



First example of water-soluble transition-metal catalysts for Oppenauer-type oxidation of secondary alcohols

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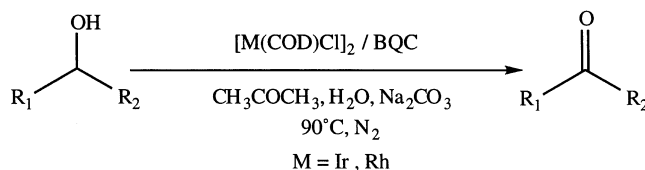
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Abstract—The first water-soluble transition-metal catalysts for Oppenauer-type oxidation of secondary alcohols have been developed. The catalytic system composed of $[\text{Ir}(\text{COD})\text{Cl}]_2$, 2,2'-biquinoline-4,4'-dicarboxylic acid dipotassium salt (BQC) and sodium carbonate is highly efficient for the selective oxidation of benzylic and aliphatic secondary alcohols to the corresponding ketones with catalyst/substrate ratios ranging from 0.4 to 2.5%. The substitution of $[\text{Ir}(\text{COD})\text{Cl}]_2$ by its rhodium analog $[\text{Rh}(\text{COD})\text{Cl}]_2$ generates a less active catalytic system. $[\text{Ir}(\text{COD})\text{Cl}]_2/\text{BQC}$ was also found to be more active than its water-insoluble analog system $[\text{Ir}(\text{COD})\text{Cl}]_2/2,2'$ -biquinoline (BC). © 2000 Elsevier Science Ltd. All rights reserved.

Catalyst recovery and recycling as well as product separation are still the most important and difficult problems of homogeneous catalysis, especially when application to industry is considered. High-temperature distillation, usually applied for separation, frequently leads to catalyst decomposition or at least significant deactivation. Aqueous organometallic catalysis has recently emerged as a very useful alternative technology to overcome these difficulties.¹ Water-soluble transition-metal complexes have been used as catalysts in several important processes.² Recently, we reported the discovery of a novel catalytic system consisting of $[\text{Rh}(\text{COD})\text{Cl}]_2/\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$ (TPPTS) which catalyzes efficiently the hydration of nitriles under basic conditions.³

The oxidation of alcohols to the corresponding carbonyl compounds is one of the most important reactions in organic synthesis. As a consequence due to the increasing demand for efficient and environmental friendly methods,⁴ numerous transition-metal-catalyzed oxidation reactions of alcohols have been developed.⁵ In this communication I am pleased to report the first water-soluble iridium and rhodium complexes containing 2,2'-biquinoline-4,4'-dicarboxylic acid dipotassium salt (BQC), which catalyze the oxidation of secondary alcohols with acetone as the oxidant (Scheme 1).⁶



Scheme 1.

A variety of catalytic systems based on different catalyst precursors and the water-soluble ligand $\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$ (TPPTS) or BQC were investigated for the oxidation of 1-phenylethanol, which was chosen as the model substrate. The first experiments showed that the presence of the catalyst precursor, acetone and sodium carbonate together is required to achieve the oxidation of 1-phenylethanol. While $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$ and $\text{PdCl}_2(\text{PhCN})_2$ exhibited no catalytic activity, $[\text{Rh}(\text{COD})\text{Cl}]_2$ and $[\text{Ir}(\text{COD})\text{Cl}]_2$ gave rise to active water-soluble systems (Table 1). The results shown in Table 1 indicate that the least active catalytic systems were provided by TPPTS (Table 1, entries 1 and 4). Treatment of 1-phenylethanol (2.5 mmol) in the presence of Na_2CO_3 (2.5 mmol) and catalytic amounts of $[\text{Rh}(\text{COD})\text{Cl}]_2$ (0.01 mmol) and BQC (0.15 mmol) in a deoxygenated mixture of water (10 mL) and acetone (5 mL) at 90°C selectively afforded acetophenone in 15% yield after 2 hours (Table 1, entry 2). An increase in the reaction time to 17 hours lead to 57% yield (Table 1, entry 3). A much more active catalyst was generated when $[\text{Rh}(\text{COD})\text{Cl}]_2$ was substituted by its iridium analog. Indeed, acetophenone was obtained in 82 and 98% yields, respectively, after 2 and 4 hours (Table 1,

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Table 1. Oxidation of 1-phenylethanol by acetone catalyzed with various catalytic systems^a

Entry	Catalyst precursor	Ligand	Time (h)	Yield (%) ^b
1	[Rh(COD)Cl] ₂	TPPTS	2	7
2	[Rh(COD)Cl] ₂	BQC	2	15
3	[Rh(COD)Cl] ₂	BQC	17	57
4	[Ir(COD)Cl] ₂	TPPTS	2	9
5	[Ir(COD)Cl] ₂	BQC	2	82
6	[Ir(COD)Cl] ₂	BQC	4	98 ^c
7 ^d	[Ir(COD)Cl] ₂	BQC	4	82
8 ^e	[Ir(COD)Cl] ₂	BQC	4	68
9 ^f	[Ir(COD)Cl] ₂	–	4	5
10 ^g	[Ir(COD)Cl] ₂	BQ	4	4
11 ^h	[Ir(COD)Cl] ₂	BQ	4	39

^a Reaction conditions: 1-phenylethanol (2.5 mmol), [M(COD)Cl]₂ (0.01 mmol), ligand (0.15 mmol), Na₂CO₃ (2.5 mmol), water (10 mL), acetone (5 mL), 90°C, N₂.

^b Yields refer to isolated ketones.

^c Full conversion of the substrate was obtained.

^d Second cycle of entry 6.⁷

^e Third cycle of entry 6.⁷

^f Reaction conditions: 1-phenylethanol (2.5 mmol), [Ir(COD)Cl]₂ (0.01 mmol), Na₂CO₃ (2.5 mmol), acetone (10 mL), 90°C, N₂.

^g The reaction conditions are the same as in entry 9 except that 2,2'-biquinoline (0.15 mmol) was added to the mixture.

^h The reaction conditions are the same as in entry 10 except that water (10 mL) was added to the mixture.

entries 5 and 6). Since one of the important aspects of aqueous-phase catalysis is the possibility of easily separating the catalyst from the reaction medium and recycling it in further experiments, the durability of the [Ir(COD)Cl]₂/BQC system was tested by carrying out three consecutive cycles with the same catalyst in aqueous solution, carefully separated from the organic phase under a nitrogen atmosphere at the end of each run (Table 1, entries 6–8).⁷ A slight decrease in the

catalytic activity was observed between each of the three recycling experiments demonstrating a good stability of the catalyst. It is relevant to point out that no metallic iridium formation was observed after the reactions and the aqueous phases remained clear-brown solutions, indicating no decomposition of the catalyst. When the oxidation was performed with [Ir(COD)Cl]₂ alone or combined with 2,2'-biquinoline (BC) in acetone containing only 0.5% water very low yields were obtained (Table 1, entries 9 and 10). Addition of water (10 mL) increased the rate of oxidation and acetophenone was isolated in 39% yield (Table 1, entry 11). A similar positive effect of water on the rate of homogeneous Oppenauer-type oxidation has already been observed for RuCl₂(PPh₃)₃.^{5a} These results which demonstrate the superiority of aqueous-phase catalysis over the homogeneous one in this Oppenauer-type oxidation are even more interesting since BQC is cheaper than 2,2'-biquinoline (BC).⁸

To demonstrate the efficiency of the [Ir(COD)Cl]₂/BQC system, a range of different alcohols were subjected to oxidation by acetone in a batch autoclave experiment (Table 2).⁹ The highest yields with full conversions, in most cases, were obtained when benzylic alcohols were used as starting materials (Table 2, entries 1–7). The catalytic system was also effective for the oxidation of aliphatic alcohols. However, higher catalyst/substrate ratios (2.5 mol%) and longer reaction times are needed (Table 2, entries 9–16). Cyclooctanol showed higher reactivity than cyclohexanol and was oxidized in 76% yield with only 0.4 mol% of [Ir(COD)Cl]₂ after 4 hours (Table 1, entry 8).

In conclusion, the first water-soluble transition-metal-catalyzed oxidation of secondary alcohols with acetone has been revealed. The system composed of [Ir(COD)Cl]₂ and the cheap water-soluble ligand 2,2'-

Table 2. Oxidation of different alcohols by acetone using water-soluble [Ir(COD)Cl]₂/BQC as the catalyst^a

Run	Substrate	Time (h)	Product	Yield (%) ^b
1	1-Phenylethanol	4	Acetophenone	98 ^c
2	1-Phenyl-1-propanol	4	Propiophenone	80
3	1-(4-Methoxyphenyl)ethanol	4	4'-Methoxyacetophenone	96 ^c
4	1-(4-Bromophenyl)ethanol	4	4'-Bromoacetophenone	90
5	1-Tetralol	4	1-Tetralone	97 ^c
6	9-Hydroxyfluorene	4	9-Fluorenone	96 ^c
7	Benzhydrol	4	Benzophenone	90
8	Cyclooctanol	4	Cyclooctanone	76
9	Cyclohexanol	4	Cyclohexanone	15
10	Cyclohexanol	17	Cyclohexanone	25
11 ^d	Cyclohexanol	17	Cyclohexanone	80
12	2-Octanol	4	2-Octanone	21
13	2-Octanol	17	2-Octanone	31
14	2-Decanol	4	2-Decanone	21
15	2-Decanol	4	2-Decanone	30
16 ^d	2-Decanol	4	2-Decanone	91

^a Unless otherwise stated, the reaction conditions are: substrate (2.5 mmol), [Ir(COD)Cl]₂ (0.01 mmol), BQC (0.15 mmol), Na₂CO₃ (2.5 mmol), water (10 mL), acetone (5 mL), 90°C, N₂.

^b Yields refer to isolated ketones.

^c Full conversion of the substrate was obtained.

^d Substrate (1 mmol), [Ir(COD)Cl]₂ (0.025 mmol) and BQC (0.375 mmol).

biquinoline-4,4'-dicarboxylic acid dipotassium salt (BQC) catalyzes the oxidation of secondary benzylic and aliphatic alcohols selectively and efficiently. The system is much more reactive than the water-insoluble analogs. I am currently examining the scope of this catalytic system using various substrates. Attempts to improve the catalyst recycling and a study of the oxidation mechanism are currently in progress.

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- The aqueous phase obtained after removal of solvents was re-used with a fresh charge of a solution of the alcohol (2.5 mmol) in degassed acetone (5 mL).
- From Aldrich Chemical Co., BQC and 2,2'-biquinoline cost 4166.7 and 5854.12 Canadian dollars per mole, respectively.
- Typical procedure for the oxidation of alcohols: In a glass liner of a 45 mL autoclave and under an atmosphere of nitrogen, [Ir(COD)Cl]₂ (0.01 mmol), BQC (0.15 mmol) and Na₂CO₃ (2.5 mmol) were dissolved in degassed water (10 mL) at room temperature. Then a solution of the substrate (2.5 mmol) in degassed acetone (5 mL) was introduced. The autoclave was flushed several times with 80 psi of N₂ and then was placed in an oil bath at 90°C for the required reaction time. The autoclave was cooled to room temperature and the mixture was extracted three times with degassed diethylether (20 mL). The combined organic layers were dried (MgSO₄) and then evaporated. The crude was analyzed by ¹H NMR¹⁰ before purification by silica gel chromatography using ethyl acetate/petroleum ether as the eluant.
- The ¹H NMR spectra of all the samples show the presence of only three compounds: the remaining substrate (where the conversions are not complete), the product and small amounts of 4-hydroxy-4-methyl-2-pentanone formed by aldol condensation of acetone.