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Determination of the Effective Redox Potentials of SmI_2, $SmBr_2$, $SmCl_2$, and their Complexes with Water by Reduction of Aromatic Hydrocarbons. Reduction of Anthracene and Stilbene by Samarium(II) Iodide–Water Complex

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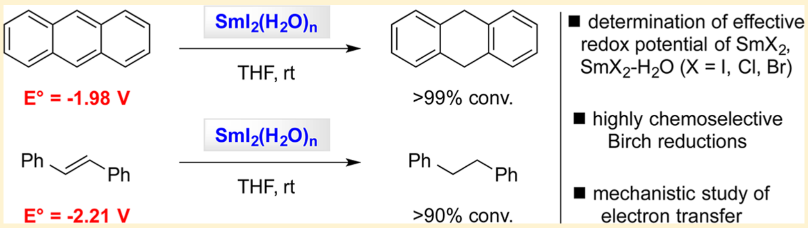
Supporting Information



ABSTRACT: Samarium(II) iodide–water complexes are ideally suited to mediate challenging electron transfer reactions, yet the effective redox potential of these powerful reductants has not been determined. Herein, we report an examination of the reactivity of $SmI_2(H_2O)_n$ with a series of unsaturated hydrocarbons and alkyl halides with reduction potentials ranging from −1.6 to −3.4 V vs SCE. We found that $SmI_2(H_2O)_n$ reacts with substrates that have reduction potentials more positive than −2.21 V vs SCE, which is much higher than the thermodynamic redox potential of $SmI_2(H_2O)_n$ determined by electrochemical methods (up to −1.3 V vs SCE). Determination of the effective redox potential demonstrates that coordination of water to SmI_2 increases the effective reducing power of Sm(II) by more than 0.4 V. We demonstrate that complexes of $SmI_2(H_2O)_n$ arising from the addition of large amounts of H_2O (500 equiv) are much less reactive toward reduction of aromatic hydrocarbons than complexes of $SmI_2(H_2O)_n$ prepared using 50 equiv of H_2O. We also report that $SmI_2(H_2O)_n$ cleanly mediates Birch reductions of substrates bearing at least two aromatic rings in excellent yields, at room temperature, under very mild reaction conditions, and with selectivity that is not attainable by other single electron transfer reductants.

■ INTRODUCTION

Since its discovery in 1977 by Kagan,[1] SmI_2 (samarium(II) iodide, Kagan's reagent) has gained status as one of the most important single electron transfer reagents in organic chemistry.[2] Of particular importance is the exquisite ability of SmI_2 to mediate reductive processes via complementary one- and two-electron pathways with chemoselectivity that cannot be achieved by other reagents.[3,4] Crucial to the successful use of SmI_2 in numerous synthetic methodologies and target oriented syntheses is the role of additives that modulate the steric requirements and redox potential of the reagent by coordination to the lanthanide(II) center, thus allowing users to fine-tune the properties of SmI_2 for a desired transformation (Figure 1).[5] In this regard, during the past decade, $SmI_2(H_2O)_n$ complexes have received increasing attention as unique Sm(II) reagents capable of mediating challenging reductive processes that for years had been thought to lie outside the redox potential of SmI_2.[6] However, despite several reports on the role of H_2O as a ligand for Sm(II),[7] mechanistic details pertaining to the effective redox potential of these powerful reductants have not been investigated, hampering the development of new chemoselective reactions mediated by $SmI_2(H_2O)_n$ and prohibiting the rational design of ligands that would expand the chemoselectivity of Sm(II) for a broad range of functional groups.[8]

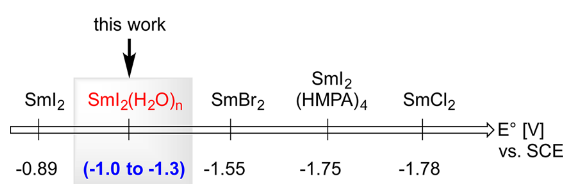


Figure 1. Redox potentials of common Sm(II) reductants (SCE = saturated calomel electrode).

In general, the reactivity of Sm(II) reductants has been found to correlate with the thermodynamic redox potentials as determined by electrochemical methods (Table 1). The seminal studies by Flowers[9] and Skrydstrup[10] demonstrated that addition of 4 equiv of HMPA results in an increase of the redox potential of SmI_2 by ca. 0.90 V (Table 1, entries 1 and 2), affording one of the most powerful reductants in organic synthesis. Due to the high redox potential, SmI_2–HMPA

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Table 1. Summary of Redox Potentials of Common Sm(II) Reductants Determined by Electrochemical Methods

entry	Sm(II) reductant	$-E_{1/2}$[a]	electrode	solvent	refs
1	SmI_2	0.89 ± 0.08[b]	SCE	THF	9, 10
2	SmI_2−HMPA	1.79 ± 0.08	SCE	THF	9, 10
3	SmI_2−DMPU	1.61 ± 0.01[c]	SCE	THF	12
4	$SmBr_2$	1.55 ± 0.07[d]	SCE	THF	14b
5	$SmCl_2$	1.78 ± 0.10[e]	SCE	THF	14b
6	$Sm(HMDS)_2$	1.5 ± 0.1[f]	SCE	THF	18
7	$SmBr_2$−HMPA	2.03 ± 0.01[g]	SCE	THF	19
8	$SmI_2(H_2O)_n$ (n = 60)	1.0 ± 0.1[h]	SCE	THF/DME	7a
9	$SmI_2(H_2O)_n$ (n = 500)	1.3 ± 0.1[i]	SCE	THF/DME	7a

[a]In volts vs SCE. $-E_{1/2}$ describes the half-reduction potential measured in DMF, refs 20−23. (The accuracy is approximately ± 0.1 V due to solvent effects.) [b]Recalculated from −1.41 ± 0.08 vs Fe^+/Fe according to ref 23. [c]Recalculated from −2.21 ± 0.01 vs Ag/$AgNO_3$; the difference between the SCE and Ag/$AgNO_3$ is 0.6 V, ref 12b. [d]Note that the value based on ref 14a, recalculated from −1.98 ± 0.01 vs Ag/$AgNO_3$, is −1.38 ± 0.01 vs SCE. [e]Note that the value based on ref 14a, recalculated from −2.11 ± 0.01 vs Ag/$AgNO_3$, is −1.51 ± 0.01 vs SCE. [f]Recalculated from −2.1 ± 0.1 vs Ag/$AgNO_3$. [g]Recalculated from −2.63 ± 0.01 vs Ag/$AgNO_3$. [h]Recalculated from −1.6 ± 0.1 vs Ag/$AgNO_3$. [i]Recalculated from −1.9 ± 0.1 vs Ag/$AgNO_3$.

complexes have found diverse applications in Barbier reactions and reductive cross-couplings utilizing unactivated π-acceptors.[11] The addition of other Lewis bases (e.g., 1,3-dimethyl-3,4,5,6-tetrahydro-2-pyrimidinone (DMPU), *N*-methyl-2-pyrrolidone (NMP), 2,2,6,6-tetramethylpiperidine (TMP), tripyrrolidino-phosphoric acid triamide (TPPA)) has been reported to increase the thermodynamic redox potential of SmI_2 (Table 1, entry 3);[12] however, despite significant progress in this area,[13] HMPA is currently the most effective Lewis basic additive for SmI_2. Furthermore, Flowers has shown that the addition of 12 equiv of metal salts, LiBr or LiCl, to SmI_2 results in the formation of soluble Sm(II) reductants characterized by redox potential much higher than that of the parent reagent (Table 1, entries 4 and 5).[14] UV−vis experiments demonstrated that this reagent combination is equivalent to the less soluble $SmBr_2$ and $SmCl_2$ prepared by independent methods by the reduction of SmX_3.[15] Recently, $SmBr_2$[16] and $SmCl_2$[17] reductants have been applied to achieve cross-coupling reactions of carbonyl precursors in complex settings. The thermodynamic redox potentials of $SmI_2(HMDS)_2$[18] and $SmBr_2$−HMPA[19] have also been reported (Table 1, entries 6 and 7) and, as expected, are much higher than those of SmI_2 and SmI_2−HMPA, respectively. Finally, in 2004, Flowers reported a seminal study on the thermodynamic redox potential of $SmI_2(H_2O)_n$ (Table 1, entries 8 and 9).[7b] It was found that the addition of 60 equiv of water with respect to SmI_2 results in an increase of redox potential of SmI_2 by ca. 0.10 V. The addition of 500 equiv of water resulted in the formation of a thermodynamically more powerful reductant (redox potential of 1.3 V vs SCE). Further addition of water had no additional impact on the redox potential of the reagent.

Studies on the determination of the effective redox potential of lanthanide reductants have also been reported (Table 2).[20−24] These methods utilize the reduction of a series of aromatic hydrocarbons with gradually increasing redox potentials to correlate the reactivity of a lanthanide reductant with the reduction potential of hydrocarbons. This indirect determination of the redox potential is particularly useful in cases of limited solubility, irreversible oxidation, precipitation, and/or instability of lanthanide reductants under the conditions of cyclic voltammetry studies. More specifically, Chauvin determined the effective redox potential of several lanthanides(0) (Ce, Nd, Sm, Yb) (Table 2, entries 1 and 2),[20] Evans demonstrated that decamethylsamarocene, $Sm(C_5Me_5)_2$, is one of the strongest lanthanide(II) reductants reported to date (Table 2, entry 3),[21] Fedushkin evaluated the reducing power of TmI_2 (Table 2, entry 4),[22] Hilmersson determined the redox potential of the powerful SmI_2−amine−H_2O and YbI_2−amine−H_2O systems (Table 2, entries 5 and 6),[23] and we have utilized this method to show that the reagent formed by complexation of MeOH to TmI_2 is characterized by a much higher redox potential than the parent lanthanide(II) iodide (Table 2, entry 7).[24] Importantly, since only simple unsaturated hydrocarbons, which react via a well-established, outer-sphere electron transfer mechanism, are used,[8,14b,18,23] these methods provide a robust and practical evaluation of the effective reducing power of a given lanthanide reductant under standard laboratory reaction conditions, thus allowing definition of a practical reactivity scale in an assay independent of the thermodynamic redox potential measurements.

Table 2. Summary of Redox Potentials of Common Ln(II) Reductants Determined by Reduction of Aromatic Hydrocarbons

entry	Ln(II) reductant	$-E_{1/2}$[a]	electrode	solvent	ref
1	Sm metal	2.02	SCE	DME	20
2	Yb metal	2.44	SCE	DME	20
3	$Sm(C_5Me_5)_2$	2.22	SCE	toluene	21
4	$TmI_2(THF)_n$	2.00	SCE	THF	22
5	YbI_2−amine−H_2O	2.30	SCE	THF	23
6	SmI_2−amine−H_2O	2.80	SCE	THF	23
7	$TmI_2(MeOH)_n$	2.65	SCE	THF	24

[a]In volts vs SCE. $-E_{1/2}$ describes the half-reduction potential measured in DMF, refs 20−23. (The accuracy is approximately ± 0.1 V due to solvent effects.)

Our laboratory has pioneered the use of $SmI_2(H_2O)_n$ complexes to expand the reactivity of SmI_2 toward carbonyl functional groups traditionally thought to lie outside the reducing range of Kagan's reagent (Scheme 2).[25−27] In particular, we reported that activation of SmI_2 with water permits a fully chemoselective reduction of six-membered lactones over other classes of lactones and esters (Scheme 2A).[25a−c] Moreover, we exploited the $SmI_2(H_2O)_n$ reagent to develop the first chemoselective monoreduction of cyclic diesters (Meldrum's acids) to afford the valuable β-hydroxy acid building blocks in a single transformation (Scheme 2B).[26] Recently, we utilized the unusual ketyl-type radical intermediates formed in $SmI_2(H_2O)_n$-mediated electron transfer to lactone carbonyls as precursors in complex cyclization and cyclization cascade processes to form polyoxygenated azulene motifs (Scheme 2C).[25c,d] We have also established that water serves a critical role with Sm(II) in the first general reductions of unactivated aliphatic esters, acids, and lactones with SmI_2, which proceed via acyl-type radical intermediates generated directly from the carboxylic acid derived functional groups.[27] These processes have resulted in very significant expansion of the synthetic scope of processes mediated by SmI_2.[28] A subtle feature of all of these reactions is that water serves as a unique additive for SmI_2; no reaction occurs with SmI_2 alone or with a variety of other additives (e.g., HMPA, DMPU, LiCl), which have been shown to form more thermodynamically powerful complexes with SmI_2 than $SmI_2(H_2O)_n$ (Table 1). Furthermore, we established that no reaction occurs at low concentration of water, which rules out the role of water as a proton donor placed in a close proximity to the radical anion after the electron transfer step.[29]

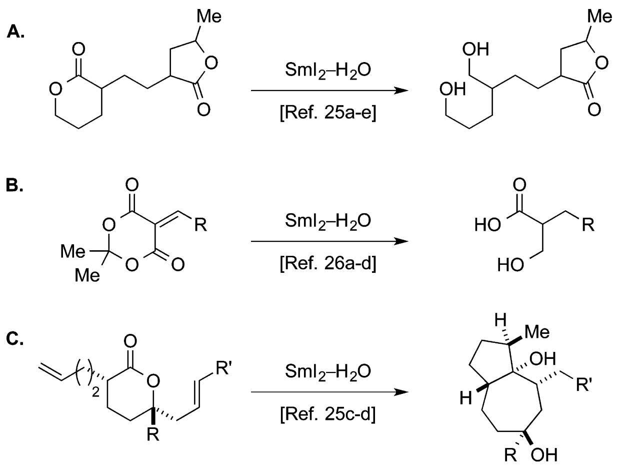


Figure 2. Recent applications of $SmI_2(H_2O)_n$ in chemoselective and stereoselective synthesis: (A) reduction of six-membered lactones; (B) monoreduction of Meldrum's acids; (C) cyclization cascades of lactones.

On the basis of our extensive experience in the reductive chemistry of lanthanides(II), we considered that the reduction of lactone carbonyls ($E_{1/2}$ = ca. −3.0 V vs SCE)[30] by $SmI_2(H_2O)_n$ ($E_{1/2}$ = ca. −1.3 V vs SCE)[7b] is inconsistent with the thermodynamic redox potential of $SmI_2(H_2O)_n$ as determined by cyclic voltammetry studies and cannot be explained exclusively by electrostatic interaction[31] between the lactone carbonyl groups and the Lewis acidic Sm(II) center.[32]

To understand in more detail the properties of $SmI_2(H_2O)_n$ reductants, we determined the effective redox potential of these reagents by examining the reactivity of $SmI_2(H_2O)_n$ complexes with a series of unsaturated hydrocarbons and alkyl halides with reduction potentials ranging from −1.6 to −3.4 V vs SCE. Remarkably, we found that $SmI_2(H_2O)_n$ reacts with substrates which have reduction potentials more positive than −2.21 V vs SCE, which is much higher than the thermodynamic redox potential of $SmI_2(H_2O)_n$ determined by electrochemical methods (up to −1.3 V vs SCE).[7b] Moreover, in contrast to literature, we demonstrated that complexes of $SmI_2(H_2O)_n$ in which n = 500 are much less reactive toward aromatic hydrocarbons than complexes of $SmI_2(H_2O)_n$ based on n = 50.[7] This has important practical implications for using $SmI_2(H_2O)_n$ reagents in organic synthesis.

Moreover, we describe herein the synthesis and determination of the effective redox potential of several reductants related to SmI_2, namely, SmX_2 and $SmX_2(H_2O)_n$ (X = Cl, Br),[16,17] which allows us to delineate the reducing power of these popular Sm(II) reductants for the first time. Furthermore, as a result of this investigation, we report that $SmI_2(H_2O)_n$ cleanly mediates Birch reduction[33] of substrates with at least two aromatic rings in excellent yields, at room temperature, under very mild reaction conditions, and with selectivity that is not attainable by other single electron transfer reductants.[3,4] Finally, we provide mechanistic studies into the role of electron transfer from Sm(II) and discuss the implications of the effective redox potentials as determined in this study for using SmX_2 and $SmX_2(H_2O)_n$ complexes in organic synthesis. This study provides the first set of guidelines with respect to reducing power to further our understanding of single electron transfer processes mediated by the extremely useful Sm(II)-based reductants.

■ RESULTS AND DISCUSSION

To determine the effective redox potential of $SmI_2(H_2O)_n$ complexes, we selected a series of aromatic hydrocarbons with reduction potentials ranging from −1.6 to −3.4 V vs SCE (Figure 3).[20−24] In addition, a series of alkyl halides ($E_{1/2}$ from

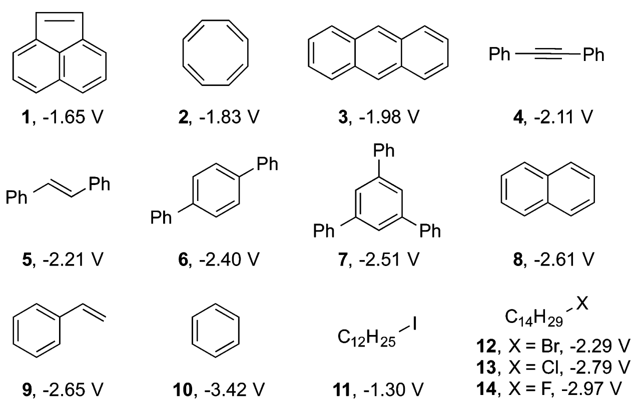


Figure 3. Structures of aromatic hydrocarbons and alkyl halides used in this study together with their half-reduction potentials ($E_{1/2}$ in volts in DMF vs SCE).

−1.30 to −3.0 V)[34] was selected for this study to gain further insight into the chemoselectivity of $SmI_2(H_2O)_n$ mediated reactions. These substrates are well-established to react via an outer-sphere mechanism[10a,14b,18,23,28o,p] and should provide complementary information on the effective reducing power of $SmI_2(H_2O)_n$ to the reactions with a set of aromatic hydrocarbons.

We started our investigation by studying in detail the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$ complexes in which n = 50 and n = 500 with respect to SmI_2 because these complexes have been shown previously to be more thermodynamically powerful than the parent SmI_2 (Table 3).[7b] In order to determine the increase of effective redox potential upon coordination of H_2O to Sm(II), the reduction by SmI_2 in THF was chosen as a benchmark. For comparison, all runs were performed in parallel, using stock solutions of SmI_2 prepared immediately prior to use[35] and titrated according to the established methods to determine the molarity of the active Sm(II) reductant.[35d,e] All reactions were performed with 3 equiv of Sm(II) reductant (1.5 molar

Table 3. Determination of Redox Potential of $SmI_2(H_2O)_n$ by Reduction of Aromatic Hydrocarbons

entry	hydrocarbon	$-E_{1/2}$[a]	reaction with SmI_2	reaction with $SmI_2(H_2O)_n$ n = 50	n = 500
1	acenaphthylene	1.65	52.6 (6 h)	73.4 (22 min)	51.9 (16 min)
2	cyclooctatetraene	1.83	>98 (6 h)	>98 (21 min)	>98 (9 min)
3	anthracene	1.98	<2 (6 h)	93.2 (37 min)	86.8 (6 min)
4	diphenylacetylene	2.11	<2 (6 h)	0.9[b] (2 h)	<2 (48 min)
5	stilbene	2.21	0.8 (5 h)	53.1 (2 h)	4.9 (20 min)
6	1,4-diphenylbenzene	2.40	<2 (5 h)	<2 (2 h)	<2 (11 min)
7	1,3,5-triphenylbenzene	2.51	<2 (5 h)	<2 (2 h)	<2 (24 min)
8	naphthalene	2.61	<2 (4 h)	<2 (2 h)	<2 (2 h)
9	styrene	2.65	<2 (4 h)	1.3 (2 h)	0.5 (2 h)
10	benzene	3.42	<2 (4 h)	<2 (2 h)	<2 (2 h)

[a]In volts vs SCE; $-E_{1/2}$ describes half-reduction potential, refs 20−23. Columns 4−6 refer to conversions in %, determined by GC or ^{1}H NMR. Conditions: 0.05 mmol of substrate, 3 equiv of SmI_2. All reactions quenched with air after the indicated time. In cases when time is <2 h, $SmI_2(H_2O)_n$ complexes were oxidized by excess of water to Sm(III). [b]0.4% bibenzyl and 0.5% stilbene. In cases when conversion is <2%, only starting material was detected in the reaction mixtures.

equiv, 2 equiv required for the reduction of a π-bond) using preformed $SmI_2(H_2O)_n$ complexes. To identify the increase of effective redox potential, all benchmark reactions using solutions of SmI_2 were quenched with air after 4−6 h (the natural decay of SmI_2 is 4.4×10^{-4} s^{-1}),[36] while the reactions using $SmI_2(H_2O)_n$ were allowed to stir for 2 h or quenched with air when decolorization from burgundy red to white or transparent occurred earlier.[7b,c] At this stage no effort was made to optimize the reactions to completion (vide infra); the focus was placed on the determination of the effective redox potential based on the well-established premise that the reduction of aromatic hydrocarbons correlates with the redox potential of the lanthanide.

Reduction of Aromatic Hydrocarbons. The results of the initial investigation are listed in Table 3. From comparison of the results it is clear that the addition of water has a profound effect on the effective redox potential of SmI_2. Most remarkably, the system consisting of $SmI_2(H_2O)_n$ is capable of reducing *trans*-stilbene ($E_{1/2}$ = −2.21 V, all values vs SCE), while under the same conditions SmI_2 in THF is unreactive. Interestingly, all three systems reduce acenaphthylene ($E_{1/2}$ = −1.65 V) and cyclooctatetraene ($E_{1/2}$ = −1.83 V), while no reaction is observed with aromatic hydrocarbons with redox potential more negative than −1.83 and −2.21 V for SmI_2 and $SmI_2(H_2O)_n$ reductants, respectively. Moreover, $SmI_2(H_2O)_n$ complexes reduce anthracene ($E_{1/2}$ = −1.98 V), with an efficiency slightly higher than that of stilbene, as is expected from the relative redox potentials of these substrates. Furthermore, the reactivity of $SmI_2(H_2O)_n$ n = 500 is lower than that of $SmI_2(H_2O)_n$ n = 50, in contrast to the thermodynamic redox potentials of these Sm(II) systems as determined by cyclic voltammetry measurements.[7b]

Overall, the results presented in Table 3 establish that (1) the effective redox potential of $SmI_2(H_2O)_n$ complexes for the reduction of aromatic hydrocarbons is in the range of ca. −2.2 V vs SCE; (2) the $SmI_2(H_2O)_n$ system with n = 500 performs less efficiently than the system comprising n = 50 of water; and (3) the effective redox potential of SmI_2 is much higher than its thermodynamic redox potential (see Table 1). From the mechanistic standpoint, we propose that the increased reactivity of $SmI_2(H_2O)_n$ complex n = 50 over n = 500 results from saturation of the coordination sphere of Sm(II) center at high concentration of water;[7c] however, lower stability of the latter system cannot be excluded at this point. Indeed, oxidation of lanthanide(II) reductants in reactions with aromatic hydrocarbons has been previously reported and is in line with the relative stability of these systems as observed in the current study.[37] We also note that although unsaturated hydrocarbons have been suggested to react with lanthanides(II) via an outer-sphere electron transfer, organometallic complexes of SmI_2 with cyclooctatetraene have been reported.[22] Moreover, the relative lack of reactivity of diphenylacetylene ($E_{1/2}$ = −2.11 V, cf. stilbene) with $SmI_2(H_2O)_n$ might be indicative of inner-sphere character in the reduction of aromatic hydrocarbons with $SmI_2(H_2O)_n$ (vide infra). In summary, results presented in Table 3 provide strong independent evidence that the effective reducing power of $SmI_2(H_2O)_n$ is at least 0.9 V higher than that obtained by ground state measurements[7b] and show that there is a significant effect of the coordination of water on the redox potential of Sm(II) reagent.

Reduction of Alkyl Halides. In order to gain further insight into the effective redox potential of $SmI_2(H_2O)_n$, we examined the reduction of alkyl halides with increasing redox potentials using $SmI_2(H_2O)_n$ (Table 4). These reactions were performed under the conditions outlined above for Table 3. Likewise, the results in Table 4 reveal that the addition of water to SmI_2 results in the formation of a much stronger reductant, capable of efficiently reducing an alkyl iodide and bromide (Table 4, entries 1 and 2). Remarkably, the reaction is not observed when alkyl chloride or fluoride are exposed to $SmI_2(H_2O)_n$ (Table 4, entries 3 and 4), which defines the reactivity of the $SmI_2(H_2O)_n$ reagent toward reduction of alkyl halides and explains the excellent chemoselectivity of this

Table 4. Determination of Redox Potential of $SmI_2(H_2O)_n$ by Reduction of Alkyl Halides

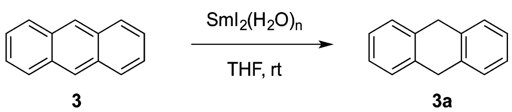
entry	alkyl halide	$-E_{1/2}$[a]	reaction with SmI_2[c]	reaction with $SmI_2(H_2O)_n$ (n = 50)[c]	(n = 500)[c]
1	$C_{12}H_{25}I$	1.30	4.6 (2 h)	94.0 (2 h)	90.7 (2 h)
2	$C_{14}H_{29}Br$	2.29	14.2 (2 h)	50.6 (2 h)	41.9 (2 h)
3	$C_{14}H_{29}Cl$	2.79	2.3 (2 h)	<2 (2 h)	<2 (2 h)
4	$C_{14}H_{29}F$	3.0[b]	<2 (2 h)	<2 (2 h)	<2 (35 min)

[a]In volts vs SCE; $-E_{1/2}$ describes half-reduction potential. Columns 4−6 refer to conversions in %. [b]Determined for ArF, ref 34. [c]Determined by GC or ^{1}H NMR.

reagent reported in our previous studies.[25−27] Finally, SmI_2 in THF (3 equiv, rt, 3 h) does not reduce an alkyl iodide and bromide to a significant extent, highlighting the preference of the reagent for an inner-sphere electron transfer and consistent with literature reports.[2,3] Overall, the results presented in Table 4 demonstrate that (1) activation of SmI_2 with H_2O affords a much stronger reductant; and (2) the effective redox potential of $SmI_2(H_2O)_n$ determined in the reduction of alkyl halides of ca. −2.3 V is in very good agreement with the reduction of stilbene ($E_{1/2}$ = −2.21 V) by $SmI_2(H_2O)_n$ complexes.

Optimization of the Reduction of Anthracene and *trans*-Stilbene. Having determined that $SmI_2(H_2O)_n$ complexes are capable of reducing aromatic hydrocarbons with redox potentials up to −2.21 V vs SCE, we next turned our attention to examining in more detail the reduction of anthracene and stilbene with $SmI_2(H_2O)_n$. The results of the optimization of the reduction of anthracene are presented in Table 5. First, we determined that the addition of as little as 3 equiv of water to SmI_2 results in the activation of SmI_2 toward the reduction (Table 5, entries 1 and 2). Extended reaction time had no impact on the reactivity of SmI_2, which is consistent with the limiting redox potential of the unactivated $SmI_2(THF)_n$ toward the reduction of anthracene (entry 6). Next, we found that the addition of 10 equiv of water to SmI_2 affords the reduction product in an excellent yield; however, the reaction rate was faster when $SmI_2(H_2O)_n$ was preformed using 50 equiv of water, consistent with the activation of lanthanide by H_2O (entries 7 and 8). Finally, we found that the stoichiometry of SmI_2 could be decreased to 3 equiv (1.5 mmol equiv), with 50 equiv of H_2O providing the best results in terms of reaction efficiency and time (entry 10).

Table 5. Optimization of the Reduction of Anthracene with $SmI_2(H_2O)_n$

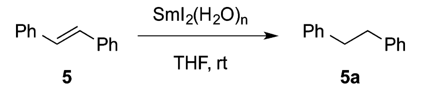


entry	SmI_2 (equiv)	H_2O (equiv/SmI_2)	time	conv[a] (%)
1[b]	3	–	2 h	<2
2[b]	3	3.3	2 h	8.2
3[c]	3	–	6 h	<2
4[c]	3	50	37 min	93.2
5[c]	3	500	6 min	86.8
6	6	–	24 h	<2
7	6	10	24 h	99.5 (98)
8	6	50	2 h	>98 (99)
9	3	10	2 h	67.6 (67)
10	3	50	2 h	>98 (99)

[a]Determined by GC or ^{1}H NMR. All reactions quenched with air after the indicated time. In cases when time is <2 h, $SmI_2(H_2O)_n$ complexes were oxidized by excess of water to Sm(III). [b]Side-by-side reactions. [c]Reproduced from Table 1. Conditions: 0.05 mmol of substrate, 3 equiv of SmI_2. Yield (^{1}H NMR) in brackets.

Table 6 summarizes the results of optimization of the reduction of *trans*-stilbene using $SmI_2(H_2O)_n$. As expected from the relative redox potentials, the reduction of stilbene is more challenging than the reduction of anthracene. The results in Table 6 demonstrate that the activation of SmI_2 with water is required for the reduction (<2.0% conversion using $SmI_2(THF)_n$ complex) and that the maximum reactivity is achieved when ca. 50 equiv of water is used to preform the $SmI_2(H_2O)_n$ reagent, in line with the findings on the reduction of anthracene using $SmI_2(H_2O)_n$. We determined that the optimum results in terms of the reaction rate and efficiency are obtained by carrying out the reaction in two iterations, which might be indicative of the substrate displacement from the coordination sphere of Sm(II). Interestingly, the reduction of *cis*-stilbene with $SmI_2(H_2O)_n$ performed under the same reaction conditions was found to be much slower than that of *trans*-stilbene. In addition, no isomerization of *cis*-stilbene to the *trans*-isomer was observed in the unreacted staring material, which suggests that the first electron transfer step is irreversible in the reduction of this substrate.

Table 6. Optimization of the Reduction of Stilbene with $SmI_2(H_2O)_n$

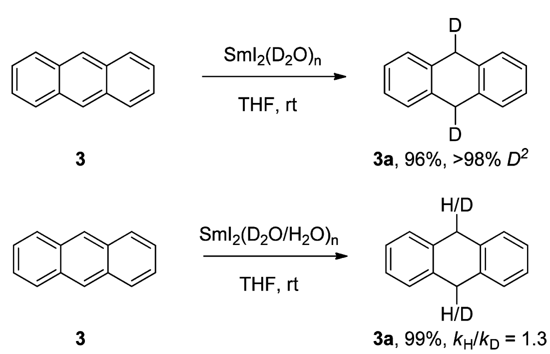


entry	stilbene	SmI_2 (equiv)	H_2O (equiv/SmI_2)	time	conv[a] (%)
1[b]	*E*	3	–	5 h	0.8
2	*E*	3	25	2 h	20.7
3[b]	*E*	3	50	2 h	53.1
4	*E*	6	–	24 h	0.8
5	*E*	6	10	24 h	2.4
6	*E*	6	25	2 h	37.5
7	*E*	6	50	2 h	47.0
8	*E*	6	100	2 h	40.0
9	*Z*	6	25	2 h	3.9
10	*Z*	6	50	2 h	14.7
11	*E*	10	25	3 h	35.1
12	*E*	10	50	3 h	75.0
13[c]	*E*	3	50	2 h	74.9
14[c]	*E*	3	100	2 h	92.7

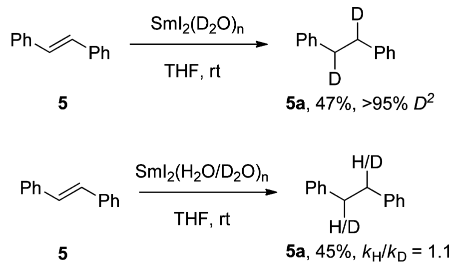
[a]Determined by GC or ^{1}H NMR. [b]Reproduced from Table 1. [c]Two iterations (sequential reactions). Conditions: 0.05 mmol of substrate, 3 equiv of SmI_2. In all entries, >95% yield based on recovered starting material. Entry 13, 57.5% conv after first iteration; entry 14, 56.9%.

Initial Studies on the Mechanism. Several experiments were performed to gain preliminary insight into the mechanism of the reduction of anthracene and stilbene with $SmI_2(H_2O)_n$. First, determination of the deuterium incorporation and kinetic isotope effect in the reduction of anthracene (Scheme 1) and *trans*-stilbene (Scheme 2) demonstrate that anions are generated and protonated by H_2O in a series of single electron

Scheme 1. Determination of Deuterium Incorporation and Kinetic Isotope Effect in the Reduction of Anthracene with $SmI_2(H_2O)_n$

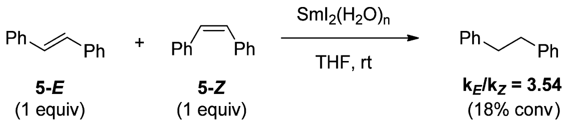


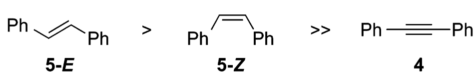
Scheme 2. Determination of Deuterium Incorporation and Kinetic Isotope Effect in the Reduction of Stilbene with $SmI_2(H_2O)_n$



transfer steps[25] and that the proton transfer is not involved in the rate determining step of the reaction.[38] Next, the relative reactivity of $SmI_2(H_2O)_n$ towards *cis*- and *trans*-stilbene was determined by performing intermolecular competition experiments. This demonstrated that under these reaction conditions *trans*-stilbene is 3.5 times more reactive than the *cis*-isomer (Scheme 3).[39] Thus, the relative reactivity of aromatic substrates decreases in order anthracene (not shown) > (*E*)-stilbene > (*Z*)-stilbene > diphenylacetylene (eq 1), which we

Scheme 3. Determination of Relative Rates of the Reduction of *E*- and *Z*-Stilbene with $SmI_2(H_2O)_n$



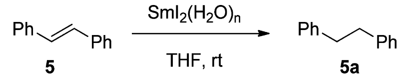


(1)

ascribe to a combination of two factors: (a) the relative redox potentials of the substrates; and (b) the ease of coordination of a π-system to the SmI_2 reductant (cf. stilbene isomers). The lower reactivity of *cis*-stilbene may be due to reduced conjugation because of steric hindrance. Taken together, these results strongly suggest that the electron transfer from Sm(II) to some of the aromatic substrates occurs through electron transfer with inner-sphere character, which would explain the dramatic difference between the thermodynamic and effective redox potentials of $SmI_2(H_2O)_n$ reductants.

Source of SmI_2. We recently reported a detailed investigation on the preparation of SmI_2.[35a] In particular, we demonstrated that the degree of dispersion of Sm metal and homogeneity of SmI_2 solutions can have a profound influence on the reactivity of the Sm(II) reagent. To determine the impact of residual Sm metal on the reactivity of $SmI_2(H_2O)_n$ solutions, we evaluated the reduction of *trans*-stilbene using SmI_2 prepared by different methods (Table 7). Under typical conditions, using stock solutions of SmI_2 in THF and taking all precautions to ensure homogeneity of the reagent, $SmI_2(H_2O)_n$ exhibits good stability (see Experimental Section for stability studies), resulting in the efficient reduction of *trans*-stilbene (Table 7, entry 1). In contrast, the use of SmI_2 powder or SmI_2 solutions prepared in situ (i.e., containing residual Sm metal) leads to much lower conversions due to decay of the reagent by formation of mixed samarium hydroxides as the major decomposition pathway.[40] We note that this is an important practical consideration and recommend that in order to achieve

Table 7. Effect of SmI_2 Source on the Reduction of Stilbene with $SmI_2(H_2O)_n$



entry	SmI_2 (equiv)	H_2O (equiv/SmI_2)	time	conv[a] (%)	SmI_2 source
1[b]	3	50	2 h	53.1	stock solution
2	3	50	10 min	15.7[d]	in situ solution
3[c]	3	50	30 min	15.0[d]	powder

[a]Determined by GC or ^{1}H NMR. [b]Reproduced from Table 3. [c]SmI_2 powder (AAPL) was used. Conditions: 0.05 mmol of substrate, 3 equiv of SmI_2. [d]15% yield.

maximum reactivity with $SmI_2(H_2O)_n$ complexes, homogeneous stock solutions of SmI_2 in THF should be used while taking all precautions outlined in our previous study to avoid contamination of the reagent with Sm metal and Sm(III) iodide.[41]

Reductions Using $SmI_2(MeOH)_n$. In addition to water, methanol has emerged as one of the most popular proton donor additives for SmI_2.[2,3] Although it has been proposed that the increased reactivity of $SmI_2(MeOH)_n$ might originate from the higher redox potential of the reagent (vs $SmI_2(THF)_n$),[29c] the effective reducing power of $SmI_2(MeOH)_n$ has not been elucidated.

To determine the redox potential of $SmI_2(MeOH)_n$ complexes, we investigated the reactivity of $SmI_2(MeOH)_n$ in the reduction of aromatic hydrocarbons (Table 8). For these experiments the stoichiometry of MeOH most commonly cited in the literature (i.e., 4:1 v/v w/THF)[2,3] was employed. The results in Table 8 indicate that the effective redox potential of $SmI_2(MeOH)_n$ is much lower than that of $SmI_2(H_2O)_n$ complexes. Moreover, $SmI_2(MeOH)_n$ shows reduced reactivity toward acenaphthylene (Table 8, entry 1) compared with that of $SmI_2(THF)_n$ (Table 3, entry 1). These results suggest that the beneficial role of MeOH in SmI_2-mediated reactions does not involve changes in the redox potential of the reagent. Furthermore, the lower reactivity of acenaphthylene with $SmI_2(MeOH)_n$ supports inner-sphere electron transfer characteristics in the reduction of aromatic hydrocarbons with SmI_2.[7,29]

Table 8. Reduction of Aromatic Hydrocarbons with $SmI_2(MeOH)_n$ Complexes (n = 150)

entry	hydrocarbon	$-E_{1/2}$[a]	SmI_2 (equiv)	MeOH (equiv, 4:1 v/v)	time	conv (%)[b]
1	acenaphthylene	1.65	3	275	1 h	9.1
2	anthracene	1.98	3	275	2 h	2.0
3	stilbene	2.21	3	275	2 h	1.1

[a]In volts vs SCE; $-E_{1/2}$ describes half-reduction potential, ref 20–23. [b]All conversions determined by GC or ^{1}H NMR. Conditions: 0.05 mmol of substrate, 3 equiv of SmI_2. All reactions quenched with air after the indicated time.

Determination of the Effective Redox Potential of $SmBr_2$, $SmCl_2$, $SmBr_2(H_2O)_n$, and $SmCl_2(H_2O)_n$. In the past decade, samarium(II) bromide and samarium(II) chloride have seen increasing application as powerful samarium(II)-based reductants.[4d] Specifically, $SmBr_2$ and $SmCl_2$ permit activation of recalcitrant substrates toward electron transfer as a result of

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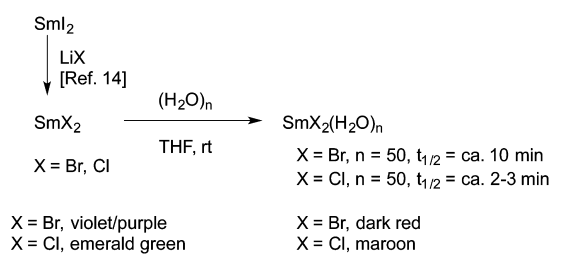
their much higher redox potential compared to SmI_2.[14] Moreover, due to the smaller radial size of the halide counterions these Sm(II)-based reductants have been shown to exhibit much higher selectivity than SmI_2 in the reductive coupling of carbonyl groups due to the enhanced inner-sphere character of the electron transfer.[16,17] The most popular method for the synthesis of samarium(II) bromide and samarium(II) chloride relies on counterion exchange from the readily available solutions of SmI_2 in THF and LiBr or LiCl reported by Flowers.[14]

In light of the increasing importance of $SmBr_2$ and $SmCl_2$ in organic synthesis, we considered that the determination of the effective redox potential of these reductants could define the functional group tolerance possible with Sm(II) reagents and provide a practical reactivity scale allowing a direct comparison with SmI_2-based systems. From the outset of our studies, a major objective was to prepare and determine the reactivity of $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ complexes as more powerful alternatives to $SmI_2(H_2O)_n$ systems with a long-term goal of utilizing a family of easily tunable $SmX_2(H_2O)_n$ complexes for chemoselective electron transfer reactions. Prior to this study, the synthesis of $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ had not been reported,[42] and it was not certain if these complexes would be sufficiently stable to permit reductions due to the much higher thermodynamic redox potential of the parent lanthanide(II) halide, which was expected to facilitate the irreversible oxidation of Sm(II) to Sm(III).[43]

$SmBr_2$ and $SmCl_2$ (THF solution) reductants were prepared by the addition of freshly prepared SmI_2 solutions in THF to the anhydrous LiBr or LiCl salts (Scheme 4). In agreement with the literature, the counterion exchange was followed by changes in color of the reaction mixtures (SmI_2: dark blue; $SmBr_2$: violet, reminiscent of SmI_2−HMPA complexes; $SmCl_2$: dark green; reminiscent of TmI_2−THF complexes). The addition of water (50 equiv with respect to SmX_2; the most reactive system as determined for SmI_2) to the stock solutions of SmX_2 in THF resulted in a color change to dark red, indicative of the formation of $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ complexes. As expected from the relative redox potentials, $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ proved to be more sensitive to oxidation than the corresponding $SmI_2(H_2O)_n$ complex ($t_{1/2}$ of $SmBr_2(H_2O)_n$, ca. 10 min; $SmCl_2(H_2O)_n$, ca. 2−3 min; $SmI_2(H_2O)_n$, more than 24 h. See Experimental Section for details). We note that from a synthetic standpoint, the high redox potential of SmX_2 (X = Cl, Br) should compensate for the lower stability of these systems.[44]

Scheme 4. Preparation and Stability of SmX_2 and $SmX_2(H_2O)_n$ Complexes



The results of determination of the effective redox potentials of SmX_2 (X = Cl, Br) and their complexes with water are presented in Table 9. Most importantly, $SmBr_2$ and $SmCl_2$ alone are capable of reducing aromatic hydrocarbons with redox potentials more positive than −2.2 V vs SCE, which is much higher than the redox potentials determined by cyclic voltammetry studies by ca. 0.4 V. Interestingly, the addition of water does not result in a significant increase in the reactivity of $SmBr_2$ and $SmCl_2$, which could be due to the formation of more sterically encumbered reductants by coordination of water (cf. SmI_2).[7c,d,14b,18] Importantly, aromatic hydrocarbons with redox potential more negative than −2.2 V vs SCE are not reduced by SmX_2 and their complexes with water, which allows to define the effective reducing power of these Sm(II) reductants as ca. −2.2 V vs SCE.

The results of our investigation of the reactivity of SmX_2 (X = Cl, Br) and $SmX_2(H_2O)_n$ with a set of alkyl halides are outlined in Table 10. Interestingly, both $SmBr_2$ and $SmCl_2$ exhibit higher reactivity toward an alkyl bromide than alkyl iodide, whereas an alkyl chloride is tolerated by these reductants. This trend of reactivity is presumably due to a combination of two effects: (a) the redox potential of the substrate; and (b) the ease of the inner-sphere electron transfer process, in agreement with previous findings.[14b] Intriguingly, an alkyl fluoride is a viable substrate for the reduction with $SmBr_2$. The increased reactivity of this substrate is most likely due to a S_N2-type displacement of fluoride by $SmXBr_2$ (X = Br, OH) with the resulting alkyl bromide being reduced. This mirrors the recently reported activation of alkyl fluorides with YbI_3.[45]

Unexpectedly, the addition of water has a deleterious effect on the reduction of alkyl halides with $SmBr_2$ and $SmCl_2$ in most cases examined. Since the solutions of $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ were effective in reducing *trans*-stilbene with a

Table 9. Determination of Redox Potential of $SmBr_2$, $SmCl_2$, $SmBr_2(H_2O)_n$, and $SmCl_2(H_2O)_n$ by Reduction of Aromatic Hydrocarbons

entry	hydrocarbon	$-E_{1/2}$[a]	reaction with $SmBr_2$[b]	reaction with $SmBr_2(H_2O)_n$[b]	reaction with $SmCl_2$[b]	reaction with $SmCl_2(H_2O)_n$[b]
1	acenaphthylene	1.65	15.3	12.2	9.8	7.1
2	cyclooctatetraene	1.83	>98	>98	>98	>98
3	anthracene	1.98	30.5	5.9	7.0	10.3
4	diphenylacetylene	2.11	<2	<2	<2	<2
5	stilbene	2.21	20.0	15.9	16.5	18.8
6	1,4-diphenylbenzene	2.40	<2	<2	<2	<2
7	styrene	2.65	<2	<2	2.0	0.4
8	benzene	3.42	<2	<2	nd	nd

[a]In volts vs SCE; $-E_{1/2}$ describes half-reduction potential. [b]Columns 4−7 refer to conversions in %. All conversions determined by GC or ^{1}H NMR. All reactions with $SmCl_2$ or $SmCl_2(H_2O)_n$ 2−3 min until decolorization; $SmBr_2(H_2O)_n$ 2−3 min until decolorization; $SmBr_2$: entry 1, rapid decolorization to yellow; entries 2−6, 2−3 min until decolorization; entries 7−8, 2 h.

Table 10. Determination of Redox Potential of $SmBr_2$, $SmCl_2$, $SmBr_2(H_2O)_n$, and $SmCl_2(H_2O)_n$ by Reduction of Alkyl Halides

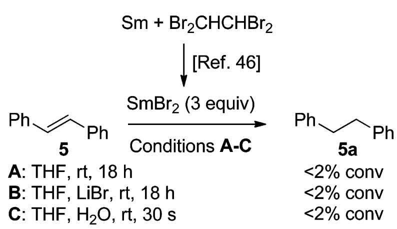
entry	alkyl halide	$-E_{1/2}$[a]	reaction with $SmBr_2$	reaction with $SmBr_2(H_2O)_n$	reaction with $SmCl_2$	reaction with $SmCl_2(H_2O)_n$
1	$C_{10}H_{21}I$	1.30	23.6 (2 h)	23.1 (3 min)[d]	36.6 (3 min)	<2[e] (3 min)
2	$C_{14}H_{29}Br$	2.29	58.0 (2 h)	<2 (3 min)	55.3 (3 min)	1.8 (3 min)
3	$C_{14}H_{29}Cl$	2.79	3.3 (2 h)	1.7 (3 min)	9.5 (3 min)	<2 (3 min)
4	$C_{14}H_{29}F$	3.0[b]	22.1 (15 min)	21.2 (3 min)	5.5 (3 min)	7.8 (3 min)

[a]In volts vs SCE; $-E_{1/2}$ describes half-reduction potential. Columns 4−7 refer to conversions in %. [b]Determined for ArF, ref 34. All conversions determined by GC or ^{1}H NMR. [d]32.6/1 h. [e]Average of two experiments (1.3, 2.3 conv). All reactions with $SmCl_2$ or $SmCl_2(H_2O)_n$ 2−3 min until decolorization; $SmBr_2(H_2O)_n$ 2−3 min until decolorization; $SmBr_2$: entries 1−3 2 h; entry 4, 15 min until decolorization.

reaction rate similar to that of $SmBr_2$ and $SmCl_2$ (Table 9), we postulate that the lower reactivity of $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ in the reduction of alkyl halides results from saturation of the coordination sphere of Sm(II) reductants.[7c,18] Further studies are ongoing to determine the role of water in the reduction of other functional groups and reductive cross-couplings with $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ complexes.

Reductions Using $SmBr_2$ Prepared from 1,1,2,2-Tetrabromoethane. It has been reported that solutions of $SmBr_2$ and $SmCl_2$ prepared by counterion exchange from SmI_2 often exhibit beneficial reactivity compared to that of $SmBr_2$ and $SmCl_2$ prepared by other methods due to the formation of solvated monomers in the synthesis from SmI_2.[14b] To probe whether the selected method of preparation contributed to the high reactivity of $SmBr_2$ in the reduction of aromatic hydrocarbons, we synthesized $SmBr_2$ via an alternative procedure from Sm metal and 1,1,2,2-tetrabromoethane (Scheme 5).[46] In agreement with previous reports, this method

Scheme 5. Attempted Reduction of Stilbene using $SmBr_2$ Prepared from Sm Metal and 1,1,2,2-Tetrabromoethane



afforded a slurry of $SmBr_2$ in THF (in contrast to clear solutions of $SmBr_2$ obtained by counterion exchange).[14b] The slurry of $SmBr_2$ in THF as well as upon activation with water or LiCl did not promote the reduction of stilbene (Scheme 5), demonstrating that the procedure reported by Flowers is at present the method of choice for the synthesis of active solutions of $SmBr_2$ and $SmCl_2$.

Birch Reductions Using $SmI_2(H_2O)_n$. Birch reductions using alkali metals in liquid ammonia are among the most important methods for dearomatization of feedstock aromatic hydrocarbons; however, these procedures are inherently limited by low functional group tolerance and require cryogenic temperatures (NH_3, bp = −33 °C), which complicates both industrial and laboratory scale applications.[33] Recent noteworthy developments to expand the scope of classic Birch reductions include ammonia-free reductions of electron-deficient aromatics using LiDBB (lithium di-*tert*-butyl biphenyl) in THF at −78 °C reported by Donohoe[47] and room temperature reductions of aromatic rings using alkali metals in silica gel reported by Jackson and co-workers,[48] among other reports.[49]

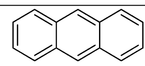
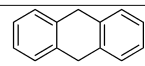
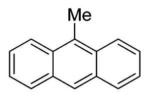
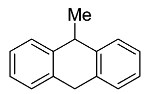
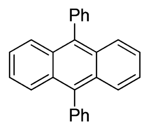
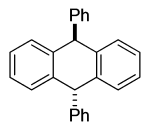
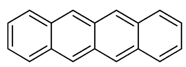
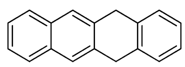
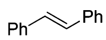
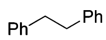
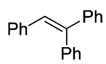
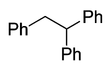
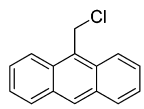
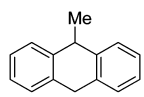
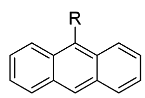
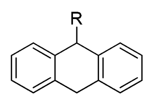
Having determined that the readily available $SmI_2(H_2O)_n$ system efficiently reduces aromatic hydrocarbons with redox potentials more positive than −2.2 V vs SCE, we recognized that this reagent would provide an attractive alternative to the classic Birch reductions of substrates bearing at least two aromatic rings. Towards this end, we subjected a broad range of aromatic hydrocarbons with redox potentials higher than −2.2 V vs SCE to the $SmI_2(H_2O)_n$ reaction conditions. Table 11 shows the synthetic scope of Birch reductions mediated by the $SmI_2(H_2O)_n$ reagent. In all cases examined the reactions are high-yielding and proceed with excellent chemoselectivity; we did not observe any products resulting from over-reduction even in cases when large excess of the reagent was used.

Entries 1−4 demonstrate the reduction of anthracene and tetracene derivatives. Interestingly, the reduction of 9,10-diphenylanthracene (entry 3) furnishes the dearomatized product with synthetically useful *trans* diastereoselectivity (dr = 98:2), which compares favorably with other protocols (vide infra).[48a] We note that several of these polycyclic dearomatized products represent important structural motifs for applications in materials chemistry, as semiconductors and optical devices. Entries 5 and 6 show the reduction of conjugated alkenes. The reduction of 9-(chloromethyl)anthracene (entry 7) demonstrates the potential of the developed process to perform reductions in tandem. Finally, we were pleased to find that this protocol could be extended to unsaturated hydrocarbons bearing carboxylic acid, ester, and amide functional groups placed at the sensitive benzylic position,[50,51] further highlighting the functional group tolerance of the reaction. At this stage, N-containing heterocycles, such as acridine and quinoline derivatives, are not efficient substrates,[52] presumably due to competing overreduction caused by the more positive reduction potential and a change of mechanism to reversible inner-sphere electron transfer by N-coordination.[53] Despite this limitation, we believe that the reaction should find useful applications as an attractive room temperature alternative to the classic Birch-type reductions using alkali metals in liquid ammonia.[33] Further studies on the reductive dearomatizing cross-coupling of aromatic hydrocarbons using the $SmI_2(H_2O)_n$ reagent are underway in our laboratories.

Studies on the Origin of Selectivity. Several studies were performed to gain insight into the reduction mechanism and to understand the observed selectivity.

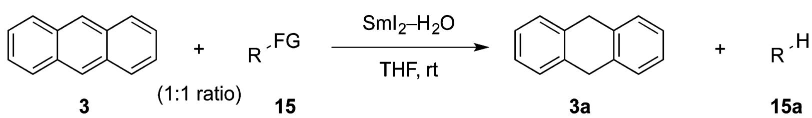
First, to illustrate the chemoselectivity observed with the $SmI_2(H_2O)_n$ reagent, we have carried out a series of competition experiments using substrates that are readily reduced with single electron transfer reagents other than $SmI_2(H_2O)_n$ (Table 12). In all cases, no reduction products arising from naphthalene, an alkyl chloride and aryl bromide were observed despite long reaction times and excess of the reagent, while anthracene underwent smooth reduction in excellent yield.

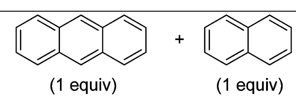
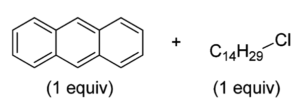
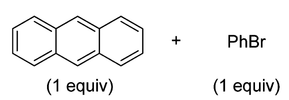
Table 11. Birch Reductions of Aromatic Hydrocarbons Using $SmI_2(H_2O)_n$ Complexes

entry	substrate	product	SmI_2–H_2O (equiv)	time	yield[a] (%)
1			3-50	0.5 h	96[b]
2			3-50	2 h	99
3			3-50	2 h	98 (trans:cis >98:2)
4			3-50	10 min	99[c]
5			6-100	4 h	72
6			3-24-24[d]	2 h	97
7			5-50	2 h	74
					
8	R = CO_2H	R = CO_2H	3-50	2 h	94
9	R = CO_2Me	R = CO_2Me	3-50	15 min	99
10	R = $C(O)NEt_2$	R = $C(O)NEt_2$	3-50	5 min	98

[a]Determined by ^{1}H NMR. In all entries, over-reduction was not detected by ^{1}H NMR and GC–MS analysis of reaction mixtures. In addition, over-reduction using large excess of SmI_2/H_2O (10–50 equiv) was not observed (entry 8). [b]Isolated yield, 1.0 mmol scale. [c]Conversion. [d]Reaction using SmI_2 (3 equiv), H_2O (24 equiv), and Et_3N (24 equiv); 34% yield using SmI_2/H_2O (3–50, 2 h).

Table 12. Chemoselectivity in Birch Reductions of Aromatic Hydrocarbons using $SmI_2(H_2O)_n$ Complexes

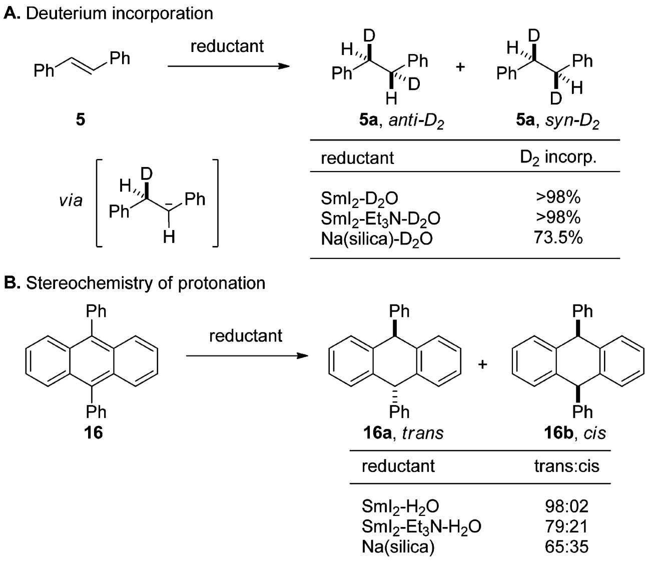


entry	substrates	conv/product yield (**3a**, %)[a]	conv/SM yield (**15**, %)[a]	k_A/k_B
1		>98/94	<2/>98	>98:2
2		>98/95	<2/>98	>98:2
3		>98/93	<2/>98	>98:2

[a]Determined by GC–MS and ^{1}H NMR. Reduction products from competition substrates **15** were <2% in all entries. Conditions: SmI_2 (3 equiv), H_2O (50 equiv/SmI_2), THF, rt, 1 h.

Next, to investigate the role of the protonation step, we studied in detail deuterium incorporation in the reduction of *trans*-stilbene and the stereoselectivity of protonation in the reaction of 9,10-diphenylanthracene using $SmI_2(H_2O)_n$ and related SET reductants (Scheme 6). The reduction of *trans*-stilbene with $SmI_2(D_2O)_n$ and with the more thermodynamically powerful $SmI_2(D_2O)_n(Et_3N)$ system gave 1,2-diphenylethane with >98% D_2 incorporation; however, the use of Na(silica) resulted in a significant loss of D_2 incorporation (Scheme 6A). Moreover, the reduction of 9,10-diphenylanthracene with $SmI_2(H_2O)_n$, $SmI_2(H_2O)_n(Et_3N)$ and Na(silica) led to a gradual decrease in stereoselectivity of the protonation (Scheme 6B). These results suggest that in the reductions with Sm(II)-based reagents, anions are generated and immediately protonated by H_2O, whereas the $SmI_2(H_2O)_n$ reagent is less sterically encumbered than $SmI_2(H_2O)_n(Et_3N)$, resulting in a highly diastereoselective protonation. Note that the intermediate monoanion in the reduction of *trans*-stilbene with $SmI_2(D_2O)_n$ does not undergo stereoselective protonation.

Scheme 6. Investigating the Protonation Step in the Reduction of Aromatic Hydrocarbons with $SmI_2(H_2O)_n$ and Related SET Reductants



reductant	D_2 incorp.
SmI_2-D_2O	>98%
SmI_2-Et_3N-D_2O	>98%
Na(silica)-D_2O	73.5%

reductant	trans:cis
SmI_2-H_2O	98:02
SmI_2-Et_3N-H_2O	79:21
Na(silica)	65:35

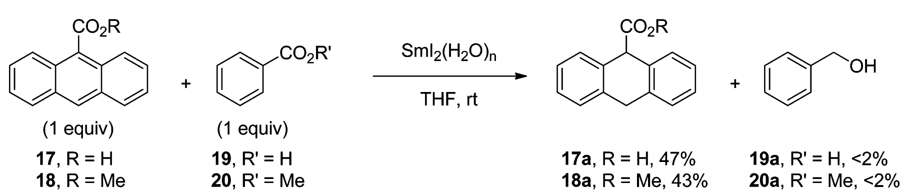
To investigate the origin of selectivity in the reduction of 9-anthracene carboxylic acid derivatives, we have carried out intermolecular competition experiments using anthracene-containing substrates and the corresponding benzoic acid analogues with limiting $SmI_2(H_2O)_n$ (Scheme 7). The reduction of aromatic carboxylic acids and esters with $SmI_2(H_2O)_n$ systems has been previously reported.[50] We determined that the reduction of 9-anthracene carboxylic acid and the methyl ester proceeds with complete selectivity over the corresponding benzoic acid analogues. In addition, control reactions using **17**–**20** (see Experimental Section) demonstrated that both classes of substrates (i.e., benzoic and anthracene carboxylic acid derivatives) undergo instantaneous reduction with $SmI_2(H_2O)_n$ (<30 s at room temperature).

Proposed Mechanism. On the basis of these studies, we conclude that the reduction of aromatic hydrocarbons with $SmI_2(H_2O)_n$ proceeds through the rate-determining first electron transfer step to give the radical anion, which is then protonated by H_2O (Scheme 8). A second electron transfer generates the anion, which is quenched by the water cosolvent. This mechanism is different from the classic Birch reductions, which have been shown to proceed via the rate-determining protonation.[54] We propose that the complete selectivity observed in reductions of aromatic hydrocarbons with redox potential more positive than −2.2 V vs SCE using $SmI_2(H_2O)_n$ originates in the rate of the first electron-transfer step. Our results suggest that the beneficial influence of water in these reductions arises from the activation of the SmI_2 reductant by increasing its redox potential.[7b] Finally, although it has been proposed that the reduction of aromatic hydrocarbons with Sm(II) proceeds via an outer sphere mechanism,[10a,14b,18,23,28o,p] the dramatic difference between the thermodynamic redox potentials of SmI_2 and $SmI_2(H_2O)_n$ determined by cyclic voltammetry and the effective redox potentials as determined in the current study suggests that these reductions may proceed via inner sphere electron transfer. We believe that the observation that $SmI_2(H_2O)_n$ is capable of reducing aromatic hydrocarbons with redox potentials as low as −2.2 V vs SCE will provide the framework for further mechanistic understanding of the electrostatic component[31] that drives the reductions mediated by Kagan's reagent.

■ CONCLUSIONS

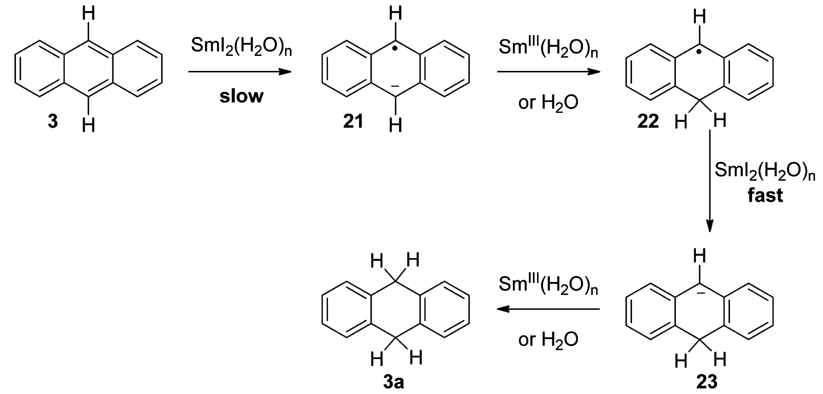
In summary, the first determination of the effective redox potential of the versatile $SmI_2(H_2O)_n$ reagent has been carried out. The reagent system has been found to reduce aromatic hydrocarbons that have reduction potentials more positive than −2.21 V vs SCE, which is much higher than the thermodynamic redox potential of $SmI_2(H_2O)_n$ determined by electrochemical methods (−1.3 V vs SCE). Determination of the effective redox potential of the parent reductant demonstrates that coordination of water to SmI_2 increases the effective reducing power of Sm(II) by more than 0.4 V. Importantly, we have identified that in the reductions of aromatic hydrocarbons the $SmI_2(H_2O)_n$ system in which $n = 50$ equiv of water is more reactive that the $SmI_2(H_2O)_n$ system based on $n = 500$, which is in contrast to the thermodynamic redox potential of $SmI_2(H_2O)_n$ complexes. Moreover, we have described the synthesis and determination of the effective redox potential of $SmX_2(H_2O)_n$ (X = Cl, Br) complexes for the first time.

Scheme 7. Investigating the Origin of Selectivity in the Reduction of 9-Anthracene Carboxylic Acid Derivatives with $SmI_2(H_2O)_n$



*Conditions: SmI_2 (1 equiv), H_2O (50 equiv)

Scheme 8. Proposed Mechanism for the Reduction of Aromatic Hydrocarbons with $SmI_2(H_2O)_n$ Complexes



The room temperature Birch reductions of substrates with at least two aromatic rings mediated by $SmI_2(H_2O)_n$ constitute an attractive practical alternative to the classic protocols employing alkali metals in liquid ammonia. From a synthetic standpoint, SmI_2 is commercially available[55] or convenient to prepare,[35a] easy to handle,[56] and the system based on $SmI_2(H_2O)_n$ does not require any toxic cosolvents or additives,[57] making this transformation a valuable addition for the preparation of dearomatized polycyclic hydrocarbons.

Experimental studies suggest that the observed selectivity in the reduction of aromatic substrates originates from the initial electron transfer step; however, some of the reductions described herein might proceed through inner-sphere electron transfer. As such, this study emphasizes the importance of electrostatic interactions in processes mediated by lanthanide(II) reductants and aids in understanding the unique role of $SmI_2(H_2O)_n$ complexes in the reduction of lactones and other polar carbonyl groups. Further studies to investigate the role of additives in Sm(II)-mediated reductions are ongoing in our laboratory, and these results will be reported shortly. We believe that the findings described herein will result in an increased application of SmX_2 and $SmX_2(H_2O)_n$ complexes in organic synthesis.

■ EXPERIMENTAL SECTION

General Methods. All experiments were performed using standard Schlenk techniques under argon atmosphere unless stated otherwise. All solvents were purchased at the highest commercial grade and used as received or after purification by passing through activated alumina columns or distillation from sodium/benzophenone under nitrogen. All solvents were deoxygenated by freeze−pump−thawing under argon (three cycles) or sparging with argon prior to use. Samarium(II) iodide was prepared as described previously.[35a] Samarium(II) bromide and samarium(II) chloride were prepared according to the procedure by Flowers and used immediately after the preparation.[7] Samarium metal was purchased as −40 mesh and stored in a closed container at room temperature on the bench without further precautions prior to use. 1,2-Diiodoethane was stored at 4 °C and used after purification as described previously.[35a] Samarium(II) iodide powder was purchased, opened and stored in an argon-containing glovebox (<1 ppm of O_2, H_2O). All other chemicals were purchased at the highest commercial grade and used as received. Reaction glassware was oven-dried at 140 °C for at least 24 h or flame-dried prior to use, allowed to cool under vacuum, and purged with argon (three cycles).

^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on spectrometers at 300, 400, and 500 MHz (^1H NMR) and 75, 100, and 125 MHz (^{13}C NMR). All shifts are reported in parts per million (ppm) relative to the residual $CHCl_3$ peak (7.27 and 77.2 ppm, ^1H NMR and ^{13}C NMR, respectively). All coupling constants (J) are reported in hertz (Hz). Abbreviations are s, singlet; d, doublet; t, triplet; q, quartet; br s, broad singlet.

Flash chromatography was performed on silica gel 60 Å, 230−400 mesh using commercial grade solvents. Samples were analyzed by thin-layer chromatography analysis on aluminum sheets coated with silica gel 60 Å F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp and/or aqueous potassium permanganate solution.

All products and starting materials used in this study are commercially available or have been previously reported. *N*,*N*-Diethylanthracene-9-carboxamide and methyl anthracene-9-carboxylate were prepared according to the previously published procedures.[58,59] Their spectroscopic properties are reported below for characterization purposes. All other products were identified using ^1H NMR, GC, and GC−MS analysis and comparison with authentic samples. All yields were obtained by ^1H NMR analysis using internal standards added after workup unless stated otherwise.

GC−MS chromatography was performed using a GC system and EI/CI MSD with triple axis detector equipped with a column (length 30 m, internal diameter 0.25 mm, film 0.25 μm) using helium as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 40 or 50 °C. The injector temperature was 250 °C. The detector temperature was 250 °C. For runs with the initial oven temperature of 40 °C, temperature was increased with a 15 °C/min ramp after 40 °C hold for 3 min to a final temperature of 300 °C and then held at 300 °C for 5 min (splitless mode of injection, total run time of 25.33 min). For runs with the initial oven temperature of 50 °C, temperature was increased with a 25 °C/min ramp after 50 °C hold for 3 min to a final temperature of 300 °C and then held at 300 °C for 5 min (splitlesss mode of injection, total run time of 18 min).

GC chromatography was performed using a gas chromatograph system equipped with a column (length 30 m, internal diameter 0.25 mm, film 0.25 μm) using hydrogen as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 40 or 70 °C. The injector temperature was 250 °C. The detector temperature was 250 °C. The temperature was increased with a 10 °C/min ramp to a final temperature of 150 or 220 °C (splitless mode of injection). For runs with the initial oven temperature of 40 °C, temperature was increased by 10 °C/min after 40 °C hold for 3 min (total run time of 13 min). For runs with the initial oven temperature of 70 °C, temperature was increased by 10 °C/min with no hold time (total run time of 15 min).

General Procedure A. Preparation of $SmBr_2$. Lithium bromide (7.65 g, 90 mmol, 12 equiv) was placed in a 500 mL Schlenk flask, carefully flame-dried under vacuum, and allowed to cool to room temperature. The flame-drying was repeated four more times. After the final cycle, the flask was backfilled with argon, and freshly prepared samarium(II) iodide solution (115 mL, 0.065 M in THF, 1 equiv) was slowly added with vigorous stirring at room temperature. At this point a change of color from deep blue indicative of samarium(II) iodide to purple/violet indicative of the formation of samarium(II) bromide was observed. After stirring for 15 min at room temperature the resulting solution was used immediately.

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General Procedure B. Preparation of $SmCl_2$. Lithium chloride (4.00 g, 96 mmol, 12 equiv) was placed in a 500 mL Schlenk flask, carefully flame-dried under vacuum, and allowed to cool to room temperature. The flame-drying was repeated four more times. After the final cycle, the flask was backfilled with argon, and freshly prepared samarium(II) iodide solution (123 mL, 0.065 M in THF, 1 equiv) was slowly added with vigorous stirring at room temperature. At this point a change of color from deep blue indicative of samarium(II) iodide to dark green indicative of the formation of samarium(II) chloride was observed. After stirring for 15 min at room temperature the resulting solution was used immediately.

General Procedure C. Preparation of $SmX_2(H_2O)_n$ (X = I, Br, Cl) Complexes. An oven-dried vial or flask equipped with a Teflon-coated magnetic stir bar and a septum was placed under a positive pressure of argon. After three evacuation/backfilling cycles a freshly prepared solution of samarium(II) halide (iodide, bromide, or chloride) was added, followed by the addition of deoxygenated deionized water (n = 50 or 500 equiv relative to SmX_2). At this point a change of color of SmX_2 (X = I, Br, Cl) to burgundy red indicative of the formation of $SmX_2(H_2O)_n$ complex was observed. The resulting solution was used immediately.

General Procedure D. Determination of Stability of $SmX_2(H_2O)_n$ Complexes. *Method A.* To an oven-dried vial equipped with a Teflon-coated magnetic stir bar and a septum was added a freshly prepared solution of SmX_2 (X = I, Br, Cl) (1.0 mL, 0.065 M in THF) followed by water (0.0586 mL, 50 equiv) with vigorous stirring at room temperature. This resulted in an immediate color change to burgundy red. The resulting solution of $SmX_2(H_2O)_n$ was stirred under argon until decolorization to white had occurred. Note that decolorization to yellow is indicative of a high concentration of O_2 and/or Sm(III) salts. The time for decolorization (average of at least three experiments) was found to be directly related to the redox potential of the parent SmX_2 reductant: $SmI_2(H_2O)_n$ more than 24 h, $SmBr_2(H_2O)_n$ ca. 15−20 min, $SmCl_2(H_2O)_n$ ca. 5−7 min. Note that the burgundy red color of $SmBr_2(H_2O)_n$ and $SmCl_2(H_2O)_n$ solutions in THF is visibly darker than that of $SmI_2(H_2O)_n$. *Method B.* To an oven-dried vial equipped with a Teflon-coated magnetic stir bar and a septum was added a freshly prepared solution of SmX_2 (X = I, Br, Cl) (1.0 mL, 0.065 M in THF) followed by the dropwise addition of water with vigorous stirring at room temperature. For all three $SmX_2(H_2O)_n$ complexes (X = I, Br, Cl) the characteristic burgundy red color appeared after addition of ca. 0.050 mL (ca. 40 equiv) of H_2O. Full decolorization to white or transparent was observed after addition of ca. 0.35−0.40 mL of H_2O ($SmBr_2$), 0.50 mL ($SmCl_2$), and more than 12.5 mL (SmI_2) for the three Sm(II) halides, respectively. Note that $SmCl_2(H_2O)_n$ exhibits a limited solubility in THF solutions: a visible precipitate forms after the addition of ca. 0.050 mL of water, which then fully dissolves upon further addition of 0.25 mL of H_2O, indicating that H_2O aids in solubilizing the $SmCl_2(H_2O)_n$ complex.

General Procedure E. Determination of Redox Potential of $SmX_2(H_2O)_n$ (X = I, Br, Cl) by Reduction of Aromatic Hydrocarbons or Alkyl Halides. To a preformed solution of $SmX_2(H_2O)_n$ prepared as described above (THF solution, 3 equiv, 0.15 mmol) was added a solution of substrate (1 equiv, 0.05 mmol) in THF (1.0 mL) at room temperature under argon atmosphere, and the mixture was stirred vigorously. After the specified time, the reaction was quenched by bubbling air through the reaction mixture until decolorization had occurred. The sample was analyzed by GC and/or ^{1}H NMR to obtain conversion using internal standard. For GC analysis, a small aliquot (typically, 0.25 mL) was removed from the reaction mixture, diluted with diethyl ether (2.0 mL) and HCl (0.1 N, 0.25 mL), and analyzed by GC and/or GC−MS to obtain conversion. For ^{1}H NMR analysis, the reaction mixture was diluted with CH_2Cl_2 (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), and the organic layers were combined, dried over $MgSO_4$, filtered, and concentrated. The product distribution was analyzed after the addition of internal standard.

General Procedure F. Reduction of Aromatic Hydrocarbons Using $SmI_2(H_2O)_n$. *Method A.* To a preformed solution of $SmI_2(H_2O)_n$ prepared as described above (THF solution, 3 equiv, typically 0.30 mmol) was added a solution of substrate (1 equiv, typically 0.10 mmol) in THF (1.0 mL) at room temperature under argon atmosphere, and the mixture was stirred vigorously. After the specified time, the reaction was quenched by bubbling air through the reaction mixture until decolorization had occurred. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and HCl (1 N, 30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), and the organic layers were combined, dried over $MgSO_4$, filtered, and concentrated. The sample was analyzed by ^{1}H NMR to obtain conversion and yield using an internal standard. *Method B.* An oven-dried vial equipped with a Teflon-coated magnetic stir bar was charged with a substrate (typically, 0.10 mmol) and placed under a positive pressure of argon. Samarium(II) iodide (THF solution, typically 3 equiv), followed by H_2O (typically, 50 equiv relative to SmI_2), was added, and the resulting mixture was stirred vigorously. Workup and analysis was performed as described for *Method A.*

General Procedure G. Reduction of Aromatic Hydrocarbons using $SmI_2(MeOH)_n$. To a freshly prepared solution of SmI_2 (THF solution, 3 equiv) was added MeOH (4:1 v/v, ca. 300 equiv), which resulted in a color change from dark blue to dark brown indicative of the formation of $SmI_2(MeOH)_n$ complex. A solution of substrate (1 equiv, typically 0.10 mmol) in THF (1.0 mL) was added at room temperature under argon atmosphere, and the mixture was stirred vigorously. Workup and analysis were as described above for reductions mediated by $SmI_2(H_2O)_n$ complexes.

General Procedure H. Determination of Deuterium Incorporation and Kinetic Isotope Effect. An oven-dried vial equipped with a Teflon-coated magnetic stir bar was charged with a substrate (0.10 mmol) and placed under a positive pressure of argon. Samarium(II) iodide (THF solution, typically 3 equiv), followed by D_2O (typically, 50 equiv relative to SmI_2; deuterium incorporation) or an equimolar mixture of D_2O and H_2O (typically, 50 equiv relative to SmI_2; kinetic isotope effect), was added, and the resulting mixture was stirred vigorously. After the workup as described above, the amount of each species was determined by ^{1}H NMR analysis (500 MHz, $CDCl_3$).

General Procedure I. Determination of Chemoselectivity in Reductions Mediated by $SmI_2(H_2O)_n$. To a preformed solution of $SmI_2(H_2O)_n$ prepared as described above (THF solution) was added a solution of an equimolar mixture of substrates (each 0.10 mmol, 1.0 mL in THF) at room temperature under argon atmosphere, and the mixture was stirred vigorously. After the specified time, the reaction was quenched by bubbling air through the reaction mixture until decolorization had occurred. After the workup as described above, the sample was analyzed by GC−MS and ^{1}H NMR to obtain product distribution using internal standard.

General Procedure J. Reduction of Aromatic Hydrocarbons using $SmI_2/Et_3N/H_2O$ Complexes. To a substrate (1 equiv, neat or as a solution in THF) was added samarium(II) iodide (THF solution, typically 3 equiv), followed by amine (typically, 24 equiv) and water (typically, 24 equiv) under argon at room temperature, and the resulting solution was stirred vigorously. Workup and analysis as described above for reductions mediated by $SmI_2(H_2O)_n$ complexes.

General Procedure K. Reduction of Aromatic Hydrocarbons using Na(silica). An oven-dried vial equipped with a Teflon-coated magnetic stir bar was charged with Na(silica) (0.63 mmol, 2.5 equiv) and placed under a positive pressure of argon. A solution of substrate (0.25 mmol, 1 equiv) in THF (3.3 mL) was added, and the resulting mixture was vigorously stirred for 5 h, followed by quenching with H_2O (3.0 mL) or D_2O (3.0 mL). Workup and analysis as described above for reductions mediated by $SmI_2(H_2O)_n$ complexes.

General Procedure L. Preparation of $SmBr_2$ from 1,1,2,2-Tetrabromoethane and its Reactivity with Aromatic Hydrocarbons. An oven-dried vial equipped with a Teflon-coated magnetic stir bar was charged with samarium metal (0.75 g, 5.0 mmol, 1.0 equiv), followed by THF (10 mL) and 1,1,2,2,-tetrabromoethane (0.865 g, 2.5 mmol, 0.5 equiv) under a positive pressure of argon at room temperature. After the reaction mixture was stirred for 3−6 h, the color of the solution turned purple reminiscent of the color of $SmBr_2$ obtained from the reaction between SmI_2 and LiBr. A solution of substrate (0.30 g, 1.67 mmol, 0.33 equiv) in THF (5 mL) was added, and the resulting mixture was stirred for the indicated time. Workup and analysis as described above for reductions mediated by $SmI_2(H_2O)_n$ complexes.

Additional Experimental Procedures for Reductions Mediated by $SmI_2(H_2O)_n$ Complex. Competition Experiments on the Origin of Selectivity in the Reduction of 9-Anthracenecarboxylic Acid. According to the general procedure I, anthracene-9-carboxylic acid or methyl anthracene-9-carboxylate (0.10 mmol) and benzoic acid or methyl benzoate (0.10 mmol) were reacted with samarium(II) iodide (1 equiv) and water (50 equiv relative to SmI_2). Decolorization to transparent occurred in the course of addition of substrates to $SmI_2(H_2O)_n$ complex. After the workup as described above, the sample was analyzed by GC−MS and ^{1}H NMR to obtain product distribution using an internal standard. *Run A.* Anthracene-9-carboxylic acid:9,10-dihydroanthracene-9-carboxylic acid = 53:47, combined yield = 99%; benzoic acid:benzyl alcohol >98:2, combined yield >99%. *Run B.* Methyl anthracene-9-carboxylate:methyl 9,10-dihydroanthracene-9-carboxylate = 57:43, combined yield = 96%; methyl benzoate:benzyl alcohol >98:2, combined yield >99%.

Control Reactions to the Origin of Selectivity in the Reduction of 9-Anthracenecarboxylic Acid. According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, (preformed complex), anthracene-9-carboxylic acid, methyl anthracene-9-carboxylate, benzoic acid, and methyl benzoate were reacted in separate vials with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) for 30 s, followed by rapid quenching with oxygen to yield yellow solutions. After the workup as described above, the samples were analyzed by GC−MS and ^{1}H NMR to obtain product distribution using internal standard. *Run A.* 9,10-Dihydroanthracene-9-carboxylic acid: >95% conversion, 99% yield. *Run B.* Methyl 9,10-dihydroanthracene-9-carboxylate: >95% conversion, 99% yield. *Run C.* Benzoic acid: 69% conversion, 68% yield. *Run D.* Methyl benzoate: 71% conversion, 66% yield.

Relative Rates of the Reduction of *E*- and *Z*-Stilbene. According to the general procedure I, *trans*-stilbene (0.10 mmol) and *cis*-stilbene (0.10 mmol) were reacted with samarium(II) iodide (1 equiv) and water (50 equiv relative to SmI_2) for 2 h. After the workup as described above, the sample was analyzed by ^{1}H NMR to obtain product distribution using internal standard. Relative reactivity values were determined based on the recovered starting material. *Run 1. cis*-Stilbene 91.7%, *trans*-stilbene 69.2%, bibenzyl 39.1%, k_E/k_Z = 3.71. *Run 2. cis*-Stilbene 91.8%, *trans*-stilbene 72.4%, bibenzyl 35.8%, k_E/k_Z = 3.37. Average k_E/k_Z = 3.54.

Competition Experiments on the Chemoselectivity in Birch Reductions of Aromatic Hydrocarbons. According to the general procedure I, anthracene (0.10 mmol) and naphthalene, 1-chlorotetradecane, or bromobenzene (0.10 mmol) were reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) for 1 h at room temperature. After the workup as described above, the sample was analyzed by GC−MS to obtain yield and product distribution using dodecane as internal standard.

Experiments with Other SET Reductants. ***A. SmI_2–Et_3N–H_2O System.*** According to the general procedure J, *trans*-stilbene (0.10 mmol) or 9,10-diphenylanthracene (0.05 mmol) were reacted with samarium(II) iodide (3 equiv), triethylamine (24 equiv), and deuterium oxide (24 equiv relative to substrate) or water (24 equiv relative to substrate), respectively, for 1 h at room temperature. After the workup as described above, the sample was analyzed by ^{1}H NMR to obtain product distribution and deuterium incorporation using internal standard. *Run A.* 1,2-D_2-1,2-Diphenylethane: yield 86%, >98% D_2 incorporation. *Run B.* 9,10-Diphenyl-9,10-dihydroanthracene: yield 82%, *trans*:*cis* = 79:21.

B. Na(silica). According to the general procedure K, *trans*-stilbene (0.25 mmol) or 9,10-diphenylanthracene (0.25 mmol) were reacted with Na(silica) (2.5 equiv) in 3.3 mL of THF for 5 h at room temperature. The reactions were quenched with 3.0 mL of deuterium oxide (*trans*-stilbene) or water (9,10-diphenylanthracene). After the workup as described above, the sample was analyzed by ^{1}H NMR to obtain product distribution and deuterium incorporation using an internal standard. *Run A.* 1,2-D_2-1,2-Diphenylethane: yield: 93%, 73.5% D_2 incorporation. *Run B.* 9,10-Diphenyl-9,10-dihydroanthracene: yield 98%, *trans*:*cis* = 65:35.

Characterization Data. *N,N*-Diethylanthracene-9-carboxamide. Prepared according to the reported procedure.[58] Spectroscopic properties were consistent with literature values. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.2 Hz, 3 H), 1.52 (t, *J* = 7.2 Hz, 3 H), 3.02 (q, *J* = 7.2 Hz, 2 H), 3.88 (q, *J* = 7.2 Hz, 2 H), 7.44−7.54 (m, 4 H), 7.91−8.03 (m, 4 H), 8.44 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 14.2, 39.2, 43.2, 125.0, 125.6, 126.6, 127.4, 127.6, 128.6, 131.3, 131.6, 169.6.

Methyl Anthracene-9-carboxylate. Prepared according to the reported procedure.[59] Spectroscopic properties were consistent with literature values. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.11 (s, 3 H), 7.39−7.51 (m, 4 H), 7.93−7.98 (m, 4 H), 8.47 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.6, 125.0, 125.5, 127.0, 127.8, 128.5, 128.6, 129.5, 131.0, 170.1.

9,10-Dihydroanthracene (Table 11, entry 1). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, anthracene (1 mmol) was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 96% (172 mg) isolated after purification by column chromatography (2% ethyl acetate/hexanes) and recrystallization from ethanol. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 4 H), 7.07−7.11 (m, 4 H), 7.16−7.20 (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.3, 126.2, 127.5, 136.8.

9-Methyl-9,10-dihydroanthracene (Table 11, entry 2). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, 9-methylanthracene was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, *J* = 7.5 Hz, 3 H), 3.81 (d, *J* = 18.4 Hz, 1 H), 3.97 (q, J = 7.2 Hz, 1 H), 4.05 (d, *J* = 18.4 Hz, 1 H), 7.08−7.17 (m, 4 H), 7.19−7.24 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5, 35.2, 41.1, 126.0, 126.4, 126.9, 127.7, 135.8, 141.8.

***trans*-9,10-Diphenyl-9,10-dihydroanthracene (Table 11, entry 3).** According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, 9,10-diphenylanthracene was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 98%; dr > 98:2 determined by ^{1}H NMR analysis of the crude reaction mixture. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.24 (s, 2 H), 6.97−7.00 (m, 4 H), 7.04−7.09 (m, 6 h), 7.11−7.14 (m, 4 H), 7.15−7.18 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.0, 126.1, 126.5, 128.2, 129.2, 129.3, 138.5, 144.4. Dr was measured by comparison with an authentic sample of *cis*-9,10-Diphenyl-9,10-dihydroanthracene obtained by the reduction of 9,10-diphenylanthracene with Na(silica) in THF (*trans*/*cis* = 65:35). *cis*-9,10-Diphenyl-9,10-dihydroanthracene (diagnostic peaks only): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (s, 2 H), 7.02−7.08 (m, 12 H), 7.13−7.17 (m, 2 H), 7.20−7.24 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.4, 126.5, 126.6, 128.5, 128.6, 129.4, 139.3, 143.8.

5,12-Dihydrotetracene (Table 11, entry 4). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, tetracene was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Conversion: >98% determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (s, 4 H), 7.12−7.16 (m, 2 H), 7.25−7.28 (m, 2 H), 7.32−7.37 (m, 2 H), 7.69 (s, 2 H), 7.69−7.74 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.8, 125.2, 125.3, 126.3, 127.2, 127.3, 132.4, 135.7, 137.1.

1,2-Diphenylethane (Table 11, entry 5). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, *trans*-stilbene was reacted with samarium(II) iodide (3 equiv) and water (100 equiv relative to SmI_2) to give the title product. Yield: 72% (two iterations). Note that the reaction using 3 equiv of SmI_2 and 50 equiv of water relative to SmI_2 afforded the title product in 62% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.10 (s, 4 H), 7.31−7.40 (m, 6 H), 7.41−7.49 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.2, 126.1, 128.5, 128.6, 141.9.

Ethane-1,1,2-triyltribenzene (Table 11, entry 6). According to the general procedure J for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, triphenylethylene was reacted with samarium(II) iodide (3 equiv), triethylamine (24 equiv), and water (24 equiv relative to substrate) to give the title product. Yield: 97%. Note that the reaction using SmI_2 (3 equiv) and water (50 equiv relative to SmI_2) afforded the title product in 34% yield, consistent with the redox potential of this substrate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.28 (d, J = 7.8 Hz, 2 H), 4.16 (t, J = 7.8 Hz, 1 H), 6.90−6.95 (m, 2 H), 7.01−7.20 (m, 13 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.1, 53.1, 125.9, 126.2, 128.1, 128.4, 129.1, 140.3, 144.5.

9-Methyl-9,10-dihydroanthracene (Table 11, entry 7). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, 9-(chloromethyl)anthracene was reacted with samarium(II) iodide (5 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, J = 7.2 Hz, 3 H), 3.81 (d, J = 18.4 Hz, 1 H), 3.97 (q, J = 7.2 Hz, 1 H), 4.05 (d, J = 18.4 Hz, 1 H), 7.08−7.17 (m, J = 4 H), 7.19−7.24 (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.5, 35.2, 41.1, 126.0, 126.4, 126.9, 127.7, 135.8, 141.8.

9,10-Dihydroanthracene-9-carboxylic Acid (Table 11, entry 8). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, anthracene-9-carboxylic acid was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 94%. Note that the reaction using large excess of SmI_2 (10 equiv) and water (50 equiv relative to SmI_2) afforded the title product in quantitative yield. Over-reduction was not observed. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (d, J = 18.3 Hz, 1 H), 4.28 (d, J = 18.3 Hz, 1 H), 4.96 (s, 1 H), 7.21−7.41 (m, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.6, 52.5, 126.5, 127.7, 128.1, 128.4, 133.0, 136.6, 177.3.

Methyl 9,10-Dihydroanthracene-9-carboxylate (Table 11, entry 9). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, methyl anthracene-9-carboxylate was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 99%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.52 (s, 3 H), 3.83 (d, J = 18.0 Hz, 1 H), 4.25 (d, J = 18.5 Hz, 1 H), 4.94 (s, 1 H), 7.15−7.22 (m, 4 H), 7.27 (d, J = 7.5 Hz, 2 H), 7.32 (dd, J = 1.5, 7.5 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.7, 52.4, 52.9, 126.4, 127.5, 128.1, 128.3, 133.7, 136.7, 172.4.

***N,N*-Diethyl-9,10-dihydroanthracene-9-carboxamide (Table 11, entry 12).** According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, *N,N*-diethylanthracene-9-carboxamide was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 98%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97 (t, J = 7.5 Hz, 3 H), 1.02 (t, J = 7.0 Hz, 3 H), 2.27−2.35 (m, 4 H), 3.89 (dd, J = 1.5, 18.5 Hz, 1 H), 4.37 (d, J = 18.5 Hz, 1 H), 5.20 (s, 1 H), 7.11−7.18 (m, 4 H), 7.21 (d, J = 7.5 Hz, 2 H), 7.25 (d, J = 7.0 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.8, 14.2, 35.5, 40.3, 42.4, 49.8, 126.3, 127.0, 127.1, 128.4, 134.9, 135.8, 172.2.

9,10-D_2-9,10-Dihydroanthracene (Scheme 1). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, anthracene was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 96%, >98% D_2 incorporation as determined by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 2 H), 7.10−7.14 (m, 4 H), 7.20−7.24 (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.8 (t, J^1 = 19.9 Hz), 126.1, 127.4, 136.7.

1,2-D_2-1,2-Diphenylethane (Scheme 2). According to the general procedure F for the reduction of aromatic hydrocarbons using $SmI_2(H_2O)_n$, *trans*-stilbene was reacted with samarium(II) iodide (3 equiv) and water (50 equiv relative to SmI_2) to give the title product. Yield: 47%, >98% D_2 incorporation as determined by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.82 (s, 2 H), 7.10−7.14 (m, 6 H), 7.19−7.23 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.5 (t, J^1 = 19.0 Hz), 125.9, 128.3, 128.5, 141.8.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Namy, J. L.; Girard, P.; Kagan, H. B. *Nouv. J. Chim.* **1977**, *1*, 5. (b) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. (c) Namy, J. L.; Girard, P.; Kagan, H. B.; Caro, P. E. *Nouv. J. Chim.* **1981**, *5*, 479.

(2) Procter, D. J.; Flowers, R. A. II; Skrydstrup, T. *Organic Synthesis Using Samarium Diiodide: A Practical Guide*; RSC Publishing: Cambridge: 2009.

(3) For general reviews on SmI_2, see: (a) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573. (b) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351. (c) Gopalaiah, K.; Kagan, H. B. *New J. Chem.* **2008**, *32*, 607. (d) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (e) Molander, G. A. *Org. React.* **1994**, *46*, 211. (f) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. (g) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321. (h) Krief, A.; Laval, A. M. *Chem. Rev.* **1999**, *99*, 745. (i) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727. (j) Skrydstrup, T. *Angew. Chem., Int. Ed.* **1997**, *36*, 345. (k) Concellón, J. M.; Rodríguez-Solla, H. *Chem. Soc. Rev.* **2004**, *33*, 599. (l) Concellón, J. M.; Rodríguez-Solla, H.; Concellón, C.; del Amo, V. *Chem. Soc. Rev.* **2010**, *39*, 4103. (m) Beemelmanns, C.; Reissig, H. U. *Chem. Soc. Rev.* **2011**, *40*, 2199. (n) Edmonds, D. J.; Johnston, D.; Procter, D. J. *Chem. Rev.* **2004**, *104*, 3371. (o) Nicolaou, K. C.; Ellery, S. P.; Chen, J. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 7140. (p) Szostak, M.; Procter, D. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7737. (q) Sautier, B.; Procter, D. J. *Chimia* **2012**, *66*, 399. (r) Berndt, M.; Gross, S.; Hölemann, A.; Reissig, H. U. *Synlett* **2004**, 422. (s) Szostak, M.; Spain, M.; Procter, D. J. *Chem. Soc. Rev.* **2013**, *42*, 9155.

(4) For reviews on metal-mediated radical reactions, see: (a) Trost, B. M.; Fleming, I. *Comprehensive Organic Synthesis*; Pergamon Press: New York, 1991. (b) Gansäuer, A.; Bluhm, H. *Chem. Rev.* **2000**, *100*, 2771. (c) Gansäuer, A. *Radicals in Synthesis I and II*. In *Topics in Current Chemistry*; Springer-Verlag: Berlin, 2006; Vol. *263−264*. (d) Szostak, M.; Procter, D. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 9238. (e) Streuff, J. *Synthesis* **2013**, *45*, 281.

(5) For reviews on the influence of additives on properties of SmI_2, see: (a) Kagan, H. B.; Namy, J. L., *Lanthanides: Chemistry and Use in Organic Synthesis*; Kobayashi, S., Ed.; Springer: New York: 1999; pp 155. (b) Dahlén, A.; Hilmersson, G. *Eur. J. Inorg. Chem.* **2004**, 3393. (c) Flowers, R. A., II *Synlett* **2008**, 1427.

(6) Szostak, M.; Spain, M.; Parmar, D.; Procter, D. J. *Chem. Commun.* **2012**, *48*, 330. See also refs 5b and 5c.

(7) (a) Chopade, P. R.; Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2004**, *126*, 44. (b) Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2005**, *127*, 18093. (c) Sadasivam, D. V.; Teprovich, J. A., Jr.; Procter, D. J.; Flowers, R. A., II *Org. Lett.* **2010**, *12*, 4140. See also: (d) Teprovich, J. A., Jr.; Balili, M. N.; Pintauer, T.; Flowers, R. A., II *Angew. Chem., Int. Ed.* **2007**, *46*, 8160.

(8) (a) Renaud, P.; Sibi, M. *Radicals in Organic Synthesis*; Wiley-VCH: New York, 2001. (b) Chatgilialoglu, C; Studer, A. *Encyclopedia of Radicals in Chemistry, Biology and Materials*; Wiley-Blackwell: New York, 2012.

(9) (a) Shabangi, M.; Flowers, R. A., II *Tetrahedron Lett.* **1997**, *38*, 1137. For selected studies on the mechanism of SmI_2−HMPA-mediated reactions, see: (b) Shabangi, M.; Kuhlman, M. L.; Flowers, R. A., II *Org. Lett.* **1999**, *1*, 2133. (c) Sadasivam, D. V.; Antharjanam, P. K. S.; Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2008**, *130*, 7228. (d) Choquette, K. A.; Sadasivam, D. V.; Flowers, R. A., II *J. Am. Chem. Soc.* **2010**, *132*, 17396.

(10) (a) Enemærke, R. J.; Daasbjerg, K.; Skrydstrup, T. *Chem. Commun.* **1999**, 343. (b) Enemaerke, R. J.; Hertz, T.; Skrydstrup, T.; Daasbjerg, K. *Chem. Eur. J.* **2000**, *6*, 3747.

(11) For selected studies, see: (a) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705. (b) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059. (c) Molander, G. A.; Harris, C. R. *J. Org. Chem.* **1997**, *62*, 2944. (d) Molander, G. A.; Czakó, B.; St. Jean, D. J., Jr. *J. Org. Chem.* **2006**, *71*, 1172. (e) Curran, D. P.; Totleben, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 6050. (f) Rivkin, A.; Nagashima, T.; Curran, D. P. *Org. Lett.* **2003**, *5*, 419. (g) Dinesh, C. U.; Reissig, H. U. *Angew. Chem., Int. Ed.* **1999**, *38*, 789. (h) Hölemann, A.; Reissig, H. U. *Org. Lett.* **2003**, *5*, 1463. (i) Saadi, J.; Lentz, D.; Reissig, H. U. *Org. Lett.* **2009**, *11*, 3334. (j) Beemelmanns, C.; Reissig, H. U. *Angew. Chem., Int. Ed.* **2010**, *49*, 8021. (k) Li, Z.; Nakashige, M.; Chain, W. J. *J. Am. Chem. Soc.* **2011**, *133*, 6553. (l) Masui, H.; Fuse, S.; Takahashi, T. *Org. Lett.* **2012**, *14*, 4090.

(12) (a) Shabangi, M.; Sealy, J. M.; Fuchs, J. R.; Flowers, R. A., II *Tetrahedron Lett.* **1998**, *39*, 4429. (b) Kuhlman, M. L.; Flowers, R. A., II *Tetrahedron Lett.* **2000**, *41*, 8049.

(13) (a) McDonald, C. E.; Ramsey, J. D.; Grant, J. A.; Howerter, K. A. *Tetrahedron Lett.* **2009**, *50*, 5308. (b) McDonald, C. E.; Ramsey, J. D.; Sampsell, D. G.; Butler, J. A.; Cecchini, M. R. *Org. Lett.* **2010**, *12*, 5178. (c) McDonald, C. E.; Ramsey, J. R.; Sampsell, D. G.; Anderson, L. A.; Krebs, J. E.; Smith, S. N. *Tetrahedron Lett.* **2013**, *69*, 2947. (d) Berndt, M.; Hölemann, A.; Niermann, A.; Bentz, C.; Zimmer, R.; Reissig, H. U. *Eur. J. Org. Chem.* **2012**, 1299.

(14) (a) Fuchs, J. R.; Mitchell, M. L.; Shabangi, M.; Flowers, R. A., II *Tetrahedron Lett.* **1997**, *38*, 8157. (b) 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.

(15) Flowers, R. A., II; Prasad, E. *Handbook on the Physics and Chemistry of Rare Earths*; Gschneidner, K. A., Jr., Bünzli, J. C., Pecharsky, V. K., Eds.; Elsevier: Amsterdam, 2006; Vol. *36*, pp 393.

(16) (a) Peltier, H. M.; McMahon, J. P.; Patterson, A. W.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 16018. (b) Asano, Y.; Suzuki, S.; Aoyama, T.; Shimizu, K.; Kajitani, M.; Yokoyama, Y. *Synthesis* **2007**, 1309. (c) Iwasaki, H.; Eguchi, T.; Tsutsui, N.; Ohno, H.; Tanaka, T. *J. Org. Chem.* **2008**, *73*, 7145. (d) Zörb, A.; Brückner, R. *Eur. J. Org. Chem.* **2010**, 4785. (e) Cha, J. Y.; Yeoman, J. T. S.; Reisman, S. E. *J. Am. Chem. Soc.* **2011**, *133*, 14964. (f) Gilles, P.; Py, S. *Org. Lett.* **2012**, *14*, 1042. (g) Yeoman, J. T. S.; Mak, V. W.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 11764.

(17) (a) Link, J. T.; Overman, L. E. *J. Am. Chem. Soc.* **1996**, *118*, 8166. (b) Ready, J. M.; Reisman, S. E.; Hirata, M.; Weiss, M. M.; Tamaki, K.; Ovaska, T. V.; Wood, J. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1270. (c) Reisman, S. E.; Ready, J. M.; Hasuoka, A.; Smith, C. J.; Wood, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 1448. (d) Reisman, S. E.; Ready, J. M.; Weiss, M. M.; Hasuoka, A.; Hirata, M.; Tamaki, K.; Ovaska, T. V.; Smith, C. J.; Wood, J. L. *J. Am. Chem. Soc.* **2008**, *130*, 2087. (e) Hughes, A. D.; Simpkins, N. S. *Synlett* **1998**, 967. (f) Hughes, A. D.; Price, D. A.; Simpkins, N. S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1295. (g) Frebault, F.; Simpkins, N. S.; Fenwick, A. *J. Am. Chem. Soc.* **2009**, *131*, 4214.

(18) (a) Prasad, E.; Knettle, B. W.; Flowers, R. A., II *J. Am. Chem. Soc.* **2004**, *126*, 6891. (b) Prasad, E.; Knettle, B. W.; Flowers, R. A., II *J. Am. Chem. Soc.* **2002**, *124*, 14663.

(19) Knettle, B. W.; Flowers, R. A., II *Org. Lett.* **2001**, *3*, 2321.

(20) Chauvin, Y.; Olivier, H.; Saussine, L. *Inorg. Chim. Acta* **1989**, *161*, 45.

(21) Evans, W. J.; Gonzales, S. L.; Ziller, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 2600.

(22) Fedushkin, I. L.; Bochkarev, M. N.; Dechert, S.; Schumann, H. *Chem. Eur. J.* **2001**, *7*, 3558.

(23) Dahlén, A.; Nilsson, Å.; Hilmersson, G. *J. Org. Chem.* **2006**, *71*, 1576.

(24) Szostak, M.; Spain, M.; Procter, D. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 7237.

(25) (a) Duffy, L. A.; Matsubara, H.; Procter, D. J. *J. Am. Chem. Soc.* **2008**, *130*, 1136. (b) Parmar, D.; Duffy, L. A.; Sadasivam, D. V.; Matsubara, H.; Bradley, P. A.; Flowers, R. A., II; Procter, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 15467. (c) Parmar, D.; Price, K.; Spain, M.; Matsubara, H.; Bradley, P. A.; Procter, D. J. *J. Am. Chem. Soc.* **2011**, *133*, 2418. (d) Parmar, D.; Matsubara, H.; Price, K.; Spain, M.; Procter, D. J. *J. Am. Chem. Soc.* **2012**, *134*, 12751. (e) Szostak, M.; Spain, M.; Choquette, K. A.; Flowers, R. A., II; Procter, D. A. *J. Am. Chem. Soc.* **2013**, *135*, 15702.

(26) (a) Guazzelli, G.; De Grazia, S.; Collins, K. D.; Matsubara, H.; Spain, M.; Procter, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 7214. (b) Collins, K. D.; Oliveira, J. M.; Guazzelli, G.; Sautier, B.; De Grazia, S.; Matsubara, H.; Helliwell, M.; Procter, D. J. *Chem. Eur. J.* **2010**, *16*, 10240. (c) Szostak, M.; Spain, M.; Procter, D. J. *Nat. Protoc.* **2012**, *7*, 970. (d) Sautier, B.; Lyons, S. E.; Webb, M. R.; Procter, D. J. *Org. Lett.* **2012**, *14*, 146. (e) Szostak, M.; Sautier, B.; Spain, M.; Behlendorf, M.; Procter, D. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 12559.

(27) (a) Szostak, M.; Spain, M.; Procter, D. J. *Chem. Commun.* **2011**, *47*, 10254. (b) Szostak, M.; Spain, M.; Procter, D. J. *Org. Lett.* **2012**, *14*, 840. (c) Szostak, M.; Collins, K. D.; Fazakerley, N. J.; Spain, M.; Procter, D. J. *Org. Biomol. Chem.* **2012**, *10*, 5820. (d) Szostak, M.; Sautier, B.; Spain, M.; Procter, D. J. *Org. Lett.* **2014**, *16*, 452. (e) Szostak, M.; Spain, M.; Eberhart, A. J.; Procter, D. J. *J. Am. Chem. Soc.* **2014**, *136*, 2268. (f) Szostak, M.; Spain, M.; Procter, D. J. *Chem. Eur. J.* **2014**, DOI: 10.1002/chem.201400295.

(28) For selected recent applications of $SmI_2(H_2O)_n$ from other groups, see: (a) Jensen, C. M.; Lindsay, K. B.; Taaning, R. H.; Karaffa, J.; Hansen, A. M.; Skrydstrup, T. *J. Am. Chem. Soc.* **2005**, *127*, 6544. (b) Hansen, A. M.; Lindsay, K. B.; Antharjanam, P. K. S.; Karaffa, J.; Daasbjerg, K.; Flowers, R. A., II; Skrydstrup, T. *J. Am. Chem. Soc.* **2006**, *128*, 9616. (c) Taaning, R. H.; Lindsay, K. B.; Schiøtt, B.; Daasbjerg, K.; Skrydstrup, T. *J. Am. Chem. Soc.* **2009**, *131*, 10253. (d) Masson, G.; Cividino, P.; Py, S.; Vallée, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 2265. (e) Cividino, P.; Py, S.; Delair, P.; Greene, A. E. *J. Org. Chem.* **2007**, *72*, 485. (f) Burchak, O. N.; Philouze, C.; Chavant, P. Y.; Py, S. *Org. Lett.* **2008**, *10*, 3021. (g) Desvergnes, S.; Py, S.; Vallée, Y. *J. Org. Chem.* **2005**, *70*, 1459. (h) Masson, G.; Philouze, C.; Py, S. *Org. Biomol. Chem.* **2005**, *3*, 2067. (i) Mai, C. K.; Sammons, M. F.; Sammakia, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 2397. (j) Phillips, E. M.; Roberts, J. M.; Scheidt, K. *Org. Lett.* **2010**, *12*, 2830. (k) Wenderski, T. A.; Huang, S.; Pettus, T. R. R. *J. Org. Chem.* **2009**, *74*, 4104. (l) Concellón, J. M.; Bernad, P. L.; Rodríguez-Solla, H. *Angew. Chem., Int. Ed.* **2001**, *40*, 3897. (m) Davies, S. G.; Rodríguez-Solla, H.; Tamayo, J. A.; Garner, A. C.; Smith, A. D. *Chem. Commun.* **2004**, 2502. (n) Davies, S. G.; Rodríguez-Solla, H.; Tamayo, J. A.; Cowley, A. R.; Concellón, C.; Garner, A. C.; Parkes, A. L.; Smith, A. D. *Org. Biomol. Chem.* **2005**, *3*, 1435. (o) Dahlén, A.; Hilmersson, G.; Knettle, B. W.; Flowers, R. A., II *J. Org. Chem.* **2003**, *68*, 4870. (p) Dahlén, A.; Hilmersson, G. *J. Am. Chem. Soc.* **2005**, *127*, 8340. (q) Wettergren, J.; Ankner, T.; Hilmersson, G. *Chem. Comm* **2010**, *46*, 7596.

(29) (a) Yacovan, A.; Bilkis, I.; Hoz, S. *J. Am. Chem. Soc.* **1996**, *118*, 261. (b) Tarnopolsky, A.; Hoz, S. *J. Am. Chem. Soc.* **2007**, *129*, 3402. (c) Amiel-Levy, M.; Hoz, S. *J. Am. Chem. Soc.* **2009**, *131*, 8280. (d) Upadhyay, S. K.; Hoz, S. *J. Org. Chem.* **2011**, *76*, 1355. (e) Tarnopolsky, A.; Hoz, S. *Org. Biomol. Chem.* **2007**, *5*, 3801. (f) Farran, H.; Hoz, S. *J. Org. Chem.* **2009**, *74*, 2075. (g) Kleiner, G.; Tarnopolsky, A.; Hoz, S. *Org. Lett.* **2005**, *7*, 4197.

(30) (a) Belotti, D.; Cossy, J.; Pete, J. P.; Portella, C. *J. Org. Chem.* **1986**, *51*, 4196. (b) Miyazaki, T.; Maekawa, H.; Yonemura, K.; Yamamoto, Y.; Yamanaka, Y.; Nishiguchi, I. *Tetrahedron* **2011**, *67*, 1598. For a recent theoretical study on SmI_2-mediated reactions of ketones, see: (c) Kefalidis, C. E.; Perrin, L.; Maron, L. *Eur. J. Inorg. Chem.* **2013**, 4042.

(31) Farran, H.; Hoz, S. *Org. Lett.* **2008**, *10*, 4875.
(32) (a) Tsuruta, H.; Yamaguchi, K.; Imamoto, T. *Chem. Commun.* **1999**, 1703. (b) Tsuruta, H.; Yamaguchi, K.; Imamoto, T. *Tetrahedron* **2003**, *59*, 10419.
(33) (a) Rabideau, P. W.; Marcinow, Z. *Org. React.* **1992**, *42*, 1. (b) Mander, L. N. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. *8*, pp 489. (c) Donohoe, T. J.; Garg, R.; Stevenson, C. A. *Tetrahedron: Asymmetry* **1996**, *7*, 317.
(34) (a) Chami, Z.; Gareil, M.; Pinson, J.; Saveant, J. M.; Thiebault, A. *J. Org. Chem.* **1991**, *56*, 586. (b) Barber, J. J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 239. (c) Loffredo, D. M.; Swartz, J. E.; Kariv-Miller, E. *J. Org. Chem.* **1989**, *54*, 5953. (d) Andrieux, C. P.; Gallardo, I.; Saveant, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 1620. (e) Hoshi, N.; Sasaki, K.; Hashimoto, S.; Hori, Y. *J. Electroanal. Chem.* **2004**, *568*, 267. (f) Lin, C. Y.; Coote, M. L.; Gennaro, A.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2008**, *130*, 12762.
(35) For a detailed study on preparation of SmI_2, see: (a) Szostak, M.; Spain, M.; Procter, D. J. *J. Org. Chem.* **2012**, *77*, 3049. For other methods of preparation of SmI_2, see: (b) Imamoto, T.; Ono, M. *Chem. Lett.* **1987**, 501. (c) Concellón, J. M.; Rodríguez-Solla, H.; Bardales, E.; Huerta, M. *Eur. J. Org. Chem.* **2003**, 1775. (d) Dahlén, A.; Hilmersson, G. *Eur. J. Inorg. Chem.* **2004**, 3020. (e) Teprovich, J. A., Jr.; Antharjanam, P. K. S.; Prasad, E.; Pesciotta, E. N.; Flowers, R. A., II *Eur. J. Inorg. Chem.* **2008**, 5015.
(36) Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2002**, *124*, 6357.
(37) Bochkarev, M. N.; Fagin, A. A.; Khoroshenkov, G. V. *Russ. Chem. Bull., Int. Ed.* **2002**, *51*, 1909.
(38) Simmons, E. M.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2012**, *51*, 3066.
(39) (a) Cotton, S. *Lanthanide and Actinide Chemistry*; John Wiley & Sons Ltd: Chichester, 2006. (b) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*, Wiley: New York, 2009. (c) Hartwig, J. F. *Organotransition Metal Chemisty: From Bonding to Catalysis*, University Science Books: Herndon, 2010.
(40) Corey, E. J.; Zheng, G. Z. *Tetrahedron Lett.* **1997**, *38*, 2045.
(41) (a) Shriver, D. F.; Drezdzon, M. A. *The Manipulation of Air-Sensitive Compounds*, John Wiley & Sons: New York, 1986. (b) Fürstner, A. *Active Metals. Preparation, Characterization, Applications*; VCH: Weinheim, 1996. For practical procedures on drying of organic solvents, see: (c) Williams, D. B. G.; Lawton, M. *J. Org. Chem.* **2010**, *75*, 8351.
(42) (a) Note that H_2O has been used as a *proton donor* in conjunction with $SmBr_2$ and $SmCl_2$. See refs 16a. and 16f. Matsukawa reported preparation of $SmCl_2$-type reagent in H_2O: (b) Matsukawa, S.; Hinakubo, Y. *Org. Lett.* **2003**, *5*, 1221. (c) Matsukawa, S.; Ichikawa, K.; Ogura, Y. *Synth. Commun.* **2010**, *40*, 1345.
(43) For an excellent perspective on recent advances in the chemistry of highly reducing non-classical lanthanides(II), see: Evans, W. J. *Inorg. Chem.* **2007**, *46*, 3435.
(44) Nief, F. *Handbook on the Physics and Chemistry of Rare Earths*; Gschneidner, K. A., Jr., Bünzli, J. C.; Pecharsky, V. K., Eds.; Elsevier: Amsterdam, 2010; Vol. *40*, pp 241.
(45) Träff, A. M.; Janjetovic, M.; Ta, L.; Hilmersson, G. *Angew. Chem., Int. Ed.* **2013**, *52*, 12073.
(46) (a) Hélion, F.; Lannou, M. I.; Namy, J. L. *Tetrahedron Lett.* **2003**, *44*, 5507. For synthesis of $SmBr_2$ and $SmCl_2$ by reduction of the corresponding SmX_3 salts, see: (b) Lebrun, A.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1993**, *34*, 2311. (c) Rossmanith, K. *Monatsh. Chem.* **1979**, *110*, 109.
(47) (a) Donohoe, T. J.; House, D. *J. Org. Chem.* **2002**, *67*, 5015. (b) Donohoe, T. J.; Johnson, D.; Mace, L. H.; Ichihara, O.; Bamford, M. *Org. Lett.* **2005**, *7*, 453. (c) Donohoe, T. J.; Sintim, H. O.; Sisangia, L.; Ace, K. W.; Guyo, P. M.; Cowley, A.; Harling, J. D. *Chem. Eur. J.* **2005**, *11*, 4227. (d) Donohoe, T. J.; Johnson, D. J.; Mace, L. H.; Thomas, R. E.; Chiu, J. Y. K.; Rodrigues, J. S.; Compton, R. G.; Banks, C. E.; Tomcik, P.; Bamford, M. J.; Ichihara, O. *Org. Biomol. Chem.* **2006**, *4*, 1071. (e) Donohoe, T. J.; Thomas, R. E. *Nat. Protoc.* **2007**, *2*, 1888.
(48) (a) Nandi, P.; Dye, J. L.; Jackson, J. E. *J. Org. Chem.* **2009**, *74*, 5790. For other recent applications of alkali metals in silica, see: (b) Constanzo, M. J.; Patel, M. N.; Petersen, K. A.; Vogt, P. F. *Tetrahedron Lett.* **2009**, *50*, 5463. (c) Bodnar, B. S.; Vogt, P. F. *J. Org. Chem.* **2009**, *74*, 2598. (d) Nandi, P.; Dye, J. L.; Bentley, P.; Jackson, J. E. *Org. Lett.* **2009**, *11*, 1689. (e) Nandi, P.; Redko, M. Y.; Petersen, K.; Dye, J. L.; Lefenfeld, M.; Vogt, P. F.; Jackson, J. E. *Org. Lett.* **2008**, *10*, 5441.
(49) (a) Evans, W. J.; Allen, N. T.; Ziller, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11749. (b) Evans, W. J.; Workman, P. S.; Allen, N. T. *Org. Lett.* **2003**, *5*, 2041. (c) Garst, M. E.; Dolby, L. J.; Esfandiari, S.; Fedoruk, N. A.; Chamberlain, N. C.; Avey, A. A. *J. Org. Chem.* **2000**, *65*, 7098. (d) Schultz, A. G. *Chem. Commun.* **1999**, 1263. (e) Findlay, N. J.; Park, S. R.; Schoenebeck, F.; Cahard, E.; Zhou, S.; Berlouis, L. E. A.; Spicer, M. D.; Tuttle, T.; Murphy, J. A. *J. Am. Chem. Soc.* **2010**, *132*, 15462. (f) Cahard, E.; Schoenebeck, F.; Garnier, J.; Cutulic, S. P. Y.; Zhou, S.; Murphy, J. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 3673. (g) Doni, E.; Mondal, B.; O'Sullivan, S.; Tuttle, T.; Murphy, J. A. *J. Am. Chem. Soc.* **2013**, *135*, 10934.
(50) Aryl carboxylic acid derivatives have been reported to undergo facile reduction with $SmI_2(H_2O)_n$: (a) Kamochi, Y.; Kudo, T. *Chem. Lett.* **1993**, 1495. (b) Kamochi, Y.; Kudo, T. *Chem. Lett.* **1991**, 893.
(51) Cleavage of benzylic heteroatoms with SmI_2 has been reported: Ankner, T.; Hilmersson, G. *Tetrahedron* **2009**, *65*, 10856.
(52) Birch, A. J.; Slobbe, J. *Heterocycles* **1976**, *5*, 905.
(53) Kamochi, Y.; Kudo, T. *Heterocycles* **1993**, *36*, 2383.
(54) (a) Zimmerman, H. E. *Acc. Chem. Res.* **2012**, *45*, 164. (b) Krapcho, A. P.; Bothner-By, A. A. *J. Am. Chem. Soc.* **1959**, *81*, 3658. (c) Greenfield, A.; Schindewolf, U. *Ber. Bunsenges. Phys. Chem.* **1998**, *102*, 1808.
(55) Solutions of SmI_2 (0.10 M in THF) are available commercially.
(56) For a recent impressive application of SmI_2 on 1.27 kg scale in a commercial synthesis of Halaven®, a novel anticancer drug, see: Austad, B. C.; Calkins, T. L.; Chase, C. E.; Fang, F. G.; Horstmann, T. E.; Hu, Y.; Lewis, B. M.; Niu, X.; Noland, T. A.; Orr, J. D.; Schnaderbeck, M. J.; Zhang, H.; Asakawa, N.; Asai, N.; Chiba, H.; Hasebe, T.; Hoshino, Y.; Ishizuka, H.; Kajima, T.; Kayano, A.; Komatsu, Y.; Kubota, M.; Kuroda, H.; Miyazawa, M.; Tagami, K.; Watanabe, T. *Synlett* **2013**, *24*, 333.
(57) HMPA has been reported to cause cancer in laboratory animals: (a) World Health Organization, International Agency for Research on Cancer, *IARC Monogr.* **1999**, *71*, 1465. (b) Dykstra, R. R. Hexamethylphosphoric Triamide, *e-EROS Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons: New York, 2001. (c) Ashby, J.; Styles, J. A.; Anderson, D. *Br. J. Cancer* **1977**, *36*, 564. (d) Keller, D. A.; Marshall, C. E.; Lee, K. P. *Fundam. Appl. Toxicol.* **1997**, *40*, 15.
(58) Gryff-Keller, A.; Terpinski, J.; Zajaczkowska-Terpinska, E. *J. Chem. Res., Synop.* **1984**, 330.
(59) Parish, R. C.; Stock, L. M. *J. Org. Chem.* **1965**, *30*, 927.