Catalytic Oxidation of Alcohols with Ru(Pybox)(Pydic) Complex

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Primary and secondary alcohols were catalytically oxidized with diacetoxyiodobenzene in the presence of Ru(Pybox)(Pydic) complex to afford the corresponding aldehydes and ketones in high yields.

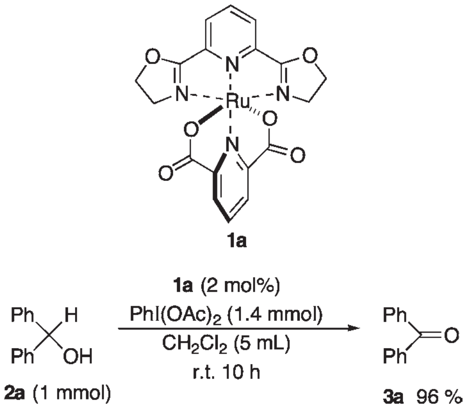
Attention has been paid for catalytic oxidation of alcohols as one of fundamental organic reactions and industrial processes under enduring efforts and consideration of efficiency and environmental consciousness.[1] Prominent successes in this direction has been recently achieved by utilization of hydroperoxide or molecular oxygen with an assistance of potent ruthenium complexes.[2,3] We disclose here an application of our epoxidation system for efficient oxidation procedure of alcohols to aldehydes or ketones since we have already reported a new epoxidation system for olefins with Ru(Pybox)(Pydic) (**1a**), ruthenium[bis(oxazolinylpyridine)-(pyridine-2,6-dicarboxylate)], and diacetoxyiodobenzene [PhI(OAc)$_2$].[4a]

Based on these previous studies, we initially applied our hydrogenperoxide oxidation of hydroxamic acid to nitroso intermediates with catalytic amount of **1a** for the oxidation of alcohols.[4b] This oxidation condition gave aldehydes and ketones up to 14–23% yields in the case of benzyl alcohol derivatives. And then we found that the addition of amines such as pyridine increased the yields slightly up to 40%. However, further optimization of the conditions shows no significant improvement on the oxidation of alcohols.

On the other hand, the use of PhI(OAc)$_2$ as an oxidant and catalytic amount of **1a** gave the corresponding products in high yields as well as high chemoselectivities.

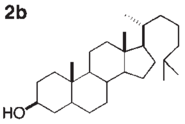
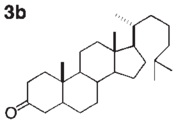
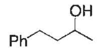
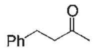
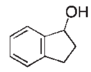
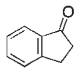
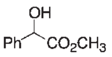
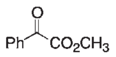
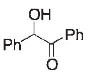
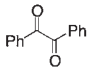
A typical procedure is as follows: To a solution of **1a** (0.02 mmol, 2 mol% to alcohol) and benzhydrol (**2a**) (1.0 mmol) in dichloromethane (5 mL) was added PhI(OAc)$_2$ (1.4 mmol) as an oxidant.[5] The mixture was stirred for 10 h at room temperature. After concentration, the residue was purified by column chromatography with ethyl acetate-hexane to give benzophenone (**3a**) in 96% yield (Scheme 1, Table 1, run 1). The oxidation of several alkyl and benzylic secondary alcohols **2b**–**j** is summarized in Table 1. Among them, 4-phenyl-2-butanol **2c**, mandelic ester **2e** and benzoin **2f** required relatively longer reaction times and an excess amount of the oxidant (run 3, 5–6).

A primary alcohol **2g**, 1-dodecanol, was readily oxidized for 6 h under catalytic condition to give dodecanal (**3g**) in 97% yield (run 7). Oxidation of benzyl alcohols **2h** and **2i** was carried out at room temperature to give the corresponding aldehydes in 74–76% yields along with the corresponding carboxylic acids as side products (run 8 and 9). In the case of cinnamyl alcohol, epoxidation of olefin skeleton proceeded, but it was much slower than the oxidation of hydroxyl groups (run 10).



Scheme 1.

Table 1. Catalytic oxidation of alcohols with Ru(Pybox)(Pydic) **1a**[a]

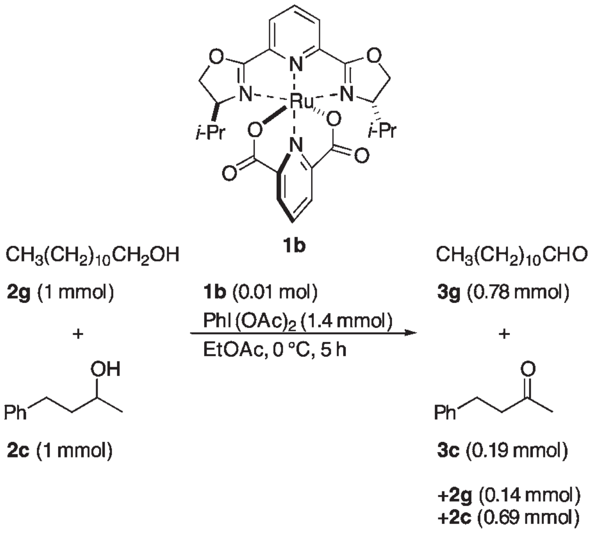
Alcohol		Product		Run	cat. **1a**		
					PhI(OAc)$_2$ /mmol	time /h	yield /%
2a	Ph_2CHOH	**3a**	$Ph_2C{=}O$	1	1.4	10	96
2b		**3b**		2	1.4	6	94
2c		**3c**		3	1.8	23	84
2d		**3d**		4	1.4	5	92
2e		**3e**		5	2.0	21	96
2f		**3f**		6	2.5	21	98
2g	$CH_3(CH_2)_{10}CH_2OH$	**3g**	$CH_3(CH_2)_{10}CHO$	7	1.4	6	97
2h	$4\text{-}CH_3OPhCH_2OH$	**3h**	$4\text{-}CH_3OPhCHO$	8	1.4	7	76[b]
2i	$4\text{-}BrPhCH_2OH$	**3i**	$4\text{-}BrPhCHO$	9	1.4	15	74[b]
2j	$PhCH{=}CHCH_2OH$	**3j**	$PhCH{=}CHCHO$	10	1.6	9	44[c, d]

[a] Alcohol (1.0 mmol), **1a** (0.02 mmol, 2 mol%), CH_2Cl_2(5 mL) at room temperature, isolated yields, unless otherwise noted. Conversion of alcohols were almost 100%. [b] The corresponding caboxylic acid was formed but not isolated. [c] The corresponding epoxide was formed in 15–20% yields, even at 0 °C. [d] The alcohol was recovered in ca. 20%.

In 1981, Müller and Gody reported catalytic oxidation of alcohols with PhIO in the presence of RuCl$_2$(PPh$_3$)$_3$ catalyst (1 mol%).[6a] In their system, 1-octanol was oxidized to 1-octanal in 45% with octanoic acid in 23%. They overcame the selectivity of the aldehyde by using PhI(OAc)$_2$ (1.3 equiv) in a short reaction time.

The similar and chiral Ru(Pybox-*i*-pr)(Pydic) complex **1b** (1 mol%) exhibited almost the same activity. The oxidation was carried out in ethyl acetate because of high solubility of **1b**.

Next, chemoselectivity between primary and secondary alcohols with **2g** and **2c** was examined by using **1b** at 0 °C (Scheme 2). Dodecanol **2g** was oxidized ca. four times faster than 4-phenyl-2-butanol **2c**. Similar selectivity for predominant oxidation of primary alcohols were reported with certain ruthenium complexes and co-oxidants, such as amine-N-oxide, molecular oxygen, peracids etc.[6b,d,i,j,q]



Scheme 2.

Thus we have demonstrated a new type of oxidation of alcohols with PhI(OAc)$_2$ and **1a**, which can be sufficiently applicable as a convenient synthetic protocol of oxidation of alcohols. In place of PhI(OAc)$_2$, other hypervalent iodo compounds such as PhIO can also be used as an oxidant. We are on the way of mechanistic investigation and isolation of higher valent active ruthenium species, and also kinetic resolution of secondary alcohol with **1b**.

Dedicated to Prof. Teruaki Mukaiyama on the occasion of his 75th birthday.

References and Notes

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