2\text{-}MeC{\equiv}CH)(PH_3)_2]^+$ (**[1]**) and thoroughly examined tautomerization of the alkyne fragment in this complex. The geometries of a rotamer (**[1′]**), two tautomers, i.e., hydride−alkynyl complex **[2]** and vinylidene complexes (**[3]**, **[3′]**), and the transition states for the isomerizations (**[TS_{12}]**, **[TS_{13}]**) are shown in Figure 1, while their relative energies are given in Figure 2.

The Ru−C distances in $[RuCp(HC{\equiv}CH)(PMe_2Ph)_2]^+$ have been reported to be 2.20(2) and 2.21(2) Å, the CC distance 1.22(2) Å, and the Ru−P distances 2.317(3) and 2.304(3) Å in the solid state.[22] The corresponding vinylidene complex $[RuCp({=}C{=}CH_2)(PMe_2Ph)_2]^+$ has distances of Ru−C 1.84(1) Å, CC 1.29(1) Å, and Ru−P 2.313(2) and 2.308(2) Å.[22] The calculated geometries of **[1]** and vinylidene complex **[3]** fit these values considering the standard deviations of the crystal analyses. Interestingly, the calculated value for Ru−C in vinylidene complex **[3]** (1.807 Å) coincides with the value observed in the crystal structure of $[RuCp^*({=}C{=}CHCO_2Me)(dippe)]^+$ (1.807(9) Å, dippe = 1,2bis(diisopropylphosphino)ethane).[23]

Complex **[2]** is formed by oxidative addition of a C−H bond of 1-alkyne. Although no hydride−alkynyl complexes have been isolated or detected by the reaction of 1-alkynes with $RuCpCl(PR_3)_2$-type complexes, the reaction with a Cp* version gives $[RuCp^*(H)(C{\equiv}CR)(dippe)]^+$ (R = CO_2Me, Ph, TMS).[23] Therefore, complex **[2]** was considered as a possible intermediate, but may have a very short lifetime. In accord with the reported structure of the Cp* complex, **[2]** has a *trans*-$(PH_3)_2$ configuration. All attempts to locate a cis-isomer were unsuccessful: apparently the cis-isomer has no stationary point but rather falls back to the η^2-alkyne complex in the process of searching for an energy minimum. Complex **[2]** was found to be slightly unstable, 9 kcal/mol higher in energy, taking the energy level of **[1]** as a standard (Figure 2). However, transition state **[TS_{12}]**, which connects **[1]** with **[2]**, via the "vertical alkyne rotamer" **[1′]**, has a transition energy as high as 40 kcal/mol. In the case of the more electron rich Cp*Ru system with an electron-releasing phosphine ligand, the barrier to Ru(IV)−hydride−alkynyl is apparently much smaller, leading to isolation of such complexes under mild conditions.

An alternative tautomer, vinylidene complex **[3]**, is more stable than the η^2-alkyne complex **[1]** by 10 kcal/mol. The transition state to it, **[TS_{13}]**, is 24.5 kcal/mol above **[1]** and its geometry corresponds to the intraligand migration of hydrogen from the α- to β-carbon. The structure of the 1-alkyne fragment in the transition state is similar to that obtained by our previous ab initio calculations for the change of $RuCl_2(HC{\equiv}CH)(PH_3)_2$ to $RuCl_2({=}C{=}CH_2)(PH_3)_2$.[24] However, a much earlier transition state was calculated for the corresponding transition state to form $[Ru(\eta^5\text{-}C_9H_7)({=}C{=}CH_2)(PH_3)_2]^+$ from its acetylene complex, reflecting the difference in Cp and indenyl ligands as well as the rather shallow potential curves in these transitions.[25] For the rearrangement of $[RuCp(HC{\equiv}CMe)(PMe_3)_2]PF_6$ to $[RuCp({=}C{=}CHMe)(PMe_3)_2]PF_6$, the kinetic study in MeCN by Bullock gave $\Delta H^{\ddagger} = 23.4 \pm 0.3$ kcal mol^{-1}, which is very close to that for **[TS_{13}]** calculated here.[26] Puerta et al. reported $\Delta H^{\ddagger} = 29 \pm 2$ kcal mol^{-1} for the change of $[RuCp(HC{\equiv}CH)(dippe)]BF_4$ to $[RuCp({=}C{=}CH_2)(dippe)]BF_4$ in MeOH.[23]

It is obvious from the experiment described in section (4) that Ru(II)−vinylidene complex **[3]** is not involved in the catalytic *anti*-Markovnikov hydration. In particular, the finding that D-labeled acetylenic hydrogen does not migrate to the substituted carbon (section (3)) is evidence that the path via **[TS_{13}]** does not occur during the catalytic reaction. Since hydride−alkynyl complex **[2]** is formed through a much higher transition state (**[TS_{12}]**) starting from the same intermediate **[1′]** (Figure 2), the path leading to **[2]** in the catalytic reaction is also very unlikely. Our original expectation that **[2]** might be an alternative route to a vinylidene complex or an acyl complex derived from it, i.e., the possibility that the addition of a water proton to C_β of **[2]** could give a Ru(IV)−vinylidene intermediate, is thus excluded by the theoretical evaluation of the transition energies.

(6.2) Protonation of η^2-Coordinated Alkyne Leading to Ru(IV)−Vinylidene. Searching for a reasonable reaction

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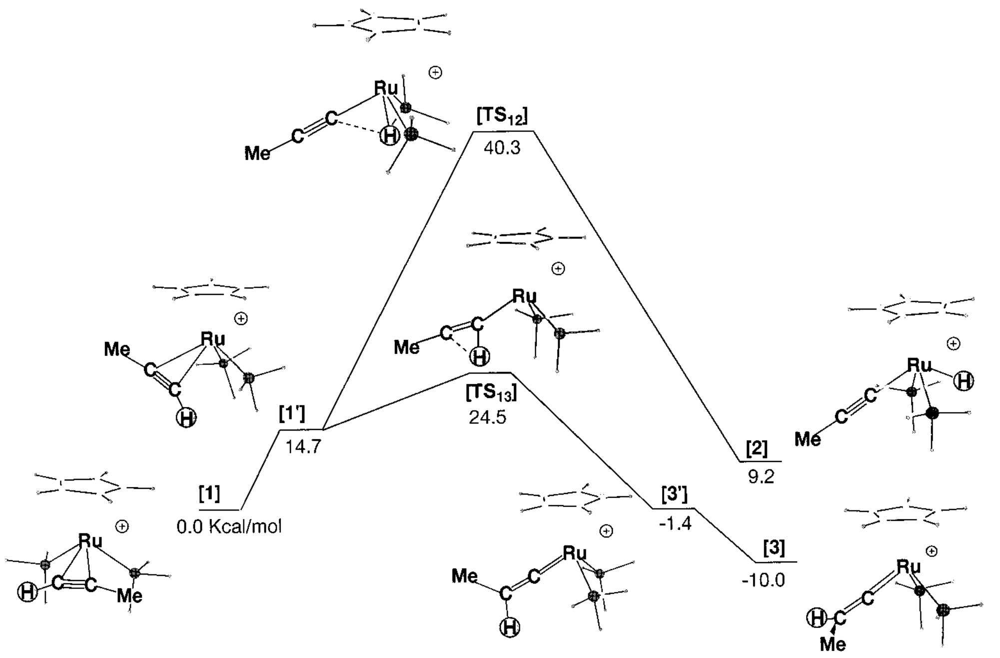
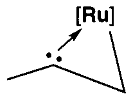


Figure 2. Energy diagram (in kcal/mol) of complexes **[1]**−**[3]**, rotational isomers, and related transition states.

process, we next examined the possibility that a proton from water may attack the η^2-MeC≡CH moiety of complex **[1]** because the protonation of a η^2-coordinated alkyne to give a cationic vinyl complex is well-known in the literature.[27]

The geometries of the proton-addition products **[4]** and a complex (**[5]**) derived from one of the vinyl intermediates, together with a transition state to it (**[TS$_{45}$]**), are shown in Figure 3 and their relative energies are shown in Figure 4. In principle, the three isomers of vinyl complexes may be formed depending on the position and direction of the proton addition. Complex **[4$_{cis}$]** is the result of addition to substituted carbon from the opposite side of the metal (outside attack), while **[4$_{trans}$]** is the addition from the same side of the metal. When protonation occurs on the terminal carbon of η^2-alkyne, **[4$_{gem}$]** will be the product. As shown in Figure 4, **[4$_{gem}$]** is the most stable vinyl complex: it is −14 kcal/mol lower in energy than the standard **[4$_{trans}$]** and this stability apparently arises from the additional interaction of Ru- -C(H$_2$), which does not exist in **[4$_{cis}$]** or **[4$_{trans}$]**. This interaction in **[4$_{gem}$]** may be regarded as a contribution of an electronic structure shown below, in which the CH$_3$CCH$_2$ carbene coordinates to the Ru atom while C(H$_2$) is σ bonded to the Ru center. As illustrated in Figure 3, the Ru−C(Me) bond is 1.893 Å in **[4$_{gem}$]** and Ru−C(H$_2$) is calculated to be 2.186 Å.



In realistic reactions, however, the phosphine ligand used, e.g. dppm, is much bulkier than (PH$_3$)$_2$ and steric repulsion would not allow such close proximity of Ru and C(H$_2$). Moreover, the 1-alkynes used in our hydration reaction have substituents (R) larger than methyl (the largest one is *tert*-butyl), and severe steric crowding at the metal center should make the addition of a proton to the unsubstituted carbon of η^2-coordinated alkyne, which leads to the metal-C(R) σ-bond, highly unfavorable.

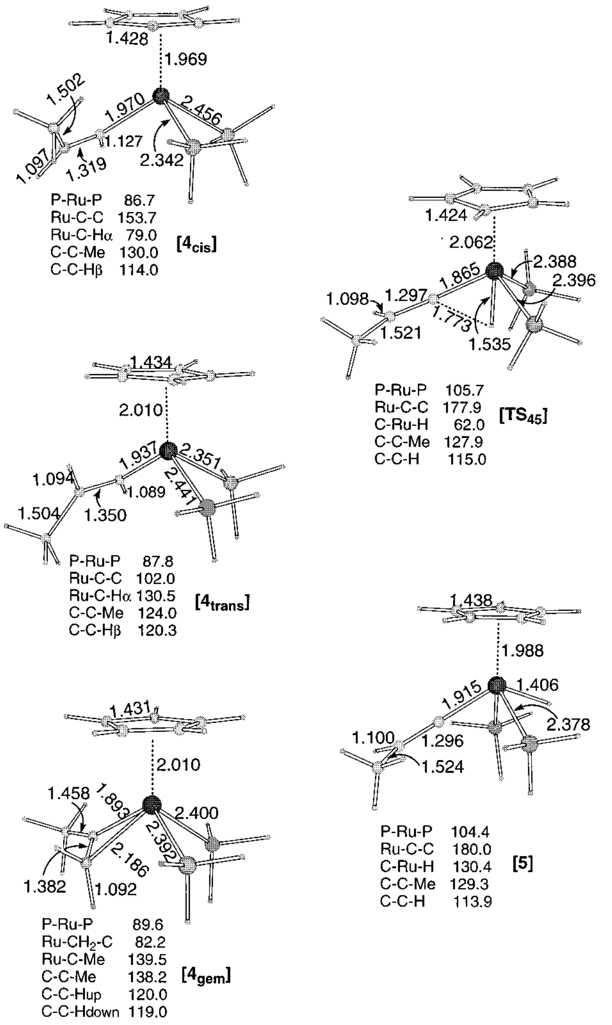


Figure 3. Calculated structures (in Å and deg) for **[4]** (three isomers), **[5]**, and the transition state.

Starting from **[4$_{trans}$]**, we found a path to a new Ru(IV)−hydride−vinylidene complex **[5]** with an activation barrier of 23 kcal (Figure 4). The net reaction is α-hydrogen migration

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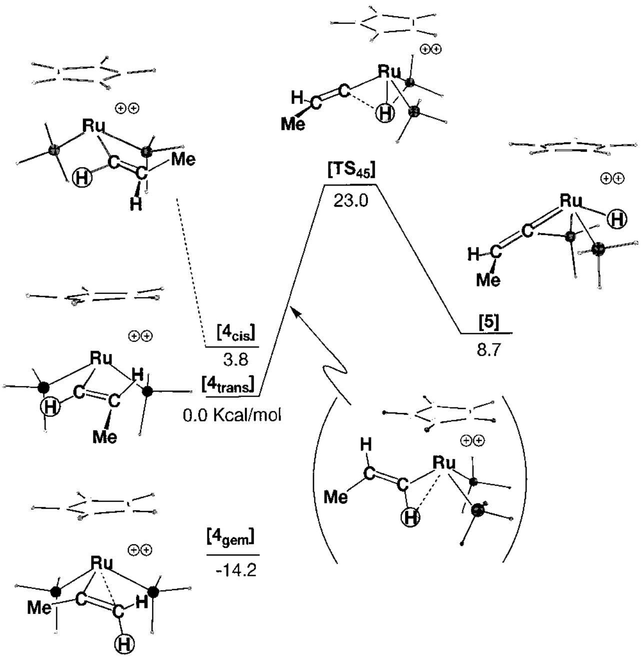


Figure 4. Energy diagram (in kcal/mol) of complexes **[4]**, **[5]**, and transition state **[TS$_{45}$]**.

from the vinyl moiety of a 16-electron complex to the metal center leading to an 18-electron complex. This type of reaction has some precedence: Caulton et al. observed the formation of Ru(II)−hydride−vinylidene complex $RuDX({=}C{=}CHPh)L_2$ in the reaction of $RuHX(H_2)L_2$ ($L = P^tBu_2Me$) with $PhC{\equiv}CD$, which proceeds via the intermediate $Ru({-}CD{=}CHPh)XL_2$.[28] This α-hydrogen migration of highly unsaturated 14-electron Ru(II) to form a 16-electron Ru(II) species was theoretically shown to have a transition energy of only 3.6 kcal/mol. It is particularly important to note here that the hydride ligand thus formed in **[5]** can be traced back to the acetylenic hydrogen in **[1]**. The orientation of the C=C vinyl plane in **[TS$_{45}$]** is almost the same as that in product **[5]**, and is nearly orthogonal to the vector C(α)−H(migrating), with a C(*β*)-C(α)−H(migrating) angle of 132°. Therefore, the geometry of **[TS$_{45}$]** is close to that of the product, while Caulton's transition state is closer to the starting complex and the migrating hydrogen is still in the plane of the vinyl group.[28b] According to our IRC calculation to follow the reaction path, a similar geometry is involved in the path from **[4$_{trans}$]** to **[TS$_{45}$]**, as illustrated in Figure 4. Important localized MO diagrams of **[TS$_{45}$]** are shown in Figure 5: Figure 5a exhibits back-donation from the occupied metal d_{xy} to p_y of C(α), indicating that empty p_y develops on this carbon as the hydrogen migrates from C(α) to Ru. Apparently, the hydrogen is best regarded as a hydride when it migrates through this transition state. As shown in Figure 5b, the hydride is accepted by an empty metal d_{z^2}-type orbital while also interacting with π^* of the CC double bond. To facilitate such orbital interactions as well as to reach the product structure, the $CH_3CH{=}C$ fragment rotates before reaching **[TS$_{45}$]**.

The next reaction step involving the resulting Ru(IV)−hidride−vinylidene **[5]** should be nucleophilic attack of the empty p_y orbital at C(α) by OH^-, as has been well established in stoichiometric reactions with more stable Ru(II)−vinylidene complexes.[10,11] The extent of back-donation from metal d_{xy} to p_y at C(α) is expected to be smaller in Ru(IV) than in Ru(II)−vinylidene complexes, and hence the reactivity of Ru(IV)−vinylidene toward OH^- should be higher than that with the Ru(II) analogue. In accord with this general consideration, the orbital population of C(α) p_y in the Ru(II)−vinylidene **[3]** was calculated to be 0.396, while that in **[5]** was 0.259 based on RHF calculations.

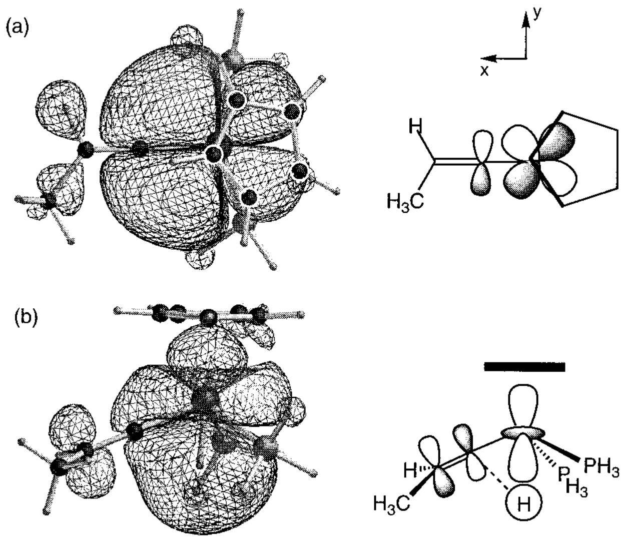
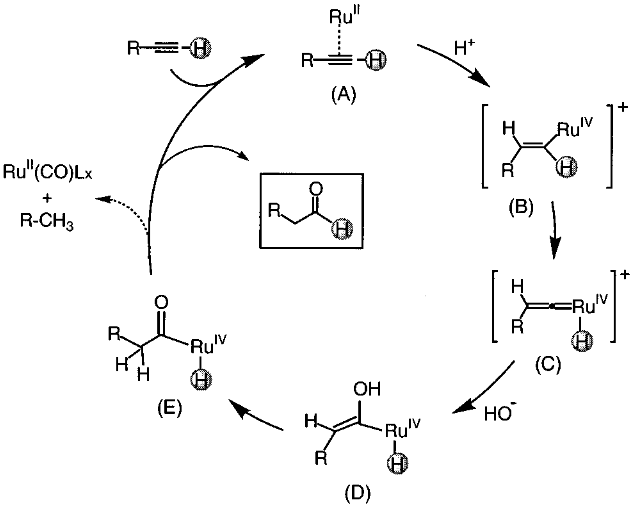


Figure 5. Localized molecular orbitals in **[TS$_{45}$]**: (a) top view of the back-donation from metal d_{xy} to vinylidene p_y and (b) side view of the metal−hydride interaction.

Scheme 4



(7) Catalytic Cycle and Regioselection. On the basis of the experimental results and calculations discussed above, the most reasonable catalytic cycle may be described as shown in Scheme 4, where Ru^{II} represents $Cl_2Ru(PR_3)_x$ (system-1) or $[RuCp(PR_3)_2]^+$ (system-2). The first key step is protonation of the η^2-alkyne complex (A), which must be faster than the well-known tautomerization of (A) to Ru(II)−vinylidene probably because water is present in large excess as a solvent, and also the increase in the positive charge in the complex might well be eased by solvation of water. Since the addition of weak protic acid does not accelerate the catalytic reaction, this is probably not the rate-determining step. The vinyl complex (B) will then undergo α-hydride transfer to form Ru(IV)−hydride−vinylidene intermediate (C). Though this step may be reversible in principle and the concentration of (C) is lower than that of (B) because (C) is less stable according to our calculations, (C) should be very reactive. The empty p-orbital at C(α) easily accepts

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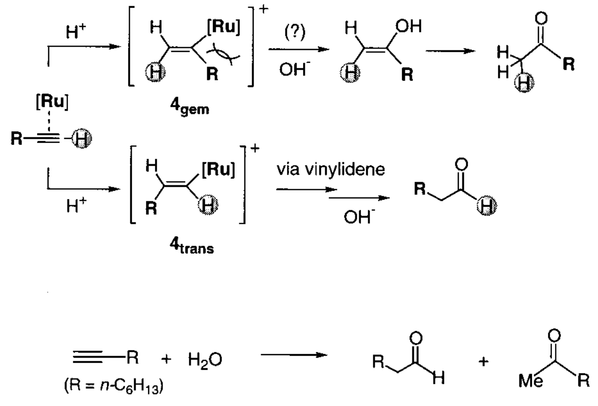
[28] (a) Oliván, M.; Eisenstein, O.; Caulton, K. G. *Organometallics* **1997**, *16*, 2227. (b) Oliván, M.; Clot, E.; Eisenstein, O.; Caulton, K. G. *Organometallics* **1998**, *17*, 3091.

Scheme 5



Ru cat	Aldehyde	Ketone
$RuCl_2(C_6H_6)[PPh_2(C_6F_5)]$	18	22 %
$RuCl_2(C_6H_6)[PPh_2(C_6F_5)]$/3 $PPh_2(C_6F_5)$	75	5 %
RuCpCl(dppm)	100	0 %

nucleophilic attack by OH^- ion since back-donation from Ru(IV) is not as extensive as with Ru(II)−vinylidene analogues. Among Ru(II)−vinylidene complexes, it is known that only electron-rich Ru(II) with electron-releasing ancillary ligands allow for the isolation of stable vinylidene complexes.[29] Therefore, isolation of a Ru(IV)−vinylidene complex should be quite difficult. α-Hydroxyvinyl complex (D) isomerizes instantaneously to acyl form (E). Finally, reductive elimination releases *n*-aldehyde in which the original acetylenic hydrogen is now bound to the carbonyl carbon. The side reaction that stops this catalytic cycle is most likely decarbonylation from (E) to give stable carbonyl complex and one-carbon-shorter organic chain (Scheme 4). The hypothesis that decarbonylation from $[HRuCp(C(O)CH_2R)(PR'_3)_2]^+$ to form $[HRuCp(CO)(CH_2R)(PR_3)]^+$ (system-2) should be suppressed by using bidentate phosphines in place of two PPh_3 ligands markedly improves the effectiveness of the catalyst, as described in our previous communication.[8b]

According to the process shown in Scheme 4, the *anti*-Markovnikov regioselection must originate from the proton addition step (A) → (B). If a proton is attached to the terminal carbon, the next reaction step of the resulting vinyl complex may well be the attack by OH^-, resulting in the formation of ketone (Scheme 5). Formation of $\mathbf{4_{gem}}$ is electronically favored (Figure 4), but should be sterically disfavored due to the presence of substituent R on C(α). In system-2, where ancillary ligands are sterically demanding Cp and strongly coordinating phosphines or diphosphines, the selection to aldehyde was perfect. In the case of system-1, the addition of free phosphine ligand was required to realize *anti*-Markovnikov selection. As exemplified in Scheme 5, the reaction of 1-octyne with the catalyst precursor $RuCl_2(C_6H_6)(PPh_2C_6F_5)$ gave almost equal amounts of *n*-aldehyde and methyl ketone. In the presence of 3 equiv of free phosphine, however, the yield of aldehyde increased to 75% while ketone was detected in only 5% yield. Apparently, the number of phosphine ligands coordinating the metal center increases in the presence of excess free phosphine, which makes the metal moiety sufficiently bulky so that $\mathbf{4_{gem}}$ is not formed in an appreciable amount while $\mathbf{4_{trans}}$ is more favored.

Conclusions

The experimental findings suggest that the ruthenium-catalyzed *anti*-Markovnikov hydration of terminal alkyne involves (1) a metal−acyl intermediate, (2) a process that changes an original acetylenic hydrogen to a formyl hydrogen, and (3) a pathway that does not include a Ru(II)−vinylidene species. DFT calculations have led to a route that satisfies the following conditions: (1) proton from water attacks the substituted carbon of a Ru(II)−η^2-coordinated alkyne, (2) the α-hydrogen of the resulting vinyl group migrates to the metal center to give a Ru(IV)−hydride−vinylidene intermediate, (3) the α-carbon of the vinylidene is attacked by OH^-, and (4) the resulting acyl group and hydride undergo reductive coupling from Ru(IV) to give aldehyde and regenerating Ru(II) species.

Therefore, the unusual *anti*-Markovnikov regioselection in the hydration reaction of terminal alkynes is attributed to attack by the water proton at the substituted carbon of the η^2-coordinated alkyne. The proton selects the substituted carbon probably because of the steric characteristics of the resulting vinyl complex. A similar regioselective protonation of η^2-methylacetylene bound to sterically crowded Mo has been reported.[27c] This step is also an entry to Ru(IV) species that plays a role in most of the catalytic cycle, leading to the efficient production of aldehyde.

Experimental Section

Column chromatography was performed with Silica Gel 60 N (spherical, neutral, 40−100 μm, Kanto Chemical Co. Inc.). Distillations were performed with a Kugelrohr apparatus (Shibata, GTO-250RS). ^1H NMR and ^{13}C NMR spectra were recorded on JEOL JNM-EX 270 (270 MHz) and JNM-AL 300 (300 MHz) spectrometers. All ^1H NMR spectra are reported in δ units, ppm downfield from tetramethylsilane as an internal standard. All ^{13}C NMR spectra are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77.0 ppm. IR spectra were recorded with use of a PERKIN ELMER Spectrum RX FT-IR System. GC analyses were performed with HP4890A and GC-MS were measured by HP-5971A with HP-5890 (GC) equipped with a 30-m capillary column (J & W, No. 122-1032, DB-1).

D_2O (D > 99.95%), *i*-C_3H_7OD (D > 98%), and $H_2{}^{18}O$ (^{18}O, 95−98%) were purchased from Merck, Acros, and Cambridge Isotope Laboratories, respectively. Deuterated 1-alkynes were synthesized by the reaction of 1-alkynes with *n*-BuLi followed by D_2O hydrolysis.

All organic substrates and solvent (2-propanol) were commercially available and degassed before use without further purification. $RuCpCl(PPh_3)_2$,[30a] RuCpCl(dppm),[30b] RuCpCl(dppe),[30b] $[RuCp(=C=CHPh)(dppm)]PF_6$,[30c] and $RuCp(C\equiv CPh)(dppm)$[30c] were synthesized as described in the literature. $RuCl_2(C_6H_6)(PPh_2C_6F_5)$ was synthesized by a procedure similar to that for $RuCl_2(C_6H_6)PPh_3$.[31] ^1H NMR (270 MHz, $CDCl_3$) δ 5.55 (s, 6H, C_6H_6), 7.34−7.50, 7.80−7.92 (m, 10H, $PPh_2(C_6F_5)$); ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.0 (t, J = 10.3 Hz). Elemental Anal. Calcd for $C_{24}H_{16}Cl_2F_5PRu$: C 47.85, H 2.68. Found: C 47.44, H 2.69. $[RuCl(C_6H_6)(TPPTS)_2]Cl$ was synthesized from $[RuCl_2(C_6H_6)]_2$[31] and 4 equiv of $P(3\text{-}C_6H_4SO_3Na)_3$ (TPPTS) in water by heating at 100 °C for 10 min. ^1H NMR (270 MHz, D_2O) δ 5.98 (s, 6H, C_6H_6), 7.54 (s, 12H), 7.98 (s, 12H), 8.19 (s, 6H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.3 (s). Elemental Anal. Calcd for $C_{24}H_{16}Cl_2F_5PRu$: C 36.37, H 2.18. Found: C 36.54, H 2.41.

Typical Procedures for Ruthenium-Catalyzed Hydration of 1-Alkynes. (a) System-1: 1-Octyne (110 mg, 1.0 mmol) was added to a mixture of $RuCl_2(C_6H_6)(PPh_2C_6F_5)$ (60.2 mg, 0.10 mmol) and $PPh_2(C_6F_5)$ (106 mg, 0.30 mmol) in 2-propanol/water (2.5/0.75 mL) in a screw-capped vial under an argon atmosphere. The mixture was stirred

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[30] (a) Bruce, M. I.; Windsor, N. J. *Aust. J. Chem.* **1977**, *30*, 1601. (b) Ashby, G. S.; Bruce, M. I.; Tomkins, I. B.; Wallis, R. C. *Aust. J. Chem.* **1979**, *32*, 1003. (c) Bruce, M. I.; Wallis, R. C. *Aust. J. Chem.* **1979**, *32*, 1471.

[31] Bennett, M. A.; Smith, A. K. *J. Chem. Soc., Dalton Trans.* **1974**, 233.

for 12 h at 65 °C, and then extracted with Et_2O (5 mL) and dried with Na_2SO_4. 1-Octanal (71%) and 2-octanone (4.5%) were determined by GC analysis. Although the other byproducts were not fully characterized, the formation of 10−15% of heptenes (1-heptene and isomers) and 5−10% of octenes (1-octene and isomers) was detected by GC and GC-MS.

When benzylacetylene was used as a substrate (70 °C, 12 h), 3-phenylpropanal (65%), 1-phenyl-2-propanone (7.0%), styrene (17.3%), 3-phenyl-1-propene (15.5%), and 1-phenyl-1-propene (6.2%) were identified.

A similar reaction with 1-hexyne, evaporation of organic materials, and washing with pentane gave a pale-yellow solid, which is soluble in CH_2Cl_2. IR spectra (CH_2Cl_2) showed, besides the peaks due to phosphine, three intense peaks in the ν(CO) region: 1974 (br), 2007 (s), and 2066 (s) cm^{-1}.

(b) System-2: 1-Hexyne (82.2 mg, 1.0 mmol) and RuCpCl(dppm) (5.9 mg, 0.010 mmol) in 2-propanol/water (2.5/0.75 mL) were stirred at 100 °C for 12 h. 1-Hexanal ($>$99% by GC) was the only detectable product, and was isolated by Kugelrohr distillation (95%).

Hydration of 1-Octyne with $RuCpCl(PPh_3)_2$. A mixture of 1-octyne (110 mg, 1.0 mmol) and $RuCpCl(PPh_3)_2$ (218 mg, 0.30 mmol) in 2-propanol/water (2.5/0.75 mL) was stirred at 100 °C for 15 h. 1-Octanal (35%), heptane (18%), and unreacted 1-octyne (25%) were detected by GC. After the evaporation of organic materials, recrystallization from CH_2Cl_2/hexane gave $RuCpCl(CO)(PPh_3)$[32] (96 mg, 65% based on Ru atom), which was characterized by ^1H NMR and IR spectra.

Hydration Reactions with D_2O. (a) System-1: 1-Dodecyne (83.2 mg, 0.50 mmol), $[RuCl(C_6H_6)(TPPTS)_2]Cl$ (13.9 mg, 0.010 mmol), and TPPTS (11.4 mg, 0.020 mmol) in i-C_3H_7OD/D_2O (1.25/0.38 mL) were reacted for 18 h at 100 °C. 1-Dodecanal (15%), 2-dodecanone (1.5%), unreacted 1-dodecyne (65%), undecenes (∼6%), and 1-dodecene (4%) were analyzed by GC. ^1H NMR analysis of unreacted 1-dodecyne suggested that acetylenic hydrogen was not exchanged with D. ^1H NMR analysis of isolated 1-dodecanal indicated $>$95% H at the formyl proton (δ 9.76, t) and 12% H at the α-position (δ 2.39, dt). ^2H NMR of the same sample was consistent with this measurement. A similar reaction condition was used for the $RuCl_2(C_6H_6)(PPh_2C_6F_5)$ system.

(b) System-2 with [RuCpCl(PPh3)2]: 1-Dodecyne (166 mg, 1.0 mmol) and $RuCpCl(PPh_3)_2$ (218 mg, 0.30 mmol) in i-C_3H_7OD/D_2O (2.5/0.75 mL) were reacted for 5 h at 100 °C. 1-Dodecanal (30%), undecane (17%), and unreacted 1-dodecyne (30%) were detected by GC analysis. ^1H NMR analysis of unreacted 1-dodecyne indicated 97% H in acetylenic proton, and that of isolated 1-dodecanal indicated 90% H at the formyl proton and 8% H at the α-CH_2-position.

The reactions of $DC{\equiv}C$-n-$C_{10}H_{21}$ with H_2O were carried out under similar conditions.

Acknowledgment. We thank the RIKEN Computer and Information Division and the Research Center for Computational Science of Okazaki National Research Institutes for providing the computational facilities. This work was in part supported by a Grant-In-Aid for Scientific Research on Priority Areas from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

Supporting Information Available: An IR ν(CO) chart of octanal after hydration of 1-octyne with $H_2{}^{18}O$, ^1H and ^2H NMR spectra of dodecanal obtained by D-labeling experiments, a GC chart of the reaction mixture after 1-octyne was hydrated by catalysis with $RuCpCl(PPh_3)_2$, and Cartesian coordinates for all optimized structures at the B3LYP level and their absolute total energy values calculated at the MP4SDQ level (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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