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Generation of Sm^{II} Reductants Using High Intensity Ultrasound

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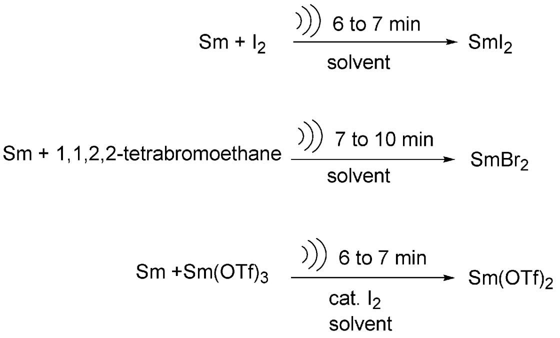
Ultrasound (20 kHz) was used to prepare samarium(II) diiodide (SmI_2), samarium(II) dibromide ($SmBr_2$), and samarium(II) triflate $(SmOTf)_2$. The method described herein provides a straightforward and rapid approach to the synthesis of Sm^{II} compounds not accessible by other means. Of particular importance is the fact that this approach can be used to produce Sm^{II}-based reductants in a wide range of solvents including alcohols.

Introduction

Although initially considered an esoteric reagent, samarium diiodide (SmI_2) is now a standard reductant in most organic laboratories and its use in synthesis is featured in nearly 100 publications a year. The unique place held by SmI_2 in the arsenal of synthetic chemists is a result of its versatility in promoting numerous fundamentally important reactions in organic synthesis including reductions, reductive couplings, and tandem reactions.[1] One of the features that makes SmI_2 useful is its ease of synthesis and availability from commercial sources. The preparation of SmI_2 typically involves treatment of excess Sm metal with iodine, 1,2-diiodoethane, or diiodomethane and reactions take up to two hours for completion.[2] While there are numerous other Sm^{II}-based reductants including samarium(II) triflate [$Sm(OTf)_2$] and samarium(II) dibromide ($SmBr_2$), their preparation involves a number of steps that are in some cases non-routine and as a result, the use of these reagents is limited in synthesis.

Recently, it has been shown that microwave-assisted heating[3] and sonication in an ultrasonic cleaning bath[4] can be used to reduce the preparation time of Sm^{II}-based reductants to under 10 min. Concellon's work,[4] utilizing an ultrasonic cleaning bath to catalyze the formation of the Sm^{II} species, is particularly interesting since it is a mild technique that does not require the use of specially designed containers. On the basis of previous precedent, it is probable that a high-intensity ultrasonic probe, specifically designed for liquid processing, could catalyze the formation of a range of Sm^{II} reductants. As a part of our research program directed towards mechanistic studies of Sm-based reductants, we have been examining alternative approaches to the synthesis of Sm^{II} compounds that are efficient and can be carried out with routine methods. Herein we report the synthesis of SmI_2, $SmBr_2$ and $Sm(OTf)_2$ in a range of solvents using high intensity ultrasound as shown in Scheme 1.



Scheme 1. Procedures for the generation of SmI_2, $SmBr_2$, and $Sm(OTf)_2$ via high-intensity ultrasound.

Results and Discussion

Generation of SmI_2

The first detailed report on the synthesis of SmI_2 using conventional cleaning-bath sonication utilized Sm powder in combination with a range of iodine sources including iodoform, diiodomethane, 1,2-diiodoethane, or iodine.[4] The rate of SmI_2 production ranged from 5 min to an hour depending on the iodine source. Low and co-workers reported that the degree of surface activation of a metal using a cleaning bath is sometimes ineffective for complete conversion of Sm and an iodine source to SmI_2.[5] To study this

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supposition in more detail, high-intensity ultrasound was examined as a means for producing SmI_2 in THF from a slight excess of Sm and either iodine or 1,2-diiodoethane. A submersible ultrasonic probe, operating at a fixed frequency of 20 kHz, was used as the source of the ultrasound. When Sm metal was combined with either iodine source in THF and sonicated, the deep blue color attributed to SmI_2 was observed after only 1 min. The maximum concentration (0.12 M as determined by iodometric titration after filtration through a glass-frit funnel) was obtained after 6 to 7 min of sonication. The reported concentration value of 0.12 M for SmI_2 in THF corresponds to a supersaturated solution, because maximum concentrations of 0.1 M are obtained from traditional methods.

Encouraged by these results, the same method employing iodine was successfully used to generate SmI_2 in CH_3CN, DME, 2-propanol, 2-methyl-2-propanol, and 2-heptanol. The concentration of SmI_2 in CH_3CN obtained (0.05 M) is comparable to existing methods and the concentration of SmI_2 obtained in DME (0.03 M) is approximately 33% higher than previous reports.[6–7] SmI_2 generated in neat 2-propanol (0.02 M), 2-methyl-2-propanol (0.05 M), and 2-heptanol (0.04 M) are new species that have not been reported in the literature to date. Figure 1 shows the UV/Vis spectrum for SmI_2 generated in each solvent using high-intensity ultrasound. The changes in absorption maxima and relative intensity of the absorption bands in each solvent clearly show that each SmI_2 solvate is unique.[7] Although the synthesis of SmI_2 in alcohols may appear somewhat surprising, recent work in our group has shown that SmI_2 is relatively stable even in the presence of high concentrations of water and glycols.[8,9] Table 1 contains the concentrations (as determined by iodometric titration), λ_{max}, and yields for the synthesis of SmI_2 in each solvent. In every case, the solution was filtered through a glass frit before examining the concentration. Precipitate of the same color as the solution remained in each case indicating that solutions were saturated.

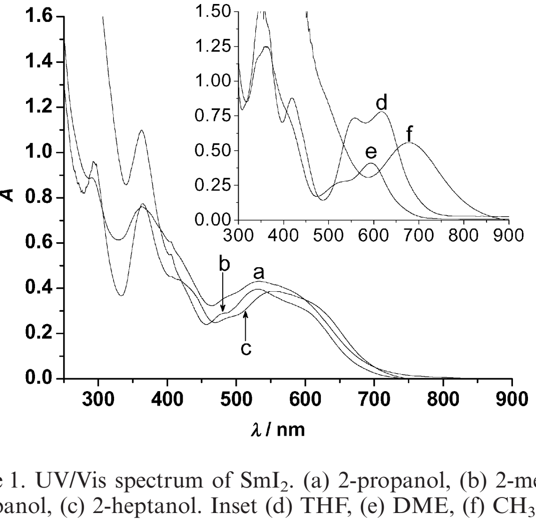

Figure 1. UV/Vis spectrum of SmI_2. (a) 2-propanol, (b) 2-methyl-2-propanol, (c) 2-heptanol. Inset (d) THF, (e) DME, (f) CH_3CN.

Table 1. Percent yield, concentration, and λ_{max} for SmI_2 in each solvent.

Solvent[a]	Yield[a]	Concentration[b] [M]	λ_{max} [nm]
THF	91%	0.12	618
CH_3CN	42%	0.05	678
DME	75%	0.03	632
2-Propanol	36%	0.02	536
2-Methyl-2-propanol	26%	0.02	531
2-Heptanol	53%	0.04	555

[a] Percent yield based on amount of iodine used in SmI_2 synthesis. [b] Concentration determined by iodometric titration of the filtered solution.

Generation of $SmBr_2$

Next the sonochemical generation of $SmBr_2$ was examined. A range of bromine sources including molecular bromine were tested but 1,1,2,2-tetrabromoethane was by far the most effective.[3,10] Sonication of 1,1,2,2-tetrabromoethane in the presence of a slight excess of Sm for 7–10 min proved to be an effective means for the generation of the sparingly soluble $SmBr_2$ reductant. During sonication, color was observed in the solution consistent with the formation of the $SmBr_2$ species (violet/blue: THF, green: CH_3CN, blue/black: DME).[10,11] A large amount of precipitate with the same color as the solution was produced in each case. The UV/Vis spectrum was also recorded for each solution (see Supporting Information) and was consistent with the generation of $SmBr_2$ in THF as previously reported.[3,11] The UV/Vis spectrum of each species resembles those of SmI_2 in each solvent except that the absorption maximum of the $SmBr_2$ species is slightly blue-shifted (≈ 20 nm).

Due to the poor solubility of $SmBr_2$ in organic solvents, the determination of the concentration and percent yield of the process is difficult through standard iodometric titration. To overcome this problem the method developed by Hilmersson to determine the active amount of Sm^{II} reductant was utilized.[3] This method uses a Sm^{II}/H_2O/amine system to rapidly and quantitatively reduce 2-heptanone to 2-heptanol. The active concentration of $SmBr_2$ is related to the amount of 2-heptanol produced, determined by GC using *n*-decane as an internal standard. The percent yield, concentration of $SmBr_2$ and λ_{max} for each solvent is shown in Table 2.

Table 2. Percent yield, concentration, and λ_{max} of $SmBr_2$ in THF, CH_3CN, and DME.

Solvent	Yield[a]	Concentration [M][b]	λ_{max} [nm]
THF	58%	0.06	599
CH_3CN	62%	0.07	659
DME	58%	0.06	584

[a] Percent yield based on amount of 1,1,2,2-tetrabromoethane. [b] Concentration of soluble and precipitated $SmBr_2$.

Generation of $Sm(OTf)_2$

Next, attention was focused on the preparation of $Sm(OTf)_2$. This reagent is typically prepared by the reaction of $Sm(OTf)_3$ with 1 equiv. of an organolithium or organomagensium reagent in THF.[12] Although, the role of the Li or Mg counterion in followup reactions of $Sm(OTf)_2$ is not known, *s*-BuLi is generally more effective than *s*-BuMgCl.[13] A number of other approaches have been developed for the synthesis of $Sm(OTf)_2$,[14] but often times require the use of reagents that are difficult to prepare or require extended periods of time. As a result, the original protocol developed by Fukuzawa is the preparative method of choice.[12,13] Inanaga reported that $Sm(OTf)_2$ could be prepared from triflic acid (TfOH) and Sm metal but the reaction in THF was sluggish and provided relatively low yields.[14c] Although this approach is the least productive method for the preparation of $Sm(OTf)_2$ under standard reaction conditions, if it could be initiated and carried out efficiently with high intensity ultrasound, it would be a viable alternative for the preparation of a salt-free reductant.

A combination of a slight excess of Sm metal with TfOH was placed in THF and sonicated using conditions identical to those employed for the preparation SmI_2. A dark purple color began to appear immediately upon sonication and $Sm(OTf)_2$ was produced. Although this method did generate $Sm(OTf)_2$, the concentration and yields were relatively low. Through trial and error it was determined that the sonication of $Sm(OTf)_3$, Sm metal, and a catalytic amount of iodine (1–5 mol-%) was the best protocol for the synthesis of the $Sm(OTf)_2$ in all solvents examined. $Sm(OTf)_2$ was rapidly generated in CH_3CN and DME in 7 min using this approach. The procedure was also attempted without iodine crystals but $Sm(OTf)_2$ generation was sluggish. Although the exact role of the iodine has not been determined, it is possible that iodine activates the surface of the metal in a manner similar to the addition of iodine to magnesium in a Grignard reaction. Regardless of the mechanism, this method is useful since it is efficient and does not have Li or Mg countercations ions present necessary for generation of $Sm(OTf)_2$ from the combination of $Sm(OTf)_3$ and alkyllithium or Grignard reagents.[12–13]

The sonochemical synthesis of $Sm(OTf)_2$ from $Sm(OTf)_3$ and Sm metal was successful in a broad range of solvents, including 2-propanol, 2-butanol, 2-methyl-2-butanol, 2-heptanol, and trifluoroethanol. $Sm(OTf)_2$ in CH_3CN was a dark green/black solution while all of the other $Sm(OTf)_2$ solutions were a dark purple/red color. $Sm(OTf)_2$ was also found to be more soluble and stable in CH_3CN than SmI_2. Solutions of SmI_2 in CH_3CN usually degrade over time (a few days) whereas we have found the $Sm(OTf)_2$-CH_3CN system to be stable for well over 6 months in an inert atmosphere with stirring. In the preparation of each $Sm(OTf)_2$ solution, a precipitate with the same color as the bulk solution was formed. This precipitate was filtered off with a glass-frit funnel before the concentration was determined by an iodometric titration as shown in Table 3. The UV/Vis spectrum of each $Sm(OTf)_2$ solution is shown in Figure 2.

Table 3. Percent yield, concentration, and λ_{max} for $Sm(OTf)_2$ in each solvent.

Solvent	Yield[a]	Concentration[b] [M]	λ_{max} [nm]
THF	85%	0.09	563
CH_3CN	87%	0.07	662
DME	44%	0.03	568
2-Propanol	60%	0.04	513
2-Butanol	30%	0.02	547
Trifluoroethanol	8%	0.01	553
2-Methyl-2-propanol	30%	0.02	517
2-Heptanol	15%	0.01	529

[a] Percent yield based on amount of $Sm(OTf)_3$ used in the synthesis of $Sm(OTf)_2$. [b] Concentration determined by iodometric titration of the filtered solution.

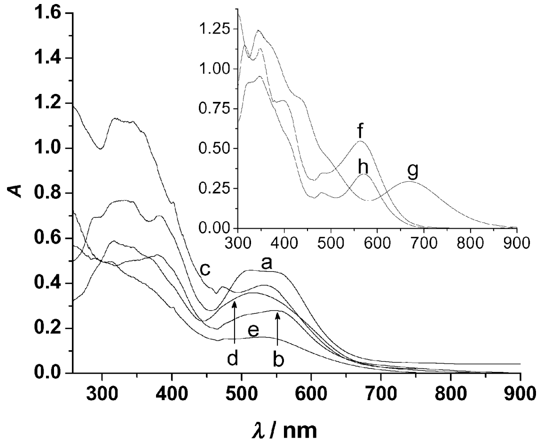

Figure 2. UV/Vis spectrum of $Sm(OTf)_2$. a) 2-Propanol, (b) 2-butanol, (c) trifluoroethanol, (d) 2-methyl-2-propanol, (e) 2-heptanol. Inset: (f) THF, (g) CH_3CN, (h) DME.

While the sonochemical preparation of $Sm(OTf)_2$ from Sm metal and $Sm(OTf)_3$ worked well in a range of solvents this method did not work for the generation of $Sm(OTf)_2$ in THF. After numerous failed attempts to develop a high-yielding one-step method for the synthesis of $Sm(OTf)_2$ in THF, an alternative method was developed. First, SmI_2 was generated sonochemically in THF. Next, 2 equiv. of potassium triflate was added to the solution and then sonicated again to generate $Sm(OTf)_2$. Presumably, the precipitation of potassium iodide drives the ligand exchange between iodide and triflate. Filtration of potassium iodide provided $Sm(OTf)_2$. The UV/Vis spectrum for the $Sm(OTf)_2$ in THF (contained in Figure 2) was identical to that formed through a salt-free (no Mg or Li salts) procedure using 1,5-dithioniabicyclo[3.3.0]octane bis(trifluoromethanesulfonate) as the triflate source.[14b] The concentration of the filtered $Sm(OTf)_2$ was determined by an iodometric titration and is displayed in Table 3.

Determination of the Total Amount of Sm^{II} Produced Through Sonication

In many of the sonochemical preparations, a precipitate the same color as the bulk solution was observed, suggesting insoluble Sm^{II} reductant was also produced in the process. To test this hypothesis, the method developed by Hilmersson[3] was used to determine the total amount of Sm^{II} produced in the sonochemical process. In an initial test, the concentration of a freshly sonicated and unfiltered solution of SmI_2 in THF was determined. This experiment showed that the total concentration of SmI_2 was 0.13 M making this a quantitative reaction. Similar results were obtained for the preparation of SmI_2 in DME. For the preparation of $Sm(OTf)_2$ in DME, the total concentration of $Sm(OTf)_2$ was found to be 0.04 M, which is higher than determined from iodometric titration of the filtered solution. The results shown in Table 4 indicate that the active amount of Sm^{II} generated is approximately 10% greater than the solution concentration. While the Hilmersson method worked well in aprotic solvents, it did not work for the alcoholic solvents examined in this study. The presence of insoluble Sm^{II} in each of the of the alcohols suggests that the total yield of reductant is likely higher than reported in Table 3.

Table 4. Determination of the active amount of Sm^{II} reductant.

Sm^{II}/Solvent	Solution concentration of Sm^{II}[a] [M]	Total Sm^{II} [M][b] (theoretical yield)[c]
SmI_2/THF	0.12	0.13 (0.13)
SmI_2/DME	0.03	0.04 (0.04)
$Sm(OTf)_2$/DME	0.03	0.04 (0.07)

[a] Concentration of a filtered Sm^{II} solution as determined by iodometric titration. [b] Total amount of Sm^{II} generated (soluble and insoluble) as determined by the Sm^{II}/H_2O/amine mediated reduction of 2-heptanone.[8] [c] Theoretical yield is based on the amount of added iodine or $Sm(OTf)_3$.

Conclusions

The use of high-intensity ultrasound provided rapid access to a number of synthetically useful Sm^{II}-based reductants. The Sm^{II} species were generated in a few minutes in a wide range of solvents including alcohols. The sonochemical method is atom-efficient and utilizes commercially available starting materials. This is advantageous, since some preparations of Sm^{II} reductants require a number of steps that are in some cases non-routine. One of the other advantages of this approach is that it can be used for small or larger scale production of Sm^{II} and we have routinely made solutions ranging in volume from 10 to 150 mL.

The generation of Sm^{II} in new solvents is interesting since solvent is known to effect the outcome of certain reactions.[7,15] More recent work has shown that changes in solvent have a large impact on the interaction of additives with Sm^{II} leading to significant changes in the physical properties and reactivity of the reductant.[16] These findings suggest that the propensity for coordination between competing additives and solvents significantly alters the stability and reactivity of Sm^{II}. If this supposition is correct, there is likely to be a rich and unexplored chemistry of Sm^{II} reductants readily available through selective changes in solvent.

Experimental Section

Materials and General Procedures: Tetrahydrofuran (THF), acetonitrile (CH_3CN), and dimethoxyethane (DME) were purified utilizing a Solvent Purification System by Innovative Technology Inc. (Newburyport, MA). Alcohols were distilled twice and dried with activated molecular sieves. All the sonochemical experiments were performed in a VCX-750 W model (Sonics & Materials Inc., Newtown, CT) with a 750-Watt 1/2" full-wave probe, working under a fixed frequency of 20 kHz and 40% of maximum amplitude. The experiments were conducted in an Innovative Technology Inc. drybox containing argon. Experiments were carried out at room temperature, with a pulser mode on for 55 s and off for 5 s to limit the amount of solvent evaporation. UV/Vis experiments were performed with a Shimadzu UV-1601 UV/Vis Spectrophotometer controlled by UV Probe (version 1.11) software. In all experiments, the ligand source (I-, Br-, and -OTf) was the limiting reagent and samarium powder was used in excess.

Generation of SmI_2: Samarium powder (40 mesh size, 0.62 g, 4 mmol) and iodine (0.64 g, 2.52 mmol) were added to 20 mL of THF at 25 °C in a flame-dried vial. The mixture was sonicated for 7 min with pulser mode. See Supporting Information for the amount of starting materials used for the other SmI_2 solvent systems.

Generation of $SmBr_2$: Samarium powder (40 mesh size, 0.25 g, 1.66 mmol) and 1,1,2,2-tetrabromoethane (0.2 g, 0.58 mmol) were added to 10 mL of dry solvent (THF, DME, or CH_3CN) in a flame-dried vial. The solution was then sonicated for 7–10 min in pulsar mode. The $SmBr_2$ precipitates out of solution in 20 min.

Generation of $Sm(OTf)_2$: Samarium powder (40 mesh size, 0.15 g, 1 mmol), $Sm(OTf)_3$ (0.60 g, 1 mmol), and iodine (0.03 g, ca. 5 mol-% relative to the total amount of Sm added) were added to 15 mL of dry CH_3CN in a flame-dried vial. The solution was then sonicated for 6–7 min in pulsar mode. For the preparation of $Sm(OTf)_2$ in THF, SmI_2 was first sonochemically generated − from 0.40 g (2.6 mmol) of Sm powder and 0.40 g (1.57 mmol) of I_2 in 15 mL of THF − then potassium triflate (0.6 g, 3.2 mmol) was added to the solution and sonicated for 4–5 additional minutes to generate $Sm(OTf)_2$ in THF. See Supporting Information for the amount of starting materials used for the other $Sm(OTf)_2$ solvent systems.

Iodometric Titration: 300–500 µL of the filtered Sm^{II} solution was diluted with 3 mL of solvent and mixed rapidly with a stir bar. Next, a solution of iodine of known concentration was added to the rapidly stirred solution until the endpoint was reached.

Determination of the Active Amount of Sm^{II} Reductant: To a freshly sonicated Sm^{II} solution, 3 equiv. of triethylamine, 4 equiv. of water, and 2 equiv. of 2-heptanone were added with stir-bar mixing. Upon work-up, the amount of 2-heptanol produced was determined by GC or GC-MS using decane as an internal standard.[3]

Supporting Information (see footnote on the first page of this article): UV/Vis spectra of Sm^{II}/solvent combinations and other experimental details are also included.

Acknowledgments

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