Acidic iridium hydrides: Implications for aerobic and Oppenauer oxidation of alcohols

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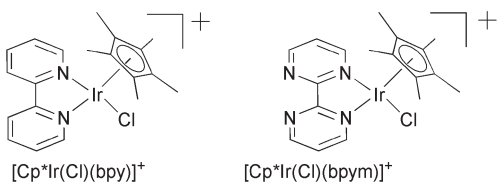
Received (in Cambridge, UK) 28th July 2006, Accepted 19th September 2006
First published as an Advance Article on the web 5th October 2006
DOI: 10.1039/b610857a

$[Cp^*Ir(H)(bpym)]^+$ and $[Cp^*Ir(H)(bpy)]^+$ are the first examples of iridium based catalysts for the aerobic oxidation of alcohols; the catalytic cycle proceeds *via* acidic hydrides. Deprotonation of the hydride leads to a highly oxygen sensitive Ir^I species that regenerate the Ir^{III} complexes upon oxidation with dioxygen.

Aldehydes are of great importance as intermediates in large scale industrial processes. Roughly half of the annual methanol production is oxidised to formaldehyde. On the smaller scale in fine chemical synthesis, aldehydes are the starting materials for many functional groups. However, the selective oxidation of alcohols to aldehydes is still a difficult procedure. Environmentally benign methods for aldehyde production with O_2 as oxidant are highly desirable: unfortunately, O_2, is a kinetically poor oxidant due to its triplet nature. A further and general problem with oxidants is the lack of selectivity; as oxidation products of primary alcohols, aldehydes are significantly easier to oxidise than the alcohol itself. One of the more exciting developments in oxidation chemistry is the palladium catalysed aerobic oxidation of alcohols without the need of a co-oxidant.[1]

The transfer hydrogenation catalysts $[Cp^*Ir(Cl)(bpy)]^+$, and $[Cp^*Ir(H)(bpym)]^+$ (Scheme 1) can act as a selective aerobic oxidation catalyst under certain conditions. Interestingly, the oxidation of alcohols to aldehydes by molecular oxygen operates through a different mechanism compared to the transfer hydrogenation pathway. The divergent mechanisms open up the possibility to tune the catalyst towards one reaction. This is the first example of iridium catalysts that promote the aerobic oxidation of alcohols to aldehydes.

The compounds $[Cp^*Ir(Cl)(bpy)]OTf$ and $[Cp^*Ir(Cl)(bpym)]OTf$ were synthesised by adaptation of a literature procedure.[2,3] When the above compounds were heated in methanol (reflux), ethanol (60 °C) or benzylalcohol (70 °C) in the presence of air and base (NaOH or Na_2CO_3) the corresponding aldehyde was formed.



$[Cp^*Ir(Cl)(bpy)]^+$ $[Cp^*Ir(Cl)(bpym)]^+$

Scheme 1

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Based on the iridium catalysed transfer hydrogenation mechanism[4,5] we assume that the catalytic intermediate is an iridium(III) hydride and that it is this hydride that reacts directly with molecular oxygen. In an attempt to trap the catalytic intermediate, the reactions of the complexes were monitored in the absence of oxygen. Addition of excess sodium methoxide to $[Cp^*Ir(Cl)(bpy)]OTf$ in methanol caused a rapid colour change from yellow to deep purple. Evaporation of the solvent and extraction into CD_3CN gave the NMR resonances in accordance with Cp*Ir(bpy) (Table 1). The assignment was also confirmed by high resolution mass spectrometry (measured; 483.1435, calculated for $C_{20}H_{22}IrN_2$; 483.1412, difference 2.3 mDa). Similarly, the reaction of $[Cp^*Ir(Cl)(bpym)](PF_6)$ yielded Cp*Ir(bpym) as determined by NMR (Table 1) and high resolution electrospray mass spectrometry (measured; 485.1339, calculated for $C_{18}H_{20}IrN_4$; 485.1317, difference 2.2 mDa). This was in stark contrast to our working hypothesis that the hydride complex formed from β-hydride elimination reacts directly with dioxygen. In a previous study, Kaim and coworkers observed that the hydride $[Cp^*Ir(H)(bpy)](PF_6)$ can be deprotonated to yield the iridium(I) complex (Cp*)Ir(bpy).[6] Note that the deprotonation step (4) results in a reduction of the formal oxidation state, while the actual reduction derives from the β-hydride elimination (3) where one proton and two electrons are transferred to the metal (Fig. 1). Regrettably, convention states that in a M–H bond the formal oxidation state of the hydrogen atom is −1 instead of +1. It can be argued that these particular "hydride" complexes would be better described as the conjugate acid of $Cp^*Ir^I(NN)$. When the reaction mixture was quenched with a weak acid, NH_4PF_6, resonances at δ −11.50 and −11.60 ppm appeared for the bpy and bpym complexes, respectively. These resonances are attributed to $[Cp^*Ir(H)(bpy)]^+$ and $[Cp^*Ir(H)(bpym)]^+$. Consequently, it can be concluded that during basic reaction conditions an alkoxide species is formed. This species is highly reactive and could only be observed by electrospray mass spectrometry. The alkoxide complexes undergo β-hydride elimination, liberating an aldehyde and forming $[Cp^*Ir(H)(bpy)]^+$ or $[Cp^*Ir(H)(bpym)]^+$. The formed hydride is deprotonated immediately to yield (Cp*)Ir(bpy) or (Cp*)Ir(bpym), thus effecting a two-electron two-proton oxidation of the alcohol.

Table 1 ^1H NMR chemical shifts (ppm)

Compound	Ir-H	Cp*	bpy/bpym	Solvent
$[Cp^*Ir(H)(bpy)]PF_6$	−11.80	1.78	7.62; 8.11; 8.29; 8.90	D_2O[4]
$[Cp^*Ir(bpy)]$	—	1.75	6.16; 6.71; 7.56; 8.94	C_6D_6[a,6]
$[Cp^*Ir(H)(bpym)]PF_6$	−11.60	1.87	7.71; 9.10; 9.12	CD_3CN[3]
$[Cp^*Ir(bpym)]$	—	1.98	6.26; 7.99; 8.89	CD_3CN[a]

[a] This work.

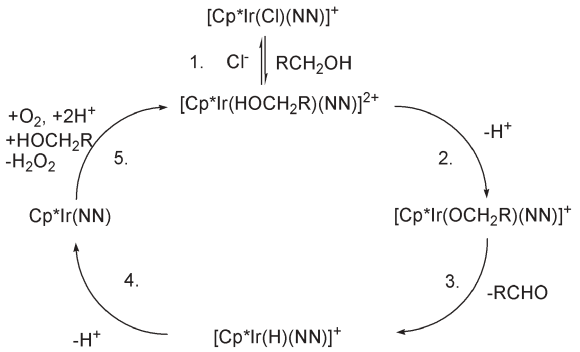

Fig. 1 Mechanism for iridium catalysed aerobic oxidation of alcohols.

The pK_a of $[Cp^*Ir(H)(bpym)]^+$ was determined to *ca.* 6 in MeCN 5% H_2O, and the pK_a of $[Cp^*Ir(H)(bpy)]^+$ is higher, as Ziessel reported it to be still in its hydride form at pH 7.[2,7]

Cp*Ir(bpy) and Cp*Ir(bpym) are particularly sensitive to molecular oxygen. When air is admitted, the dark violet colour of the Ir^I compound rapidly disappears and an Ir^{III} species is formed. This allows us to establish the following cycle (Fig. 1). Substitution of the halide by the alcohol gives an alcohol complex (1), deprotonation results in an alkoxide complex (2) which rapidly undergoes β-hydride elimination to give a hydride (3). Deprotonation of the hydride generates Cp*Ir(bpy) or Cp*Ir(bpym) (4). Oxidation followed by solvation (5) returns the alcohol complex. The reoxidation of the Ir^I complexes presumably forms a peroxide species. This reaction is most likely similar to the reoxidation of the more common palladium based catalysts.[8] The iridium peroxide species could not be isolated but when tri-*o*-tolylphosphine is added to the reaction medium it acts as peroxide scavenger and tri-*o*-tolylphosphine oxide can be detected by ^{31}P NMR. Even in the absence of a peroxide scavenger, hydrogen peroxide never builds up in the solution as it is reduced by Cp*Ir(bpy) or Cp*Ir(bpym). An alternative explanation would be that the iridium complexes catalyse the disproportionation of H_2O_2, this has been observed for some palladium based catalysts.[9] Consequently, one mole of oxygen oxidises two moles of alcohol selectively to the corresponding aldehyde.

The resulting iridium(I) compound cannot be reoxidised by organic carbonyl compounds hindering completion of the Oppenauer oxidation cycle. However, under acidic conditions using an acidic hydrogen equivalent such as formic acid, the $[Cp^*Ir(H)(bpy)]^+$ complex can be used as a transfer hydrogenation catalyst.[4]

The turnover number for the aerobic oxidation of benzyl alcohol using GC was determined to be a modest 5 for the bipyridine complex and 70 for the bipyrimidine catalyst.† The catalytic runs were performed in a vial open to air, no bubbling of oxygen or air was required. The turnover numbers are likely to be minimum values as no efforts to protect the liberated benzaldehyde towards auto-oxidation or air oxidation were taken. No catalytic activity was observed in the absence of a base.

The bipyrimidine complex is the more efficient catalyst, and easier to reduce than the bipyridine complex by 0.15 V.[3,10] This means that the reoxidation of Ir^I by O_2 is not the rate limiting step as it would have given an inverse correlation with the reduction potential. It is more likely that the stronger π-accepting ligand favours the reduction to Ir^I by either increasing the rate of methoxide formation or the rate of β-hydride elimination.

It is now clear why these complexes cannot act as transfer hydrogenation catalysts using an alcohol as hydrogen donor, but work so well with acidic hydrogen equivalents such as formic acid.

The hydride complex formed from the β-hydride elimination step is more acidic than the OH proton of the alcohol complex. Thus at the pH required for the catalytic cycle to commence, the hydride intermediate is deprotonated as well (Fig. 1).

The reaction described can essentially be viewed as a transfer hydrogenation reaction with the difference that the oxidant is not an organic carbonyl functionality but molecular oxygen. There is however, a striking difference in the mechanism. The iridium(I) compounds formed under basic condition are not able to reduce organic carbonyl functionalities and can in fact be characterised by NMR in dry degassed d_6-acetone. In basic media, however, the catalyst is selective towards molecular oxygen as oxidant, thus inhibiting the undesirable back reaction with the liberated carbonyl product. This mechanism also explains the striking pH dependence in transfer hydrogenation catalysed by $[Cp^*Ir(H)(bpy)]^+$ using formate as a hydrogen donor.[4] The turn-over frequency for the transfer hydrogenation is at its highest at around pH = 2 and drastically decreases as the pH is increased; the catalytic activity ceases at around pH = 6.[4] In light of the above presented results the inability to catalyse transfer hydrogenation at basic pH was ascribed to the deprotonation of the hydride. Indeed, when [Cp*Ir(Cl)(bpy)]Cl was heated in the presence of sodium formate and cyclohexanone under basic conditions the solution turned deep violet/blue, indicative of the formation of $Cp^*Ir^I(bpy)$, and no formation of cyclohexanol was observed.

We gratefully acknowledge Zoraida Freixa and Josep Maria López for advise and technical help, financial support from the Alexander von Humboldt Stiftung and the Deutsche Forschungs gemeinschaft.

Notes and references

† Turn-over numbers where measured in benzyl alcohol containing 10% 1 M Na_2CO_3 at 70 °C in a vail open to air and sampled over 2 h after which the activity had significantly decreased.

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