SmI2(H2O)n Reduction of Electron Rich Enamines by Proton-Coupled Electron Transfer

Scott S. Kolmar and **James M. Mayer**[*]

Department of Chemistry, Yale University, New Haven, Connecticut, 06520

Abstract

Samarium diiodide in the presence of water and THF ($SmI_2(H_2O)_n$) has in recent years become a versatile and useful reagent, mainly for reducing carbonyl-type substrates. This work reports the reduction of several enamines by $SmI_2(H_2O)_n$. Mechanistic experiments implicate a concerted proton-coupled electron transfer (PCET) pathway, based on various evidence against initial outer-sphere electron transfer, proton transfer or substrate coordination. A thermochemical analysis indicates that the C-H bond formed in the rate determining step has a bond dissociation free energy (BDFE) of ~32 kcal mol^{-1}. The O–H BDFE of the samarium aquo ion is estimated to be 26 kcal mol^{-1}, which is among the weakest known X–H bonds of stable reagents. Thus $SmI_2(H_2O)_n$ should be able to form very weak C-H bonds. The reduction of these highly electron rich substrates by $SmI_2(H_2O)_n$ shows that this reagent is a very strong hydrogen atom donor as well as an outer sphere reductant.

Graphical abstract
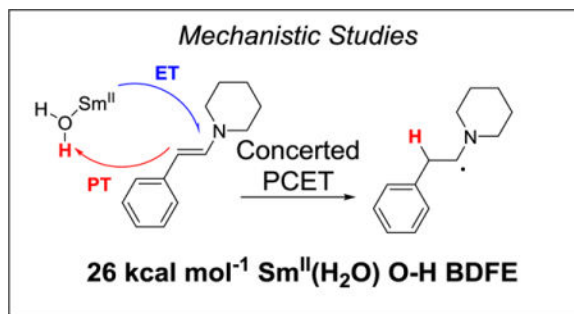
Introduction

Samarium diiodide (SmI_2) is a ubiquitous reagent in organic synthesis, typically used as a single electron transfer (SET) agent to reduce alkyl halides and carbonyl functionalities.[1] Additives are commonly used to increase the effectiveness and versatility of SmI_2. These are Lewis bases which make SmI_2 more reducing and often provide protons, such as methanol

Corresponding Author: James M. Mayer, james.mayer@yale.edu.
orcid.org/0000-0002-3943-5250

and water. Water has been the most unique and useful additive, allowing reduction of the most challenging substrates.[2] Solutions of SmI_2 and water in THF likely contain an equilibrium mixture of species,[3] which are denoted here as $SmI_2(H_2O)_n$.

Kinetic investigations of SmI_2 reductions with proton donors have been reported by Hoz and coworkers.[4] The broad scope of $SmI_2(H_2O)_n$ has been explored by Procter and coworkers with different carbonyl type functionalities and polycyclic aromatic compounds.[2,5] They defined an "effective redox potential" of $SmI_2(H_2O)_n$ as the boundary between the outersphere (pure electron) reduction potentials of reactive and non-reactive aromatic substrates.[5b] Flowers et al. showed that H_2O makes SmI_2 more reducing by cyclic voltammetry (CV),[6,] and they showed how the coordination strength of proton donors affects SmI_2 reductions.[7] A mechanistic study by this group later indicated that $SmI_2(H_2O)_n$ reduces anthracene through a concerted proton coupled electron transfer (PCET) mechanism.[8] Most recently, they proposed that the electrostatic interaction between carbonyl substrates and SmI_2 can tune the PCET character of the reaction coordinate.[9] Overall, Flowers et al. have shown that $SmI_2(H_2O)_n$ reductions of widely used substrates can involve PCET reactivity of $SmI_2(H_2O)_n$.

Reported here are $SmI_2(H_2O)_n$ reductions of a new substrate class, enamines (Scheme 1), as well as evidence that these reactions proceed through a concerted PCET pathway. A thermochemical analysis shows that the related aqueous Sm^{2+} ion has an extraordinarily weak O–H bond. These studies thus show that the PCET perspective significantly broadens the range of substrates that are likely to be reduced by $SmI_2(H_2O)_n$.

Enamines have very electron rich carbon-carbon double bonds due to the resonance donation of the nitrogen lone pair into the C=C π-bond. They are very resistant to the addition of an electron,[10] but they can add a hydrogen atom ($e^- + H^+$) to form a neutral, stabilized α-amino radical (Figure 1). Therefore, enamines were chosen as an attractive substrate class to explore the ability of $SmI_2(H_2O)_n$ to react by concerted PCET. This mechanism involves transfer of H^+ and e^- together in a single kinetic step, which for enamines bypasses the high energy radical anion. From this perspective, $SmI_2(H_2O)_n$ should be able to reduce enamines, which are resistant to accepting an electron but have a moderate ability to accept a hydrogen atom. Additionally, this reactivity can be rationalized through analysis of the bond dissociation energies (BDEs) of the broken O–H bond in $SmI_2(H_2O)_n$ and the formed C–H bond in the neutral intermediate.

Results

I. Preparative Results

Enamines are rapidly reduced to amines by $SmI_2(H_2O)_n$ (Scheme 1). The addition of enamines to air-free $SmI_2(H_2O)_n$ solutions caused bleaching of the red color and formation of a white Sm^{3+} precipitate within 10 min at ambient temperatures. The piperidine and morpholine substrates in Table 1 are generally reduced in good isolated yields. Simple methods of product isolation, such as filtration of the crude reaction mixtures, were unsuccessful because the amine product was bound to the insoluble metal salts. This also prevented straightforward ^{1}H NMR analysis of products. Acid-base workup conditions to

isolate the amine product were similarly unsuccessful, so basic alumina or reverse phase column chromatography was used. Substrates include compounds bearing conjugated phenyl groups either β (**1p**, **1m** and **1pOMe**) or α (**2p** and **2m**) to the nitrogen. An enamine with a benzyl group β to the nitrogen (**3**) is also reduced, albeit in lower yield. The substrates were chosen with varying electronic character, pK_as, and conjugation in order to answer specific mechanistic questions (see below). Nitrogen containing aromatic compounds such as imidazole, indole, pyrrole, and their N-methyl analogues did not react under these conditions, despite formally containing enamine motifs.

II. Mechanistic Results

Four mechanistic possibilities have been considered for the enamine reductions: (i) initial outer-sphere electron transfer followed by proton transfer (ET/PT); (ii) initial proton transfer followed by electron transfer (PT/ET); (iii) concerted PCET with transfer of a proton and an electron in a single kinetic step; and (iv) initial substrate coordination. The first three cases are illustrated in Scheme 2 and would all be considered PCET mechanisms within the current wider PCET framework,[11] though we note that within the organic chemistry literature "PCET" still typically refers only to the concerted process. Mechanistic experiments probing each of these are discussed in turn below.

(a) Initial electron transfer—Initial *ET* is very unlikely because of the electron rich character of the enamine substrates. This is evident from the cyclic voltammetry (CV) of **1p** in THF, which displayed no reduction wave within the solvent window, to $^-$3.5 V vs. Fc$^{0/+}$ (Supporting Information (SI) Section 4.1).

To further test this mechanistic possibility, a competition experiment was done with **1p** and the more electron rich **1pOMe**.

A reaction with a 1 : 1 mixture of **1p** and **1pOMe** with limited $SmI_2(H_2O)_n$ gave a 1.2 : 1 mixture of reduced products (Table 2). This is inconsistent with initial rate-limiting ET because the *p*-OMe substituted **1pOMe** would form a much less stable radical anion intermediate than the unsubstituted **1p**, and consequently would be reduced with a much slower rate. This result could in principle be consistent with pre-equilibrium ET followed by rate limiting PT. However, this seems very unlikely because the difference in the rate constants for protonation of the radical anions would have to precisely balance the difference in ET equilibrium constants. For the related oxidation of these styrenes, the difference in the CV oxidation peak in MeCN is 0.56 V;[12] if the difference in reduction potentials are similar, this would imply a ~10^9 difference in K_{eq} for ET.

(b) Initial proton transfer—The possibility of initial PT was similarly probed with a competition experiment between **1p** and **1m**. The β-carbon is the most basic site on an enamine, and the pK_a's of piperidine-containing enamines in acetonitrile are *ca.* 2.5 units more basic than the corresponding morpholine-containing enamines.[13] Reduction of a 1 : 1 mixture of **1p** and **1m** gave a 4.0 : 1 ratio of products (Table 2). A larger rate difference in protonation rates would have been expected for a difference of 2.5 pK_a units.

To further explore this mechanistic scenario, reductions were investigated with an added bulk solvent acid, trifluoroethanol (TFE), 1:1 with the added H_2O. TFE is known to be non-coordinating with SmI_2.[4a] TFE has an aqueous pK_a of ca. 12.4,[14] which is likely more acidic than aqueous Sm^{2+}.[15] Monitoring reactions by optical spectroscopy with and without substantial TFE showed that the time courses increased, but by less than a factor of 1.3 in all cases (SI Section 5.1). Thus, both in changing the enamine and in adding an acid, significant changes in basicity or acidity caused only small changes in rate, arguing against rate-limiting PT.

The occurrence of pre-equilibrium proton transfer was explored via isotope-exchange experiments.[16] Enamine reductions were done with D_2O and with half of the stoichiometric requirement of $SmI_2(H_2O)_n$, and the unreacted starting material was examined by ^1H NMR. For both **1p** and **1m**, no exchange of the β-H for deuterium was observed (eq 1 and SI Sections 3.6 and 7.4). Pre-equilibrium PT is also very unlikely because deprotonation of the C–H bond of the cationic imine in the slightly acidic solution would have to be faster than electron transfer from the highly reducing $SmI_2(H_2O)_n$. This path is also unlikely based on the large product isotope effects reported in the next section.
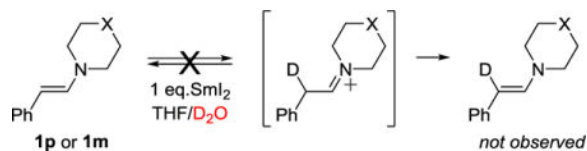
(1)

(c) Product isotope effects—Enamine reductions were performed using SmI_2 in THF with H_2O/D_2O mixtures. The relative ratios of protonated and deuterated products were determined by integrating the relevant CH peaks in the ^1H NMR spectra of the products. Large H/D product isotope effects (PIEs) were found in the reductions of substrates **1p**, **1m**, and **2m** (Table 3). Substrates **1m** and **2m** were reduced using a 1:1 ratio of $D_2O:H_2O$, while a 4.5:1 ratio was used for **1p** to obtain more reliable integrations. Effects at the β-carbons range from 3.5 - 7.3, indicating that H/D transfer to the β-carbon is involved in the selectivity-determining step of reduction. This is consistent with a concerted PCET mechanism or an ET/PT pathway, but would be difficult to rationalize with pre-equilibrium PT. Effects at the α-carbons are much closer to unity, but accurate determinations were precluded by overlap of ^1H NMR resonances for these protons and piperidinyl or morpholinyl α protons.

(d) Substrate coordination—It is also possible that the substrates can coordinate to SmI_2 during the reaction, increasing their electrophilicity and allowing initial ET to occur. No coordination of **1p** was observed by optical spectroscopy when monitoring the reactions, as the initial spectra are unchanged upon addition of substrate (as the reaction starts). The visible absorption spectrum of SmI_2 in THF is known to be sensitive to changes in coordination.[6,17] However, this does not exclude a small equilibrium amount of coordinated substrate.

The similar reactivity of **1p** and **1m** also indicates the unimportance of coordination. These substrates should have different affinities for the metal center due to their different basicities.[13b] This should result in significantly different rates of reduction if binding through the alkene or the nitrogen moiety occurred along the reaction pathway.

The reactivity of **1p** was also compared with substrates incapable of coordination to the metal center (Table 2). **1p** reacted 4.3 times faster than *trans*-stilbene (**S**), and 2.0 times slower than anthracene (**A**), both of which have no coordinating group. This is not a simple comparison because the driving forces for the reactions are different.[18] However, the results suggest that the presence of a potentially coordinating nitrogen atom does not substantially increase the rate of reduction. In sum, these experiments are not definitive, but they suggest that coordination does not play a major role in the enamine reductions.

Discussion

I. Mechanism

All the experimental results above are consistent with a concerted PCET mechanism for the first step of enamine reduction by $SmI_2(H_2O)_n$. We note that this is not an ideal system for mechanistic study, as the speciation of the samarium reactant is not well defined, the samarium product is insoluble, the acidity of the solutions is not easily controlled over the course of the reactions, and the remaining organic reactant is unstable to the workup conditions. Still, the body of experiments point to the concerted transfer of e^- and H^+ from $SmI_2(H_2O)_n$ to the enamines. This is consistent with recent studies by Flowers for the reduction of anthracene.

The concerted PCET mechanism can be described as transfer of a proton from a H_2O coordinated to Sm(II) to the β-carbon of the enamine concerted with transfer of an electron from Sm(II) to the α-carbon of the enamine (Scheme 3, top left). This same step could equivalently be described as the transfer of a hydrogen atom from $SmI_2(H_2O)_n$ to the enamine β-carbon. Subsequent conversion of the radical to the saturated amine product occurs by transfers of an additional electron and proton, which could be stepwise or concerted.

II. Thermochemistry

Describing these reductions as the transfer of a hydrogen atom implies that the free energy of the concerted PCET step can be quantified as the difference between the bond dissociation energies (BDFEs) of the O–H bond being cleaved and the C–H bond being formed. While the use of bond dissociation enthalpies (BDEs) is common in organic free radical chemistry, free energies are preferred because they connect with equilibrium constants and a Marcus theory approach.[19]

(a) Strength of the C–H bond formed—While no thermochemical data is available for the specific enamines used in this study, C–H bond strengths can be well estimated for **3** based on values for related compounds. We take the heat of heat of hydrogenation of **3** to be the same as that for closely related compound N-(1-propenyl)piperidine (**4**), −23.6 kcal mol^{-1}.[20] The resulting hydrogenated compound **3H₂** is taken to have a BDE of its α-C–H bond

that is that same as that of triethylamine. 90.7 kcal mol^{-1}.[21] Using these values, the thermochemical cycle in Scheme 4 gives the BDE of the C–H bond formed upon reduction of **3**, labelled (i) in the Scheme. Steps (i)-(iii) in the Scheme separate the overall hydrogenation (step iv) into the two BDEs. This analysis gives the BDE of the initially formed C–H bond to be ~37 kcal mol^{-1} using eqs 2 and 3.

$$(i) + (ii) + (iii) = (iv) \quad (2)$$

$$\text{BDE of interest} \cong -90.7 + 104 - (-23.7) = 37 \, \text{kcal mol}^{-1} \quad (3)$$

A C–H bond dissociation enthalpy, such as that derived in Scheme 4 and eq 3, is related to its bond dissociation free energy by the differences in entropy between the reaction components, RH, R• and H•. For the cleavage of C–H bonds in organic solvents, the entropies of RH and R• are typically very similar,[11b] so the BDFE and BDE are related by $TS°(H•)_{solv}$, which is ~4.6 kcal mol^{-1} in polar organic solvents (eq 4).[11b] Thus, the BDFE of the C–H bond formed upon addition of H• to **3** is ~32 kcal mol^{-1}.

$$\text{BDFE (R–H)} \cong \text{BDE (R–H)} - 4.6 \, \text{kcal mol}^{-1} \, \text{for cleavage of C–H bonds in organic solvents}^{11b}$$

$$(4)$$

(b) Sm^{II}O–H bond strength—In order for the hydrogen atom transfer reaction in Scheme 3 to occur at a reasonable rate, the O-H BDFE in $SmI_2(H_2O)_n$ cannot be much stronger than 32 kcal mol^{-1}. Because the O–H bond in water is incredibly strong (BDFE(HO–H) = 111 kcal mol^{-1} in the gas phase),[11b] this means the O–H BDFE has decreased dramatically upon coordination to SmI_2, by *ca.* 79 kcal mol^{-1}. Such O–H bond weakening upon coordination to a reducing metal center is well precedented,[22] and Flowers and coworkers have estimated a 73 kcal mol^{-1} bond weakening for $SmI_2(H_2O)_n$ based on its successful reduction of anthracene.[8] The same group also demonstrated that coordination of SmI_2 to the carbonyl of 2-pyrrolidinone weakens the N-H bond by approximately 70 kcal mol^{-1}.[23]

To obtain a more direct estimate of the O–H bond strength for a water molecule bound to Sm^{2+}, we determine here the O-H BDFE of the related *Sm^{2+} aquo ion*, $Sm(H_2O)_n^{2+}$ (aq). This can be determined directly[11b] from the aqueous Sm$^{3+/2+}$ standard reduction potential of –1.55 V[24] and the pK_a of $Sm(H_2O)_n^{3+}$ (aq) as shown in Scheme 5. This determination of X–H bond strengths from the separate thermochemistry of removal of the electron ($E°$) and proton (pK_a) has a long history and was developed extensively by Bordwell; in some cases when there is separation of the e^- and H$^+$, what is determined might better be called an 'effective BDFE.'[11b] The pK_a of $Sm(H_2O)_n^{3+}$ (aq) has not been reported but is taken to be

the same as that of $Eu(H_2O)_n^{3+}$ (aq), 3.3,[25] because radii and pK_a's are fairly constant across the lanthanide row.[26] The analysis in Scheme 5 gives an O-H BDFE of 26 kcal mol^{-1} for $Sm(H_2O)_n^{2+}$ (aq) [BDE = ~25 kcal mol^{-1}].[11b]

A similar analysis was very recently reported by Szostak and coworkers for SmI_2 in a THF/water mixture.[27] They obtained BDFE = 37.4 kcal mol^{-1} but this calculation unfortunately is in error because it used values from different solvents and it used an estimated pK_a for Sm^{2+} instead of the appropriate Sm^{3+} value (Scheme 5).

To our knowledge,[11b] the O-H BDFE of the *Sm^{2+} aquo ion*, $Sm(H_2O)_n^{2+}$ (aq), and the N–H bond in the related pyrrolidinone complex[23] are *the weakest X–H bonds for any species stable enough to be used as a reagent under ambient conditions.*

We believe that the value for $SmI_2(H_2O)_n$ in THF is likely similar to the aqueous value derived above. While many thermochemical quantities such as reduction potentials and pK_a values are very solvent-dependent, bond strengths typically vary only small amounts between solvents. This is why, for instance, gas-phase BDEs are typically given in chemistry textbooks to rationalize various solution reactivity. As we have shown in a recent review,[11b] the origin of limited solvent dependence can be illustrated in Scheme 6, which shows that solution and gas-phase BDFEs are related by the free energies of solution. For most large molecular systems, the solvation of XH and X$^•$ are similar, except perhaps due to a difference in the number of hydrogen bonds.[11b] For instance, $Sm(H_2O)_n^{2+}$ and $Sm(H_2O)_{n-1}(OH)^{2+}$ are the same size and charge, so they are likely solvated similarly in different solvents.

The samarium(II) system discussed here, however, could be an exception to the general rule of low solvent dependence of BDEs and BDFEs, due to differences in the speciation of the cation in different solvents. The analysis in Scheme 5 involves $Sm(H_2O)_n^{2+}$ [equivalently, Sm^{2+} (aq)], while the speciation of SmI_2 in THF/H_2O mixtures is likely complicated. Some iodide anion coordination to the 2+ cation would be expected given the low dielectric constant of THF with 6.5% water ($\varepsilon \cong 10$)[17c,28] and the iodide-coordinated crystal structures obtained from SmI_2/THF solutions.[29] Given the uncertainty in speciation and the insolubility of the Sm^{III} product, rigorous thermodynamic measurements on this system would be very challenging. We conclude that the aqueous BDFE of 26 kcal mol^{-1} for $Sm(H_2O)_n^{2+}$ is the best available value and is likely to be a good approximation.

III. Reactivity

Using the BDFE values from the last section, transfer of a hydrogen atom from $SmI_2(H_2O)_n$ to **3** is exoergic by $G° = -6$ kcal mol^{-1}. This thermochemical analysis thus supports the mechanistic conclusion of a concerted PCET/hydrogen atom transfer mechanism (Scheme 3).

The uniqueness of Sm^{2+} PCET chemistry is not just the weakness of the O–H but also that these solutions do not rapidly evolve H_2.[30] Based on the BDFE above, the formation of H_2 gas (eq 5) should be ~45 kcal mol^{-1} exoergic. The traditional 'rule of thumb' is that H_2 will be produced by reducing agents that are ca. 0.5 V (~25 kcal mol^{-1}) below the reversible H_2

potential (RHE).[31] Still, Sm^{2+} has some stability in water despite its -1.55 V standard potential, and solutions of $SmI_2(H_2O)_n$ in THF/H$_2$O are stable for hours under our reaction conditions. There is evidently no facile kinetic pathway for Sm^{2+} to make H$_2$, despite the large driving force.

$$2\,Sm\,(H_2O)_n{}^{2+}{}_{(aq)} \rightarrow 2\,Sm\,(H_2O)_{n-1}(OH)^{2+}{}_{(aq)} + H_{2(g)} \quad (5)$$
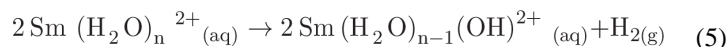
Kinetic factors also must be responsible for the lack of hydrogenation of simple alkenes by $SmI_2(H_2O)_n$ in THF/H$_2$O. The transfer of H· to cyclohexene is ~ 4 kcal mol^{-1} less favorable than for enamine **3** (S.I. Section 6.1.1),[32] yet we observed no reduction over an hour at ambient temperatures.[33] This energetic difference should translate into a rate difference of roughly 30 based on the Marcus cross relation [($\Delta G^{\ddagger}$) $\cong$ ½ (ΔG°), other things being equal].[19] Given the rapidity of the reduction of enamines (typically seconds by preliminary kinetic studies, SI section 5), reduction of cyclohexene should have been observed. Similarly puzzling is that 1,1-diphenylethylene is not reduced while trans-stilbene is readily hydrogenated. The origin of these kinetic factors is not known, but we note that reaction conditions more forcing than a few hours at 25 C are not possible. Perhaps the faster reactions of enamines are due to a polar effect, well known in organic systems, that H-atom transfers from an acidic X–H bond are more facile to a reagent that has a higher HOMO.[34]

Conclusion

$SmI_2(H_2O)_n$ in THF has been shown to reduce a new substrate class, enamines. Enamines would not normally have been thought of as a possible substrate for reduction by SmI_2 because of their resistance to outer-sphere electron transfer. The mechanism has been probed with competition experiments, product isotope effects, and other studies using substrates of varying electron richness, basicity, and coordinative capability. The results are all consistent with a mechanism of initial concerted transfer of e^- and H$^+$ (H atom) from $SmI_2(H_2O)_n$ to the enamine. There are strong arguments against stepwise PCET mechanisms of initial electron transfer or proton transfer, and there is no indication of a mechanism involving coordination of the enamine substrate. A thermochemical analysis indicates that the O–H bond in $Sm(H_2O)_n{}^{2+}$ (aq), and by implication $SmI_2(H_2O)_n$, is incredibly weak. This O–H bond has a bond dissociation free energy of only 26 kcal mol^{-1}, being the weakest O–H bond for any stable material. This BDE analysis therefore shows why $SmI_2(H_2O)_n$ can reduce such recalcitrant substrates, but also raises questions about the origin of the larger kinetic barriers for other substrates. This study thus provides a more detailed understanding of the important and varied chemistry of $SmI_2(H_2O)_n$ and opens the door to new applications of this reagent as a hydrogen atom donor.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References

1. (a) Szostak M, Fazakerley NJ, Parmar D, Procter DJ. Chem Rev. 2014; 114:5959. [PubMed: 24758360] (b) Szostak M, Spain M, Procter DJ. Chem Soc Rev. 2013; 42:9155. [PubMed: 24013846]

2. Szostak M, Spain M, Parmar D, Procter DJ. Chem Commun. 2012; 48:330.

3. (a) Zhao X, Perrin L, Procter DJ, Maron L. Dalton Trans. 2016; 45:3706. [PubMed: 26865402] (b) Kefalidis CE, Perrin L, Maron L. Eur J Inorg Chem. 2013; 2013:4042.

4. (a) Tarnopolsky A, Hoz S. Org Biomol Chem. 2007; 5:3801. [PubMed: 18004459] (b) Amiel-Levy M, Hoz S. J Am Chem Soc. 2009; 131:8280. [PubMed: 19507909] (c) Halder S, Hoz S. J Org Chem. 2014; 79:2682. [PubMed: 24559471]

5. (a) Szostak M, Spain M, Procter DJ. J Am Chem Soc. 2014; 136:8459. [PubMed: 24810096] (b) Szostak M, Spain M, Procter DJ. J Org Chem. 2014; 79:2522. [PubMed: 24517639] (c) Huang HM, Procter DJ. J Am Chem Soc. 2016; 138:7770. [PubMed: 27243379] (d) Huang HM, Procter DJ. J Am Chem Soc. 2017; 139:1661. [PubMed: 27995785] (e) Duffy LA, Matsubara H, Procter DJ. J Am Chem Soc. 2008; 130:1136. [PubMed: 18183982]

6. Prasad E, Flowers RA. J Am Chem Soc. 2005; 127:18093. [PubMed: 16366561]

7. Chciuk TV, Anderson WR, Flowers RA. Angew Chem Int Ed. 2016; 55:6033.

8. Chciuk TV, Flowers RA. J Am Chem Soc. 2015; 137:11526. [PubMed: 26273964]

9. Chciuk TV, Anderson WR, Flowers RA. J Am Chem Soc. 2016; 138:8738. [PubMed: 27367158]

10. Cook, AG. Enamines: Synthesis, Structure and Reactions. 2nd. CRC Press: New York, New York, USA; 1987.

11. (a) Cukier RI, Nocera DG. Annu Rev Phys Chem. 1998; 49:337. [PubMed: 9933908] (b) Warren JJ, Tronic TA, Mayer JM. Chem Rev. 2010; 110:6961. [PubMed: 20925411] (c) Weinberg DR, Gagliardi CJ, Hull JF, Murphy CF, Kent CA, Westlake BC, Paul A, Ess DH, McCafferty DG, Meyer TJ. Chem Rev. 2012; 112:4016. [PubMed: 22702235]

12. Schepp NP, Johnston LJ. J Am Chem Soc. 1996; 118:2872.

13. (a) Based on pK$_a$ values of 3.07, and 2.48 for cyclopent-1-en-1-yl, cyclohex-1-en-1-yl, and cyclohept-1-en-1-yl derivativesCook AG, Absi ML, Bowden VK. J Org Chem. 1995; 60:3169.

14. Donghi D, Beringhelli T, D'Alfonso G, Mondini M. Chem Eur J. 2006; 12:1016. [PubMed: 16267862]

15. The aqueous pK$_a$ of Sm(H$_2$O)$_n^{2+}$ is not known, but the acidity of 'hard' aquo ions is well known to vary as Z^2/r, where Z is the charge on the ion and r is the radius. Comparing dications, Sm^{2+} is likely very similar in size to Sr^{2+} (1.32 Å) since neighboring Eu^{2+} has r = 1.31 Å. Sr^{2+} has a pK$_a$ of 13.3, almost an order of magnitude weaker than TFE. Principles and values from:Wulfsberg, G. Principles of Descriptive Inorganic Chemistry. Brooks/Cole; Belmont, CA: 1987. p. 24-30.and inside back cover

16. We thank the reviewer for suggesting a version of this experiment.

17. (a) Teprovich JA, Antharjanam PKS, Prasad E, Pesciotta EN, Flowers RA. Eur J Inorg Chem. 2008; 2008:5015.(b) Yacovan A, Hoz S, Bilkis I. J Am Chem Soc. 1996; 118:261.(c) Sadasivam DV, Teprovich JA, Procter DJ, Flowers RA. Org Lett. 2010; 12:4140. [PubMed: 20722385]

18. Assuming a rate-limiting transfer of a hydrogen atom from SmI$_2$(H$_2$O)$_n$ to a carbon atom of the substrate (see below), the rate constants should parallel the strengths of the C–H bonds formed. Preliminary estimates are that these fall in the order 1p < stilbene < anthracene. The dependence of rate constants on driving force in SmI$_2$(H$_2$O)$_n$ reactions will be analyzed in more detail in future publications.

19. Mayer JM. Acc Chem Res. 2011; 44:36. [PubMed: 20977224]

20. Prochazka M, K V, Palecek M, Pecka K. Collection Czechoslov, Chem Commun. 1970; 35:3813.

21. Luo, YR. Comprehensive Handbook of Chemical Bond Energies. CRC Press; Boca Raton, Florida, USA: 2007.

22. (a) Bezdek MJ, Guo S, Chirik PJ. Science. 2016; 354:730. [PubMed: 27846601] (b) Spiegel DA, Wiberg KB, Schacherer LN, Medeiros MR, Wood JL. J Am Chem Soc. 2005; 127:12513. [PubMed: 16144398] (c) Campaña AG, Estévez RE, Fuentes N, Robles R, Cuerva JM, Buñuel E, Cárdenas D, Oltra JE. Org Lett. 2007; 9:2195. [PubMed: 17480090]

23. Chciuk TV, Li AM, Vazquez-Lopez A, Anderson WR, Flowers RA. Org Lett. 2017; 19:290. [PubMed: 28001419]

24. The value of –1.55 V vs. NHE for the standard reduction potential of $Sm^{3+/2+}$ appears in a number of reviews of standard electrode potentials and of the thermochemistry of lanthanide elements, including(a) Morss LR. Chem Rev. 1976; 76:827.(b) Bratsch SG. J Phys Chem Ref Data. 1989; 18:1–21.It appears to be relatively independent of the nature of the anions present:Timnick A, Glockler G. J Am Chem Soc. 1948; 70:1347–1350. [PubMed: 18915743]

25. Mohapatra PK, Khopkar PK. Polyhedron. 1989; 8:2071.

26. Shannon R. Acta Crystallographica Section A. 1976; 32:751.

27. Shi S, Szostak R, Szostak M. Org Biomol Chem. 2016; 14:9151. [PubMed: 27714249]

28. Critchfield FE, Gibson JA, Hall JL. J Am Chem Soc. 1953; 75:6044.

29. Evans WJ, Gummersheimer TS, Ziller JW. J Am Chem Soc. 1995; 117:8999.

30. We thank a reviewer for raising this issue and encouraging us to address it.

31. Wulfsberg, G. Principles of Descriptive Inorganic Chemistry. Brooks/Cole; Belmont, CA: 1987. p. 146-149.

32. (a) Value calculated in SI Section 6.1.1. from experimental values, which matches well with the following reference;Zhang XM. J Org Chem. 1998; 63:1872.

33. Reaction done in an NMR tube with 0.024 mM cyclohexene, 0.072 mM SmI_2, 3.6 M H_2O, 0.6 mL THF-d_8.

34. (a) Free Radicals. Vol. 1. Wiley; New York, N.Y., U.S.A.: 1973. (b) Especially KU. Ingold. 1:69. chap. 2. and G. A. Russell, vol. 1, chap. 7, pp. 283-293. (c) Tedder JM. Angew Chem Int Ed. 1982; 21:401.
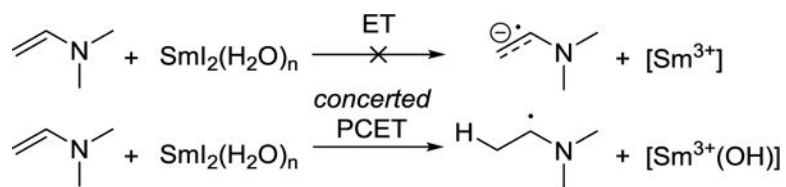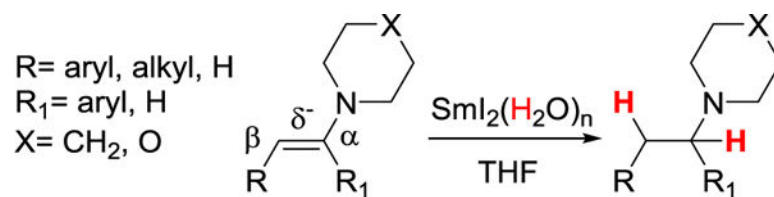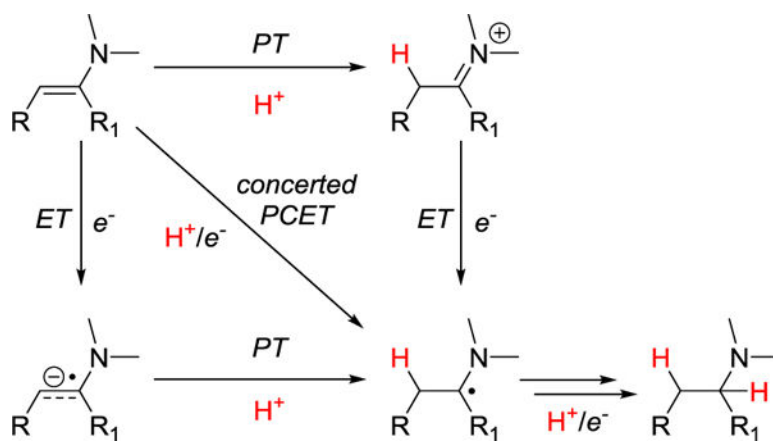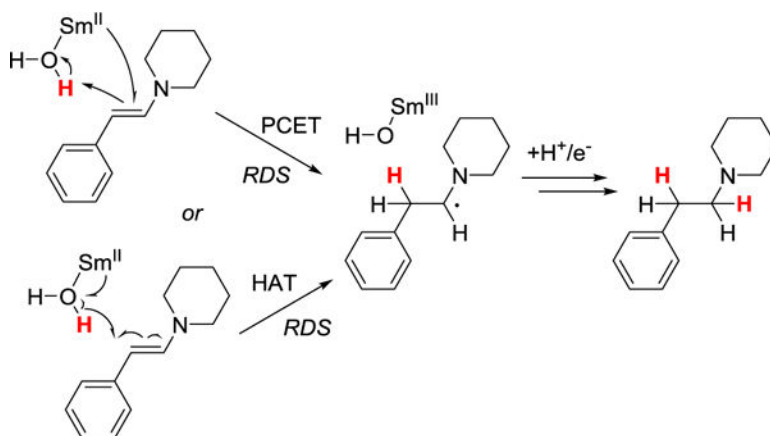
Figure 1.
$SmI_2(H_2O)_n$ reductions of enamines via ET and concerted PCET Pathways
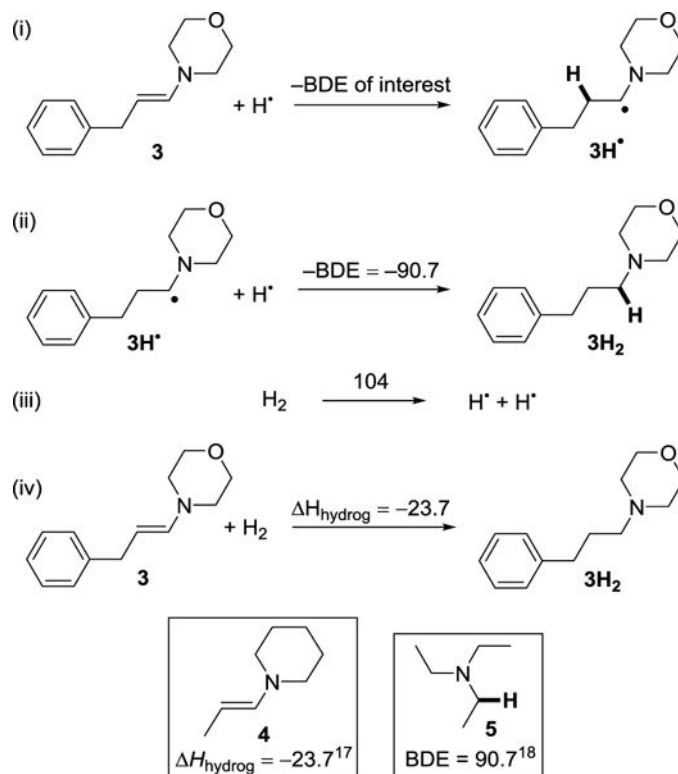
Scheme 1.
$SmI_2(H_2O)_n$ Reduction of Enamines

Scheme 2.
Square Scheme showing PCET Mechanisms for Enamine Reduction by $SmI_2(H_2O)_n$
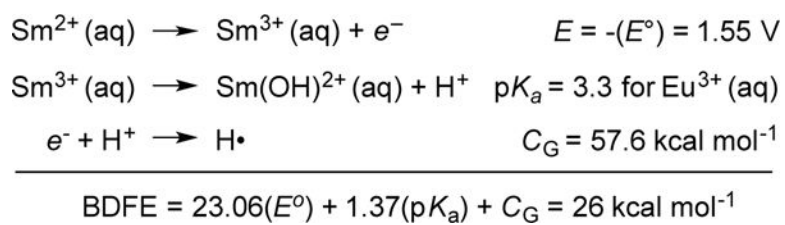
Scheme 3.
Two Descriptions of the Proposed Mechanism for $SmI_2(H_2O)_n$ Reduction of Enamines
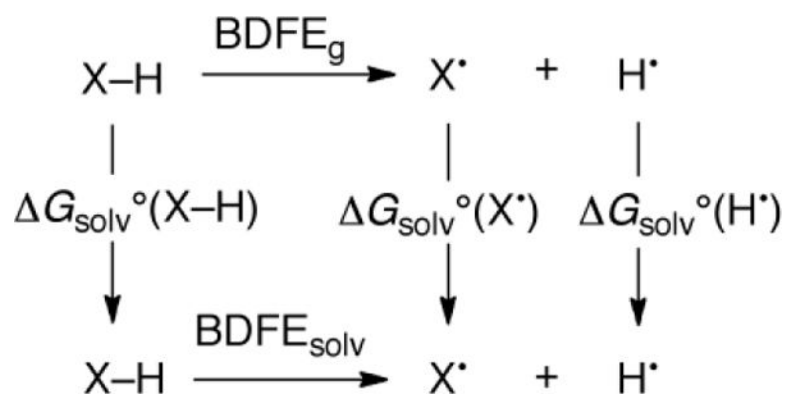
Scheme 4.
Estimation of the initially formed C–H BDE in the reduction of 3.[a]

[a] All values in kcal mol^{-1}. Step (ii) is assumed to be equivalent to that of **5**, and step (iv) is assumed to be equal to that of **4**.
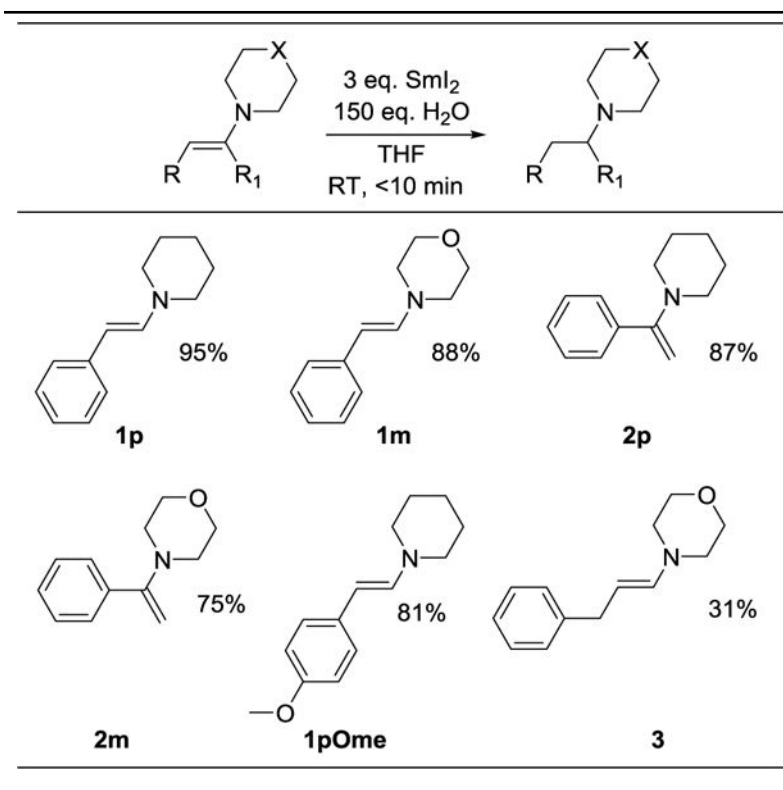
$$Sm^{2+}(aq) \longrightarrow Sm^{3+}(aq) + e^- \qquad\qquad E = -(E°) = 1.55 \text{ V}$$

$$Sm^{3+}(aq) \longrightarrow Sm(OH)^{2+}(aq) + H^+ \quad pK_a = 3.3 \text{ for } Eu^{3+}(aq)$$

$$e^- + H^+ \longrightarrow H\bullet \qquad\qquad C_G = 57.6 \text{ kcal mol}^{-1}$$

$$\overline{\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad}$$

$$BDFE = 23.06(E°) + 1.37(pK_a) + C_G = 26 \text{ kcal mol}^{-1}$$

Scheme 5.
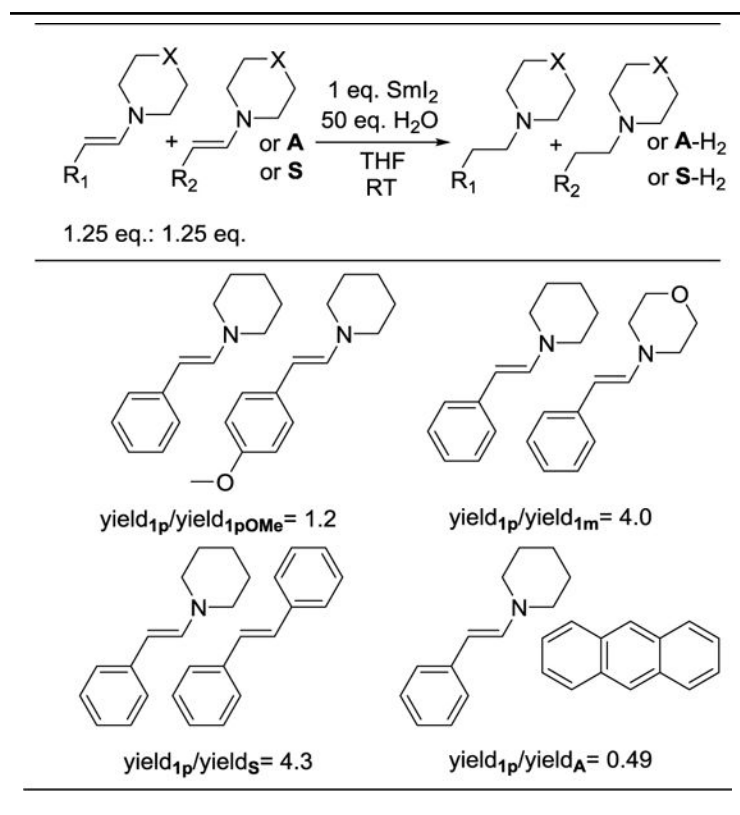The O-H bond dissociation enthalpy in $Sm(H_2O)_n^{2+}(aq)$

Scheme 6.
Relationship between gas-phase and solution bond dissociation free energies (from[11b]).

Table 1

Enamine Reduction Substrates[a]

[a]Non-optimized conditions: 0.024 M substrate, 0.072 M SmI$_2$, 3.6 M H$_2$O, 4.9 mL THF. Isolated yields of products. **p** = piperidinyl; **m** = morpholinyl.
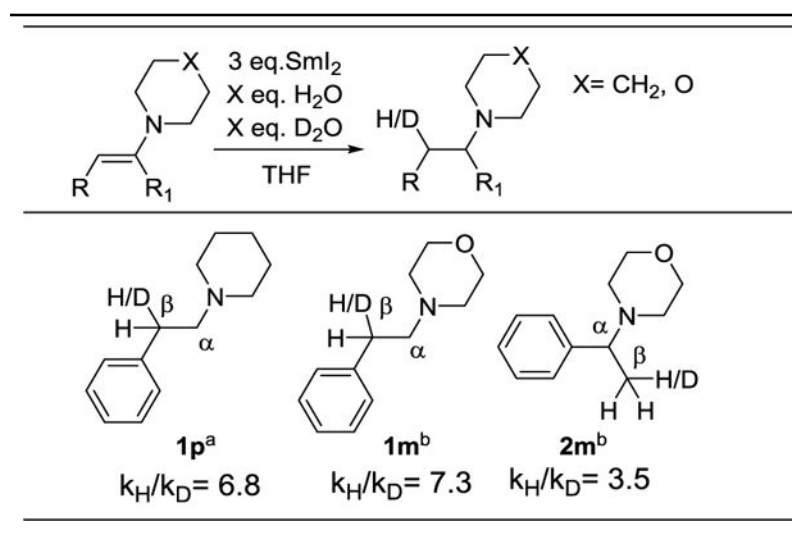
Table 2

Competition Experiments[a,b]

yield$_{1p}$/yield$_{1pOMe}$ = 1.2

yield$_{1p}$/yield$_{1m}$ = 4.0

yield$_{1p}$/yield$_S$ = 4.3

yield$_{1p}$/yield$_A$ = 0.49

[a]Non-optimized conditions: 0.025 M substrate 1, 0.025 M substrate 2, 0.020 M SmI$_2$, 1.0 M H$_2$O, 8.0 mL THF.

[b]Under these conditions, less than 20% total substrate conversion was achieved. **S** = stilbene, **A** = anthracene.

Table 3

Deuterium product isotope effects

[a]Non-optimized conditions: 0.024 M substrate, 0.072 M SmI_2, 0.65 M (27 eq.) H_2O, 2.9 M (123 eq.) D_2O, 4.9 mL THF.

[b]Same as a except 1.8 M (75 eq.) H_2O and 1.8 M (75 eq.) D_2O.