The Mechanism of Aqueous Ruthenium(II)-Catalyzed Olefin Isomerization†

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Olefin isomerization of allylic ethers and alcohols is catalyzed by $Ru^{II}(H_2O)_6(tos)_2$ (tos = *p*-toluenesulfonate) (1) under mild conditions in aqueous solution to yield the corresponding carbonyl compounds. Non-allylic olefins are also isomerized, although homoallylic alcohols exhibit stability toward isomerization. An exclusive 1,3-hydrogen shift is observed in the isomerization of allyl-*1,1-d*$_2$ alcohol to propionaldehyde-*1,3-d*$_2$ and allyl-*1,1-d*$_2$ methyl ether to 1-propenyl-*1,3-d*$_2$ methyl ether by 1 in aqueous solution. The presence of crossover products from the isomerizations of mixtures of (a) allyl-*3*-^{13}C alcohol and allyl-*1,1-d*$_2$ alcohol and (b) allyl-*1,1-d*$_2$ methyl ether and allyl ethyl ether demonstrates that the isomerization of both alcohols and ethers occurs via intermolecular hydrogen shifts. A modified metal hydride addition–elimination mechanism involving exclusive Markovnikov addition to the double bond directed by the oxygen functionality of the substrate has been proposed.

Introduction

The coordination complex $Ru^{II}(H_2O)_6(tos)_2$ (tos = *p*-toluenesulfonate) (1)[1,2] is a highly active catalyst for the ring-opening metathesis polymerization (ROMP)[3-6] of strained cyclic olefins.[7-11] During the course of our studies on the preparation of functionalized olefin complexes of 1[12] we discovered that this aqueous ruthenium(II) complex is also an efficient catalyst for the isomerization of olefins. Although olefin isomerization[13] is an important transformation in a number of transition-metal-catalyzed reactions such as hydrozirconation,[14,15] hydroformylation,[16-22] hydrosilylation,[23-25] and hydrocyanation,[26-28] none of these processes involves water as a solvent. Indeed, to the best of our knowledge, this study is the first example of fully aqueous metal catalysis of olefin isomerization. Water continues to emerge as an important solvent for transition-metal catalysis with its advantages lying in economy, safety, and its ability to facilitate catalyst–product separation.[29] This, coupled with the lack of data regarding organometallic transformations catalyzed by 1, led us to probe the mechanism of olefin isomerization in this system.

Our initial observations regarding olefin isomerizations catalyzed by 1[12] concerned the isomerization of allylic alcohols and ethers to the corresponding carbonyl compounds. Although most mechanistic studies on olefin isomerization have centered on strictly hydrocarbon substrates such as 1-butene, 1-pentene, and 3-phenyl-1-propene, olefin isomerization has seen its widest application in the isomerization of functionalized substrates. Allylic alcohols are isomerized to saturated aldehydes or ketones, via an intermediate enol, and allyl ethers are isomerized to enol ethers by a number of transition-metal catalysts (allylic alcohols: Mo,[30] Fe,[31,32] Ru,[33-38] Co,[39] Rh,[33,40-43] Ir,[40,44,45] and Pt[46-48]; allylic ethers: Mo,[30] Fe,[49,50]

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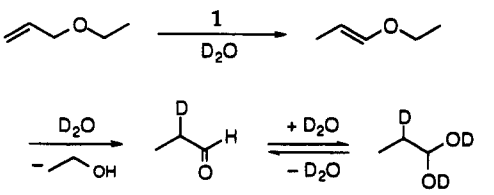
Rh,[42,51] Ir,[44] Pd,[52] and Pt[47,48]). In particular, rhodium[53-56] and iridium[57] complexes are used as deprotecting agents for allyl ethers which often serve as protecting groups in carbohydrate chemistry.[53,56,58,59] Some of the systems reported can produce aldehydes and ketones from allylic alcohols in sufficient yields to be synthetically useful.[32,34,41] Transition-metal catalysts also have been reported to isomerize various other functionalized olefins including, but not limited to, allylic acetates,[60] allylic siloxanes,[61] *N*-allylamides and -imides,[62] and unsaturated nitriles.[26] Allylamines are isomerized asymmetrically by [Rh(binap)-S_2]$^+$ (binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; S = solvent or other coordinative molecule) in what is by far the most successful asymmetric isomerization system developed to date (ee ≥ 90%).[63-66] This system is also active for the isomerization of allylic alcohols and ethers, but with only moderate optical yields (ee ≈ 40–50%).[35,42]

The two established pathways for transition-metal-catalyzed olefin isomerization are the π-allyl metal hydride and the metal hydride addition–elimination mechanisms.[67,68] The fundamental differences between the two mechanisms are that (1) the π-allyl metal hydride mechanism involves a 1,3-hydrogen shift while the metal hydride addition–elimination mechanism can involve a 1,2-hydrogen shift and (2) the π-allyl metal hydride mechanism is an intramolecular hydrogen shift while the metal hydride addition–elimination mechanism is an intermolecular hydrogen shift. Of the various mechanistic studies on transition-metal-catalyzed isomerizations of allylic functionalized substrates,[42-44,48,69-72] all but one[48] claim a π-allyl metal hydride-type mechanism. The studies detailed below determine the nature of the isomerization mechanism for the aqueous ruthenium(II)-catalyzed isomerization of allylic alcohols and ethers through isotopic labeling experiments. Our results are consistent with a modified metal hydride addition–elimination mechanism which involves exclusive 1,3-hydrogen shifts through oxygen-directed Markovnikov addition of the metal hydride to the olefin substrate.

Scheme 1



Results

Isomerizations. When the reaction of allyl ethyl ether and 1 (10 mol %) in D_2O is followed by ^1H NMR, four organic products are observed in addition to the starting material and Ru^{II}(allyl ethyl ether)$(D_2O)_5(tos)_2$.[12] After complete consumption of the starting material the organic products can be extracted into C_6D_6 and analyzed by ^1H NMR. In this organic solvent, however, only three products are observed. These products can be isolated by preparative gas chromatography and identified by ^1H NMR as *trans*-1-propenyl ethyl ether (J_{CH-CH} = 13 Hz), propionaldehyde-2-*d*, and ethyl alcohol. The fourth product observed in aqueous medium is the hydrate of propionaldehyde-2-*d*. *cis*-1-Propenyl ethyl ether is not observed at any time during the course of the reaction. The formation of these products is consistent with the reaction pathway shown in Scheme 1. Aqueous ruthenium(II) catalyzes the isomerization of allyl ethyl ether to *trans*-1-propenyl ethyl ether which then undergoes acid-catalyzed hydrolysis[73,74] to ethanol and propionaldehyde-2-*d*. With a substrate to catalyst ratio of 10:1 the conversion to aldehyde is complete in 4–5 h at 45 °C. The appearance and disappearance of the products in the ^1H NMR are consistent with the pathway shown in Scheme 1. The olefin complex Ru^{II}(allyl ethyl ether)$(D_2O)_5(tos)_2$ can be isolated by removing the volatiles of the reaction in vacuo. This complex is stable for up to 1 week at room temperature in D_2O solution.

Allylic alcohols also undergo isomerization in the presence of 1 and the reaction is quite general (Scheme

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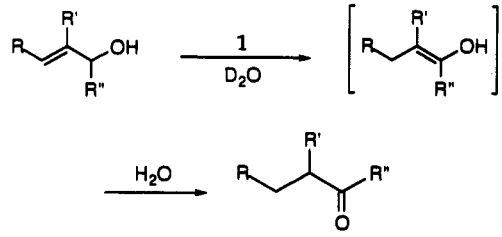
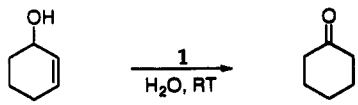
Scheme 2



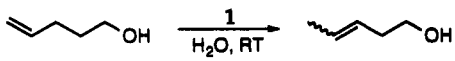
R, R' = H; R" = H, Me, Et
R = Me; R', R" = H
R, R" = H; R' = Me

2). Greater than 90% conversion to the isomeric aldehyde is observed by ^{1}H NMR in all cases. Oxidation products are also observed in some instances. In the case of crotyl alcohol (2-buten-1-ol), ca. 5% crotonaldehyde is observed in the product mixture by ^{1}H NMR and ca. 18% of the ruthenium is present as a crotonaldehyde complex. In the case of (±)-3-buten-2-ol ca. 33% of the ruthenium is present as a complex with methyl vinyl ketone after total consumption of starting material. Small but detectable amounts of free methyl vinyl ketone are observed during the course of the reaction. Cyclic olefins are also isomerized (eq 1).



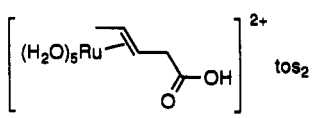
(1)

The isomerization reaction is not restricted to olefins with activated allylic hydrogens. Although isomerization of 3-buten-1-ol is not observed, isomerization of 4-penten-1-ol to a mixture of *cis*- and *trans*-3-penten-1-ol proceeds in high yield (eq 2). Isomerization stops at this stage and does not continue along the hydrocarbon chain to yield valeraldehyde.



(2)

This isomerization of a substrate olefin moiety to a specified distance from a pendant oxygen-containing functional group is also observed for unsaturated carboxylic acids. 2-Pentenoic acid reacts with 1 to yield the olefin complex of 3-pentenoic acid **2**.[12] Catalytic production of free 3-pentenoic acid is not observed. When the reaction is carried out in D_2O, one of the diastereotopic hydrogens on C-2 is selectively deuterated during isomerization, as evidenced by the disappearance of the resonance at 2.15 ppm and the collapse of the doublet of doublets at 3.46 ppm to a doublet in the ^{1}H NMR. The position of the deuterated site with respect to the metal (endo/exo) was not determined. Eventual formation of the bis(olefin)-bis(carboxylate) complex $Ru(H_2O)_2(\eta^1\text{-}(O),\eta^2\text{-}(C,C')\text{-}OCOCH_2CH{=}CHCH_3)_2$ is observed.[12]



2

Labeling Studies. A deuterium labeling study employing allyl-*1,1-d*$_2$ alcohol (**3**) has been undertaken to probe the nature of the hydrogen shift during the

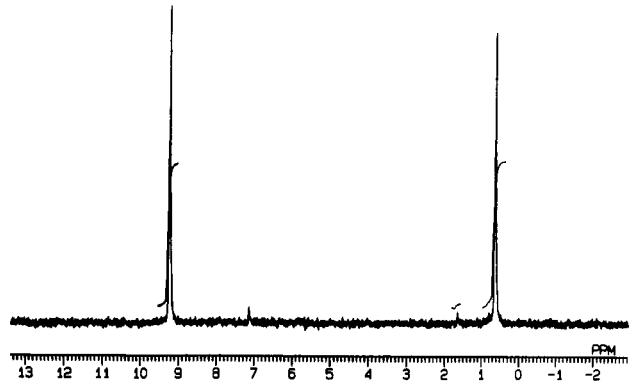
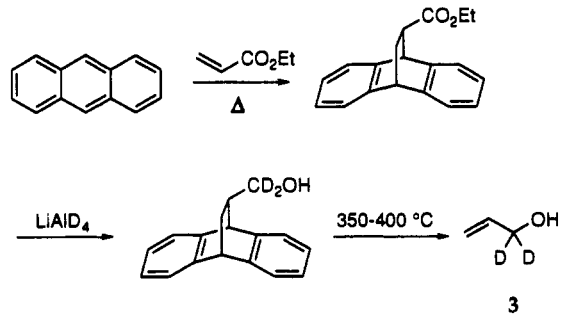


Figure 1. ^{2}H NMR (C_6D_6) spectrum of the reaction product from the aqueous (H_2O) Ru^{II}-catalyzed isomerization of allyl-*1,1-d*$_2$ alcohol.

Scheme 3

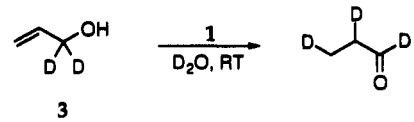


3

isomerization of allylic alcohols. Compound **3** is prepared

3 **4**

in the manner outlined by Hendrix et al.: a Diels–Alder reaction between ethyl acrylate and anthracene, followed by reduction to the alcohol with lithium aluminum deuteride, and then pyrolysis at 350–400 °C (Scheme 3).[69] When reaction of **3** (20 equiv) with **1** is carried out in D_2O at room temperature and followed by ^{1}H NMR spectroscopy, an equilibrium mixture of propionaldehyde-*1,2,3-d*$_3$ and the corresponding hydrate[75] is observed (eq 3a, hydrate is omitted for clarity). Integration[76] of the



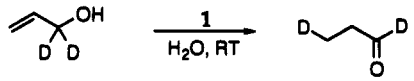
(3a)

3

methyl vs methylene peaks of the aldehyde (0.75 and 1.45 ppm, respectively) yields a ratio of 2.02 and the corresponding peaks for the hydrate (0.88 and 2.38 ppm, respectively) integrate with a ratio of 2.07.

When this aqueous mixture is extracted with C_6H_6 and analyzed by ^{2}H NMR, three peaks of equal intensity are observed at 9.3, 1.6, and 0.7 ppm. When the same reaction is carried out in H_2O and extracted with benzene, the ^{2}H NMR spectrum contains only two resonances, of equal integration, at 9.3 and 0.7 ppm (Figure 1), indicating exclusive production of propionaldehyde-*1,3-d*$_2$ (eq 3b).

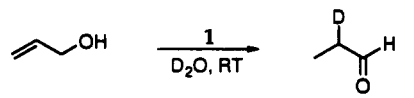
(75) K_{eq} for the aldehyde–acetal equilibrium is approximately 0.75.
(76) All NMR integrations were referenced to the aromatic tosylate protons. ^{1}H NMR spectra were taken with a pulse angle of ≤15° and a pulse delay of ≥10 s to ensure relaxation of all spins between accumulations.



(3b)

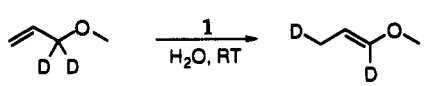
3

The mass spectrum obtained with minimal fragmentation (GC–CIMS) is consistent with two deuterium per molecule of product. Incorporation of deuterium into the C-1 or C-3 positions of the substrate from the solvent is ruled out by the absence of deuterium in the propionaldehyde product from the isomerization of unlabeled allyl alcohol in D_2O. Analysis by ^2H NMR in C_6H_6 indicates exclusive production of propionaldehyde-*2-d* by a single resonance at 1.6 ppm, the single deuterium in the C-2 position resulting from enol tautomerization (eq 3c). The ^1H NMR confirms that there is also a single proton at this position.



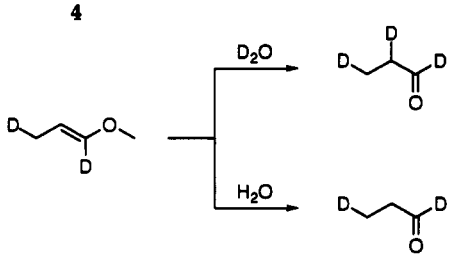
(3c)

The hydrogen shift during allylic ether isomerization has been probed with the deuterium labeled substrate allyl-*1,1-d*$_2$ methyl ether (4). When reaction of 4 (20 equiv) with 1 in D_2O at room temperature is followed by ^1H NMR, exclusive production of labeled 1-propenyl-*1,3-d*$_2$ methyl ether is observed (eq 4a). The resonance arising from the



(4a)

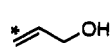
4



(4b)

methyl of the propenyl moiety appears as a doublet of 1:1:1 triplets (J_{HH} = 6.6 Hz, J_{HD} = 2.2 Hz) at 1.32 ppm. Hydrolysis to propionaldehyde-*1,2,3-d*$_3$ and methanol subsequently occurs (eq 4b). The ^2H NMR spectrum of the C_6H_6-extracted reaction carried out in H_2O reveals the absence of deuterium on the C-2 position of propionaldehyde. Two resonances of equal integration appear at 9.3 and 0.7 ppm, indicating exclusive production of propionaldehyde-*1,3-d*$_2$ (eq 4b), identical to the observation made with allyl-*1,1-d*$_2$ alcohol.

The intra/intermolecularity of the allylic alcohol isomerization has been investigated through a crossover labeling study. A $^{13}C/^2H$ crossover, rather than a $^1H/^2H$ crossover, has been designed to identify specific site-to-site crossover and allow analysis by NNR techniques, while avoiding the difficulty in observing aldehyde molecular ion peaks by mass spectrometry. Allyl-*3-*^{13}C alcohol 5 is prepared



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as a solution in water (Scheme 4). After a mixture of 1, 3, and 5 in a 1.0:6.6:2.9 ratio is allowed to react in D_2O solution ([Ru(II)] ~ 25 mM) for 18–24 h at room temperature, extraction of the resulting yellow solution with C_6D_6 gives a colorless solution of isotopically labeled

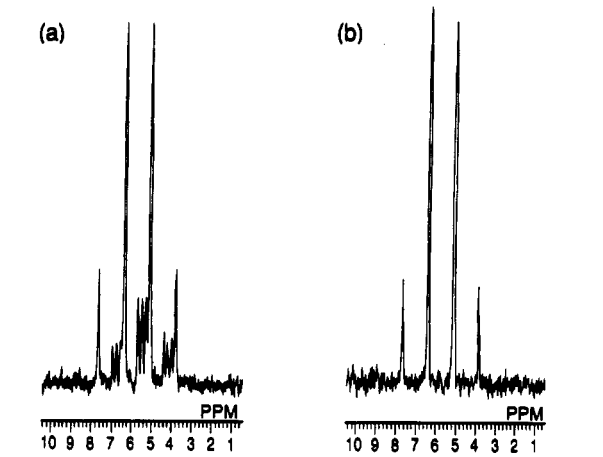
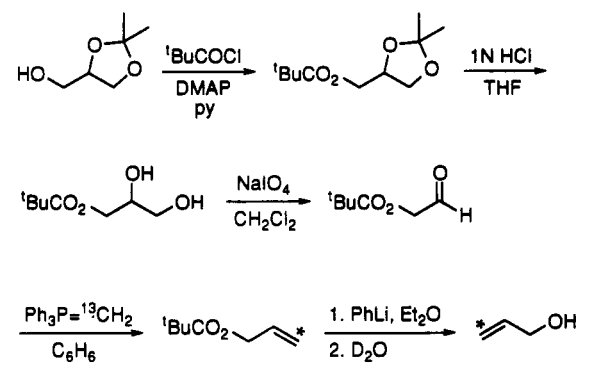


Figure 2. Methyl region of the ^1H nondecoupled ^{13}C NMR (C_6D_6) of the products from the aqueous (D_2O) Ru^{II}-catalyzed isomerization of (a) allyl-*1,1-d*$_2$ alcohol and allyl-*3-*^{13}C alcohol and (b) allyl-*3-*^{13}C alcohol.

Scheme 4



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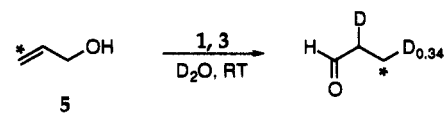
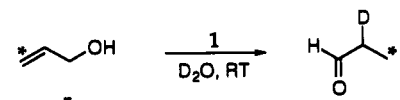
propionaldehydes. In the ^1H-nondecoupled ^{13}C NMR spectrum (Figure 2a) a quartet (J_{CH} = 127 Hz) at 5.79 ppm overlaps a triplet of 1:1:1 triplets (J_{CH} = 130 Hz, J_{CD} = 20 Hz) at 5.51 ppm. On the basis of the resonance intensities, approximately 34% of the ^{13}C label is present as $^{13}CH_2D$, the remainder being $^{13}CH_3$ (eq 5a).[77] No ^{13}-



(5a)

5

CHD_2 groups are observed. When the ^{13}C-labeled substrate alone is isomerized in D_2O under identical conditions the ^1H-nondecoupled ^{13}C NMR spectrum (Figure 2b) contains only the quartet resonance at 5.79 ppm, confirming that 3 is the source of deterium on the methyl position of the product in the crossover experiment (eq 5b).



(5b)

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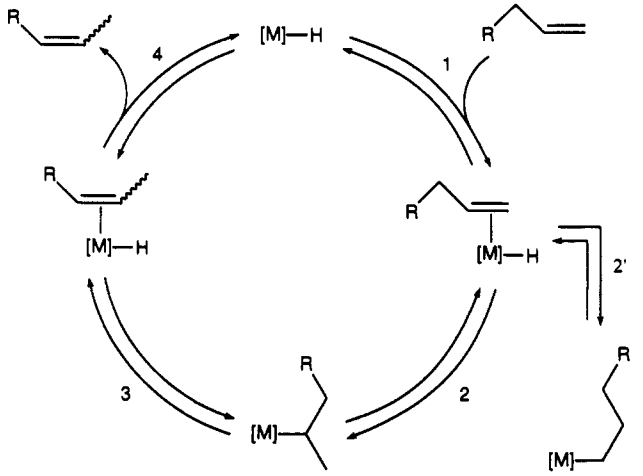
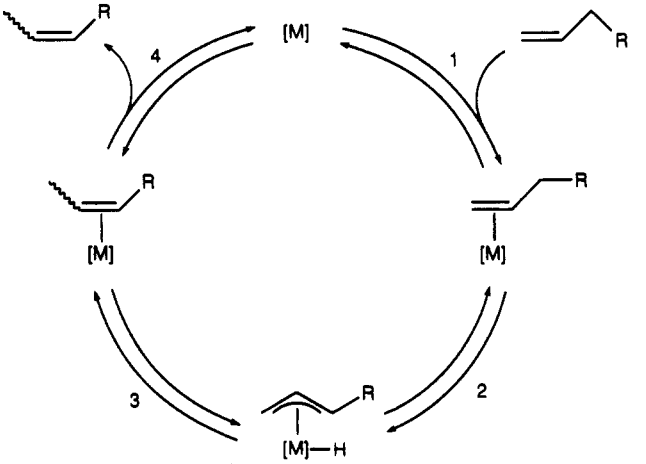
The intra/intermolecularity of the allylic ether isomerization has been investigated through a $^1H/^2H$, rather than a $^{13}C/^2H$, crossover labeling study because of synthetic difficulties. The propionaldehyde product from the isomerization of a mixture of allyl methyl ether (10 equiv)

(77) While we are comparing the resonance intensities of identical methyl carbons, this estimate is indeed tenuous since the isotopic substitution renders the relaxation times of the nuclei different.

Scheme 5



Scheme 6



and 4 (10 equiv) with 1 in H_2O has been analyzed by GC–CIMS to determine the deuterium content of the labeled product. Although fragmentation by loss of the aldehyde hydrogen (or deuterium) atom precludes quantitative measurement of the relative abundancies of molecular ions for the different labeled propionaldehydes in the mass spectrum, the molecular ion pattern indicates a mixture of d_0, d_1, and d_2 propionaldehydes. A large peak at m/e 60 $(M + H)^+$ is the result of a significant amount of propionaldehyde-d_1 among the product mixture. Comparison with the mass spectra of authentic samples of propionaldehyde and propionaldehyde-*1,3*-d_2 confirms that this peak does not solely arise from fragmentation of these species.

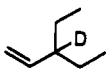
Discussion

Mechanism. The two established pathways for transition-metal-catalyzed olefin isomerization are the π-allyl metal hydride and the metal hydride addition–elimination mechanisms.[67,68] The metal hydride addition–elimination mechanism (Scheme 5) is the more prevalent pathway for transition-metal-catalyzed isomerizations. In this mechanism, free olefin coordinates to a kinetically long-lived metal hydride species. Subsequent insertion into the metal–hydride bond yields a metal alkyl. Formation of a secondary metal alkyl followed by β-elimination yields isomerized olefin and regenerates the initial metal hydride. Nonproductive addition–elimination of the olefin through formation of and subsequent β-elimination from a primary metal alkyl generally occurs to a great extent since formation of the primary alkyl is thermodynamically favored. If all steps are truly reversible, eventual equilibration to a thermodynamic ratio of olefins is observed. Various catalyst systems based on cobalt,[18,78] rhodium,[79,80] iridium,[81] platinum,[48] and nickel[82] have been reported to isomerize olefins through this mechanism. Although some of these catalyst systems consist of stable, isolable metal hydrides (e.g., $HCo(CO)_4$, $RhH(CO)(PPh_3)_3$, $IrH(CO)(PPh_3)_3$, $RuHCl(PPh_3)_3$), many are not (e.g., $RhCl_3$, $RhCl(PPh_3)_3$, $Ni[P(OEt)_3)]_4$). These systems require cocatalysts, such as acids[79,80,82,83] and hydrogen,[44,84] which are responsible for the generation of the initial metal hydride. A number of pathways are known for the generation of the initial metal hydrides with the latter catalysts.[85]

Certain modifications have been placed on the generic metal hydride addition–elimination mechanism of Scheme 5 to fit observed data for individual systems. Deuterium incorporation, or lack thereof, into the substrate from deuterated solvents or cocatalysts can give some idea of the relative rates of the individual steps in the catalytic cycle. The ratio of nonproductive (step 2′) to productive (step 2) insertion is indicative of the relative rates of Markovnikov versus anti-Markovnikov addition of the metal hydride across the olefin bond and is determined by examining the position of deuterium incorporation in the products after isomerization. From the ratio of $CH_2DCH{=}CHCH_3$ versus other deuterated butenes in the isomerization of 1-butene by DCl-activated rhodium catalysts, Cramer estimated the rates of Markovnikov: anti-Markovnikov addition to be approximately 1:15.[79] This ratio seems consistent with the thermodynamics of metal alkyls, although conflicting results have been reported for other systems. For example, both Hendrix and von Rosenberg[78] and Taylor and Orchin[18] reported isomerization product compositions from the $HCo(CO)_4$-catalyzed isomerization of deuterated olefins to be consistent with a 65–70% preference for Markovnikov metal hydride addition.

The π-allyl hydride mechanism (Scheme 6) is the less commonly observed pathway for olefin isomerization. In this mechanism, free olefin coordinates to a transition metal fragment that does not have a hydride ligand. Oxidative addition of an activated allylic C–H bond to the metal yields a π-allyl metal hydride. Transfer of the coordinated hydride to the opposite end of the allyl group yields isomerized olefin. Again, if all steps are truly reversible, eventual equilibration to a thermodynamic ratio of olefins is observed. Casey and Cyr,[86] in a study that presented clear evidence in favor of the π-allyl hydride mechanism for the $Fe_3(CO)_{12}$-catalyzed isomerization of 3-ethyl-1-pentene-*3*-d_1 (6), concluded that the equilibria leading to isomerization (steps 2 and 3) are fast relative to decomplexation of bound olefin (step 4). They based

(78) Hendrix, W. T.; von Rosenberg, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 4850–4852.
(79) Cramer, R. *J. Am. Chem. Soc.* **1966**, *88*, 2272–2282.
(80) Cramer, R.; Lindsey, R. V., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 3534–3544.
(81) Bingham, D.; Webster, D. E.; Wells, P. B. *J. Chem. Soc., Dalton Trans.* **1974**, 1514–1518.
(82) Tolman, C. A. *J. Am. Chem. Soc.* **1972**, *94*, 2994–2999.
(83) Cramer, R. *Acc. Chem. Res.* **1968**, *1*, 186–191.
(84) Adams, R. W.; Batley, G. E.; J. C. Bailar, Jr. *J. Am. Chem. Soc.* **1968**, *90*, 6051–6056.
(85) Kaesz, H. D.; Saillant, R. B. *Chem. Rev.* **1972**, *72*, 231–281.
(86) Casey, C. P.; Cyr, C. R. *J. Am. Chem. Soc.* **1973**, *95*, 2248–2253.



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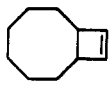

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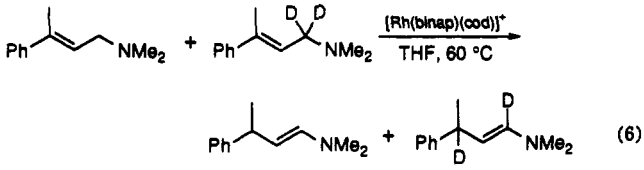
these conclusions on observations regarding deuterium label scrambling in recovered starting material and the relative rates of isomerization versus deuterium label scrambling within the product. The generality of their conclusions is unknown, but a similar effect was seen by Barborak et al. in the isomerization of bicyclo[6.2.0]dec-9-ene (7).[87]

Mechanistic Studies. While both mechanisms yield the same product—a thermodynamic mixture of olefins—two differences make them distinguishable through labeling studies. First, the π-allyl hydride mechanism is a formal 1,3-hydrogen shift in the sense that a hydrogen in the allylic position undergoes a metal-mediated transfer to a terminal position (in an α-olefin). The metal hydride addition–elimination mechanism, however, can involve a 1,2-hydrogen shift through formation of a primary metal alkyl and β-elimination of a different hydrogen. Readdition of the metal hydride to the olefin to yield a secondary metal alkyl followed by appropriate β-elimination completes the 1,2 shift. These shifts become distinguishable through isotopic labeling of the individual hydrogen atoms in the substrate. Second, the π-allyl hydride mechanism is intramolecular: a single substrate molecule is rearranged by the metal and released as product. The metal hydride addition–elimination mechanism, however, is intermolecular: hydrogen atoms from one substrate molecule are transferred to the catalyst and then to another substrate molecule. The intra/intermolecularity of the process is the ultimate distinguishing feature between the two mechanisms.

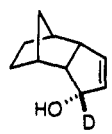
A useful substrate for probing the nature of the hydrogen shift in metal-catalyzed olefin isomerizations is allyl-*1,1-d*$_2$ alcohol (**3**)[43,69] as well as the corresponding methyl ether **4**.[44,88] Isomerization of allyl-*1,1-d*$_2$ alcohol through the π-allyl metal hydride mechanism should yield exclusively propionaldehyde-*1,3-d*$_2$, while a mixture of deuterated propionaldehydes with deuterium incorporation into the C-2 position should be obtained through competitive nonproductive olefin insertion–elimination (Scheme 5, step 2′ with Ru–D) if the metal hydride mechanism is operative. This particular labeling study is common and is often taken by itself as convincing evidence for the π-allyl hydride mechanism.[43,44,69] Baudry et al. cited an observed 1,3 shift in the isomerization of allyl-*1,1-d*$_2$ methyl ether to 1-propenyl-*1,3-d*$_2$ methyl ether as evidence for the π-allyl metal hydride mechanism even though the catalyst, [Ir(η^4-1,5-cyclooctadiene)(PCy$_3$)(C$_5$H$_5$N)]PF$_6$, was activated by hydrogen.[44] Hendrix et al.[69] observed propionaldehyde-*1,3-d*$_2$ as the product of the Fe(CO)$_5$-catalyzed isomerization of allyl-*1,1-d*$_2$ alcohol. They reasoned that exclusive Markovnikov addition of an iron hydride was unlikely, since formation of a primary metal alkyl is thermodynamically favored over formation of a secondary metal alkyl, and thus could not be responsible for the exclusive 1,3-shift. Indeed, while predominant Markovnikov addition has been observed in some metal-hydride-catalyzed olefin isomerization systems,[18,78] anti-Markovnikov addition is always a competing pathway.

Tests for intra/intermolecularity in olefin isomerization systems are less common and are based on mass spectrometry or ^{2}H NMR data. Tani et al. reported obtaining GC–MS data consistent with an intramolecular process in the isomerization of a mixture of nonlabeled and labeled identical allylamines by [Rh(binap)(η^4-1,5-cyclooctadiene)]$^+$ (eq 6).[42] No monodeuterated enamine was detected.



(6)

Strauss and Ford[71] reported a crossover experiment that supported the previous results of Hendrix et al. on the Fe(CO)$_5$-catalyzed isomerization of allylic alcohols.[69,70] Their crossover experiment, however, utilized two vastly different substrates, the tricyclic alcohol 8 and cyclohex-



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2-enol, and they did not indicate whether the reaction was monitored at low conversion in order to rule out preferential reactivity of either substrate. Casey and Cyr,[86] in their study of the Fe$_3$(CO)$_{12}$-catalyzed isomerization of **6**, also utilized different substrates in a crossover experiment, but the difference in this case was small. They observed negligible crossover (<1%) between **6** and an excess of 3-methyl-1-butene after isomerization was carried to 55% and 89% conversion, respectively.

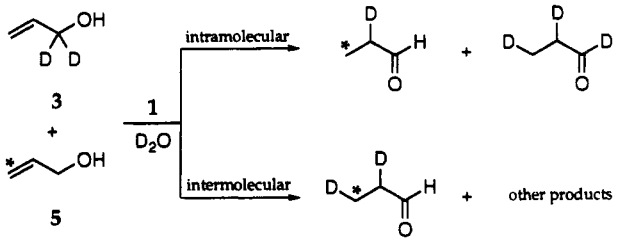
Mechanism of Aqueous Ruthenium(II)-Catalyzed Olefin Isomerization. The results from the ^{2}H and ^{13}C labeling studies presented here are consistent with a metal hydride isomerization mechanism involving exclusive Markovnikov addition of the metal hydride to the olefin substrate for the aqueous ruthenium(II)-catalyzed isomerization of allylic functionalized olefins. The isomerization of allyl-*1,1-d*$_2$ alcohol to exclusively propionaldehyde-*1,2,3-d*$_3$ in D$_2$O (eq 3a) and propionaldehyde-*1,3-d*$_2$ in H$_2$O (eq 3b) indicates that **1** isomerizes allyl alcohol through a selective 1,3-hydrogen shift to the intermediate enol which tautomerizes in the acidic medium.[73] The isomerization of allyl-*1,1-d*$_2$ methyl ether to 1-propenyl-*1,3-d*$_2$ methyl ether (eq 4a), and propionaldehyde-*1,3-d*$_2$ after hydrolysis in H$_2$O (eq 4b), is also indicative of a selective 1,3-hydrogen shift during allyl ether isomerization. Although this lack of deuterium incorporation at the C-2 position of the allyl moiety suggests that isomerization occurs through the π-allyl hydride mechanism, exclusive Markovnikov addition of a metal hydride is also consistent with the lack of scrambling and formation of 1,3 shift product.

The ^{13}C/^{2}H crossover experiment establishes the intermolecularity of the isomerization. An intramolecular pathway would yield only propionaldehyde-*3-*^{13}*C* and propionaldehyde-*1,3-d*$_2$, while an intermolecular pathway would statistically incorporate deuterium onto the ^{13}C labeled site to yield propionaldehyde-*3-*^{13}*C-3-d* (Scheme

(87) Barborak, J. C.; Herndon, J. W.; Wong, J.-W. *J. Am. Chem. Soc.* **1979**, *101*, 7430–7431.

(88) Allyl-2-*d* methyl ether has also been used for the same purpose. See ref 48.

Scheme 7



7) in addition to propionaldehyde-3-^{13}C.[89] The ^1H nondecoupled ^{13}C NMR spectrum of the product propionaldehydes (Figure 2a) identifies the substitution on the labeled carbon as both $^{13}CH_3$, responsible for the quartet at 5.79 ppm, and $^{13}CH_2D$, arising as the triplet of 1:1:1 triplets at 5.51 ppm. The control experiment where the isomerization of **5** is conducted in the absence of **3** (Figure 2b) definitively identifies **3** as the source of deuterium in the crossover experiment, ruling out incorporation of deuterium from the solvent. The mass spectrometry results of the $^1H/^2H$ crossover between labeled and unlabeled allyl methyl ether is also indicative of an intermolecular mechanism for the isomerization of allylic ethers.

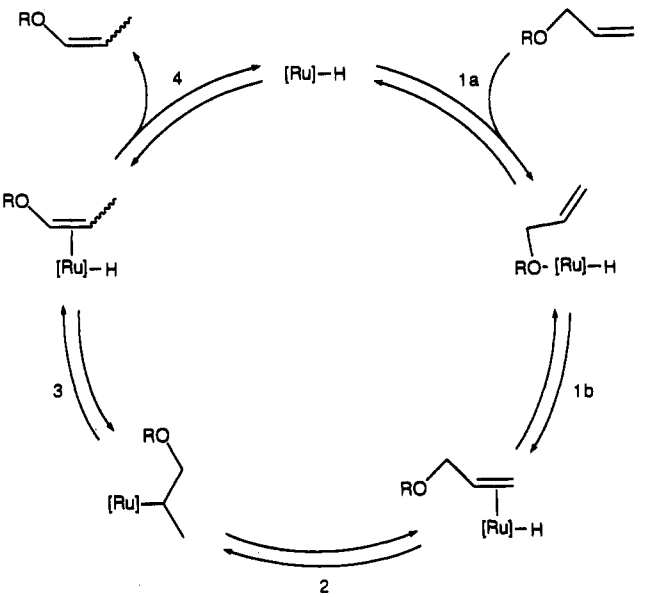
The intermolecularity of the isomerization mechanism is suggestive of the intermediacy of a metal hydride species. This, coupled with the results from the deuterium-labeling experiment, leads us to propose that isomerization occurs through a metal hydride-catalyzed 1,3-hydrogen shift. The metal hydride addition to the olefin substrate occurs in an exclusive Markovnikov fashion to yield a secondary metal alkyl. This metal alkyl subsequently undergoes β-hydride elimination to yield the enol or enol ether product. Contrary to other studies, no formation of a primary metal alkyl species occurs through anti-Markovnikov addition of the metal hydride to the olefin during the isomerization cycle in this system. This is evidenced by the lack of deuterium incorporation into the C-2 position of the product aldehydes and enol ethers. Furthermore, we propose that the exclusive Markovnikov metal hydride addition is the result of the directing effect of the oxygen functionality.

Our modified metal hydride mechanism for the directed isomerization of allylic alcohols and ethers by aqueous ruthenium(II) is shown in Scheme 8. Precoordination of the substrate oxygen directs subsequent coordination of the olefin to the metal center such that insertion occurs in a Markovnikov fashion. It is possible that the trans labilizing effect of the hydride, relative to aquo, ligand favors precoordination of the oxygen to the trans position, thus ensuring the coordination of the olefin in a cis position with the terminal carbon proximal to the hydride. Subsequent β-hydride elimination yields the enol or enol ether which decomplexes and tautomerizes or hydrolyzes to the product aldehyde. This is the first example of a metal hydride olefin isomerization system exhibiting *exclusive* Markovnikov addition to the substrate.

The directing effect of functional groups on the selectivity of transition metal catalysts is well precedented. Crabtree and Davis reported high stereoselectivity in the homogeneous hydrogenation of allylic and homoallylic

(89) The total list of possible products for this crossover experiment includes the previously mentioned propionaldehyde-3-^{13}C and propionaldehyde-1,3-d_2 as well as propionaldehyde-1-d. More products are possible if steps 1 and/or 2 in Scheme 8 are reversible.

Scheme 8

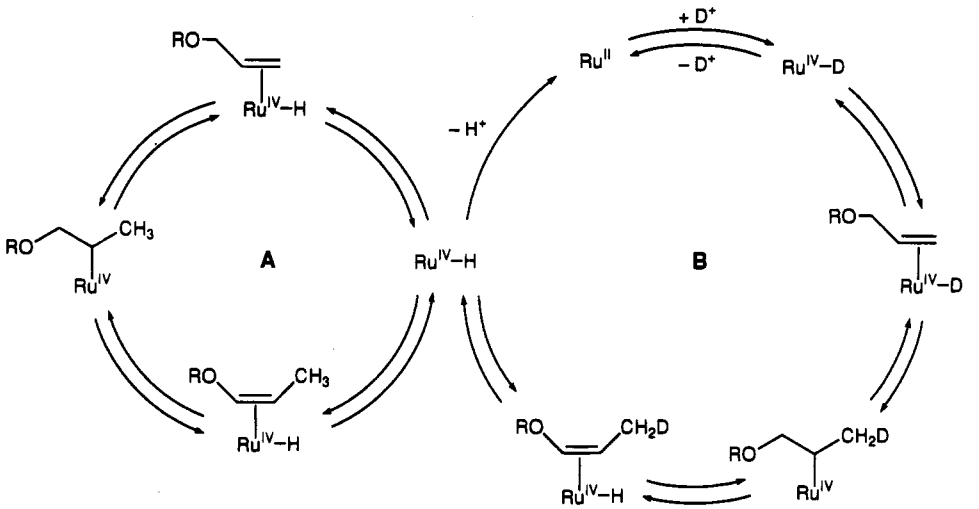


cyclohexenols with [Ir(η^4-1,5-cyclooctadiene)(PCy_3)-(C_5H_5N)]PF_6 (Cy = C_6H_{11}).[90,91] Brown and co-workers observed moderate to high stereoselectivity in the homogeneous hydrogenation of both acyclic allylic and homoallylic alcohols[92] as well as allylic and homoallylic methylenecyclohexanols[93] with [Rh(η^4-norbornadiene)($Ph_2P(CH_2)_4PPh_2$)]BF_4. Evans and Morrissey extended this work to acyclic chiral allylic alcohols.[94,95] Other oxygen-containing functional groups such as alkoxides,[96] carboxylates,[91,97] ethers,[91] and ketones[91] have also been shown to exhibit directing effects in transition-metal-catalyzed homogeneous hydrogenation. Hydroxyls and other basic functional groups are responsible for stereoselective transition-metal-catalyzed methylenation,[98,99] epoxidation,[100,101] and hydroboration.[102]

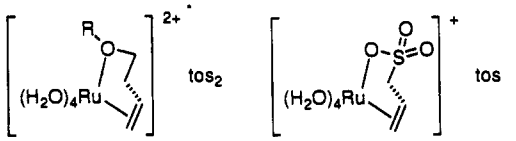
Directing effects have also been observed in an olefin isomerization system. McKinney has proposed that the directing effect of a pendant cyano group is responsible for the selective isomerization of 3-pentenenitrile to 4-pentenenitrile by $HNi[P(OR)_3]_4^+$.[26] High kinetic ratios of 4-pentenenitrile to 2-penetenenitrile are produced in this system even through the thermodynamic distribution of pentenenitrile isomers is 78.3:20.1:1.6 (2PN:3PN:4PN). The author attributes this kinetic control to nitrile-directed olefin orientation during the insertion step. Nondirected insertion would result in a thermodynamic mixture of olefins. In the aqueous ruthenium(II) system certain oxygen functionalities coordinate to the Ru^{II} center, as

(90) Crabtree, R. H.; Davis, M. W. *Organometallics* **1983**, *2*, 681–682.
(91) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655–2661.
(92) Brown, J. M.; Naik, R. G. *J. Chem. Soc., Chem. Commun.* **1982**, 348–350.
(93) Brown, J. M.; Hall, S. A. *Tetrahedron Lett.* **1984**, *25*, 1393–1396.
(94) Evans, D. A.; Morrissey, M. M. *J. Am. Chem. Soc.* **1984**, *106*, 3666–3668.
(95) Evans, D. A.; Morrissey, M. M. *Tetrahedron Lett.* **1984**, *25*, 4637–4640.
(96) Thompson, H. W.; MacPherson, E. *J. Am. Chem. Soc.* **1974**, *96*, 6232–6233.
(97) Brown, J. M.; Hall, S. A. *J. Organomet. Chem.* **1985**, *285*, 333–341.
(98) Winstein, S.; Sonnenberg, J.; DeVries, L. J. *Am. Chem. Soc.* **1959**, *81*, 6523–6524.
(99) Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468–472.
(100) Henbest, H. B.; Wilson, R. A. *J. Chem. Soc.* **1957**, 1958–1965.
(101) Sharpless, K. B.; Michaelson, *J. Am. Chem. Soc.* **1973**, *95*, 6136–6137.
(102) Evans, D. A.; Fu, G. C. *J. Am. Chem. Soc.* **1988**, *110*, 6917–6918.

Scheme 9



demonstrated by the preparation and isolation of $Ru^{II}(H_2O)_4(\eta^1(O):\eta^2(C,C')$-$HOCH_2CH_2CH{=}CH_2)(tos)_2$ (**9**) and the ^1H and ^{13}C NMR characterization of $Ru^{II}(H_2O)_4(\eta^1(O):\eta^2(C,C')$-$CH_3OCH_2CH_2CH{=}CH_2)(tos)_2$ (**10**) and $Ru^{II}(H_2O)_4(\eta^1(O):\eta^2(C,C')$-$OSO_2CH_2CH{=}CH_2)(tos)$ (**11**).[12,103]



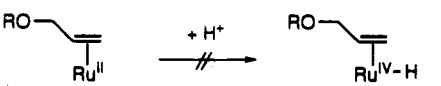
9 R = H **11**

10 R = Me

Deuterium Incorporation. Further restrictions are placed on the mechanism in Scheme 8 by several additional observations. The total lack of deuterium incorporation into the substrate or products from D_2O, aside from the deuterium on the C-2 carbon from enol tautomerization/enol ether hydrolysis, indicates that the proposed active metal hydride does not exchange with the solvent on the time scale of the isomerizations. However, we do observe deuterium incorporation in the stoichiometric isomerization of 2-pentenoic acid to 3-pentenoic acid (vide supra) which leads us to conclude that the hydride originates from the solvent but is formed in a rate limiting step. Tolman has previously observed a similar lack of deuterium incorporation from deuterated media in a nickel hydride olefin isomerization system.[82] The isomerization of 1-butene to a mixture of 2-butenes by $Ni[P(OEt)_3]_4$ in CH_3OD initiated by D_2SO_4 occurs with a ratio of isomerization to deuterium incorporation of 170:1. Tolman attributed this to a much higher rate of isomerization versus hydride exchange between the $HNi[P(OEt)_3]_4^+$ catalyst and the solvent.

A catalytic cycle illustrating initial hydride formation from deuterated solvent is shown in Scheme 9. Free ruthenium(II) (cycle B, upper left) is oxidized to ruthenium(IV) deuteride. The substrate coordinates and undergoes a directed insertion in an exclusive Markovnikov fashion to yield a secondary metal alkyl. This metal alkyl undergoes β-hydride elimination, producing the enol or enol ether product and ruthenium(IV) hydride. Cycle B, therefore, could be responsible for any observed deuterium incorporation. The ruthenium(IV) hydride can then either reduce back to ruthenium(II) or continue to isomerize substrate as shown in cycle A, which would result in isomerization without deuterium incorporation. Since we do not observe deuterium incorporation to the limits of our detection methods, cycle A must predominate in the isomerization mechanism under the conditions studied. The rate of olefin coordination to ruthenium(IV) hydride must be much greater than reduction back to ruthenium(II).

In addition, the stability of isolated ruthenium(II) allyl ethyl ether complex (vide supra) suggests that deuterium cannot enter the cycle by exchange with the ruthenium(IV) hydride olefin complex (eq 7). If the reaction shown



(7)

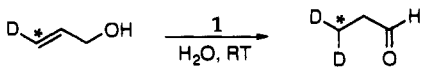
in eq 7 were occurring, the isolated ruthenium(II) allyl ethyl ether complex would decompose to yield isomerize olefin. The stability of the isolated ruthenium(II) complex of allyl ethyl ether under the isomerization conditions also dictates that metal hydride formation precedes olefin coordination. In other words, the substrate ruthenium(II) olefin complex is not protonated to yield an olefin hydride complex. Note also that the stability of Ru^{II}(allyl ethyl ether)$(D_2O)_5(tos)_2$[12] under the reaction conditions precludes an allyl hydride pathway for the isomerization of allylic ethers.

The other possible origin of the initial metal hydride is the substrate itself. For instance, the olefin could coordinate to the metal center and an allylic hydrogen could be abstracted as in the first steps of the π-allyl hydride mechanism (Scheme 6). This allyl hydride could then act as the active metal hydride catalyst. However, isotopic scrambling of an olefin lacking allylic hydrogens has been observed in an independent study in this laboratory.[104] When a mixture of styrene (5 equiv) and styrene-α,β,β-d_3 (5 equiv) is reacted with 1 (1 equiv) in methanol-d_4 at 55 °C, incorporation of deuterium into the unlabeled styrene vinyl moiety is observed. In the absence of labeled styrene deuterium incorporation is not observed, identifying styrene-α,β,β-d_3 as the source of deuterium in the crossover. This crossover undoubtedly occurs through a series of olefin insertion–elimination sequences involving a kinetically stable ruthenium hydride.

(103) McGrath, D. V.; Grubbs, R. H. Submitted for publication.

(104) France, M. B.; Paciello, R. A.; Grubbs, R. H. Unpublished results.

A further restriction placed on the proposed isomerization mechanism in Scheme 8 is the irreversibility of steps 1 and/or 2. This is required by the absence of di- and trideuterio-^{13}C-labeled methyl groups in the alcohol crossover experiment. If both substrate coordination and olefin insertion were reversible, then more than one deuterium could be placed on the ^{13}C-labeled carbon through production of allyl-*3*-^{13}*C*-*3*-d_1 alcohol. This substrate could then be isomerized by Ru–D to yield propionaldehyde-*3*-^{13}*C*-*3,3*-d_2 (eq 8). The doublet of 1:2:2:1



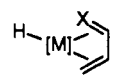
(8)

not observed

quartets resonance which would arise from this $^{13}CHD_2$ group is absent from the ^{1}H nondecoupled ^{13}C NMR of the product propionaldehydes (Figure 1a).

Other Possible Mechanisms. The mechanism proposed above for the allylic allylic alcohol and ether isomerizations accounts for the available data from the labeling studies as well as additional observations concerning deuterium incorporation and observed complex stabilities. The one piece of evidence not taken into account is the formation of small amounts of oxidation products during the allylic alcohol isomerizations. The central question is whether these products are formed as intermediates in the initiation, isomerization, or are the products of a parallel oxidation pathway.

An isomerization mechanism involving the intermediacy of α,β-unsaturated carbonyl species has recently been proposed by Trost and Kulawiec[36,37] for the selective isomerization of allylic alcohols by $(\eta^5\text{-Cp})(PPh_3)_2RuCl$. This "internal redox" mechanism involves the coordination of the allylic alcohol as a bidentate ligand. β-Hydride elimination from the coordinated alkoxide[105] leads to an enone hydride complex **12** (X = O) which rearranges to an



12

oxaallyl species, presumably through exclusive Markovnikov addition of the metal hydride to the coordinated olefin moiety. Protonation liberates the product. This system demonstrates selectivity for allylic alcohols, leaving other alcohol and isolated olefin functionalities untouched.[106] Evidence for this pathway includes an observed intramolecular 1,3-hydride shift as well as the detection of small amounts of enone in the reaction mixture. A similar mechanism has been proposed by Inoue et al.[72] for the asymmetric isomerization of allylamines by $[Rh(binap)S_2]^+$.[63-65] This "nitrogen triggered" mechanism, which involves the intermediacy of the α,β-unsaturated iminium complex **12** (X = NR_2^+), is based on ^{1}H and ^{31}P NMR studies, kinetic measurements, and deuterium labeling experiments. This system exhibits selectivity for allylic amines over isolated olefins. Convincing evidence for the necessity of the amine functionality for isomerization activity is the displacement of solvent from $[Rh(binap)S_2]^+$ by triethylamine, to form [Rh(binap)(S)-(triethylamine)]$^+$, but not by 2-methyl-2-butene. More importantly, the rate of isomerization of diethylgeranylamine is inhibited by addition of triethylamine but not affected by the presence of a large excess of 2-methyl-2-butene.

There are differences in reactivity between our system and those of Trost and Inoue which shed doubt on the validity of adapting an internal redox mechanism to the aqueous ruthenium(II) system. The key difference is the inability of the latter systems to isomerize isolated olefins, while the aqueous ruthenium(II) system can isomerize, for instance, 4-penten-1-ol to 3-penten-1-ol and 2-pentenoic acid to 3-pentenoic acid.[107] We also observe isomerization of allyl ethers to 1-propenyl ethers, a transformation which clearly does not involve the participation of an alcohol functionality, although it may be possible that aqueous ruthenium(II) isomerizes allylic ethers and allylic alcohols by separate mechanisms (infra vide). In addition to the alcohol functionality not being necessary for the isomerization of double bonds in the aqueous ruthenium(II) system, the reaction is not inhibited by excess alcohol. Isomerization of allyl alcohol can be carried out in neat methanol and occurs at approximately the same rate as in water. Excess olefin, however, in contrast to the rhodium system, inhibits the isomerization reaction.[108] We are also able to prepare aqueous ruthenium(II) olefin complexes in methanol solution and isolated olefin complexes of aqueous ruthenium(II) do not decompose through loss of olefin when dissolved in methanol.[103] In addition, the rhodium system is intramolecular, as shown by the absence of monodeuterated enamine by GC–MS in the products of the isomerization of a mixture of nonlabeled and (*dideuterio*allyl)amines (eq 6).[42] The aqueous ruthenium(II) system, however, is intermolecular (eq 5a).

Separate mechanisms for the isomerization of allylic alcohols and allylic ethers is a distinct possibility. The most likely alternative mechanism for allylic alcohol isomerization is the aforementioned enone mechanism proposed by Kulawiec and Trost.[36,37] The intermolecularity of the aqueous ruthenium(II) isomerization, however, would require significant disassociation of the enone from the species analogous to **12**, followed by directed Markovnikov addition of Ru–H(D) to the free, as well as the remaining bound, α,β-unsaturated carbonyl compound, satisfying the 1,3-hydride shift criterium.[109] If this mechanism were in operation, however, we would expect the amount of free α,β-unsaturated carbonyl compound produced to be dependent on the steric requirements of the enone. This does not seem to be the case, however, as crotyl alcohol yields 5–10% crotonaldehyde, but 2-methyl-2-propen-1-ol and 3-buten-2-ol yield only negligible amounts of the corresponding oxidation products while

(105) Sheldon, R. A.; Kochi, J. K. *Matal-Catalyzed Oxidations of Organic Compounds*; Academic Press: San Francisco, 1981; p 424.

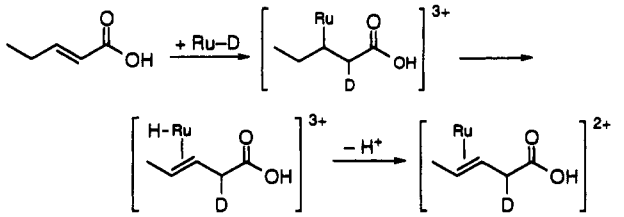
(106) Similar selectivity is also observed in the closely related $RuCl_2(PPh_3)_3/Me_3SiOOSiMe_3$ oxidation system: Kanemoto, S.; Matsubara, S.; Takai, K.; Oshima, K.; Utimoto, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3607–3612.

(107) Trost and Kulawiec do observe isolated olefin isomerization at prolonged reaction times.[37] However, we observe isomerization of 4-penten-1-ol to 3-penten-1-ol on the same time scale as allylic alcohol isomerization.

(108) France, M. B.; Grubbs, R. H. Unpublished results.

(109) This mechanism may also explain the observed nonstatistical crossover According to Scheme 8, with a 6.6:2.9 ratio of **3** to **5**, Ru–X (X = H or D) reacts with **3** and **5** in 69:31 ratio, assuming no substrate preference. When Ru–X reacts with **3**, Ru–D is produced, and when Ru–X reacts with **5**, Ru–H is produced. Therefore Ru–D is the active catalyst 69% of the time and should react with **5** resulting in 69% observed crossover. If allylic alcohols were isomerizing through species **12**, however, dissociation of enone from this enone hydride complex would be responsible for the crossover. An isotope effect on this disassociation would result in a nonstatistical crossover.

Scheme 10



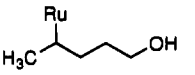
having similar or greater steric requirements than crotonaldehyde. The rather unhindered steric environment around the ruthenium center, however, brings this argument into question, and electronic factors may play a more important role in this respect. Unfortunately, the reactivity of α,β-unsaturated carbonyl compounds with 1 has not been extensively investigated.

Oxidation of allylic alcohols may indeed be a pathway independent of olefin isomerization. However, nonactivated alcohols such as methanol, ethanol, and various other primary aliphatic alcohols are not oxidized by aqueous ruthenium(II). When benzyl alcohol is reacted with 1 (10:1) in water no benzaldehyde is formed within 24 h at room temperature or for an extended time at 65 °C.

Non-Allylic Substrates. The selective deuteration of only one of the C-2 hydrogens during the formation of 2 from 1 and free 2-pentenoic acid in D_2O is also indicative of specific addition of a metal hydride across an olefin bond. In this case it is directed by the carboxylic acid functionality. The irreversibility of the formation of this complex is evidenced by (a) the lack of exchange between these two diastereotopic positions on the NMR time scale and (b) the presence of exactly one deuterium at the C-2 position. We are therefore observing the original metal deuteride formed from Ru^{II} and D^+ (D_2O) in the form of the deuterium at C-2 (see Scheme 9). Since the addition/isomerization/complex formation sequence is irreversible, metal hydride is not liberated and we see essentially 100% deuterium incorporation. This is in contrast to allyl alcohol isomerization and all other isomerizations where metal hydride is liberated (i.e., the reaction is catalytic). A reaction sequence is shown in Scheme 10.

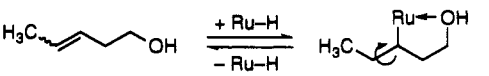
The stability of homoallylic substrates such as 3-buten-1-ol and 3-penten-1-ol with regard to isomerization has been observed previously in a system which is claimed to isomerize olefins through a π-allyl hydride mechanism.[43] This stability was attributed to the formation of a stable chelate structure which prevented allylic hydrogen abstraction by the metal. We have prepared such a chelate complex of aqueous ruthenium(II) with 3-buten-1-ol (9).[12] However, in the aqueous ruthenium(II) system, metal hydride formation precedes olefin coordination and insertion (vide supra). The stability of the olefin complex, therefore, should not be responsible for the olefin's stability toward isomerization. An alternate explanation is that the 3-buten-1-ol quickly binds to all metal sites and prohibits the formation of metal hydride. However, 3-penten-1-ol does not isomerize although, as an internal olefin, it is a relatively weak complexing agent.

We note, however, that the ratio of *cis/trans*-3-penten-1-ol during the isomerization of 4-penten-1-ol is 40:60, as observed by ^1H NMR, while after all 4-penten-1-ol is consumed the ratio changes to 27:73, indicating that 3-penten-1-ol is still reacting with ruthenium hydride but in such a way as to only isomerize the double bond geometry. There are two possible explanations for this. Either (a) the alcohol oxygen is directing the addition of the olefin to the ruthenium hydride to yield a ruthenium alkyl species such as 13 which can only β-eliminate to give



13

4-penten-1-ol or 3-penten-1-ol, or (b) coordination of the alcohol oxygen to the metal center in the ruthenium alkyl species shown in eq 9 prevents β-elimination to yield



(9)

2-penten-1-ol. Both possibilities allow *cis/trans* isomerization of the double bond. The interaction of the terminal olefin 3-buten-1-ol with the catalyst in this fashion would have to be probed through labeling studies. We do acknowledge, however, the additional possibility that 3-buten-1-ol does bind the metal well enough to prevent hydride formation from unbound ruthenium(II) while 3-penten-1-ol does not. Ruthenium hydride can form from unbound ruthenium(II) in the latter case and catalyze *cis/trans* isomerization.

Summary and Conclusions

Olefin isomerization of allylic ethers and alcohols of various substitution patterns is catalyzed by aqueous ruthenium(II) under mild conditions. Nonallylic olefins are also isomerize, although homoallylic alcohols exhibit stability toward isomerization. Labeling studies indicate that isomerization occurs by a modified metal hydride addition–elimination mechanism involving exclusive Markovnikov addition to the double bond directed by the oxygen functionality of the substrate. The mechanistic experiments detailed here illustrate that although a 1,3-hydrogen shift strongly implies a π-allyl hydride mechanism for transition-metal-catalyzed olefin isomerization, ruling out the metal hydride addition-elimination mechanism by establishing the intramolecularity of the process is of increased importance with functionalized substrates because of the directing power of functional groups in transition-metal catalysis. An observed 1,3-hydrogen shift might be the result of directed olefin insertion and is not in itself evidence of the π-allyl metal hydride mechanism.

Experimental Section

General Procedures. All manipulations involving air- and/or moisture-sensitive compounds were carried out using standard high vacuum or Schlenk techniques. Argon was purified by passage through columns of BASF RS-11 (Chemalog) and Linde 4-Å molecular sieves. Solids were transferred and stored in a N_2-filled Vacuum Atmospheres glovebox equipped with a MO-40-1 purification train, a DK-3E Dri-Kool conditioner, and a Dri-Cold Freezer.

Instrumentation. NMR spectra were recorded on a JEOL FX-90Q (89.6 MHz ^1H, 22.5 MHz ^{13}C), a JEOL GX-400 (399.65 MHz ^1H, 61.25 MHz ^2H, 100.40 MHz ^{13}C), a Varin XL-200 (200 MHz ^1H), a Varian EM-390 (90 MHz ^1H), and a Bruker AM-500 (500.14 MHz ^1H, 76.78 MHz ^2H). Proton chemical shifts are referenced to internal residual solvent protons. Carbon chemical shifts are referenced to the carbon signal of the deuterated solvents. Deuterium chemical shifts are referenced to natural abundance deuterium in the solvent. Gas chromatography

analyses were performed on a Shimadzu GC-Mini-2 flame-ionization instrument equipped with a 50-m capillary column and a Hewlett-Packard Model 3390A integrator. Low-resolution mass spectrometry analyses were performed on a Hewlett-Packard Model 5970 mass selective detector in conjunction with a Series 5890 GC equipped with a 15-m SE-30 capillary column or at the Southern California Mass Spectrometry Facility at the University of California, Riverside. Elemental analysis was performed at the analytical facilities of the California Institute of Technology.

Materials. Benzene, diethyl ether, and tetrahydrofuran were distilled from sodium-benzophenone ketyl. Methylene chloride was distilled from calcium hydride. Dried, degassed solvents were stored under argon in dry glass vessels equipped with Teflon valve closures. Water was either housed deionized or purchased from Aldrich (HPLC grade) and degassed prior to use. Chloroform-*d* and benzene-d_6 were purchased from Cambridge Isotope Laboratories and used as received. Deuterium oxide was purchased from Aldrich or Cambridge Isotope Laboratories and degassed prior to use. Allyl alcohol, 3-buten-1-ol, and 4-penten-1-ol were purchased from Aldrich and purified by distillation. *trans*-2-Pentenoic acid, anthracene, ethyl acrylate, sodium hydride, iodomethane, 4-(dimethylamino)pyridine, solketal (2,2-dimethyl-1,3-dioxolane-4-methanol), and trimethylacetyl chloride were purchased from Aldrich and used as received. Lithium aluminum deuteride was purchased from Aldrich and purified by Soxhlet extraction into anhydrous diethyl ether and stored as a solid in the dark before use. Sodium periodate was purchased from EM Science and used as received. Bromobenzene was purchased from Aldrich and distilled under argon before use. Thin-layer chromatography (TLC) was performed on precoated TLC plates (silica gel 60 F-254, EM Reagents). Flash chromatography was performed by the method of Still et al.[110] using silica gel 60 (230–400 mesh ATM, EM Reagents). Reagent grade petroleum ether (35–60 °C), pentane, and ethyl acetate were used without further purification. Paul Bernhard is gratefully acknowledged for initial samples of $Ru^{II}(H_2O)_6(tos)_2$[2] and for a modified procedure for its preparation prior to publication.[1] All samples of $Ru^{II}(H_2O)_6(tos)_2$ prepared in this laboratory were according to the literature procedure.[1] The preparation of allyl-*1,1-*d_2 alcohol (**3**) was outlined by Hendrix et al.[69] and is reported in full below.

General Isomerization Procedure. Olefin (0.1–0.2 mmol) is added to a solution of $Ru^{II}(H_2O)_6(tos)_2$ (5.5 mg, 0.01 mmol) in degassed water (0.5 mL). The solution is stirred at room temperature or 45 °C for a period of 12–48 h, during which time it turns from pale pink to yellow. The reaction is monitored by ^{1}H NMR or TLC. After completion, the product aldehyde is isolated by ether extraction (3 × 100 μL) and distilled.

$Ru^{II}(H_2O)_5(\eta^2(C,C)$-$CH_3CH{=}CHCH_2CO_2H)(tos)_2$ (2). *trans*-2-Pentenoic acid (11 μL, 10.9 mg, 0.11 mmol) was added to a solution of $Ru^{II}(H_2O)_6(tos)_2$ (5.5 mg, 0.01 mmol) in degassed water (0.5 mL). The solution was allowed to stand at room temperature overnight, during which time it turned from a pale pink to a deep yellow color. After removal of solvent in vacuo, the solid residue was washed with ethyl acetate (3 × 0.5 mL) and ether (3 × 0.5 mL) and dried at reduced pressure. ^{1}H NMR (D_2O): δ 7.51 (d, 4, J = 8.3 Hz, H_{aryl} tos), 7.18 (d, 4, J = 8.3, H_{aryl} tos), 4.96 (m, 0.8, =CH–), 4.89 (m, 0.8, =CH–), 3.46 (dd, 0.8, J = 17.2, 5.1, –CH_2CO_2H), 2.21 (s, 6, Me tos), 2.15 (dd, 0.8, J = 17.2, 9.3, –CH_2CO_2H), 1.32 (d, 2.6, J = 5.7, CH_3–). When prepared in D_2O, ^{1}H NMR (D_2O): δ 7.51 (d, 4, J = 8.3, H_{aryl} tos), 7.18 (d, 4, J = 8.3, H_{aryl} tos), 4.96 (m, 0.8, =CH–), 4.89 (m, 0.8, =CH–), 3.46 (d, 0.8, J = 5.1, –CH_2CO_2H), 2.21 (s, 6, Me tos), 1.32 (d, 2.6, J = 5.7, CH_3–).

9,10-Dihydro-9,10-ethano-11-carboethoxyanthracene. Anthracene (15.3 g, 86 mmol) was dissolved in ethyl acrylate (200 mL), and the solution was heated to reflux for 48 h. The solution was cooled to room temperature, excess ethyl acrylate was removed in vacuo, and the residue was washed with pentane and dried at reduced pressure to yield 21.7 g (78 mmol, 91%) of the product as a white solid. ^{1}H NMR ($CDCl_3$): δ 7.25 (m, 4H), 7.07 (m, 4H), 4.65 (d, 1H), 4.31 (t, 1H), 4.03 (m, 2H), 2.84 (m, 1H), 2.17 (m, 1H), 1.96 (m, 1H), 1.18 (t, 3H).

9,10-Dihydroxy-9,10-ethano-11-(hydroxymethyl-d_2)-anthracene. 9,10-Dihydro-9,10-ethano-11-carboethoxyanthracene (21.7 g, 78 mmol) was added slowly to a slurry of lithium aluminum deuteride (LAD) (2.7 g, 64 mmol) in THF (400 mL) at room temperature. The slurry was heated to reflux for 24 h, during which time all solids dissolved. The reaction was then cooled to room temperature and then worked up by the standard procedure[111] followed by a pentane wash to yield 16.2 g (68 mmol, 87% yield) of the product as a white solid. Residual proton content at the methanol carbon was less than 2% as measured by ^{1}H NMR. ^{1}H NMR ($CDCl_3$): δ 7.26 (m, 4H), 7.10 (m, 4H), 4.40 (d, 1H, J = 2.2), 4.25 (t, 1H, J = 2.7), 2.14 (br, 1H), 1.92 (ddd, 1H, J = 2.9, 10.3, 12.2), 1.33 (br s, 1H), 1.06 (ddd, 1H, J = 2.7, 4.9, 12.2).

Allyl-*1,1-*d_2 Alcohol (3). 9,10-Dihydro-9,10-ethano-11-(hydroxymethyl-d_2)anthracene was heated to 350–400 °C under argon with the use of a sand bath. After 30 min a slight vacuum was applied and the product was collected in a receiver flask cooled to 77 K. The residual proton content at C-1 was less than 2% as measured by ^{1}H NMR. The product was freeze–pump–thaw degassed at 77 K and stored at room temperature in a glass vessel equipped with a Teflon valve closure. ^{1}H NMR ($CDCl_3$): δ 5.96 (dd, 1H, J = 10.3, 16.6), 5.26 (d, 1H, J = 16.6), 5.13 (d, 1H, J = 10.3). ^{2}H NMR ($CHCl_3$): δ 4.33 (s).

Reaction of Allyl-*1,1-*d_2 Alcohol (3) with $Ru^{II}(H_2O)_6(tos)_2$ (1). To a clean dry NMR tube equipped with a Teflon valve closure was added allyl-*1,1-*d_2 alcohol (12 mg, 0.20 mmol) and water (H_2O or D_2O) (400 μL), and the sample was degassed by three freeze–pump–thaw cycles at 77 K. $Ru^{II}(H_2O)_6(tos)_2$ (5.5 mg, 0.010 mmol) was added under a flow of argon and the reaction was monitored by ^{1}H NMR in the case of D_2O samples. Integration of the ^{1}H NMR (D_2O) was measured under conditions of low pulse angle (≤15°) and long pulse delay (≥10 s) to ensure relaxation of all spins between accumulations. After the reaction was complete, the solution was extracted with C_6H_6 (3 × 200 μL). The resulting C_6H_6 solution was vacuum transferred at 77 K to a clean dry NMR tube and sealded under dynamic vacuum with a torch. The ^{2}H NMR spectrum was recorded at room temperature (see text).

9,10-Dihydro-9,10-ethano-11-(methoxymethyl-d_2)-anthracene. 9,10-Dihydro-9,10-ethano-11-(hydroxymethyl-d_2)-anthracene (10.0 g, 42 mmol) was added slowly to a slurry of sodium hydride (2.0 g, 83 mmol) and iodomethane (11.9 g, 84 mmol) in THF (200 mL) at 0 °C. The mixture was stirred overnight and allowed to warm to room temperature. Standard aqueous workup yielded 7.2 g (29 mmol, 68%) of product as a white solid. ^{1}H NMR ($CDCl_3$): δ 7.25 (m, 4H), 7.08 (m, 4H), 4.36 (d, 1H, J = 2.4), 4.23 (t, 1H, J = 2.7), 3.27 (s, 3H), 2.20 (br, 1H), 1.91 (ddd, 1H, J = 2.9, 10.0, 12.2), 1.00 (ddd, 1H, J = 2.7, 4.9, 12.2).

Allyl-*1,1-*d_2 Methyl Ether (4). 9,10-Dihydro-9,10-ethano-11-(methoxymethyl-d_2)anthracene was heated to 350–400 °C under argon with the use of a sand bath. After 30 min a slight vacuum was applied and the product was collected in a receiver flask cooled to 77 K. The residual proton content at C-1 was less than 2% as measured by ^{1}H NMR. The product was freeze–pump–thaw degassed at 77 K and stored at room temperature in a glass vessel equipped with a Teflon valve closure. ^{1}H NMR ($CDCl_3$): δ 5.88 (dd, 1H, J = 10.5, 17.3), 5.25 (d, 1H, J = 17.3), 5.17 (d, 1H, 10.5), 3.32 (s, 3H).

Reaction of Allyl-*1,1-*d_2 Methyl Ether (4) with $Ru^{II}(H_2O)_6(tos)_2$ (1). To a clean dry NMR tube was added allyl-*1,1-*d_2 methyl ether (17 mg, 0.24 mmol), water (H_2O or D_2O) (400 μL), and $Ru^{II}(H_2O)_6(tos)_2$ (6.7 mg, 0.012 mmol). The sample was degassed

(110) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(111) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, pp 581–585.

by three freeze–pump–thaw cycles at 77 K and sealed under dynamic vacuum with a torch. The reaction was monitored by ^1H NMR in the case of D_2O samples. After the reaction was complete, the solution was extracted with C_6H_6 (3 × 200 μL). The resulting C_6H_6 solution was vacuum transferred at 77 K to a clean dry NMR tube and sealed under dynamic vacuum with a torch. The ^2H NMR spectrum was recorded at room temperature (see text).

1-[(Trimethylacetyl)oxy]-2,3-acetonidoglycerine. 4-(Dimethylamino)pyridine (DMAP) (0.1 g) was dissolved in pyridine (30 mL) in a clean, dry flask. Solketal (2,2-dimethyl-1,3-dioxolane-4-methanol) (13.2 g, 0.10 mol) was added, and the solution was cooled to 0 °C with an ice bath. Pivaloyl chloride (trimethylacetyl chloride) (18.1 g, 0.15 mol) was added by syringe. After the addition, during which white solids began to precipitate, the mixture was stirred at 0 °C and allowed to warm to room temperature over 12 h. After this time the white slurry was poured into ice water (50 mL) and the organic layer separated. The aqueous layer was extracted with methylene chloride (3 × 20 mL) and the organic solutions were combined and dried over Na_2SO_4. Residual solvent and side products (pivalic acid) were distilled away at 3–4 Torr. Further distillation at 50 μm yielded 16.2 g (75 mmol, 75%, bp 65–70 °C) of product as a colorless liquid. ^1H NMR ($CDCl_3$): δ 4.28 (m, 1H), 4.10 (m, 2H), 4.04 (dd, 1H), 3.75 (dd, 1H), 1.42 (s, 3H), 1.34 (s, 3H), 1.19 (s, 9H).

2,3-Dihydroxypropyl Pivalate. 1-[(Trimethylacetyl)oxy]-2,3-acetonidoglycerine (16 g, 75 mmol) was dissolved in THF (600 mL). To this solution was added hydrochloric acid (370 mL, 1 N), and the mixture was stirred at room temperature. The reaction was followed by ^1H NMR. After completion (ca. 2.5 h) the mixture was poured into methylene chloride (500 mL) and sodium bicarbonate (37 g) was added carefully to neutralize the aqueous layer. The organic layer was separated, and the remaining aqueous layer was extracted with methylene chloride (3 × 100 mL). The organic solutions were combined and dried over $MgSO_4$. Solvent was removed in vacuo to yield 12.1 g (69 mmol, 93%) product as a white solid which can be recrystallized from methylene chloride/pentane. ^1H NMR ($CDCl_3$): δ 4.16 (m, 2H), 3.19 (m, 1H), 3.67 (m, 1H), 3.57 (m, 1H), 2.50 (d, 1H, J = 5.4), 2.11 (dd, 1H, J = 5.9, 6.6), 1.20 (s, 9H). Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.40; H, 8.82.

2-[(Trimethylacetyl)oxy]acetaldehyde. This procedure was adapted from Shiao et al.[112] 2,3-Dihydroxypropyl pivalate (1.76 g, 10 mmol) was dissolved in methylene chloride (100 mL). To this solution was added a solution of sodium periodate ($NaIO_4$) (22.5 g, 105 mmol) in water (200 mL) and the emulsion was stirred at room temperature. The reaction was followed by TLC. After completion the organic layer was separated and washed with water (50 mL). Removal of solvent in vacuo afforded 1.44 g (10 mmol, 100%) of the product as a colorless liquid which was stored at −50 °C to prevent decomposition. ^1H NMR ($CDCl_3$): δ 9.53 (s, 1H), 4.60 (s, 2H), 1.22 (s, 9H).

Phenyllithium. A solution of butyllithium in hexanes (140 mL, 2.5 M, 0.35 mol) was added dropwise over 75 min to a solution of bromobenzene (55.0 g, 0.35 mol) in hexane (400 mL) at −20 °C. After stirring for an additional 1 h at −20 °C the solution was cooled to −50 °C and stored overnight. The solution was then warmed to room temperature. The solvent was removed in vacuo to leave a white solid which was washed with hexane (3 × 50 mL) and dried in vacuo to yield the product as a fluffy white solid (27.6 g, 94%). A titration assay (*sec*-butanol, 1,10-phenanthroline indicator) indicated the solid to be 100% lithium reagent.

Allyl-*3*-^{13}C Alcohol (5). 2-[(Trimethylacetyl)oxy]acetaldehyde (560 mg, 3.9 mmol) was added slowly to a stirred solution of methylene-^{13}C-triphenylphosphorane (1.43 g, 5.2 mmol) in C_6H_6 (80 mL) at 5 °C, and then the solution was warmed to room temperature. All the volatile components of this reaction were then vacuum transferred at 77 K to a clean flask, and the solvent was distilled through a 21-cm Vigreaux column. The crude allyl-*3*-^{13}C pivalate was added by syringe to a diethyl ether (15 mL) solution of phenyllithium (0.82 g, 9.8 mmol), and the reaction was allowed to stir at room temperature for 8 h. Extraction of the reaction mixture with water (3 × 1 mL) yields an aqueous solution of **5** which is vacuum transferred at 77 K to remove the lithium salts and stored degassed in a glass vessel equipped with a Teflon valve closure. Traces of ether can be removed by pentane extraction followed by removal of residual pentane by solvent evaporation in vacuo at 0 °C. The yield based on 2-[(trimethylacetyl)oxy]acetaldehyde was approximately 10% on the basis of ^1H NMR integration versus an internal standard. ^1H NMR (D_2O): δ 5.82 (m, 1H), 5.09 (dd, 1H, J_{HH} = 17.5, J_{CH} = 55.4), 5.00 (dd, 1H, J_{HH} = 10.5, J_{CH} = 59.2), 3.92 (t, 1H, J = 5.1).

Reaction of Allyl-*3*-^{13}C Alcohol (5) and Allyl-*1,1*-d_2 Alcohol (3) with $Ru^{II}(H_2O)_6(tos)_2$ (1). To a clean dry NMR tube equipped with a Teflon valve closure was added 400 μL of a solution of allyl-*3*-^{13}C alcohol in water (H_2O or D_2O). Allyl-*1,1*-d_2 alcohol was added by syringe and the sample was degassed by three freeze–pump–thaw cycles at 77 K. $Ru^{II}(H_2O)_6(tos)_2$ was added under a flow of argon and the reaction was monitored by ^1H NMR in the case of D_2O samples. After the reaction was complete, the solution was extracted with C_6D_6 (3 × 200 μL). The resulting C_6D_6 solution was vacuum transferred at 77 K to a clean dry NMR tube and sealed under dynamic vacuum with a torch. The ^{13}C NMR spectrum was recorded at room temperature (see text).

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