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Reduction of Ketones and Alkyl Iodides by SmI_2 and Sm(II)-HMPA Complexes. Rate and Mechanistic Studies

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Abstract: The effect of HMPA on the electron transfer (ET) rate of samarium diiodide reduction reactions in THF was analyzed for a series of ketones (2-butanone, methyl acetoacetate, and *N*,*N*-dimethylacetoacetamide) and alkyl iodides (1-iodobutane and 2-iodobutane) with stopped flow spectrophotometric studies. Activation parameters for the ET processes were determined by temperature-dependence studies over a range of 30−50 °C. The ET rate constants and the activation parameters obtained for the above systems in the presence of different equivalents of HMPA were compared to understand the mechanism of action of HMPA on various substrates. The results obtained from these studies indicate that coordination or chelation is possible in the transition state geometry for SmI_2/ketone systems even in the presence of the sterically demanding ligand HMPA. After the addition of 4 equiv of HMPA the ET rate and activation parameters for ketone reduction by Sm is unaffected by further HMPA addition while a linear dependence of ET rate on the equivalents of HMPA was found in the SmI_2/alkyl iodide system. The results of these studies are consistent with an inner-sphere-type ET for the reduction of ketones by SmI_2 (and SmI_2−HMPA complexes) and an outer-sphere-type ET for the reduction of alkyl iodides by SmI_2 or SmI_2−HMPA complexes.

Introduction

Ligands play a crucial role in promoting many organic reactions mediated by organometallic catalysts or reagents. Despite its high carcinogenicity, HMPA remains the ligand of choice for many lithium- and SmI_2-promoted bond-forming reactions.[1,2] While HMPA exhibits unique behavior as a ligand for Ln(III) species, its use in reactions of SmI_2 and other Sm(II)- based reductions has a number of synthetic advantages.[3] The addition of HMPA increases the rate of many reductions and reductive coupling reactions promoted by SmI_2.[4] In addition to accelerating the rate of SmI_2-mediated reactions, HMPA enhances the stereochemical outcome of these reactions as well.[5]

Although there is a paucity of mechanistic work in the area of Sm(II) chemistry, a picture has emerged for the SmI_2−HMPA-promoted reductive coupling of alkyl halides and carbonyl-containing compounds.[6] The work of Curran demonstrates the importance of organosamarium intermediates in Barbier reactions. Curran and co-workers found that primary and secondary radicals are reduced by SmI_2 in THF/HMPA to form primary and secondary alkylsamarium reagents. These reagents were found to have moderate stability in solution and to react with a wide variety of electrophiles. Molander also proposed that organosamarium species are key intermediates in intramolecular Barbier reactions.[7] Ito and co-workers have successfully used an organosamarium-based reagent as a synthetic equivalent for the α-hydroxyacetyl anion.[8] More recently, Fukuzawa and co-workers have employed samarium(II) triflate−HMPA to generate organosamarium reagents.[9]

Though there is little doubt that organosamarium intermediates generated from SmI_2−HMPA are important in the coupling of alkyl halides and ketones, the mechanistic picture is less clear in the case of other reductive coupling reactions. Molander has pointed out that while intramolecular Barbier reactions of certain isolated ketones containing a pendant iodoalkyl side chain proceed through a carbanionic intermediate, other types of coupling reactions clearly do not.[10] For example, a number of iodoalkyl-substituted β-dicarbonyl substrates react without intermediate formation of an organometallic species via reduction of the halide.[11] It is clear that multifunctional substrates can alter the mechanistic course of SmI_2−HMPA-promoted reactions.

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Until recently, little was known about the solution structures and energetics of Sm(II)−HMPA complexes. Upon the addition of 4 equiv of HMPA the complex $[Sm(THF)_2(HMPA)_4]I_2$ is formed.[12] Further addition of HMPA produces the octahedral complex $[Sm(HMPA)_6]I_2$ at greater than 10 equiv of cosolvent. On the basis of their redox potentials, both Sm−HMPA complexes are powerful reductants. Although experimental evidence suggests that both complexes exist in solution, a number of questions remain, including the following: (1) How does the successive addition of HMPA impact the rates of reduction of alkyl halides and ketones? (2) What are the differences between the two complexes in their interactions with various functional groups involved in Sm-mediated reductions and reductive coupling reactions? (3) To what degree does the sterically demanding HMPA influence the reduction of functional groups and their ability to interact with the metal center? While the seminal studies of Curran and Dassjberg have begun to address these questions to some degree, a thorough activation study has not been forthcoming. Knowledge of the rate of reduction of alkyl halides and carbonyl-containing functionalities by SmI_2 and SmI_2−HMPA complexes (and the mechanism through which they proceed) will help to establish the sequence of events involved in these reactions. Herein we report the rates of reduction of ketone, β-dicarbonyl substrates, and alkyl halides by SmI_2 and SmI_2−HMPA complexes in THF. Activation parameters were determined to examine the impact of HMPA on the transition states of alkyl halide and ketone reduction.

Experimental Section

Materials and General Procedures. THF was distilled from sodium benzophenone ketyl under a nitrogen atmosphere. HMPA was dried by vacuum distillation from CaO. Dried solvents were stored in an Innovative Technology, Inc. drybox containing a nitrogen atmosphere and a platinum catalyst for drying. The SmI_2 was prepared according to literature procedure[13] and its concentration was determined by iodometric titration.[14] All substrates (alkyl iodides and ketones) were received from Aldrich and distilled under vacuum from CaO before use.

Stopped-Flow Rate Studies. Kinetic experiments in THF were performed with a computer-controlled SX.18 MV stopped-flow spectrophotometer (Applied Photophysics Ltd. Surrey, UK). The SmI_2 or SmI_2−HMPA complex and substrates were taken separately in airtight Hamilton syringes from a drybox and injected into the stopped-flow system. The cell block and the drive syringes of the stopped flow reaction analyzer were flushed a minimum of three times with dry, degassed THF to make the system anaerobic. The concentration of SmI_2 used for the study was 5 mM. The concentration of the substrates was kept high relative to $[SmI_2]$ (0.05 to 0.45 M) in order to maintain pseudo-first-order conditions. The pseudo-first-order rate constants were determined by using standard methods.[15] Reaction rates were determined from the decay of the SmI_2 absorbance at 555 nm or the SmI_2−HMPA absorbance at 540 nm. The decay of SmI_2 (or the HMPA complex) displayed first-order behavior over >4 half-lives for all SmI_2−substrate combinations. The kinetics for the ketones followed the rate law shown in eq 1. The kinetics for the alkyl iodides followed the rate law shown in eq 2. A representative stopped flow trace for the reduction of methyl acetoacetate by SmI_2 and SmI_2 containing 4 equiv of HMPA is contained in Figure 1. The temperature studies used to determine activation parameters were carried out over a range of 30−50 °C with use of a Neslab circulator connected to the sample handling unit of the stopped flow system. The step size used for the temperature study was 5 °C and each kinetic trace was recorded at a known temperature that was monitored by a thermocouple in the reaction cell.

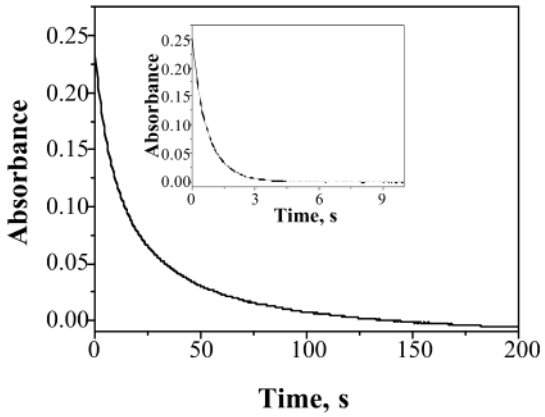

Figure 1. Stopped flow trace showing the decay of SmI_2 absorbance at 555 nm in the presence of methyl acetoacetate (0.25 M) at 25 °C. The inset shows the same in the presence of 4 equiv of HMPA.

$$-\text{d[Sm(II) complex]}/\text{d}t = k\text{[Sm(II) complex][ketone]} \quad (1)$$

$$-\text{d[Sm(II) complex]}/\text{d}t = 2k\text{[Sm(II) complex][alkyl iodide]} \quad (2)$$

Results and Discussion

The goal of this work was to determine the rates and activation parameters for the reduction of ketones, β-dicarbonyls, and alkyl halides by SmI_2 to examine the impact of HMPA on the electron-transfer process. Recent work in our laboratory showed that the SmI_2-mediated reduction of ketones proceeds through an ordered transition state.[16] In particular, the presence of a β-ester or an amide was found to enhance the rate of ketone reduction. Subsequent activation studies provided strong evidence that the reduction proceeded through a chelated transition state. Since HMPA is known to have a high affinity for SmI_2, it is not clear whether its presence will affect the ability of a ketone to coordinate to the Sm since a number of examples exist that show the presence of HMPA can be deleterious to the diastereoselectivity of samarium-induced α- and β-hydroxy ketone−olefin couplings.[17] To address this, the rates and activation parameters for the reduction of 2-butanone, methyl acetoacetate, and *N*,*N*-dimethylacetoacetamide by SmI_2, $[Sm(THF)_2(HMPA)_4]I_2$, and $[Sm(HMPA)_6]I_2$ were determined with stopped-flow decay experiments (Table 1).

The rate constant for the reduction of 2-butanone was just above the measured rate for the natural decay of SmI_2 in THF, but the value is consistent with the rate constant recently reported for the reduction of 3-heptanone by SmI_2.[18] Addition of 4 equiv of HMPA to the reduction enhances the rate by an order of

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Table 1. Rate Constants and Activation Parameters for the SmI_2/Ketone System

system	k,[a,b] $M^{-1}s^{-1}$	E_a,[c] kcal/mol	$\Delta S^{\ddagger}$,[d] cal/(mol K)	$\Delta H^{\ddagger}$,[d] kcal/mol	$\Delta G^{\ddagger}$,[e] kcal/mol
SmI_2−2-butanone	$(7 \pm 3) \times 10^{-4}$	-	-	-	-
$[Sm(THF)_2(HMPA)_4]I_2$−2-butanone	$(8 \pm 1) \times 10^{-3}$	7.6 ± 0.8	-43 ± 3	7.0 ± 0.8	20 ± 1
$[Sm(HMPA)_6]I_2$−2-butanone	$(8 \pm 1) \times 10^{-3}$	7.3 ± 0.3	-44 ± 1	6.7 ± 0.3	20.3 ± 0.4
SmI_2−methyl acetoacetate	$(2.0 \pm 0.4) \times 10^{-1}$	17 ± 1	-6 ± 1	16 ± 1	18 ± 1
$[Sm(THF)_2(HMPA)_4]I_2$−methyl acetoacetate	9.5 ± 0.4	4.1 ± 0.2	-41 ± 1	3.5 ± 0.2	16.2 ± 0.5
$[Sm(HMPA)_6]I_2$−methyl acetoacetate	9 ± 2	3.5 ± 0.2	-43 ± 1	2.8 ± 0.2	16.3 ± 0.5
SmI_2−*N*,*N*-dimethylacetoacetamide	$(7.5 \pm 0.4) \times 10^{2}$	10.6 ± 0.4	-15 ± 1	10.0 ± 0.4	14.6 ± 0.5
$[Sm(THF)_2(HMPA)_4]I_2$−*N*,*N*-dimethylacetoacetamide	$(1.6 \pm 0.1) \times 10^{3}$	2.9 ± 0.1	-40 ± 1	2.3 ± 0.1	14.5 ± 0.2
$[Sm(HMPA)_6]I_2$−*N*, *N*-dimethylacetoacetamide	$(1.6 \pm 0.1) \times 10^{3}$	3.2 ± 0.4	-39 ± 1	2.6 ± 0.4	14.7 ± 0.5

[a] All rate data are the average of at least two independent runs. [b] Experimental uncertainties were propagated through these calculations and all values are reported as $\pm\sigma$. [c] Calculated from $E_a = \Delta H^{\ddagger} + RT$. [d] Eyring activation parameters were obtained from $\ln(k_{obs}h/kT) = -\Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R$. [e] Calculated from $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$.

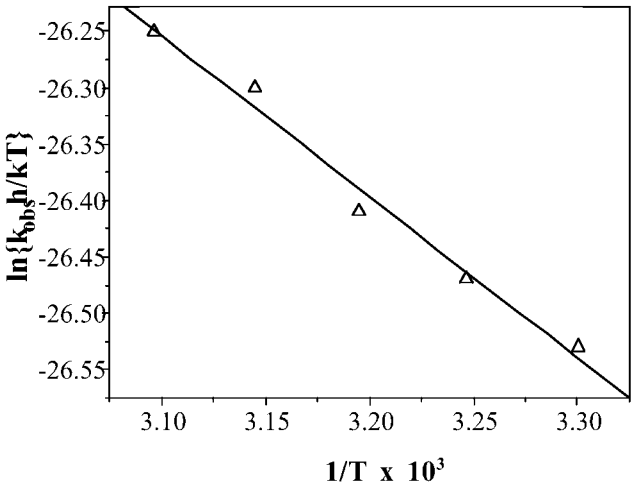

Figure 2. Eyring plot for $Sm[(HMPA)_6]I_2$/methyl acetoacetate system.

magnitude. On the basis of redox potentials, the $[Sm(HMPA)_6]I_2$ complex should be a stronger reductant than $[Sm(THF)_2(HMPA)_4]I_2$.[12] Surprisingly, addition of 10 equiv of HMPA to produce $[Sm(HMPA)_6]I_2$ has no effect on the rate of reduction of 2-butanone. The rate constants for the reduction of methyl acetoacetate by $[Sm(THF)_2(HMPA)_4]I_2$ and $[Sm(HMPA)_6]I_2$ are nearly 50 times greater than reduction by SmI_2 alone, while the rate constants for reduction of *N*,*N*-dimethylacetoacetamide by the same complexes are 2 times greater than that obtained by reduction by SmI_2. Once again, the addition of either 4 or 10 equiv of HMPA provides the same rate constant (within experimental error) for reduction of the β-keto substrates.

To acquire a more detailed understanding of the electron-transfer process and the possible role of chelation in the presence of HMPA, rates were measured over a temperature range to obtain activation enthalpies ($\Delta H^{\ddagger}$) and entropies ($\Delta S^{\ddagger}$) from the linear form of the Eyring eq 3. Figure 2 contains the Eyring plot for the $[Sm(THF)_2(HMPA)_4]I_2$−methyl acetoacetate system over a range of 30−50 °C. Activation data were not determined

$$\ln(k_{obs}h/kT) = -\Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R \qquad (3)$$

for 2-butanone since the measured rate of reduction was on the same order as the natural decay of SmI_2 under our experimental conditions. The results of these experiments are contained in Table 1. While direct comparison of the activation parameters for the reductions of 2-butanone by SmI_2 and its HMPA complexes cannot be made, the data for the two Sm−HMPA complexes are remarkable in the sense that they are nearly indistinguishable within experimental error. Nonetheless, the negative $\Delta S^{\ddagger}$ and the relatively low $\Delta H^{\ddagger}$ are consistent with an ordered transition state.

Reduction of methyl acetoacetate and *N*,*N*-dimethylacetoacetamide by SmI_2 provides activation parameters consistent with chelation with the β-amide providing a more ordered transition state than a β-ester.[16] Upon the addition of HMPA to SmI_2, the activation results change drastically for both β-substituted substrates. The $\Delta H^{\ddagger}$ values for reduction of methyl acetoacetate by either Sm−HMPA complex are approximately 13 kcal/mol less than reduction by SmI_2 alone while the $\Delta S^{\ddagger}$ values decrease by roughly 36 eu. Similar but slightly less pronounced trends are observed for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ during the reduction of *N*,*N*-dimethylacetoacetamide by all three Sm complexes. The increase in rates and changes in the activation parameters upon addition of HMPA to SmI_2 are to be expected since a more powerful reductant is produced, but does HMPA alter the ability of Sm to coordinate to a ketone or chelate to β-substituted ketone during the electron-transfer process? Comparison of the $\Delta S^{\ddagger}$ values for the reduction of the ketone substrates by the Sm−HMPA complexes clearly shows that values are all approximately −40 eu. The $\Delta H^{\ddagger}$ values decrease from roughly 7 kcal/mol for butanone, 3 kcal/mol for methyl acetoacetate, and 2 kcal/mol for *N*,*N*-dimethylacetoacetamide. The $\Delta H^{\ddagger}$ values parallel the rates, indicating that the reduction in the ketone series is enthalpically driven. If HMPA completely inhibited coordination or chelation, the rates and activation parameters for all three ketones would be similar. Although the $\Delta S^{\ddagger}$ values suggest a similar amount of order in each of the ketone reductions by the Sm−HMPA complexes, the lower $\Delta H^{\ddagger}$ values for the β-substituted ketones parallel their ability to chelate to Sm in the absence of HMPA, indicating that chelation is occurring to some extent, even in the presence of the sterically bulky ligand.

The lack of difference in the rate and activation values for the reduction of ketones by $[Sm(THF)_2(HMPA)_4]I_2$ and $[Sm(HMPA)_6]I_2$ is curious. Examination of the crystal structure of $[Sm(HMPA)_6]I_2$ shows that the complex is very sterically hindered.[19] While displacement of a THF ligand from $[Sm(THF)_2(HMPA)_4]I_2$ by a ketone during reduction is reasonable, it should be more difficult for a ketone to access the metal center of the sterically encumbered octahedral Sm−HMPA complex. A recent elegant study by Daasbjerg and co-workers showed

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Table 2. Rate Constants and Activation Parameters for the SmI_2/Alkyl Iodide System

system	k_1,[a,b] $M^{-1}s^{-1}$	E_a,[c] kcal/mol	$\Delta S^{\ddagger}$,[d] cal/(mol K)	$\Delta H^{\ddagger}$,[d] kcal/mol	$\Delta G^{\ddagger}$,[e] kcal/mol
SmI_2−1-iodobutane	$(8 \pm 2) \times 10^{-4}$	-	-	-	-
$[Sm(THF)_2(HMPA)_4]I_2$−1-iodobutane	1.0 ± 0.1	8.9 ± 0.4	-30 ± 1	8.3 ± 0.4	17.7 ± 0.5
$[Sm(HMPA)_6]I_2$−1-iodobutane	2.6 ± 0.1	9.3 ± 0.2	-28 ± 1	8.7 ± 0.2	17.3 ± 0.3
SmI_2−2-iodobutane	$(6 \pm 2) \times 10^{-4}$	-	-	-	
$[Sm(THF)_2(HMPA)_4]I_2$−2-iodobutane	4.7 ± 0.3	8.3 ± 0.8	-35 ± 3	7.7 ± 0.8	19 ± 1
$[Sm(HMPA)_6]I_2$−2-iodobutane	13.4 ± 0.1	8.7 ± 0.4	-31 ± 1	8.1 ± 0.4	18.1 ± 0.5

[a] All rate data are the average of at least two independent runs. [b] Experimental uncertainties were propagated through these calculations and all values are reported as $\pm\sigma$. [c] Calculated from $E_a = \Delta H^{\ddagger} + RT$. [d] Eyring activation parameters were obtained from $\ln(k_{obs}h/kT) = -\Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R$. [e] Calculated from $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$.

that it is likely that upon addition of 10 or more equiv of HMPA the octahedral $[Sm(HMPA)_6]I_2$ is formed.[12a] Their work was based on electrochemical, conductance, and spectroscopic data. Conversely, calorimetric work in our lab was found to be consistent with the addition of 4 HMPA molecules to SmI_2, even in the presence of excess HMPA.[20] Careful reexamination of the system was carried out and provided identical results. If the octahedral complex is formed in solution, the calorimetric data suggest that either the coordination of two HMPA ligands is thermoneutral or they have such a low affinity for the Sm that their coordination cannot be measured by this experimental technique. While we do not wish to dispute the presence of the octahedral complex in solution since there is compelling evidence for its existence, the rate and activation data above suggest that the transition states for ketone reduction by either Sm−HMPA complex are similar. Additional experiments showed that subsequent addition of HMPA (>10 equiv) had little effect on the rate of reduction or activation parameters for 2-butanone and the β-substituted ketones.

Next the impact of HMPA on the reduction of a primary and secondary alkyl iodide by SmI_2 was examined. Table 2 contains the rate and activation data for the reduction of 1-iodobutane and 2-iodobutane by SmI_2, $[Sm(THF)_2(HMPA)_4]I_2$, and $[Sm(HMPA)_6]I_2$. The rate constants for reduction of either 1- or 2-iodobutane by SmI_2 were just above the natural decay of SmI_2. Addition of 4 equiv of HMPA to SmI_2 showed a large increase (1000-fold) in the rate of reduction of both alkyl halides. Further addition of 10 equiv of HMPA to SmI_2 showed a rate increase of approximately 2.5 and 3 for 1-iodobutane and 2-iodobutane, respectively, compared to addition of 4 equiv of HMPA. While the rate of reduction of the alkyl halides by the Sm−HMPA complexes is consistent with their thermodynamic redox potentials[21] in contrast to the reduction of ketones, the addition of >4 equiv of HMPA further increases the rate of reduction of primary and secondary alkyl iodides. Activation parameters were obtained to provide insight into the electron-transfer process. While care must be taken in evaluation of the activation data since they are within experimental error of each other, a general trend is present for both alkyl halides. Comparison of the activation data for reduction of the alkyl iodides by $[Sm(THF)_2(HMPA)_4]I_2$ and $[Sm(HMPA)_6]I_2$ shows that E_a, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ increase slightly for the latter case. Nonetheless, the reduction of both alkyl iodides by Sm−HMPA complexes proceeds through an ordered transition state.

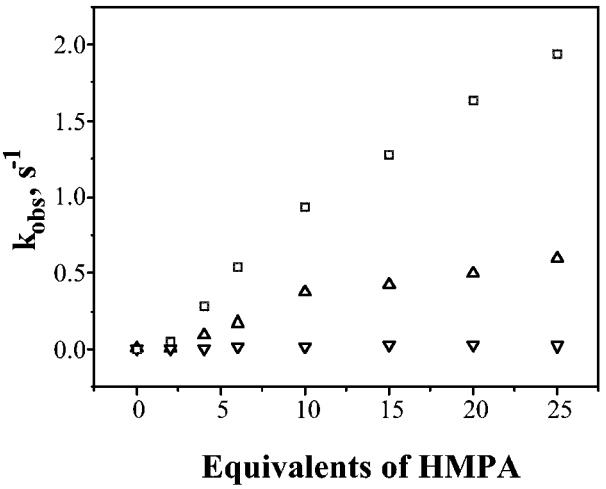

Figure 3. Plot of k_{obs} vs equivalents of HMPA for the reduction of 2-butanone (▽), 1-iodobutane (△), and 2-iodobutane (□) by SmI_2.

The difference in the behavior of the ketones and alkyl iodides toward the Sm−HMPA complexes indicated that either the weak Lewis basic iodide interacts with the hindered complexes differently or that possibly solvent polarity may play a role in the reduction. Daasbjerg recently reported that while increasing the ionic strength of the medium had no effect on the rate of reduction of benzyl chloride by Sm(II)−HMPA complexes, there was a notable rate enhancement in the reduction of 1-iodobutane.[12a] The effect of HMPA concentration on SmI_2/ketone as well as in SmI_2/alkyl halide reductions was investigated by measuring the pseudo-first-order rate constants for electron transfer in the above systems in the presence of increasing quantities of HMPA (from 2 to 25 equiv based on the concentration of SmI_2). The results of these experiments are contained in Figure 3.

The data in Figure 3 clearly show that addition of HMPA produces a monotonic increase in k_{obs} for both 1- and 2-iodobutane whereas 2-butanone shows little variance. This finding indicates that there could be a change in the electron-transfer mechanism between SmI_2 and these substrates. Earlier work in our lab provided evidence that SmI_2−HMPA reduced alkyl iodides through a predominantly outer-sphere electron transfer (ET).[22] The recent work of Daasbjerg indicates that ketones are reduced through an inner-sphere ET by SmI_2 and SmI_2−HMPA complexes and that while reduction of alkyl halides cannot be characterized as purely outer-sphere, the outer-sphere character increases in the order $I^- > Br^- > Cl^-$. In other words, alkyl

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iodide reduction has more outer-sphere character than alkyl chloride reduction.[12a] Another way to look at the reduction is in terms of substrate-reductant affinity. The fact that Sm is oxophilic suggests that there should be strong interaction between Sm and oxygen in the SmI_2/ketone system leading to the electron transfer toward an inner-sphere pathway. Since iodide is a relatively soft substituent, it does not have a high affinity for the hard Sm.

The existence of considerable bonding interaction between Sm and oxygen provides an inner-sphere pathway for ET in SmI_2 (or SmI_2−HMPA complexes)/ketone systems. Inner-sphere ET is characterized by (a) a temperature-independent rate constant, which is considerably higher than predicted by Marcus theory, (b) low sensitivity to kinetic salt effects, and (c) weak dependency on solvent polarity. Kochi et al. recently reported the ET behaviors in a series of substituted arenes, which show a shift in the mechanism of ET from an inner-sphere character to the outer-sphere character as the bulkiness of the substituents increases.[23] Their study shows that the rate constant for ET in the unhindered donor−acceptor pairs (where inner sphere ET takes place) does not vary as the solvent polarity is changed from acetonitrile ($\epsilon = 35.9$) to carbon tetrachloride ($\epsilon = 2.2$). This is reasonable since an inner-sphere ET is always expected to proceed through a strong electronic coupling of donor and acceptor in the transition state where the solvent role in assisting the ET will be marginal. The general conclusion one could extract from this study is that solvent polarity has little role in determining the inner-sphere (adiabatic) ET rate constant due to the considerable orbital overlap of the donor−acceptor pair in the activated complex. Our experiments indicate that the solvent polarity change due to the addition of a cosolvent (HMPA) to the system does not affect the ET rate constant for SmI_2 (or SmI_2−HMPA complexes) reduction of ketones due to the high inner-sphere character of the ET.

Conversely, the ET rate constant for outer-sphere ET is solvent dependent as predicted by Marcus theory. Change in the polarity of the solvent medium alters both the reorganization energy and the free energy of ET, and consequently the ET rate is expected to be higher in a more polar medium.[24] Kochi et al. showed that the ET rate constants for hindered donor−acceptor pairs (where outer-sphere ET takes place) show a decrease up to 4 orders of magnitude from the polar solvent acetonitrile to the nonpolar solvent carbon tetrachloride.[23] In our experiments, the addition of HMPA to THF certainly alters the polarity of the solvent milieu. While we did not attempt to determine quantitatively the change in reorganization or free energy in these systems, our results are consistent with the reduction of alkyl iodides occurring through an outer-sphere-type mechanism (by SmI_2−HMPA). Thus our experiments suggest that there is a striking difference in the electron-transfer mechanism with SmI_2/HMPA complex toward alkyl iodide and ketone, consistent with ET leading to an outer-sphere character type process in the former one.

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(24) Smitha, M. A.; Prasad, E.; Gopidas, K. R. *J. Am. Chem. Soc.* **2001**, *123*, 1159.

Regardless of the complexities of electron transfer, the rate data presented above clearly show that both primary and secondary alkyl iodides are reduced faster by SmI_2−HMPA complexes than dialkyl ketones. Curran has provided strong evidence that during the SmI_2−(HMPA)-mediated coupling of alkyl halides and ketones, reduction of the alkyl halide occurs preferentially to produce an organosamarium species that attacks the ketone to produce a carbinol upon workup.[6] To provide a more comprehensive picture of the reductive coupling of ketones and alkyl iodides, a series of rate experiments were carried out in which SmI_2−HMPA was exposed to an equimolar amount of 1-iodobutane and 2-butanone. The decay was found to be identical with that obtained for the reduction of 1-iodobutane alone and fit to a single exponential. The rates were measured over a series of substrate concentrations to extract the bimolecular rate constant for the reduction. The rate constant was found to be $0.9 \pm 0.1\ M^{-1}\ s^{-1}$, which is within experimental error for the rate constant determined for 1-iododbutane alone ($1.0 \pm 0.1\ M^{-1}\ s^{-1}$). While no spectroscopic evidence was found to support the existence of discrete organosamarium species in our experiments, these results are consistent with the mechanistic hypothesis developed by Curran.

Conclusions

The rate and activation parameters for the reduction of 2-butanone, methyl acetoacetate, *N*,*N*-dimethylacetoacetamide, 1-iodobutane, and 2-iodobutane by SmI_2, $[Sm(THF)_2(HMPA)_4]I_2$, and $[Sm(HMPA)_6]I_2$ were examined with stopped-flow experiments. Examination of the activation parameters for the reduction of the ketones shows that coordination or chelation to Sm occurs to some extent even in the presence of the sterically bulky HMPA ligand. Surprisingly, there was no difference in the rate and activation parameters when the reductant was changed from $[Sm(THF)_2(HMPA)_4]I_2$ to $[Sm(HMPA)_6]I_2$ even though the latter complex is a more powerful reductant. This finding suggests that the transition states for reduction of ketones by either Sm(II)−HMPA reductant are similar. In contrast to ketones, the rate of reduction of primary and secondary alkyl iodides was found to be dependent on the concentration of HMPA. Rate experiments in the presence of increasing quantities of HMPA show that while increasing medium polarity influences the rate of alkyl iodide reduction, it has a minimal influence on the rate of ketone reduction. These results were interpreted to be consistent with outer-sphere reduction of alkyl iodides and inner-sphere reduction of ketones by SmI_2 and SmI_2−HMPA complexes.

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Supporting Information Available: Decay traces and plots of rate data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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