Functionalization of Rhenium Aryl Bonds by O-Atom Transfer

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Supporting Information

ABSTRACT: Aryltrioxorhenium (ArReO₃) has been demonstrated to show rapid oxy-functionalization upon reaction with O-atom donors, YO, to selectively generate the corresponding phenols in near quantitative yields. ¹⁸O-Labeling experiments show that the oxygen in the products is exclusively from YO. DFT studies reveal a 10.7 kcal/mol barrier (Ar = Ph) for oxy-functionalization with H₂O₂ via a Baeyer–Villiger type mechanism involving nucleophilic attack of the aryl group on an electrophilic oxygen of YO coordinated to rhenium.

A fundamental challenge in the development of hydrocarbon hydroxylation catalysts based on C–H bond activation¹ is the requirement for efficient and compatible oxy-functionalization of the LnM–R intermediates to generate R–OH.²,³ The most effective catalysts for methane hydroxylation are based on strongly electrophilic and oxidizing cations such as Hg(II),⁴ Pt(II),⁵ Pd(II),⁶ and Au(I/III)⁷ in strongly acidic media where both C–H activation and oxy-functionalization of the electrophilic LnM–CH₃ intermediates are facile. However, well-defined oxy-functionalization catalysts for hydrocarbons based on less electrophilic and less oxidizing metals such as Re, Ru, Ir, and Os have not yet been well developed.⁸ This is likely because, while C–H activation is known with these systems,⁹ oxy-functionalization reactions of less electrophilic LnM–R intermediates are not well developed and have only recently been reported when R = alkyl group.¹⁰ For electrophilic late transition metals, C–O bond formation proceeds via nucleophilic attack of an O-based nucleophile (e.g., water) on the electrophilic hydrocarbyl group. Not surprisingly, the functionalization reactions of LnM–R complexes with more electropositive metals operate by very different mechanisms, where the hydrocarbyl group is the nucleophile. For example, Brown and Mayer reported oxy insertion into a phenyl ligand from a Re(VII) bis-oxo system.¹¹ However, examples of oxo ligands that are sufficiently electrophilic for migration of a nucleophilic hydrocarbyl ligand are rare.¹¹,¹² More recently, some of us have reported the reaction of methyl rhenium trioxide (CH₃ReO₃) with various O-atom donors, YO, such as IO₄⁻, H₂O₂, or PhIO, in aqueous solvents that proceeds at room temperature (RT) to rapidly and cleanly generate methanol and [ReO₅]⁻ presumably via the rhenium methoxy species (Figure 1, R = Me).¹³

A Baeyer–Villiger (BV) type mechanism has been proposed for this reaction based on DFT studies and could provide the basis for the design of new catalysts that operate via C–H activation for hydrocarbon oxidation reactions. However, relatively little is known about the scope and details of oxy-functionalization reactions of poorly electrophilic LnM–R systems by this or other reaction mechanisms. To begin addressing this using the R–ReO₃ motif as a well-behaved system with a nucleophilic hydrocarbyl, we have begun to systematically explore the scope of oxy-functionalization chemistry where R = aryl. Since the bonds of metal–aryls are typically stronger than metal–alkyls, it is plausible that higher barriers could be possible and reactions proceed through different mechanisms. However, in organic BV reactions, aryl migration is more facile than alkyl, and it will be interesting to contrast the organic and organometallic systems based on this precedent.¹³

The aryl complexes of rhenium trioxide, ArReO₃, have been previously reported.¹⁴ Our initial studies involved reaction of the phenyl (PhReO₃) and para-tolyl trioxorhenium (p-TolReO₃) derivatives of ArReO₃ with 3 equiv of H₂O₂ in a THF-D₂O/D₂O (5:1) mixture. A color change was observed instantaneously upon shaking at RT. Subsequent analysis by NMR and GC-MS showed formation of phenol and only para-cresol. However, full quantitative and kinetic analyses of these and other known monosubstituted ArReO₃ complexes were complicated by their characteristic thermal-instabilities.¹⁴

Since the 2,4,6-trimethylphenyl trioxorhenium (MesReO₃) complex¹⁴b was reported to be thermally stable, we focused our studies on this system. Significantly, similar to the parent phenyl complexes. To begin addressing this using the R–ReO₃ motif as a well-behaved system with a nucleophilic hydrocarbyl, we have begun to systematically explore the scope of oxy-functionalization chemistry where R = aryl. Since the bonds of metal–aryls are typically stronger than metal–alkyls, it is plausible that higher barriers could be possible and reactions proceed through different mechanisms. However, in organic BV reactions, aryl migration is more facile than alkyl, and it will be interesting to contrast the organic and organometallic systems based on this precedent.¹³

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Received: March 17, 2011
Published: March 29, 2011

Figure 1. Oxy-functionalization of a M–R complex proposed to proceed via a Baeyer–Villiger-type oxidation.
analagues, treatment of a THF-D$_8$/D$_2$O (5:1) solution of MesReO$_3$ with 3 equiv of H$_2$O$_2$ led to an instantaneous color change at RT and selective formation of only 2,4,6-trimethylphenol on the basis of $^1$H NMR and GC-MS analysis. Examination of this reaction using an external standard showed that the reaction is essentially quantitative with no evidence of MesReO$_3$ decomposition. Also, the functionalization reaction proceeds efficiently under both air and argon.

To determine whether the oxygen in the 2,4,6-trimethylphenol was derived from H$_2$O$_2$, the ReO$_3$ motif, or D$_2$O solvent, we examined the reaction with >95% $^{18}$O-labeled hydrogen peroxide (which does not undergo O-atom exchange on the time scale of the reaction with water or Re). Confirming that the oxygen atom was derived from H$_2$O$_2$, analysis of the reaction mixture by GC-MS showed that the 2,4,6-trimethylphenol was >95% $^{18}$O-labeled. A similar result was obtained from our previous report involving the reaction of CH$_3$ReO$_3$ with NaI$_{18}$O$_4$.

To examine the scope of the reaction with respect to O-atom donors, we examined the reaction with NaIO$_4$, DMSO, and PyO. We were particularly interested in O-atom donors such as PyO and DMSO, as these can be generated from O$_2$. As can be seen in Table 1, all of these O-donors generated 2,4,6-trimethylphenol but with different efficiencies. Detailed kinetic studies were not carried out, but as shown in column 3, the reactions with H$_2$O$_2$ and NaIO$_4$ were fast and selective with essentially quantitative yields of the 2,4,6-trimethylphenol after 1 h at RT. In contrast, reactions with PyO and DMSO were much slower, and these O-atom donors showed no reaction under our standard conditions. However, heating the PyO and DMSO reaction mixtures at 75 °C for 24 h and 100 °C for 72 h, respectively, showed clean formation of 2,4,6-trimethylphenol, albeit in low yields (column 4, Table 1). These reactions are selective, as the phenol and unreacted starting material accounted for >90% mass balance.

To compare the relative reactivity of alkyl and aryl derivatives of R–ReO$_3$ complexes, we investigated competitive reactions between CH$_3$ReO$_3$ and MesReO$_3$. The study was carried out under pseudo-first-order conditions by treatment of a 5:1 THF-D$_8$/D$_2$O solution containing 33 mM of both CH$_3$ReO$_3$ and MesReO$_3$ with 0.05 equiv of H$_2$O$_2$ (based on total added Re). After shaking at RT, in situ analysis of the crude reaction mixture by $^1$H NMR showed formation of 2,4,6-trimethylphenol and CH$_3$OH in a 3.8:1 ratio along with unreacted CH$_3$ReO$_3$ and MesReO$_3$ with >90% mass balance. These results suggest that the aryl complex is ∼4 times more reactive than the alkyl complex. Examination of the competitive oxidation in THF by DFT confirmed this result to give $\Delta G^\ddagger$ barriers of 25.5 and 26.9 kcal/mol for MesReO$_3$ and CH$_3$ReO$_3$, respectively, for aryl and alkyl migration ($\Delta \Delta G^\ddagger$ ∼1 kcal/mol for ∼4:1 ratio of rates).

In order to gain further insight into the functionalization of the ArReO$_3$ complexes, we examined the reactions of PhReO$_3$, 1, with H$_2$O$_2$ by DFT and continuum solvation representing water. These studies show that, as for organic BV-type mechanisms, on the most favorable pathway the reaction proceeds in two steps: (1) YO coordination to the Re type mechanism, on the most favorable pathway the reaction proceeds in two steps: (1) YO coordination to the Re type center and (2) concerted migration of the aryl group to the oxygen of the coordinated YO, Figure 2. Other

### Table 1. Functionalization Results of MesReO$_3$ and Predicted DFT Barriers for the BV TS

<table>
<thead>
<tr>
<th>complex</th>
<th>YO</th>
<th>std cond % aryl–OH</th>
<th>max yield % aryl–OH</th>
<th>BV TS $^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MesReO$_3$</td>
<td>H$_2$O$_2$</td>
<td>&gt;90</td>
<td>&gt;90</td>
<td>10.7</td>
</tr>
<tr>
<td>MesReO$_3$</td>
<td>NaIO$_4$</td>
<td>&gt;90</td>
<td>&gt;90</td>
<td>12.8</td>
</tr>
<tr>
<td>MesReO$_3$</td>
<td>PyO</td>
<td>0</td>
<td>~20</td>
<td>35.1</td>
</tr>
<tr>
<td>MesReO$_3$</td>
<td>DMSO</td>
<td>0</td>
<td>~15</td>
<td>35.1</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: A screw cap NMR tube with PTFE insert was loaded with 5 mg of MesReO$_3$. The solid was dissolved in 0.6 mL of a THF-D$_8$/D$_2$O (5:1) solution to which 3 equiv of YO was added, and the NMR tube was shaken at RT and allowed to sit for 1 h before monitoring. 24 h, 75 °C. 72 h, 100 °C. $^b$Calculated $\Delta G^\ddagger$ between PhReO$_3$ and phenyl migration barrier in water and in DMSO, respectively.

Figure 2. Standard Gibbs free energy surfaces (kcal/mol, including aqueous solvation using M06) of the Baeyer–Villiger oxidation at pH = 7 and 298 K.
pathways involving a migration of the aryl group to either oxo or μ²-peroxo groups result in much higher barriers (>23 kcal/mol).

Since coordination of H₂O₂ to the Re center is expected to be pH dependent, we examined the reaction profile at pH = 7 to mimic the reaction conditions. Neutral adducts between 1 and H₂O₂ were found to be less stable than monodeprotonated adducts with no stable adduct between 1 and neutral H₂O₂ located in our survey of the reaction surface. With a pKₐ of 11.6 for H₂O₂,¹⁸ proton dissociation is uphill by 6.3 kcal/mol at pH = 7 and coordination of HOO⁻ to the Re center to generate the monodeprotonated adduct, 3, is stabilizing, −0.2 kcal/mol, and is slightly favorable relative to 1. As shown in Figure 1, the overall reaction to generate the O-atom insertion product, PhOReO₃, is highly favorable, −78.4 kcal/mol downhill. The lowest calculated pathway (10.9 kcal/mol) was found from the monodeprotonated species, 3, proceeding through a BV-type aryl migration to coordinated hydroperoxide (TS₁).

These values are consistent with the observed high functionalization yields and rapid reaction upon mixing at RT. We have assumed that the hydrolysis of the ArReO₃ intermediate to the corresponding aryl alcohol is fast. Electronically the reaction proceeds as a concerted displacement of the O–O σ-bonding pair of electrons by the attacking carbon σ-bond. It is interesting that the mono-
derprotonated TS₁, where OH⁻ is the leaving group, is substantially lower in energy than the neutral TS₂, where the leaving group is H₂O. This would seem to suggest that with these more electropositive organometallics, inducing nucleophilic character on the aryl group by operating under basic conditions could be more beneficial than stabilizing the leaving group through protonation under more acidic conditions. It will be interesting to examine the pH dependency of these reactions.

Given the experimental observation that potentially air recyclable oxidants such as PyO and DMSO can functionalize MesReO₃, we examined the oxidation of PhReO₃ with DMSO by DFT. Interestingly, unlike the case for H₂O₂ calculations predicted that no stable DMSO adduct exists. Instead, consistent with the observed slow reaction, a concerted insertion transition state was located with an activation free energy of 35.1 kcal/mol, leading to the formation of PhOReO₃ and dimethylsulfoxide (Scheme 1).

These results suggest a parallel to the BV reactions observed in organic chemistry, where conversion of aryl ketones to the corresponding esters by treatment with O-atom donors such as H₂O₂ are more facile than with alkyl ketones.¹⁵ This is typically explained by the greater stabilization of charge by delocalization in the transition state that is possible in aryl versus alkyl migration. To address this, a Hammett study of substituted ArReO₃ complexes would be ideal. However, our attempts at Hammett studies were hampered since, as noted above, the known class of phenyl 4-substituted trioxorhenium complexes were thermally unstable. The 2,6-dimethylphenyl trioxorhenium complexes can be utilized in such a study, but the required family of para-substituted complexes are not known and are currently being synthesized in our laboratories.

These results show that the functionalization of LnM–R complexes where M is not of the class of strongly electrophilic metals can undergo facile oxy-functionalization when R = alkyl or aryl. As in the case of the alkyl systems, theoretical calculations for when R = Ar are consistent with the reactions proceeding via a BV-type reaction mechanism, which would be consistent with the observed faster rates for the aryl systems. Importantly, the results disclosed herein suggest similarity between the organic and organometallic BV transformation and showcase the broad potential for facile oxy-functionalization of more electropositive organometallic intermediates by a BV-type reaction mechanism.

Given the facile characteristics of these oxy-functionalization reactions, we are exploring the possibility of coupling with C–H activation to design new hydroxylation catalysts. It should be noted that the Re center in the R–ReO₃ motif is formally d⁰, and thus competitive oxidation by YO of the metal center versus the R group is not possible. Since lower oxidation state metal centers are typically more active for C–H activation, we anticipate that this undesirable oxidation of the metal center versus the R group could be a key challenge in utilizing this type of functionalization reaction to design new hydrocarbon functionalization catalysts based on a C–H activation/M–R functionalization cycle. Consequently, an important focus of our ongoing work will be to determine if the BV-type mechanism is possible with non-d⁰, more electropositive organometallics.

## ASSOCIATED CONTENT

Supporting Information. Synthetic procedures, characterization data, experimental details, and DFT coordinates are available free of charge via the Internet at http://pubs.acs.org.

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### ACKNOWLEDGMENT

The authors acknowledge the Chevron Corporation, the Center for Catalytic Hydrocarbon Functionalization, a DOE Energy Frontier Research Center (DOE DE-SC000-1298), and The Scripps Research Institute for financial support of this research.

### REFERENCES


(14) Added YO was based on total added Re such that 0.05 equiv allows for either MesReO3 or MTO to be under pseudo-first-order conditions if reaction went to completion with the added YO.

(15) See Supporting Information for more details.