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Oxy-Functionalization of Nucleophilic Rhenium(I) Metal Carbon Bonds Catalyzed by Selenium(IV)

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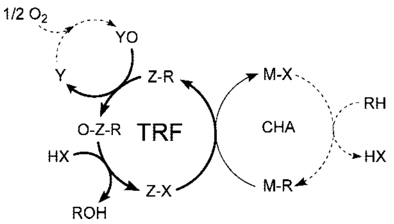
Electrophilic C−H bond activation (CHA) with strong electrophiles,[1,2] such as Pt^{II}, Pd^{II}, Au^{III}, and Hg^{II}, followed by reductive oxy-functionalization (OF) of the resulting positively polarized metal alkyl ($M-R^{\delta+}$) intermediate is a well-known strategy for hydrocarbon hydroxylation.[3] However, water and alcohol inhibition of the CHA reaction renders this strategy commercially impractical. We[4] and others[5] have shown that CHA with *weakly* electrophilic cations, such as Ir^{III} and Ru^{II}, are less prone to such inhibition. However, the reductive OF reactions utilized with highly electrophilic catalysts are generally not applicable to weakly electrophilic systems because the reduced oxidation potential thermodynamically disfavors reductive functionalization and/or the reduced electrophilicity can result in $M-R^{\delta-}$ polarized bonds that exhibit high barriers for nucleophilic attack at the carbon.[6] Therefore we have set out to design new approaches for functionalization of $M-R^{\delta-}$ polarized bonds.

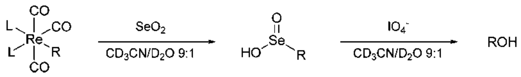
We recently proposed a new strategy for facile, nonredox, OF of electron-rich M−C bonds that involves insertion of O-electrophiles, YO.[6] A related strategy is to functionalize by alkyl transfer to a more electrophilic, redox active, Z−X co-catalyst, followed by oxidation and reductive OF from Z−R (Scheme 1). This trans-alkylation reductive functionalization (TRF) sequence, when coupled to the C−H bond activation and oxidant regeneration reactions (dashed lines, Scheme 1), could lead to tandem catalytic systems for alkane hydroxylation.

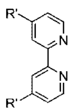
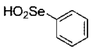
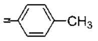
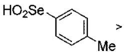
Scheme 1. Generalized Scheme for Coupling a TRF Catalytic Cycle (Solid Lines) to CHA and Oxidant Regeneration Reactions (Dashed Lines)



We focused on designing TRF reactions with d^6, octahedral, low oxidation state $M-R^{\delta-}$ complexes that would be good models for M−R intermediates generated from weakly electrophilic, water insensitive CHA systems.[4] Key to facilitating study of these M−R complexes is identifying systems where undesired reactions, such as metal centered oxidations and alkyl protonolysis, can be minimized. In actual catalytic systems, strategies will have to be developed to addresses these types of undesired reactions. We chose to study the OF reactions of the $(CO)_5Re^IR$ and the more electron-rich analogue $(CO)_3(bpy)Re^IR$ motifs because our screens showed these complexes were relatively soluble and sufficiently stable in aqueous media to allow reactions to be examined without special techniques (Table 1). Here we report conditions for the facile, stochiometric as well as catalytic OF of $Re-R^{\delta-}$ complexes to the corresponding alcohols via a TRF mechanism.

Table 1. TRF Reactions Studied[a]



L, L	R	Product	% Yield	Product
CO, CO	CH_3	CH_3SeO_2H	> 95 %	CH_3OH
	R' = H, R = CH_3	CH_3SeO_2H	> 95 %	CH_3OH
	R' = H, R = CH_2CH_3	$CH_3CH_2SeO_2H$	~ 90 %	CH_3CH_2OH
	R' = H, R = n-Propyl	n-$PrSeO_2H$	~ 90 %	$CH_3CH_2CH_2OH$
	R' = OMe, R = C_6H_5		> 95 %	---
	R' = OMe, R = 		> 95 %	---

[a] General reaction conditions: 0.01 mmol Re complex (1 equiv) and SeO_2 (2 equiv) in a J-Young NMR tube are dissolved in 0.45 mL of CD_3CN/D_2O (9:1). The reaction is heated to 100 °C for the pentacarbonyl complexes and stirred at rt for the bpy complexes. The yield of the seleninic acids is determined by ^1H NMR comparison to an external standard. $NaIO_4$ (2 equiv) is added and the reaction is heated to 100 °C for 14 h for oxidation to the alcohols.

In contrast to earlier reports of high yield OF reactions of CH_3ReO_3 that occur via O-atom insertion,[6] reactions of $(CO)_5ReCH_3$ with electrophilic O-donors, such as PhIO and $NaIO_4$, in a 9:1 acetonitrile/water solution at 100 °C gave low yields of methanol (∼20−30%, see Supporting Information, SI), and PyO yielded no methanol. Oxidants such as Cu^I/Cu^{II} and Pd^{II} salts in the presence or absence of air did not yield methanol. We considered reactions with selenium oxides since (1) similar to SO_2, SeO_2 is known to react with M−R to generate $R-Se^{IV}$species,[7] (2) $R-Se^{IV}(O)OH$ can be oxidized to $R-Se^{VI}(O)_2OH$ that readily converts to alkanols and Se^{IV},[8] and (3) Se oxides are commercially utilized as co-catalysts in hydrocarbon oxidation reactions.[9,10]

The reaction of $(C\text{-}O)_5ReCH_3$ with excess SeO_2, which exists as $D_2Se^{IV}O_3$ in D_2O,[11] in a 9:1 v/v solution of CD_3CN/D_2O produced methaneseleninic acid, $CH_3-Se^{IV}O_2D$, in quantitative yield as identified by comparison of the ^1H, ^{13}C NMR, and GC/MS spectra to an authentic sample (Table 1). This reaction was slow at room temperature, but heating to 50 °C for 2 h gave nearly

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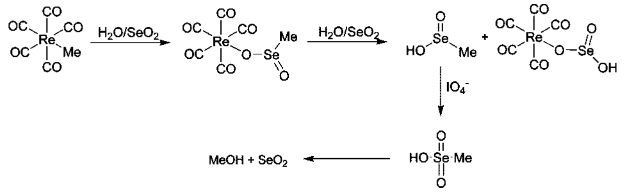
quantitative formation of CH_3SeO_2D as monitored by ^{1}H NMR. Control experiments using $(CO)_5Re^{13}CH_3$ confirmed that the CH_3SeO_2D was derived from the $(CO)_5ReCH_3$ and not from side reactions with the solvent. The formation of CH_3SeO_2D followed first-order kinetics with an experimental $\Delta H^{\ddagger} = 8.0 \pm 1.7$ kcal/mol. Given the observed ~100% methyl mass balance, the likely reaction stoichiometry is shown in eqs 1 and 2.

$$2H_2SeO_3 + (CO)_5ReCH_3 \rightarrow (CO)_5Re(OSeO_2H) + CH_3SeO_2H + H_2O \tag{1}$$

$$(CO)_5Re(OSeO_2H) + H_2O \rightarrow (CO)_5Re(OH) + H_2SeO_3 \tag{2}$$

The expected Re products, $(CO)_5Re(OSeO_2H)$ or $(CO)_5ReOH$, could not be directly observed, likely due to known oligomerization reactions[12] and displacement of CO ligands by the coordinating solvent. Significantly, no methane was observed in the headspace or solution. This, along with the high reaction yield, suggests that the transalkylation reaction with D_2SeO_3 is much faster than protonolysis of the Re−CH_3 bond or oxidation at the Re center by D_2SeO_3. To directly obtain methanol from $(CO)_5Re^ICH_3$ we examined whether it would be possible to *in situ* oxidize $CH_3Se^{IV}(O)OH$ to $CH_3Se^{VI}(O)_2OH$ which could generate methanol and regenerate $H_2Se^{IV}O_3$. Significantly, heating $(CO)_5ReCH_3$ to 100 °C for 12 h in an ~8:2 v/v mixture of CD_3CN/D_2O with excess IO_4^- along with a *catalytic amount* of D_2SeO_3 (10 mol %) gave an ~80% yield of methanol. Controls carried out in the dark show the reactions are not light induced. $CH_3Se^{IV}O_2H$ was observed as a reaction intermediate by ^{1}H NMR, indicating that oxidation of $CH_3Se^{IV}O_2H$ to methanol, likely via $CH_3Se^{VI}(O)_2OH$, is the rate limiting step in the overall conversion to methanol. Control experiments confirmed that treatment of $CH_3Se^{IV}(O)OH$ with IO_4^- under the conditions of the catalytic reaction generates methanol without observation of $CH_3Se^{VI}(O)_2OH$ (Scheme 2).[8]

Scheme 2. Proposed Mechanism of Methanol Formation



Seeking a more reactive system that could also generate a well-defined Re product that could be characterized, we reasoned that replacing CO groups with more electron-donating, less labile bipyridine (bpy) should increase the nucleophilicity of the Re−$CH_3^{\delta-}$ group and lead to cleaner, faster reactions with electrophiles such as Se^{IV}. Consequently, we examined the reaction of $(CO)_3(bpy)ReCH_3$[13] with 1 equiv of H_2SeO_3 in a 9:1 mixture of CH_3CN/H_2O. This system was indeed found to be more reactive, and the reaction was very efficient at rt and even to temperatures as low as −35 °C to generate $(CO)_3(bpy)Re(OSe(O)CH_3)$ in high yield on mixing. This species was isolated as a fine yellow solid in 65% yield after precipitation by diethyl ether and characterized by ^{1}H NMR and elemental analysis. Use of excess H_2SeO_3 produced CH_3SeO_2H and $(CO)_3(bpy)Re(OSeO_2H)$ which was also isolated in high yield and characterized analogously.

It is significant that the rate of methyl transfer can be substantially increased by the use of more electron donating ligands since fast reactions will be required for the trapping of M−R intermediates when coupling functionalizations to CHA reactions. Also relevant to eventual coupling of these reactions to CHA is the lack of competitive protonolysis or oxidation of the Re(I) center. However, at low temperatures the stoichiometric reaction of $(CO)_3(bpy)ReCH_3$ with SeO_2 gives fast quantitative methyl transfer, but attempted reaction of $(CO)_3(bpy)ReCH_3$ with IO_4^- and *catalytic* amounts of H_2SeO_3 at 100 °C led only to formation of methane. We suspect that this is the result of a higher rate of protonolysis for $(CO)_3(bpy)ReCH_3$ vs $(CO)_5ReCH_3$ (due to a more basic Re−$CH_3^{\delta-}$ bond) even though the transalkylation reactions with H_2SeO_3 are also more efficient. In actual tandem catalytic systems, when coupled to a *reversible* CHA system, this M−R protonolysis will not prevent product formation. The relative reactivity of $(CO)_5Re^ICH_3$ and $(CO)_3(bpy)Re^ICH_3$ with SeO_2 and oxidants is currently being examined in detail.

To examine the scope of these OF reactions, we also studied the reaction of $(CO)_3(bpy)$Re−R complexes where R = methyl, ethyl, and *n*-propyl (Table 1). Of particular interest was whether primary rhenium alkyls would generate primary, rather than rearranged, seleno-functionalized products upon treatment with SeO_2. Significantly, as in the case of R = CH_3, reaction of the ethyl and *n*-propyl Re^I complexes led to essentially quantitative yields of the corresponding seleno-functionalized product, $RSe^{IV}(O)OH$, where R is ethyl and *n*-propyl, respectively. Since Se^{IV} is a relatively strong oxidant and used for oxidation of activated CH bonds in organic chemistry,[9] it is significant that no rearrangements or oxidation of the ethyl and *n*-propyl groups take place during functionalization. Equally significant, treatment of the resulting $RSe^{IV}(O)OH$ solutions with IO_4^- led to regioselective formation of the corresponding alcohols, CH_3CH_2OH and $CH_3CH_2CH_2OH$, Table 1. These results are encouraging and show the potential for Se^{IV} based tandem CHA/TRF catalysis that can lead to alcohols where the regioselectivity is set by the CH activation step. This observation, coupled with the known higher selectivity for CHA for primary over secondary or tertiary C−H bonds with weakly electrophilic catalysts,[1,4] could suggest methods for the selective C–H functionalization of alkanes to primary alcohols.

To determine if the seleno-functionalization could be also extended to aryl rhenium bonds, we examined the reaction of SeO_2 with $(CO)_3(bpy)$Re-R, R = phenyl and *para*-tolyl. These complexes also reacted quantitatively and rapidly to generate the corresponding RSe(O)OH products. Significantly, R = *para*-tolyl led to exclusive formation of the *para*-tolyl seleninic acid, *p*-$CH_3C_6H_4Se(O)OH$, and shows that functionalization likely proceeds by attack at the ipso carbon of the aryl ring. Treatment of $(CO)_3(bpy)$Re-Ph with catalytic amounts of SeO_2 and excess IO_4^- did not generate phenol and gave only $PhSe^{IV}(O)OH$ and $PhSe^{VI}(O)_2OH$. Consistent with this observation, control studies show that, unlike $CH_3Se^{VI}(O)_2OH$ (*vide infra*), $C_6H_5Se^{VI}(O)_2OH$ is a thermally stable species in aqueous solution and can be readily synthesized by treatment of $PhSe^{IV}(O)OH$ with oxidants such as MnO_4^- (or IO_4^-).[14] Since methods to convert these aryl metal complexes to phenol will be important, efforts are underway to identify conditions to convert $(CO)_5RePh$, $PhSe^{IV}(O)OH$, and/or $PhSe^{VI}(O)_2OH$ to phenol.

The mechanism for the transalkylation step was also studied using density functional theory.[15] The most favorable reaction pathway was found to be nucleophilic attack by Re−$CH_3^{\delta-}$ on the electrophilic Se^{IV} center (Figure 1). All reactions involving prior dissociation of CO are energetically disfavored. Consistent with this, experiments run at 70 °C under 1 atm of CO gas showed no decrease in rate relative to those without added CO. The initial step in the reaction mechanism is the conversion of ground state H_2SeO_3 to the more electrophilic SeO_2, with the H_2O weakly bound to selenium (Se−OH_2 2.6 Å). As expected, this reaction was calculated to be endothermic with a ΔH of 5.5 kcal/mol. The electrophilic Se center is then attacked by the negatively polarized methyl group of $(CO)_5$Re−$CH_3^{\delta-}$. We found that keeping the water molecule associated with the SeO_2 moiety in the transition state lowers the reaction barrier by 3.0 kcal/mol, most likely due to a stabilization of the partial negative charge built up at the oxygen atoms. We calculated the reaction to have an enthalpic barrier of 7.6 kcal/mol, giving an overall barrier of 13.2 kcal/mol relative to selenious acid and $(CO)_5ReCH_3$. This is consistent with our experimental $\Delta H^\ddagger$ value of 8.0 ± 1.7 kcal/mol.[16] For the overall reaction from H_2SeO_3 and $(CO)_5ReCH_3$ we calculated an entropic barrier of ~4.4 kcal/mol ($T\Delta S^\ddagger = -14.8$ eu) (298 K), yielding a $\Delta G^\ddagger$ of 17.6 kcal/mol at rt. This relatively large negative entropy is consistent with the associative nature of the transition state.

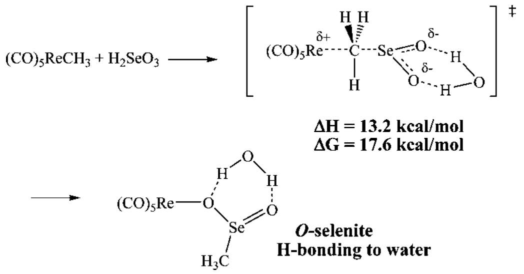


Figure 1. Proposed mechanism for methyl transfer to H_2SeO_3.

A scan of the intrinsic reaction coordinate (IRC) shows that the transition state collapses to a structure where one of the oxygen atoms of the methylseleninic moiety coordinates to Re (Figure 2, bottom right). The overall reaction of $(CO)_5ReCH_3$ with selenious acid to form the *O*-methylseleninate complex is exothermic by 21.5 kcal/mol. Interestingly, we found that rearrangement to the *S*-methylseleninate is unfavorable by 15.4 kcal/mol.

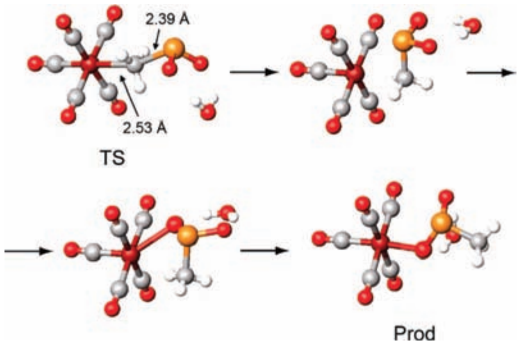


Figure 2. Transition state (top left) and snapshot views from the IRC of the subsequent decomposition to *O*-seleninate product.

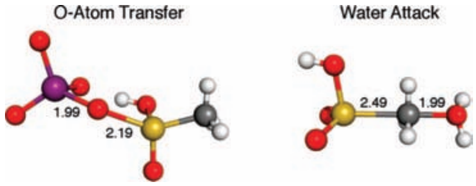


Figure 3. Solvent (MeCN) optimized transition states for O-atom transfer and H_2O attack.

The direct O-atom transfer between $CH_3Se^{IV}(O)OH$ and IO_4^- to generate $CH_3Se^{VI}(O)_2OH$ has an activation free energy of 24 kcal/mol, relative to the methyl Se^{IV} intermediate, which is consistent with the need to heat the reaction to 100 °C for several hours to give methanol (Figure 3). Selenium oxidation is most likely followed by S_N2 attack of the CH_3Se^{VI} bond by water ($\Delta G^\ddagger = 18$ kcal/mol). An alternative pathway without Se oxidation via a Baeyer−Villiger type mechanism has a large activation barrier ($\Delta G^\ddagger = 53$ kcal/mol).

In conclusion, we have identified a facile, catalytic OF route for Re^I-CH_3 bonds with Se^{IV} and iodine based O-atom donors. We are exploring strategies to incorporate this reaction sequence into catalytic cycles for the overall conversion of hydrocarbons to alcohols utilizing low-valent, weakly electrophilic transition metals for C−H bond activation.[17]

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Supporting Information Available: Synthetic procedures, experimental and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) (a) All calculations were performed using the B3LYP hybrid density functional as implemented in Jaguar 6.5 and 7.5. For all atoms except Se, the LACV3P** basis set was used for geometry optimizations and solvation energies, and LACV3P**++ for single-point gas phase energy corrections. For Se, the augmented MSV all electron basis set was used. See Supporting Information for details. (b) *Jaguar*, version 7.5; Schrodinger, LLC: New York, 2008.
(16) We believe that part of the discrepancy between the experimental and theoretical activation enthalpy is due to the theoretical solvation model. This computes the free energy of solvation and therefore contains entropic contributions from solvent rearrangement.
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