Inner-Sphere Oxygen Activation Promoting Outer-Sphere Nucleophilic Attack to Olefins

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Abstract: Alkoxylation and hydroxylation reactions of 1,5-cyclooctadiene (cod) in an iridium complex with alcohols and water promoted by the reduction of oxygen to hydrogen peroxide are described. The *exo* configuration of the OH/OR groups in the products agrees with the nucleophilic attack at the external face of the olefin as the key step. The reactions also require the presence of a coordinating protic acid (such as picolinic acid, HpPic) and involve the participation of a cationic diolefin Ir^{III} complex, [Ir(pic)₂(cod)]⁺, which has been isolated. Independently, this cation is also involved in easy alkoxy group-exchange reactions, which are very unusual for organic ethers. DFT studies on the mechanism of the olefin alkoxylation mediated by oxygen show a low-energy PCET step connecting a superoxide-iridium(II) complex with hydroperoxide-iridium(III) intermediates rather than peroxide complexes. Accordingly, a quite more complex reaction with up to four different products occurred on reacting the diolefin-peroxide iridium(III) complex with picolinic acid. Moreover, such hydroperoxide intermediates are the origin of the regio- and stereo-selectivity of the hydroxylation/alkoxylation reactions. If this protocol was applied to the diolefin-rhodium(I) complex [Rh(pic)(cod)] the free alkyl ethers resulted, and the reaction is enantioselective if a chiral amino acid such as L-proline is used instead of HpPic.

Introduction

The electrophilic activation of alkenes by coordination to transition metals is a key for the linkage of a wide range of functional groups to a hydrocarbon skeleton.^[1] In particular, the nucleophilic attack of oxygen-based nucleophiles to metal-coordinated olefins is the central step in the palladium-catalyzed Wacker process,^[2] as well as in its variants using alternative oxidants such as peroxides^[3] or nitrites^[4] as co-catalysts, or

copper-free catalytic methods.^[5] It also represents a key step in the hydration of olefins to produce alcohols^[6] or in hydroalkoxylation reactions leading to ethers.^[7] In general terms, two main pathways are commonly accepted to account for the formation of the new C–O bond, either the migratory insertion of a coordinated olefin into a M–OH/OR bond or an external nucleophilic attack of H₂O/OH[–] (or ROH/RO[–]) to the coordinated olefin. The former (inner-sphere or *syn*-attack) produces *endo* products while the later (outer-sphere or *anti*-attack) give the *exo* ones.^[8]

Iridium complexes have been poorly explored in this field, represented by the following cases reported in the literature. An apparent insertion of ethylene into an Ir–OH bond was observed in the reaction of [Ir(C₅Me₅)(PMe₃)(Ph)(OH)] with ethylene to give the hydroxyethyl complex [Ir(C₅Me₅)(PMe₃)(Ph)(CH₂CH₂OH)].^[9] However, further studies suggested a bimolecular mechanism involving an outer-sphere attack of the hydroxo ligand in [Ir(C₅Me₅)(PMe₃)(Ph)(OH)] to the η^2 -ethylene in [Ir(C₅Me₅)(PMe₃)(Ph)(C₂H₄)]⁺.^[10] More recently, a *syn*-nucleophilic attack of an Ir–OH group to one of the double bonds of a cod ligand has been proposed by Bera in the preparation of 1-irida-2-oxetane complexes.^[11]

Regarding the second alternative (*anti*-attack), 2-R-cyclooct-5-enyl complexes (R = benzyl, allyl) have been prepared by reactions of carbanions (such as RMgCl) with [Ir(cod)(PMe₃)₃]Cl, while a 2-indenylcyclooct-5-enyl was directly obtained from the addition of trimethylphosphane to [Ir(η^5 -indenyl)(cod)].^[12] Moreover, nucleophilic attack of sodium/potassium alkoxides have been only reported for a couple of cationic complexes: [Ir(bipy)(cod)(fumarionitrile)]Cl and [Ir(MeBP₃)(cod)]Cl (MeBP₃ = MeC{CH₂PPh₂}₃) described by Camus^[13] and Caulton,^[14] respectively. In this context, it would be highly interesting if non-deprotonated alcohols and neutral complexes could be used to form C–O bonds, thus avoiding the formation of stoichiometric amounts of inorganic salts.

In this paper we showcase the easy olefin alkoxylation with alcohols, and hydroxylation with water in an iridium(III) complex via nucleophilic attack in a reaction promoted by oxygen.

It is interesting to remark that the chemistry of Rh(I) and Ir(I) complexes with oxygen is dominated by their high tendency to form peroxide complexes.^[15] Notable exceptions are few rhodium(I) compounds in which oxygen remains coordinated as a simple η^2 -ligand,^[16] superoxide iridium(III) derivatives,^[17] or dinuclear iridium(IV) μ -oxo complexes.^[18] In other instances, oxygenation reactions^[19] involving C–O bond formation to 1-metalla-2-oxetanes,^[20] highly unstable 1-metalla-2,3-dioxolanes,^[21] and alkyl-hydroxy-allyl species^[22] have been

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described, whereas hydroxide or hydroperoxide complexes result either by oxygen insertion into the M–H bond,^[23] or by protonation of peroxide complexes.^[24] Therefore, the reactions reported here promoted by oxygen have not precedent in rhodium and iridium chemistry.

Results and Discussion

Alkoxylation and hydroxylation reactions on iridium.

Air-exposure of a solution of $[\text{Ir}(\text{pic})(\text{cod})]$ (**1**, Hpic = picolinic acid) in dichloromethane:methanol 4:1 and in the presence of one mol-equiv. of Hpic produced a color change from red to yellow in 90 min. From these solutions the complex $[\text{Ir}(\text{pic})_2(\text{MeOC}_8\text{H}_{12})]$ (**2**) was isolated as a yellow solid in 80% yield after working-up (86% by ^1H NMR). The overall reaction involves not only the oxidation of iridium, but also the incorporation of the second picolinate ligand and, more significant, the functionalization of the cod ligand by the formation of a new C–O bond with a methoxide group (Scheme 1).

Scheme 1. Synthesis of complexes $[\text{Ir}(\text{pic})_2(\text{ROC}_8\text{H}_{12})]$.

Simultaneously, the incoming oxygen was released as hydrogen peroxide.^[25] Moreover, oxygen uptake measurements indicated the consumption of almost one-mol of oxygen per mol of **1**, which agrees with the formation of one mol of hydrogen peroxide (Scheme 1). In addition, the possibility of a side reaction of **1** with H_2O_2 , present in the reaction media, was checked by adding one mol-equiv. of H_2O_2 to a suspension of **1** in CD_3OD under argon. ^1H NMR spectrum revealed that the reaction occurred, but it led to a complicated mixture of complexes including **2a/2b**, but in lower yields. Most probably, this side reaction accounts for the 86% yield in the reaction with oxygen.

NMR studies of the product revealed that it was isolated as a mixture of the two isomers **2a/2b** shown in Scheme 1 in a 45/55 relative ratio; one of them (**2a**) was separated as single monocrystals by slow diffusion of diethyl ether into a solution of **2a/2b** in methanol.^[26] DFT calculations (TPSSH-D3/BS2)^[27] pointed out the thermodynamic feasibility of the reaction depicted in Scheme 1, with $\Delta G = -24.0 \text{ kcal mol}^{-1}$ computed in methanol for **2b**.

In the molecular structure of **2a** (Figure 1) the octahedral iridium center is bound to a $\text{MeOC}_8\text{H}_{12}$ fragment through a σ -bond with C1 and a π -bond of the intact olefin, $\text{C5}=\text{C6}$, and to two chelating picolinate ligands in a relative *trans*-O,O

configuration. The methoxide group was found to be in an *exo*- or *anti*-configuration. In addition, DFT calculations^[27] of both isomers revealed that **2b** is slightly more stable than **2a** in $1.0 \text{ kcal mol}^{-1}$. The *exo*-configuration of the methoxide group in **2a/2b** strongly suggests a reaction pathway involving an outer-sphere nucleophilic attack of methanol (or methoxide) to the hypothetical cationic complex $[\text{Ir}(\text{pic})_2(\text{cod})]^+$ and indeed, it represents the key step in the synthesis of **2a/2b** (see below).

Complexes **2a/2b** were characterized according to their analytical and spectroscopic data in solution. Relevant resonances are sharp singlets for the OMe groups and two multiplets from the H^5 and H^6 protons of the intact C=C bond in the ^1H NMR spectrum. The C^1 carbon directly bonded to iridium was observed at high field ($\delta = 16.6$ and 18.3 ppm , for **2a** and **2b**, respectively) in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum, whereas the *exo*-configuration of the methoxide in **2b** was confirmed by the $^1\text{H}, ^1\text{H}$ -noesy NMR spectrum.

Figure 1. Structures (ORTEP at 50% level) of complexes **2a** (left) and **4b** (right). Hydrogen atoms (except those bonded to C1 and C2) have been omitted for clarity. Selected angles ($^\circ$) and bond distances ($\text{\AA}$) for **2a**: Ir–O2, 2.065(3); Ir–O4, 2.063(3); Ir–N1, 2.073(4); Ir–N2, 2.141(4); Ir–C1, 2.082(5); C1–C2, 1.517(8); C2–O1, 1.460(7); O2–Ir–O4, 163.8(2); N1–Ir–Ct1, 172.3(2); N2–Ir–C1, 172.5(2). For **4b**: Ir–O2, 2.058(4); Ir–O4, 2.053(4); Ir–N1, 2.054(5); Ir–N2, 2.144(5); Ir–C1, 2.080(6); C1–C2, 1.515(8); C2–O1, 1.447(7); O2–Ir–O4, 166.1(2); N1–Ir–Ct1, 172.3(2); N2–Ir–C1, 177.0(2).

This original reaction is not particular of methanol, because if ethanol was used as solvent the related ethoxy complexes $[\text{Ir}(\text{pic})_2(\text{EtOC}_8\text{H}_{12})]$ (**3a/3b**) resulted, which were isolated in very good yields. Moreover, if this reaction was carried out in acetone-water (4:1) the products were found to be the hydroxyl complexes $[\text{Ir}(\text{pic})_2(\text{HOC}_8\text{H}_{12})]$ (**4a/4b**). Complexes $[\text{Ir}(\text{pic})_2(\text{EtOC}_8\text{H}_{12})]$ (**3a/3b**) as well as $[\text{Ir}(\text{pic})_2(\text{HOC}_8\text{H}_{12})]$ (**4a/4b**) were characterized according to their analytical and spectroscopic data (See Supporting Information); the structure of complex **4b** was also determined by X-ray diffraction studies (Figure 1, right).

On the whole, the structure of **4b** is quite similar to that described for the methoxide complex **2a**, with the hydroxide group bound to C2 in a *exo* disposition and the picolinate ligands in a relative O,O-*trans* disposition. As found for the pair **2a/2b**,

DFT calculations^[27] indicate that again, isomer **4b** is slightly more stable than **4a** in 0.6 kcal mol⁻¹.

RO/R'O exchange reactions.

Solutions of **2a/2b** in CD₃OD showed the gradual disappearance of the signals of the OCH₃ groups simultaneously with an enhancement of the signal of CH₃OD (Figure 2). No other change in the ¹H NMR spectrum was detected, and accordingly, the ²H NMR spectrum at the end of the experiment showed only the signals of the OCD₃ groups in the deuterated complexes [Ir(pic)₂(cod)₂(CD₃OC₈H₁₂)] (**2a^D/2b^D**). Moreover, this OCH₃/OCD₃ exchange was found to be fully reversible. Thus, complexes **2a/2b** were recovered if the isolated deuterated complexes **2a^D/2b^D** were dissolved in CH₃OH. These facts strongly support that **only** the methoxide groups are involved in the H/D exchange and, consequently, any pathway encompassing the extrusion of CH₃OH from the OCH₃ group and protons of the C₈H₁₂ fragment can be excluded, since this fragment remains non-deuterated.

Figure 2. Change of the ¹H NMR spectrum of complexes **2a/2b** in CD₃OD over time in the selected region, and plot of the intensity of the signals of OCH₃ in **2a/2b** (%) vs time (min). The inset shows the ²H NMR spectrum at the end of the experiment (the asterisks denote the signals of CD₃OD).

A reasonable mechanism for this OCH₃/OCD₃ exchange accounting for all observations is shown in Scheme 2. The first step would correspond to the cleavage of the C–OCH₃ bond to form the ionic pair [Ir(pic)₂(cod)]OCH₃⁺ ([5]OCH₃). This pair was calculated by DFT methods^[27] as the complex [Ir(pic)₂(cod)][OMe⁺(MeOH)₅], in which a small cluster of five molecules of methanol^[28] was incorporated to stabilize the methoxide anion. It was found to be only 11.0/12.0 kcal mol⁻¹ above **2a/2b**, respectively. In addition, this bond cleavage should be facilitated by acid catalysis, and indeed, the time for this OCH₃/OCD₃ exchange is considerably reduced from 20h (Figure 2) up to 40 min by adding catalytic amounts of a protic acid (1% of Hpic, Figure 3).

Scheme 2. Proposed mechanism for the OCH₃/OCD₃ exchange and isomerization of **2a/2b** into **2a^D/2b^D** in CD₃OD.

The second step involves the fast equilibrium: CH₃O⁻ + CD₃OD ⇌ CH₃OD + CD₃O⁻, while the third step represents the nucleophilic attack of CD₃O⁻ to the olefinic carbon in the cation [5]⁺ to give **2a^D/2b^D**. Notice that the C₂ symmetry of [5]⁺ makes the olefinic carbons 1, 5 (blue) as well as 2, 6 (red) equivalent (Scheme 2), and consequently, the binding of the OMe group to one of the blue carbons gives **2a**, whereas **2b** results if the binding takes place at the red carbons.

Pseudo-first order kinetics $v = k_{\text{obs}}[\mathbf{2a}]$ and $v = k_{\text{obs}}[\mathbf{2b}]$ were observed for this exchange (Figure 2), which indicates that the rate-determining step in this mechanism is the cleavage of the C–OCH₃ bond. Values of k_{obs} of 0.0015±3 and 0.0023±2 min⁻¹ (0.104±2 and 0.138±2 min⁻¹ in the presence of 1% Hpic) were obtained for **2a** and **2b**, respectively, indicating that the cleavage of the C–OCH₃ bond is slightly easier in **2b**. Moreover, according to DFT calculations^[27] the process in Scheme 2 takes place through fairly accessible transition states of 20.9 kcal mol⁻¹ (TSa) for the reaction: **2a** + (MeOH)₅ → [5][OMe⁺(MeOH)₅] and 20.0 kcal mol⁻¹ starting from **2b** (TSb, see Supporting Information). The slightly lower value for TSb relative to TSa agrees with the values for k_{obs} commented before.

The proposed mechanism also denotes that starting from pure samples of **2a**, the H/D exchange should be associated not only to its transformation into **2a^D**, but also to its isomerization into **2b^D**, and indeed, it certainly occurs. As shown in Figure 3, the time for the OCH₃/OCD₃ exchange (**2a** → **2a^D**, black circle), which is associated to the disappearance of the signal corresponding to OCH₃ in **2a**, is similar to that required for the isomerization of **2a** (blue diamond) directly into **2b^D** (red triangle).

Figure 3. Intensity of the signals of OMe-**2a** (black circle), **2a+2a^D** (blue diamond) and **2b^D** (red triangle) in %, vs time (min) for the isomerization **2a** ⇌ **2b^D** and exchange **2a** → **2a^D** of pure **2a** in CD₃OD in the presence of Hpic (1% mol).

In the same line, the pairs of complexes **3a/3b** and **4a/4b** were also found to be in equilibrium, most probably via the cationic **[5]⁺**, as described above for complexes **2a/2b** (Scheme 2). Moreover, solutions of the hydroxyl complexes **4a/4b** transformed into the corresponding methyl-ethers **2a/2b** in methanol, whereas they evolve to the ethyl ones **3a/3b** in ethanol. Furthermore, treatment of the methoxy complexes **2a/2b** with ethanol gave the ethoxy complexes **3a/3b**, and conversely the ethoxy complexes **3a/3b** transform into **2a/2a** by dissolving them in methanol (NMR evidence).

These 'exchange' reactions are remarkable and reflect the weakness of the C–O bond in complexes **[Ir(pic)₂(ROC₈H₁₂)]**. In sharp contrast, the cleavage of the C–O bond in free ethers requires hard reaction conditions such as the protonation with concentrated sulfuric acid. In this regard, the main difference between both approaches is that the cleavage of the C–O bond in organics of the type R₂CH–OR gives highly unstable carbocations (R₂CH⁺) whereas in complexes **2** and **3**, the C–O bond cleavage does not result in the corresponding carbocation, but the regeneration of the C=C bond and the shift of the positive charge to iridium, thus providing an elegant way for the stabilization of the 'organic carbocation'.

Furthermore, the equilibria in Scheme 2 also allow one to predict that the methoxide anion will be protonated upon addition of a strong acid to the mixture of isomers, thus liberating the cationic Ir(III) complex. Certainly, the addition of one mol-equiv. of HBF₄ to dichloromethane solutions of **2a/2b** gave the complex **[Ir(pic)₂(cod)]⁺** (**[5]⁺**), which was isolated as the BF₄[−] salt in almost quantitative yield. The regeneration of an intact cod ligand in this reaction as well as the C₂ symmetry of the complex are evident from the ¹H and ¹³C{¹H} NMR spectra of **[5]⁺**.

As expected, **[5]BF₄** immediately reacts with NaOMe in methanol to give **2a/2b** quantitatively, and with Me₄NOH in acetonitrile to give the hydroxyl complexes **4a/4b** (see Supporting Information). These experiments are consistent with the mechanism shown in Scheme 2.

Role of oxygen in the synthesis of complexes 2-4.

With experimental confirmation in hand of the participation of the cation **[Ir(pic)₂(cod)]⁺** (**[5]⁺**) in the synthesis of **2-4**, attention was focused to the way in which **1** transforms into **[5]⁺** by the combined action of oxygen and Hpic. Unfortunately, all attempts to detect intermediates by monitoring the reaction in CD₂Cl₂-CD₃OD by NMR were unsuccessful, and only the starting material and the products (as **2a^D/2b^D**) could be observed. Nonetheless, relevant insights were gathered from DFT calculations.^[27]

The reaction of **1** with oxygen starts in the open-shell triplet potential surface to give a superoxide-Ir(II) intermediate (**I1**) (Figure 4). This superoxide (**I1**) was found to be 9.8 kcal mol^{−1} above **1**+O₂+Hpic (ΔG = 0) and it is formed across an accessible transition state (**TS0**) located at 18.4 kcal mol^{−1}. A subsequent electron transfer (ET, from iridium to oxygen) transforms the superoxide **I1** into the singlet peroxide **[Ir(pic)(cod)(O₂)]** (**6**), which is more stable than **I1** in 15.1 kcal mol^{−1}, and takes place through a minimum-energy crossing point (**MECP1**) at 17.8 kcal mol^{−1} (Figure 4).

Noticeably, a second minimum-energy crossing point (**MECP2**), lower in energy than **MECP1**, was found. Through **MECP2**, the superoxide **I1** directly transforms into the diamagnetic hydroperoxide iridium(III) complex **[Ir(pic)(cod)(OOH)(κ¹-pic)]** (**I2**), which is 8.2 kcal mol^{−1} more stable than the peroxide **6** (Figure 4). In this step, the protonation of the superoxide ligand, the oxidation of iridium(II) to iridium(III), and the O-coordination of the picolinate ligand take place in one single step. In other words, a proton coupled electron transfer reaction (PCET), accomplished by coordination of the second picolinate ligand transforms the superoxide complex **I1** into **I2** with a lower energy profile than that leading to the peroxide **6**.

Figure 4. DFT computed (TPSSH-D3/BS2) Gibbs energy profile for the reaction of **1** with O₂ in presence of Hpic in CH₂Cl₂. Relative ΔG values are given in kcal mol^{−1}. Spin states of the stationary points are depicted in red (triplet) and green (singlet). Code color for the figures: Ir (green), O (red), N (blue), C (gray), H (black).

The next steps correspond to the extrusion of the hydroperoxide ligand in **I2** as H₂O₂, and coordination of the free N-end of the second picolinate ligand to form the ionic complex **[Ir(pic)₂(cod)]pic** (**[5]pic**). The DFT computed^{[27],[28]} profile of this part of the reaction is shown in Figures 5 and 6, in which a small cluster of five molecules of methanol was incorporated to stabilize the picolinate anion. This reaction requires the assistance of a proton, which is provided by the picolinic acid (Hpic) present in the reaction medium.

Initially the −OOH ligand is protonated by Hpic. This step is almost barrierless (**TS1** is only 1.7 kcal mol^{−1} above **I2**⋯Hpic) and yields the product (**[I2H]⁺pic(MeOH)₅**) at practically the same energy than the initial species (Figure 5).

In this step, it is remarkable the stabilization undergone by **I2** when interacting with the cluster Hpic(MeOH)₅ (3.7 kcal mol^{−1}), due to the formation of a rather strong hydrogen bond between the proton of picolinic acid and the oxygen atom of the anionic hydroperoxo ligand as the initial step of the proton transfer reaction.

Figure 5. DFT computed (TPSSH-D3/BS2) Gibbs energy profile for the protonation of **I2** with Hpic in methanol. Relative ΔG values are given in kcal mol⁻¹. Code color for the figures: Ir (green), O (red), N (blue), C (gray), H (black).

From $[I2H] \cdots pic(MeOH)_5$ the coordinated hydrogen peroxide is replaced by the coordination of the N-atom of the initially κ^1 -O picolinate ligand (Figure 6). This step entails the highest barrier (19.9 kcal mol⁻¹, **TS2**) and yields the very stable intermediate $[5]^+$, which provides the thermodynamic driving force for the reaction. Indeed, this intermediate is also involved in the **2a/2b** isomerization described above (Scheme 2).

Figure 6. DFT computed (TPSSH-D3/BS2) Gibbs energy profile for the removal of the H_2O_2 ligand and formation of intermediate $[5]^+$ in methanol. Relative ΔG values are given in kcal mol⁻¹. Code color for the figures: Ir (green), O (red), N (blue), C (gray), H (black).

The last part of the reaction consists in the nucleophilic attack of one methanol molecule to the C=C bond of $[5]^+$ to form the new C–O bond. The attack of the alcohol to the C=C bond takes place with a very low energy barrier (10.5 kcal mol⁻¹, **TS3b**) due to the assistance of the picolinate anion formed in the first step (Figure 7). The picolinate anion activates the nucleophile and

picks up the proton of methanol, playing a similar role than carboxylate residues in natural and artificial metallohydrolases.^[29]

Once **2b** and Hpic have been formed, the picolinic acid interacts with **I2**. In this way, a cycle for the transformation of **I2** into **2a/2b** catalyzed by Hpic is closed.

On a preparative scale, the addition of CD_3OD to the ionic complex $[Ir(pic)_2(cod)]BF_4$ (**[5]BF4**) in the presence of small amounts of picolinate (as Kpic) immediately gives complexes **2a/2b** and Dpic, thus providing a further support to the DFT-calculated final step. Consequently, the nucleophilic attack of methanol to $[5]^+$ (assisted by a base, the picolinate anion in this case) represents the key step for the formation of C–O bond. Moreover, the addition a different base such as solid Me_4NOH to a solution of **[5]BF4** in methanol again gave the thermodynamic mixture **2a/2b** immediate and quantitatively (¹H NMR evidence). On the contrary, no reaction was observed when dissolving $[5]^+$ in methanol in the absence of a base.

Figure 7. DFT computed (TPSSH-D3/BS2) Gibbs energy profile for the picolinate-assisted nucleophilic attack of MeOH to $[5]^+$ in methanol. Relative ΔG values are given in kcal mol⁻¹. Code color for the figures: Ir (green), O (red), N (blue), C (gray), H (black).

Reaction of $[Ir(pic)(cod)(O_2)]$ with Hpic.

The energy-profiles shown in Figures 4-7 revealed that the highest energy barrier for the whole reaction corresponds to the formation of the superoxide complex $[Ir(pic)(cod)(\eta^1-O_2)]$ (**I1**) through **TS0** (Figure 4). Since kinetic measurements cannot discriminate between the two critical possibilities: an ET reaction to the peroxide $[Ir(pic)(cod)(O_2)]$ (**6**, through **MCEP1**) versus a PCET reaction to the hydroperoxide $[Ir(pic)(cod)(OOH)(\kappa^1-pic)]$ (**I2**, through **MCEP2**), the following experiment was carried out.

As we had the peroxide complex $[Ir(pic)(cod)(O_2)]$ (**6**) in hand,^[20a] its reaction with Hpic was studied. Thus, addition of a solution of Hpic in CD_3OD to a solution of **6** in dichloromethane resulted in a complicated reaction that gave a mixture of four major products (Figure 8). Among them, complexes **2a/2b** (blue diamond and red triangle, respectively) were formed, but they

only represent the 36.5 % of the products, whereas the main species are those marked with black and white circles in Figure 8 (50 %). As the later compounds do not result in the original and cleaner reaction of $[\text{Ir}(\text{pic})(\text{cod})](\text{O}_2)$ (**1**) + Hpic + O_2 to give **2a/2b** (86.0%), this experiment clearly indicates that the peroxide **6** (formed by the ET transfer step through **MECP1**) is not involved in the reaction, and it is consistent with the PCET step through **MECP2** (Figure 4).

The major component in the reaction mixture (black circle, ca. 34 %) was further characterized by NMR as the ketonic complex *trans*-O,O- $[\text{Ir}(\text{pic})_2(\text{OC}_8\text{H}_{11})]$ (**7**), whereas a X-ray diffraction study revealed that complex **2c** (white circle, 16 %) is a third isomer of complex **2**, similar to **2b**, but having the picolinate ligands in a *cis*-O,O-*cis*-N,N disposition (see Supporting Information).

Figure 8. Selected region of the ^1H NMR spectrum of the products of the reaction $[\text{Ir}(\text{pic})(\text{cod})(\text{O}_2)]$ (**6**) + Hpic/ CD_3OD after 24 h. The mixture contains four major products including **2a** (blue diamond) and **2b** (red triangle) in a 36.5 % total yield.

As shown in Scheme 3, protonation of the peroxide ligand in **6** can take place on each one of the oxygen atoms. If the oxygen O^1 *trans* to the oxygen is protonated the intermediate **12** results, which develops into **2a/2b**, as commented before. Protonation of the oxygen O^2 *trans* to the olefin gives **12'**, which could transform into **2c** by nucleophilic attack of methanol to the carbon marked in green through a similar pathway to that described for **2a/2b**.

Scheme 3. Reaction of $[\text{Ir}(\text{pic})(\text{cod})(\text{O}_2)]$ (**6**) with Hpic in MeOH to give complexes **2a**, **2b**, **2c** and **7**.

In addition, a nucleophilic attack of the hydroperoxide ligand in **12'** to one of the olefinic carbons of cod would give intermediate

A, which has a *fac*-1-irida-2,3-dioxolane- η^2 -cyclooctenyl fragment. The transformation of **A** into the ketonic aquo intermediate **B** would result from O–O bond cleavage and hydrogen transfer, a known reaction for neutral 1-rhoda/irida-2,3-dioxolanes^{[15g],[21]} and related complexes.^[30] The last step would involve dissociation of the molecule of water, bonding isomerization of the η^1 -coordinated picolinate, and coordination of the N-end to give complex **7** with the picolinate ligands in a *trans*-O,O-configuration. Notice that this alternative is only possible from isomer **12'** because of the *fac*-stereochemistry of the two olefinic bonds and the hydroperoxide ligand (*mer* in **12**).

Reductive-elimination steps.

In order to close a plausible catalytic cycle for the synthesis of alkyl ethers, complexes **2a/2b** were warmed in methanol in the presence of cod. However, the reductive-elimination step was not observed. Moreover, if the warming was carried out in acetonitrile, extrusion of methanol to give the complexes **8a/8b** (Scheme 4) was observed.

Scheme 4. Transformation of complexes **2a/2b** into **8a/8b**.

Complexes **8a/8b** were isolated as white solids and further characterized according to their analytical and spectroscopic data (see the Supporting Information). The most relevant signals in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum were those corresponding to the carbon σ -bonded to iridium (which resonates at high field, δ = 17.9 and 17.6 ppm) and to the uncoordinated C=C double bond (δ = 136.6 and 135.9 ppm) in the region typical of free olefins. The formation of **8a/8b** can be easily understood assuming the participation of the ionic species $[\text{Ir}(\text{pic})_2(\text{cod})]\text{OMe}$, which under these conditions transforms into **8a/8b** via abstraction of an allylic hydrogen by the methoxide.

Knowing the greater ability of rhodium complexes to undergo reductive-elimination reactions than iridium, the response of the rhodium counterpart $[\text{Rh}(\text{pic})(\text{cod})]$ (**9**) towards the combined action of oxygen and Hpic in alcohols was studied. The reactions required around four days to reach completion and the products were found to be the organic ethers 1-alkoxy-2,5-cyclooctadiene (OMe, **10**; OEt, **11**), as a result of the reductive-elimination of the organic fragment (Scheme 5). The reactions were accomplished with the precipitation of a white solid further identified as the previously reported^[31] $[\text{Rh}(\text{pic})_3]$ (**12**) and accordingly, the reactions run better in the presence of an extra equiv.-mol of Hpic.

Scheme 5. Synthesis of the organic ethers **10** and **11**.

The organics **10** and **11** were isolated as colourless oils after chromatographic separation and further characterized by spectroscopic methods. Although we are not aware of previous examples of such reactions in rhodium chemistry, mixtures of isomers of 1-methoxy-cyclooctadiene have been prepared by reaction of $[\text{Pd}(\text{cod})\text{Cl}_2]$ with bases (Na_2CO_3 or NaOMe) in refluxing methanol^[32] or $[\text{Pd}(\text{cod})\text{Br}_2]$ with NaOMe in the presence of PCy_3 .^[33] In this regard, the regioselectivity shown by complex $[\text{Rh}(\text{pic})(\text{cod})]$ (**9**) to the single 2,5-diene isomer is remarkable (Scheme 5). Moreover, in our case, the reaction does not require the addition of bases or high temperatures.

Most probably, the reaction of complex $[\text{Rh}(\text{pic})(\text{cod})]$ (**9**) with oxygen and Hpic in methanol follows a similar mechanism to that described for the iridium counterpart **1** to give $[\text{Rh}(\text{pic})_2(\text{MeOC}_8\text{H}_{12})]$. Then, dissociation of one of the ends of the picolinate ligands (or the olefinic bond) would provide a coordination vacancy for a β -hydride elimination to give $[\text{Rh}(\text{pic})_2(\text{H})(\text{MeOC}_8\text{H}_{11})]$. Protonation of the hydride ligand by the extra Hpic,^[34] followed by coordination of the resulting picolinate anion would give $[\text{Rh}(\text{pic})_3]$ (**12**) and free 1-methoxy-2,5-cyclooctadiene (**10**). Unfortunately, no intermediates could be observed by NMR, so that any mechanistic proposal would remain speculative.

Interestingly, if the related complex $[\text{Rh}(\text{L-pro})(\text{cod})]$ (**13**), containing the deprotonated form of the aminoacid L-proline (L-Hpro), is used instead of the achiral $[\text{Rh}(\text{pic})(\text{cod})]$ (**9**), the reaction with oxygen in the presence of L-proline as proton source in methanol gave compound **10*** in an enantioselective way, with an e.e > 98 % by NMR.

Conclusions

In summary, the results reported here represent a novel stoichiometric way to the hydroxylation/alkoxylation of a diolefin on iridium associated to the reduction of oxygen. Alcohols or simply water are the source for the hydroxy/alkoxy groups in the products, *trans*-O,O- $[\text{Ir}(\text{pic})_2(\text{ROC}_8\text{H}_{12})]$ (R = Me, **2a/2b**; Et, **3a/3b**; H, **4a/4b**). From a conceptual point of view, oxygen is reduced to H_2O_2 with two protons and two electrons provided by the oxidation of iridium(I) to iridium(III). The resulting picolinate anion becomes coordinated to iridium whereas the hydroxy/alkoxy groups are incorporated into the complex through the formation of a new C–O bond in an *exo* or *anti* configuration.

A key step that accounts for the selectivity of this original reaction disclosed by DFT-calculations is a PCET step that provides an alternative pathway from the initial OST-superoxide

complex $[\text{Ir}^{\text{II}}(\text{pic})(\text{cod})(\eta^1\text{-O}_2)]$ to the hydroperoxide complex $\text{CSS-}[\text{Ir}^{\text{III}}(\text{pic})(\text{cod})(\eta^1\text{-O}_2\text{H})(\eta^1\text{-pic})]$ (**12**) rather than the most common ET reaction to the peroxide. This finding is highly valuable because previous examples for the evolution of an open-shell triplet (OST) superoxide complex into a diamagnetic (closed-shell singlet, CSS) hydroperoxide compound through a PCET reaction are almost absent in the literature.^[35]

In marked contrast, open-shell superoxide complexes are well-known to transform into the corresponding hydroperoxide derivatives, via hydrogen atom abstraction reactions without change in the spin state of the overall reaction.^[36] In addition, it is remarkable the key role of the picolinic acid, actor vs spectator, in the analyzed evolution of the superoxide complex **11** to the hydroperoxide **12** vs the peroxide **6**.

A second relevant step is a nucleophilic attack of alcohol/water to the olefin in the cationic species $[\text{Ir}(\text{pic})_2(\text{cod})]^+$ assisted by a base generated in situ. This step has been observed experimentally via isolation of the cationic complex and further reaction with alkoxides and hydroxide. Moreover, indirect evidence of the proposed pathway comes from the complexity of the products if the peroxide iridium(III) complex $[\text{Ir}^{\text{III}}(\text{pic})(\text{cod})(\text{O}_2)]$ is reacted with picolinic acid in methanol compared with the high selectivity observed in the original reaction of $[\text{Ir}^{\text{I}}(\text{pic})(\text{cod})]$ with Hpic and oxygen from air.

If this protocol is applied to the diolefin-rhodium(I) complex $[\text{Rh}(\text{pic})(\text{cod})]$, the free alkyl ethers $\text{ORC}_8\text{H}_{11}$ (R = Me, Et) and $[\text{Rh}(\text{pic})_3]$ resulted, and the reaction is enantioselective if a chiral aminoacid such as L-proline is used.

Finally, we have found a reversible and easy exchange of the alkoxy groups in the complexes $[\text{Ir}(\text{pic})_2(\text{ROC}_8\text{H}_{12})]$ just by dissolving them in a different alcohol (R'OH). This exchange is speed up by small amounts of a protic acid and reflect the weakness of the C–O bond in complexes $[\text{Ir}(\text{pic})_2(\text{ROC}_8\text{H}_{12})]$, in sharp contrast with the cleavage of the C–O bond in free ethers that requires hard reaction conditions.

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Keywords: oxygen • iridium • DFT-studies • hydroperoxide • nucleophilic attack

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- [26] The monocrystal studied was disordered with a 86.9(4)% of **2a** and 13.1(4)% of **2b**.
CCDC 1907971 (**2a/2b**·0.125C₆H₁₄), 1907972 (**5b**·1.5CH₂Cl₂) and 1910243 (**2c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [27] DFT calculations have been performed with the TPSSH-D3 functional (see Computational Details in the Supporting information). All reported energies correspond to TPSSH-D3 Gibbs energies in solvent at 298.15 K.

- [28] When computing the reactions in methanol, in addition to the continuum solvent (SMD model), we have considered a cluster of five molecules of methanol solvating the methanol molecule, the acid (Hpic), and the bases (pic⁻ or MeO⁻) (see Supporting Information).
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Layout 2:

FULL PAPER

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**Inner-Sphere Oxygen Activation
Promoting Outer-Sphere Nucleophilic
Attack to Olefins**

Combined action of oxygen, two protons and one 'Ir(diolefin)' fragment causes an unusual and easy hydroxylation/alkoxylation of the diolefin bound to iridium with reduction of O_2 to hydrogen peroxide as shown in the figure. Experimental and theoretical studies reveal a novel PCET reduction of oxygen to hydroperoxide as well as unusual and straightforward exchange reactions of alkyl ethers. Code color: Ir (green), O (red), N (blue), C (gray).