Catalytic Synthesis of α-Hydroxy Ketones Using Organic–Inorganic Hybrid Polymer

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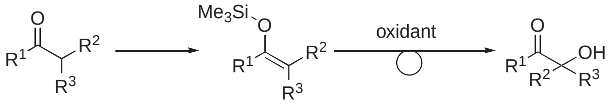
Oxidation of silyl enolates was found to be smoothly catalyzed by $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$ (bpy = 4,4′-bipyridine) under molecular oxygen, and provided the corresponding α-hydroxy carbonyl compounds in high yield. The insoluble organic–inorganic hybrid polymer was readily recovered by centrifugation after the completion of reaction, and the recovered catalyst could be reused.

The α-hydroxy carbonyl functionality is found in abundance in the realm of organic molecules, either derived from natural sources or generated as products of the chemical industry. Moreover, realization of the biological phenomenon regulated by an α-hydroxy carbonyl-derived hydrogen-bonding network has promoted the development of various techniques for preparing the fascinating functionality. Among the reported synthetic methods for preparing α-hydroxy carbonyls, the most widely used method would be a reaction of the silyl enolate of a ketone with organic peracids (Scheme 1).

Despite the availability of reliable peracid oxidant (e.g., *m*CPBA), these methods suffer from explosion and disposal issues associated with the co-production of acid (e.g. *meta*-chlorobenzoic acid). To circumvent these problems a number of techniques have been developed by employing dioxiranes, hypervalent iodines, ozone, and singlet oxygen.[1,2] A recent remarkable advance has made the oxidation possible using gasiform molecular oxygen and late transition metal catalysts.[3] Here, we report a new molecular oxygen-derived α-hydroxylation of silyl enolate which is catalyzed by an organic–inorganic hybrid polymer "$[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$ (bpy = 4,4′-bipyridine)."

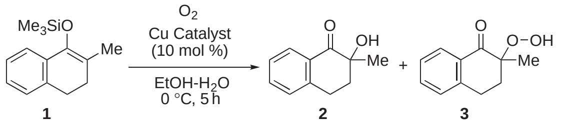
Initially, we screened the catalytic activity of various metal salts for the transformation of the trimethylsilyl enolate of 2-methyl-1-tetralone (**1**) to α-hydroxy ketone **2**. Among the metal salts we examined, $Cu(BF_4)_2$ showed good catalytic activity under an oxygen atmosphere to give the adduct **2** in 47% yield with co-production of α-hydroperoxy ketone (**3**) (Entry 1, Table 1).

The only detectable side product was the parent ketone, which would be produced by an acidic hydrolysis of silyl enolate **1**. To avoid the undesired hydrolysis the addition of pyridine in the reaction mixture was effective (Entry 2, Table 1). The Cu(II)–Py catalyst system prompted us to investigate the utilization of an organic–inorganic hybrid polymer "$[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$." The $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$, in which the position and orientation of the Cu atom and bpy are strictly controlled in atomic order, has been realized as a new type of gas adsorption/desorption material in the recent progress of gas storage chemistry.[4] The unique feature of gas adsorption might also be effective for the activation of gaseous small molecules. We were pleased to find the silyl enolate **1** was smoothly converted to the desired product **2** by $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$ under molecular oxygen, and provided the corresponding α-hydroxy carbonyl compound **2** in high yield (Entry 3, Table 1).



Scheme 1. Synthesis of α-hydroxy ketone.

Table 1. Cu(II)-catalyzed oxidation of Si-enolate



Entry	Cu Catalyst	Yield/%[b]
1	$Cu(BF_4)_2$	47
2	$Cu(BF_4)_2$–4Py	66
3[a]	$[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$	75

[a]Catalyst amount is based on the monomeric structure. [b]Combined yield of **2** and **3**.

For the α-hydroxylation catalyzed by $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$, the role of molecular oxygen as the oxidant was clearly proved by the production of α-hydroperoxy ketone **3** and the fact that negligible reaction occurred under argon.[5] The α-siloxy ketone reported in the bis(3-methyl-2,4-pentanedionato)nickel(II)-catalyzed reaction[3b] was not detected in the present Cu(II)-catalyzed reactions. Moreover, remarkable is the high catalyst activity of $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$ equal to or higher than that of a solution-phase catalyst. Generally, heterogeneous catalysis restricts an encounter of substrates with the catalyst, and results in a decline of the catalyst efficiency. The observed high catalytic activity in the present system may partly be attributed to the new reaction sphere constructed by the orderly arranged plural Cu atoms on the surface of $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$.

Encouraged by the success with the $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$-catalyzed synthesis of α-hydroxy ketone, the synthetic procedure was optimized for obtaining the desired α-hydroxy ketones, predominantly. Thus, the resulting crude mixture was treated with triethyl phosphite for reducing the α-hydroperoxy ketones.[6] In the optimized experimental procedure, not only the tetralones (**1**, **4**–**7**), but also various types of silyl enolates including acyclic substrate **10** were converted to the corresponding α-hydroperoxy ketones in good yield (Table 2). Noteworthy is the observation that the olefin functionality in the substrate was intact in the present oxidation even after 24 h reaction time (Entry 5, Table 2). In the reaction of **11**, the α-hydroxy ketone was obtained in 62% with a co-production of

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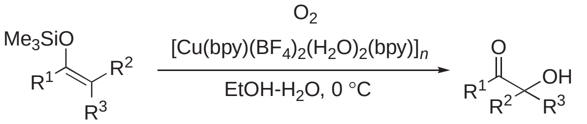
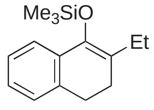
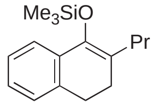
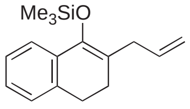
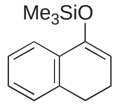
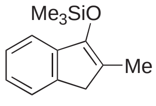
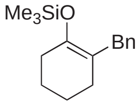
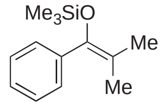
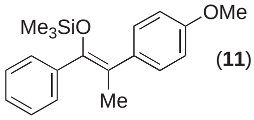
Table 2. $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$-catalyzed synthesis of various α-hydroxy ketones



Entry	Substrate		Catalyst Amount (mol %)[a]	Time/h	Yield/%[b]
1	**1**		10	4.5	85
2			1	24	74
3		(**4**)	10	5	81
4		(**5**)	10	5	84
5		(**6**)	10	24	72
6		(**7**)	10	4	32
7		(**8**)	10	5	68
8		(**9**)	10	13	60
9		(**10**)	10	24	79
10		(**11**)	10	18	62

[a]Catalyst amount is based on the monomeric structure. [b]Isolated yield after treatment with $P(OEt)_3$.

p-methoxyacetophenone (30%).

Furthermore, we examined the reuse of the insoluble organic–inorganic hybrid polymer. The recovery of the catalyst was readily performed by centrifugation under air, and it was revealed that the recovered catalyst could be recycled five times without significant loss of catalyst activity (Table 3). The use of molecular oxygen and a reusable catalyst, combine with a broadly applicable method that exhibits low toxicity, establishes this as clean, sustainable chemistry.

In summary, we have developed a Cu(II) ion containing organic–inorganic hybrid polymer-catalyzed synthesis of α-hydroxy ketones. Further studies on the application of the organic–inorganic hybrid polymer to other reactions are under progress.[7]

Table 3. Reuse of $[Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n$ catalyst

$$\mathbf{1} \xrightarrow[\text{EtOH-H}_2\text{O, 0 °C, 4.5 h}]{\substack{O_2 \\ [Cu(bpy)(BF_4)_2(H_2O)_2(bpy)]_n\ (10\ \text{mol}\ \%)^a}} \mathbf{2}$$

Run[b]	Yield/%[c]	Recovery of catalyst/%
1	85	98
2	82	96
3	82	95
4	80	95
5	80	94

[a]Catalyst amount is based on the monomeric structure. [b]Catalyst was recovered by centrifugation (3000 rpm for 3 min in 3 times each) after treatment with $P(OEt)_3$. [c]Isolated yield.

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