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Oxidation Catalysis in Air with Cp*Ir: Influence of Added Ligands and Reaction Conditions on Catalytic Activity and Stability

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We describe the systematic evaluation of Cp*Ir catalysts for the aerobic oxidation of alcohols. Our results demonstrate turnover numbers up to 270 per $[Cp*IrCl_2]_2$ which have not been previously achieved for this reaction. Using air as the sole oxidant under base-free conditions, the effects of solvent systems and additives on the catalytic activity are documented systematically. We further elucidate the role of additives in catalyst decomposition processes and establish a novel buffer system which results in significant catalyst stabilization upon prolonged reaction times.

Introduction

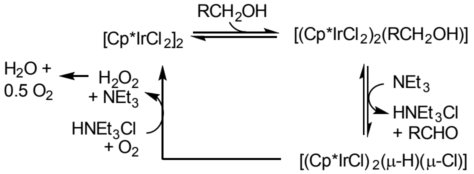
Cp*Ir complexes have received considerable attention lately as catalyst precursors for reactions relevant to sustainable energy and green chemistry: water oxidation,[1] O_2 reduction,[2] H_2 activation,[3] CO_2 hydrogenation,[4],[5] formic acid decomposition,[5] acceptorless dehydrogenation,[6] ammonia alkylation with alcohols,[7] transfer (de)hydrogenation,[6a,8] and C-H activation.[9] The majority of these reactions are oxidation/reduction reactions, and as such the use of sustainable reductants and oxidants (i.e., H_2 and O_2) is an important goal for the development of green catalytic methodologies.[2]

Studying Cp*Ir complexes as oxidation catalysts has so far mainly focused on reactions in the presence of strong oxidants[10] or on alcohol dehydrogenation reactions which produce H_2 as side product.[6,11] Catalysis with strong oxidants is often not well-defined, as ligand oxidation and subsequent ligand loss can occur, leading to nanoparticles which can also be catalytically active.[10b] Dehydrogenative catalysis, on the other hand, suffers from the drawback that it needs to be performed under conditions that successfully drive off H_2; as such, high temperatures are inherently necessary in these reactions to provide a thermodynamic driving force. In contrast to dehydrogenative Cp*Ir catalysis, aerobic oxidations have in principle the potential to enable mild catalytic conditions due to the higher thermodynamic driving force of oxidative reactions. Additionally, excellent atom economies can be realized with H_2O as the only by-product of catalysis. Furthermore, ligand decomposition can be expected to be less problematic than with other oxidants, since O_2 is a kinetically hindered oxidant.

Despite these interesting features of aerobic oxidations and recent advances that elucidate stoichiometric reactions of O_2 with organometallic Ir complexes,[2,12] Cp*Ir catalysts in reactions with O_2 are rather rare. Few reports of O_2 coupled catalysis using Cp*Ir complexes have been published[13,14] and all of them exhibit fundamental drawbacks: high catalyst loadings (5-10 mol % [Ir]) indicating significant catalyst decomposition or low efficiencies of the used catalysts, stoichiometric amounts of strong bases (KO^tBu, NEt_3, Na_2CO_3), or a large excess of O_2 as oxidant (open-flask, air balloon, pure O_2 gas). The latter issue is particularly important when considering large scale aerobic oxidation reactions, as an excess of O_2 in the presence of large amounts of organic solvent constitutes a considerable explosion hazard.[15] The role of ancillary ligands in these Cp*Ir catalyst systems is not well understood, as they exhibit a wide variety of structural differences (no ligands vs. bidentate N,N/C,N ligands; secondary amines vs. pyridines) and the used conditions are not comparable from one protocol to another.

One recent report elucidates the mechanism of aerobic alcohol oxidations with simple $[Cp*IrCl_2]_2$ in the presence of NEt_3 as additive.[14] In these studies, employing 1 atm of O_2 and 10 mol % [Ir] are crucial for high yields (39-86%, depending on the substrate). The use of NEt_3 (20-100 mol %) has been rationalized with the need to deprotonate the coordinated alcohol substrate in order to achieve β-H elimination (Scheme 1). The proposed mechanism also speculates that the by-product H_2O_2 decomposes to 0.5 O_2 and H_2O under the reaction conditions (toluene, 80 ºC) based on the O_2 uptake stoichiometry and fast H_2O_2 disproportionation in independent experiments. However, no information is provided regarding the speciation of the Ir catalyst after its reaction with O_2,[16] the effects of other bases on catalysis, or regarding catalytic activity in the absence of bases. Due to these limitations, general predictions for the design of efficient and stable Cp*Ir catalysts in aerobic transformations cannot be made.

In order to address these issues (requirement for 1 atm of O_2, high catalyst loadings, and base; lack of information on additive effects), we have performed a comparative study of additives that can potentially serve as ligands to Ir and reaction conditions for the air oxidation of alcohols at low catalyst loadings. The herein described investigations reveal that water content, solvents, and additives all play a crucial role for catalyst stability and need to be taken into account when establishing efficient aerobic oxidation protocols. In contrast to previous reports[12,13] the presence of a strong base is not required for high activity in our systems.



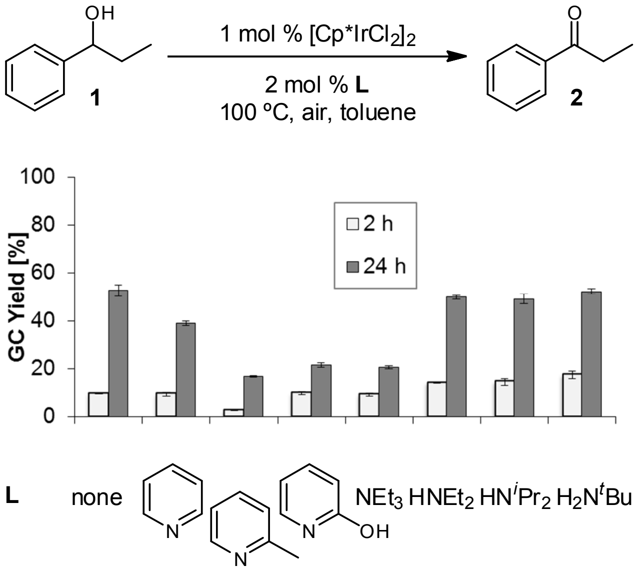
Scheme 1. Previously Proposed Mechanism of $[Cp^*IrCl_2]_2$ Catalyzed Aerobic Alcohol Oxidation.

Results and discussion

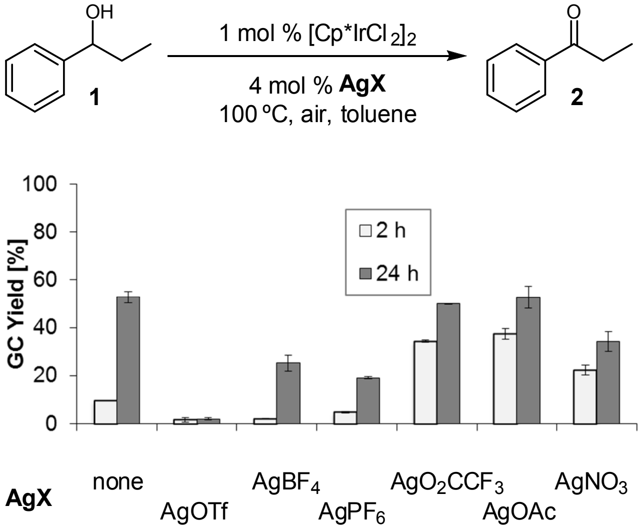
1.1 L-type Additive Effects on Catalytic Activity. Initial studies focused on evaluating the effect of various pyridine and amine additives on the activity of $[Cp^*IrCl_2]_2$,[17] as these bases represent the most common catalyst modifications used in the literature for Cp*Ir catalyzed aerobic oxidations (Scheme 2).[13a,b,18] Previous detailed studies of $[Cp^*IrCl_2]_2$ and related complexes[,19] suggest that addition of pyridines in non-coordinating solvents result in formation of complexes of the formula $[Cp^*IrCl_2(pyridine)]$, which might be the active catalysts in the reactions in Scheme 2. 1-Phenyl-1-propanol (**1**) was chosen as a substrate for this study due to its low volatility and electron-neutral character, which is expected to help in the development of a widely applicable catalyst system.[14] An additional advantage of using **1** as substrate is a simplified GC analysis of the reaction mixture, as ketone **2** is the only obtained oxidation product.[20] In order to benefit catalyst development, all subsequent reactions involving Ir catalysts were performed at a low catalyst loading of 1 mol % $[Cp^*IrCl_2]_2$ (2 mol % [Ir]) using sealed vials in toluene as solvent.[21] Reaction yields were measured after 2 and 24 h in order to account for initial reactivity and long-term stability.

Employing simple $[Cp^*IrCl_2]_2$ as the catalyst under these conditions resulted in formation of 53% of **2** after 24 h with the reaction yielding only 10% after 2 h (Scheme 2).[22] Addition of 2 mol % of L-type additives to form 2 mol % of $Cp^*IrCl_2(L)$ (**3**) *in situ* did not result in higher yields after 24 h. However, several primary and secondary amine bases ($HNEt_2$, HN^iPr_2, H_2N^tBu) increased the short-term reactivity of the catalyst, as shown by higher yields of **2** after 2 h. NEt_3 and all used pyridines (see the SI for more examples) resulted in inhibition of the catalytic activity compared to simple $[Cp^*IrCl_2]_2$.

1.2 Ag Additive Effects on Catalytic Activity. The next step in our systematic study of additives aimed at evaluating the effects of different Ag salts. In order to exchange the chloride ligands bound to Ir, we reacted 1 mol % $[Cp^*IrCl_2]_2$ with 4 mol % of several Ag salts *in situ* (Scheme 3). This approach has been used widely in the literature to synthesize Ir compounds with different X-type ligands from chloride precursor complexes[23] and to evaluate the activity of Cp*Ir complexes with different X-type ligands for C-H activation under catalytically relevant conditions.[19,24]



Scheme 2. L-Type Additive Effects on Catalytic Activity of $[Cp^*IrCl_2]_2$.

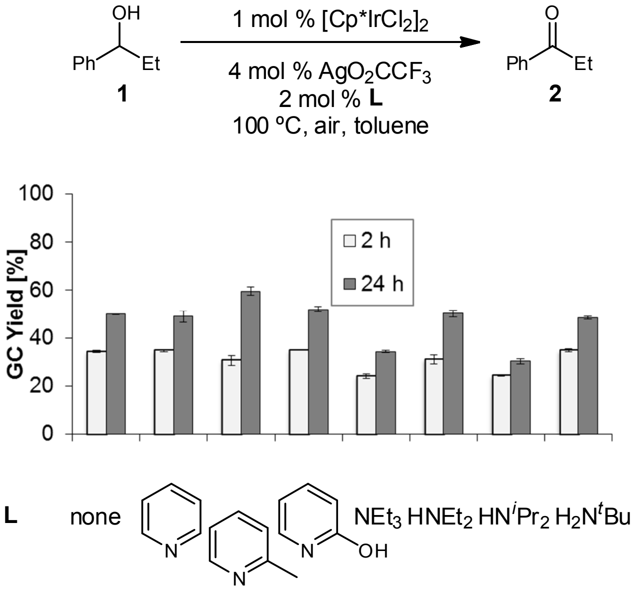


Scheme 3. Ag Additive Effects on Catalytic Activity of $[Cp^*IrCl_2]_2$.

As illustrated in Scheme 3, addition of silver salts with non-coordinating anions (TfO^-, BF_4^-, PF_6^-) resulted in lower catalytic activities in the aerobic oxidation of **1** compared to reactions with [Cp*IrCl$_2$]$_2$.

In contrast, Ag carboxylate additives (AcO$^-$, F$_3$CCO$_2^-$) resulted in a remarkable increase of the initial reactivity as illustrated by the yields of **2** after 2 h. However, the yield after 24 h was not improved by addition of any Ag additive. This suggests either that catalyst decomposition occurs in these systems with all tested additives or that the formed catalysts are not very effective.

1.3 Combining L-type Additive and Ag Additive Effects. Next, we explored the simultaneous effects of both L-type additives and Ag additives on catalysis. We chose the most reactive Ag additive AgO$_2$CCF$_3$ for this study and varied the added L-type additives (Scheme 4). Interestingly, in all of these reactions, the initial reactivity as described by the yields of **2** after 2 h showed improvement when compared to reactions with [Cp*IrCl$_2$]$_2$ (10% after 2 h). No additive combinations, however, showed a significantly increased 2 h activity in comparison to the parent system [Cp*IrCl$_2$]$_2$/AgO$_2$CCF$_3$, while only one additive combination (AgO$_2$CCF$_3$/ 2-picoline) provided a higher yield of **2** (60%) after 24 h.



Scheme 4. Combination of L-type additives with AgO$_2$CCF$_3$.

Based on the described studies, we hypothesized that several factors could contribute to limiting the long-term yields of **2**. (i) The oxygen content (0.77 equiv.) in the used vials might be too low to reach complete conversion;[25] (ii) decomposition of the catalyst might occur under all explored reaction conditions; (iii) the by-product of Ag additive evaluation, AgCl, could affect the stability of the catalysts in all reactions using Ag additives. These hypotheses were tested in order to understand and prevent factors that contribute to catalyst decomposition in aerobic Cp*Ir catalysis.

2.1 Effects of Oxygen Content and Reaction Time. In all reactions described above, the content of oxygen can be calculated to be 0.15 mmol (0.77 eq).[25] If O$_2$ cannot be regenerated by disproportionation of H$_2$O$_2$ under the reaction conditions, the maximum obtainable yield would be 77%. To examine if the yields in this experimental setup are thus limited, we performed catalytic reactions in larger reaction vials, which contained 0.32 mmol (1.6 eq) O$_2$ under otherwise unchanged conditions. This setup provides enough O$_2$ for quantitative conversion of **1**, even if the disproportionation of H$_2$O$_2$ to produce H$_2$O and O$_2$ is slow (see Scheme 1). However, the yields after 24 h remained almost unchanged for [Cp*IrCl$_2$]$_2$ (53% vs. 53%) and [Cp*IrCl$_2$]$_2$/AgO$_2$CCF$_3$ (57% vs. 50%) as catalyst systems. These data show that the availability of oxygen in the reaction system does not play a major role in limiting the yield after 24 h.

In order to determine if the catalyst would retain its activity upon prolonged heating, we performed experiments with extended reaction times. The resulting yield of ketone **2** after 48 h with [Cp*IrCl$_2$]$_2$ as catalyst was only slightly higher (56%) than the yield after 24 h (53%). In the presence of AgO$_2$CCF$_3$, the yield was even lower after 48 h (39%) than after 24 h (50%), indicating catalyst or product decomposition. This is further supported by the high standard deviations (4 to 7%) of the measured reaction yields after 48 h.

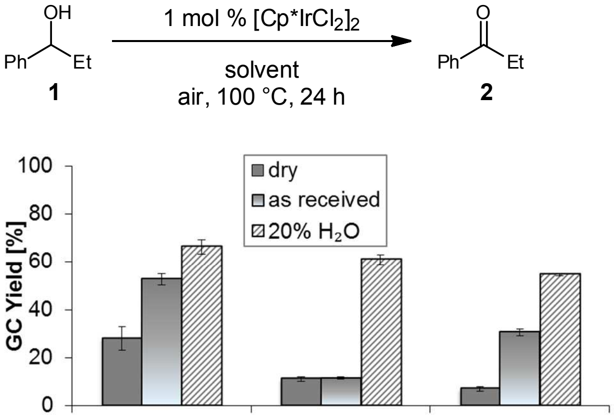
Finally, we reacted **1** with [Cp*IrCl$_2$]$_2$ in toluene under a N$_2$ atmosphere. Under these conditions, only 2% of oxidation product **2** was formed with [Cp*IrCl$_2$]$_2$ as catalyst after 24 h. The [Cp*IrCl$_2$]$_2$/AgO$_2$CCF$_3$ catalyst system showed a slightly higher activity under analogous conditions (12%); however, this value is still drastically reduced in comparison to the yield obtained after 24 h in the presence of air (50%).

These data combined suggest that the reactions studied herein proceed mainly through an O$_2$-driven pathway instead of a dehydrogenation mechanism. Furthermore, when super-stoichiometric amounts of O$_2$ are present in the reaction mixture the mediocre yields after 24 h are likely due to decomposition processes. Concurrently, the rates of decomposition are not strongly affected by differences in reaction times or oxygen loading.

2.2 Non-Innocence of AgCl. Based on these findings, we decided to explore the effect of AgCl on the catalytic activity of [Cp*IrCl$_2$]$_2$. Highly insoluble AgCl is formed as byproduct in our Ag additive studies and is also commonly assumed to not take part in other reactions in which it is formed as a side product.[26] To test the validity of this assumption for the herein studied aerobic oxidations, we evaluated the performance of 1 mol % [Cp*IrCl$_2$]$_2$ in the presence of 4 mol % AgCl. Surprisingly, the activity of [Cp*IrCl$_2$]$_2$ was reduced under these conditions, affording only 46% of ketone **2** after 24 h (compared with 53% in the absence of AgCl). This observation suggests that the presence of AgCl lessens the catalytic performance, even though the exact mechanism of this observation is not understood at this time.

3.1 Effect of Solvents and Water Content on Catalyst Stability. Since the solubility of $[Cp^*IrCl_2]_2$ in toluene is low,[27] we speculated that the reaction of Ir-H intermediates or inorganic byproducts with O_2 leading to catalyst regeneration could suffer from their low solubilities in the reaction mixture. Therefore, we studied the effect of more polar solvents (PhCl, PhBr, $PhCF_3$, DMF) on the catalytic turnover. Unfortunately, experiments in these solvents did not afford higher yields of **2** than experiments in toluene (53%). Interestingly, adding small amounts of chlorinated solvents to toluene was already detrimental for the catalytic activity: the 24 h yield dropped to 13% with 5 vol-% CH_2Cl_2 in toluene and to 17% with 5 vol-% $CHCl_3$ in toluene.

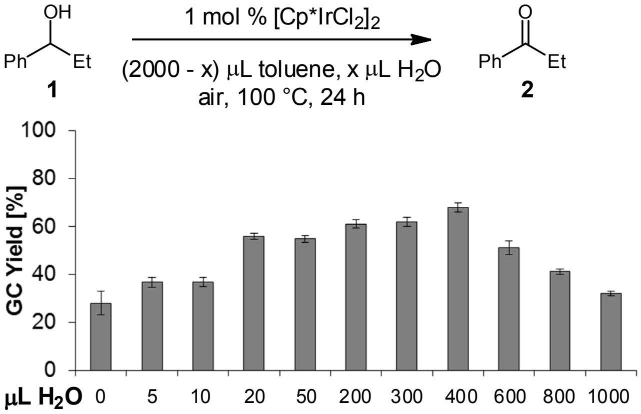
Next, we investigated the effect of H_2O on the reaction, as the presence of H_2O has shown to have accelerating effects on transfer hydrogenations with Cp*Ir species[28] as well as on aerobic Wacker oxidations and on alcohol oxidations with Pd catalysts.[29] We further postulated that H_2O could be a suitable proton shuttle, acting as both base and acid and thus accelerating the proton transfer steps of the catalytic cycle (Scheme 1). To test this hypothesis, 1 mol % $[Cp^*IrCl_2]_2$ was used as catalyst in toluene, which was either used as received or dried over activated molecular sieves (4Å) for at least 24 h prior to use. Remarkably, the reaction in dry toluene resulted in a much lower yield (28% vs. 53%; see Scheme 5), suggesting that the water content indeed contributes to catalyst stabilization. An analogous reaction performed in the presence of 500 mg activated molecular sieves (4Å) afforded an even lower yield (12% after 24 h), further supporting this hypothesis.



Scheme 5. Effect of Water in Different Solvents.

To systematically study the influence of the H_2O content on catalytic activity, various amounts of water were added to the reaction mixture, while keeping the overall volume at 2 mL (Scheme 6). Remarkably, substituting the solvent with considerable amounts of H_2O (toluene:H_2O 4:1) enhances the 24 h yield of **2** to up to 68%; however, the reactivity decreased when adding large amounts of H_2O. The activity enhancing effect of water was also observed when using other solvents (Scheme 5; for more examples see SI) and in the presence of most L -type additives and Ag additives (see SI), suggesting that catalyst stabilization by H_2O is a general phenomenon. This finding is particularly interesting, as formation of H_2O as a by-product of oxidation has been proposed (Scheme 1); thus, H_2O can be expected to affect even reactions that are originally prepared in dry solvents particularly after several turnovers.

We conclude from these studies that the presence of H_2O results in higher yields at low catalyst loadings. The higher catalyst activity could be attributed to H_2O serving as a ligand for Ir.



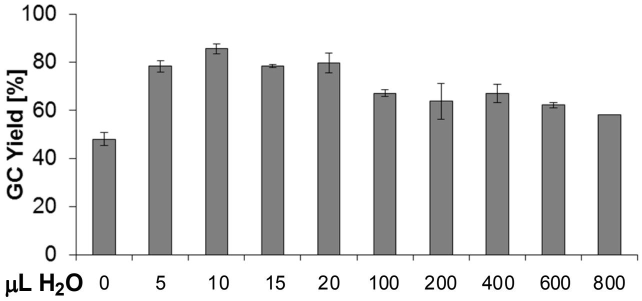
Scheme 6. 24 h Reactivity vs. Water Content.

Nevertheless, additional strategies for catalyst stabilization need to be found, as yield and conversions are not quantitative even with the best solvent system above. One strategy to this end could be the use of L -type additives and Ag additives as detailed in the initial sections of this manuscript. However, when using different catalyst precursors, no catalyst stabilizing effects or higher yields of ketone **2** after 24 h were found in toluene/H_2O (4:1; see SI). This outcome can be rationalized when considering that H_2O can serve as ligand for Ir[9b,30] and that its coordination is expected to be strongly favored due to its high concentration in the reaction mixture. This observation is also in agreement with our previous result that additives mainly enhance the short-term reactivity (yields after 2 h) without improving catalyst stability (yields after 24 h).

3.2 Basic and Acidic Additives and Buffer Systems. In order to identify additional strategies for catalyst stabilization, we again considered the proposed reaction mechanism for catalysis by $[Cp^*IrCl_2]_2$ (see Scheme 1).[14] Even though the overall reaction is pH neutral, proton transfer reactions play a crucial role during catalysis. Previous research on aerobic catalysis with Cp*Ir complexes has identified bases as particularly useful additives, which was explained by their role in deprotonating the alcohol substrate.[13,14] Thus, we tested the effects of various bases (NaO_2CCF_3, NaOAc, Na_2CO_3, K_2CO_3, NEt_3) and acids (AcOH, CF_3CO_2H, *p*-TsOH, HCl) on catalyst stabilization under our best reaction conditions thus far (1 mol % $[Cp^*IrCl_2]_2$, toluene/H_2O 4:1 volume-%, 18 mL air, 100 °C, 24 h). Interestingly, the weakest acid (AcOH) and the weakest base (NaO_2CCF_3) tested provided the best yields (48% and 56%, respectively; see SI for all results), but without enhancing the overall yield in the absence of additives (68%).

Based on these outcomes, we speculated that the catalytic cycle would be accelerated by a proton buffer, which could both accept and donate protons independently. According to the proposed mechanism (see Scheme 1), deprotonation of the alcohol substrate is important for catalysis; however, a protonation step is also necessary for catalyst regeneration and formation of H_2O_2 from O_2. Consequently, AcOH/NaOAc and CF_3CO_2H/NaO_2CCF_3 buffer systems were tested in various toluene/H_2O mixtures (2.3:1 to 399:1), ratios, and concentrations (see SI). In all cases, the AcOH/NaOAc buffer provided higher 24 h yields of **2** up to 83%.

Interestingly, a water content study in the presence of AcOH/NaOAc buffer (Scheme 7) differs remarkably from the data obtained in the absence of buffer (Scheme 6):



Scheme 7. GC Yields of **2** with AcOH/NaOAc Buffer vs Water Content.

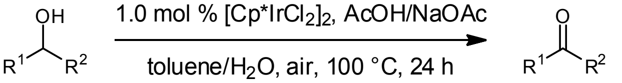
(i) Oxidizing **1** in dry toluene with buffer in the mixture resulted in a relatively high yield of **2** (48%). The analogous reaction in the absence of buffer provides only 28% yield. (ii) Addition of only small amounts of water (10 μL) resulted in an enhancement of the yield up to 83% (Scheme 7) with buffer, while the maximum yield without additives required more water (400 μL) for peak activity (68%; Scheme 6). We conclude from these data that the presence of buffer and water contribute to catalyst stability independently, resulting in the highest yield of air oxidation product **2** observed so far.

In order to challenge this new catalyst system, reactions were performed at 0.1 mol % catalyst loading. These experiments afforded 270 TONs after 72 h.[31] This is to our knowledge the highest TON achieved to date for Ir catalyzed aerobic alcohol oxidations, which do not proceed through acceptorless dehydrogenation.[32] In order to gain preliminary insight on the catalytically active species under our best conditions, the compound $Cp^*Ir(H_2O)_3(OTf)_2$ was prepared[30,33] and used as catalyst. Interestingly, only 19% of ketone **2** were obtained after 24 h, confirming that the active Ir catalyst in solution is not identical to $Cp^*Ir(H_2O)_3(OTf)_2$. Furthermore, this low activity suggests that other ligands such as chloride and acetate can coordinate to Ir and thus influence the catalytic activity under our best aerobic oxidation conditions.

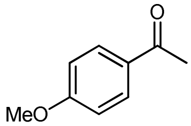
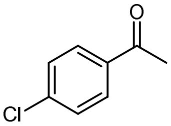
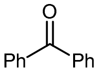
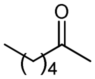
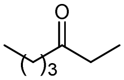
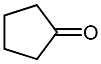
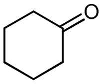
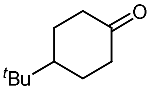
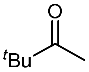
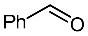
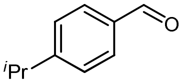
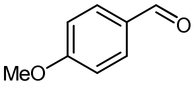
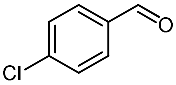
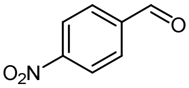
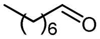
3.3 Substrate Scope Study. A variety of secondary alcohols were readily transformed into the resulting ketones (see Table 1). Overall, benzylic secondary alcohols (entries 1 to 3) were reactive substrates with both electron-rich and electron-neutral substituents. Exceptions to this good reactivity were the substrate 1-(4-chlorophenyl)ethanol (38%, entry 4), which was not dissolved under the reaction conditions, and di(phenyl)methanol (50%, entry 5), which might suffer from steric hindrance during the substrate coordination step. The importance of steric effects around the alcohol group can also be observed when reacting aliphatic alcohol substrates: 2-Octanol (entry 6) and 3-octanol (entry 7) are efficiently converted to the corresponding ketones (72% and 87%, respectively), while the formation of tert-butyl methyl ketone (entry 11) occurs with only 38% yield after 24 h. The reactivity of cyclic aliphatic substrates (entries 8 to 10) shows an interesting differentiation with a five-membered cyclic alcohol being a good substrate (77%), while lower yields are obtained with six-membered cyclic alcohols (53% and 59%, respectively). Compared to secondary alcohols, primary benzylic alcohol substrates react more sluggishly and afford only moderate yields (12 to 34%); at the same time, electron-rich and electron-neutral substrates (e.g. entry 14) show better reactivity than substrates with electron-poor substituents (entry 16). The least reactive substrate investigated was 1-octanol (entry 17) with only 3% of aldehyde product observed.

A possible explanation for these observations could be that primary alcohols can form esters or acids as over-oxidized side products; however, the mass balances (aldehyde yield plus remaining starting material) were close to 100% in all reactions with primary alcohols and no over-oxidized products were detected by GCMS. Another possibility is that primary alcohols are less electron-rich than secondary alcohols; thus, β-hydride elimination would be expected to be slower in these cases. Interestingly, the herein documented preference for secondary alcohol oxidation has also been observed with a structurally related Cp*Ir dehydrogenation catalysts,[6d] which suggests that the preference for β-hydride elimination of secondary alcohols is related to the type of catalyst.[34,35]

Table 1. Substrate Scope of Ir Catalyzed Air Oxidation of Alcohols.[a)]



Entry	Product	GC Yield[b)]
1		83%
2		75%

3		83%
4		38%$^{c)}$
5		50%
6		72%
7		87%
8		77%
9		59%
10		53%
11		38%
12		34%
13		23%
14		24%
15		23%
16		12%
17		3%

$^{a)}$ Conditions: $[Cp^*IrCl_2]_2$ (2.0 μmol, 1.0 mol %; 2.0 mol % [Ir]), NaOAc (5 mol %), AcOH (10 mol %), alcohol substrate (0.20 mmol, 1.0 equiv.), toluene (1990 μL), H_2O (10 μL), 100 °C, 24 h. $^{b)}$ Tabulated yields are the average of at least 2 repeated trials. $^{c)}$ Substrate did not dissolve.

Furthermore, stoichiometric studies of Ir complexes suggest that β-hydride elimination is faster for substrates with alkyl substituents at the β-C.[36] Thus, we hypothesize that the less electron-rich nature of primary alcohols results in slow β-hydride elimination in our system, which is responsible for the observed sluggish aerobic oxidation reactivity.

This suggests that our Cp*Ir catalyst systems can be used complementary to known Cu-based catalysts which achieve the selective oxidation of primary alcohols in a molecule.[37]

Conclusions

In summary, we have established a catalyst system for the air oxidation of secondary alcohols. Moreover, we have provided criteria for improving catalytic activity and catalyst stability in aerobic, Cp*Ir-catalyzed reactions proceeding through Ir-H intermediates. While L-type additives and Ag additives mainly influence the initial catalytic activity of the Cp*Ir catalysts, catalyst decomposition is an important issue at low oxygen pressures and low catalyst loadings and we propose decomposition to be the main reason for non-quantitative yields. However, this challenge can partially be met by controlling the water content in the reaction mixture and by employing a buffer system, which is in agreement with the proposed importance of proton transfer steps in the catalytic cycle. We further conclude that base-free, aerobic alcohol oxidations are possible with Cp*Ir catalysts. We thus hypothesize that literature-known, base-dependent protocols with similar catalysts probably do not require base *per se*; instead the employed bases might simply serve as suitable proton transfer reagents in these reactions. In contrast to the promoting effects of water and buffer system, Ag^I salts contribute to catalyst decomposition and should therefore be used with caution in aerobic protocols with low catalyst loadings. Efforts to characterize relevant decomposition processes and to identify relevant catalytic intermediates are currently underway in our laboratory.

Experimental Section

General Procedure for Evaluating Additives, and Conditions. To a 20 mL scintillation vial, equipped with a Teflon-coated stirbar, was added 1.6 mg of $[Cp^*IrCl_2]_2$ (2.0 μmol, 1.0 mol %; 2.0 mol % [Ir]) and solid additives. Whenever possible, additives were added as standard solutions in toluene. 100 μL (0.20 mmol, 1.0 equiv.) of a standard solution of 1-phenyl-1-propanol (**1**) (2.74 mL, 2.72 g, 20 mmol) in 10 mL toluene was added. The resulting solution was diluted to a total volume of 2.0 mL with toluene. The vial was sealed with a Teflon-lined cap and heated to 100 °C on a pre-heated vial plate under vigorous stirring (1500 rpm). After the reaction time was completed (2 or 24 h) the vial was taken off the heating block and the mixture was allowed to cool to room temperature. 100 μL (80 μmol, 8.6 mg, 0.40 equiv.) of a standard solution of *p*-xylene (1.00 mL, 0.861 g, 8.10 mmol) in 10 mL toluene was added as GC-standard. The solution was diluted to a total volume of 4 mL with toluene or isopropanol. If the solution was cloudy, it was filtered through celite; subsequently, the yield of **2** was determined by calibrated GC analysis.

Reactions at 0.1 mol % Catalyst Loading. 0.2 mg of $[Cp^*IrCl_2]_2$ (0.16 mg, 0.2 μmol, 0.1 mol %; 0.2 mol % [Ir]), NaOAc (0.8 mg, 10 μmol, 5 mol %), AcOH (1.2 μL, 1.3 mg, 20 μmol, 10 mol %), 1990 μL toluene, 10 μL H_2O, and **1** (0.20 mmol, 1.0 equiv.) were added to a 20 mL scintillation vial, equipped with a Teflon-coated stirbar. The vial was sealed with a Teflon-lined cap and heated to 100 °C on a pre-heated vial plate under vigorous stirring (1500 rpm). After the reaction time was completed (24 or 72 h) the vial was taken off the heating block and the mixture was allowed to cool to room temperature. 100 µL (corresponding to 80 µmol, 8.6 mg, 0.40 equiv. of *p*-xylene) of a standard solution of *p*-xylene (1.00 mL, 0.861 g, 8.10 mmol) in 10 mL toluene were added as internal GC-standard and the yield of **2** was determined by calibrated GC analysis (110 TONs after 24 h; 270 TONs after 72 h).

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Notes and references

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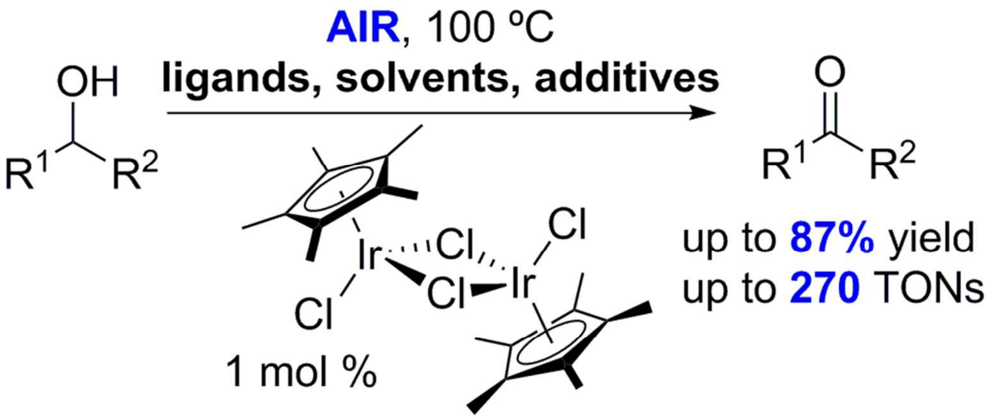

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