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Proton Coupled Electron Transfer in the Reduction of Arenes by SmI$_2$-Water Complexes

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ABSTRACT: The presence of water has a significant impact on the reduction of substrates by SmI$_2$. The reactivity of the Sm(II)-water reducing system and the relationship between sequential or concerted electron-transfer, proton-transfer is not well understood. In this work, we demonstrate that the reduction of an arene by SmI$_2$-water proceeds through an initial proton-coupled electron transfer. The use of thermochemical data available in the literature shows that upon coordination of water to Sm(II) in THF, significant weakening of the O-H bond occurs. The derived value of nearly 73 kcal/mol for the decrease in the bond dissociation energy of the O-H bond in the Sm(II)-water complex is the largest reported to date for low valent reductants containing bound water.

Introduction

The addition of water and alcohols to samarium diiodide (SmI$_2$) in THF has a significant impact on the selectivity and reactivity of the reagent.[1] A wide range of highly selective reductions and reductive coupling reactions can be carried out with high efficiency.[2] In each case, the effectiveness of the approach is dependent on proton donor concentration, competition for Sm(II) coordination between substrate and proton donor and other reaction components. Functional group reductions and bond-forming reactions initiated by SmI$_2$-proton donor systems are complicated by the interplay between proton donor coordination to Sm(II) and their ability to donate a proton through cleavage of the O-H bond. Given this, proton donors employed in reactions of SmI$_2$ are distinguished by those which have a high affinity for Sm(II) (water, methanol, glycols) and those that do not (phenol, 2,2,2,-trifluoroethanol, t-butanol, etc.).[3]

Among Sm(II)-proton donor systems, those that employ water or coordinating proton donors are the most effective at reducing substrates typically recalcitrant to reduction through electron transfer.[4] The seminal work of Curran and Hasegawa demonstrated that water addition to SmI$_2$ accelerated the rate of functional group reduction and they proposed that the effectiveness of the reducing system was a consequence of water coordination to Sm(II).[5] This hypothesis was later confirmed by the groups of Hoz and Flowers.[3,6,7] Since these earlier studies, a number of reductions and bond-forming reactions initiated by the reduction of lactones and other carboxylic acid derivatives by SmI$_2$-water have been developed predominantly through the work of Procter.[8,9] The interesting feature of these reductions is that substrates are being reduced that have significantly higher reduction potentials than SmI$_2$-water.[7] Since this process and others are endergonic (based on redox potentials), it raises the question: Are these events stepwise or does the initial reduction of substrates occur through a proton coupled electron transfer? The reactivity of the Sm(II)-water reducing system and the relationship between the

sequential (or concerted) electron-transfer proton-transfer (ET-PT) process is not well understood. Herein we present a detailed mechanistic study on the reduction of non-coordinating substrates by SmI$_2$-water. This work demonstrates that in the case of arenes, the reduction by Sm(II)-water occurs through a proton-coupled electron transfer (PCET).

Results and Discussion

Given the complexity of Sm(II)-water systems and possible multiple coordination of substrate, water and other reaction components to Sm, we sought out substrates that would simplify a mechanistic study and enable us to examine the interplay between the impact of water on the reducing power of the complex (thermodynamic) and the rate of reaction (kinetic). To this end we chose two classes of substrates, an arene (anthracene) and a primary alkyl iodide (1-iodododecane). These substrates were chosen since they are known to be reduced by Sm-water systems[4] and studies would not be complicated by competition with water for coordination sites on Sm(II) since both are reduced through predominantly an outer-sphere process.[10, 11] In addition, the choice of these substrates enable us to examine the impact of water on the rate of reduction by SmI$_2$. Alkyl halides are reduced through a dissociative electron transfer mechanism where initial electron transfer (ET) is rate limiting.[12, 13] Conversely arenes may be reduced by a rate-limiting ET, a rate-limiting second proton transfer (PT) in the second step, or a proton-coupled electron transfer (PCET).

To examine the systems in detail, a series of rate experiments were performed on SmI$_2$-mediated reductions of anthracene and 1-iodododecane using water and methanol (MeOH) over a wide range of concentrations in THF as shown in equations 1 and 2. Reactions without proton donors led to the recovery of starting material in the case of anthracene whereas partial reduction of the alkyl halide occurred. The rate of reduction of anthra-

cene was relatively fast using water, whereas reduction by MeOH was too slow to be measured by stopped-flow spectrophotometry. Reduction of the alkyl iodide occurred in the presence of water and MeOH, but was considerably slower than the reduction of anthracene.
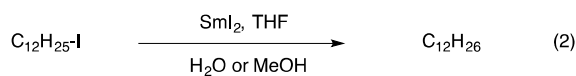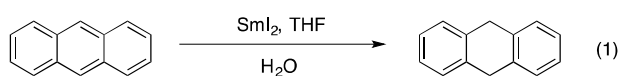
These studies show that water is critical for the reduction of anthracene. Rate studies were performed under pseudo first-order conditions with anthracene and 1-iodododecane in a 10-fold excess (100 mM) with respect to [SmI_2] which was maintained at 10 mM. The reaction was monitored using stopped-flow spectrophotometry to observe [SmI_2] (see SI). Water concentrations were monitored under pseudo first-order conditions over a range of 75 mM to 12 M in the case of anthracene and 70 mM to 5 M in the case of 1-iodododecane. Each rate measurement was repeated thrice with freshly prepared samples. To verify that the rate of substrate reduction was not influenced by the instability of the SmI_2-water complexes at high concentrations of proton donor, the natural decay of the complex was acquired and found to be less than 5% of the value obtained for the decay of Sm(II) in the presence of substrate. A plot of k_{obs} vs. proton donor concentration up to 5 M for the reduction of anthracene and 1-iodododecane is contained in Figure 1.
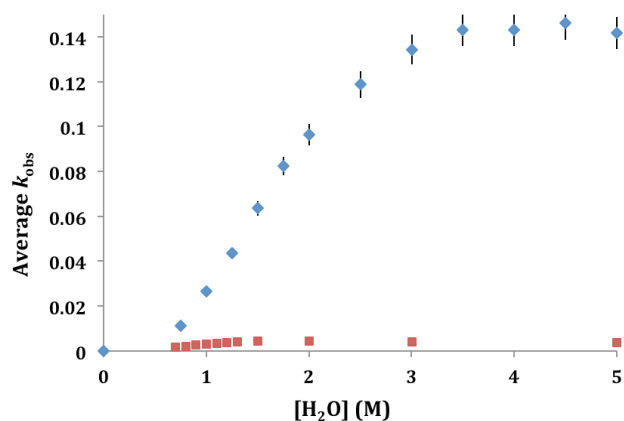

Figure 1. Plot of k_{obs} vs water concentration for the reduction of anthracene (♦) and 1-iodododecane (■) by SmI_2 (10 mM).

Examination of the data shows that water has a significantly greater impact on the reduction of anthracene by

SmI_2 than it does on the reduction of 1-iodododecane. At low concentrations of water, there is a rapid increase in the rate of reduction of anthracene until saturation occurs at approximately 3 M water. At higher concentrations of water above 4.5 M, the rate decreases and displays an inverse order in water (see SI). Although the impact of water on the reduction of 1-iodododecane by SmI_2 is modest in comparison to anthracene, there is a 40 fold rate increase at 2 M water (200 equiv based on [SmI_2]) in comparison to reduction in the absence of water.[13]

The fascinating feature of this data is the relative impact of water on reduction of anthracene by SmI_2 in comparison to 1-iodododecane. The redox potentials of SmI_2, anthracene and a primary alkyl iodide vs. SCE are known.[14-16] As a consequence, the ΔG of the initial electron transfer to each substrate can be determined as shown in Scheme 1. The data below clearly show that reduction of anthracene is a significantly more endothermic process. The caveat of this analysis is the fact that as water is added to SmI_2, a more powerful reductant is formed.[17] However, the reduction of anthracene initiates at concentrations of water below the level where it impacts the reducing power of Sm(II) and the full impact of water on the reducing power of water isn't realized until nearly 1000 equiv. of water.[7] Additionally, if the only role of water in the reduction was to produce a more powerful reductant, a similar rate enhancement should be observed in both cases given that a primary alkyl iodide is thermodynamically easier to reduce through single electron transfer.
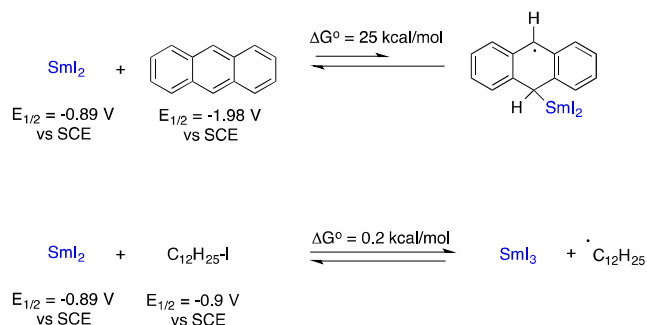
Scheme 1

To further examine the unusual impact of water on anthracene reduction, rate orders were determined. We focused on water concentrations below 2 M (200 equiv based on [SmI_2]) since this is the range of water typically employed in reactions carried out by synthetic chemists.[1,2] Rate orders for SmI_2, water, and anthracene were determined for each of the components and are shown in Table 1. The rate order of water was

Table 1. Rate orders for reduction of anthracene by SmI_2-water.

Reaction component	Rate order

SmI$_2$	1[a]
Anthracene	0.9 ± 0.1[b]
water	2.0 ± 0.1 (0-1.75 M)

Conditions: [a]Fractional times method. 10 mM SmI$_2$, 100 mM anthracene, 0.75-2M H$_2$O. [b]5 mM SmI$_2$, 60-100 mM anthracene, 625 mM H$_2$O. [c]10 mM SmI$_2$, 100 mM anthracene, 0-1.75M H$_2$O. The rate orders are the average of 3 independent experiments.

obtained from the non-linear region of the plot of k_{obs} vs [water] up to 2 M as shown in Figure 2. The rate orders of anthracene and SmI$_2$ are near unity whereas water displays a rate order of 2 in the initial non-linear regions displayed in Figures 1 and 2.
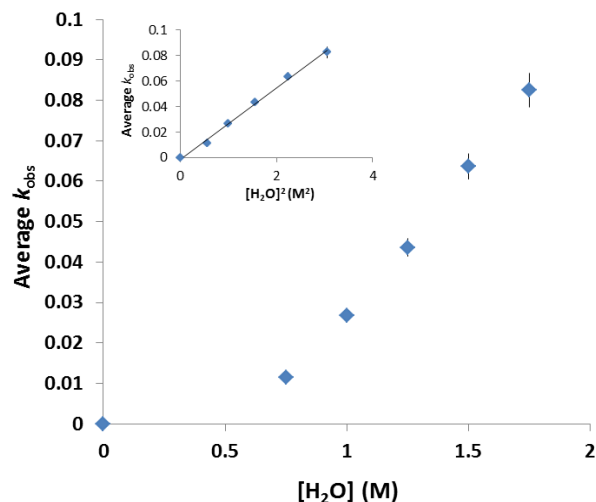

Figure 2. Plot of Average k_{obs} vs water concentration for the reduction of anthracene (100 mM) by SmI$_2$ (10 mM). Inset displays a plot of k_{obs} vs [H$_2$O]^2 with a linear least squares fit (R^2 = 0.997).

The empirical rate law for the reduction of anthracene at modest concentrations of water typically employed in reductions (50 mM – 2 M) is shown in equation 3. The

$$-d[Sm^{II}]/dt = k'[Sm^{II}][anthracene][water]^2 = k_{obs}[Sm^{II}]$$
(3)

high molecularity of the empirical rate law and the rate order of 2 for water are consistent with a complex mechanism and a role for water beyond serving as a proton donor.

Water has a high affinity for Sm(II) even in bulk THF and as a consequence, at least one water is likely coordinated to Sm(II) at lower concentrations of the proton donor. Given this, it is probable that the initial electron transfer-proton transfer to anthracene occurs through two possible pathways: 1) electron transfer from Sm(II)-water followed by protonation from donors in bulk solvent, or 2) electron transfer from a Sm(II)-intermediate requiring two equivalents of bound water. To evaluate if proton donation from the bulk solution was occurring, trifluoroethanol (TFE) was examined since it does not

coordinate to Sm(II), but is significantly more acidic than water and has been shown to donate protons to anionic intermediates from bulk solution.[6] The rate of reduction of anthracene by SmI$_2$ containing equimolar amounts of water and TFE was measured over a range of 1-3 M proton donor. It was our supposition that if protonation from the bulk was important, that the more acidic TFE would lead to a faster reduction. Despite the presence of a substantial amount of TFE, the rate of reduction decreased slightly. This finding is consistent with bulk proton not playing a role in the proton transfer and suggests that two waters associated with Sm(II) are responsible for the rate order of 2.

To obtain further insight into the mechanistic role of water in the Sm(II)-mediated reduction of anthracene, the rate was measured using D$_2$O. Data were determined from individual rate experiments for the reduction of anthracene using either water or D$_2$O. A plot of the k_H/k_D vs. water concentration is shown in Figure 3. At low concentrations of water (50 mM), the
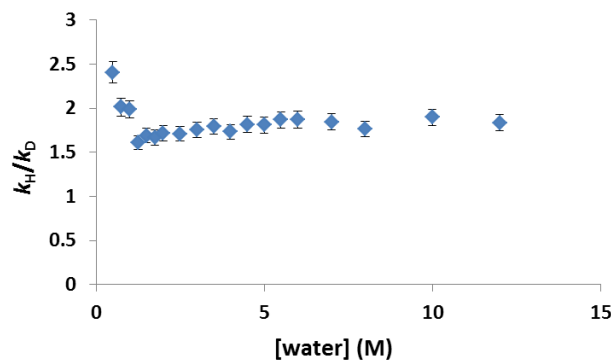

Figure 3. Plot of k_H/k_D vs. [water] for the reduction of anthracene by SmI$_2$. [SmI$_2$] = 10 mM; [anthracene] = 100 mM.

k_H/k_D is 2.1 ± 0.1 and as additional water is added, the isotope effect gradually drops to 1.7 ± 0.1 at 1 M water (100 equiv vs [SmI$_2$]). The k_H/k_D = 1.7 ± 0.1 across concentrations up to 10 M water. The results are somewhat larger in magnitude than those reported by Procter for the reduction of anthracene by Sm(II) reductants where a value of 1.3 was obtained.[14] It should be noted that the KIE experiments described by Procter and colleagues were carried out as competition experiments using equimolar amounts of H$_2$O and D$_2$O in the reaction to determine the degree of deuterium incorporation in the final reduced product to determine k_H/k_D. Regardless of this difference, it is our supposition that the data is clearly consistent with a primary isotope effect whose magnitude is a consequence of PCET. The relationship between PCET and the observed deuterium isotope effect will be discussed *vide infra.*

To acquire further detail about the reduction of anthracene by SmI$_2$, and water, rates were measured over a 30 degree temperature range to obtain activation parameters from the linear form of the Eyring equation. The data are contained in Table 2. The concentration of water was maintained at 1.25 M (125 equiv) which is in the region where water exhibits a rate order

Table 2. Activation parameters for the reduction of anthracene by SmI_2 and water.

[proton donor]^a	$\Delta H^{\ddagger\,b}$ (kcal/mol)	$\Delta S^{\ddagger\,b}$ (cal/mol*K)	$\Delta G^{\ddagger\,c}$ (kcal/mol)
1.25 M H_2O	0.1 ± 0.1	-64 ± 4	19 ± 1

^aConditions: 10 mM SmI_2 and 100 mM anthracene in THF. The activation parameters are the average of 3 independent experiments from 20-40 °C and are reported as ±σ. ^bObtained from $\ln(k_{obs}h/kT)$- $\Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R$. ^cCalculated from $\Delta G^{\ddagger =} \Delta H^{\ddagger}$-$T\Delta S^{\ddagger}$.

of 2. Examination of the data in Table 2 shows that the reduction has a small degree of bond reorganization and that the reduction is entropy controlled.

It is important to consider the present results in the context of earlier studies of the Sm(II)-water system and classic studies on proton transfer to arene radical anions. Previous studies have demonstrated that water has a high affinity for Sm(II).[3, 18] Coordination of water to the Lewis acidic Sm increases the acidity of the O-H bond.[19] Concomitant with this process, the ease of oxidation of Sm(II) is enhanced by producing a more powerful reductant.[7] In other words, as water coordinates to Sm(II) a more powerful reductant is formed in concert with a better proton donor. In addition to work on Sm(II)-water complexes, there is a great deal of classic work on the protonation of anthracene radical anions by water and other proton donors.[20] The work of Bank is quite useful in this regard.[20a] In this report, he found that protonation of the sodium generated anthracene radical anion by water in THF occurred through water bound to the sodium countercation.[20a]

In light of the data and framework from previous studies, the question that arises is: What is the procession of events that leads to the initial electron and proton transfer in the reduction of anthracene by Sm(II)-water? To answer this question, it is useful to keep a number of points in mind: 1) SmI_2 is incapable of reducing anthracene in the absence of water. 2) Addition of successive amounts of water to SmI_2 in THF likely drives coordination to result in the formation of a Sm(II)-water complex. 3) Reduction of anthracene initiates with amounts of water well below that required to influence the reducing power of SmI_2. 4) The rate order of water is 2 and has a k_H/k_D of 1.7. 5) The rate law describing the reduction provides the stoichiometry of the activated complex relative to reactants but only the transition state for the rate-limiting step can be probed with any certainty.[21]

Given the points above, there are several possible events that can occur in the initial electron-proton transfer from the Sm(II)-water complex to anthracene: 1) A rate-limiting electron transfer (ET) followed by a proton transfer (PT);[14] 2) An ET followed by a rate-limiting PT, or 3) a PCET. The key difference between 1 or 2 and 3 is whether the electron and proton are transferred sequentially or in one kinetic step.

In a classic review by Mayer, he notes that it is a common supposition that stepwise transfers of a proton and electron are favored over the concerted PCET, but this intuition is incorrect in most cases since ΔG is always lower for PCET than ΔG for the initial PT or ET.[22] Although sequential ET-PT is the accepted process in the chemistry of Sm(II) reductions and reductive couplings, bond-weakening processes are extremely common in the PCET literature for a wide range of complexes that lead to significant weakening of N-H and O-H bonds.[23] In the present case, concerted transfer of a proton and electron from Sm(II)-water to anthracene is thermodynamically equivalent to hydrogen atom transfer between the same reactants. As a consequence, an alternative way to view the process is one where water complexation to Sm(II) lowers the homolytic bond dissociation energy (BDE) of the O-H of the bound water enabling it to donate an H-atom to the anthracene acceptor.

A consequence of the line of reasoning described above is that it enables us to make quantitative conclusions about the ability of the Sm(II)-water complex to function as a PCET donor as exemplified in Scheme 2. The BDE of the O-H bond of water is 117.6 kcal/mol.[24] However, the BDE of the initial radical formed via hydrogen atom transfer to anthracene is comparably weak with a value of 44.9 kcal/mol.[25] This analysis demonstrates that the BDE of the O-H bond in the Sm(II)-water complex is decreased by at least 72.7 kcal/mol.

Bond weakening of water is well precedented in the literature. Pioneering work of Wood and Renaud showed that
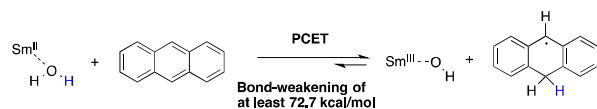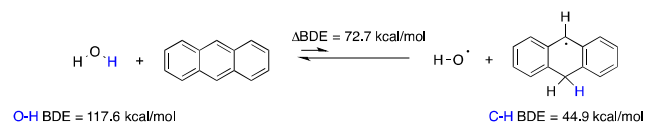
Scheme 2

borane-water or borane-alcohol complexes could be used as H-atom donors to radicals.[26] In 1997, Stack demonstrated that coordination of alcohols to non-heme iron models of lipoxygenases significantly reduces the O-H bond strength of the bound ligand.[27] More recently, experiments by Cuerva and coworkers revealed that water bound to $Cp_2Ti^{III}Cl$ decreased the O-H BDE by approximately 60 kcal/mol.[28] As a consequence, Ti^{III}-water complexes serve as efficient H-atom donors for alkyl radicals. These findings were exploited in elegant work by Knowles for the development of a catalytic bond-weakening protocol for the conjugate amination.[29] In each of the examples cited above, bond weakening is significant but the decrease in the O-H bond of the Sm(II)-water complex of at least 72.7 kcal/mol derived from the analysis shown in Scheme 2 is the largest reported to date.

The thermochemical analysis described above is consistent with PCET, but do the mechanistic studies support a concerted process? The inclusion of water in the empirical rate law is consistent with a role in the rate-limiting step, but the low magnitude of the deuterium isotope has previously been interpreted as a secondary effect.[14] It is our supposition that the k_H/k_D determined for the reduction of anthracene is clearly a primary isotope effect. From a classical perspective, the activation parameters displayed in Table 2 are consistent with a highly ordered early transition state where very little O-H(D) bond cleavage has occurred and very little C-H(D) bond formation has taken place in the activated complex. In this case, the isotope effect is predicted to be small since the zero point vibrational energy differences for H and D are small between the reactant and transition state.[30] In systems where PCET is operating, isotope effects are significantly more complex than classical systems. Proton vibrational wavefunction overlap plays an important role in determining deuterium isotope effects but the KIE is complicated due to differing length and timescales for electron proton exchange, dynamic effects, and differing contributions from excited vibronic states.[31] As a consequence, reactions occurring through PCET can have isotope effects that vary a great deal and many well-characterized examples occur with primary isotope effect only slightly above unity.[32] It is our supposition that the observed deuterium KIE is consistent with PCET.

On the basis of the points described above, the remaining question is: Does the kinetic study support sequential ET-PT or PCET? If the electron and proton transfer were successive processes, an expression cannot be derived that fits the experimentally determined data. However, application of a steady-state approximation to the concentration of the Sm(II)-water complex followed by a concerted, rate-limiting PCET as shown in Scheme 3 provides equation 4, which matches the empirical rate-law (equation 3) obtained from experimental data. The
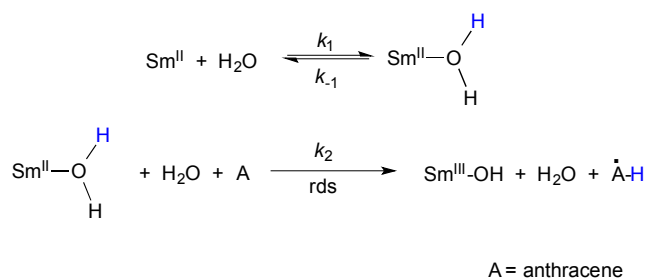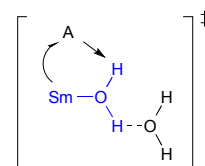
Scheme 3

$$\frac{-d[Sm(II)]}{dt} = K_1 k_2 [Sm(II)] \, [H_2O]^2 \, [A] \quad (4)$$

high molecularity of the empirical rate law which is second order in water and the large degree of order in the activated complex are consistent with the transition state shown below in Scheme 4. In this scenario, the coordi-

nation of water to Sm(II) increases the acidity of the O-H bond and also enhances its ability to hydrogen bond to another water facilitating the rate-limiting PCET to anthracene. Alternatively, the activated complex could have both waters bound to Sm(II).

Scheme 4

Overall, it is our supposition that the collection of studies and experimental work described above support a PCET for the reduction of anthracene by SmI$_2$ containing modest concentrations of water typically employed in reductions. Although the majority of the work described above is focused on concentrations of water typically employed in reductions by SmI$_2$, we believe it is useful to consider why higher concentrations of water lead to saturation and eventual inverse order of the proton donor. As higher concentrations of water are added, THF and iodide are displaced from the coordination sphere of Sm(II) and replaced by water.[18b] Once Sm(II) is saturated, additional water is likely to hydrogen bond in the second coordination sphere. Second sphere interactions are recognized to be important in rare earth mediated reactions.[33] In the present case, anthracene would have to displace water in the second coordination sphere leading to a change in the mechanism where water displacement is likely rate-limiting. A caveat with this hypothesis is the fact that as high amounts of water are added to THF, the solvent polarity changes significantly and as a consequence may impact the mechanism of ET.[34]

One final point to consider is whether arenes are a suitable measure of the redox potential of Sm(II)-water or other coordinating proton donor systems. Classic studies on the reduction of arenes by rare-earth reductants in the absence of any additive showed that arene dimerization occurred through radical-radical coupling.[35] The present study shows that SmI$_2$ alone is incapable of reducing anthracene and the reduction initiates at concentrations of water below the level where it impacts the reducing power of Sm(II) and is inhibited at higher concentrations where the proton donor has a maximal impact on the redox potential of the metal. Additionally, the concerted nature of the ET-PT makes estimation of the redox potential tenuous at best. Given this, we recommend that caution is employed in the use of arenes as a measure of redox potential of SmI$_2$-water systems given the mechanistic complexity of the reaction.

Conclusions

The results described herein show that the reduction of an arene by SmI$_2$ containing modest concentrations of water proceeds through a highly-ordered transition state where the initial transfer of an electron and proton pro-

ceed through PCET. The complexity of the reduction resulting from PCET shows that care should be employed when interpreting deuterium isotope effects or mechanisms deduced from empirical models based on knowledge of ground state reductants and reaction products alone. Although the studies presented herein reveal the complexity of arene reduction by Sm(II)-water, these results may have an important impact for the reduction of other functional groups. This is especially important for carbonyls and related functional groups that are likely to compete with water for coordination to Sm(II). We are currently examining these systems and the results of these studies will be reported in due course.

ASSOCIATED CONTENT

Experimental procedures, kinetic and spectral data. This material is available free of charge via the Internet at **http://pubs.acs.org**.

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Author Contributions

The manuscript was written through contributions of both authors who have given approval to the final version of the manuscript.

ABBREVIATIONS

ET, electron transfer; PT, proton transfer; PCET, proton coupled electron transfer; THF, tetrahydrofuran.

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TOC

A = anthracene