Proton Donors

International Edition: DOI: 10.1002/anie.201601474
German Edition: DOI: 10.1002/ange.201601474

High-Affinity Proton Donors Promote Proton-Coupled Electron Transfer by Samarium Diiodide

*Tesia V. Chciuk, William R. Anderson, Jr., and Robert A. Flowers II**

Abstract: *The relationship between proton-donor affinity for Sm^{II} ions and the reduction of two substrates (anthracene and benzyl chloride) was examined. A combination of spectroscopic, thermochemical, and kinetic studies show that only those proton donors that coordinate or chelate strongly to Sm^{II} promote anthracene reduction through a PCET process. These studies demonstrate that the combination of Sm^{II} ions and water does not provide a unique reagent system for formal hydrogen atom transfer to substrates.*

The presence of additives in reactions of samarium diiodide has a profound impact on their rate and selectivity.[1] There are three classes of additives used in reactions of SmI_2: Lewis bases, proton donors, and transition-metal salts. Among these groups of additives, proton donors have been shown to be quite effective in accelerating substrate reduction and altering the selectivities of reactions.[2] In particular, the combination of SmI_2 and water is unusual in that it is effective in reacting with substrates that are difficult to reduce through single electron transfer.[3] The distinguishing feature of this class of reductions is that they are significantly endergonic. This raises the question as to whether substrate reduction proceeds through an electron transfer followed by a proton transfer, or whether the process occurs through a formal hydrogen-atom transfer (HAT). We recently examined this question through a series of rate and mechanistic studies to examine the reduction of anthracene by SmI_2–water. These studies showed that substrate reduction occurred through initial proton-coupled electron transfer (PCET).[4] The key component of this transformation was strong coordination of water to Sm^{II} ions that significantly weakens the O–H bond. Proton donors such as methanol, which do not have a high affinity for Sm^{II} ions, are ineffective for arene reduction. Since initial studies showed that the affinity of water for Sm^{II} is critical, it raises several important questions: 1) Does the combination of SmI_2 and water provide a unique combination for HAT to substrates? 2) Can high-affinity proton donors be used in place of water to promote reductions? 3) Is there a relationship between proton-donor affinity for Sm^{II} ions and initial HAT to substrate? Herein we present studies designed to answer these important questions. Overall, the experiments presented here demonstrate that strong proton-donor coordination to Sm^{II} ions is a prerequisite for reduction through PCET.

To examine the importance of proton-donor coordination to Sm^{II} ions, we chose several proton donors: diethylene glycol (dg), diethylene glycol monomethyl ether (dgme), ethylene glycol (eg), ethylene glycol monomethyl ether (egme), water, and 2,2,2-trifluoroethanol (TFE). Proton donors dg, eg, and water are known to coordinate strongly to Sm^{II} ions, and the monomethyl ethers dgme and egme were chosen since the replacement of a hydroxy proton with a methyl group has a deleterious impact on the affinity of proton donors for Sm^{II} ions.[5] The proton donor TFE does not coordinate to Sm^{II} ions even at high concentrations.[2d,e,h] Anthracene and benzyl chloride were chosen as substrates since studies would not be complicated by competition with proton donors for coordination sites on Sm^{II} ions. Additionally, benzyl chloride is reduced through a rate-limiting dissociative electron transfer,[6] whereas anthracene has been shown to be reduced through a PCET by Sm^{II}–water. If proton-donor coordination is important for PCET from a Sm^{II} donor complex, we expect high-affinity donors to have a larger relative impact on the rate of reduction of anthracene than benzyl chloride.

To test the assertion described above, the rate of reduction of anthracene and benzyl chloride by SmI_2 containing increasing amounts of proton donor were measured under pseudo-first-order conditions with substrates in a 12.5-fold excess with respect to $[SmI_2]$. Unfortunately, the use of dg led to significant precipitation, which prevented rate studies, although substrate reduction was fast as observed by rapid decoloration of the solution, consistent with oxidation of Sm^{II} ions. Additionally, dgme and egme did not facilitate the reduction of anthracene in the timescale of the rate studies although dgme had a modest impact on the rate of benzyl chloride reduction by Sm^{II} ions. A plot of proton-donor concentration versus k_{obs} for reactions where rates could be measured is displayed in Figure 1.

There are several interesting features of the data displayed in Figure 1. Among the reductions that could be measured by stopped-flow experiments, only water and eg facilitate the reduction of anthracene by SmI_2, whereas all proton donors (except TFE) slightly accelerate the reduction of benzyl chloride. The reduction of benzyl chloride through an initial ET from SmI_2 is exergonic by approximately $-3.7\ kcal\,mol^{-1}$, whereas an initial ET to anthracene is endergonic by approximately $25\ kcal\,mol^{-1}$. While the impact of proton donors on the reduction of benzyl chloride is apparent, they are not as significant as those that facilitate reduction of anthracene, a substrate considerably harder to reduce through ET.

[*] T. V. Chciuk, W. R. Anderson Jr., Prof. R. A. Flowers II
Department of Chemistry, Lehigh University
6 E. Packer Ave., Bethlehem, PA 18015 (USA)
E-mail: rof2@lehigh.edu

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under http://dx.doi.org/10.1002/anie.201601474.

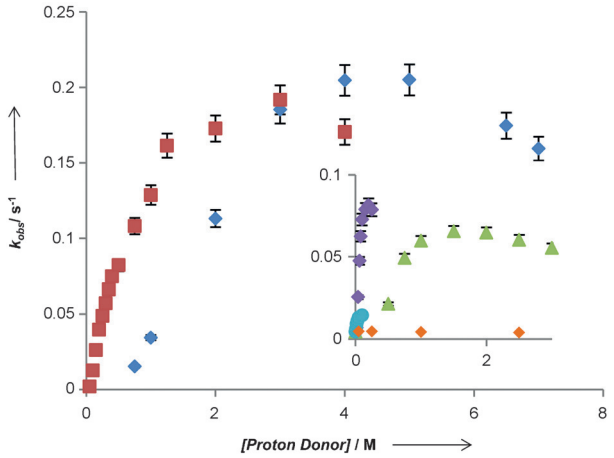


Figure 1. Rate of reduction of anthracene (125 mM) by SmI_2 (10 mM) in the presence of increasing amounts of eg (red ■) and water (dark blue ◆) at 25 °C. Inset: Rate of reduction of benzyl chloride (125 mM) by SmI_2 (10 mM) in the presence of increasing concentration of eg (purple ◆), water (green ▲) dgme (light blue ●) and TFE (orange ◆).

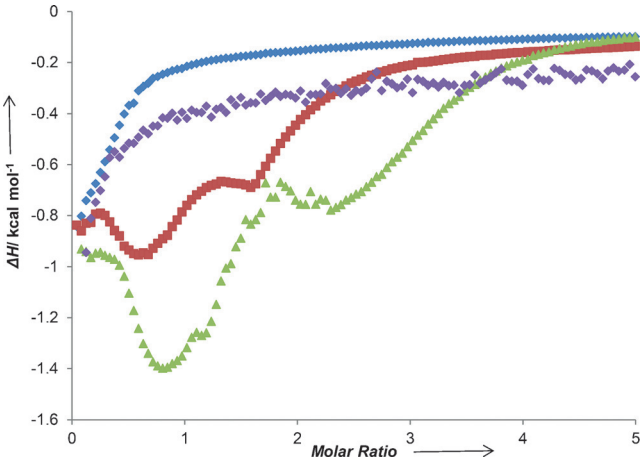


Figure 2. ITC binding isotherms for the addition of 2 µL aliquots of 90 mM egme (purple ◆), dgme (blue ◆), eg (red ■), and dg (green ▲) to SmI_2 (1.4 mL, 3 mM) in THF.

Closer inspection of the rate data obtained in the reduction of both substrates by SmI_2–proton donor combinations reveals other important findings. In cases where reduction is facilitated upon addition of water or a glycol derivative, lower concentrations of proton donors are second-order in the additive in all cases. Higher concentrations of proton donor provide rate orders closer to unity and even higher concentrations lead to zero order or a slight inverse order in additive. Additionally, kinetic isotope studies on deuterated eg and D_2O provide isotope effects of 1.8 ± 0.1 in the reduction of anthracene and 1.1 ± 0.1 in the reduction of benzyl chloride (see the Supporting Information). The rate order of SmI_2 and substrate are first order under all concentrations of proton donor. The consequences of these findings will be discussed below.

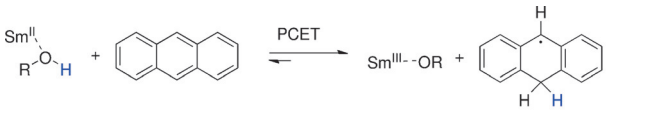
To examine the impact of proton-donor affinity for SmI_2 we employed isothermal titration calorimetry (ITC) and UV/Vis studies. In both studies, increasing amounts of proton donor were added to SmI_2 in THF. Data obtained for ITC studies of eg, dg, egme, and dgme with SmI_2 are displayed in Figure 2. It was our expectation that we would be able to fit the data to determine the solution stoichiometry of Sm^{II}–proton donors since the stoichiometry of the SmI_2-dg and SmI_2–dgme complexes are known from X-ray crystal structures.[5] A caveat with this supposition is that X-ray structures were obtained from the slow evaporation of solvent from solutions of proton donors and SmI_2, creating an environment that may not represent the structures in relatively dilute solutions (< 0.1 M) of Sm^{II}–glycol complexes. Several attempts were made to fit the data, but all fits provided a significant amount of error. Nonetheless, the data clearly show that the interaction of eg and dg with SmI_2 are distinct from egme and dgme. The binding isotherms for egme and dgme are consistent with low-affinity coordination, whereas the data for eg and dg are consistent with higher-affinity binding. Furthermore, the parabolic shape in the initial portion of the eg and dg binding isotherms are consistent with systems where a higher affinity binding site has a less exothermic enthalpy change than the lower binding affinity sites.[7] It is our supposition that the less exothermic coordination of eg and dg is a consequence of the displacement of iodide from the inner sphere of Sm^{II} ions upon addition of these additives.[8] Regardless of the complexity of proton-donor coordination to SmI_2, UV/Vis studies on these additives clearly show the same trends providing affinities that follow the trend dg > eg > H_2O ≫ dgme > egme (see the Supporting Information).

Experimental observations from rate studies, ITC, and spectroscopic experiments are consistent with the supposition that proton-donor coordination to Sm^{II} ions has an impact on the reduction of benzyl chloride, and is critical for reduction of anthracene. There are several likely mechanistic scenarios for anthracene reduction by Sm^{II}–proton donor complexes: 1) A rate-limiting electron transfer followed by a rapid proton transfer, 2) an electron transfer followed by a rate-limiting proton transfer, and 3) PCET. Previous initial work on the reduction of anthracene by SmI_2–water demonstrated that reduction likely occurs through a PCET process. Comparisons of the impact of water and glycols on SmI_2 are useful to determine the likely pathway of reduction and similarities between both types of proton donors.

The data presented above demonstrate that in the systems studied here, proton-donor coordination accelerates substrate reduction.[5,9] Another facet of coordination that may influence the mechanism of substrate reduction is the alteration of the reducing power (ease of oxidation) of Sm^{II} ions upon ligation of proton donors.[10] Addition of cosolvents and additives are known to have an impact on the redox potential of SmI_2 through the production of a thermodynamically more powerful reductant or through stabilization of the Sm^{III} state.[11] When water is employed as an additive, large amounts (1000 equiv based on [SmI_2]) are required to significantly influence the redox potential.[12] Additionally, glycols have a limited impact on the redox potential of SmI_2 with dg providing a modest change of 0.13 V (3 kcal).[5] In the reductions studied herein, it is our supposition that the

modest increase in the rate of reduction of benzyl chloride by SmI_2–proton donor reagent systems is a consequence of the small change in the redox potential of Sm^{II}-containing ligated proton donor since the electron transfer is already exergonic. Conversely, it is unlikely that the reductions of anthracene proceed through an initial electron transfer since the process is significantly endergonic under the conditions of the experiment and as a consequence, an initial electron transfer is unlikely in the timescale measured by stopped-flow studies. If an initial electron transfer is unlikely, then how does reduction proceed? The seminal work of Mayer and co-workers demonstrates that PCET is favored over sequential electron-proton transfer when the stepwise pathways are significantly endergonic.[13] The small k_H/k_D measured for the reduction of anthracene by SmI_2–eg is consistent with PCET.[14] Additionally, there is a great deal of precedence for the coordination of water or alcohols to low-valent metals leading to significant weakening of the O–H bond.[15,16] Based on previous reports,[4] the impact of coordination on the ability of the Sm^{II}–proton donor complex can be evaluated for eg, dg, and H_2O in THF using the calculated O–H bond dissociation free energy (BDFE) for each donor and the calculated BDFE of the initial radical formed through hydrogen-atom transfer to anthracene.[17] The degree of bond weakening for each coordinating donor is shown in Table 1. A previous estimate for the decrease in the homolytic

Table 1: Impact of Sm^{II} coordination on the O–H bond strength of coordinating proton donors.



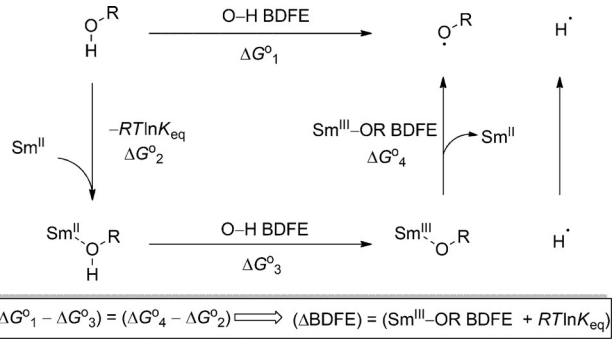
R = H, CH_2CH_2OH, $CH_2CH_2OCH_2CH_2OH$

Entry	Proton donor	Bond weakening [kcal mol^{-1}][a]
1	eg	49.8
2	dg	50.1
3	H_2O	66.8

[a] Values obtained from the difference between the BDFE values of proton donors and that of the radical obtained through HAT to anthracene.

dissociation energy of the O–H bond of water upon coordination to SmI_2 was determined by using experimental gas phase BDEs and found to be 72.7 kcal mol^{-1}. The present estimate of bond weakening determined from calculated BDFE values in THF is nearly 6 kcal mol^{-1} smaller, but in reasonable agreement with previous data. The degree of bond weakening for eg and dg upon coordination to SmI_2 is approximately 50 kcal mol^{-1}. The smaller values for eg and dg are a consequence of the lower BDFE of the glycols compared to water and not their affinity for Sm^{II} ions. Although these values are substantial, it is our supposition that the decrease in BDFE values obtained using this approach are a measure of the minimum impact of coordination to Sm^{II} on the ability to reduce anthracene through a formal hydrogen atom transfer. Further experiments will be required to determine the limits (i.e., maximum impact) of coordination.

An alternative approach for evaluating the impact of coordination of proton donors to Sm^{II} ions and the resulting bond weakening of the Sm^{II}–proton donor complex is through the construction of a thermochemical cycle (Scheme 1). This



Scheme 1. Thermochemical cycle demonstrating the relationship between proton donor affinity for Sm^{II} ions and bond weakening.

cycle demonstrates that the difference in energy between the O–H bond strength of free (ΔG^o_1) and Sm^{II}-bound proton donor (ΔG^o_3) is equal to the difference in energy between the strength of the resulting Sm^{III}–OH or –OR BDFE (ΔG^o_4) and the free energy of coordination between the proton donor and Sm^{II} (ΔG^o_2). Since all BDFE values are positive (ΔG^o_1, $\Delta G^o_{3\text{-}4}$) the ΔBDFE (O–H bond weakening) will be greater for proton donors that have a high affinity for Sm^{II} ions. This construct further supports our hypothesis that high affinity donors lead to a higher degree of bond-weakening.

Although the present work describes OH-based proton donors, any high-affinity ligand containing a strong X–H bond that is weakened upon coordination to a low-valent metal should be effective for reduction. Knowles,[18] Gansäuer,[19] and their respective co-workers have demonstrated that activation of an amide N–H bond by low-valent Ti is an effective method for promoting HAT. To determine if this approach could be employed in the reduction of anthracene, five equivalents of 2-pyrrolidone (based on [SmI_2]) was added to a solution of anthracene and SmI_2. The solution discolored quickly to provide 9,10-dihydroanthracene in quantitative yield. This finding demonstrates that PCET is not limited to water or other hydroxy-based proton donors with a high affinity for Sm^{II} ions.

Overall, the studies presented herein demonstrate that the combination of Sm^{II}–water does not provide a unique reagent system for hydrogen atom transfer. The use of isothermal titration calorimetry and UV/Vis spectroscopy from this work and previous studies shows that only those proton donors that coordinate to SmI_2 promote substrate reduction through PCET. The present work, in concert with the seminal work of Cuerva and co-workers on Ti^{III}–proton donor systems,[20] demonstrates that this approach can likely be extended to a range of low-valent metals. As a consequence, this method may enable an alternative approach for the generation of radical intermediates important in synthetic processes as

recently demonstrated through the elegant work of Knowles and co-workers.[9] We are currently examining this hypothesis and the results of this work will be reported in due course.

Acknowledgements

We thank the National Science Foundation (CHE-1266333) for support of this work. We thank Gabrielle Haddad-Weiser for assistance with the ITC experiments and Dr. Joseph Teprovich for initial UV/Vis studies. We also thank the reviewers for constructive evaluation and feedback.

Keywords: hydrogen-atom transfer · proton-coupled electron transfer · proton donors · reduction · samarium diiodide

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 6033 – 6036
Angew. Chem. **2016**, *128*, 6137 – 6140

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Received: February 10, 2016
Revised: March 9, 2016
Published online: April 8, 2016

