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Aqueous Phase C−H Bond Oxidation Reaction of Arylalkanes Catalyzed by a Water-Soluble Cationic Ru(III) Complex $[(\text{pymox-Me}_2)_2\text{RuCl}_2]^+\text{BF}_4^-$

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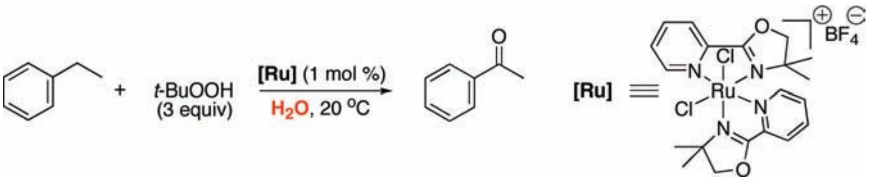
ABSTRACT



The cationic complex $[(\text{pymox-Me}_2)\text{RuCl}_2]^+\text{BF}_4^-$ was found to be a highly effective catalyst for the C−H bond oxidation reaction of arylalkanes in water. For example, the treatment of ethylbenzene (1.0 mmol) with *t*-BuOOH (3.0 mmol) and 1.0 mol % of the Ru catalyst in water (3 mL) cleanly produced PhCOCH_3 at room temperature. Both a large kinetic isotope effect ($k_H/k_D = 14$) and a relatively large Hammett value ($\rho = -1.1$) suggest a solvent-caged oxygen rebounding mechanism via a Ru(IV)-oxo intermediate species.

Aqueous phase homogeneous catalysis has emerged as an important tool for attaining new "green" chemical technology in both industrial and fine chemical processes.[1] Particular attention has been centered on the development of water-soluble metal catalysts for the C−H bond oxidation reactions, and in this regard, late transition metal complexes with nitrogen ligands have been shown to be effective for mediating catalytic oxidation of saturated hydrocarbons in protic media.[2] A number of chemoselective allylic and propargylic C−H bond oxidation and oxidative coupling reactions of amines have recently been achieved by using water-soluble dirhodium[3] and ruthenium[4] catalysts, respectively. Fukuzumi reported an efficient C−H bond oxidation of arylalkanes mediated by CAN/$[\text{Ru(tpa)(H}_2\text{O)}_2]^+$ system in aqueous media.[5] Li and co-workers devised a number of oxidative coupling reactions involving C−H bond activation in water.[6] Surface-modified heterogeneous ruthenium-hydroxo catalysts have also been found to mediate selective oxidation of benzylamines to arylamides in water.[7] Despite these recent advances, only a few well-defined synthetic metal catalysts have been shown to mediate aerobic C−H bond oxidation reactions in the aqueous phase, and considerable controversies still persist on the issues of reaction mechanisms and the nature of reactive species.

As part of an ongoing effort to develop ruthenium-catalyzed C−H bond activation reactions,[8] we initially screened several chelating nitrogen ligands to synthesize

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(1) Recent reviews and monographs: (a) Lindström, U. M. *Chem. Rev.* **2002**, *102*, 2751–2772. (b) *Aqueous-Phase Organometallic Catalysis*; Cornils, B., Herrmann, W. A., Eds.; Wiley-VCH: Weinheim, 2004. (c) *Multiphase Homogeneous Catalysis*; Cornils, B., Herrmann, W. A., Horváth, I. T., Leitner, W., Mecking, S., Olivier-Bourbigou, H., Vogt, D., Eds.; Wiley-VCH: Weinheim, 2005; Vol. 1. (d) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095–3165.

(2) (a) Sen, A.; Lin, M. *Chem. Commun.* **1992**, 508–510. (b) Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504–512. (c) Periana, R. A.; Taube, D. J.; Gamble, S.; Taube, H.; Satoh, T.; Fujii, H. *Science* **1998**, *280*, 560–564.

(3) (a) Choi, H.; Doyle, M. P. *Org. Lett.* **2007**, *9*, 5349–5352. (b) McLaughlin, E. C.; Doyle, M. P. *J. Org. Chem.* **2008**, *73*, 4317–4319.

(4) Murahashi, S.-I.; Zhang, D. *Chem. Soc. Rev.* **2008**, *37*, 1490–1501.

(5) Hirai, Y.; Kojima, T.; Mizutani, Y.; Shiota, Y.; Yoshizawa, K.; Fukuzumi, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 5772–5776.

(6) (a) Li, C.-J. *Acc. Chem. Res.* **2002**, *35*, 533–538. (b) Herrerías, C. I.; Yao, X.; Li, Z.; Li, C.-J. *Chem. Rev.* **2007**, *107*, 2546–2562.

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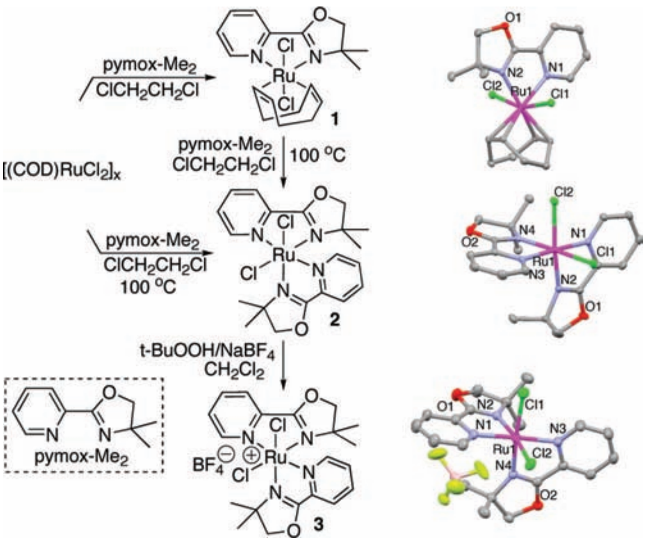
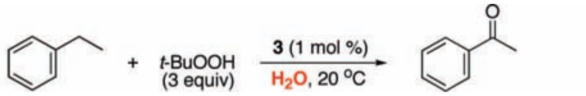
water-soluble ruthenium catalysts. Thus, the treatment of $[(COD)RuCl_2]_x$ with 1.2 equivalents of 4,4-dimethyl-2-(2-pyridyl)oxazoline (pymox-Me_2) ligand in 1,2-dichloroethane at 50 °C produced an orange-yellow colored complex (pymox-Me_2)Ru(COD)Cl_2 (**1**), which was isolated in 65% yield after recrystallization in *n*-hexanes/CH_2Cl_2 (Scheme 1).

Scheme 1



The treatment of **1** (0.4 mmol) with pymox-Me_2 (1.9 mmol) in 1,2-dichloroethane at 100 °C led to the isolation of a deep blue-purple colored complex (pymox-Me_2)$_2$RuCl_2 (**2**) in 55% yield. Alternatively, the complex **2** could be directly produced from the treatment of $[(COD)RuCl_2]_x$ with excess amount of pymox-Me_2 in 1,2-dichloroethane at 100 °C (65% yield).

The subsequent treatment of **2** with $NaBF_4$ and *t*-BuOOH in CH_2Cl_2 led to the cationic Ru(III) complex $[(\text{pymox-}Me_2)_2RuCl_2]^+BF_4^-$ (**3**) in 73% isolated yield. The structure of these ruthenium complexes was completely established by both spectroscopic and X-ray crystallographic methods. The molecular structure of both **2** and **3** showed an octahedral geometry with cis coordination of the chloride and anti pyridine ligands. The average Ru−Cl bond distance of the cationic Ru(III) complex **3** (2.33 Å) was found to be considerably shorter than the neutral complex **2** (2.41 Å). The magnetic moment of **3** ($\mu_{eff} = 1.55\ B_M$) as determined by using the Evans NMR method was also consistent with a paramagnetic Ru(III) complex.[9]

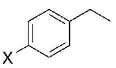
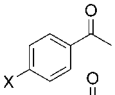
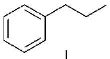
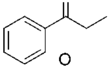
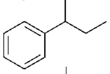
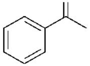
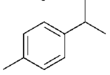
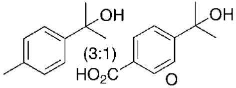
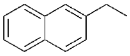
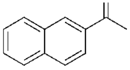
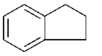
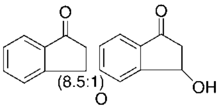
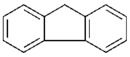
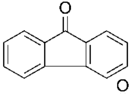
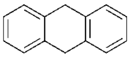
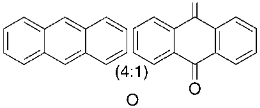
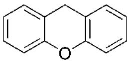
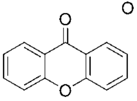
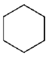
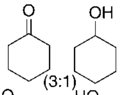
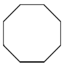
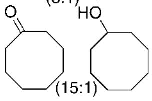


(1)

In a strikingly different reactivity pattern, only complex **3** was found to exhibit high catalytic activity for the C−H bond oxidation reaction in aqueous solution, even though both **2** and **3** are soluble in water. Thus, the treatment of ethylbenzene (1.0 mmol) with *t*-BuOOH (3 mmol, 70 wt % in aqueous solution) in the presence of 1 mol % of **3** in water (3 mL) cleanly produced $PhCOCH_3$ in >95% conversion within 16 h at room temperature (eq 1). Salient features of the catalyst **3** are that it retains significant activity after repeated runs (61% yield after third run), and it can be readily separated from the reaction mixture by simple extraction.

The scope of the oxidation reaction was surveyed by using **3** as the catalyst (Table 1). In general, the C−H bond oxidation of benzylic compounds occurred smoothly at room temperature to give the ketone products. The formation of C−C bond cleavage product for isobutylbenzene is reminiscent of the oxidation reaction promoted by transition metal complexes (entry 5), where benzyloxy radical species has

Table 1. Aqueous Phase C−H Bond Oxidation of Arylalkanes[a]

entry	substrate	product(s)	t (h)	convn (%)	yield (%)[b]
1		 X = H	16	95	83(90)
2		X = OMe	16	97	87(95)
3		X = Cl	16	87	77(83)
4			16	88	72(80)
5			24	56	41(47)
6			16	90	74(80)[c]
7			16	94	89(90)
8			2	>99	80(90)[d]
9[e]			2	93	86(92)
10[e]			2	>99	88(95)
11[e]			2	>99	87(95)
12			24	33	--(29)[f]
13			24	66	54(62)

[a] Reaction conditions: substrate (1.0 mmol), *t*-BuOOH (3.0 mmol, 70 wt % in water), **3** (1.0 mol %), H_2O (3 mL), 20−22 °C. [b] Isolated product yields. The GC product yields are listed in parenthesis. [c] Less than 5% of benzaldehyde derivative is formed. [d] Five percent of 1,3-indandione is formed. [e] Substrate was dissolved in 1 mL of CH_2Cl_2. [f] Products were not isolated due to low conversion and difficulty in separation.

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(8) (a) Yi, C. S.; Yun, S. Y. *J. Am. Chem. Soc.* **2005**, *127*, 17000–17006. (b) Yi, C. S.; Zhang, J. *Chem. Commun.* **2008**, 2349–2351.

(9) See the Supporting Information for experimental details.

been implicated for the C−C bond cleavage reactions of alkylbenzenes.[10] The oxidation of tertiary benzylic C−H bond is favored over the primary ones to give the alcohol product (entry 6). The dehydrogenation product was favored over the oxidation product for the 9,10-anthracene case (entry 10). The oxidation of cyclic alkanes was found to be sluggish, giving only modest conversions under the similar reaction conditions (entry 12, 13).

We performed the following experiments to gain further mechanistic insights on the oxidation reaction. (1) A very large kinetic isotope effect of $k_H/k_D = 14$ was obtained from the pseudo-first order plots of the oxidation reaction of ethylbenzene vs ethylbenzene-d_{10} at 20 °C ($k_{obs} = 2.1 \times 10^{-2}$ h^{-1} and 1.5×10^{-3} h^{-1}, respectively) (Figure S1, Supporting Information).[9] Such a large deuterium isotope effect has been rarely observed in C−H bond oxidation reactions mediated by synthetic metal catalysts, but more commonly observed in enzyme-catalyzed oxidation reactions where quantum mechanical tunneling effect has been ascribed to effect the rate-limiting C−H activation step.[11]

(2) The Hammett correlation of *para*-substituted ethylbenzene substrates p-X-$C_6H_4CH_2CH_3$ (X = OMe, CH_3, H, F, Cl) led to $\rho = -1.1$ (Figure 1). The observed ρ value is substantially higher than the oxidation reactions catalyzed by free radical species such as t-BuO• and t-BuOO• (ρ = −0.4 to −0.6), but somewhat lower than the ones catalyzed by $(PPh_3)_3RuCl_2$/t-BuOOH and cytochrome P-450 and their synthetic model systems ($\rho = -1.3$ to -1.6).[12] A relatively high -ρ value suggested of a substantial charge transfer from a metal-oxo species to the substrate during the C−H bond cleavage step.

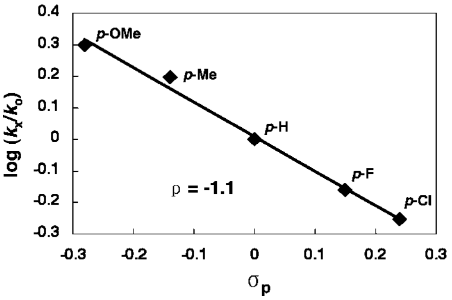

Figure 1. Hammett plot for the oxidation reaction of ρ-X-$C_6H_4CH_2CH_3$ (X = OMe, CH_3, H, F, Cl) in water.

(3) The initially inactive **2** became an active catalyst upon addition of $NaBF_4$ for the oxidation reaction. This fact and a relatively low Ru(II)/Ru(III) redox potential ($E_o = +0.22$ V) clearly indicate that the cationic Ru(III) complex is the catalytically active species for the oxidation reaction.[13] The observation of a strong metal-to-ligand charge transfer band at 360 nm (dp-π*) from the reaction mixture of **2** with t-BuOOH and $NaBF_4$ also supports the formation of a Ru(III) species (Figure S2, Supporting Information). These data are most consistent with a "solvent-caged" oxygen rebound mechanism of the rate-limiting C−H oxidation step from a Ru(IV)-oxo species.[12,13] The fact that a radical scavenger TEMPO (10 mol %) did not significantly affected the rate of the oxidation reaction also supports the notion of a solvent-caged mechanism.

In summary, the cationic Ru(III) complex **3** was found to be a highly effective catalyst for the benzylic C−H bond oxidation reaction in water. While high valent metal-oxo species have been invoked in both nonheme and Gif-type oxidations,[2b,14] catalytic C−H bond oxidation reactions mediated by well-defined Ru(III) complexes have been rarely reported.[13] Efforts are currently underway to extend the scope of the oxidation reaction as well as to establish the nature of reactive species.

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Supporting Information Available: Experimental procedures and crystallographic data of **1**, **2**, and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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