

## Ruthenium-catalyzed Isomerization of Alkenol into Alkanone in Water under Irradiation of Microwaves

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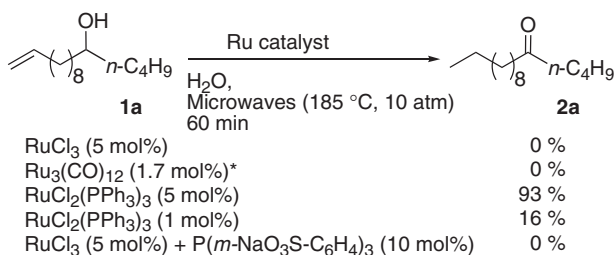
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Ruthenium catalyzed isomerization of alkenol into alkanone through a migration of C–C double bond was performed in water under irradiation of microwaves. When the reaction was performed in deuterium oxide instead of water, the trail of the migration was shown by H–D exchange reaction.

Isomerization of allylic alcohols into carbonyl compounds via C–C double bond migration has been performed efficiently using transition metal catalysts.<sup>1a,b</sup> In the reactions starting from allylic alcohols, the reaction pathway may be considered to be the result of formation of an enol via a 1,3-hydride shift. The corresponding reactions starting from homoallylic alcohols or  $\omega$ -alkenols which have more than three sp<sup>3</sup> carbons between the alkene group carbon and the hydroxyl group substituted carbon have not been performed efficiently, except for a few examples.<sup>2</sup> In the case of ruthenium catalyzed reactions, allylic alcohols are isomerized into carbonyl compounds efficiently, but homoallylic alcohols cannot be converted into carbonyl compounds even at high temperature.<sup>3</sup> We have found that treatment of alkenes with ruthenium catalyst in water under irradiation of microwaves shows an effective alkene migration reaction. Here we wish to report the novel ruthenium catalyzed isomerization of  $\omega$ -alkenols into carbonyl compounds in water.<sup>3c,d</sup>

A mixture of 14-pentadecen-5-ol (**1a**, 1.0 mmol), water (3.0 mL), and Ru catalyst (5 mol %) in a 10-mL sealed vial was heated by irradiation of microwaves (185 °C, 10 atm).<sup>4</sup> After irradiation of microwaves for 60 min, the resulting mixture was extracted with ether. As shown in Scheme 1, tris(triphenylphosphine)ruthenium(II) dichloride (RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>) showed good efficiency as a catalyst for the isomerization of **1a** into alkanone **2a**.

Results using other substrates are summarized in Table 1. The reaction mixture became acidic as ruthenium catalyst was hydrolyzed to form hydrochloric acid. As shown in Runs 2 and 5, the reaction should be performed in 0.1 M NaOH to prevent the decomposition of the acid sensitive substrate. The sub-



\*Warning: In the case of Ru<sub>3</sub>(CO)<sub>12</sub> catalyst, internal pressure increased extraordinary during microwaves irradiation.

**Scheme 1.** Isomerization of 14-pentadecen-5-ol (**1a**) with various ruthenium catalysts.

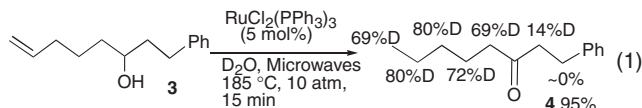
**Table 1.** Isomerization of alkenol into alkanone<sup>a</sup>

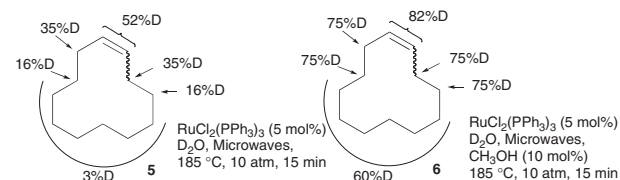
$\text{R}-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{OH} \xrightarrow[\text{H}_2\text{O, Microwaves } 185^\circ\text{C, 10 atm}]{\text{RuCl}_2(\text{PPh}_3)_3 \text{ (5 mol\%)}} \text{R}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{R}'$		
Run	Substrates (1)	Yield of 2
1		96%
2		77 <sup>b,c</sup>
3		87
4		<5 <sup>d</sup> 80 <sup>b</sup>
5		82 <sup>b,e</sup>
6		93

<sup>a</sup>Condition: substrate (1.0 mmol) and RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (5 mol %) in H<sub>2</sub>O (3.0 mL) at 185 °C/10 atm for 15–60 min. <sup>b</sup>Reaction was performed in 0.1 M NaOH (3.0 mL). <sup>c</sup>4-Nonanone was also formed in 6% yield. <sup>d</sup>An acid-catalyzed cyclization occurred to give 2,2,6-trimethyltetrahydropyran quantitatively. <sup>e</sup>1,3-Diphenyl-1-propanone was also formed in 14% yield.

strate in Run 4 gave cyclic ether via acid catalyzed ether formation.<sup>5</sup> In this case too, the isomerization reaction should be performed in 0.1 M NaOH to obtain the saturated ketone.

In all reactions in Table 1, a small amount of unsaturated ketones (<1% yield) accompanied the main process as byproducts. As we reported previously, hydrogen-transfer type oxidation by ruthenium catalyst may explain such formation of the ketone.<sup>6</sup> From this point of view, the reactions in Table 1 may not be intramolecular isomerizations of alkene, but may be intermolecular or intramolecular hydrogen-transfer-type oxidations between alkene and alcohol. The reaction in deuterium oxide, however, implies that the intramolecular alkene isomerization into enol is more plausible. As shown in Eq 1, alkenol **3** was treated with ruthenium catalyst in deuterium oxide under irradiation of microwaves. The hydrogen-atoms on the carbons between the alkene group and hydroxy group were exchanged with D-atoms. These D-atoms can be regarded as a track of the migration of the alkene.

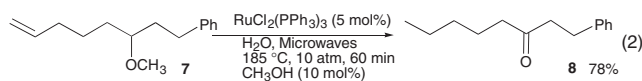




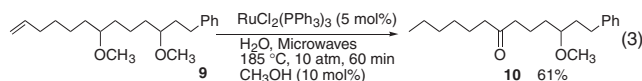
**Figure 1.** H-D-exchange reaction of cyclododecene with  $\text{RuCl}_2(\text{PPh}_3)_3$ - $\text{D}_2\text{O}$ -microwaves (**5**) and  $\text{RuCl}_2(\text{PPh}_3)_3$ - $\text{D}_2\text{O}$ -methanol-microwaves (**6**).

Isomerization of simple alkene was also observed. As shown in Figure 1, a migration of alkene was demonstrated by H-D exchange reaction of cyclododecene.<sup>7,8</sup> Treatment of cyclododecene with  $\text{RuCl}_2(\text{PPh}_3)_3$  in  $\text{D}_2\text{O}$  under irradiation of microwaves for 15 min at  $185^\circ\text{C}/10\text{ atm}$  gave **5**, while that in the presence of catalytic amount of methanol gave the more deuterium enriched **6**. It is clear that an addition of a catalytic amount of methanol improved the efficiency of H-D exchange reaction dramatically. The saturated hydrocarbon cyclododecane was not deuterated under any condition in Figure 1, so the ratio of D-atom in the product **5** and **6** showed the alkene migration frequency. In these H-D exchange reactions, that is alkene migration reaction, an active catalyst should be ruthenium hydride species, which is formed effectively from methanol and  $\text{RuCl}_2(\text{PPh}_3)_3$ .<sup>3a,b,6</sup>

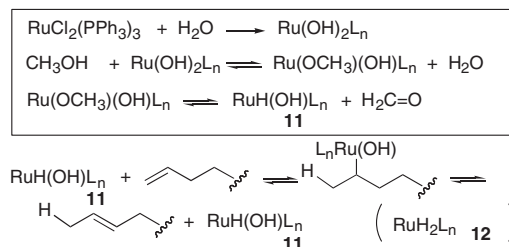
In the reaction in Table 1, ruthenium hydride species will be formed by an oxidative interaction of  $\text{RuCl}_2(\text{PPh}_3)_3$  with an alcohol function in the substrate. The addition of alcohol was necessary in the isomerization reaction of the protected alkenol into the corresponding ketone. This is consonant with the result in Figure 1. As shown in Eq 2, a methyl ether of alkenol was converted into alkanone **8** via enol ether hydrolysis in situ. Without some addition of methanol, the ketone **8** was not obtained at all, although isomerization of terminal alkene into an internal one was observed in some extent.



As shown in Eq 3, one of two methyl ether groups in dimethoxy alkene **9** can be converted into the methoxyketone **10** selectively via the isomerization reaction. Alkene migrated from the end in good order.



In these isomerization reactions, water (or deuterium oxide) was indispensable as a solvent. Treatment of alkenol **1a** with  $\text{RuCl}_2(\text{PPh}_3)_3$  in dioxane under irradiation of microwaves ( $185^\circ\text{C}$ , 10 atm, 60 min) did not give any saturated ketone, although isomerization of a terminal alkene group into an internal one occurred to some extent. As shown in Scheme 2, we assume that the reactive catalyst is monohydride **11**. Water and alcohol are necessary to form **11**. Without water, dihydride **12** may be formed, and this will not be an efficient isomerization catalyst.<sup>9</sup> The isomerization will proceed via hydrometallation and  $\beta$ -elimination.<sup>1,3</sup> It was demonstrated by Krische that a lifetime of organometallic intermediate was extended in  $\text{R-Mtl-X}$  species compare to  $\text{R-Mtl-H}$  one.<sup>9a</sup> The former will be formed via hydrometallation of monohydride **11** to alkene, and the latter will be formed via hydrometallation of dihydride **12** to alkene. The H-D exchange reactions in Eq 1 and Figure 1 are under-



**Scheme 2.** Plausible mechanism of the isomerization.

standable, as H-D exchange ruthenium monohydride with deuterium oxide was shown by Whittlesey.<sup>10</sup> Irradiation of microwaves accelerates both formation of **11** and the addition-elimination process in Scheme 2.

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