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# Efficient and Selective Aerobic Oxidation of Alcohols into Aldehydes and Ketones Using Ruthenium/TEMPO as the Catalytic System

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**Abstract:** The combination of  $\text{RuCl}_2(\text{PPh}_3)_3$  and TEMPO affords an efficient catalytic system for the aerobic oxidation of a variety of primary and secondary alcohols, giving the corresponding aldehydes and ketones, in >99% selectivity in all cases. The Ru/TEMPO system displayed a preference for primary vs secondary alcohols. Results from Hammett correlation studies ( $\rho = -0.58$ ) and the primary kinetic isotope effect ( $k_{\text{H}}/k_{\text{D}} = 5.1$ ) for the catalytic aerobic benzyl alcohol oxidations are inconsistent with either an oxoruthenium ( $\text{O}=\text{Ru}$ ) or an oxoammonium based mechanism. We postulate a hydridometal mechanism, involving a “ $\text{RuH}_2(\text{PPh}_3)_3$ ” species as the active catalyst. TEMPO acts as a hydrogen transfer mediator and is either regenerated by oxygen, under catalytic aerobic conditions, or converted to TEMPH under stoichiometric anaerobic conditions.

## Introduction

The oxidation of alcohols into their corresponding aldehydes and ketones is of significant importance in synthetic organic chemistry.<sup>1–3</sup> Many reagents for alcohol oxidations are known,<sup>3</sup> e.g., hypochlorite,<sup>4</sup> chromium(VI) oxide,<sup>5</sup> dichromate,<sup>6</sup> manganese(IV) oxide,<sup>7</sup> permanganate,<sup>8</sup> and ruthenium(VIII) oxide.<sup>9</sup> Unfortunately, one or more equivalents of these—often hazardous or toxic—oxidizing agents are required. From both an economic and environmental point of view, the quest for effective catalytic oxidation processes that use clean, inexpensive primary oxidants, such as molecular oxygen or hydrogen peroxide, i.e., a “green method” for converting alcohols to carbonyl compounds on an industrial scale, remains an important challenge.<sup>10</sup>

Most examples of alcohol oxidations, both homogeneous and heterogeneous, involve the use of group 8 metal complexes as catalysts. Especially ruthenium compounds, which are widely used as catalysts in organic synthesis,<sup>11</sup> have been thoroughly investigated.  $\text{RuCl}_2(\text{PPh}_3)_3$ ,  $\text{RuCl}_3$ , and some high-valent oxoruthenium complexes are known to mediate in alcohol oxida-

tions using a variety of stoichiometric oxidants such as iodosobenzene,<sup>12</sup> methylmorpholine *N*-oxide,<sup>2,13</sup> bromate,<sup>14</sup> hypochlorite,<sup>15</sup> peroxides,<sup>16</sup> or a combination of oxygen and an aldehyde. In the latter case, 1 equiv of carboxylic acid is also formed.<sup>17</sup>

The number of ruthenium-catalyzed alcohol oxidations, employing oxygen (or air) as the sole oxidant, is limited.<sup>18</sup> For example,  $\text{RuCl}_2(\text{PPh}_3)_3$ ,<sup>19</sup> hydrated  $\text{RuO}_2$ ,<sup>20</sup> and Ru-hydrotalcite<sup>21</sup> have been shown to catalyze the oxidation of alcohols using oxygen as the primary oxidant, but in these cases the scope was generally limited to activated alcohols, i.e., allylic and benzylic alcohols. On the other hand, tetrapropylammoniumper-ruthenate (TPAP), either as such<sup>22</sup> or supported on an ion-exchange resin<sup>23</sup> or MCM-41,<sup>24</sup> catalyzes the aerobic oxidation of nonactivated aliphatic alcohols (reaction 1). Other examples

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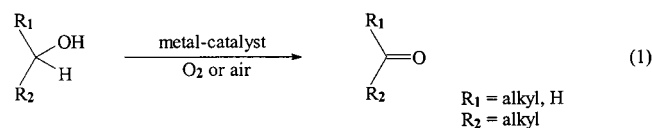
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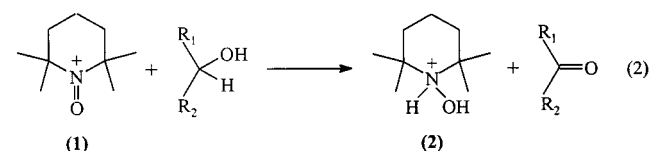
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of catalytically active ruthenium systems are trinuclear ruthenium complexes,<sup>25</sup> ruthenium complexes in combination with hydroquinone as cocatalyst,<sup>26</sup> Ru/CeO<sub>2</sub>,<sup>27</sup> and the improved Ru/Co-hydrotalcite.<sup>28</sup> Besides ruthenium, a few other metals, e.g., palladium,<sup>29</sup> cobalt,<sup>30</sup> and copper,<sup>10,31</sup> have also been shown to catalyze reaction 1. However, most reported systems require relatively large quantities of catalyst (5–10 mol %) and/or additives, i.e., cocatalyst (10–20 mol %) and drying agents (2 equiv), to achieve their activity.

In addition to metal complexes, stable nitroxyl radicals, such as 2,2',6,6'-tetramethylpiperidine *N*-oxyl (TEMPO), have been used as catalysts for the mild and selective oxidation of alcohols to aldehydes, ketones, and carboxylic acids.<sup>32</sup> Typically, these transformations employ 1 mol % of the nitroxyl radical and a stoichiometric amount of a terminal oxidant, e.g., sodium hypochlorite,<sup>33,34</sup> trichloroisocyanuric acid,<sup>35</sup> *m*-chloroperbenzoic acid,<sup>36</sup> sodium bromite,<sup>37</sup> sodium chlorite,<sup>38</sup> and oxone.<sup>39</sup> In these systems, an oxoammonium cation is generated and acts as the active oxidant (reaction 2). The hydroxylamine (2), which



is formed, is reoxidized by the terminal oxidant to regenerate 1.<sup>40</sup> Alternatively, the use of TEMPO in combination with copper salts and oxygen as the primary oxidant was reported by Semmelhack.<sup>41</sup> However, this system was effective only with

**Table 1.** Aerobic Ruthenium/TEMPO-Catalyzed Oxidation of Octan-2-ol<sup>a</sup>

entry	S/C ratio	time (h)	convn (%) <sup>b</sup>	sel. (%) <sup>b</sup>	TON <sup>c</sup>
1	no Ru	24	0		
2 <sup>d</sup>	100	24	18	>99	18
3	100	7	98 (90)	>99	98
4 <sup>e</sup>	100	7	89	>99	89
5 <sup>f</sup>	1225	1	8.5	>99	104
		5	17	>99	208
		22	38	>99	466

<sup>a</sup> Reaction conditions: 15 mmol of substrate, Ru:TEMPO = 1:3, 30 mL of chlorobenzene, 10 mL/min O<sub>2</sub>/N<sub>2</sub> (8/92; v/v), *p* (total pressure) = 10 bar, *T* = 100 °C (see Experimental Section). <sup>b</sup> Conversions and selectivities based on GC results using *n*-hexadecane as internal standard; numbers in parentheses are isolated yields (see Experimental Section). <sup>c</sup> TON = turnover number in mmol of product per mmol of Ru catalyst. <sup>d</sup> No TEMPO. <sup>e</sup> Toluene as solvent. <sup>f</sup> Neat octan-2-ol as solvent.

easily oxidized benzylic and allylic alcohols, with simple primary and secondary alcohols being largely unreactive.

**Ruthenium/TEMPO as Catalytic System.** On the basis of the catalytic systems described above, we reasoned that the combination of ruthenium and TEMPO would likely lead to an efficient catalytic system for the aerobic oxidation of alcohols. For our initial experiments, we selected octan-2-ol as a test substrate and allowed it to react in chlorobenzene with catalytic quantities of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub><sup>42</sup> in the presence of TEMPO<sup>43</sup> and oxygen.

As shown in Table 1, RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> alone is a poor catalyst for the aerobic oxidation of octan-2-ol to octan-2-one (entry 2). On the other hand, addition of TEMPO, which itself is not active as catalyst (entry 1), to RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> leads to a substantial increase in activity (entry 3). The use of chlorobenzene as a solvent is not essential and was chosen merely to simplify the GC analysis. Toluene can also be employed (entry 4), and even better results were obtained in neat octan-2-ol (entry 5). In this case, a turnover number (TON) of approximately 100 was achieved within 1 h compared to the 7 h needed for the same TON in chlorobenzene (entry 3).

Besides RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>, other ruthenium compounds were also tested. RuCl<sub>3</sub> gave lower rates and 18e complexes of ruthenium, e.g., RuCl<sub>2</sub>(bipy)<sub>2</sub> and RuCl<sub>2</sub>(DMSO)<sub>4</sub>, were completely unreactive. Also, other metal chlorides, e.g., Fe(II and III), Ni(II), Pd(II), Cu(I and II), Mn(II), and Co(II and III), show no activity in combination with TEMPO. Similarly, the combination of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> and other hydrogen/electron-transfer systems, such as ABTS and 2-ethylanthraquinone, is not able to catalyze the aerobic oxidation of octan-2-ol. In conclusion, the best results were obtained when using 1.0 mol % of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> and 3.0 mol % of TEMPO. In this case, the turnover frequency (TOF) was 14 h<sup>-1</sup>, which is superior to the most active aerobic ruthenium system described in the literature, i.e., TPAP,<sup>22</sup> which in our hands gave a TOF of 5.5 h<sup>-1</sup> for octan-2-ol.<sup>44</sup>

The dependence of the initial rate of the catalytic oxidation on the temperature can be employed to determine the activation energy of the reaction (Arrhenius plot). The data for the Ru/

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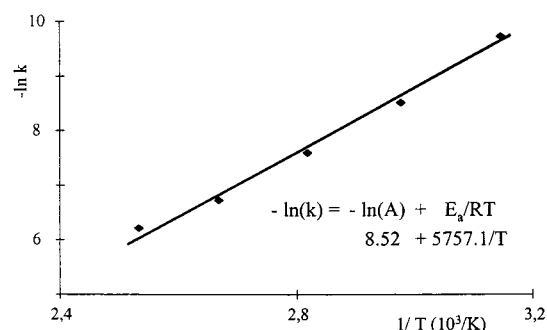
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**Table 2.** Ruthenium/TEMPO-Catalyzed Aerobic Oxidation of Several Alcohols<sup>a</sup>

entry	substrate	product	S/C ratio	time (h)	convn (%) <sup>b</sup>
1	octan-2-ol	octan-2-one	100	7	98 (90)
2 <sup>c</sup>	octan-1-ol	octanal	50	7	85
3	benzyl alcohol	benzaldehyde	200	2.5	>99 (90)
4	<i>p</i> -nitrobenzyl alcohol	<i>p</i> -nitrobenzaldehyde	200	6	97
5	1-phenylethanol	acetophenone	100	4	>99 (93)
6	cyclooctanol	cyclooctanone	100	7	92
7	adamantan-2-ol	adamantan-2-one	100	6	98
8 <sup>c</sup>	geraniol	geranial	67	7	91
9 <sup>c</sup>	3-methyl-2-buten-1-ol	3-methyl-2-butenal	67	7	96
10 <sup>c</sup>	octan-2-ol/octan-1-ol	octan-2-one/octanal	50	7	10/80
11	benzyl alcohol/1-phenylethanol	benzaldehyde/acetophenone	200	3	90/5

<sup>a</sup> Reaction conditions: 15 mmol of substrate, RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>/TEMPO ratio of 1:3, 30 mL of chlorobenzene, 10 mL min<sup>-1</sup> O<sub>2</sub>/N<sub>2</sub> (8/92; v/v), *p* = 10 bar, *T* = 100 °C. <sup>b</sup> Conversions based on GC results (selectivity >99% in all cases) using *n*-hexadecane as internal standard; numbers in parentheses are isolated yields. <sup>c</sup> O<sub>2</sub> atmosphere (see Experimental Section).

**Figure 1.** The correlation of the initial rate and the temperature (40–120 °C) for the Ru/TEMPO-catalyzed aerobic oxidation of octan-2-ol.

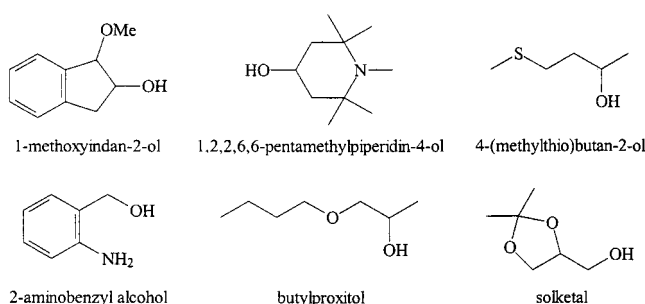
TEMPO-catalyzed aerobic oxidation of octan-2-ol plotted in Figure 1 can be readily fitted to the familiar expression  $k = A \exp(-E_a/RT)$ , to give an activation energy ( $E_a$ ) of 47.8 kJ/mol.

#### Scope of the Ru/TEMPO-Catalyzed Aerobic Oxidation.

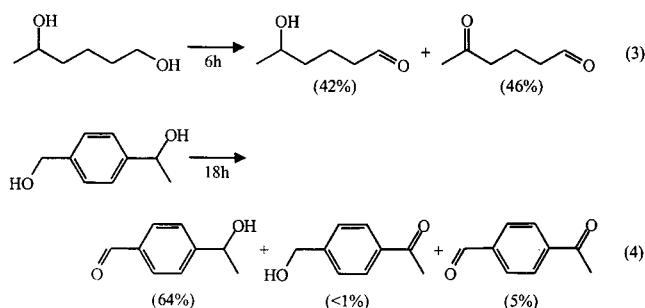
The use of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>/TEMPO as catalyst for the aerobic oxidation of alcohols was applied to a range of representative primary and secondary alcohols. As shown in Table 2, octan-1-ol is oxidized selectively into octanal (entry 2). TEMPO not only accelerates the oxidation of octan-1-ol but also completely suppresses the overoxidation of octanal to octanoic acid. Attempted oxidation of octanal under the same reaction conditions, in the presence of TEMPO, gave no reaction in 1 week. On the other hand, without TEMPO octanal was converted completely to octanoic acid within 1 h. The ability to suppress overoxidation is due to the well-known antioxidant activity of TEMPO. This stable nitroxyl radical efficiently scavenges free radical intermediates during autoxidation and thereby terminates free radical chains.

Allylic alcohols were selectively converted into the corresponding unsaturated aldehydes in high yields without intramolecular hydrogen transfer (entries 8 and 9). Some ruthenium(II) phosphine complexes are known to catalyze the rearrangement of allylic alcohols to saturated ketones via intramolecular hydrogen transfer,<sup>45</sup> which obviously is not occurring in the present system. Besides aliphatic and allylic alcohols, cyclic and benzylic alcohols were also smoothly oxidized into the corresponding ketones and aldehydes (entries 3–7). In these cases lower catalyst loadings ( $S/C \geq 100$ ) were sufficient to obtain the same results.

The Ru/TEMPO system displayed a preference for primary versus secondary alcohols, as was observed in competition experiments (entries 10 and 11). Since ruthenium-catalyzed

**Figure 2.** Unreactive alcohols.

oxidations are generally believed to involve the intermediate formation of an alkoxy-ruthenium complex,<sup>46</sup> we interpret this result as an indication that the ruthenium preferentially complexes with primary alcohols, leading to selective oxidation of the latter. In addition to the (intermolecular) competition experiments, the same behavior was observed in the intramolecular competition of two primary/secondary diols, i.e., 1,5-hexanediol and 4-(1'-hydroxyethyl)benzyl alcohol (see Experimental Section). As shown in reactions 3 and 4, the Ru/TEMPO system again displayed a preference for the primary versus the secondary hydroxyl group of either an aliphatic or a benzylic diol.

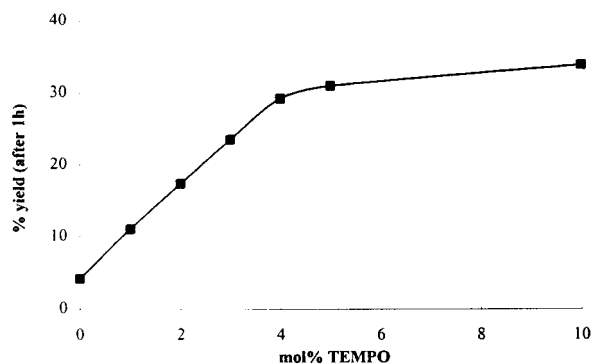


In summary, the combination of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> and TEMPO affords an efficient catalytic system for the aerobic oxidation of a variety of primary and secondary alcohols, e.g., aliphatic, allylic, benzylic, and cyclic ones. Unfortunately, a number of alcohols remain that are unreactive toward this system. Generally, these unreactive alcohols (Figure 2) contain heteroatoms (O, N, S), which probably coordinate to ruthenium and thereby inactivate the catalyst.

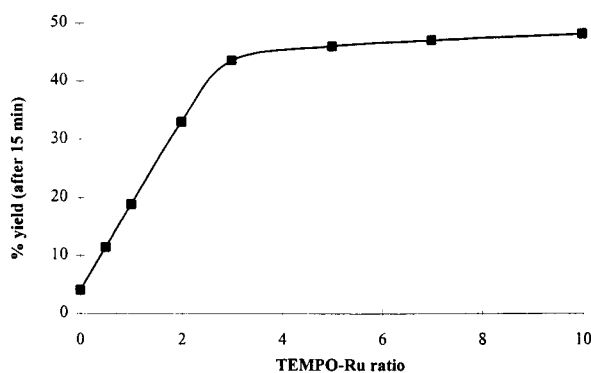
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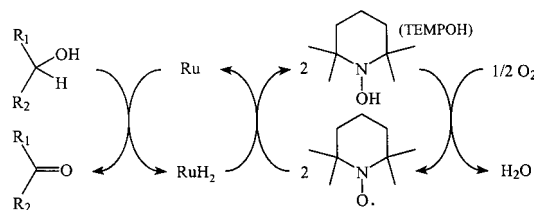




**Figure 3.** Yield after 1 h in  $\text{RuCl}_2(\text{PPh}_3)_3$  (1 mol %)/TEMPO catalyzed aerobic oxidation of octan-2-ol in chlorobenzene at 100 °C at different concentrations of TEMPO.



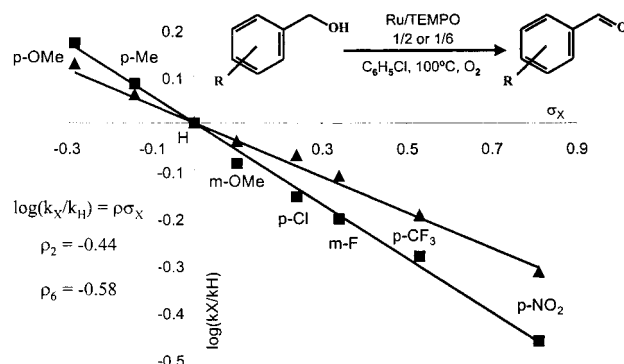
**Figure 4.** Yield after 15 min in the  $\text{RuCl}_2(\text{PPh}_3)_3$  (0.5 mol %)/TEMPO catalyzed aerobic oxidation of benzyl alcohol in chlorobenzene at 100 °C at different TEMPO/Ru ratios.



**Figure 5.** Schematic mechanism of Ru/TEMPO catalyzed aerobic oxidation of alcohols.

**Mechanistic Studies.** The effect of the TEMPO concentration on the rate of the oxidation was investigated. An almost linear increase was observed with respect to the TEMPO concentration in the range of 0–4 mol % in the oxidation of octan-2-ol (Figure 3). Above 4 mol % the increase starts to level out, and further addition of TEMPO led to only a minor increase in the yield obtained after 1 h. In addition, the oxidation of benzyl alcohol to benzaldehyde using only 0.5 mol % of Ru and different concentrations of TEMPO showed the same trend (Figure 4). In this case, no significant increase in rate was observed above a TEMPO/Ru ratio of about 3.

The same “mediator” dependency was observed with a ruthenium/benzoquinone/ $\text{MnO}_2$  system, reported by Bäckvall et al.,<sup>47</sup> in which a ruthenium-centered dehydrogenation takes place with ruthenium hydrides as the intermediates. For the Ru/TEMPO-catalyzed aerobic oxidation of alcohols, we propose a similar mechanism (Figure 5). The result can be explained in terms of a change in the rate-limiting step. At low concentrations of TEMPO, reoxidation of the “ruthenium hydride” species may be the slowest step, whereas at high concentrations of TEMPO dehydrogenation is probably rate limiting.



**Figure 6.** Hammett plots for the aerobic oxidation of substituted benzyl alcohols using different Ru/TEMPO ratios: (▲)  $1/2$ ; (■)  $1/6$ .

Indeed, results obtained in the aerobic oxidation of various substituted benzyl alcohols using different TEMPO/Ru ratios are consistent with this notion. Using either a TEMPO/Ru ratio of 6:1 or 2:1, the logarithm of the initial rate plotted against the  $\sigma$  value of the *para*- or *meta*-substituent resulted in a linear relationship (Figure 6). However, the slopes of the lines were different, i.e., at a low TEMPO/Ru ratio a  $\rho$  value of  $-0.44$  was obtained, whereas at a high ratio a  $\rho$  value of  $-0.58$  was found. The increase of the  $\rho$  value is consistent with dehydrogenation playing a more significant role at higher TEMPO/Ru ratios.

Besides Hammett plots, kinetic isotope effects ( $k_H/k_D$ ) also give information regarding the rate-determining step. As shown in Table 3, for both inter- (entries 2 and 3) and intramolecular (entries 1 and 4) H/D competition in aliphatic and benzylic alcohols (see Experimental Section), the values for the kinetic isotope effect increase with increasing amounts of TEMPO. These results provide further support for the notion that dehydrogenation plays a more important role at higher TEMPO/Ru ratios.

Using TEMPO and ruthenium in a ratio of 5:1 at 100 °C, the intramolecular kinetic isotope effect for the aerobic oxidation of *p*-methyl- $\alpha$ -deuteriobenzyl alcohol is 3.9 (entry 1). This value indicates that dehydrogenation plays a substantial role. To provide more insight into the mechanism and to compare the system with other ruthenium-catalyzed oxidations of alcohols, the catalytic aerobic oxidation of *p*-methyl- $\alpha$ -deuteriobenzyl alcohol was also performed at different temperatures (Table 4).

The hydride ion transfer may take place either by a concerted cyclic process or by an acyclic one. Kwart et al. showed that a dependence of the kinetic isotope effect ( $k_H/k_D$ ) on the temperature could provide a basis for distinguishing between the two processes.<sup>48</sup> The data for the Ru/TEMPO-catalyzed aerobic oxidation of *p*-methyl- $\alpha$ -deuteriobenzyl alcohol listed in Table 4 and plotted in Figure 7 can be readily fitted to the familiar expression  $k_H/k_D = A_H/A_D \exp(-\Delta E_a/RT)$ . They correspond with the properties of a symmetrical transition state in which the activation energy difference ( $\Delta E_a$ ) for  $k_H/k_D$  is equal to the zero-point energy difference for the respective C–H and C–D bonds ( $\approx 4.3$  kJ/mol) and the frequency factors ( $A_H/A_D = 0.92$ ) and thus entropies of activation of the respective reactions are nearly equal.

The primary kinetic isotope effect ( $k_H/k_D$ ) for the Ru/TEMPO-catalyzed aerobic oxidation of *p*-methyl- $\alpha$ -deuteriobenzyl alcohol at 25 °C was 5.1 (Table 4, entry 1). Although this value indicates substantial C–H bond cleavage on progressing to the transition state, it is still far smaller than those reported for the stoichiometric benzyl alcohol oxidations by ruthenium–oxo

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**Table 3.** Ruthenium/TEMPO-Catalyzed Aerobic Oxidation of Several Alcohols<sup>a</sup>

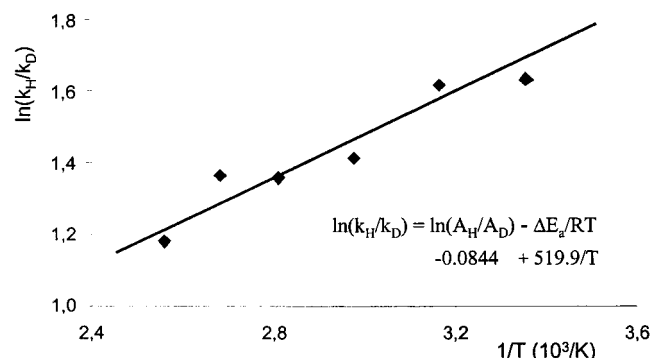
entry	substrate	convn (%)	kinetic isotope effect ( $k_H/k_D$ ) <sup>b</sup>	
			TEMPO/Ru = 2	TEMPO/Ru = 5
1	<i>p</i> -methyl- $\alpha$ -deuteriobenzyl alcohol	100	3.2	3.9
2	1-deuterio-1-phenylethanol/1-phenylethanol (1/1)	35	2.3	3.0
3	2-deuteriooctan-2-ol/octan-2-ol (1/1)	25	2.2	2.4
4	1-deuterioheptan-1-ol	70	2.1	2.8

<sup>a</sup> Reaction conditions: 5 mmol of substrate, 0.05 mmol (1 mol %) of  $\text{RuCl}_2(\text{PPh}_3)_3$ , 0.10–0.25 mmol (2–5 mol %) of TEMPO, 10 mL of chlorobenzene,  $\text{O}_2$  atmosphere,  $T = 100^\circ\text{C}$ . <sup>b</sup> H/D ratio determined by  $^1\text{H}$  NMR.

**Table 4.** Kinetic Isotope Effect for the Ru/TEMPO-Catalyzed Aerobic Oxidation of *p*-Methyl- $\alpha$ -deuteriobenzyl Alcohol at Different Temperatures<sup>a</sup>

entry	temp ( $^\circ\text{C}$ )	time (h) for 100% convn	kinetic isotope effect ( $k_H/k_D$ ) <sup>b</sup>
1	25	67	5.1
2	43	40	5.0
3	63	6	4.1
4	83	3	4.0
5	100	2	3.9
6	118	1.5	3.4

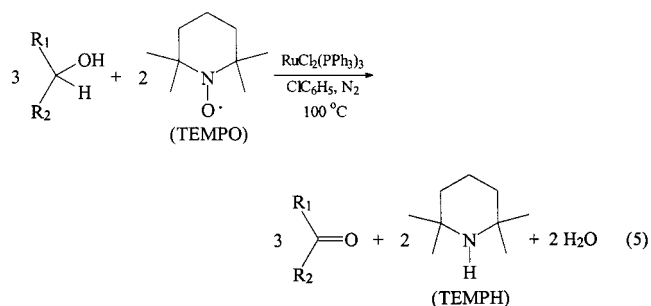
<sup>a</sup> Reaction conditions: 5 mmol of *p*-methyl- $\alpha$ -deuteriobenzyl alcohol, 0.05 mmol of  $\text{RuCl}_2(\text{PPh}_3)_3$ , 0.25 mmol of TEMPO, 10 mL of chlorobenzene,  $\text{O}_2$  atmosphere. <sup>b</sup> H/D ratio determined by  $^1\text{H}$  NMR.

**Figure 7.** The correlation of the kinetic isotope effect and the temperature (25–118  $^\circ\text{C}$ ) for the Ru/TEMPO catalyzed aerobic oxidation of *p*-methyl- $\alpha$ -deuteriobenzyl alcohol.

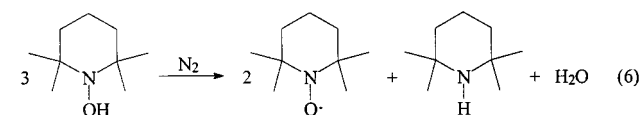
complexes, e.g., *trans*- $[\text{Ru}^{\text{VI}}(\text{tpy})(\text{O})_2(\text{CH}_3\text{CN})]^{2+}$  ( $k_H/k_D = 12.1$ ),<sup>49</sup> *cis*- $[(\text{N}_4)\text{Ru}^{\text{VI}}\text{O}_2]^{2+}$  ( $k_H/k_D = 21$ ),<sup>50</sup>  $[(\text{bpy})_2(\text{py})\text{Ru}^{\text{IV}}(\text{O})]^{2+}$  ( $k_H/k_D = 50$ ),<sup>51</sup> and  $[\text{Ru}^{\text{IV}}(\text{tpy})(\text{CH}_3\text{CN})_2(\text{O})]^{2+}$  ( $k_H/k_D = 61.5$ ).<sup>49</sup> On the other hand, the value is substantially larger than that found for the stoichiometric oxidation of benzyl alcohols by the oxoammonium cation (1) (reaction 2) at  $25^\circ\text{C}$  ( $k_H/k_D = 1.7$ – $2.3$ ).<sup>52</sup> We suggest that these results indicate that neither a ruthenium–oxo complex ( $\text{Ru}^{\text{IV}}\text{O}$ ,  $\text{Ru}^{\text{VI}}\text{O}_2$ ) nor the oxoammonium cation is the active oxidant, consistent with the proposed schematic mechanism in Figure 5.

The absence of a ruthenium–oxo complex ( $\text{Ru}^{\text{IV}}\text{O}$ ,  $\text{Ru}^{\text{VI}}\text{O}_2$ ) or the oxoammonium cation as the active oxidant can also be derived from the slope of the Hammett plots ( $\rho$  value). The  $\rho$  value for the Ru/TEMPO-catalyzed oxidation of benzyl alcohols ( $-0.58$ ) is significantly higher than that of the stoichiometric oxidation by the oxoammonium cation ( $\rho \approx -0.3$ ).<sup>52</sup> On the other hand, the value is much lower than those obtained in the stoichiometric oxidations by ruthenium–oxo compounds, e.g., *cis*- $[(\text{N}_4)\text{Ru}^{\text{VI}}\text{O}_2]^{2+}$  ( $\rho = -1.2$  to  $-1.9$ ).<sup>50</sup>

According to the mechanism presented in Figure 5, no regeneration of TEMPOH should take place under an inert atmosphere. In this case,  $\text{RuCl}_2(\text{PPh}_3)_3$  catalyzes the oxidation of octan-2-ol when a stoichiometric amount of TEMPO is used. We performed this experiment (see Experimental Section) and found octan-2-one and TEMPH as products in a 3:2 ratio (reaction 5). We assume that TEMPH is formed by disproportionation of the extremely unstable TEMPOH (reaction 6).



Attempts to prepare TEMPOH<sup>53</sup> under an inert atmosphere always resulted in the formation of TEMPH. On the other hand, in the presence of oxygen TEMPOH is rapidly oxidized to TEMPO. These results support the mechanism depicted in Figure 5 and indicate that TEMPO acts as a hydrogen transfer mediator.



Similarly, the  $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed stoichiometric reaction of TEMPO and benzyl alcohol at either  $25$  or  $100^\circ\text{C}$  afforded TEMPH and benzaldehyde in a 3:2 ratio. By using *p*-methyl- $\alpha$ -deuteriobenzyl alcohol as substrate, the kinetic isotope effect of the  $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed anaerobic oxidation could also be studied. The results were similar to those obtained in the catalytic aerobic oxidations presented in Table 4 (entries 1 and 5). At  $25^\circ\text{C}$  a kinetic isotope effect ( $k_H/k_D$ ) of 5.1 was obtained, whereas at  $100^\circ\text{C}$  a value of 3.4 was found. These results are consistent with the aerobic and anaerobic oxidation following the same pathway and, therefore, support the mechanism depicted in Figure 5, whereby TEMPO acts as a hydrogen transfer mediator.

A likely candidate for the active ruthenium hydride species is  $\text{RuH}_2(\text{PPh}_3)_3$ , as observed in  $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed hydrogen-transfer reactions.<sup>54</sup> In the ruthenium/TEMPO-catalyzed aerobic oxidation of octan-2-ol,  $\text{RuH}_2(\text{PPh}_3)_4$  was as active as  $\text{RuCl}_2$ -

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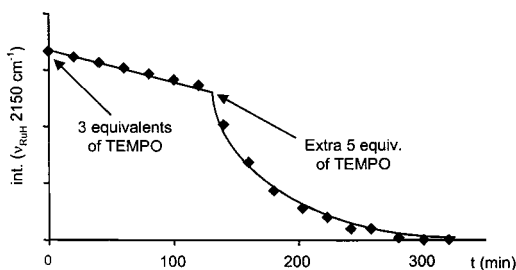
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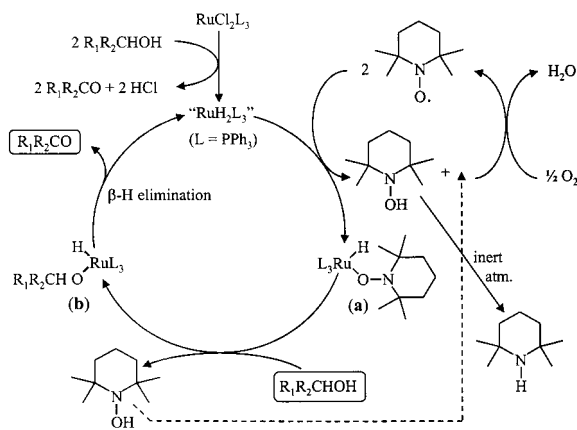
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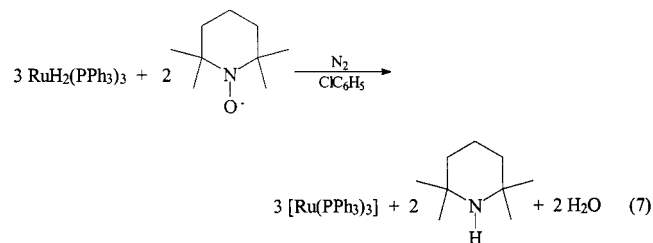
**Figure 8.** Stoichiometric reaction of “RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>” with TEMPO in chlorobenzene under an inert atmosphere at 25 °C, followed by in situ IR.



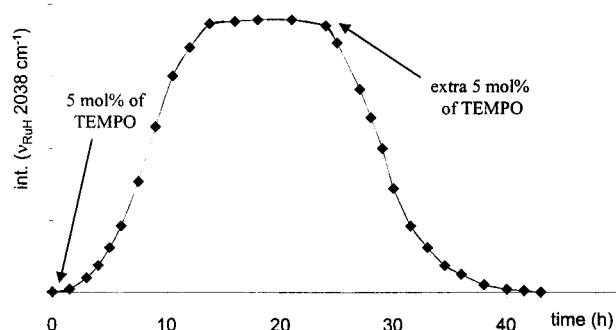
**Figure 9.** Proposed mechanism for the Ru/TEMPO catalyzed aerobic oxidation of alcohols.

(PPh<sub>3</sub>)<sub>3</sub>, i.e., octan-2-ol was quantitatively converted to octan-2-one within 9 h using 1.5 mol % of either catalyst and 4.5 mol % of TEMPO under an oxygen atmosphere at 100 °C. Additional support for a dihydride as the active catalyst was obtained from stoichiometric reaction of “RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>” (generated from RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>4</sub><sup>55</sup> in situ) with TEMPO in chlorobenzene, under an inert atmosphere at 25 °C, monitored by in situ IR (see Experimental Section). Following the intensity of the Ru–H vibration of “RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>” (2150 cm<sup>-1</sup>) in time, it was found that the ruthenium dihydride slowly decreased in the presence of 3 equiv of TEMPO but rapidly disappeared upon addition of another 5 equiv (Figure 8) without formation of any other ruthenium hydride complex.

On the other hand, TEMPO was again converted to TEMPH in a 2:3 ratio with respect to the molar amount of RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>4</sub> added (reaction 7). These results can be explained on the basis



of the catalytic cycle for the RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>/TEMPO-catalyzed aerobic oxidation of alcohols shown in Figure 9. In the catalytic system, where there is a large excess of alcohol, it is likely that proton transfer from the alcohol to the piperidinyloxy ligand in complex **a** takes place, leading to an exchange of “alkoxy” groups to give complex **b**. In contrast, in reaction 7 no alcohol



**Figure 10.** RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> catalyzed oxidation of benzyl alcohol with TEMPO (up to 0.1 equiv) in chlorobenzene under an inert atmosphere at 25 °C, followed by in situ IR.

is present and therefore a formal reductive elimination to give a Ru<sup>0</sup> species would predominate.

The above-described intermediate (**a**) is postulated by analogy with other ruthenium-based hydrogen transfer systems, in which no reduction of Ru<sup>2+</sup> to Ru<sup>0</sup> takes place during catalysis.<sup>54,56</sup> To provide support for the formation of (mono)hydride species in the catalytic cycle, the RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> (5 mol %) catalyzed anaerobic oxidation of benzyl alcohol with only 5 mol % of TEMPO was performed in chlorobenzene at 25 °C. During this reaction, both TEMPH and a (mono)hydride ruthenium species (ν<sub>RuH</sub> 2038 cm<sup>-1</sup>) were formed. Further addition of TEMPO (5 mol %) resulted again in the disappearance of the ruthenium hydride complex (Figure 10).

In summary, we propose that the Ru/TEMPO-catalyzed aerobic oxidation of alcohols proceeds via a hydridometal mechanism, involving a “RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>” species as the active catalyst (Figure 9). This ruthenium dihydride complex reacts with two molecules of TEMPO to form complex **a** and one molecule of TEMPOH. Proton transfer from the incoming alcohol to the piperidinyloxy ligand in complex **a** affords complex **b** and another molecule of TEMPOH. In the aerobic oxidation, the two molecules of TEMPOH are oxidized by oxygen to regenerate two molecules of TEMPO. Under anaerobic conditions, in the Ru-catalyzed stoichiometric reaction of an alcohol with TEMPO, TEMPH is formed by disproportionation of TEMPOH. In both cases, complex **b** undergoes normal β-hydrogen elimination to produce the ketone/aldehyde and the active ruthenium dihydride species.

**Heterogenization of the Catalyst.** A problem in the present aerobic Ru/TEMPO-catalyzed oxidation of alcohols is the slow deactivation of both ruthenium and TEMPO during catalysis. Unfortunately, the combination of PIPO<sup>34</sup> (polymer-immobilized TEMPO) and RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> in chlorobenzene is not able to catalyze the aerobic oxidation of octan-2-ol,<sup>57</sup> probably owing to coordination of ruthenium to the polyamine leading to an 18e complex. Similarly, attempts to use silica and MCM-41 supported TEMPO systems<sup>58</sup> lead to an inactive system.<sup>57</sup> Most probably, adsorption of ruthenium on the silica and MCM-41 surface took place, leading to an inactive catalyst. Indeed, our attempts to perform the (homogeneous) Ru/TEMPO-catalyzed

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aerobic oxidation of octan-2-ol in the presence of silica<sup>59</sup> resulted in much lower activities. In addition, a discoloration of the reaction mixture from dark brown to light orange took place, due to adsorption of ruthenium on the silica surface. Because of these disappointing results and the fact that ruthenium is much more expensive than TEMPO, we are currently focusing our attention on the heterogenization of ruthenium and will report our results in due course.

## Conclusion

The combination of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> and TEMPO affords an efficient catalytic system for the aerobic oxidation of a variety of primary and secondary alcohols, giving the corresponding aldehydes and ketones in >99% selectivity in all cases. To our knowledge this is one of the most reactive catalysts reported to date for the aerobic oxidation of (aliphatic) alcohols. Unfortunately, alcohols containing a heteroatom (O, N, S), such as butylproxitol and 4-(methylthio)butan-2-ol, are unreactive. In both inter- and intramolecular competition experiments, the Ru/TEMPO system displayed a preference for primary versus secondary alcohols.

Results from Hammett correlation studies ( $\rho = -0.58$ ) and the primary kinetic isotope effect ( $k_H/k_D = 5.1$ ) for the catalytic aerobic oxidation of benzyl alcohol are inconsistent with either an oxoruthenium (O=Ru) or an oxoammonium based mechanism. On the basis of this and the results from stoichiometric and in situ IR experiments, we postulate a hydridometal mechanism, involving a "RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>"-species as the active catalyst. TEMPO acts as a hydrogen transfer mediator and is regenerated by oxygen. Under anaerobic conditions, TEMPO acts as a stoichiometric oxidant.

## Experimental Section

**Aerobic Oxidation of Octan-2-ol at High Pressure.** Octan-2-ol (15.0 mmol, 1.96 g), *n*-hexadecane (internal standard; 3.0 mmol, 0.69 g), RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> (0.225 mmol, 216 mg), and TEMPO (0.675 mmol, 106 mg) were dissolved in 30 mL of chlorobenzene, heated in a high-pressure reactor (10 bar) to 100 °C under a continuous stream (10 mL min<sup>-1</sup>) of an oxygen–nitrogen mixture (8:92; v/v), and stirred (1000 rpm) for 7 h. Octan-2-ol conversion and octan-2-one selectivity were determined using GC analysis (50 m × 0.53 mm CP-WAX 52 CB column).

**Aerobic Oxidation of Octan-1-ol at Atmospheric Pressure.** Octan-1-ol (15.0 mmol, 1.96 g), *n*-hexadecane (internal standard; 3.0 mmol, 0.69 g), RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> (0.30 mmol, 286 mg), and TEMPO (0.90 mmol, 141 mg) were dissolved in 30 mL of chlorobenzene, heated to 100 °C under an oxygen atmosphere, and stirred (1000 rpm) for 7 h. Octan-1-ol conversion and octan-1-one selectivity were determined using GC analysis (50 m × 0.53 mm CP-WAX 52 CB column).

**Product Isolation.** The reaction mixture was diluted with *n*-hexane (to precipitate ruthenium compounds) and dried over MgSO<sub>4</sub>. The resulting mixture was filtered and the solvent was removed in vacuo. The product was separated from chlorobenzene using Kugelrohr distillation.

**Oxidation of 1,5-Hexanediol.** The oxidation of 1,5-hexanediol was carried out under the standard conditions. The reaction mixture was analyzed by GC and the products were identified by GCMS and were identical to literature values.

**1,5-Hexanediol:** *m/z* 100 (M<sup>+</sup> – H<sub>2</sub>O, 1), 85 (17), 75 (25), 67 (21), 57 (32), 56 (75), 45 (100).

**5-Hydroxyhexanal:** *m/z* 116 (M<sup>+</sup>, 2), 98 (M<sup>+</sup> – H<sub>2</sub>O, 11), 88 (21), 83 (13), 70 (25), 69 (17), 57 (56), 55 (38), 45 (100), 44 (76).

**5-Oxohexanal:** *m/z* 114 (M<sup>+</sup>, 14), 99 (13), 85 (4), 71 (27), 70 (100), 55 (67).

(59) Purchased from ACROS, for column chromatography, 0.060–0.200 mm, pore diameter 6 nm.

**Synthesis of 4-Acetylbenzoic Acid.** A mixture of *p*-acetylbenzonitrile (34.5 mmol, 5 g) in sulfuric acid (20 mL, 96%) and water (20 mL) was refluxed for 45 min. After the reaction, the solution was cooled to room temperature and water (200 mL) was added to precipitate an off-white solid. This solid was filtered off and dried via azeotropic distillation with toluene (50 mL) to give a fine pale-yellow powder. <sup>1</sup>H NMR (300 MHz, DMSO, TMS):  $\delta$  13 (s, 1H, COOH), 8.05 (s, 4H, 2H<sub>ortho</sub> and 2H<sub>meta</sub>), 2.63 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, DMSO, TMS):  $\delta$  198.2 (CO), 167.1 (COOH), 140.3 (C<sub>para</sub>), 135.0 (C<sub>ipso</sub>), 130.0 (2C<sub>meta</sub>), 128.8 (2C<sub>ortho</sub>), 27.5 (CH<sub>3</sub>).

**Synthesis of 4-(1'-Hydroxyethyl)benzyl Alcohol.** A mixture of 4-acetylbenzoic acid and LiAlH<sub>4</sub> (132 mmol, 4 g) in anhydrous THF (50 mL) was refluxed overnight under dry nitrogen. The usual workup gave 2.2 g (14.5 mmol, 42%) of a viscous orange-yellow oil which was used without further purification: *m/z* 152 (M<sup>+</sup>, 19), 137 (M<sup>+</sup> – Me, 96), 134 (M<sup>+</sup> – H<sub>2</sub>O, 19), 121 (22), 107 (31), 105 (28), 91 (60), 79 (100), 77 (58), 63 (16), 51 (35). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  7.28 (d, 2H, <sup>3</sup>J<sub>HH</sub> = 8.4 Hz, 2H<sub>meta</sub>), 7.24 (d, 2H, <sup>3</sup>J<sub>HH</sub> = 8.4 Hz, 2H<sub>ortho</sub>), 4.81 (q, 1H, <sup>3</sup>J<sub>HH</sub> = 6.6 Hz, CHCH<sub>3</sub>), 4.60 (s, 2H, CH<sub>2</sub>–OH), 2.72 (s, 2H, CH<sub>2</sub>OH and CH(CH<sub>3</sub>)OH), 1.43 (d, 3H, <sup>3</sup>J<sub>HH</sub> = 6.6 Hz, CH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  145.1 (C<sub>ipso</sub>), 140.0 (C<sub>para</sub>), 127.1 (2C<sub>meta</sub>), 125.6 (2C<sub>ortho</sub>), 70.0 (CHOH), 64.7 (CH<sub>2</sub>OH), 25.1 (CH<sub>3</sub>).

**Oxidation of 4-(1'-Hydroxyethyl)benzyl Alcohol.** The oxidation of 1-(4'-hydroxymethylphenyl)ethanol was carried under the standard conditions. The reaction mixture was analyzed by GC and the products were identified by GCMS and were identical to literature values.

**4-(Hydroxymethyl)acetophenone:** *m/z* 150 (M<sup>+</sup>, 31), 135 (100), 107 (23), 89 (37), 77 (29).

**4-(1'-Hydroxyethyl)benzaldehyde:** *m/z* 150 (M<sup>+</sup>, 5), 149 (5), 107 (100), 79 (74), 77 (50), 51 (21).

**4-Acetylbenzaldehyde:** *m/z* 148 (M<sup>+</sup>, 41), 134 (17), 133 (100), 105 (49), 77 (33), 51 (24), 50 (15).

**Synthesis of  $\alpha$ -Deuterio-*p*-methylbenzyl Alcohol.**  $\alpha$ -Deuterio-*p*-methylbenzyl alcohol was synthesized according to a literature procedure.<sup>60</sup> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  7.25 (d, 2H, <sup>3</sup>J<sub>HH</sub> = 8.0 Hz, 2H<sub>ortho</sub>), 7.16 (d, 2H, <sup>3</sup>J<sub>HH</sub> = 7.8 Hz, 2H<sub>meta</sub>), 4.60 (s, 1H, CHDOH), 2.35 (s, 3H, CH<sub>3</sub>), 1.69 (d, 1H, <sup>3</sup>J<sub>HH</sub> = 5.1 Hz, OH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  137.8 (C<sub>ipso</sub>), 137.4 (C<sub>para</sub>), 129.2 (2C<sub>meta</sub>), 127.2 (2C<sub>ortho</sub>), 64.9 (t, <sup>1</sup>J<sub>CD</sub> = 21.8 Hz, CHDOH), 21.2 (CH<sub>3</sub>). *m/z*: 124 (17), 123 (M<sup>+</sup>, 92), 122 (25), 108 (100), 106 (33), 94 (50), 93 (31), 92 (32), 91 (48), 80 (71), 78 (52), 77 (36), 65 (28).

**Synthesis of 2-Deuteriooctan-2-ol.** 2-Deuteriooctan-2-ol was synthesized according to a literature procedure.<sup>60</sup> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  1.42 (m, 2H, C<sup>3</sup>H<sub>2</sub>), 1.29 (m, 8H, C<sup>4–7</sup>H<sub>2</sub>), 1.18 (s, 3H, C<sup>1</sup>H<sub>3</sub>), 0.89 (t, 3H, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, C<sup>8</sup>H<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  67.5 (t, <sup>1</sup>J<sub>CD</sub> = 21.4 Hz, C<sup>2</sup>HDOH), 39.3 (C<sup>3</sup>H<sub>2</sub>), 31.9 (C<sup>6</sup>H<sub>2</sub>), 29.3 (C<sup>5</sup>H<sub>2</sub>), 25.7 (C<sup>4</sup>H<sub>2</sub>), 23.7 (C<sup>7</sup>H<sub>2</sub>), 22.6 (C<sup>1</sup>H<sub>3</sub>), 14.1 (C<sup>8</sup>H<sub>3</sub>). *m/z*: 116 (M<sup>+</sup> – CH<sub>3</sub>, 30), 113 (M<sup>+</sup> – H<sub>2</sub>O, 30), 98 (53), 84 (41), 70 (27), 56 (35), 46 (100).

**Synthesis of 1-Deuterio-1-phenylethanol.** 1-Deuterio-1-phenylethanol was synthesized according to a literature procedure.<sup>61</sup> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  7.33 (m, 4H, 2H<sub>meta</sub> and 2H<sub>ortho</sub>), 7.25 (m, 1H, H<sub>para</sub>), 2.13 (s, 1H, OH), 1.46 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS)  $\delta$  145.7 (C<sub>ipso</sub>), 128.4 (2C<sub>meta</sub>), 127.4 (C<sub>para</sub>), 125.4 (2C<sub>ortho</sub>), 70.0 (t, <sup>1</sup>J<sub>CD</sub> = 22.1 Hz, CDOH), 25.0 (CH<sub>3</sub>). *m/z*: 123 (M<sup>+</sup>, 27), 108 (100), 105 (M<sup>+</sup> – H<sub>2</sub>O, 40), 80 (91), 79 (25), 78 (49), 77 (36), 51 (35).

**Synthesis of 1-Deuterioheptan-1-ol.** 1-Deuterioheptan-1-ol was synthesized according to a literature procedure.<sup>62</sup> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  3.61 (t, 1H, <sup>3</sup>J<sub>HH</sub> = 6.6 Hz, CHDOH), 1.56 (m, 3H, C<sup>2</sup>H<sub>2</sub> and OH), 1.30 (m, 8H, C<sup>3–6</sup>H<sub>2</sub>), 0.96 (t, 3H, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, C<sup>7</sup>H<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  62.7 (t, <sup>1</sup>J<sub>CD</sub> = 21.4 Hz, CHDOH), 32.7 (C<sup>3</sup>H<sub>2</sub>), 31.8 (C<sup>2</sup>H<sub>2</sub>), 29.1 (C<sup>4</sup>H<sub>2</sub>), 25.7 (C<sup>5</sup>H<sub>2</sub>), 22.6 (C<sup>6</sup>H<sub>2</sub>), 14.1 (C<sup>7</sup>H<sub>3</sub>). *m/z*: 99 (M<sup>+</sup> – CH<sub>3</sub>, 7), 84 (10), 71 (40), 70 (100), 69 (50), 58 (18), 57 (68), 56 (88), 55 (58), 44 (18).

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**Determination of Intramolecular Kinetic Isotope Effect.** The oxidation of the deuterated primary alcohols,  $\alpha$ -deuterio-*p*-methylbenzyl alcohol and 1-deuterioheptan-1-ol, was carried out under the standard conditions. The reaction mixture was analyzed by GC, and the products, ( $\alpha$ -deuterio)-*p*-methylbenzaldehyde and (1-deuterio)heptanal, respectively, were isolated using Kugelrohr distillation. The intramolecular kinetic isotope effect was determined by  $^1\text{H}$  NMR.

***p*-Methylbenzaldehyde:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  9.95 (s, 1H, CHO), 7.75 (d, 2H,  $^3J_{\text{HH}} = 7.8$  Hz,  $2H^{\text{ortho}}$ ), 7.31 (d, 2H,  $^3J_{\text{HH}} = 7.8$  Hz,  $2H^{\text{meta}}$ ), 2.42 (s, 3H,  $\text{CH}_3$ ).

**$\alpha$ -Deuterio-*p*-methylbenzaldehyde:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  7.75 (d, 2H,  $^3J_{\text{HH}} = 7.8$  Hz,  $2H^{\text{ortho}}$ ), 7.31 (d, 2H,  $^3J_{\text{HH}} = 7.8$  Hz,  $2H^{\text{meta}}$ ), 2.42 (s, 3H,  $\text{CH}_3$ ).

**Heptanal:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  9.78 (s, 1H, CHO), 2.42 (t, 2H,  $^3J_{\text{HH}} = 6.7$  Hz,  $\text{C}^2\text{H}_2$ ), 1.30 (m, 8H,  $\text{C}^{3-6}\text{H}_2$ ), 0.96 (t, 3H,  $^3J_{\text{HH}} = 7.0$  Hz,  $\text{C}^7\text{H}_3$ ).

**1-Deuterioheptanal:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  2.42 (t, 2H,  $^3J_{\text{HH}} = 6.7$  Hz,  $\text{C}^2\text{H}_2$ ), 1.30 (m, 8H,  $\text{C}^{3-6}\text{H}_2$ ), 0.96 (t, 3H,  $^3J_{\text{HH}} = 7.0$  Hz,  $\text{C}^7\text{H}_3$ ).

**Determination of Intermolecular Kinetic Isotope Effect.** Oxidation of the deuterated secondary alcohol mixtures, (2-deuterio)octan-2-ol and (1-deuterio)-1-phenylethanol, was carried out by using the standard conditions. The reaction mixture was followed by GC and the reaction was stopped at 25–35% conversion. The unreacted substrate was isolated using Kugelrohr distillation, and the intermolecular kinetic isotope effect was determined by  $^1\text{H}$  NMR.

**Octan-2-ol:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  3.81 (m, 1H,  $\text{C}^2\text{HOH}$ ), 1.42 (m, 2H,  $\text{C}^3\text{H}_2$ ), 1.29 (m, 8H,  $\text{C}^{4-7}\text{H}_2$ ), 1.18 (d, 3H,  $^3J_{\text{HH}} = 5.9$  Hz,  $\text{C}^1\text{H}_3$ ), 0.89 (t, 3H,  $^3J_{\text{HH}} = 6.4$  Hz,  $\text{C}^8\text{H}_3$ ).

**2-Deuteriooctan-2-ol:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  1.42 (m, 2H,  $\text{C}^3\text{H}_2$ ), 1.29 (m, 8H,  $\text{C}^{4-7}\text{H}_2$ ), 1.18 (s, 3H,  $\text{C}^1\text{H}_3$ ), 0.89 (t, 3H,  $^3J_{\text{HH}} = 6.4$  Hz,  $\text{C}^8\text{H}_3$ ).

**1-Phenylethanol:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  7.33 (m, 4H,  $2H^{\text{meta}}$  and  $2H^{\text{ortho}}$ ), 7.25 (m, 1H,  $H^{\text{para}}$ ), 4.90 (m, 1H, CHO), 2.10 (s, 1H, OH), 1.46 (d,  $^3J_{\text{HH}} = 6.4$  Hz, 3H,  $\text{CH}_3$ ).

**1-Deuterio-1-phenylethanol:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  7.33 (m, 4H,  $2H^{\text{meta}}$  and  $2H^{\text{ortho}}$ ), 7.25 (m, 1H,  $H^{\text{para}}$ ), 2.10 (s, 1H, OH), 1.46 (s, 3H,  $\text{CH}_3$ ).

**Stoichiometric Reaction of Octan-2-ol with TEMPO.** Octan-2-ol (2.5 mmol, 0.33 g),  $\text{RuCl}_2(\text{PPh}_3)_3$  (0.025 mmol, 23.8 mg), and TEMPO (5 mmol, 0.78 g) were dissolved in 5 mL of chlorobenzene, heated to 100 °C under an inert atmosphere ( $\text{N}_2$ ), and stirred for 24 h. Substrate (octan-2-ol/TEMPO) conversion and product (octan-2-one and TEMPH) selectivity were determined using GC analysis (50 m  $\times$  0.53 mm CP-WAX 52 CB column).

**Stoichiometric Reaction of  $\text{RuH}_2(\text{PPh}_3)_4$  with TEMPO.** TEMPO (1.35 mmol, 211 mg) and  $\text{RuH}_2(\text{PPh}_3)_4$  (0.45 mmol, 517 mg) were dissolved in 15 mL of chlorobenzene and stirred at 25 °C under an inert atmosphere ( $\text{N}_2$ ) for 6 h. After 2 h, an extra portion of TEMPO (2.25 mmol, 351 mg) was added. Conversion of TEMPO and  $\text{RuH}_2(\text{PPh}_3)_4$  was determined using respectively GC analysis (50m  $\times$  0.53 mm CP-WAX 52 CB column) and an in situ IR technique (ASI Applied Systems ReactIR 1000;  $\nu_{\text{RuH}}$  2150  $\text{cm}^{-1}$ ).

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