Article

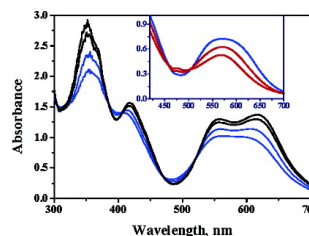# Mechanistic Impact of Water Addition to SmI: Consequences in the Ground and Transition State

Edamana Prasad, and Robert A. Flowers

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 5 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

Mechanistic Impact of Water Addition to SmI₂: Consequences in the Ground and Transition State

Edamana Prasad and Robert A. Flowers II*

Contribution from the Department of Chemistry, Lehigh University, Bethlehem, Pennsylvania 18015

Received September 15, 2005; E-mail: rof2@lehigh.edu

Abstract: The mechanistic impact of water addition to SmI₂ on the ground state and rate-limiting transition state structures in the reduction of benzyl bromide was determined using UV−vis spectroscopy, cyclic voltammetry, vapor pressure osmommetry, and stopped-flow spectrophotometric studies. The results obtained from these studies show that, upon addition of water, SmI₂ in THF (or DME) becomes partially water-solvated by displacing metal-coordinated solvent. Further addition of water displaces remaining bound solvent and induces a monomer−dimer equilibrium of the SmI₂−water complex. Concomitant with this process, a thermodynamically more powerful reductant is created. Rate studies on the reduction of benzyl bromide by SmI₂−water are consistent with reaction occurring through a dimeric transition state with the assembly of the activated complex requiring an equivalent of water at low concentrations but not at higher concentrations. The mechanistic complexity of the SmI₂−water system shows that simple empirical models describing the role of water in SmI₂-mediated reductions are likely to contain a high degree of uncertainty.

Introduction

The role of additives in samarium diiodide (SmI₂)-mediated reactions have been the focus of considerable attention for the past decade.[1] Additives used in reactions of SmI₂ generally belong to either of the following two classes: (a) electron donors such as HMPA,[2] DMPU,[3] and inorganic bases[4] or (b) proton donors such as water and alcohols.[1,5] While great efforts have been made to unravel the mechanism of SmI₂ reactions in the presence of electron donors such as HMPA,[6] comparatively little research has been initiated to understand the role of proton donors in SmI₂-mediated reactions. This is surprising since proton donors have been shown to have an important influence on the regiochemical and stereochemical outcome of numerous Sm(II)-mediated reactions.[5] Since proton donors may coordinate to Sm(II) as well as donate a proton through heterolytic cleavage of the O−H bond, the interplay between coordination and proton donor acidity is likely to play an important mechanistic role. The seminal work of Hoz et al. addressed this point and showed that the reduction of activated olefins by SmI₂ and proton donors occurred through two mechanistic pathways, one in which free SmI₂ reacts with substrate prior to protonation by an alcohol and another where the SmI₂−alcohol complex reacts with substrate.[7] The identity of the proton source, reactant concentration, and mode of addition were factors that dictated the mechanistic pathway of reductions. More recent studies on the role of alcohols and water on the SmI₂-mediated reduction of acetophenone lead to two important findings: (1) There was a direct correlation between the rate of acetophenone reduction and the pK$_a$ of the alcohol and (2) water has a higher affinity for SmI₂ than the alcohols examined, leading to reduction of acetophenone through a unique mechanistic pathway.[8]

Careful examination of the early literature on the applications of proton donors in reactions of SmI₂ show that water clearly plays a unique role in reductions and bond-forming reactions. Although water was initially thought to quench reactions of SmI₂, Hasegawa and Curran's seminal report describing the enhanced rate of reductions of a series of functional groups by SmI₂ in the presence of water generated a great deal of interest in this proton source.[9] While the origin of the enhanced rate of reduction was not explicitly studied, Hasegawa and Curran suggested that coordination of water to the SmI₂ played a role in the process. Later work of Kamochi et al. showed that reduction of a wide range of functional groups including carboxylic acids, esters, amides, and nitriles usually resistant to reduction by SmI₂ could be carried out by the addition of

(1) (a) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29−68. (b) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307−338. (c) Miller, R. S.; Sealy, J. M.; Shabangi, M.; Kuhlman, M. L.; Fuchs, J. R.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2000**, *122*, 7718−7722. (d) Edmonds, D. J.; Johnston, D.; Procter, D. J. *Chem. Rev.* **2004**, *104*, 3371−3404. (e) Dahlen, A.; Hilmersson, G. *Eur. J. Inorg. Chem.* **2004**, *17*, 3393−3403.
(2) Inanaga, J.; Ishikawa M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485−1486.
(3) Curran, D. P.; Wolin, R. L. *Synlett* **1991**, 317−318.
(4) Kamochi, Y.; Kudo, T. *Tetrahedron Lett.* **1991**, *32*, 3511−3514.
(5) (a) Yoshida, A.; Mikami, K. *Synlett* **1997**, 1375−1376. (b) Yoshida, A.; Manamoto, T.; Inanga, J.; Mikami, K. *Tetrahedron Lett.* **1998**, *39*, 1777−1780. (c) Keck, G. E.; Wager, C. A.; Sell, T.; Wager, T. T. *J. Org. Chem.* **1999**, *64*, 2172−2173. (d) Edmonds, D. J.; Muir, K. W.; Procter, D. J. *J. Org. Chem.* **2003**, *68*, 3190−3198.
(6) (a) Molander, G. A.; McKie, J. *J. Org. Chem.* **1992**, *57*, 3132−3139. (b) Curran, D. P.; Totleben, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 6050−6058. (c) Hasegawa, E.; Curran, D. P. *Tetrahedron Lett.* **1993**, *34*, 1717−1720. (d) Fukuzava, S.-I.; Mutoh, K.; Tsuchimoto, T.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 5400−5405. (e) Curran, D. P.; Gu, X.; Zhang, W.; Dowd, P. *Tetrahedron* **1997**, *53*, 9023−9042. (f) Enemaerke, R. J.; Heretz, T.; Skrydstrup, T.; Daasbjerg, K. *Chem. Eur. J.* **2000**, *6*, 3747−3754. (g) Knettle, B. W.; Flowers, R. A., II. *Org. Lett.* **2001**, *3*, 2321−2324. (h) Prasad, E.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2002**, *124*, 6895−6899.
(7) Hoz, S.; Yacovan, A.; Bilkis, I. *J. Am. Chem. Soc.* **1996**, *118*, 261−262.
(8) Chopade, P. R.; Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2004**, *126*, 44−45.
(9) Hasegawa, E.; Curran, D. P. *J. Org. Chem.* **1993**, *58*, 5008−5010.

water.[10] More recent work of Hilmersson and co-workers has shown that water is the critical component in the SmI$_2$/H$_2$O/ amine reducing system and its replacement by alcohols leads to inactivation of the reductant.[11]

In numerous SmI$_2$-mediated reductions and reductive coupling reactions of important synthetic utility, water is shown to be a unique proton source compared to alcohols. Conversion of β-hydroxyketones to 1,3-diols by SmI$_2$ leads to high diastereo-selectivities at low water concentrations while at higher concentrations selectivity is lost, whereas use of a broad concentration range of methanol as a proton donor in the same reactions provides high diastereoselectivities.[5c] In bond-forming reactions, the addition of water to the SmI$_2$-initiated reductive coupling of nitrones with α,β-unsaturated esters substantially increased the rate and yield of the reaction[12] and was also recently shown to be a critical additive in SmI$_2$-promoted radical additions of *N*-acyl oxazolidinones to acrylamides and acry-lates.[13] Despite the importance of SmI$_2$/water in a variety of reactions, very little mechanistic detail is known about this powerful and useful combination of reagents. To have a fundamental understanding of the reactivity of the SmI$_2$/water reducing system, it is necessary to determine the interplay between solvation and the affinity of water for SmI$_2$, and the role of water and its concentration on the ground-state reductant and the rate-limiting transition structures. A detailed mechanistic understanding of the role of water in reductions and bond-forming reactions of SmI$_2$ will provide chemists with the fine points necessary to plan reaction protocols appropriately and possibly develop new reactions using this combination of reagents.

Results and Discussion

UV–Vis Studies. Previous studies have shown that the presence of large amounts of proton donors (water and alcohols) result in coordination between SmI$_2$ and the proton source in THF and other solvents.[7,8] Clear changes have been observed for absorption peaks in the visible spectrum of SmI$_2$ in the presence of excess proton sources such as methanol. While a large amount of methanol (>1 M) is needed for the alcohol–samarium coordination, water coordination to samarium begins in much lower concentration range (~0.10 M). Upon addition of water, the long wavelength absorption peaks of SmI$_2$ (λ_{max} = 555 and 618 nm) begin to merge (λ_{max} = 570 nm), indicating Sm–water coordination. To study the SmI$_2$–water system in detail, careful UV–vis experiments were initiated and the visible absorption bands of SmI$_2$ ([SmI$_2$] = 2.5 mM) were monitored in the presence of an increasing amount of water (Figure 1). Examination of Figure 1 clearly shows that water competes effectively with the bulk solvent (THF) for SmI$_2$. The two long wavelength absorption peaks of SmI$_2$ started to combine upon
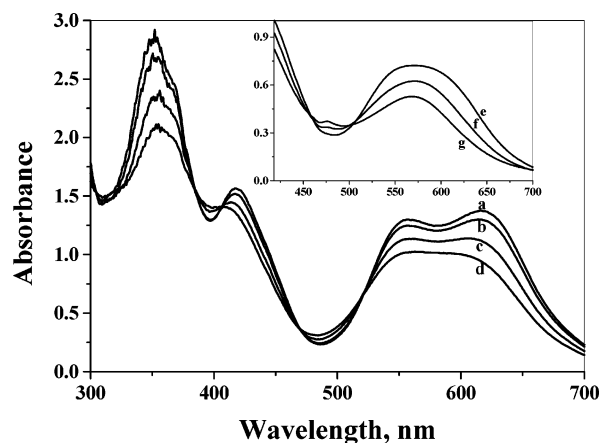

Figure 1. Absorption spectra of SmI$_2$ (2.5 mM) in the presence of increasing amount of water. (a) [H$_2$O] = 0.025 M, (b) [H$_2$O] = 0.05 M, (c) [H$_2$O] = 0.125 M, (d) [H$_2$O] = 0.188 M. Inset shows the absorption spectra of SmI$_2$ upon the addition of larger amounts of water. (e) [H$_2$O] = 0.15 M, (f) [H$_2$O] = 0.30 M, (g) [H$_2$O] = 0.45 M.
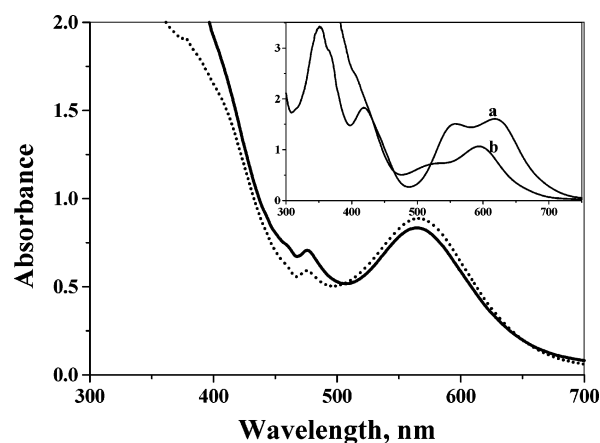

Figure 2. Absorption spectra of SmI$_2$ in THF (dot) and DME (solid) containing 1.25 M water. Inset shows the absorption spectra of SmI$_2$ in THF (a) and DME (b). In all spectra [SmI$_2$] = 2.5 mM.

the addition of 50 equiv of water (0.125 M H$_2$O). Further addition of water (>100 equiv) resulted in a second absorption peak centered at 476 nm (inset of Figure 1), which is isobestic with the initially formed SmI$_2$–water complex peak at 570 nm. Addition of 50 equiv of water turns the deep blue solution of SmI$_2$ in THF purple and continued addition of water changes the color from purple to bright red. The absorption experiments are consistent with the generation of two different types of SmI$_2$–water complexes. No further changes occur in the absorption spectrum of SmI$_2$ even at large excess of water (2.5 M), suggesting the two species exist at equilibrium in the presence of excess water.

Intrigued by these initial results, further absorption experiments were conducted in dimethoxyethane (DME). The UV–vis spectrum of SmI$_2$ in DME is notably different from that in THF (inset of Figure 2). Nonetheless, addition of water to SmI$_2$–DME solution generates the identical absorption spectrum in both THF and DME. Successive addition of water to SmI$_2$ in DME resulted in similar changes to that in THF, although greater amounts of water are required to generate the intermediates; i.e., initial addition of water (<120 equiv) generates a peak centered at 585 nm and further addition (up to 500 equiv) generates a second peak at 476 nm (see Supporting Information).

(10) (a) Kamochi, Y.; Kusudo, T.; Daiichi, C. P. S.; Fukuoka, J. *Chem. Lett.* **1993**, 1495−1498. (b) Kamochi, Y.; Kusudo, T.; Daiichi, C. P. S.; Fukuoka, J. *Heterocycles* **1993**, *36*, 2383−2396.
(11) (a) Dahlen, A.; Hilmersson, G. *Tetrahedron Lett.* **2002**, *43*, 7197−7200. (b) Dahlen, A.; Hilmersson, G. *Chem. Eur. J.* **2003**, *9*, 1123−1128. (c) Dahlen, A.; Hilmersson, G.; Knettle, B. W.; Flowers, R. A., II. *J. Org. Chem.* **2003**, *68*, 4870−4875. (d) Dahlen, A.; Sundgren, A.; Lahmann, M.; Oscarson, S.; Hilmersson, G. *Org. Lett.* **2003**, *5*, 4085−4088. (e) Dahlen, A.; Petersson, A.; Hilmersson, G. *Org. Biomol. Chem.* **2003**, *1*, 2423−2436. (f) Davis, T. A.; Chopade, P. R.; Hilmersson, G.; Flowers, R. A., II. *Org. Lett.* **2005**, *7*, 119−122.
(12) Masson, G.; Cividino, P.; Py, S.; Vallée, Y. *Angew. Chem.* **2003**, *42*, 2265−2268.
(13) Jensen, C. M.; Lindsay, K. B.; Taaning, R. H.; Karaffa, J.; Hansen, A. M.; Skrydstrup, T. *J. Am. Chem. Soc.* **2005**, *127*, 6544−6545.

Addition of an excess amount of water results in a hypsochromic shift for the initial SmI$_2$−water absorption to 565 nm in both THF and DME. Figure 2 shows a comparison of the UV−vis spectra of SmI$_2$ obtained in THF and DME in the presence of excess (1.25 M) water. Spectra of SmI$_2$ in THF and DME in the absence of water are also shown in the inset of Figure 2. This spectroscopic data is consistent with identical species being generated in both solvents by the addition of water. Since the spectra of SmI$_2$ in THF and DME are unique, the identical spectra obtained upon addition of water are consistent with displacement of bulk solvent from the inner sphere of Sm and its replacement by water. Unlike the results obtained in THF and DME, addition of water to a solution of SmI$_2$ in acetonitrile resulted in complete precipitation and byproducts consistent with reduction of solvent, indicating that SmI$_2$−water complexes are not stable in acetonitrile.

Crystal structures published by Evans and co-workers show that the SmI$_2$−THF complex is surrounded by five THF molecules whereas SmI$_2$ obtained from DME shows that three DME molecules are coordinated to Sm.[14] The experiments described thus far are consistent with the ability of water to displace THF and DME from SmI$_2$, suggesting that water has a greater affinity for Sm(II) than bulk THF and DME. Furthermore, the higher amount of water needed to generate the SmI$_2$−water complexes in DME compared to THF implies that (1) the bidentate DME is a better ligand for SmI$_2$ than THF or (2) the differential solvation of water in DME and THF leads to less free water available for complexation in DME.

Cyclic Voltammetry Studies. To further examine the hypothesis that identical reductants are generated in THF and DME and to study their energetics, cyclic voltammetry (cv) experiments of SmI$_2$−water combinations were initiated. Previous cv studies of SmI$_2$ in THF and DME have shown that the voltammograms are quasireversible and the redox potentials of SmI$_2$ are identical within experimental error, with potentials of −1.5 ± 0.1 V vs a saturated Ag/AgNO$_3$ reference electrode.[15] Addition of 60 equiv of water to a solution of SmI$_2$ in THF generated an irreversible cyclic voltammogram with an oxidation peak potential of −1.6 ± 0.1 V vs a saturated Ag/AgNO$_3$. Further addition of water (500 equiv) resulted in a more negative oxidation peak potential of −1.9 ± 0.1 V with a similar irreversible voltammogram. Further addition of water up to 1000 equiv (5 M) had no further influence on the oxidation peak potential. Cyclic voltammetry experiments in DME at lower water concentrations were hampered by the limited solubility of the supporting electrolyte (tetraheptylammonium iodide). Fortunately, the solubility of electrolyte in DME was good enough at high concentrations of water (∼5 M) and cv experiments were conducted at these higher concentrations. Figure 3 shows the cyclic voltammograms of SmI$_2$ containing 500 equiv of water in THF and the inset shows SmI$_2$ in DME containing 1000 equiv of water. The oxidation potential values were identical within experimental error. The cv experiments lead to two conclusions: (1) Addition of water to SmI$_2$ in THF or DME creates a more powerful reductant (in thermodynamic terms) and (2) addition of water to SmI$_2$ dissolved in either solvent produces reductants with identical redox properties.
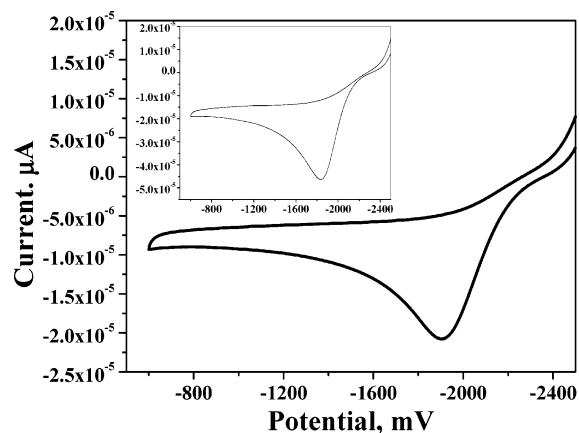
Figure 3. Cyclic voltammogram of SmI$_2$ (5 mM) in THF containing 2.5 M water. Cyclic voltammetry was performed using platinum wire auxiliary electrodes, glassy carbon working electrodes, and Ag/AgNO$_3$ reference electrodes. The electrolyte used was tetraheptylammonium iodide (0.1 M). Inset shows the cyclic voltammogram for the same experiment in DME containing 5 M water.

These data in combination with the previously described spectrophotometric studies show that addition of water to SmI$_2$ in THF or DME likely produces water-solvated SmI$_2$, which is a more powerful reductant (thermodynamically) than SmI$_2$ alone. Furthermore, absorption experiments suggest that higher concentrations of water produce two different SmI$_2$−water complexes that exist in equilibrium in the system.

VPO Studies. Although previous studies have shown that SmI$_2$ exists as a monomer in THF and DME,[16] the addition of water could alter the aggregation state. Since water is a relatively small ligand compared to THF or DME, it is possible that displacement of solvent from the inner sphere of Sm and replacement by water could potentially lead to aggregation of SmI$_2$ either through bridging water or iodide ligands.[17] To obtain a better understanding of the nature of these complexes, vapor pressure osmommetry (VPO) experiments were undertaken to determine the average solution molecular weights and aggregation numbers of SmI$_2$ in THF and DME containing water. While it can be reasonably argued that reliance on measurements based on colligative properties have potential drawbacks because structural detail is inferred, previous studies have shown that this approach can provide insight into the solution MW and aggregation state of Sm-based complexes not easily obtained by other methods.[16,18]

Table 1 contains the VPO-generated molality, MW, and aggregation number of SmI$_2$ in THF and DME in the presence of moderate amounts of water (12 and 15 equiv, respectively) and in the presence of larger amounts of water (146 and 192 equiv, respectively). Higher concentrations of water were used in the VPO experiments for SmI$_2$ in DME since UV−vis data indicate this solvent has a higher affinity for Sm (i.e., a larger amount of water is required to displace DME from SmI$_2$). Each experiment is an average of five independent VPO runs.

(14) (a) Evans, W. J.; Gummersheimer, T. S.; Ziller, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 8999−9002. (b) Evans W. J.; Broomhall-Dillard, R. N. R.; Ziller, J. W. *Polyhedron* **1998**, *17*, 3361−3370.
(15) Shabangi, M.; Flowers, R. A., II. *Tetrahedron Lett.* **1997**, *38*, 1137−1140.

(16) Shotwell, J. B.; Sealy, J. M.; Flowers, R. A., II. *J. Org. Chem.* **1999**, *64*, 4, 5251−5255.
(17) Bridging iodides and oxides are known for a number of Sm(II) complexes. (a)Evans, W. J.; Grate, J. W.; Bloom, I., Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 405−409. (b) Evans, W. J.; Grate, J. W.; Choi, H. W.; Bloom, I.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 941−946. (c) Evans, W. J.; Drummond, D. K.; Zhang, H.; Atwood, J. L. *Inorg. Chem.* **1988**, *27*, 575−579.
(18) Prasad, E.; Knettle, B. W.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2004**, *126*, 6891−6894.

Table 1. SmI$_2$ Concentration and Aggregation Numbers (VPO) in THF and DME Containing Water
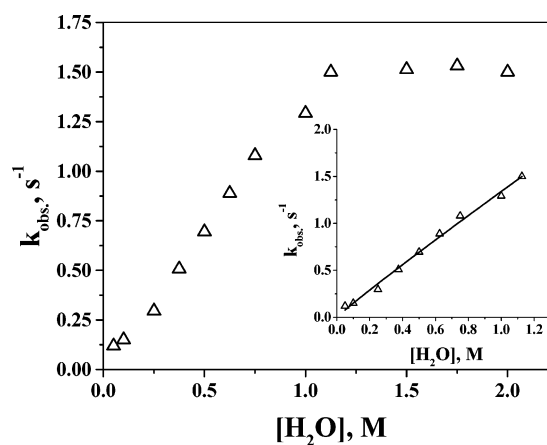
concentrations (mM)	concentration (m*m*)	VPO concentration (m*m*)	aggregation number	avg. MW
SmI$_2$–THF (0.15 M H$_2$O)	13.2	15.0	16.6	0.9 ± 0.1	380 ± 40
SmI$_2$–DME (0.19 M H$_2$O)	13.0	15.0	16.7	0.9 ± 0.1	410 ± 40
SmI$_2$–THF (1.9 M H$_2$O)	13.2	15.0	10.3	1.5 ± 0.1	590 ± 50
SmI$_2$–DME (2.5 M H$_2$O)	13.0	15.0	10.1	1.5 ± 0.1	600 ± 50

Examination of the VPO-derived data in Table 1 shows that the addition of moderate amounts of water to SmI$_2$ in THF or DME has little effect on the aggregation state and hence SmI$_2$ is monomeric under these conditions. The VPO data for SmI$_2$ in THF and DME that contains higher amounts of water provides MWs of 590 ± 50 and 600 ± 50, respectively, which substantially deviate from the 404 MW of SmI$_2$. The resulting aggregation number for both solvents is 1.5. This data clearly shows that SmI$_2$ does not exist as a monomer upon the addition of excess water.

In ideal cases, a monomer would provide an aggregation number of 1 whereas a dimer would provide an aggregation number of 2. The average values of 1.5 obtained for SmI$_2$ in THF or DME containing large amounts of water indicates the likelihood of a monomer–dimer equilibrium under the conditions of this experiment. Another possibility is that the VPO data represents a more complex equilibrium between a small amount of a higher order aggregate and monomer. While that latter possibility cannot be excluded based on VPO data alone, higher order aggregates typically precipitate out of solution. The absence of precipitation during these experiments and rate studies described in the following paragraphs are consistent with the VPO data, representing a monomer–dimer equilibrium.

Kinetic Studies. To further study the impact of water concentration on the mechanistic behavior of SmI$_2$, a series of kinetic experiments were carried out in THF, employing benzyl bromide as the substrate in the presence of a range of water concentrations. Benzyl bromide was chosen as a model compound because the first electron transfer from Sm(II) to this substrate is likely to be the rate-limiting step in this reduction.[19] As a consequence, the overall kinetic analysis and determination of reaction orders necessary to ascertain the role of various SmI$_2$–water intermediates is more straightforward. While the use of DME in the previously described experiments was useful in providing a clear picture of the solution structure of SmI$_2$ upon the addition of water and providing a basis of comparison to THF, most reactions of SmI$_2$ using water as a proton donor are carried out in THF. As a consequence, all rate studies were performed in THF.

Initial experiments were designed to determine the rate orders of water, benzyl bromide, and SmI$_2$. All rate studies were carried out at 15 °C under pseudo first-order conditions with [benzylBr] kept high relative to [SmI$_2$] using a stopped flow spectrophotometer. The decay of the absorption at 570 nm was monitored when examining moderate water concentrations whereas the

(19) (a) Andrieux, C. P.; Gallardo, I.; Saveant, J.-M.; Su, K.-B. *J. Am. Chem. Soc.* **1986**, *108*, 638–647. (b) Saveant, J.-M. *J. Am. Chem. Soc.* **1987**, *109*, 6788–6795.

Figure 4. Plot of $k_{obs.}$ vs [water] in THF for the reduction of benzyl bromide (0.05 M) by SmI$_2$ (5 mM) at 15 °C. The inset shows the same up to 1.125 M of water and the line corresponds to an unweighted fit to $k_{obs.} = k[\text{water}]^n$ ($n = 0.95 ± 0.04$).

absorption at 476 nm was monitored when higher water concentrations were being examined since these absorptions represent the monomer and dimer, respectively.

To determine the rate order of water, a series of kinetic experiments were initiated where the rate of reduction of benzyl bromide was monitored over a wide range of water concentrations. These data are contained in Figure 4. Below a concentration of 1.1 M H$_2$O, a first-order dependence of water on the rate was observed, whereas at higher concentrations a zeroth-order dependence was obtained. Further studies with D$_2$O over a broad range of concentrations provided a deuterium isotope effect of 1.0 ± 0.1, clearly showing that proton transfer does not occur in the rate-limiting step of the reduction.

Next, the rate order for SmI$_2$ was determined. Since SmI$_2$ is the limiting reagent in these experiments, the rate order was extracted from ln A vs time plots, where A corresponds to the absorption of SmI$_2$.[20] A clear change was observed for the rate order for SmI$_2$–water complexes depending on whether the decay was monitored at 570 or 476 nm. When the decay trace was monitored at 476 nm, ln A vs time graphs provide linear plots. On the other hand, such graphs deviate substantially from linear behavior when the decay traces were monitored at 570 nm (see Supporting Information). These findings are consistent with a second-order behavior for SmI$_2$–water monomer and a first-order behavior for SmI$_2$–water dimer.[20]

Further experiments were carried out to determine the rate order of SmI$_2$ at lower concentration of water from ln rate vs ln [SmI$_2$] plots, which provide a slope of 2.1 ± 0.1, confirming the second-order behavior of SmI$_2$ under these conditions (Figure 5). Reduction of benzyl bromide by SmI$_2$ provides linear plots for $k_{obs.}$ vs [benzyl bromide] at all concentrations of water, providing a rate order of 1.0 ± 0.1 (Figure 6).

Table 2 summarizes the VPO and rate order study for the reduction of benzyl bromide by SmI$_2$ over a range of concentrations. It is important to keep in mind that the solution structures are necessary in determining the rate expressions for the reactions since the rate law provides the stoichiometry of the activated complex relative to the reactants.[21] As a consequence, the rate equations for the reduction of benzyl bromide in THF

(20) Espenson, J. H. In *Chemical Kinetics and Reaction Mechanism*; Speer, J. B., Morris, J. M., Eds.; McGraw-Hill: New York, 1995.
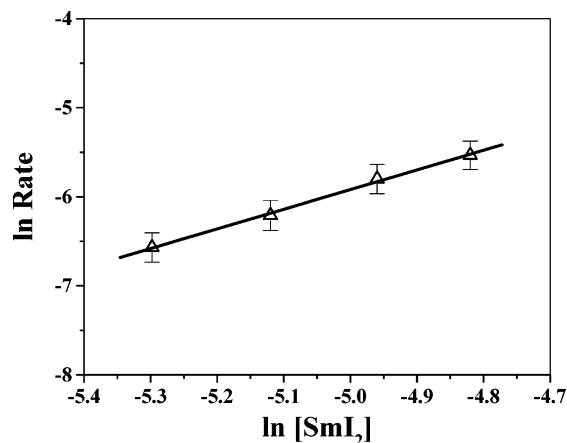
Figure 5. Plot of ln rate vs ln [SmI₂] for the reduction of benzyl bromide (0.05 M) in the presence of water (0.44 M) at 15 °C.
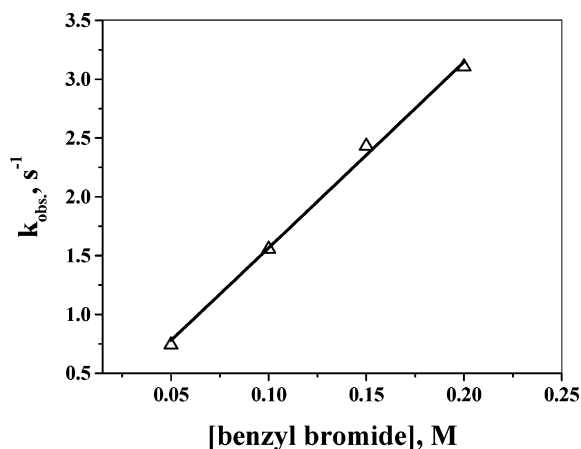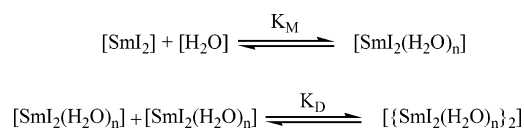

Figure 6. Plot of $k_{obs.}$ vs [benzyl bromide] in THF for the reduction of benzyl bromide by SmI₂ (5 mM)−water (1 M) at 15 °C. The line corresponds to an unweighted fit to $k_{obs.} = k[\text{benzyl bromide}]^n$ ($n = 1.0 \pm 0.1$).

Table 2. Summary of Rate and VPO Studies for the Reduction of Benzyl Bromide by SmI₂ over a Range of Water Concentrations in THF

	Rate order				
[H₂O]	SmI₂	H₂O	benzyl bromide	aggregation number	avg. MW
0.15−1.1 M	2.1 ± 0.1	0.95 ± 0.04	1.0 ± 0.1	0.90 ± 0.1	380 ± 40
>1.1 M	1.0 ± 0.1	0	1.0 ± 0.1	1.5 ± 0.1	590 ± 50

by SmI₂ in the presence of water were derived based on the determined rate orders in combination with the data extracted from the VPO studies. At moderate concentrations of water, UV−vis spectra are consistent with the formation of two SmI₂−water complexes (Figure 1). Careful VPO analysis of the system indicates a monomer−dimer equilibrium of the SmI₂−water complexes. Although the discrete structural details of these complexes, including the number of water molecules bound to samarium and the type of bridging interaction responsible for dimerization, are uncertain, it is reasonable to assume that displacement of bound solvent by water assists the dimerization of SmI₂ by providing a less hindered solvate. Since addition of water in excess does not drive the equilibrium exclusively to dimer under the conditions utilized in these experiments, it is

(21) Wiedemann, S. H.; Ramirez, A.; Collum, D. B. *J. Am. Chem. Soc.* **2003**, *125*, 15893−15901.

Scheme 1

$$[\text{SmI}_2] + [\text{H}_2\text{O}] \underset{}{\overset{K_M}{\rightleftharpoons}} [\text{SmI}_2(\text{H}_2\text{O})_n]$$

$$[\text{SmI}_2(\text{H}_2\text{O})_n] + [\text{SmI}_2(\text{H}_2\text{O})_n] \underset{}{\overset{K_D}{\rightleftharpoons}} [\{\text{SmI}_2(\text{H}_2\text{O})_n\}_2]$$

likely that the monomer utilizes bound water for bridging. Thus, addition of water initially generates SmI₂−water monomer and, presumably, when an appreciable amount of water-solvated SmI₂ monomer is formed, dimerization commences. This supposition is consistent with the two different isobestic points observed in the UV−vis studies. The equilibria among SmI₂, water, and the initially formed complex shown in Scheme 1 represent this mechanistic scenario where $[\text{SmI}_2(\text{H}_2\text{O})_n]$ represents SmI₂−water monomer concentration and $[\{\text{SmI}_2(\text{H}_2\text{O})_n\}_2]$ represents SmI₂−water dimer concentration.

Taken together, the rate results and spectroscopic studies provide the following experimental observations: (1) The rate of the reaction is first-order in water at lower water concentrations and zero-order at higher concentrations. (2) The rate of the reaction is second-order for the Sm−water monomer and first-order in Sm-water dimer. The reaction order of the benzyl bromide is 1 at all concentrations of water. Hence, at concentrations of water <1.1 M,

$$\text{rate} = k_1[\text{SmI}_2(\text{H}_2\text{O})_n]^2[\text{H}_2\text{O}][\text{RX}]$$
$$= k_{obs.} [\text{SmI}_2(\text{H}_2\text{O})_n]^2 \tag{1}$$

where

$$k_{obs.} = k_1[\text{H}_2\text{O}][\text{RX}] \tag{2}$$

At higher concentrations of water (>1.1 M), Sm−water monomer and dimer exist in equilibrium. Thus, both species can react with RX. As a result, the rate expression under these conditions is

$$\text{rate} = k_1[\text{SmI}_2(\text{H}_2\text{O})_n]^2[\text{RX}] + k_2[\{\text{SmI}_2(\text{H}_2\text{O})_n\}_2][\text{RX}] \tag{3}$$

From Scheme 1,

$$K_D = \frac{[\{\text{SmI}_2(\text{H}_2\text{O})_n\}_2]}{[\text{SmI}_2(\text{H}_2\text{O})_n]^2}$$

Thus,

$$\text{rate} = \{k_1/K_D + k_2\}[\{\text{SmI}_2(\text{H}_2\text{O})_n\}_2][\text{RX}]$$
$$= k_{obs.}[\{\text{SmI}_2(\text{H}_2\text{O})_n\}_2] \tag{4}$$
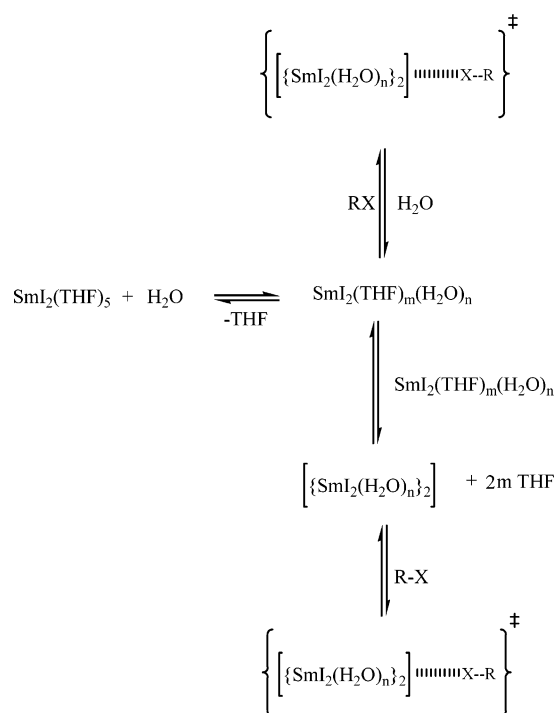
where

$$k_{obs.} = \{k_1/K_D + k_2\}[\text{RX}] \tag{5}$$

Scheme 2 provides a pictorial representation of the data in Table 2. Upon addition of water, SmI₂ in THF becomes water solvated by displacing metal-coordinated solvent. Further addition of water displaces THF and induces dimerization of the SmI₂−water complex. At lower concentrations of water (relative to [SmI₂]), the second-order rate dependence of the Sm−water monomer is consistent with reduction of benzyl bromide through

Scheme 2

$$\left\{ \left[\{SmI_2(H_2O)_n\}_2 \right] \!\!\!\!\!\mid\!\mid\!\mid\!\mid\!\mid\!\mid\!\mid\! X\text{--}R \right\}^{\ddagger}$$

$$\Big\Uparrow \quad RX \quad\parallel\quad H_2O$$

$$SmI_2(THF)_5 \;+\; H_2O \;\rightleftharpoons\; SmI_2(THF)_m(H_2O)_n$$
$$\text{-THF}$$

$$\Big\Uparrow \quad SmI_2(THF)_m(H_2O)_n$$

$$\left[\{SmI_2(H_2O)_n\}_2 \right] \quad + 2m\ THF$$

$$\Big\Uparrow \quad R\text{-}X$$

$$\left\{ \left[\{SmI_2(H_2O)_n\}_2 \right] \!\!\!\!\!\mid\!\mid\!\mid\!\mid\!\mid\!\mid\!\mid\! X\text{--}R \right\}^{\ddagger}$$

a dimeric transition state.[22] Since no deuterium isotope effect was found over the entire concentration range of water studied, the first-order rate dependency of water at lower concentrations is consistent with water being involved in the assembly of the dimeric activated complex. At higher concentrations of water where an appreciable amount of dimer is present, the rate is first order in dimer (as determined by monitoring the decay of absorption band at 476 nm).

With this mechanistic data in hand, it is instructive to consider the observations described herein in the context of previous findings reported in the literature. One of the striking features of this work is the observation that water has an unusually high affinity for SmI_2 and competes for coordination with THF at comparatively low concentrations compared to bulk solvent. Coordination of water with SmI_2 in THF (or DME) produces a thermodynamically more powerful reductant that approaches the ease of oxidation of the SmI_2−HMPA combination.[1c,15,23] Although water does not have the steric bulk of HMPA proposed to be necessary for achieving the high diastereoselectivities important in bond-forming reactions of SmI_2−HMPA, it provides a means to accelerate reductions in concert with providing a proton donor in the medium. This suggests that, in functional group reductions, addition of water as a cosolvent may be sufficient for reaction (i.e., HMPA is unnecessary). Additionally, coordination of water to SmI_2 is also likely to decrease the heterolytic bond dissociation energy of the O−H bond, producing a better proton donor. While proton transfer has been shown to be mechanistically inconsequential in the present system, it is likely to be important in the reduction of carbonyl-containing substrates since proton transfer has previously been shown to be important in these systems.[7,8,24] Thus,

coordination of water to SmI_2 potentially accelerates reactions through a dual mode, increased reducing power and enhanced acidity of the proton donor. This mechanistic mode of action is likely to be important in the reduction of carboxylic acids, esters, and amides by SmI_2−water which cannot be reduced by SmI_2 alone.[10]

Another interesting finding from this work was the unexpected stability of SmI_2 in water. Until recently, the prevailing view has been that SmI_2 can be utilized in a narrow range of solvents including THF, DME, and acetonitrile. During the course of this work, SmI_2 in THF was introduced into neat water and found to be stable for a few days in solutions containing 98% water as long as the solution was sufficiently deaerated (Supporting Information, Figure S6). Inspection of the literature shows although water has not been used as a medium for SmI_2, pinacol couplings have been carried out in water using a combination of $SmCl_3$ and Sm.[25] Spectroscopic data were consistent with $SmCl_2$ as the active reductant in this system. Since $SmCl_2$ is known to be a substantially better reductant than SmI_2,[26] reactions of SmI_2 in water should be accessible. A rational extension of this line of reasoning suggests that common alcohols such as ethanol or 2-propanol may be suitable solvents as well.

Conclusion

The spectroscopic, thermochemical, and mechanistic data described herein collectively show that upon addition of water to SmI_2 in THF (or DME), water displaces bulk solvent. The replacement of metal-bound solvent with water creates a thermodynamically more powerful reductant, and once a sufficient amount of ligated solvent is displaced by water, a monomer−dimer equilibrium is established. Careful rate studies on the reduction of benzyl bromide are consistent with reaction occurring through a dimeric transition state with the assembly of the activated complex requiring an equivalent of water at low concentrations but not at higher concentrations. The mechanistic complexity of the SmI_2−water system is driven by the high affinity of water for Sm(II) and these results suggest that simple empirical models describing the role of proton donors (including, but not necessarily limited to, water) in more complex systems are likely to be fraught with a high degree of uncertainty. The role of water and other proton donors in SmI_2-initiated reductions and bond-forming reactions of carbonyl-containing substrates is currently being initiated and the results of these studies will be reported in due course.

Experimental Section

Materials and General Procedures. THF was purified after purging argon gas and passing over a column of activated alumina by a Solvent Purification System (Innovative Technology Inc.; MA). DME was distilled from sodium benzophenone ketyl, under an argon atmosphere. Water was doubly distilled and deaerated with argon for 24 h prior to use. Dried solvents and reagents were stored in an Innovative Technology, Inc. drybox containing an argon atmosphere and a platinum catalyst for drying. SmI_2 was prepared by stirring Sm metal and iodine in THF and DME until the characteristic color of Sm^{2+} appeared. The concentration of the Sm complex in both solvents (0.10 M in THF and 0.02 M in DME) was determined by iodometric titration. Benzyl

(22) Dahlen, A.; Hilmersson, G. *J. Am. Chem. Soc.* **2005**, *127*, 8340−8347.
(23) (a) Enemaerke, R. J.; Daasbjerg, K.; Skrydstrup, T. *Chem. Commun.* **1999**, 343−344. (b) Shabangi, M.; Kuhlman, M. L.; Flowers, R. A., II *Org. Lett.* **1999**, *1*, 2133-2135.
(24) Kleiner, G.; Tarnopolsky, A.; Hoz, S. *Org. Lett.* **2005**, *7*, 4197−4200.

(25) Matsukawa, S.; Hinakubo, Y. *Org. Lett.* **2003**, *5*, 1221−1223.
(26) Fuchs, J. R.; Mitchell, M. L.; Shabangi, M.; Flowers, R. A., II *Tetrahedron Lett.* **1997**, *38*, 8157−8158.

bromide was purchased from Aldrich and distilled under vacuum from CaO before use.

Stopped-Flow Studies. (a) Rate Equation. Kinetic studies in THF were performed using a computer-controlled SX-18 MV stopped-flow reaction spectrophotometer (Applied Photophysics Ltd., Surrey, UK). Rate order for water and benzyl bromide was derived from the plots of $k_{obs.}$ vs [substrate]. The rate order for SmI_2 was determined from ln rate (initial rate) vs ln $[SmI_2]$ plots. The rate plots were generated from the absorption decay traces obtained from a stopped-flow spectrophotometer. The rate equation utilized at [water] < 1.1 M was

$$rate = k_1[SmI_2(H_2O)_n]^2[H_2O][RX]$$

where $[SmI_2(H_2O)_n]$ represents SmI_2-water monomer concentration and [RX] represents benzyl bromide concentration. At [water] >1.1M, the rate equation utilized was

$$rate = k_1[SmI_2(H_2O)_n]^2[RX] + k_2[\{SmI_2(H_2O)_n\}_2][RX]$$

where $[\{SmI_2(H_2O)_n\}_2]$ represents SmI_2−water dimer concentration.

(b) Rate Constants. The SmI_2−water combination and substrate were taken separately in airtight Hamilton syringes from a drybox and injected into the stopped-flow system. The cell box and the drive syringes of the stopped-flow reaction analyzer were flushed a minimum of three times with degassed solvents to make the system oxygen-free. The concentration of SmI_2 used for the study was 5 mM. The concentration of the substrates was kept high relative to SmI_2−water combination (0.05 to 0.20 M) to maintain pseudo first-order conditions. Observed reaction rate constants were determined from exponential fitting of the decays of SmI_2−water complex at 570 and 476 nm. The decay of the SmI_2−water combination displayed first-order behavior over >4 half-lives for SmI_2−water−substrate combinations.

Cyclic Voltammetric (cv) Studies. The redox potential of SmI_2−water combination in THF and DME was measured by cyclic voltammetry, employing a BAS 100B/W MF-9063 Electrochemical Workstation. The working electrode was a standard glassy carbon electrode. The electrode was polished with polishing alumina and cleansed in an ultrasonic bath. The auxiliary electrode was a platinum wire, and the reference electrode was a saturated $Ag/AgNO_3$ electrode. The scan rate for all experiments was 100 mV/s. The electrolyte used was tetraheptylammonium iodide. The concentrations of the Sm(II) species and the electrolyte in each experiment were 5 mM and 0.1 M, respectively. All solutions were prepared in the drybox and transferred to the electrochemical analyzer for analysis.

UV−Vis Studies. UV−vis experiments were performed on a Shimadzu UV-1601 UV−Visible Spectrophotometer controlled by UV Probe (version 1.11) software.

VPO Experiments. The VPO experiments were carried out on a Wescor 5500-XR vapor pressure osmometer operating at 25 °C in a drybox. Calibration curves of VPO reading vs molality were obtained using biphenyl as the calibration standard in THF−water and DME−water (water concentration between 0.15 and 2.5 M) mixtures. From the calibration curve, an "observed molality" can be extracted. The aggregation number "n" is determined by

$$n = known\ molality/observed\ molality$$

Solution molecular weights can be extracted from VPO data when the total weight of the solute added is known and the final VPO molality is measured. Total solute concentration was calculated from the standardized concentration and formula weights. A solution molecular weight was generated by dividing the total solute mass by the number of moles present as calculated from the VPO-generated molality. Each VPO datum was generated by making five concentrations and measuring each solution a minimum of five times.

Note Added after ASAP Publication. In the version published on the Internet December 3, 2005, there was an error in Scheme 2. This has been corrected in the version published December 5, 2005, and in the print version.

Supporting Information Available: General experimental details, decay traces, and plots of rate data. This material is available free of charge via the Internet at http://pubs.acs.org. See any current masthead page for ordering information and Web access instructions.

JA056352T