

Research Article

Cyclopentadienyl Ruthenium(II) Complex-Mediated Oxidation of Benzylic and Allylic Alcohols to Corresponding Aldehydes

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Received 2 May 2019; Revised 9 July 2019; Accepted 17 July 2019; Published 18 August 2019

Academic Editor: Guillaume Berionni

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This work reports an efficient method for the oxidation reaction of aliphatic, aromatic allylic, and benzylic alcohols into aldehydes catalyzed by the cyclopentadienyl ruthenium(II) complex ($\text{RuCpCl}(\text{PPh}_3)_2$) with bubbled O_2 . Through further optimizing controlled studies, the tendency order of oxidation reactivity was determined as follows: benzylic alcohols > aromatic allylic alcohols >> aliphatic alcohols. In addition, this method has several advantages, including a small amount of catalyst (0.5 mol%) and selective application of high discrimination activity of aliphatic, aromatic allylic, and benzylic alcohols.

1. Introduction

Oxidation reactions are very useful functional transformations in organic synthesis [1, 2]. Many of the metal-based oxidizing reagents have been developed to achieve the efficient oxidation of alcohols such as PI Au [3], ARP-Pt [4], $\text{Ru/Al}_2\text{O}_3$ [5, 6], Pd/HAP [7, 8], Au-Pd/TiO_2 [9], and HB Ru [10]. However, these catalysts are generally difficult to obtain because of their expensive cost and harsh production. In addition, other oxidation methods for alcohols using the readily available carbon-supported metal catalysts [11–14] including many famous Pd/C [15–17], Pt/C [18–23], or Au/C [24–30] catalysts [31, 32] were also enthusiastically investigated. Unfortunately, these catalysts needed addition of

adjunction metals such as Co or Cd , or presence of oxygen or air under higher pressure and/or temperature, and/or stronger basic conditions to obtain the desired products. Furthermore, the rare earth elements have occupied an especially important place in the past two decades because of their high reactivity in various catalytic processes [33–39]. One of these rare elements is ruthenium. Some species of ruthenium have been widely developed and used as efficient catalysts for oxidation reactions [40, 41].

Among a variety of catalysts reported in the literature for the redox process of carbonyl compounds [42], the use of ruthenium complexes has garnished significant attention. For example, several ruthenium complexes have been employed as catalysts for the hydrogenation of carbonyl compounds,

TABLE 1: Study of oxidation conditions of benzyl alcohol **1a** with RuCpCl(PPh₃)₂.

c1ccc(cc1)CO $\xrightarrow[\text{O}_2, \text{ solvent, at reflux}]{\text{RuCpCl(PPh}_3)_2}$ c1ccc(cc1)C=O

Entry	Substrate	Solvent	Reaction condition	Product	Yield (%)
1	1a	CH ₂ Cl ₂	Reflux for 24 h	2a	Trace
2	1a	CH ₂ Cl ₂	Reflux for 48 h	2a	<10
3	1a	Benzene	Reflux for 24 h	2a	Trace
4	1a	Benzene	Reflux for 48 h	2a	<6
5	1a	Acetone	Reflux for 24 h	2a	Nondetectable
6	1a	Acetone	Reflux for 48 h	2a	Nondetectable
7	1a	THF	Reflux for 24 h	2a	54
8	1a	THF	Reflux for 48 h	2a	71

providing an efficient access to their corresponding alcohols. For example, several ruthenium complexes [43] including RuCpCl(PPh₃)₂, Ru(indenyl)Cl(PPh₃)₂, [RuCp(MeCN)₂(PR₃)]PF₆ [44], [RuCp(MeCN)₃]PF₆ [45], and RuCpCl(diphosphine) have been employed as catalysts for the isomerization of both aliphatic [46] and aromatic [47–50] allylic alcohols into ketones or aldehydes.

Literature has reported oxidation of allylic and benzylic alcohols for functional transformation such as that reported by Prof. Pearson using trimethylamine-*N*-oxide in the presence of iron carbonyl as a significant catalyst [51]. However, several issues limit these catalysts' applications such as the need for a toxic solvent, tedious complex reagents, and troublesome procedures. Therefore, we reported a novel and interesting cyclopentadienyl ruthenium(II) complex (RuCpCl(PPh₃)₂), which oxidizes aromatic allylic and benzylic alcohols into carbonyl compounds. Based on the further controlled experimental studies, we found the tendency order of oxidative reactivity as benzylic alcohols > aromatic allylic alcohols >> aliphatic alcohols.

2. Results and Discussion

Benzyl alcohol **1a** is an important precursor for organic synthesis and a useful solvent because of its polarity, low toxicity, mildly pleasant aromatic odor, and low vapor pressure [52–54]. The chemoselective oxidation property of compound **1a** was also very useful in functional transformations for the preparation of aldehydes [55, 56] and their dicarboxyl analogues [57, 58]. For these reasons, we carried out a plausible oxidation of benzyl alcohol **1a**. We preliminarily investigated a versatile oxidation method for compound **1a** with 0.5 mol% amount of the cyclopentadienyl ruthenium(II) complex (RuCpCl(PPh₃)₂) catalyst with bubbled O₂ in CH₂Cl₂ solution at reflux for 24 h. However, only trace amounts of benzaldehyde **2a** were achieved (entry 1 in Table 1). We then increased the reaction time to 48 h, which resulted in the desired oxidation product **2a**, but at a low yield (<10%; entry 2 in Table 1). To identify the optimal reaction conditions, we attempted to screen the

ACS grade of solvents (i.e., benzene, acetone, and THF) and the reaction time at room temperature or reflux. Based on the experimental results in Table 1, we observed that the ideal conditions for this reaction were to use THF as the reaction solvent and to reflux for 48 h. The corresponding oxidation product **2a** can be afforded in 71% isolated yield (entry 8 in Table 1). Consequently, optimization of the amount of the catalyst from 0.5, 1.0, 2.0, to 5 mol% was performed. However, this did not lead to any further improvement. The structure of product **2a** was completely characterized by spectroscopic methods and consistent with an Aldrich-authentic sample. Following the results in Table 1, we found that RuCpCl(PPh₃)₂ possessed the oxidation reactivity necessary for transferring benzyl alcohols to the corresponding benzaldehydes.

In order to explore the substrate scope of the new oxidation reaction, we first examined the reactions of substituted benzylic alcohols **1b–f** containing either electron-donating or electron-withdrawing groups **1b–d** and disubstituted benzylic alcohols **1e–f**. Fortunately, most of the substituted benzylic alcohols **1b–f** were successfully converted to the corresponding aldehyde products **2b–f** in moderate yields (>68%; Table 2). On the contrary, benzylic alcohols with *para*-Me (**1b**) and *para*-OMe (**1c**) electron-donating groups were oxidized to give the corresponding aldehyde products **2b–c** in 73% and 80% yields, respectively (entries 1 and 2 in Table 2). In addition, the conversion of *para*-CN-benzylic alcohol **1d** to aldehyde **2d** in 68% yield seemed to have lower reactivity compared to benzylic alcohols with electron-donating groups **1b–c** (entries 1 and 2 in Table 2). For disubstituted benzylic alcohols **1e** and **1f**, the most effective results were achieved in 82% and 86% yields, respectively, demonstrating a strong and significant electron-assisted effect (entries 4 and 5 in Table 2). Following the above study, it was found the cyclopentadienyl ruthenium(II) complex (RuCpCl(PPh₃)₂) possessed significant oxidizing activity for discrimination of benzylic alcohols.

To further expand our study, we investigated simplified allylic systems such as (*E*)-3-arylprop-2-en-1-ols (**1g**) and cyclohex-2-enol (**1h**). The RuCpCl(PPh₃)₂ catalyst (0.5 mol%) successfully reacted towards (*E*)-3-arylprop-2-en-1-ols (**1g**)

TABLE 2: Oxidation results of alcohols with $\text{RuCpCl}(\text{PPh}_3)_2$ at reflux in anhydrous THF solution.

Entry	Alcohols 1b-k	Reaction time (h)	Yields of products 2b-k	Yields (%)
1	1b 	~48 h	2b 	73
2	1c 	~48 h	2c 	80
3	1d 	~48 h	2d 	68
4	1e 	~48 h	2e 	82
5	1f 	~48 h	2f 	86
6	1g 	~48 h	2g 	68
7	1h 	~48 h	2h 	69
8	1i 	~48 h	2i 	17 ^a
9	1j $\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{OH}$	~48 h	2j $\text{CH}_3(\text{CH}_2)_5\text{CHO}$	35
10	1k 	~48 h	2k —	— ^a

^aThe starting material was recovered.

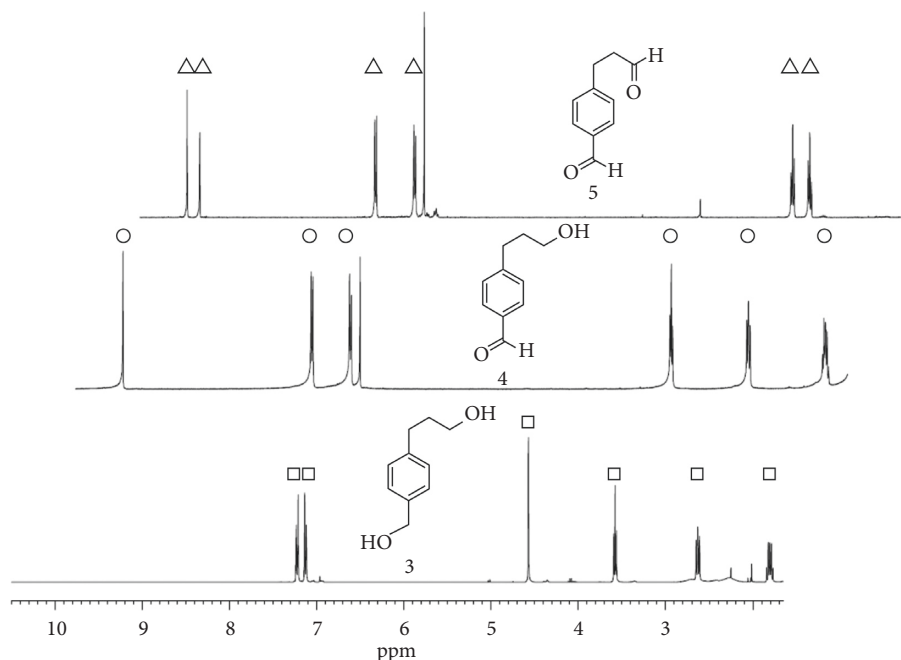
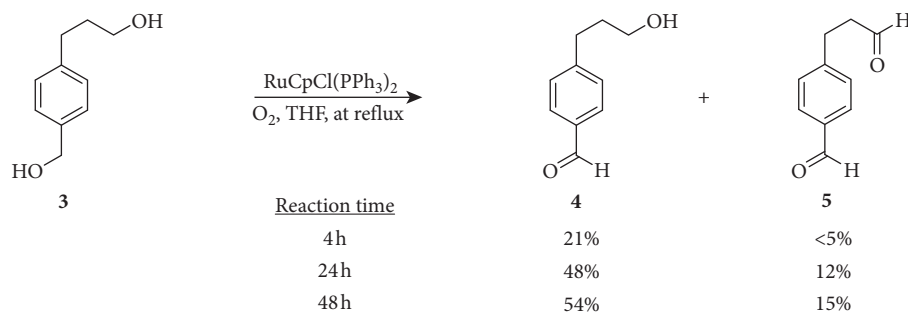


FIGURE 1: ^1H NMR characteristic identification of compounds **3** (\square), **4** (\circ), and **5** (Δ).



SCHEME 1: Chemoreactivity oxidation results of 4-(hydroxymethyl)benzenepropanol **3**.

and cyclohex-2-enol (**1h**) in the presence of THF at reflux for ~48 h to give the desired oxidation products **2g** and **2h** in 68% and 69% yields, respectively (entries 6 and 7 in Table 2). The yielding results of the allylic system **1g-h** were noticeably lower than the conversion of benzylic alcohols **1e-f**.

To evaluate the substrate scope and limitation, this study has been extended to a variety of aliphatic or alicyclic alcohols such as 3-arylpropan-1-ols (**1i**), heptan-1-ol (**1j**), and 2-isopropyl-5-methylcyclohexanol (**1k**). In general, a longer reaction time (~60 h) was required compared to benzyl and allylic alcohols **1a-h** for oxidation reaction (entries 8–10 in Table 2). Under the same condition, aliphatic or alicyclic alcohols **1i-k** presented poor oxidizing reactivity, resulting in trace to 35% yields. For compound **1k**, no trace of the oxidation product was detected in the ^1H NMR spectrum of the crude reaction mixture (entry 10 in Table 2). Following the above study, it was found the cyclopentadienyl ruthenium(II) complex ($\text{RuCpCl}(\text{PPh}_3)_2$) possessed significant oxidizing activity for discrimination of aromatic allylic and benzylic

alcohols. In addition, the oxidation reaction of benzylic alcohol **1a** with the $\text{RuCpCl}(\text{PPh}_3)_2$ catalyst (0.5 mol%) was found to produce better isolated yields compared to both allylic alcohol **1g** and aliphatic alcohol **1i**.

4-(Hydroxymethyl)benzenepropanol **3** was synthesized by the reported method as the important bifunctional substrate for the chemoreactivity oxidation study [59]. We initially carried out a careful study of possible oxidations of compound **3** with 1.25 mol% amount of the cyclopentadienyl ruthenium(II) complex ($\text{RuCpCl}(\text{PPh}_3)_2$) catalyst with bubbled O_2 in CH_2Cl_2 solution at reflux for 48 h. The versatile oxidation was monitored by TLC and sampled for ^1H NMR characteristic identification (see Figure 1). When the reaction was performed for 4 h, the crude solution was sampled, worked up, and eluted from the column. Most of starting material **3** was recovered, and the corresponding mixture products 4-(3-hydroxypropyl)benzaldehyde **4** and the small amount of 4-(3-oxopropyl)benzaldehyde **5** were given out in 21% and <5% yields, respectively (see Scheme 1 and Figure 1). When the reaction time was prolonged from 4 h to

24 h or 48 h under the same condition, we observed that the expected oxidation product **4** was significantly promoted from 21% to 48% or 54% yields, respectively [60]. Comparatively, only a small amount of oxidation product 4-(3-oxopropyl)benzaldehyde **5** was achieved (~5% to 12% and 15%; Scheme 1) [60]. Based on the above experimental results, we proved again that the benzylic alcohol possessed more efficient oxidative reactivity than the aliphatic alcohol.

3. Conclusions

We have successfully developed the oxidation reaction for aliphatic, aromatic allylic, and benzylic alcohols with 0.5 mol% of the cyclopentadienyl ruthenium(II) complex (RuCpCl(PPh₃)₂). Based on the further controlled studies, the reactive tendency was determined as follows: benzylic alcohols > aromatic allylic alcohols >> aliphatic alcohols. On the contrary, mono- and disubstituted benzylic alcohols with electron-donating groups can provide the best oxidation results. In addition, this new method has several advantages including a small amount of catalyst (0.5 mol%) and high discrimination activity of aliphatic, aromatic allylic, and benzylic alcohols.

4. Experimental Section

All reagents were used as obtained commercially. All reactions were carried out under argon or nitrogen atmosphere and monitored by TLC. Flash column chromatography was carried out on silica gel (230–400 mesh). An analytical thin-layer chromatography (TLC) was performed using precoated plates (silica gel 60 F-254) purchased from Merck Inc. Flash column chromatography purification was carried out by gradient elution using *n*-hexane in ethyl acetate (EtOAc) unless otherwise stated. Infrared (IR) spectra were measured with a Bomem Michelson Series FT-IR spectrometer. The wavenumbers reported are referenced to the polystyrene absorption at 1601 cm⁻¹. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; and w, weak. All proton and carbon-13 NMR spectra were obtained by Bruker instruments (400 MHz and 100 MHz, respectively). Proton and carbon-13 NMR spectra were acquired using deuteriochloroform (CDCl₃) solvent. Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and *J*, coupling constant (Hz). ESI-MS analyses were performed on an Applied Biosystems API 300 mass spectrometer. High-resolution mass spectra were obtained from a JEOL JMS-HX110 mass spectrometer.

4.1. Standard Procedure for the Oxidation of Aliphatic, Aromatic Allylic, and Benzylic Alcohols 1a–j to Corresponding Aldehydes 2a–j with Cyclopentadienyl Ruthenium(II) Complex. Aliphatic, aromatic allylic, or benzylic alcohols (**1a–j**, ~1.0 mmol, 1.0 equiv) and RuCpCl(PPh₃)₂ (~0.5 mol %) with bubbled O₂ were stirred in anhydrous THF (2.0 mL) and heated at reflux for 24–48 h under the argon

atmospheric pressure. When the oxidization reaction was completed, the solution was filtered through Celite, and the Celite bed was washed with hot THF. The filtrate was concentrated to remove THF under reduced pressure. The residue was added (CH₂Cl₂, 15 mL), washed with saturated aqueous NaHCO₃ (15 mL), and extracted with CH₂Cl₂ (10 mL × 2). The combined organic layers were washed with brine (15 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (*n*-hexane/EtOAc = 4/1) on silica gel to give the corresponding aldehyde products **2a–j** in 17–86% yields. The physical properties and spectroscopic characteristics of the isolated aliphatic, aromatic allylic, and benzylic alcohols, including **2a–j**, were consistent with those of the authentic sample [61].

Benzaldehyde (**2a**) [61]: light yellow liquid; ¹H NMR (CDCl₃, 400 MHz): δ 7.48–7.52 (m, 2H, ArH), 7.58–7.63 (m, 1H, ArH), 7.84–7.87 (m, 2H, ArH), and 9.99 (s, 1H, CHO); ¹³C NMR (CDCl₃, 100 MHz): δ 129.94 (2 × CH), 129.69 (2 × CH), 134.41, 136.34, and 192.37; IR (KBr): 3071, 2832, 2674, 2560, 1686, 1424, 1325, 1291, 934, and 709 cm⁻¹; MS (EI): 106 (78), 105 (100), 78 (15), 77 (83), 51 (37), and 50 (13).

4-Tolualdehyde (**2b**) [61]: colorless liquid; ¹H NMR (CDCl₃, 400 MHz): δ 2.42 (s, 3H, Me), 7.31 (d, *J* = 7.9 Hz, 2H, ArH), 7.75 (dd, *J* = 6.6 and 1.6 Hz, 2H, ArH), and 9.94 (s, 1H, CHO); ¹³C NMR (CDCl₃, 100 MHz): δ 21.85, 129.68 (2 × CH), 129.83 (2 × CH), 134.16, 145.54, and 192.01; IR (KBr): 3043, 2945, 1672, 1574, 1282, 959, 947, 838, and 752 cm⁻¹; MS (EI): 120 (34), 119 (100), 92 (11), 91 (97), and 65 (18).

4-Methoxybenzaldehyde (**2c**) [61]: light yellow liquid; ¹H NMR (CDCl₃, 400 MHz): δ 3.79 (s, 3H, OMe), 6.90–6.93 (m, 2H, ArH), 7.73–7.76 (m, 2H, ArH), and 9.79 (s, 1H, CHO); ¹³C NMR (CDCl₃, 100 MHz): δ 54.74, 113.61 (2 × CH), 129.24, 131.16 (2 × CH), 163.89, and 189.98; IR (KBr): 3520, 3356, 2969, 2839, 2741, 1682, 1601, 1577, 1512, 1315, 1260, 1158, and 1026 cm⁻¹; MS (EI): 136 (72), 135 (100), 92 (14), 77.0(24), and 65 (10).

4-Cyanobenzaldehyde (**2d**) [61]: white crystal, m.p. 99–102°C; ¹H NMR (CDCl₃, 400 MHz): δ 7.83 (d, *J* = 8.2 Hz, 2H, ArH), 7.98 (d, *J* = 8.2 Hz, 2H, ArH), and 10.07 (s, 1H, CHO); ¹³C NMR (CDCl₃, 100 MHz): δ 117.57, 117.74, 129.90 (2 × CH), 132.92 (2 × CH), 138.74, and 190.70; IR (KBr): 2850, 2231, 1707, 1608, 1571, 1387, 1295, 1203, 1172, 832, 737, and 546 cm⁻¹; MS (EI): 131 (84), 130 (100), 105 (28), 103 (23), 102.0(57), 91 (12), 77 (16), 76 (18), 75 (12), and 51 (12).

3,4-Dimethoxybenzaldehyde (**2e**) [61]: light yellow liquid; ¹H NMR (CDCl₃, 400 MHz): δ 3.93 (s, 3H, -OMe), 3.96 (s, 3H, -OMe), 6.98 (d, *J* = 8.2 Hz, 1H, ArH), 7.40 (d, *J* = 7.6 Hz, 1H, ArH), 7.45 (dd, *J* = 8.2 and 1.9 Hz, 1H, ArH), and 9.84 (s, 1H, CHO); ¹³C NMR (CDCl₃, 100 MHz): δ 55.60, 55.80, 108.63, 110.11, 126.42, 129.79, 149.26, 154.13, and 190.47; IR (KBr): 2938, 2840, 1683, 1588, 1513, 1462, 1421, 1268, 1243,

1135, 1021, 811, and 731 cm^{-1} ; MS (EI): 167 (18), 166 (100), 165 (71), 159 (22), 95 (33), 91.0(40), 79 (14), 77 (22), 73 (26), and 60 (15).

4-Benzyloxy-3-methoxybenzaldehyde (**2f**) [61]: orange liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 3.89 (s, 3H, OMe), 5.19 (s, 2H, OCH_2), 6.95 (d, $J=8.2$ Hz, 1H, ArH), 7.30 (d, $J=7.3$ Hz, 1H, ArH), 7.33–7.37 (m, 3H, ArH), 7.39–7.42 (m, 3H, ArH), and 9.79 (s, 1H, CHO); ^{13}C NMR (CDCl_3 , 100 MHz): δ 55.85, 70.67, 109.22, 112.24, 126.39, 127.08 ($2 \times \text{CH}$), 128.05, 128.56 ($2 \times \text{CH}$), 130.14, 135.87, 149.90, 153.44, and 190.72; IR (KBr): 2938, 2833, 2731, 1683, 1588, 1509, 1462, 1424, 1264, 1237, 1135, 1026, and 734 cm^{-1} ; MS (EI): 242 (45), 92 (43), 91 (100), and 65 (41).

Cinnamaldehyde (**2g**) [61]: light yellow liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 6.71 (qd, $J=1.82$ and 7.70 Hz, 1H, Me), 7.41–7.43 (m, 3H, ArH), 7.44 (d, $J=1.88$ Hz, 1H, Me), 7.54–7.56 (m, 2H, ArH), and 9.69 (dd, $J=7.70$ and 2.42 Hz, CHO); ^{13}C NMR (CDCl_3 , 100 MHz): δ 128.42 ($3 \times \text{CH}$), 129.01 ($2 \times \text{CH}$), 131.21, 133.88, 152.81, and 193.73; IR (KBr): 3024, 2844, 1681, 1634, 1449, 1311, and 1286 cm^{-1} ; MS (EI): 132 (38), 131 (69), 130 (36), 103 (98), 102 (63), 91 (59), 78 (41), 77 (94), 76 (40), and 51 (65).

2-Cyclohexen-1-one (**2h**) [61]: colorless liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 1.90–1.96 (m, 2H), 2.24–2.29 (m, 2H), 2.33 (t, $J=13.48$ Hz, 2H), 5.92 (d, $J=10.12$ Hz, 1H), and 6.89–6.94 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 22.56, 25.49, 37.92, 129.63, 150.61, and 199.40; IR (KBr) 3299, 2918, 2847, 1513, 1707, 1380, 1241, 1210, and 832 cm^{-1} ; MS (EI): 96 (36) and 68 (100).

3-Phenylpropionaldehyde (**2i**) [61]: colorless liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 2.77 (td, $J=7.28$ and 0.87 Hz, 2H), 2.96 (t, $J=7.56$ Hz, 2H), 7.20 (t, $J=7.38$ Hz, 3H), 7.30 (t, $J=7.30$ Hz, 2H), and 9.81 (t, $J=1.34$ Hz, CHO); ^{13}C NMR (CDCl_3 , 100 MHz): δ 28.08, 45.18, 126.28 ($2 \times \text{CH}$), 128.35, 128.60 ($2 \times \text{CH}$), 140.57, and 201.46; IR (KBr): 3029, 2929, 1709, 1604, 1496, 1456, and 1298 cm^{-1} ; MS (EI): 135 (22), 134 (100), 133 (10), 118 (12), 117 (20), 105 (27), 92 (58), 91 (96), 78 (23), and 77 (11).

Heptanal (**2j**) [61]: colorless liquid; ^1H NMR (CDCl_3 , 400 MHz): δ 0.87 (t, $J=6.9$ Hz, 3H, Me), 1.25–1.33 (m, 6H), 1.57–1.63 (m, 2H, $\text{CH}_2\text{CH}_2\text{CHO}$), 2.40 (td, $J=7.4$ and 1.9 Hz, 2H, CH_2CHO), and 9.75 (t, $J=1.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): δ 13.96, 22.02, 22.42, 28.80, 31.50, 43.89, and 202.94; IR (KBr): 3421, 2955, 2928, 2856, 1716, 1461, 1376, 1145, and 947 cm^{-1} ; MS (EI): 96 (23), 86 (20), 81 (27), 72 (13), 71 (25), 70 (100), 69 (10), 68 (21), 67 (12), 60 (12), 57 (47), and 55 (59).

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

This manuscript was also presented at National Annual Meeting of Chinese Chemical Society, National Sun Yat-sen University (Kaohsiung), Taiwan, Nov 8–9, 2018.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Ching-Yuh Chern and Ching-Chun Tseng contributed equally to this work.

Acknowledgments

The authors are grateful to the Tsuzuki Institute for Traditional Medicine and the Ministry of Science and Technology of the Republic of China (MOST 107-2113-M-039-006) for financial support. This work was also financially supported by Taiwan Ministry of Health and Welfare Clinical Trial Center (MOHW107-TDU-B-212-123004) and Chinese Medicine Research Center, China Medical University, through The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan (CMRC-CHM-4).

Supplementary Materials

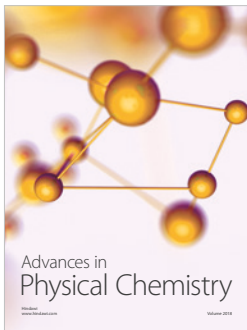
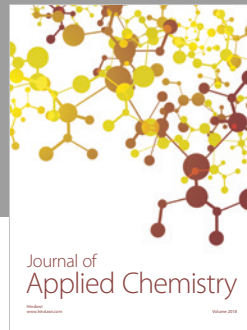
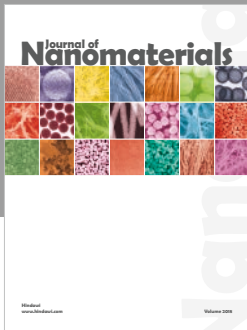
The supplementary materials contain experimental details, characterization data of all compounds, and copies of ^1H and ^{13}C NMR spectra and low mass. (*Supplementary Materials*)

References

- [1] T. Kondo, Y. U. Kimura, H. Yamada, and A. Toshimitsu, "Ruthenium-based catalysts for aerobic oxidation of alcohols: transition metal catalysis in aerobic alcohol oxidation," in *Green Chemistry Series*, F. Cardona and C. Parmeggiani, Eds., pp. 70–91, Royal Society of Chemistry, London, U.K, 2014.
- [2] G. N. I. Rapenne, "Synthesis of technomimetic molecules: towards rotation control in single-molecular machines and motors," *Organic & Biomolecular Chemistry*, vol. 3, no. 7, pp. 1165–1169, 2005.
- [3] H. Miyamura, R. Matsubara, Y. Miyazaki, and S. Kobayashi, "Aerobic oxidation of alcohols at room temperature and atmospheric conditions catalyzed by reusable gold nanoclusters stabilized by the benzene rings of polystyrene derivatives," *Angewandte Chemie International Edition*, vol. 46, no. 22, pp. 4151–4154, 2007.
- [4] Y. M. A. Yamada, T. Arakawa, H. Hocke, and Y. Uozumi, "A nanoplatinum catalyst for aerobic oxidation of alcohols in water," *Angewandte Chemie International Edition*, vol. 46, no. 5, pp. 704–706, 2007.
- [5] K. Yamaguchi and N. Mizuno, "Supported ruthenium catalyst for the heterogeneous oxidation of alcohols with molecular oxygen," *Angewandte Chemie International Edition*, vol. 41, no. 23, pp. 4538–4542, 2002.

- [6] S. Mori, M. Takubo, K. Makida et al., "A simple and efficient oxidation of alcohols with ruthenium on carbon," *Chemical Communications*, no. 34, pp. 5159–5161, 2009.
- [7] K. Mori, K. Yamaguchi, T. Hara, T. Mizugaki, K. Ebitani, and K. Kaneda, "Controlled synthesis of hydroxyapatite-supported palladium complexes as highly efficient heterogeneous catalysts," *Journal of the American Chemical Society*, vol. 124, no. 39, pp. 11572–11573, 2002.
- [8] K. Mori, T. Hara, T. Mizugaki, K. Ebitani, and K. Kaneda, "Hydroxyapatite-supported palladium nanoclusters: a highly active heterogeneous catalyst for selective oxidation of alcohols by use of molecular oxygen," *Journal of the American Chemical Society*, vol. 126, no. 34, pp. 10657–10666, 2004.
- [9] D. I. Enache, J. K. Edwards, P. Landon et al., "Solvent-free oxidation of primary alcohols to aldehydes using Au-Pd/TiO₂ catalysts," *Science*, vol. 311, no. 5759, pp. 362–365, 2006.
- [10] T. Matsumoto, M. Ueno, N. Wang, and S. Kobayashi, "Immobilization of ruthenium in organic-inorganic hybrid copolymers: a reusable heterogeneous catalyst for oxidation of alcohols with molecular oxygen," *Chemistry—An Asian Journal*, vol. 3, no. 2, pp. 239–243, 2008.
- [11] T. Mallat and A. Baiker, "Oxidation of alcohols with molecular oxygen on solid catalysts," *Chemical Reviews*, vol. 104, no. 6, pp. 3037–3058, 2004.
- [12] T. Matsumoto, M. Ueno, N. Wang, and S. Kobayashi, "Recent advances in immobilized metal catalysts for environmentally benign oxidation of alcohols," *Chemistry—An Asian Journal*, vol. 3, no. 2, pp. 196–214, 2008.
- [13] A. Carella, J.-P. Launay, R. Poteau, and G. Rapenne, "Synthesis and reactivity of [Penta(4-halogenophenyl)cyclopentadienyl][hydrotris(indazolyl)borato]ruthenium(II) complexes: rotation-induced fosbury flop in an organometallic molecular turnstile," *Chemistry—A European Journal*, vol. 14, no. 27, pp. 8147–8156, 2008.
- [14] F. Chiaravalloti, L. Gross, K.-H. Rieder et al., "A rack-and-pinion device at the molecular scale," *Nature Materials*, vol. 6, no. 1, pp. 30–33, 2007.
- [15] M. Hronec, Z. Cveňgrošová, and J. Kizlink, "Competitive oxidation of alcohols in aqueous phase using Pd/C catalyst," *Journal of Molecular Catalysis*, vol. 83, no. 1–2, pp. 75–82, 1993.
- [16] T. Mallat and A. Baiker, "Oxidation of alcohols with molecular oxygen on platinum metal catalysts in aqueous solutions," *Catalysis Today*, vol. 19, no. 2, pp. 247–283, 1994.
- [17] H. Rhee, G. An, M. Lim, and K.-S. Chun, "Environmentally benign oxidation reaction of benzylic and allylic alcohols to carbonyl compounds using Pd/C with sodium borohydride," *Synlett*, vol. 2007, no. 1, pp. 0095–0098, 2007.
- [18] C. Brönnimann, Z. Bodnar, R. Aeschmann, T. Mallat, and A. Baiker, "Platinum catalysts modified by adsorbed amines: a new method of enhancing rate and selectivity of sorbose oxidation," *Journal of Catalysis*, vol. 161, no. 2, pp. 720–729, 1996.
- [19] T. Mallat, C. Brönnimann, and A. Baiker, "Modification of supported Pt catalysts by preadsorbed phosphines: enhanced selectivity in the oxidation of sorbose," *Applied Catalysis A: General*, vol. 149, no. 1, pp. 103–112, 1997.
- [20] P. Korovchenko, C. Donze, P. Gallezot, and M. Besson, "Oxidation of primary alcohols with air on carbon-supported platinum catalysts for the synthesis of aldehydes or acids," *Catalysis Today*, vol. 121, no. 1–2, pp. 13–21, 2007.
- [21] C. Donze, P. Korovchenko, P. Gallezot, and M. Besson, "Aerobic selective oxidation of (hetero)aromatic primary alcohols to aldehydes or carboxylic acids over carbon supported platinum," *Applied Catalysis B: Environmental*, vol. 70, no. 1–4, pp. 621–629, 2007.
- [22] M. Lopp, I. Reile, A. Paju, M. Eek, and T. Pehk, "Aerobic oxidation of cyclopentane-1,2-diols to cyclopentane-1,2-diones on Pt/C catalyst," *Synlett*, vol. 3, pp. 347–350, 2008.
- [23] Y. H. Ng, S. Ikeda, T. Harada, Y. Morita, and M. Matsumura, "An efficient and reusable carbon-supported platinum catalyst for aerobic oxidation of alcohols in water," *Chemical Communications*, no. 27, pp. 3181–3183, 2008.
- [24] S. Carrettin, P. McMorn, P. Johnston, K. Griffin, and G. J. Hutchings, "Selective oxidation of glycerol to glyceric acid using a gold catalyst in aqueous sodium hydroxide," *Chemical Communications*, no. 7, pp. 696–697, 2002.
- [25] L. Prati and F. Porta, "Oxidation of alcohols and sugars using Au/C catalysts," *Applied Catalysis A: General*, vol. 291, no. 1–2, pp. 199–203, 2005.
- [26] M. Comotti, C. D. Pina, R. Matarrese, M. Rossi, and A. Siani, "Oxidation of alcohols and sugars using Au/C catalysts," *Applied Catalysis A: General*, vol. 291, no. 1–2, pp. 204–209, 2005.
- [27] N. Dimitratos, J. A. Lopez-Sanchez, D. Lennon, F. Porta, L. Prati, and A. Villa, "Effect of particle size on monometallic and bimetallic (Au,Pd)/C on the liquid phase oxidation of glycerol," *Catalysis Letters*, vol. 108, no. 3–4, pp. 147–153, 2006.
- [28] G. J. Hutchings, S. Carrettin, P. Landon et al., "New approaches to designing selective oxidation catalysts: Au/C a versatile catalyst," *Topics in Catalysis*, vol. 38, no. 4, pp. 223–230, 2006.
- [29] A. H. Begli, C. Baatz, N. Decker, U. Pruesse, and K.-D. Vorlop, PCT Int. Appl., WO2008095629A1, 2008.
- [30] Y. Önal, S. Schimpf, and P. Claus, "Structure sensitivity and kinetics of D-glucose oxidation to D-gluconic acid over carbon-supported gold catalysts," *Journal of Catalysis*, vol. 223, no. 1, pp. 122–133, 2004.
- [31] M. C. Jiménez, C. Dietrich-Buchecker, and J.-P. Sauvage, "Towards synthetic molecular muscles: contraction and stretching of a linear rotaxane dimer," *Angewandte Chemie*, vol. 39, no. 18, pp. 3284–3287, 2000.
- [32] M. Barboiu, G. Vaughan, N. Kyritsakas, and J.-M. Lehn, "Dynamic chemical devices: generation of reversible extension/contraction molecular motion by ion-triggered single/double helix interconversion," *Chemistry—A European Journal*, vol. 9, no. 3, pp. 763–769, 2003.
- [33] G. A. Molander and J. A. C. Romero, "Lanthanocene catalysts in selective organic synthesis," *Chemical Reviews*, vol. 102, no. 6, pp. 2161–2186, 2002.
- [34] Z. Hou and Y. Wakatsuki, *Science of Synthesis*, T. Imamoto and R. Noyori, Eds., Vol. 2, Thiem, Stuttgart, Germany, 2002.
- [35] Z. Hou and Y. Wakatsuki, "Recent developments in organo-lanthanide polymerization catalysts," *Coordination Chemistry Reviews*, vol. 231, no. 1–2, pp. 1–22, 2002.
- [36] G. A. Molander and E. D. Dowdy, "Lanthanide and group 3 metallocene catalysis in small molecule synthesis," *Lanthanides: Chemistry and Use in Organic Synthesis*, vol. 2, pp. 119–154, 1999.
- [37] H. Yasuda, "Organo rare earth metal catalysis for the living polymerizations of polar and nonpolar monomers," *Lanthanides: Chemistry and Use in Organic Synthesis*, vol. 2, pp. 255–283, 1999.
- [38] M. Ephritikhine, "Synthesis, structure, and reactions of hydride, borohydride, and aluminohydride compounds of the f-elements," *Chemical Reviews*, vol. 97, no. 6, pp. 2193–2242, 1997.

- [39] H. Schumann, J. A. Meese-Marktscheffel, and L. Esser, "Synthesis, structure, and reactivity of organometallic π -complexes of the rare earths in the oxidation state Ln^{3+} with aromatic ligands," *Chemical Reviews*, vol. 95, no. 4, pp. 865–986, 1995.
- [40] L. Grill, K.-H. Rieder, F. Moresco et al., "Rolling a single molecular wheel at the atomic scale," *Nature Nanotechnology*, vol. 2, no. 2, pp. 95–98, 2007.
- [41] M. Schmittel and P. Mal, "Towards technomimetic spoked wheels: dynamic hexakis-heteroleptic coordination at a hexakis-terpyridine scaffold," *Chemical Communications*, no. 8, pp. 960–962, 2008.
- [42] J. Gimeno, V. Cadierno, and P. Crochet, "Ruthenium-Catalyzed Isomerizations of Allylic and Propargylic Alcohols in Aqueous and Organic Media: Applications in Synthesis," *Synlett*, vol. 2008, no. 8, pp. 1105–1124, 2008.
- [43] G. Vives and J. M. Tour, "Synthesis of single-molecule nanocars," *Accounts of Chemical Research*, V. Cadierno, P. Crochet, J. Gimeno, *Synlett* 2008, vol. 42, no. 3, pp. 473–487, 2009.
- [44] C. Slugovc, E. Růba, R. Schmid, and K. Kirchner, "Improved efficiency of the ruthenium-catalyzed redox isomerization of allyl alcohols," *Organometallics*, vol. 18, no. 20, pp. 4230–4233, 1999.
- [45] A. Bouziane, B. Carboni, C. Bruneau, F. Carreaux, and J.-L. Renaud, "Pentamethylcyclopentadienyl ruthenium: an efficient catalyst for the redox isomerization of functionalized allylic alcohols into carbonyl compounds," *Tetrahedron*, vol. 64, no. 51, pp. 11745–11750, 2008.
- [46] A. J. A. Watson, A. C. Maxwell, and J. M. J. Williams, "Ruthenium-catalyzed aromatic C-H activation of benzylic alcohols via remote electronic activation," *Organic Letters*, vol. 12, no. 17, pp. 3856–3859, 2010.
- [47] B. M. Trost and R. J. Kulawiec, "A chemoselective internal redox of allyl alcohols to saturated aldehydes or ketones," *Tetrahedron Letters*, vol. 32, no. 26, pp. 3039–3042, 1991.
- [48] B. M. Trost and R. J. Kulawiec, "Chemoselectivity in the ruthenium-catalyzed redox isomerization of allyl alcohols," *Journal of the American Chemical Society*, vol. 115, no. 5, pp. 2027–2036, 1993.
- [49] R. C. van der Drift, M. Vailati, E. Bouwman, and E. Drent, "Two reactions of allylic alcohols catalysed by ruthenium cyclopentadienyl complexes with didentate phosphine ligands: isomerisation and ether formation," *Journal of Molecular Catalysis A: Chemical*, vol. 159, no. 2, pp. 163–177, 2000.
- [50] R. C. van der Drift, M. Gagliardo, H. Kooijman, A. L. Spek, E. Bouwman, and E. Drent, "Scope, mechanism and diene inhibition of isomerization of allylic alcohols to saturated ketones catalyzed by ruthenium(II)-cyclopentadienyl complexes," *Journal of Organometallic Chemistry*, vol. 690, no. 4, pp. 1044–1055, 2005.
- [51] A. J. Pearson and Y. Kwak, "A new method for the selective oxidation of allylic and benzylic alcohols," *Tetrahedron Letters*, vol. 46, no. 32, pp. 5417–5419, 2005.
- [52] G. B. Gardner, Y.-H. Kiang, S. Lee, A. Asgaonkar, and D. Venkataraman, "Exchange properties of the three-dimensional coordination compound $1,3,5\text{-Tris(4-ethynylbenzotrile)benzene}\cdot\text{AgO}_3\text{SCF}_3$," *Journal of the American Chemical Society*, vol. 118, no. 29, pp. 6946–6953, 1996.
- [53] J. W. Johnson, A. J. Jacobson, W. M. Butler, S. E. Rosenthal, J. F. Brody, and J. T. Lewandowski, "Molecular recognition of alcohols by layered compounds with alternating organic and inorganic layers," *Journal of the American Chemical Society*, vol. 111, no. 1, pp. 381–383, 1989.
- [54] Y.-H. Liu, H.-L. Tsai, Y.-L. Lu, Y.-S. Wen, J.-C. Wang, and K.-L. Lu, "Assembly of a robust, thermally stable porous cobalt(II) nicotinate framework based on a dicobalt carboxylate unit," *Inorganic Chemistry*, vol. 40, no. 25, pp. 6426–6431, 2001.
- [55] J. S. Xiang and P. L. Fuchs, "Mechanistic aspects of the CH alkynylation reaction of acetylenic triflones. Determination of phenyl versus cyclohexyl migratory aptitude for a vinylidene carbene," *Tetrahedron Letters*, vol. 37, no. 30, pp. 5269–5272, 1996.
- [56] M. E. Blake, K. L. Bartlett, and M. Jones, "Am-benzyne to o-benzyne conversion through a 1,2-shift of a phenyl group," *Journal of the American Chemical Society*, vol. 125, no. 21, pp. 6485–6490, 2003.
- [57] D. S. Mannel, M. S. Ahmed, T. W. Root, and S. S. Stahl, "Discovery of multicomponent heterogeneous catalysts via admixture screening: PdBiTe catalysts for aerobic oxidative esterification of primary alcohols," *Journal of the American Chemical Society*, vol. 139, no. 4, pp. 1690–1698, 2017.
- [58] R. Semwal, C. Ravi, R. Kumar, R. Meena, and S. Adimurthy, "Sodium salts (NaI/NaBr/NaCl) for the halogenation of imidazo-fused heterocycles," *The Journal of Organic Chemistry*, vol. 84, no. 2, pp. 792–805, 2019.
- [59] S. Kuwano, S. Harada, R. Oriez, and K.-I. Yamada, "Chemoselective conversion of α -unbranched aldehydes to amides, esters, and carboxylic acids by NHC-catalysis," *Chemical Communication*, vol. 48, no. 1, pp. 145–147, 2012.
- [60] I. Sho and H. Togo, "Synthetic utility of iodic acid in the oxidation of benzylic alcohols to aromatic aldehydes and ketones," *Tetrahedron*, vol. 72, no. 44, pp. 6948–6954, 2016.
- [61] Compounds are available from Aldrich-Sigma Chemical Co.



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