Microwave-Assisted Generation of Lanthanide(II) Halides in THF and Simple Quantitative Determination

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Lanthanide(II) reagents (SmI_2, $SmBr_2$, YbI_2, EuI_2) have been prepared rapidly in high yields using microwave-assisted heating. Samarium diiodide is obtained as a saturated solution in THF (0.13 M) within 5 min and ytterbium diiodide (0.065 M) after 45 min. A simple method for quantitative determination of LnX_2 in THF is also described by utilizing the instantaneous reaction with ketones in the presence of an amine and water. This method establishes the concentration of the active single-electron-donor species, i.e. Ln^{2+}.

Introduction

The introduction of the versatile and highly selective single-electron-transfer reagent SmI_2 has had a great impact on the development of organic chemistry during the last 10−15 years.[1−4] The reduction potential of SmI_2 is in the range of -1.3 to -2.2 V,[5] depending on solvents and ligands, which makes SmI_2 particularly useful for selective reduction and various coupling reactions.[6,7] Since SmI_2 has become commercially available, the development of SmI_2-mediated reactions has rapidly entered different areas of organic synthesis. Recently, there have also been reports on the use of other anions (Br^- and amides)[8−10] and lanthanides (Yb, Nd and Dy)[11−13] for various selective reduction reactions. However, reagents such as $SmBr_2$, YbI_2, EuI_2 and ThI_2 are still far from being widely used, much due to the lack of simple methods and long reaction times needed for their preparation. Recent progress in microwave-assisted synthesis is particularly attractive due to dramatically shorter reaction times and higher yields relative to conventional reaction conditions.[14,15]

We have realised that research groups that currently explore the chemistry mediated by e.g. SmI_2 are lacking a reliable method for a simple, rapid and quantitative determination of the concentration of the reducing reagent itself. It is important that the concentration of the reducing reagent is known before the success of a new SmI_2-mediated reaction can be fully evaluated. The concentration of the commercially available SmI_2 reagent (0.1 M) has been found to vary from 0.05 to 0.10 M. (Evaluating the concentrations from several different batches from commercial sources showed that the concentration of SmI_2 varied dramatically.) Today there are only a few volumetric titration methods known for e.g. SmI_2; however, these methods only establish the total concentration of I^- or Sm^{2+} and Sm^{3+} (i.e. they also measure inactive reagents such as SmI_3).[16−18] There is, to the best of our knowledge, no method known for a direct and quantitative method for the titration of the single-electron-transfer reagent Ln^{2+} itself. Recently, we reported on the SmI_2/amine/water instantaneous reduction of ketones.[19] This reaction constitutes a key for quantitative determination of the concentration of various LnX_2 solutions, since the reduction of simple ketones is very clean and proceeds extremely fast. Furthermore, the progress of the reaction may be monitored by the disappearance of the characteristic dark blue colour of SmI_2 in THF (Scheme 1).

$$2\ SmI_2\ \textit{(dark blue)} + R_2C{=}O \xrightarrow[-R_3N\cdot HI]{R_3N/H_2O} 2\ Sm(OH)_3\ \textit{(white)} + R_2CHOH$$

Scheme 1. The colour changes from dark blue to white during the reduction of ketones

Results and Discussion

Generation of LnX_2

Microwave-assisted heating of THF mixtures of samarium metal and iodine, iodoform or diiodoethane for 5 min (at 180 °C) results in rapid formation of dark blue solutions of SmI_2. The resulting SmI_2 solutions are of similar quality whether they are made from iodine, iodoform or diiodoethane. However, the use of iodine is preferred since this source of I^- does not involve the generation of gaseous

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by-products (i.e. acetylene or ethene)[20,21] that may cause the maximum pressure allowed in the microwave reaction vessel to be exceeded during heating. Crystals of iodine are also more easily handled inside the glove box. There is a significant difference in the rate of SmI_2 formation from samarium metal if it is used as chunks or as a powder. The formation of SmI_2 using powder of mesh −40 is rapid; the reaction is complete within 3−5 min, while chunks require about 20−30 min. When SmI_2 is generated from more than the necessary amount of I_2 and Sm, the excess SmI_2 precipitates leaving a saturated THF solution. After centrifugation of excess undissolved SmI_2, the maximum concentration of SmI_2 in THF is 0.13 M. The UV/Vis spectrum of the microwave-generated SmI_2 was identical to that previously reported (Supporting Information; for Supporting Information see also the footnote on the first page of this article).[22]

Ytterbium diiodide (YbI_2) has not been used much in organic synthesis since the first report by Kagan.[21] This is in part due to its reported low solubility in THF (0.040 M) and lower reactivity than that of SmI_2. In contrast to the large number of reports on SmI_2-mediated reactions, the development of YbI_2 as a single-electron-transfer reagent is still in its infancy. It was, therefore, with great interest that we prepared YbI_2 from ytterbium metal and iodine crystals using microwave-assisted heating. The saturated clear yellow THF solution of YbI_2 (maximum solubility 0.065 M in THF) is formed in less than 45 min under microwave heating at 180 °C, which results in a pressure of 13 bar. YbI_2 can be stored for extended periods of time inside the glove box without any observable change in colour, concentration or reactivity, as long as there is a slight excess of ytterbium metal present. The UV/Vis spectrum of the microwave-generated YbI_2 is identical to that previously reported (Supporting Information).[22]

We were also interested in the preparation of $SmBr_2$ since it is known to have a considerably larger oxidation potential (−2.07 V) than SmI_2 in THF.[23] Recently, Namy and co-workers reported on the preparation of $SmBr_2$ from tetrabromoethane.[10] We found that the predicted concentration of $SmBr_2$ has to be significantly higher than that of SmI_2, otherwise the preparation failed; the use of approximately 0.45 mmol of $SmBr_2$ per mL of THF gives reproducible results. The samarium bromide could be prepared in a microwave oven from samarium powder and either bromine or tetrabromoethane. However, we recommend preparation of $SmBr_2$ from tetrabromoethane since it gives somewhat cleaner reactions relative to $SmBr_2$ prepared from bromine. (The GC chromatograms of reduced 2-heptanone with $SmBr_2$/triethylamine/water shows no impurities for tetrabromoethane-generated $SmBr_2$, while $SmBr_2$ generated from bromine gives several smaller, unidentified peaks.) In agreement with previous studies we conclude that the solubility of $SmBr_2$ is very low in THF, and it exists predominantly as a suspension. The UV/Vis spectrum agrees with the spectrum for $SmBr_2$ prepared from SmI_2 and LiBr previously reported by Flowers and co-workers (Supporting Information).[23]

Table 1. Microwave-assisted generation of LnX_2 and the resulting concentration in THF[a]

Entry	Ln (mmol)	X_2 (mmol)	V [mL]	$[LnX_2]_{theor.}$ [M]	$[LnX_2]_{titrated}$ [M]
1	Sm (1.3)[b]	I_2 (0.10)	10.0	0.010	0.010
2	Sm (1.0)	I_2 (0.32)	5.0	0.063	0.063
3	Sm (1.0)	I_2 (0.39)	5.0	0.078	0.076
4	Sm (1.0)	I_2 (0.47)	5.0	0.094	0.091
5	Sm (1.1)	I_2 (0.50)	5.0	0.100	0.099
6	Sm (13)[b]	I_2 (11.0)	100.0	0.110	0.108
7	Sm (5.0)	I_2 (0.25)	5.0	0.050	0.048
8	Sm (5.0)	I_2 (0.50)	5.0	0.100	0.102
9	Sm (5.0)	I_2 (0.75)	5.0	0.15	0.15[c]
10	Sm (5.0)	I_2 (1.00)	5.0	0.20	0.21[c]
11	Sm (5.0)	I_2 (1.50)	5.0	0.30	0.31[c]
12	Sm (5.0)	I_2 (2.00)	5.0	0.40	0.36[c]
13	Sm (5.0)[b]	I_2 (1.50)	5.0	0.30	0.29[c]
14	Sm (5.0)[b]	I_2 (2.00)	5.0	0.40	0.35[c]
15	Sm (3.0)	$C_2H_2Br_4$ (0.75)	3.5	0.43	0.42[c]
16	Sm (3.0)[b]	$C_2H_2Br_4$ (0.75)	3.5	0.43	0.43[c]
17	Sm (2.3)[d]	$C_2H_2Br_4$ (0.75)	3.5	0.43	0.44[c]
18	Sm (2.3)[d]	Br_2 (1.50)	3.5	0.43	0.40[c]
19	Yb (2.9)	I_2 (0.16)	5.0	0.032	0.031
20	Yb (2.9)	I_2 (0.276)	5.0	0.055	0.057
21	Yb (2.9)	I_2 (0.33)	5.0	0.063	0.064
22	Yb (2.9)	I_2 (0.355)	5.0	0.071	0.069[c]
23	Yb (2.9)	I_2 (0.48)	5.0	0.100	0.108[c]
24	Yb (2.9)	I_2 (0.59)	5.0	0.118	0.119[c]

[a] The starting materials were mixed inside a glove box. YbI_2 was microwave-irradiated for 45 min, and SmI_2 and $SmBr_2$ for 5 min. $[LnX_2]$ was titrated according to the method described below to yield the concentration with an error of approximately ±2%. [b] Prepared in ultrasonic bath for 2−4 h. [c] Suspension, maximum solubility is exceeded, and the given value is an expected concentration provided that all reagents would dissolve. [d] Prepared inside a glove box with magnetic stirring for at least 15 h.

The use of microwave heating was also explored in the preparation of EuI_2. We found that EuI_2 is prepared within 45 min (this reaction time was not optimised) to yield a clear, light yellow solution. The UV/Vis spectrum is identical to that previously reported (Supporting Information).[22]

Volumetric Titration of SmI_2 Solutions

The reduction of 2-heptanone has been studied using mixtures of SmI_2, amine and water. There is no side-reaction, thus two molecules of SmI_2 are consumed for every reduced molecule of ketone. An excess of I^-, I_2, Sm^0 or Sm^{3+} is not capable of reducing even trace amounts of ketone, hence the reduction of the ketone proceeds only by reaction with the single-electron-transfer reagent SmI_2, and the amount of reduced ketone is directly proportional to the molar concentration of SmI_2 in THF according to Equation (1).

$$R_2C{=}O + 2\,SmI_2 + 6\,H_2O + 4\,R_3N \rightleftharpoons R_2CH_2OH + 2\,Sm(OH)_3 + 4\,R_3N{\cdot}HI \quad (1)$$

Triethylamine (approximately 3 equiv.) and water (approximately 4 equiv.) were added to a solution of unknown concentration of SmI_2 in THF (10−130 mM). The resulting mixture of unknown concentration of the single-electron-transfer reagent SmI_2 was volumetrically titrated with a ketone (2-heptanone) dissolved in THF until the end point, i.e. when the characteristic dark blue colour of SmI_2 had disappeared and a white precipitate and colourless liquid remained. The reduction is instantaneous, even when there is excess precipitated SmI_2 present, which therefore allows rapid titration. The titrant reacts immediately, and there is no delay time during the titration. The added titrant volume was read when the colour changed from light green to white (Table 2).

Table 2. Comparison of volumetric titration with GC-based determinations of $[SmI_2]$[a]

$[SmI_2]_{\text{Volumetric titration}}$ [M][b]	$[SmI_2]_{\text{Conversion}}$ [M][c]	$[SmI_2]_{\text{Internal standard}}$ [M][d]
0.077	0.075	0.074
0.077	0.076	0.075
0.074	0.074	0.075
0.074	0.075	0.074

[a] SmI_2 (5 mL) was added to a dry Schlenk tube, then Et_3N (3 equiv.) and water (4 equiv.) were added by syringe. [b] 2-heptanone was dissolved in dry THF (0.070 M) and added dropwise to the SmI_2/H_2O/amine mixture. The colour of the solution changed from dark blue to green and finally white. The added titrant volume was noted when the colour changed from light green to white. $[SmI_2]$ was calculated according to the balanced Equation (1). [c] The determined $[SmI_2]$ calculated from the conversion of 2-heptanone to 2-heptanol after integration of the separate peaks of the GC chromatogram. [d] The determined $[SmI_2]$ based on the concentration of unreduced 2-heptanone relative to an internal standard (1-hexanol) after integration of the separate peaks of the GC chromatogram.

It may be argued that SmI_2 decomposes rapidly in the presence of excess water and amine. The stability of the reagent mixture of SmI_2 with excess water and amine in THF was therefore also studied (Figure 1). There is an observed decomposition of a 0.075 M solution of SmI_2 in THF in the presence of 4 equiv. of water and 3 equiv. of amine. However, the decomposition of SmI_2 after 1 h is only about 5%. We therefore conclude that the decomposition of SmI_2 is only of marginal consequence for the analysis. The volumetric addition of the ketone to the THF solution should only require approximately 1−2 min, which corresponds to a maximum error of about 1% in the analysis.

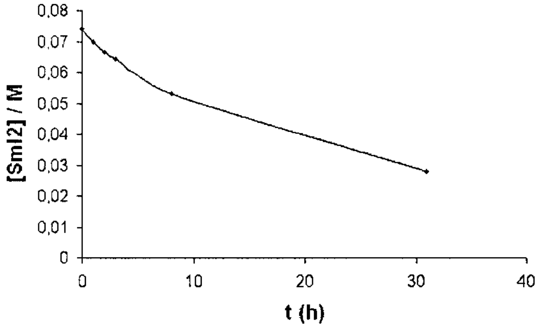
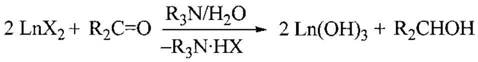


Figure 1. Decomposition of SmI_2 in the presence of triethylamine (3 equiv.) and water (4 equiv.) over an extended period of time (30 h)

GC-Based Titration of SmI_2 and YbI_2

Since the other lanthanide(II) halides do not have such a characteristic colour as SmI_2, another method for the determination of their concentrations was developed. Triethylamine (3 equiv.), water (4 equiv.) and 2-heptanone (1 equiv.) were added to a 5 mL solution or suspension of SmI_2 or YbI_2 in THF (10−400 mM). Provided that the amount of ketone is more than half of the actual amount of LnX_2, the instantaneous reaction of the excess ketone with SmI_2/amine/water results in a mixture of 2-heptanol and 2-heptanone (Scheme 2). Analysis of the amounts of 2-heptanol and 2-heptanone by GC chromatography (verified by an internal standard) yields the initial concentration of LnX_2 (Tables 1 and 2).



$$2\,LnX_2 + R_2C{=}O \xrightarrow[-R_3N\cdot HX]{R_3N/H_2O} 2\,Ln(OH)_3 + R_2CHOH$$

Scheme 4. Unbalanced formula for the LnX_2/amine/H_2O reductions

GC-Based Titration of Suspensions of $SmBr_2$, SmI_2 and YbI_2

Initially, we did not expect to be able to determine the amount of precipitated SmI_2 or $SmBr_2$ utilizing the reduction of 2-heptanone in the presence of amine and water. On the contrary, the reduction of the ketone is extremely fast (instantaneous), even with suspensions of YbI_2, SmI_2 and $SmBr_2$; this allows the quantitative titration of suspensions of up to at least 0.4 M (Table 1). These results also indicate that suspensions of either YbI_2, SmI_2 or $SmBr_2$ can be used as single-electron-transfer reagents in the instantaneous reduction of, for example, ketones by the amine/water method.

Titration of EuI_2

Titrations of EuI_2 in THF were unsuccessful. Apparently, the oxidation potential of Eu^{2+} is too low to mediate the reduction of, for example, 2-heptanone in the presence of triethylamine and water.

Conclusion

There should be numerous reduction reactions for which the oxidation potential of SmI_2 is nonideal, and in which other lanthanide halides and also samarium with different counter anions may play a crucial role. We believe that the exploration of the chemistry mediated by these reagents is dependent on simple methods for their preparation. Due to the very low oxidation potential of EuI_2 its synthetic utility as a single-electron-reagent is somewhat limited, nevertheless its use may increase once this rapid and reliable method of preparation is known. Microwave-assisted generation of LnX_2 from metal (Ln = Sm, Yb and Eu) and halides (I_2 and Br_2) appear to be a viable alternative to the recently reported fast sonication technique.[20] Preliminary results indicate that LnX_2 reagents can be prepared in situ in the presence of reducible substrates. In an ideal situation that would allow the use of less solvent as the actual concentration of LnX_2 could be kept low during the reaction.

The direct method of determining the concentration of LnX_2 solutions by utilizing the instantaneous reaction between, for example, SmI_2 and ketones in the presence of excess amine and water has proven to be a very powerful and reliable method. The major advantage with this method is that the determination is made only on the active single-electron-donor species, i.e. LnX_2. Previously reported methods also include inactive species such as LnX_3 and therefore tend to overestimate the concentration of the reagent. This simple method of determining accurate concentrations of LnX_2 will therefore become useful among those working with single-electron-transfer reagents.

Experimental Section

Generation of SmI_2: Samarium powder (113 mg, 0.75 mmol, 1.5 equiv.) and iodine (127 mg, 0.5 mmol, 1 equiv.) were weighed and diluted with dried THF (5 mL) in a microwave-approved vessel inside a glove box under nitrogen. A magnetic stirrer bar was added, and the vessel was sealed. The mixture was inserted in the microwave oven and irradiated at 180 °C for 5 min to yield a dark blue solution of SmI_2 in THF, which could be used without further purification.

Volumetric Titration of SmI_2: SmI_2 was centrifuged, and the solution (5 mL) was added to a test tube containing a magnetic stirrer bar, located inside a glove box and fitted with a septum. Triethylamine (approximately 3 equiv.) and water (approximately 4 equiv.) were then added to the SmI_2 solution by syringe. While vigorously stirring, 2-heptanone diluted in THF (0.07 M) was added dropwise until the dark blue solution turned colourless with the formation of a white suspension, and the volume of added 2-heptanone was read. The final calculation of $[SmI_2]$ could then be carried out using the balanced formula [Equation (1)].

General GC-Based Determination of the Active Amount of $SmBr_2$, SmI_2 and YbI_2: A solution or suspension of SmI_2 (5 mL) was added to a test tube containing a magnetic stirrer bar, located inside a glove box and fitted with a septum. Triethylamine (approximately 3 equiv.) and water (approximately 4 equiv.) were added into the SmI_2 solution by syringe. While vigorously stirring, excess 2-heptanone diluted in THF (0.070 M) (i.e. more ketone than would be possible to reduce with the estimated amount of the prepared lanthanide reagent) was added in one portion, which caused the solution to decolourise. With the use of gas chromatography, the amount of consumed 2-heptanone was determined with an internal standard added, e.g. 1-hexanol. The final calculation of $[SmI_2]$ could then be performed according to Equation (1).

Supporting Information Available (see also the footnote on the first page of this article): UV/Vis spectra of THF solutions of SmI_2, YbI_2, $SmBr_2$ and EuI_2. Further experimental details are also included.

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