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Cp*Ir Complexes Bearing N-Heterocyclic Carbene Ligands as Effective Catalysts for Oppenauer-Type Oxidation of Alcohols

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*Summary: The catalytic activity of Cp*Ir complexes in the Oppenauer-type oxidation of alcohols was considerably enhanced by introduction of N-heterocyclic carbene (NHC) ligands. High turnover numbers (up to 950) were achieved in the oxidation of secondary alcohols.*

Recently, there has been considerable effort devoted to the studies on transition-metal complexes with N-heterocyclic carbene (NHC) ligands, and their intriguing catalytic activities in organic reactions have been rapidly disclosed.[1,2] NHC ligands possess strong σ-donating properties with negligible π-back-bonding, and they have shown great promise of effective and environmentally benign ligands which could replace the commonly used tertiary phosphines. While a large number of reports on the synthesis and catalytic application of NHC palladium and ruthenium complexes have appeared,[2] NHC complexes of iridium have been relatively unexplored.[3,4]

Meanwhile, development of oxidation reactions of organic compounds in an environmentally benign fashion has attracted considerable attention. Thus, several transition-metal-catalyzed systems for oxidation of alcohols using oxygen or hydrogen peroxide as an oxidant have been reported very recently.[5] Oppenauer-type oxidation of alcohols is another promising method for oxidation of alcohols, because the non-noxious acetone can be used as an oxidant. Some transition-metal-catalyzed systems for Oppenauer-type oxidation have been reported;[6,7] however, a highly effective system has rarely been realized.[7] We have recently reported the prominent catalytic activity of Cp*Ir complexes (Cp* = η^5-pentamethylcyclopentadienyl) in hydrogen transfer reactions[8] and have examined the Oppenauer-type oxidation of alcohols catalyzed by $[\mathrm{Cp^*IrCl_2}]_2$ (**1**).[8a,9] However, the catalytic activity of **1** was unsatisfactory, since the turnover number (TON) of the reaction was less than 200. To improve the activity of the Cp*Ir catalyst, we planned to introduce fine-tunable ligands on the catalyst and found a considerable enhancement of the catalytic activity by introduction of NHC ligands. In this paper, we report the synthesis of new Cp*Ir NHC complexes and their high catalytic activity in Oppenauer-type oxidation of alcohols.

Treatment of $[\mathrm{Cp^*IrCl_2}]_2$ (**1**) with 2 equiv of the imidazol-2-ylidene (NHC) ligands **2a**−**c** gave Cp*Ir(L)-$\mathrm{Cl_2}$ (**3a**−**c**; L = NHC ligand) as air-stable crystals in 79, 49, and 73% yields, respectively (Scheme 1).[10] The structures of **3a**−**c** were elucidated by their spectral data (see the Supporting Information). Treatment of **3a**−**c** with 2 equiv of AgOTf followed by acetonitrile gave the dicationic complexes $[\mathrm{Cp^*Ir(L)(MeCN)_2}]^{2+}$ (**4a**−**c**) as air-stable crystals in 84, 61, and 59% yields, respectively. Complex **3a** could be also converted into

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(10) Full details of the syntheses and structures of the complexes **3**−**5** will be reported in due course.

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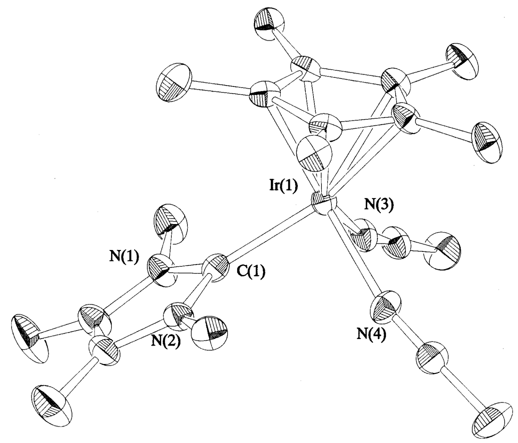


Figure 1. ORTEP drawing of the cation part of **4a**. Hydrogen atoms are omitted for clarity. Selected bond distances (Å): Ir(1)−C(1) = 2.055(8); Ir(1)−N(3) = 2.088(7); Ir(1)−N(4) = 2.060(7); C(1)−N(1) = 1.364(9); C(1)−N(2) = 1.347(9).

Scheme 1

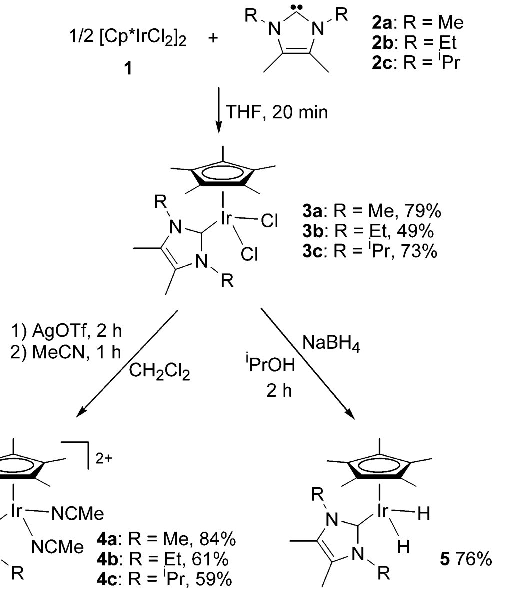
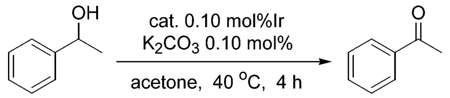


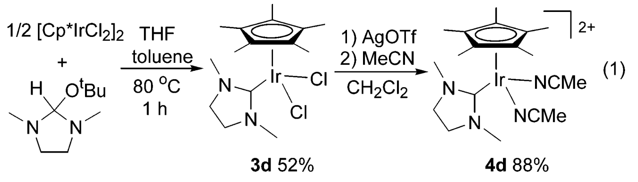
Table 1. Oxidation of 1-Phenylethanol to Acetophenone Catalyzed by Various Cp*Ir Complexes[a]



entry	cat.	conversn (%)	yield (%)	TON
1	**1**	48	43	430
2	**3a**	3	1	10
3	**3a**[b]	95	92	920
4	**4a**	95	95	950
5	**4a**[c]	88	85	850
6	**4b**	92	91	910
7	**4c**	29	20	200
8	**4d**	87	85	850
9	**5**	4	0	0
10	**6**	8	1	10

[a] Conditions: 1-phenylethanol (20 mmol), catalyst (0.020 mmol), K_2CO_3 (0.020 mmol), acetone (16 mL), 40 °C, 4 h. The conversion and yield were determined by GC. [b] AgOTf (0.045 mmol) was added. [c] Et_3N (0.020 mmol) was used instead of K_2CO_3.

the dihydrido complex Cp*Ir(L)H_2 (**5**; L = **2a**) in 76% yield by a reaction with excess $NaBH_4$. The structure of **4a** was confirmed by an X-ray diffraction study.[11] The ORTEP diagram is shown in Figure 1. Cp*, the NHC ligand, and two molecules of MeCN are attached to the iridium center. The iridium−carbene carbon bond distance (Ir(1)−C(1)) is 2.055(8) Å. The geometry around the iridium center could be described as a three-legged piano stool, which is common in Cp^*Ir^{III} complexes. The saturated analogous Cp*Ir complex **3d**, bearing the 4,5-dihydroimidazol-2-ylidene ligand **2d**, was prepared by the reaction of **1** with 2-*tert*-butoxy-4,5-dihydroimidazole generated from 1,3-dimethyl-4,5-dihydroimidazolium tetrafluoroborate and KO^{t}Bu,[12] and transformation into the dicationic complex **4d** was also carried out (eq 1).



With a series of new Cp*Ir NHC complexes in hand, we next examined the Oppenauer-type oxidation of 1-phenylethanol to acetophenone in the presence of a catalytic amount (0.10 mol % Ir) of complexes **3**−**5** and other Cp*Ir complexes at 40 °C for 4 h. The results are summarized in Table 1. $[Cp^*IrCl_2]_2$ (**1**) showed some catalytic activity to give acetophenone in 43% yield (entry 1). While the neutral complex **3a** showed almost no catalytic activity (entry 2), addition of AgOTf considerably improved the yield to 92% (entry 3). The dicationic complex **4a** showed very high activity to give the product in 95% yield (entry 4). Triethylamine could be used as a base instead of K_2CO_3, although the yield was slightly decreased (entry 5). As the steric bulkiness of the N substituent in the NHC ligand increased, the catalytic activity was lowered (entries 4, 6, and 7). The complex **4d**, bearing 4,5-dihydroimidazol-2-ylidene ligand, showed activity slightly lower than that of **4a** (entry 8). Reaction with the dihydrido complex **5** as a catalyst was also examined; however, no reaction was observed (entry 9), suggesting no incorporation of dihydride species in the catalytic cycle. The dicationic phosphine complex $[Cp^*Ir(PBu_3)(MeCN)_2][OTf]_2$ (**6**),[13] isoelectronic with **4**, showed almost no catalytic activity (entry 10), indicating that strong σ-donating ability and/or reduced steric requirements of the NHC ligand are essential to enhance the catalytic activity.

Time-resolved reaction profiles for the oxidation of 1-phenylethanol to acetophenone catalyzed by **1** and **4a**

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[11] X-ray crystallographic analysis was performed with a Rigaku AFC-5S diffractometer. Crystal data: $C_{23}H_{33}F_6N_4O_6S_2Ir$, fw = 831.87, crystal size 0.30 × 0.30 × 0.50 mm^3, monoclinic, $P2_1/c$, $Z = 4$, a = 9.055(2) Å, b = 21.448(2) Å, c = 16.176(1) Å, β = 91.865(9)°, V = 3140.1(5) Å^3, D_{calcd} = 1.759 g cm^{-3}, T = 203 K, $F(000)$ = 1640, Mo Kα radiation (λ = 0.710 69 Å), μ = 44.74 cm^{-1}, 7841 reflections measured ($2\theta_{max}$ = 55.0°), 7391 unique (R_{int} = 0.022). The structure was refined by using full-matrix least squares on F to R = 0.042 and R_w = 0.046, with a goodness of fit of 1.75 for 4755 reflections ($I > 3\sigma(I)$) and 379 variable parameters.

[12] Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.

[13] The complex **6** was prepared by the reaction of $[Cp^*IrCl_2]_2$ (**1**) with PBu_3 and AgOTf (see the Supporting Information).

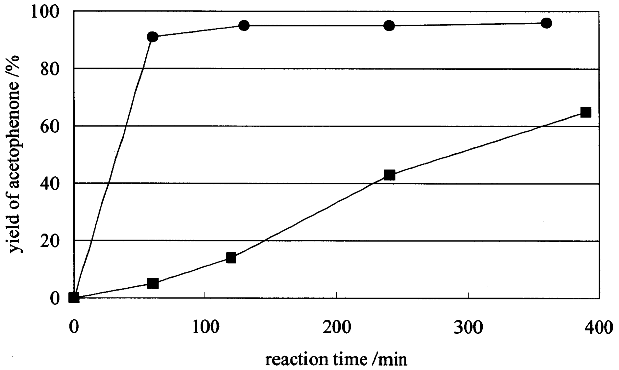


Figure 2. Time-resolved reaction profiles observed for the oxidation of 1-phenylethanol catalyzed by **1** (■) and **4a** (●). Reactions were carried out as shown in footnote *a* of Table 1.

Table 2. Oxidation of Secondary Alcohols to Ketones Catalyzed by 4a[a]

entry	alcohol	time	conversn (%)	yield (%)	TON
1	1-phenylethanol	4	95	95	950
2	cyclopentanol	4	91	90	900
3[b]	cyclohexanol	4	58	56	560
4[b]	1-indanol	4	91	81	810
5	2-octanol	7	78	76	760

[a] Conditions: secondary alcohol (20 mmol), catalyst **4a** (0.020 mmol), K_2CO_3 (0.020 mmol), acetone (16 mL), 40 °C. The conversion and yield were determined by GC. [b] Et_3N (0.020 mmol) was used instead of K_2CO_3.

Table 3. Oxidation of Primary Alcohols to Aldehydes Catalyzed by 4a[a]

entry	alcohol	time	conversn (%)	yield (%)	TON
1	benzyl alcohol	4	89	86	172
2[b]	4-methoxybenzyl alcohol	2	98	98	196
3	4-chlorobenzyl alcohol	4	76	75	150
4	1-octanol	6	57	54	108

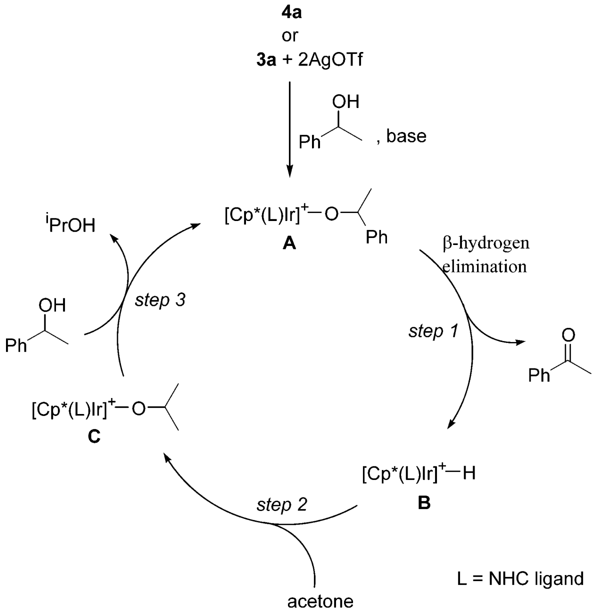
[a] Conditions: primary alcohol (2.0 mmol), catalyst **4a** (0.010 mmol), K_2CO_3 (0.010 mmol), acetone (60 mL), 40 °C. The conversion and yield were determined by GC. [b] Et_3N (0.010 mmol) was used instead of K_2CO_3.

are shown in Figure 2. In the case of catalyst **4a**, the turnover number (TON) after 1 h was 910, in contrast to TON = 50 in the case of **1**, indicating 18 times greater catalytic activity of **4a** compared to **1** in the first 1 h.

To evaluate the catalytic activity of **4a**, we examined the scope of the reaction with several substrates. Results of oxidation of secondary alcohols to the corresponding ketones are summarized in Table 2. Oxidation of 1-phenylethanol, cyclopentanol, 1-indanol, and 2-octanol gave ketones with high TONs (entries 1, 2, 4, and 5). Oxidation of cyclohexanol gave cyclohexanone in rather lower yield (entry 3), showing a tendency similar to that observed in the reaction catalyzed by **1**.[8a]

The oxidation of primary alcohols was also examined. Results are summarized in Table 3. Although a larger amount of catalyst (0.50 mol %Ir) and acetone were required, oxidation of primary alcohols proceeded in reasonable yields.

Scheme 2 Possible Mechanism for Oppenauer-Type Oxidation of 1-Phenylethanol Catalyzed by Cp*Ir NHC Complexes



A possible mechanism for the oxidation of 1-phenylethanol catalyzed by the Cp*Ir NHC complex is shown in Scheme 2. The initial step of the reaction would involve the formation of the iridium alkoxide **A** by the reaction of catalyst precursor **4a** with 1-phenylethanol and base (K_2CO_3 or Et_3N). Then, acetophenone and the iridium hydride **B** would be formed by β-hydrogen elimination (step 1). Insertion of acetone into the iridium−hydride bond to give the iridium isopropoxide **C** (step 2) followed by alkoxy exchange would occur to regenerate the catalytically active species **A** (step 3). This mechanism is closely related to the one we have reported for the Oppenauer-type oxidation catalyzed by $[Cp^*IrCl_2]_2$ (**1**).[8a] The observed enhancement of the catalytic activity by introduction of NHC ligands can possibly be attributed to the increased nucleophilicity of the iridium hydride **B**, since NHC ligands are better electron donors. This characteristic would lead to a more facile interaction with acetone.

In summary, an efficient system for Oppenauer-type oxidation of primary and secondary alcohols catalyzed by Cp*Ir NHC complexes has been developed using acetone as an oxidant. High turnover numbers (up to 950) were achieved in the oxidation of secondary alcohols by use of NHC ligands. Further details of the synthesis and structures of complexes **3**−**5** and the scope and limitation of the present catalytic oxidation will be reported in due course.

Supporting Information Available: Text giving experimental procedures and characterization data for the products obtained and CIF files giving crystallographic data for **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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