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Mechanism of Reduction of Primary Alkyl Radicals by SmI_2–HMPA

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ABSTRACT

$$R\bullet \xrightarrow[\text{THF}]{SmI_2\text{-HMPA}} R{-}SmI_2$$

R = primary alkyl $\qquad k_{obs} / k_{ET} = 2$

The measured value of $E°(SmI_2^{+}$–HMPA – SmI_2–HMPA) was used in combination with literature values for the $E°$ of primary radicals to estimate the bimolecular rate constant for an outer-sphere electron transfer (ET). Comparison with the experimentally measured rate constant is consistent with an outer-sphere ET.

Samarium diiodide (SmI_2) is one of the most important reducing reagents utilized by organic chemists. It is useful in functional group reductions, the coupling of halides with π bonds, and the coupling of two π bonds.[1] The most important feature of SmI_2 is its ability to promote one-pot, sequential reactions including both one- and two-electron processes.[2] The success of many SmI_2-mediated reactions is often dependent on the addition of a ligating cosolvent such as HMPA,[3] which accelerates reactions of SmI_2.[4] In addition to accelerating reductions by SmI_2, HMPA also enhances the stereochemical outcome and diastereoselectivity of many reactions.[3,5] Although the combination of SmI_2−HMPA in THF produces an extremely versatile reductant, there is a paucity of detail on its interaction with organic substrates.

Recent results in our laboratory suggest that $SmI_2(HMPA)_4$ is the species responsible for the unique reactivity of the SmI_2−HMPA combination in THF.[6] Careful examination of the recently published X-ray crystal structure of the SmI_2-$(HMPA)_4$ reductant shows that the complex is sterically crowded.[7] There are two potential ways that a reducible functional group (alkyl halide, carbonyl, or radical) can be reduced by the sterically crowded reductant (Scheme 1). The first would involve displacement of an $SmI_2(HMPA)_4$ ligand by substrate which could lead to an inner-sphere electron transfer (ET). The second potential mechanistic pathway would have the ligands remain intact and the ET take place through an outer-sphere process. Since radicals are formed during numerous reductive coupling processes mediated by SmI_2, we carried out the experiments described below to determine the mode of electron transfer from $SmI_2(HMPA)_4$ to primary radicals.

One of the most important values that needs to be defined in order to determine the mode of electron transfer is the standard potential of the $SmI_2(HMPA)_4 - SmI_2^{+}-(HMPA)_4$ redox couple in THF. We recently utilized linear sweep voltammetry (LSV) to examine the influence of HMPA concentration on the reducing power of SmI_2.[8] While these experiments showed unequivocally that HMPA increases the reducing power of SmI_2, the reported values were not standard potentials. Figure 1 contains the cyclic voltammogram of SmI_2 and $SmI_2(HMPA)_4$ in THF. The CV of SmI_2 containing HMPA did not change with the addition of more than 4 equiv of HMPA. Both voltammograms contained in Figure 1 are quasireversible, so we employed the model recently described by Skrydstrup for the $SmI_2^{+}-SmI_2$ redox

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(1) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943−961.

(2) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307−338.

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(4) (a) Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485−1486. (b) Hasegawa, E.; Curran, D. P. *Tetrahedron Lett.* **1993**, *34*, 1717−1720.

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(7) (a) Hou, Z.; Wakatsuki, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 1205−1206. (b) Hou, Z.; Zhang, Y.; Wakatsuki, Y. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 149−153.

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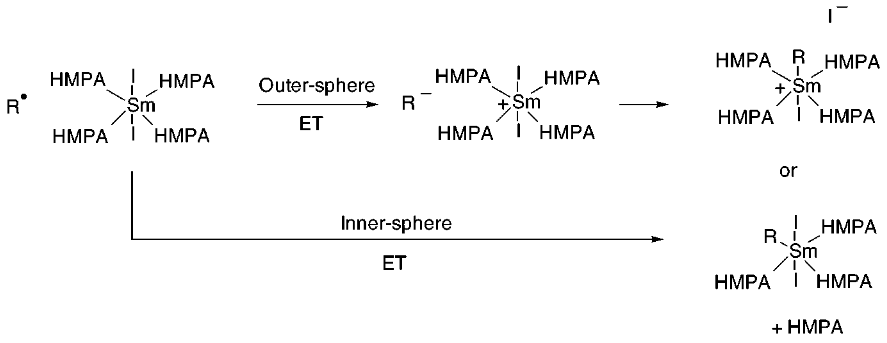
Scheme 1



couple to determine the standard potentials.[9] Digital simulations of both voltammograms revealed that the standard potential (vs SCE in THF) for SmI_2 is −0.98 ± 0.04 V vs SCE,[10] while the standard potential for $SmI_2(HMPA)_4$ is −1.75 ± 0.06 V vs SCE. These findings indicate that the change in the reducing power of reductant is 0.8 V (18 kcal/mol), a finding in close agreement with our earlier LSV experiments.

The standard redox potential of the $R^\bullet/R^-$ couple for a primary butyl radical was estimated by Saveant and coworkers to be in the range −1.30 to −1.42 V vs SCE.[11] With these limiting values, it is possible to estimate the bimolecular rate constant for outer-sphere ET from $SmI_2(HMPA)_4$ to a primary radical using the Marcus equation (1): [12]

$$k_{ET} = k_d/[1 + 0.2\exp\{(\lambda/4)(1+\Delta G^\circ_{ET}/\lambda)^2/RT\}] \qquad (1)$$

where k_d is the diffusion-controlled rate constant in THF, ΔG°_{ET} is the free energy of electron transfer, and λ is the reorganization energy.[12,13] Utilizing this approach we were able to estimate the bimolecular rate constant for electron transfer from $SmI_2(HMPA)_4$ to a primary radical (Table 1).

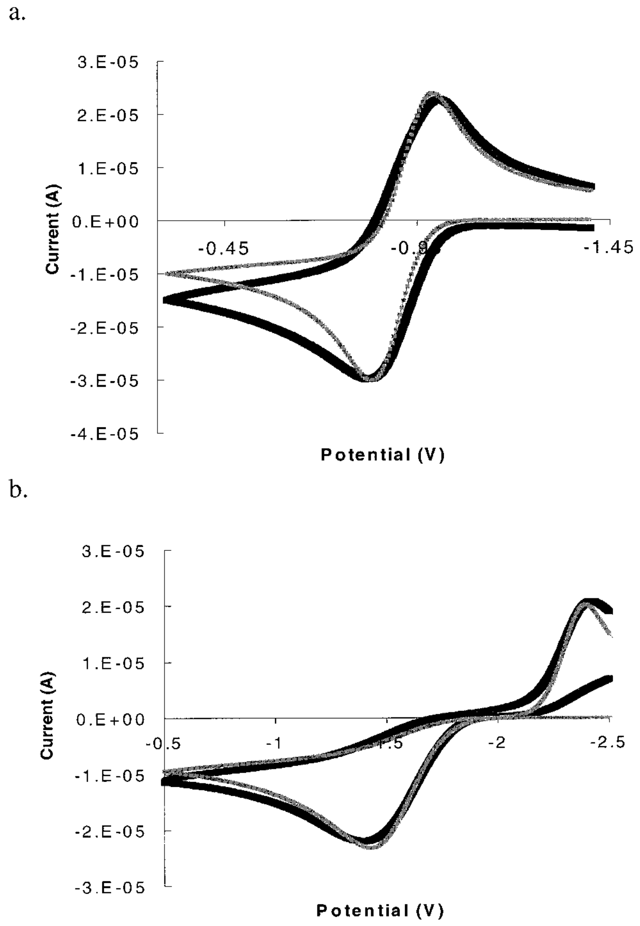


Figure 1. (a) Cyclic voltammogram of 2.5 mM SmI_2 recorded in THF−0.5 M LiI electrolyte at a glassy carbon electrode (diameter = 1 mm) at a sweep rate of 100 mV s^{-1}. The gray curve represents the simulated voltammogram based on the model utilized in ref 9. (b) Cyclic voltammogram of 2.5 mM $SmI_2(HMPA)_4$ recorded under the same conditions. The gray curve represents the simulated voltammogram.

Table 1. Total Reorganization Energy (λ), Free Energy of Electron Transfer (ΔG°_{ET}), Marcus Rate (k_{ET}), and Measured Rate (k_{obs}) for the Reduction of a Primary Alkyl Radical by $SmI_2(HMPA)_4$

λ (kcal/mol)[a]	ΔG°_{ET} (kcal/mol)[b]	k_{ET} (× 10^6 M^{-1} s^{-1})	k_{obs} (× 10^6 M^{-1} s^{-1})
40	−9 ± 1	3 ± 1	6 ± 1 7[c]

[a] The total reorganization energy (λ) is the average of the self-exchange reorganization energies for the electron donors and acceptors. [b] ΔG°_{ET} = 23.06 (E°_{ox} − E°_{red}), where E°_{ox} is the standard potential of the $SmI_2(HMPA)_4$ − SmI_2^+−$(HMPA)_4$ redox couple and E°_{red} is the standard potential of the $R^\bullet$ − R^- couple for a primary radical. [c] See ref 14.

Curran and Hasegawa utilized the 6-iodo-1-hexene radical clock to estimate the bimolecular rate constant for the

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(9) Enemaerke, R. J.; Daasbjerg, K.; Skrydstrup, T. *Chem. Commun.* **1999**, 343−344.

(10) The redox potential of SmI_2 is −1.45 ± 0.04 vs Fc^+−Fc. This value is within the experimental error of the same value reported in ref 9.

(11) Andrieux, C. P.; Gallardo, I.; Saveant, J.-M. *J. Am. Chem. Soc.* **1989**, *111*, 1620−1626.

(12) Marcus, R. A. *Annu Rev. Phys. Chem.* **1964**, *15*, 155.

reduction of a primary radical by SmI_2 containing varying amounts of HMPA.[14] They found that a solution of SmI_2 containing between 4 and 5 equiv of HMPA produced a reductant capable of reducing a primary radical. We repeated their experiment and found the same rate constant (within experimental error) for the reduction of a primary radical by $SmI_2(HMPA)_4$. The bimolecular rate constants determined experimentally with the radical clock and utilizing Marcus theory are contained in Table 1. Surprisingly, these values only differ by a factor of 2, suggesting that the SmI_2(HMPA) reductant reduces primary radicals through predominantly an outer-sphere process.

The recent work of Skrydstrup indicates that ET from THF-solvated SmI_2 to acetophenone is clearly an inner-sphere process while ET to benzyl bromide is closer to an outer-sphere process.[9] These results suggest that SmI_2 has a higher affinity for THF than a benzyl halide, while carbonyls are capable of displacing THF ligands bound to SmI_2. The electrochemical results reported here show that a primary radical does not displace ligands from the $SmI_2(HMPA)_4$ complex. The consequence of this finding is that there is very little interaction between Sm reductant and the primary radical in the transition state leading to carbanion formation.[15]

An apparent quandary arises because Curran[16] and Molander[17] have shown that organosamarium species are the reactive intermediates responsible for carbon−carbon bond formation in the SmI_2−HMPA-mediated Barbier reaction. The term organosamarium implies that a bond is formed between samarium and carbon, and Curran postulated that radicals and SmI_2 combine directly (though an inner-sphere ET) to form alkylsamarium(III) reagents.[1] Our experiments support a mechanism where the primary radical is reduced to an anion through an outer-sphere ET. The existence of organosamarium intermediates proposed by Molander and Curran does not exclude the possibility of outer-sphere electron transfer in reductive couplings mediated by SmI_2−HMPA. It is possible that the reduction of a primary radical by a hindered SmI_2−HMPA complex produces a carbanion that can displace a ligand *after the electron transfer*, thereby producing a stable organosamarium species (Scheme 1). Littler provides a detailed account of a number of cases where ligand displacement on oxidants and reductants to produce organometallic species occurs by an outer-sphere process.[18]

We have recently shown that different ligating cosolvents can be utilized to “fine tune” the reducing power of SmI_2.[19] If different ligating cosolvents produce Sm-based reductants that carry out ET via an outer-sphere process, chemists will be able to estimate the rates of reduction of various functional groups and radicals using their standard redox potentials. A complete analysis of the influence of various ligating cosolvents and additives on the energetics, rates, and mechanism of ET between SmI_2 and various functional groups and radicals will be presented in a forthcoming paper.

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Supporting Information Available: Full experimental detail including electrochemical procedures and digital simulation data. This material is available free of charge via the Internet at http://pubs.acs.org.

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[13] We used −1.36 ± 0.06 V as the standard potential for a primary radical. The total reorganization energy (λ) is the average of the self-exchange reorganization energies for the electron donors and acceptors and was estimated to be approximately 40 kcal/mol. The diffusion-controlled rate constant (k_d) in THF was determined using $k_d = 8RT/3000\eta$ and found to be 1.4×10^{10} M^{-1} s^{-1}.

[14] Hasegawa, E.; Curran, D. P. *Tetrahedron Lett.* **1993**, *34*, 1717−1720.

[15] Eberson, L. *Electron-Transfer Reactions in Organic Chemistry*; Springer-Verlag: New York, 1987; p 18.

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