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Preparation of Samarium(II) Iodide: Quantitative Evaluation of the Effect of Water, Oxygen, and Peroxide Content, Preparative Methods, and the Activation of Samarium Metal

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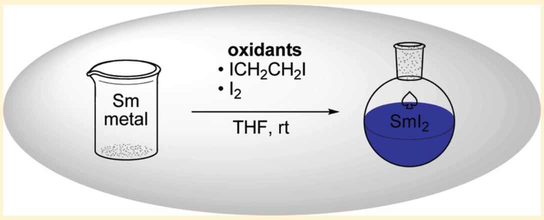
Supporting Information

ABSTRACT: Samarium(II) iodide (SmI_2) is one of the most important reducing agents in organic synthesis. Synthetic chemistry promoted by SmI_2 depends on the efficient and reliable preparation of the reagent. Unfortunately, users can experience difficulties preparing the reagent, and this has prevented realization of the full synthetic potential of SmI_2. To provide synthetic chemists with general and reliable methods for the preparation of SmI_2, a systematic evaluation of the factors involved in its synthesis has been carried out. Our studies confirm that SmI_2 is a user-friendly reagent. Factors such as water, oxygen, and peroxide content in THF have little influence on the synthesis of SmI_2. In addition, the use of specialized glovebox equipment or Schlenk techniques is not required for the preparation of SmI_2. However, our studies suggest that the quality of samarium metal is an important factor and that the use of low quality metal is the main cause of failed preparations of the reagent. Accordingly, we report a straightforward method for activation of "inactive" samarium metal and demonstrate the broad utility of this protocol through the electron transfer reductions of a range of substrates using SmI_2 prepared from otherwise "inactive" metal. An investigation into the stability of SmI_2 solutions and an evaluation of commercially available solutions of the reagent is also reported.

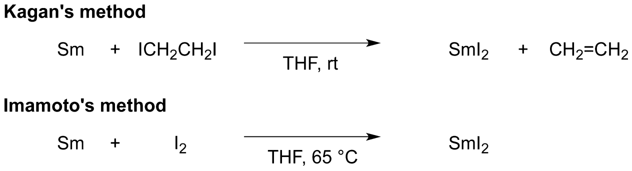


INTRODUCTION

Samarium(II) iodide (SmI_2) is one of the most important reducing agents available in the laboratory. Since its introduction to synthetic chemistry by Kagan in 1977,[1] functional group transformations and C−C bond-forming reactions mediated by SmI_2 have ranked among the most useful tools available to organic chemists.[2] These processes proceed through either one-electron or two-electron pathways or sequences involving both modes of activation and have been extensively used in new synthetic strategies, natural product synthesis, and cascade reactions.[3,4] Many SmI_2-mediated transformations proceed with exquisite control of structure and stereochemistry to furnish bond disconnections impossible to achieve with other reagents. An important feature of SmI_2 is the ability to tune its properties through the use of appropriate additives.[5,6] However, to fully exploit the versatility of SmI_2, laboratories involved in synthetic chemistry require efficient and reliable methods for its preparation.

As first reported by Kagan, SmI_2 can be conveniently prepared by the reaction of samarium metal with 1,2-diiodoethane in THF (Scheme 1).[1] This procedure is typically carried out using carefully dried and deoxygenated solvents and strict Schlenk or glovebox techniques. Several years after Kagan's seminal work, Imamoto described a more atom-economical method for the synthesis of SmI_2 using samarium metal and iodine as the oxidant in refluxing THF (Scheme 1).[7] However, the detailed mechanism for the formation of SmI_2 using this method has not been elucidated. The methods of Kagan and Imamoto are the two most common protocols used for the preparation of SmI_2 for organic chemistry applications.

Scheme 1. Synthesis of SmI_2 Using 1,2-Diiodoethane (Kagan's Method) and Iodine (Imamoto's Method)



Several other methods for the preparation of SmI_2 have been reported and are shown in Scheme 2. Kagan reported the use of diiodobutane or diiodomethane as oxidants (the latter method was subsequently popularized in elegant studies by Molander);[8] Ishii described the preparation of a SmI_2 equivalent from samarium metal, TMSCl and NaI;[9] Concellón found that sonication of samarium metal and iodoform at room temperature gave SmI_2 in THF after short reaction times;[10] Flowers utilized high intensity ultrasound to synthesize SmI_2 from samarium metal and iodine in a wide range of solvents;[11] and finally, Hilmersson reported a rapid synthesis of SmI_2 using iodine and microwave heating.[12] These new procedures have yet to experience the widespread take-up associated with the original Kagan and Imamoto methods.[13] The development of

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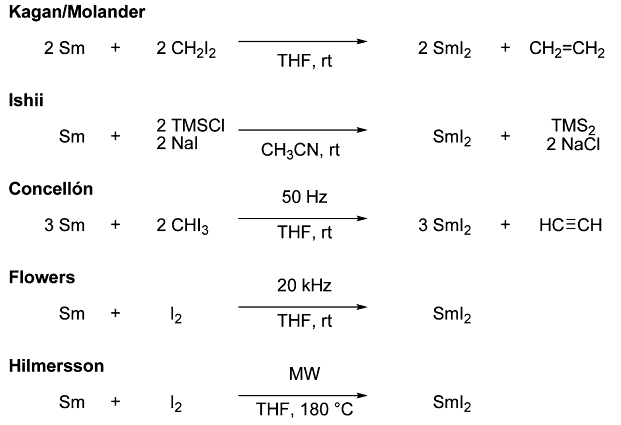
Scheme 2. Additional Procedures for the Synthesis of SmI_2



new methods for the preparation of SmI_2 by groups working in the area suggests that a "foolproof" protocol for the synthesis of the reagent is not yet available.

Traditionally, care is taken to use absolutely dry solvents, an oxygen-free atmosphere, and good quality samarium metal when preparing SmI_2 using Kagan's and Imamoto's methods.[14−17] Relatively expensive solvent drying columns and highly reactive metals have been typically employed to dry THF for use in the preparation of SmI_2,[16] and the careful deoxygenation of solvents means that significant effort has been devoted to the preparation of the reagent.[17] The quality of samarium metal from commercial suppliers may vary on a batch to batch basis, and glovebox systems are often used to store samarium metal and/or to prepare the reagent.[15]

Although various techniques for activating samarium metal have been described, a quantitative study of their efficacy has not been described.[18] Reports describing the negative influence of peroxide content in THF on the formation and stability of SmI_2 have also been published.[19] A survey of the literature reveals many examples in which the yields of SmI_2-mediated reactions are likely compromised due to low quality reagent that in turn arises from a poor understanding of the factors governing the synthesis of SmI_2.[20] Clearly, difficulties in preparing SmI_2 hinder the spread of its use in synthesis and perpetuate the myth that the reagent is difficult to work with.

Furthermore, the need for a "foolproof" protocol for the synthesis of SmI_2 in THF is underlined by the fact that the preparation of SmI_2 in solvents other than THF has met with limited success despite considerable efforts devoted toward this goal.[21] Factors that hinder the use of SmI_2 in solvents other than THF include less predictable solution properties that can lead to limited substrate and/or reaction scope. In addition, although solutions of SmI_2 in THF are available from commercial suppliers it is often noted that the stability and quality of the commercial reagent is variable and its use problematic.[22] Finally, since SmI_2 is used for the preparation of other Sm(II)-based reagents, the requirement for a reliable preparation of the reagent reaches beyond the chemistry of SmI_2 alone.[23]

Our laboratory has been at the forefront of developing reactions promoted by SmI_2.[24] In our recent studies on reactions mediated by the SmI_2-H_2O complex,[24e,25] we required a method of preparation that would reliably provide reagent solutions with sufficient low-valent lanthanide purity for mechanistic and rate studies. As the reports of Kagan and Imamoto did not give the information needed for our studies, and in light of contrasting literature evidence regarding the preparation of SmI_2, we began a systematic investigation of the potential factors affecting the preparation of SmI_2. For our study, we selected Kagan's method using 1,2-diiodoethane[1] and Imamoto's method using iodine[7] as the two most practical and most commonly utilized methods for the preparation of SmI_2. The formation of the reagent was followed by titration using the method developed by Hilmersson[12] and by standard iodometric titration.[11] However, Hilmersson's method is most informative as it measures only the amount of active Sm(II) reagent. Since during the last 15 years we have noted that the quality of samarium metal can dramatically affect the efficiency of synthesis of SmI_2 (in extreme cases, some batches of commercial samarium metal failed to provide SmI_2), we therefore investigated different methods for the activation of samarium metal and its use for the synthesis of SmI_2.

Herein we report the accumulation of sufficient experimental data to allow us to dispel several myths surrounding the reagent and to report practical, robust and reliable protocols for the preparation of SmI_2 for use by the synthetic chemistry community.

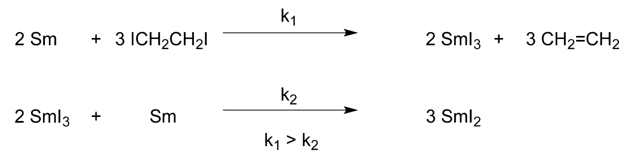
RESULTS AND DISCUSSION

For our study, we selected water, oxygen, and peroxide content, the quality of samarium metal, and the preparation procedure as the most likely factors affecting the formation of SmI_2.[15−20] We started our investigation by studying in detail the synthesis of SmI_2 using Kagan's method employing 1,2-diiodoethane as the oxidant.

For comparison, all reactions were run for the same period of time, with runs typically performed in parallel to facilitate the identification of key factors influencing the synthesis of SmI_2. To impart reasonable stability on the resultant SmI_2 solutions, and following Kagan's seminal report,[1] a 2-fold excess of samarium metal was typically used relative to the oxidant. In all cases, in addition to the concentration of the active Sm(II) species, the induction time—that is, the time after which the solution turned blue—was noted. However, it should be noted that the blue color of the reaction mixture does not indicate that the synthesis of SmI_2 is complete.[15−20] For example, we have found that blue solutions of SmI_2 in THF with concentrations lower than 0.005 M are visually indistinguishable from saturated solutions of 0.1 M in THF, which corresponds to at least a 20-fold difference in molarity.

All runs were performed on two preparative scales (5.5 and 16.5 mmol with respect to the oxidant), solutions of SmI_2 were allowed to settle for at least 30 min prior to titration to ensure homogeneous solutions, and titration was performed in triplicate. For the synthesis of SmI_2 using 1,2-diiodoethane, the oxidant was freshly purified by washing with sodium thiosulfate prior to each preparation of the reagent and stored in the absence of light prior to use. In contrast to literature reports,[15b,20h] we found that 1,2-diiodoethane is relatively stable when purified and stored under inert atmosphere in the absence of light (<5% decomposition after 24 h at room temperature as determined by ^{1}H NMR analysis). To aid in identifying key factors affecting the synthesis of SmI_2, the same batch of samarium metal, solvent and oxidant was typically used for the preparation of SmI_2 under a specific set of conditions. It should be noted that the reaction of samarium metal and 1,2-diiodoethane initially gives SmI_2. However, in the presence of a large excess of 1,2-diiodoethane, the initially formed SmI_2 is oxidized to SmI_3, which is subsequently reduced to SmI_2 by samarium metal (Scheme 3).[26] These changes in the oxidation state of samarium can be followed by the color changes of the reaction mixture.

Scheme 3. Synthesis of SmI_2 Using 1,2-Diiodoethane



$$2\ Sm + 3\ ICH_2CH_2I \xrightarrow{k_1} 2\ SmI_3 + 3\ CH_2{=}CH_2$$

$$2\ SmI_3 + Sm \xrightarrow[k_1 > k_2]{k_2} 3\ SmI_2$$

Finally, it should be noted that our studies pertain to *solutions* of SmI_2 rather than *suspensions* of SmI_2. We focused our investigation on solutions of the reagent for the following reasons: (1) suspensions of SmI_2 contain variable quantities of samarium metal and display different properties to solutions of SmI_2 or pure SmI_2 solid,[27] and (2) some of the reactions mediated by SmI_2 are not compatible with the samarium metal present in suspensions of SmI_2. In all of the examples presented in the current study (with the exception of Table 7), reactions between samarium metal and the oxidant proceed quantitatively to yield suspensions of SmI_2. We propose that different physicochemical stimuli during the synthesis of SmI_2 (e.g., changes in mechanical agitation, temperature or physical properties of the system) might be responsible for different properties of the resultant solutions/suspensions. At present, we cannot exclude that complex solution equilibria are also responsible for this difference.[28] Moreover, the variable and limited solubility of SmI_2 in THF also plays a role in determining the molarity of solutions of SmI_2.[29]

Effect of Water. Because of its potential to react with Sm metal, SmI_3, or SmI_2, the presence of water appeared to be a likely factor impeding the synthesis of SmI_2.[26] To evaluate the influence of water on the formation of SmI_2, the synthesis was performed using THF with gradually increasing water content, as determined by a coulometric Karl Fischer titration (Table 1).

To unambiguously determine the impact of water content in THF on the synthesis of SmI_2, the THF used in entries 1−3 was prepared by sequential dilution of the same batch of THF.[30] For comparison, three other batches of THF were also used. All reactions were carried out using literature conditions for the synthesis of SmI_2: carefully degassed THF, standard Schlenk techniques and samarium metal handled in a glovebox.

Table 1. Effect of Water Content in THF on the Synthesis of SmI_2[a]

entry	water content[b] (ppm)	THF purity	induction time[c]	$[SmI_2]$[d] (M)
1	15	anhydrous, dried over MS 4 Å	15 min	0.076
2	167	anhydrous, dried over MS 4 Å + H_2O	45 min	0.072
3	328	anhydrous, dried over MS 4 Å + H_2O	>2 h	0.073
4	59	anhydrous	30 min	0.070
5	50	HPLC grade	30 min	0.075
6	34	HPLC grade, distilled from Ph_2CO/Na	10 min	0.075

[a] All reactions carried out using standard Schlenk techniques for handling air-sensitive reagents; samarium metal (ABCR) handled in a glovebox; THF purchased from Sigma-Aldrich, rt, 18−24 h, 5.5 mmol scale. Sm (2 equiv) and 1,2-diiodoethane (1 equiv) were used. [b] Determined by coulometric Karl Fischer titration. [c] Induction time indicates time after which color of reaction mixture turned blue; note that induction time varies with the scale of the reaction. [d] Refers to solutions of SmI_2, performed according to ref 12 in triplicate.

As outlined in Table 1, water content was found to have little influence (within experimental error) on the synthesis of SmI_2 under the conditions of our experiments. For example, in the extreme case (entry 3) using very wet THF (commercially available bottles of THF of HPLC grade typically contain <150−250 ppm of water), SmI_2 was formed with similar efficiency. Interestingly, the induction time was found to correlate directly with the water content, with slower reaction time corresponding to higher water concentration.

From these experiments, we conclude that when minimal care is taken to exclude water (the standard operating protocol in most synthetic chemistry laboratories), water is not the major factor hindering the synthesis of SmI_2. We hypothesize that in cases when "wet" THF was used, the longer induction time may arise from the initial reaction of samarium metal with water thus slowing down the reaction of the metal with 1,2-diiodoethane. Overall, these results demonstrate that in the synthesis of SmI_2 using 1,2-diiodoethane, water is not the major factor in failed preparations of the reagent, although long activation times are indicative of high water content, and that commercially available THF can be used.

Effect of Oxygen. It is well-known that the Ln(II) oxidation state is less stable than the Ln(III) oxidation state.[1−3,23,26] Consequently, SmI_2 is unstable when exposed to air and easily oxidizes to Sm(III) with an accompanying color change from blue to yellow. Therefore, we next investigated the influence of oxygen concentration on the synthesis of SmI_2 using several experimental protocols involving gradually less rigorous conditions for the exclusion of air.

Details of these experiments are outlined in Table 2. As expected, the use of standard Schlenk techniques and the

Table 2. Effect of Oxygen on the Synthesis of SmI_2[a]

entry	degassing method of THF[b]	rxn setup method	induction time[c] (min)	$[SmI_2]$[c] (M)
1	freeze-pump thawing	standard Schlenk techniques	15	0.076
2	distillation from Na/ Ph_2CO/N_2	standard Schlenk techniques	10	0.075
3		standard Schlenk techniques	20	0.074
4		Ar sparging, no vacuum[d]	15	0.060
5		"open flask conditions"[e]	15	0.058

[a] Unless noted otherwise, all reactions were carried out using standard Schlenk techniques for handling air-sensitive reagents; samarium metal (ABCR) handled in a glovebox; THF purchased from Sigma-Aldrich; rt, 18−24 h, 5.5 mmol scale. [b] Entry 1, three cycles of freeze−pump−thawing; entry 2, freshly distilled prior to use; entries 3−5, commercial THF without any pretreatment was used. [c] See Table 1. [d] Reaction was carried out without the use of high vacuum: in air, an oven-dried flask was charged with samarium metal and 1,2-diiodoethane, sealed with septum and placed under argon atmosphere. THF was added in one portion, the flask was sealed with Parafilm, and the reaction mixture was stirred for indicated time. [e] Reaction was carried out without the use of high-vacuum or inert gas techniques: in air, an oven-dried flask was charged with samarium metal and 1,2-diiodoethane, fitted with septum and THF was added in one portion. The flask was sealed with Parafilm, and the reaction mixture was stirred for indicated time.

degassing of THF by means of freeze−pump−thawing or distillation under inert atmosphere gave comparable results in terms of reaction efficiency and induction time (entries 1 and 2).

Strikingly, similar results were obtained when commercially available solvents without any special pretreatment were used (entry 3). Furthermore, simple argon sparging or even 'open flask' conditions allowed the efficient synthesis of SmI_2 (entries 4−5). *These unexpected results require us to change our view on the importance of excluding oxygen during the formation of SmI_2.* (*NB* after formation of SmI_2, the reagent should be handled under inert gas atmosphere to prevent oxidation to Sm(III) species).[31] In cases where oxygen was deliberately allowed into reaction vessels, excess samarium metal may react with oxygen prior to the formation of SmI_2, thus permitting efficient synthesis of the reagent. Interestingly, when using 1,2-diiodoethane as oxidant, the induction time does not seem to depend on the amount of oxygen present in the reaction vessel (however, compare to the use of Imamoto's method, Table 5). Importantly, these findings show that the use of strict Schlenk techniques is not necessary for the synthesis of SmI_2 and that commercially available THF can be used for the synthesis of SmI_2 *without prior degassing*.

Effect of Peroxides. Peroxide-contamination is a common problem with ethereal solvents such as THF.[32] The presence of peroxides in THF has been suggested to have a detrimental impact on the synthesis of SmI_2.[19] However, by testing different sources of THF with varying degrees of peroxide content (the peroxide content was determined by standard reaction with potassium iodide followed by iodometric titration with sodium thiosulfate), we determined that it is unlikely that peroxides interfere with the formation of SmI_2 to a significant degree (Table 3). From this study it is useful to know that both types of THF, stabilized and unstabilized, can be used for the synthesis of SmI_2.[33] Caution: when using unstabilized THF, standard precautions regarding the handling of peroxides should be taken.

Table 3. Effect of Peroxide Content in THF on the Synthesis of SmI_2[a]

entry	peroxide content[b] (M)	THF[c]	induction time (min)[d]	$[SmI_2]$[d] (M)
1	0.0015	Aldrich, anhyd, 1 L, w/o BHT	30	0.070
2	0.002	Aldrich, anhyd, 2 L, w/o BHT	15	0.076
3	0.002	Acros, anhyd, 1 L, w/o BHT	30	0.069
4	<0.001	Aldrich, HPLC, w/BHT	20	0.074
5	<0.001	Fisher Sci., anhyd, w/BHT	15	0.071

[a] All reactions carried out using standard Schlenk techniques for handling air-sensitive reagents; samarium metal (ABCR) handled in a glovebox, rt, 18−24 h, 5.5 mmol scale. BHT = 3,5-di-*tert*-butyl-4-hydroxytoluene. [b] Determined by reaction with sodium thiosulfate, followed by iodometric titration. [c] See the Supporting Information for details regarding batch number of THF used. [d] See Table 1.

Effect of THF Quality. THF is the mainstay solvent for the synthesis and use of SmI_2.[1−5] The influence of different sources of THF on the formation of SmI_2 was tested alongside studies on the effect of peroxide content (Table 3). Additional experiments showing the influence of the source of THF can be found in Tables 1 and 2. Overall, these findings indicate that it is unlikely that the quality of THF (including variable water, oxygen, and peroxide content) is the major factor in failed attempts to prepare SmI_2. These results suggest that the use of standard sources of THF available in organic chemistry laboratories give rise to the efficient formation of the reagent.

Effect of Preparation Procedure. Three different approaches for the combination of reagents and solvents in the preparation of SmI_2 have been reported in the literature.[34] As outlined in Table 4, we found no significant difference in the efficiency of formation of SmI_2 using the three variants. From a practical perspective, the procedure described in entry 1, namely adding THF to the reaction vessel charged with samarium metal and 1,2-diiodoethane, is the most convenient and time-efficient (see the Experimental Section).

Table 4. Effect of Preparation Procedure on the Synthesis of SmI_2[a]

entry	addition procedure[b]	induction time[c] (min)	$[SmI_2]$[c] (M)
1	addition of THF to Sm metal and ICH_2CH_2I	15	0.071
2	addition of ICH_2CH_2I in THF to Sm metal	20	0.072
3	addition of solid ICH_2CH_2I to Sm metal in THF	20	0.069

[a] All reactions carried out using standard Schlenk techniques for handling air-sensitive reagents; samarium metal (ABCR) handled in a glovebox, commercial THF was used w/o special pretreatment, water content 100 ppm; rt, 18−24 h, 5.5 mmol scale. [b] Entry 1: THF was added to a flask charged with Sm metal and 1,2-diiodoethane. Entry 2: a solution of 1,2-diiodoethane in THF was added to a flask charged with Sm metal. Entry 3: solid 1,2-diiodoethane was added to a flask charged with Sm metal and THF. [c] See Table 1.

Factors Affecting the Synthesis of SmI_2 Using Imamoto's Method with Iodine as the Oxidant. Imamoto's method is an important procedure for the preparation of SmI_2.[7] Having examined potential factors affecting the synthesis of SmI_2 using 1,2-diiodoethane, we turned our attention to the use of iodine as the oxidant (Table 5). In general, the effect of the factors examined mirrors our findings for the formation of SmI_2 using 1,2-diiodoethane. Overall, these results demonstrate that rigorous drying of solvents is not required for Imamoto's method, commercial solvents can be used as received, and simple argon sparging and "open flask" conditions are adequate.[31]

Effect of Samarium Metal Quality on the Preparation of SmI_2. In the early 1990s, Brown and co-workers described the mechanical activation of magnesium for the synthesis of Grignard reagents, whereby solid magnesium turnings were stirred under inert atmosphere to provide highly reactive magnesium powder.[35] This convenient procedure for the removal of oxide from the magnesium surface provided a platform for advances in organometallic chemistry based on the activation of metals under simple laboratory conditions.[36] To our knowledge the dry-stirring method described by Brown has not been used for the activation of samarium metal.

In the course of studying reactions mediated by SmI_2, we and others have noticed the negative impact of the quality of some batches of samarium metal on the efficiency of SmI_2 formation.[37] In the worst cases, it has been noted that the preparation of SmI_2 using a batch of samarium metal might fail completely under standard conditions. Since lanthanide metals

Table 5. Effect of Selected Parameters on the Synthesis of SmI_2 Using I_2[a]

entry	water content[b] (ppm)	reaction setup method	peroxides[c] (M)	induction time[d]	$[SmI_2]$[d] (M)
1	100	Schlenk techniques	<0.001	1 h	0.060
2	110	Schlenk techniques	0.002	1.5 h	0.062
3	110	Schlenk techniques/ 60 °C[e]	0.002	30 min	0.066
4	100	Ar sparging[f]	<0.001	2 h	0.061
5	100	"open flask"[f]	<0.001	>5 h	0.061
6	380	Schlenk techniques	<0.001	2 h	0.055

[a] Unless noted otherwise, all reactions carried out using standard Schlenk techniques for handling air-sensitive reagents; samarium metal (ABCR) handled in a glovebox; commercial THF without special pretreatment was used; rt, 18−24 h, 5.5 mmol scale. [b] Determined by coulometric Karl Fischer titration. [c] Determined by reaction with sodium thiosulfate, followed by iodometric titration. [d] See Table 1. [e] Reaction performed at 60 °C. [f] See Table 2.

Table 6. Effect of Handling and Storage of Samarium Metal on the Synthesis of SmI_2[a]

entry	samarium metal[b]	notes	induction time[c] (min)	$[SmI_2]$[c] (M)
1	ABCR, glovebox		5	0.072
2	Acros, glovebox		5	0.065−0.073
3	Acros, air[d]		15	0.069
4	ABCR, glovebox	kept in air for 10 days[e]	15	0.062
5	Acros, glovebox	activated by flame-drying[f]	5	0.068

[a] Unless noted otherwise, all reactions carried out using standard Schlenk techniques for handling air-sensitive reagents; rt, 18−24 h, 5.5 or 16.5 mmol scale. [b] See the Supporting Information for the batch number of samarium metal used. [c] See Table 1. [d] Stored in a closed container in air and frequently opened in air for use without any precautions to exclude oxygen. [e] Samarium metal removed from glovebox, stored in air in an open vessel, and mixed at least two times per day to ensure homogeneous exposure of metal surface to oxygen. [f] Vigorous flame-drying of samarium metal under high-vacuum.

are oxygen sensitive, we hypothesized that the major factor preventing efficient formation of SmI_2 using "inactive" batches of samarium metal is an oxide coating on the metal surface.

Interestingly, we found no pattern in encountering "inactive" batches of samarium metal from commercial suppliers. For example, following a long period of good quality samarium metal from a supplier, an "inactive" batch would be encountered, followed again by bottles of good quality metal. As we have encountered this problem with different suppliers at different times, it appears to indicate potential issues with the storage of samarium metal prior to distribution or an occasional issue with the quality of the world supply of samarium metal.

In light of our findings (Tables 1−5), we propose that most of the difficulties reported in the preparation of SmI_2 over the last 30 years originate from "inactive" batches of samarium metal from commercial suppliers. In some cases, such an experience prevents users from pursuing the use of the reagent. Moreover, it is likely that literature reports of low yields from SmI_2-mediated reactions may often arise from the use of low quality samarium metal in the preparation of the reagent. It is important to note that SmI_2 solutions prepared from low quality samarium metal are likely to contain an unusually high content of SmI_3 and exhibit low stability. Clearly, the inability to reliably prepare SmI_2 from *all* batches of commercial samarium metal has prevented an even wider use of SmI_2 in synthesis and slowed the full realization of the reagent's potential.

To investigate the problem of variable samarium metal quality, we first studied the impact of different conditions for the storing and handling of samarium metal (Table 6). For this study we selected batches of samarium metal that had already been shown to be effective for the formation of the reagent. As outlined above, literature procedures for the synthesis of SmI_2 often emphasize the importance of handling samarium metal under inert atmosphere conditions and involve metal flame-drying techniques aimed at activating the metal surface.[15,17,18] However, in our studies (Table 6) we found no significant difference in the efficiency of SmI_2 formation using the same batches of samarium metal that were (a) handled under strictly inert atmosphere conditions in a glovebox (entries 1 and 2), (b) stored in a closed container in air and frequently opened for use in air without taking any precautions (entry 3), or (c) stored in a completely open container in air (entry 4). Our study therefore suggests that samarium metal is much more stable in air than has been indicated in the literature.

Overall, our findings demonstrate that as long as the samarium metal is "active", which in our experience is the case with the majority of commercial batches, simple techniques and equipment are sufficient to handle samarium metal for the formation of SmI_2. Notably, the metal can be stored on the bench in air and special precautions are not necessary during the weighing of samples.

Activation of "Inactive" Samarium Metal. Next, we addressed the problem of activating "inactive" samarium metal. Our objective was to develop a convenient, "foolproof" method for the preparation of SmI_2 from any batch of samarium metal.[38,39] For this study we selected different batches of samarium metal that failed to form SmI_2 under standard and more forcing conditions (Table 7, entries 1 and 2). We reasoned that the dry-stirring method described by Brown could provide a convenient method for the activation of "inactive" samarium metal for use in the synthesis of SmI_2.

After some experimentation, we were delighted to find that activation of an "inactive" batch of samarium metal by dry-stirring under argon, followed by oxidation with iodine, gave SmI_2 in excellent yield (Table 7, entries 3 and 4). Furthermore, we demonstrated that SmI_2 prepared from "inactive" samarium metal is an efficient electron transfer reductant in a variety of challenging SmI_2-mediated transformations (Table 8).[25] In all cases, yields were comparable to or higher than those previously reported, testifying to the utility of the SmI_2 solutions prepared using our activation protocol.

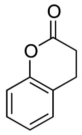
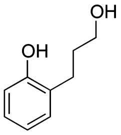
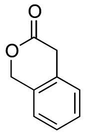
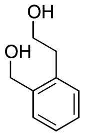
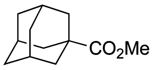
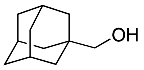
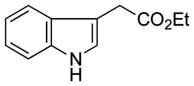
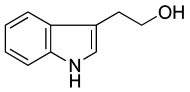
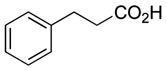
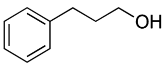
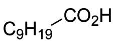
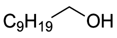
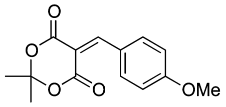
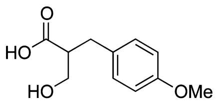
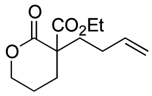
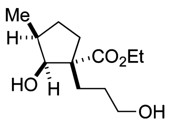
Next, we applied this activation method to other "inactive" batches of samarium metal (Table 7). Interestingly, we found that the dry-stirring activation method does not work when 1,2-diiodoethane is used as oxidant (entries 5 and 6). We hypothesize that additional activation of samarium metal surface by iodine under thermal conditions might explain the efficiency of the processes described in entries 3 and 4 of Table 7. However, for some "inactive" batches of samarium metal, the use of 1,2-diiodoethane at higher concentrations activates the

Table 7. Synthesis of SmI_2 from "Inactive" Samarium Metal[a]

entry	samarium metal[b]	activation of samarium metal	synthesis method	notes[c]	induction time[d]	$[SmI_2]^d$ (M)
1	Strem	n/a	ICH_2CH_2I	rt, 6 d		not formed[e]
2	Strem	n/a	I_2	60 °C, 3 d		not formed[e]
3	Strem	dry-stirring under Ar, 24 h[f]	I_2	60 °C, 18 h	2 h	0.084
4	Strem	dry-stirring under vacuum, 150 °C, 20 h[g]	I_2	60 °C, 18 h	5 h	0.081
5	Strem	dry-stirring under Ar, 24 h[f]	ICH_2CH_2I	rt, 18 h		not formed[e]
6	Strem	thermal activation[h]	ICH_2CH_2I	rt, 18 h		not formed[e]
7	Strem	10−55 mL[i]	ICH_2CH_2I	rt, 2 d, 1 d	>5 h	0.057
8	Strem	10−55 mL[i]	ICH_2CH_2I	rt, 1 d, 1 d	>5 h	0.072
9	Strem	10−55 mL[i]	I_2	rt, 1 d, 1 d	>5 h	0.047
10	AlfaAesar	n/a	ICH_2CH_2I	rt, 1 d		not formed[e]
11	AlfaAesar	dry-stirring under Ar, 24 h[f]	I_2	60 °C, 18 h	15 min	0.083
12	ABCR	n/a	ICH_2CH_2I	rt, 1 d		not formed[e]
13	ABCR	dry-stirring under Ar, 24 h[f]	I_2	60 °C, 18 h	15 min	0.099

[a] All reactions carried out using standard Schlenk techniques for handling air-sensitive reagents; all reactions performed on 5.5 mmol scale. [b] See the Supporting Information for batch number of samarium metal used. [c] Refers to conditions used for the synthesis of SmI_2. [d] See Table 1; the concentration for entries 11 and 13 was determined for suspensions of SmI_2. [e] Indicates that the blue color characteristic of SmI_2 did not form. [f] Samarium metal was stirred under argon at rt for indicated time, followed by addition of THF and oxidant. [g] Samarium metal was stirred under high-vacuum at 150 °C for indicated time, followed by addition of THF and oxidant. [h] Activation of metal by vigorous flame-drying under vacuum. [i] 1,2-Diiodoethane and samarium metal stirred in 10 mL of THF for indicated time, followed by addition of the remaining portion of THF.

Table 8. Electron-Transfer Reductions Mediated by SmI_2 Prepared from "Inactive" Samarium Metal

entry	starting material	product	conditions	time (h)	yield (%)[a]
1			SmI_2-H_2O	0.5	99
2			SmI_2-H_2O	1	65
3			SmI_2-H_2O-Et_3N	18	97
4			SmI_2-H_2O-Et_3N	1	99
5			SmI_2-H_2O-Et_3N	15	84
6			SmI_2-H_2O-Et_3N	15	89
7			SmI_2-H_2O	1	98
8			SmI_2-H_2O	1	88 (7:1 dr)

[a] Determined by ^1H NMR.

samarium metal surface (entries 7−9). However, this protocol has not been found to be as general as the dry-stir method followed by reaction with iodine (entries 3 and 4).

Having worked with samarium metal of differing quality, we have noticed that "active" and "inactive" batches of samarium metal often differ in physical appearance. Consequently, we have developed a simple test to determine whether a particular batch of samarium metal is likely to be "active" or "inactive" for the synthesis of SmI_2.[40]

In summary, our studies have shown that the synthesis of SmI_2 using "active" samarium metal is remarkably robust and that "inactive" samarium metal can be activated by dry-stirring. Thus, we have developed a "foolproof" protocol for the synthesis of SmI_2 from *any* batch of commercial samarium metal.

Stability of Solutions of SmI_2 in THF. The stability of solutions of SmI_2 in THF is a key issue in the study of reactions mediated by the reagent. In general, it has been recommended that SmI_2 should be freshly prepared before each use as problems with the stability of the reagent have been frequently reported.[2−5,20]

We have therefore examined the stability of SmI_2 prepared by Kagan's method, and in contrast to some literature reports, we have found that solutions of the reagent are reasonably stable. No sign of decomposition was detected after a period of one month when the reagent was simply sealed under inert atmosphere and stored on the bench at room temperature with stirring. On the other hand, we have noticed a propensity for SmI_2 to precipitate with time from unstirred THF solutions. The limited solubility of SmI_2 in THF may affect dynamic equilibria between SmI_2, Sm metal, SmI_3 and other complexes of Sm(II) and likely plays an important role in the stability of the reagent.[27−29] Furthermore, we have found that SmI_2 can be conveniently stored at room temperature under inert atmosphere without stirring for long periods of time (>2 weeks). However, the reagent should be stirred for at least 1 h prior to use. Studies to elucidate these intriguing features of SmI_2 solutions are currently ongoing in our group.

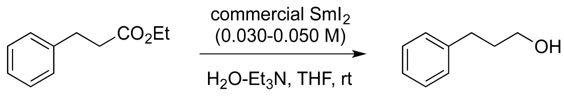
In contrast to SmI_2 prepared from 1,2-diiodoethane, we determined that THF solutions of SmI_2 prepared from iodine are significantly less stable; visible decomposition was observed after several days. We ascribe this difference to more efficient activation of samarium metal by 1,2-diiodoethane than by iodine. Accordingly, we recommend that in cases when SmI_2 solutions prepared using Imamoto's method give variable results, reactions should be repeated using SmI_2 prepared from 1,2-diiodoethane. From an experimental perspective, it is very useful to know that THF solutions of SmI_2 can be stored provided they are stirred prior to use.

Working with Commercial Solutions of SmI_2. SmI_2 is available from several commercial suppliers as a "0.1 M solution in THF". Examination of the literature suggests that commercial solutions of SmI_2 vary significantly in concentration from the advertized value.[12] Furthermore, the use of commercial solutions of SmI_2 have been reported to give variable results and low yields in SmI_2-mediated reactions, suggesting that there are problems with the stability of commercial solutions of the reagent.[22]

To gain independent insight into this issue, we evaluated several different batches of SmI_2 from commercial sources (see the Supporting Information, Table SI-1, for full details). We found that the average concentration of commercial SmI_2 (0.04 M from four different suppliers) was much lower than the advertised 0.1 M concentration. This finding is in good agreement with other literature reports.[12]

Since the commercial availability of SmI_2 solutions in THF contributes to the widespread use of the reagent, we sought to demonstrate that commercial solutions are viable sources of SmI_2. Toward this end, we performed a series of challenging electron transfer reductions using aliphatic ester **1** as a model substrate[25e] (Scheme 4, see the Supporting Information for additional examples). In all cases, after taking into account the low concentration of the commercial solutions, the yields obtained were comparable to those obtained with SmI_2 prepared fresh using Kagan's or Imamoto's method. Thus, commercial THF solutions are effective sources of SmI_2 for preliminary studies.

Scheme 4. Evaluating the Use of Commercial SmI_2 Solutions for the Reduction of Aliphatic Esters



1

2, 93-99%

CONCLUSIONS

Our studies show that the use of samarium metal and 1,2-diiodoethane or iodine for the formation of SmI_2 reliably provides the reagent under experimental conditions that are more convenient than those typically employed in literature. We have found that the formation of SmI_2 is remarkably resilient to the presence of water, oxygen and peroxides and thus we have dispelled many of the myths surrounding the reagent. In fact, SmI_2 is ideally suited for widespread use in all synthetic chemistry laboratories, including those that do not have access to specialized glovebox or high-vacuum equipment, high quality solvents and reagents. We have shown that when SmI_2 fails to form efficiently it is likely to be a result of low quality samarium metal. Accordingly, we have developed a "foolproof" protocol for the activation of "inactive" batches of samarium metal and have demonstrated the utility of SmI_2 generated in this way. Our studies also suggest that SmI_2 solutions can be stored, however, complex equilibria might play a role in altering the properties of the solutions if they are not stirred. Finally, we have showed that commercially available solutions of SmI_2 in THF are effective, although much lower than advertized molarities should be expected. We expect our findings to be of broad utility for all practitioners of organic chemistry who require a user-friendly electron transfer reductant, such as SmI_2.

EXPERIMENTAL SECTION

General Methods. All experiments were performed under an atmosphere of argon or nitrogen, using anhydrous solvents, unless stated otherwise. THF was purchased and purified by passing through activated alumina columns, distillation from sodium/benzophenone, or used as received. Samarium metal was purchased and used as received. 1,2-Diiodoethane was stored at 4 °C and used after purification as described below. All other solvents and chemicals were used without further purification or drying procedures. Reaction glassware was oven-dried overnight at 140 °C or flame-dried prior to use and cooled under vacuum then purged with argon. ^1H and ^{13}C NMR spectra were recorded on 300, 400, and 500 MHz spectrometers. Unless otherwise noted, all samples were dissolved in $CDCl_3$, and the shifts are reported in parts per million (ppm) relative to residual $CHCl_3$ as an internal standard (^1H NMR $\delta = 7.27$ or ^{13}C NMR $\delta = 77.2$). Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; br s, broad singlet. All coupling constants (J) are reported in hertz (Hz). All flash chromatography was performed using silica gel, 60 Å, 230−400 mesh. TLC analysis was carried out on aluminum sheets coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. Products were identified using ^1H NMR analysis and comparison with authentic samples.

Typical Procedure for the Preparation of SmI_2. An oven-dried 100 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar and a septum was placed under vacuum and evacuated/backfilled with argon three times. Note: the flask can also be flame-dried under vacuum, followed by three evacuation/backfilling cycles. In air, 1.65 g (11.0 mmol) of samarium metal and 1.55 g (5.5 mmol) of freshly washed 1,2-diiodoethane (see, below) was weighed out and added to the reaction flask. The flask was sealed with a septum, evacuated/backfilled with argon three times, and stirring was started at medium speed. 55 mL of commercial THF (Sigma-Aldrich, anhyd, used as received) was added using a 60 mL syringe. The flask was evacuated/backfilled with argon three times (this process removes ethylene formed during the insertion of Sm into 1,2-diiodoethane), the argon line was removed, and the septum was sealed with Parafilm. Note: the reaction can also be conveniently stirred under a positive pressure of argon. After stirring overnight, the stirring was turned off, and the solution of SmI_2 was allowed to settle for 30 min and titrated according to ref 12 and/or 11.

Procedure for Purifying Commercial 1,2-Diiodoethane. 1,2-Diiodoethane (20 g) was dissolved in approximately 400 mL of diethyl ether, and the organic layer was washed with aqueous saturated sodium thiosulfate solution (5 × 100 mL) and water (1 × 100 mL), dried over sodium sulfate, and concentrated to give a white solid. The flask containing 1,2-diiodoethane was wrapped in aluminum foil and placed under high-vacuum for 30 min.

Typical Procedure for the Preparation of SmI_2 from "Inactive" Samarium Metal. A 100 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar (24 × 12 mm) and a septum was flame-dried under vacuum. Note: an oven-dried Schlenk tube can also be used. The tube was allowed to cool to room temperature and evacuated/backfilled with argon three times. 1.65 g (11.0 mmol) of "inactive" samarium metal was added, the tube was sealed with a septum and subjected to three evacuation/backfilling cycles. After the final cycle, the tube was left under a positive pressure of argon, and stirring was started at medium to high speed. After the mixture was stirred for 24 h, 45 mL of THF was added, followed by 1.40 g (5.5 mmol) of iodine dissolved in 10 mL of THF under argon. The reaction flask was sealed with Parafilm and heated at 60 °C for 18 h. The stirring was turned off and the solution of SmI_2 was allowed to settle for 2 h and titrated according to ref 12 and/or 11.

Typical Procedure for the Preparation of SmI_2 with Inert Gas Sparging. Kagan's Method. An oven-dried 100 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar and a septum was placed under a positive pressure of inert gas (argon or nitrogen). In air, 1.65 g (11.0 mmol) of samarium metal and 1.55 g (5.5 mmol) of freshly washed 1,2-diiodoethane (see, above) were weighed out and added to the reaction flask. The flask was sealed with a septum, and stirring was started at medium speed. Commercial THF (55 mL, Sigma-Aldrich, anhyd, used as received) was added using a 60 mL syringe, the argon line was removed, and the septum was sealed with Parafilm. Note: the reaction can also be conveniently stirred under a positive pressure of argon. After stirring overnight, stirring was stopped and the solution of SmI_2 was allowed to settle for 30 min and titrated according to ref 12 and/or 11.

Typical Procedure for the Preparation of SmI_2 with Inert Gas Sparging. Imamoto's Method. An oven-dried 100 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar and a septum was placed under a positive pressure of inert gas (argon or nitrogen). In air, 1.65 g (11.0 mmol) of samarium metal was weighed out and added to the reaction flask. Commercial THF (55 mL, Sigma-Aldrich, anhyd, used as received) was then added using a 60 mL syringe. Finally, 1.40 g (5.5 mmol) of iodine was added, the flask was sealed with a septum, and stirring was started at medium speed. The argon line was then removed, and the septum was sealed with Parafilm. Note: the reaction can also be conveniently stirred under a positive pressure of argon. After stirring overnight at room temperature or 60 °C, stirring was stopped (when the reaction was performed at 60 °C, it was allowed to cool to room temperature), the solution of SmI_2 was allowed to settle for 30 min, and titrated according to ref 12 and/or 11.

Experimental Procedures for Reactions Mediated by SmI_2 Prepared from Inactive Samarium Metal. *General Procedure I (for Reactions in Table 8).* To cyclic ester was added samarium(II) iodide (THF solution) followed by water under inert atmosphere at room temperature and the mixture stirred vigorously. After the specified time, 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 (3 × 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered and concentrated. The sample was analyzed by ^{1}H NMR to obtain conversion and yield using internal standard.

General Procedure II (for Reactions in Table 8). To acyclic ester or carboxylic acid was added samarium(II) iodide (THF solution) followed by amine and water under inert atmosphere at room temperature and the mixture stirred vigorously. After the specified time, the excess of SmI_2 was oxidized by bubbling air through the reaction mixture. 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 (3 × 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^{1}H NMR to obtain conversion and yield using internal standard.

2-(3-Hydroxypropyl)phenol (Table 8, Entry 1). According to the general procedure I, the cyclic ester was reacted with samarium(II) iodide (8 equiv) and water (200 equiv) to give the title product in 99% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.78−1.84 (m, 2H), 2.51 (br, 1H), 2.71 (t, J = 6.8 Hz, 2H), 3.57 (t, J = 5.8 Hz, 2H), 6.76−6.82 (m, 2H), 7.02−7.05 (m, 2H), 7.06 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.1, 32.2, 60.8, 116.1, 120.8, 127.2, 127.6, 130.7, 154.6. Spectroscopic properties matched those previously described.[25a]

2-(2-(Hydroxymethyl)phenyl)ethanol (Table 8, Entry 2). According to the general procedure I, the cyclic ester was reacted with samarium(II) iodide (8 equiv) and water (200 equiv) to give the title product in 65% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.75 (t, J = 6.0 Hz, 2H), 3.64 (t, J = 6.0 Hz, 2H), 4.07 (br, 2H), 4.43 (s, 2H), 7.07−7.21 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.1, 62.9, 63.2, 126.7, 128.5, 129.7, 130.1, 138.3, 139.2. Spectroscopic properties matched those previously described.[25a]

1-Adamantanemethanol (Table 8, Entry 3). According to the general procedure II, the ester was reacted with samarium(II) iodide (12 equiv), triethylamine (72 equiv), and water (72 equiv) to give the title product in 97% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (br, 1H), 1.44 (m, 6H), 1.57 (m, 1H), 1.59 (m, 2H), 1.65 (m, 2H), 1.68 (m, 1H), 1.92 (m, 3H), 3.13 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.2, 34.5, 37.2, 39.0, 73.9. Spectroscopic properties matched those previously described.[25e]

2-(1H-Indol-3-yl)ethanol (Table 8, Entry 4). According to the general procedure II, the ester was reacted with samarium(II) iodide (8 equiv), triethylamine (36 equiv) and water (36 equiv) to give the title product in 99% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (br, 1H), 2.97 (t, J = 6.3 Hz, 2H), 3.84 (t, J = 6.3 Hz, 2H), 7.01 (d, J = 1.5 Hz, 1H), 7.06 (t, J = 7.0 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.99 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.8, 62.6, 111.3, 112.3, 118.9, 119.5, 122.3, 122.5, 127.4, 136.5. Spectroscopic properties matched those previously described.[25e]

3-Phenylpropan-1-ol (Table 8, Entry 5). According to the general procedure II, the acid was reacted with samarium(II) iodide (6 equiv), triethylamine (36 equiv) and water (36 equiv) to give the title product in 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (br, 1H), 1.80−1.86 (m, 2H), 2.64 (t, J = 7.5 Hz, 2H), 3.61 (t, J = 6.5 Hz, 2H), 7.10−7.24 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.1, 34.3, 62.3, 125.9, 128.4, 128.5, 141.8. Spectroscopic properties matched those previously described.[25e]

Decan-1-ol (Table 8, Entry 6). According to the general procedure II, the acid was reacted with samarium(II) iodide (6 equiv), triethylamine (36 equiv) and water (36 equiv) to give the title product in 89% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.81 (t, J = 6.9 Hz, 3H), 1.15−1.33 (m, 15H), 1.47−1.52 (m, 2H), 3.57 (t, J = 5.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.7, 25.7, 29.3, 29.4, 29.6, 29.6, 31.9, 32.8, 63.1. Spectroscopic properties matched those previously described.[25e]

3-Hydroxy-2-(4-methoxybenzyl)propanoic Acid (Table 8, Entry 7). To a solution of samarium(II) iodide (THF solution, 8 equiv) was added water (1200 equiv), followed by cyclic 1,3-diester dissolved in 2.0 mL of THF under inert atmosphere at room temperature and the mixture stirred vigorously. After the specified time, 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 (3 × 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^{1}H NMR to obtain conversion and yield using internal standard: yield 98%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.81−2.90 (m, 2H), 2.99−2.08 (m, 1H), 3.72−3.77 (m, 1H), 3.79−3.83 (m, 1H), 3.81 (s, 3H), 6.86 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.2, 49.0, 55.3, 61.9, 114.0, 130.0, 130.2, 158.3, 179.7. Spectroscopic properties matched those previously described.[25b]

rac-(1R,2S,3S)-Ethyl 2-Hydroxy-1-(3-hydroxypropyl)-3-methylcyclopentanecarboxylate (Table 8, Entry 8). To a solution of cyclic ester in THF (2.0 mL) and water (1200 equiv) was added samarium(II) iodide (THF solution, 7 equiv) via syringe pump over 1 h under inert atmosphere at room temperature. When the addition was complete, 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 (3 × 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^{1}H NMR to obtain conversion and yield using internal standard: yield 88%, dr = 7:1; ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer) δ 0.96 (d, J = 6.6 Hz, 3H), 1.19 (t, J = 6.9 Hz, 3H), 1.25−2.02 (m, 10H), 2.14−2.26 (m, 1H), 3.49−3.65 (m, 2H), 4.07 (q, J = 6.9 Hz, 2H), 4.12 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 14.2, 28.8, 29.2, 29.9, 32.5, 38.1, 59.6, 60.6, 62.8, 78.7, 176.5. Spectroscopic properties matched those previously described.[25a]

Experimental Procedures for Reactions Mediated by Commercial Solutions of SmI_2. *Experimental Procedure for Reduction of Aliphatic Esters and Carboxylic Acids.* To acid or ester (neat) was added SmI_2 (THF solution, typically, 6 equiv), followed by amine (typically, 36 equiv) and water (typically, 36 equiv) under inert atmosphere at room temperature and the mixture stirred vigorously. After the specified time (typically, 15−18 h), the excess of SmI_2 was oxidized by bubbling air through the reaction mixture. 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 (3 × 30 mL), and the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^{1}H NMR to obtain conversion and yield (vs internal standard). Spectroscopic properties of all products matched those previously described.[25]

Additional Experiments and Procedures. *Titration Procedures. Titration with H_2O-Et_3N System.*[12a] An oven-dried 4-dram vial equipped with a stirring bar and septum was placed under a high-vacuum line, subjected to three evacuation/backfilling cycles with argon, and left under a positive pressure of argon. A solution of SmI_2 (typically, 1.0 mL, the exact volume of added SmI_2 has to be carefully noted) was added, followed by Et_3N (0.21 mL) and H_2O (33 mg). The resulting solution was titrated with cyclohexanone (THF solution) until the color changed from dark brown to white. The end point was recorded when the solution changed from light green to white. Note: other ketones can also be used for the titration procedure. Note: all syringes and solvents used in the procedure should be flushed with argon (three times) and degassed prior to use to obtain reproducible results. The titration should be repeated to give the average of three experiments.

2. Iodometric Titration.[11] An oven-dried 4-dram vial equipped with a stirring bar and septum was charged with iodine (26.5 mg), placed under a high-vacuum line, and subjected to three evacuation/backfilling cycles with argon, and THF was added (1.0 mL). Another vial, equipped with a stirring bar and septum, was placed under a high-vacuum line, subjected to three evacuation/backfilling cycles with argon, and charged with a solution of SmI_2 (typically, 1.0 mL, the exact volume of added SmI_2 has to be carefully noted). A solution of SmI_2 was titrated with iodine solution, prepared as described above. The end point is reached when the solution changes to a yellow color. Note: all syringes and solvents used in the procedure should be flushed with argon (three times) and degassed prior to use to obtain reproducible results. The titration should be repeated to give the average of three experiments.

3. Procedure for Titration of Suspensions of SmI_2.[12a] To a stirred suspension of SmI_2 (approximately 5.5 mmol) was added 4-*tert*-butylcyclohexanone (5.5 mmol), followed by triethylamine (22.0 mmol) and water (22.0 mmol). After 5 min, the reaction was transferred to a separatory funnel, diluted with CH_2Cl_2 (100 mL) and 1.0 M HCl (100 mL), extracted with CH_2Cl_2 (5 × 100 mL), dried, and concentrated. The molarity of the suspension of SmI_2 was determined from analysis of the product distribution by ^{1}H NMR (400 MHz). Note: other ketones can also be conveniently used for this titration. The amount of ketone used must be less than the amount required for full reduction by the formed suspension of SmI_2.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Discussion regarding commercial solutions of SmI_2, Table SI-1, detailed list of reagents used, ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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