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Reduction and reductive coupling of imines by Sm(II)-based reagents

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Abstract—The reductive coupling of aldimines and ketimines by a series of Sm(II)-based reagents (SmI_2, SmI_2–HMPA, $SmBr_2$, $Sm\{N[Si(CH_3)_3]_2\}_2$, and SmI_2/triethylamine/water) were examined. In general, aldimines and ketimines were efficiently reduced or coupled using reductants that are more powerful than SmI_2, and the use of $Sm\{N[Si(CH_3)_3]_2\}_2$ led to higher diastereoselectivities in reductive coupling reactions. Surprisingly, only the combination of SmI_2/triethylamine/water was capable of reducing and coupling *para*-substituted benzaldimines and coupling ketimines.

1. Introduction

Reductants based on samarium have widespread applicability in reductions and reductive couplings of numerous functional groups including alkyl and aryl halides, aldehydes, epoxides, and α,β-unsaturated ketones, esters, and amides.[1–4] In many SmI_2 mediated reactions, HMPA or other additives are required for successful reduction of alkyl bromides, chlorides and ketones.[5] While SmI_2 or SmI_2-additive combinations have been enormously useful for the reduction and reductive coupling of several functional groups, relatively little work has been carried out using this reagent in the reduction of imines.

The first reports of SmI_2 mediated reduction of aldimines were carried out independently by Enholm[6] and Imamoto[7] in 1990. In both reports, reductions and reductive coupling reactions required prolonged reaction times or elevated temperatures. More recently, Namy has reported that the use of catalytic amounts of NiI_2 with SmI_2 facilitates the reductive coupling of aldimines.[8] Although the diastereoselectivity is relatively low, the reactions proceed under mild conditions and tolerate a wide variety of phenyl and N-substitution. Another recent report utilized a combination of SmI_2 and $Yb(OTf)_3$ to reductively couple aldimines to the corresponding 1,2-diamines.[9] Other Sm-based reductants including $[Sm(OTf)_2(DME)_2]$,[10] $SmBr_2$,[11] and Sm metal containing catalytic amounts of I_2[12] have been used to reduce imines with some success as well. To circumvent some of the more forcing conditions required for imine reduction by SmI_2, nitrones (iminium ion equivalents) have been used to carry out cross coupling reactions between aldehydes or ketones[13] and α,β-unsaturated esters and amides.[14] In both reports, nitrones were efficiently reduced under mild conditions with SmI_2.

Recently, we have been examining two alternative approaches to facilitate the reaction of functional groups typically resistant to reduction by single electron transfer from Sm(II). The first approach utilizes $Sm\{N[Si(CH_3)_3]_2\}_2$. This reductant was first prepared by Evans[15] and has been found to reduce ketones at a much faster rate than SmI_2 or SmI_2–HMPA.[16] The second approach utilizes the combination of SmI_2 with amines and H_2O to drive precipitation of Sm(III) and I^-. The combination of SmI_2/amines/H_2O also reduces conjugated double bonds[17] and ketones.[18] Initial results indicate that both systems should be efficient reductants for imines.[19] Herein, we communicate the results for reduction of an iminium salt, aldimines, and ketimines under mild, room temperature conditions. Comparisons of these reagents with SmI_2 (in the case of the iminium salt) and $SmBr_2$ (in the case of aldimines and ketimines) are presented.

2. Results

2.1. Reduction of iminium salt by Sm(II) reductants

Reduction of the *N*-benzyliminium perchlorate of benzaldehyde (**1**) was carried out using SmI_2, SmI_2–HMPA,

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Keywords: reductive coupling; aldimines; ketimines; samarium.

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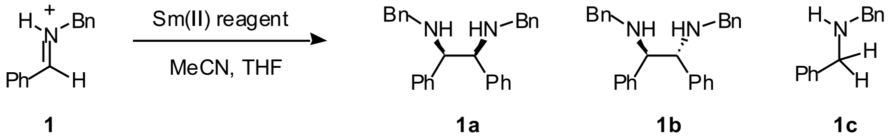
Table 1. Reactions of iminium perchlorate **1** with Sm(II) reductants



Entry	Substrate	Sm(II) reagent	Yield of **1a** and **1b** (**1a**:**1b**)	Reduced product **1c**
1	**1**	SmI_2 (1.5 equiv.)	80^a $(70:30)^b$	–
2	**1**	SmI_2 (1.5 equiv.) HMPA (15 equiv.)	80^a $(60:40)^b$	–
3	**1**	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	Trace $(0:100)^b$	–
4	**1**	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	45^b $(65:35)^b$	55^b

[a] Isolated yield.
[b] Determined by ^1H NMR and GC.

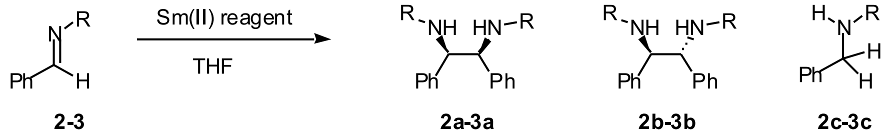
$Sm\{N[Si(CH_3)_3]_2\}_2$, and $SmI_2/Et_3N/H_2O$. All of these reactions were carried out in 50% acetonitrile in THF since **1** was insoluble in THF alone. In all cases the reactions were determined to be quantitative by GC and NMR examination of the crude product mixture. The results of these experiments are contained in Table 1. Reaction of **1** with SmI_2 was completed within minutes and examination of the ^1H NMR showed that only coupled product was obtained. The isolated yield for this reaction was 80% and the ratio of the *meso* and *d*/*l* coupled products was 70:30. Next, the reaction was performed using SmI_2–HMPA as the reductant. The isolated yield was 80% with a slight change in the observed diastereoselectivity. Since little change was found in the diastereoselectivity upon addition of HMPA to SmI_2, $Sm\{N[Si(CH_3)_3]_2\}_2$ was examined as an alternative. While **1b** was the only observed coupling product, the yield was low and products consistent with reduction of acetonitrile were observed. Finally, the combination of $SmI_2/Et_3N/H_2O$ was examined. This protocol was recently introduced by Hilmersson and Dahlén and appeared to have great potential for the reduction of functional groups not typically reduced by SmI_2 and SmI_2–HMPA.[19] Reduction of **1** by $SmI_2/Et_3N/H_2O$ was instantaneous. Analysis by GC and ^1H NMR showed only reduced (**1c**) and reductively coupled products (**1a** and **1b**). The reductively coupled products showed a low diastereoselectivity similar to that obtained with SmI_2 and SmI_2–HMPA.

2.2. Reduction of aldimines by Sm(II) reductants

Reduction of a series of aldimines by the previous series of Sm(II) reductants was examined to determine the influence of reagent and reductant structure on the outcome of the reactions. A number of reactions of substrate **2** with SmI_2 or SmI_2 additive combinations have been reported.[6–8] Furthermore, reduction of aldimines by SmI_2 requires long reaction times or elevated temperatures so we did not examine this reagent any further. Kagan and co-workers have reported that $SmBr_2$ was useful in imine couplings, so it was examined in place of SmI_2.[11] Table 2 contains the results of the reduction of the *N*-benzyl and *N*-butyl imines of benzaldehyde. All of the reactions were found to be quantitative by GC and NMR analysis and good isolated yields were obtained in some cases. Reduction of substrate **2** by $SmBr_2$ and $SmI_2/Et_3N/H_2O$ produced diamines **2a** and **2b** in good yields. Unfortunately, there was no diastereoselectivity in the coupling reaction. The combination of $SmI_2/Et_3N/H_2O$ also produced a significant amount (35%) of the reduced product **2c**. Reduction of **2** by $Sm\{N[Si(CH_3)_3]_2\}_2$ resulted in an isolated yield of 76% and a much higher diastereoselectivity with a preference of 4:1 for the anti (*d*/*l*) coupled product.

Substrate **3** was examined to determine the impact of N-substitution on the product distributions and yields. Reaction of **3** with $SmBr_2$ and $SmI_2/Et_3N/H_2O$ provided nearly identical results. Both reductants provided nearly 80% of the coupled product with the balance being reduced product. Both reductants provided essentially no diastereoselectivity. In contrast, reaction of **3** with $Sm\{N[Si(CH_3)_3]_2\}_2$ provided predominantly the coupled diamine and the diastereoselectivity was 5:1 with a preference for the *d*/*l* pair.

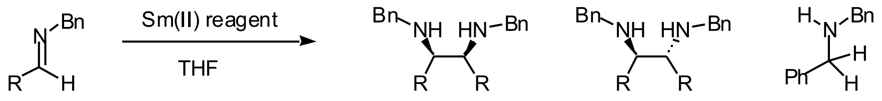
Table 2. Reactions of **2** and **3** with Sm(II) reductants



Substrate	R	Sm(II) reagent	Yield of **a** and **b** (**a**:**b**)	Reduced product **c**
2	Bn	$SmBr_2$ (3.0 equiv.)	70^a $(50:50)^b$	–
2	Bn	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	76^a $(20:80)^b$	–
2	Bn	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	65^b $(50:50)^b$	35^b
3	n-C_4H_9	$SmBr_2$ (3.0 equiv.)	78^b $(55:45)^b$	22^b
3	n-C_4H_9	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	95^b $(16:84)^b$	5^b
3	n-C_4H_9	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	79^b $(54:46)^b$	21^b

[a] Isolated yield.
[b] Determined by ^1H NMR and GC.

Table 3. Reactions of substrates **4–6** with Sm(II) reductants



4-6 **4a-6a** **4b-6b** **4c-6c**

Substrate	R	Sm(II) reagent	Yield of **a** and **b** (**a**:**b**)	Reduced product **c**
4	*p*-$CH_3C_6H_5$	$SmBr_2$ (3.0 equiv.)	–	Trace
4	*p*-$CH_3C_6H_5$	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	–	–
4	*p*-$CH_3C_6H_5$	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	65[a] (45:55)	35[a]
5	*p*-$CH_3OC_6H_5$	$SmBr_2$ (3.0 equiv.)	–	Trace
5	*p*-$CH_3OC_6H_5$	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	–	–
5	*p*-$CH_3OC_6H_5$	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	70[a] (30:70)	30[a]
6	*p*-$CF_3C_6H_5$	$SmBr_2$ (3.0 equiv.)	–	Trace
6	*p*-$CF_3C_6H_5$	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	–	–
6	*p*-$CF_3C_6H_5$	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	65[a] (45:55)	35[a]

[a] Determined by ^1H NMR and GC.

Next substrates **4** and **5** with electron donating *para*-substituents, and substrate **6** with an electron withdrawing *para*-substituent were examined to determine the electronic effects on reductions and reductive coupling reactions of imines. The results of these experiments are contained in Table 3. Reactions of substrates **4–6** with $SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$ were unsuccessful, and resulted in predominantly unreduced starting material.

In each of the reactions between substrates **4–6** and $Sm\{N[Si(CH_3)_3]_2\}_2$, only starting material was recovered after workup. In the case of $SmBr_2$, a trace amount of the reduced products **4c–6c** were obtained, but the balance of the reaction was unreduced starting material.

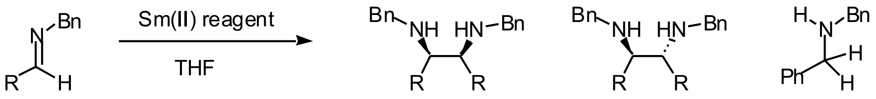
Reaction of substrates **4–6** with $SmI_2/Et_3N/H_2O$ were also examined. Typically, this reductant reacts with substrates within minutes, but reaction with the *para*-substituted imines took about 30 min to proceed to completion. Examination of the reactions after completion clearly showed the presence of both reduced and coupled products exclusively. No starting materials or other side products were apparent from examination of the ^1H NMR spectra or GC chromatographic traces. While the reactions proceeded, the yield of coupled to reduced products was approximately 2:1. The reductive coupling of substrates **4** and **6** provided no diastereoselectivity. However, the reductive coupling of substrate **5** showed a preference for the *d*/*l* pair over the *meso* product in an approximate 2:1 ratio. With substrates **4–6**, there is a significant amount of reduction using $SmI_2/Et_3N/H_2O$.

The unexpected results obtained with **4–6** led us to examine reactions of the *meta* derivative, **7** with the Sm(II) reductants. The results are contained in Table 4. These reactions proceeded to completion and examination of the products clearly showed the presence of both reduced and coupled products. Surprisingly, $SmBr_2$ provided predominantly reduced product **7c** and 20% of **7a** and **7b**. Reaction of **7** with $Sm\{N[Si(CH_3)_3]_2\}_2$ and $SmI_2/Et_3N/H_2O$ provided 70 and 75% yields, respectively of the coupled product and only trace amounts of reduced **7c**. Reductive coupling of **7** by $SmBr_2$ or $SmI_2/Et_3N/H_2O$ showed very little stereoselectivity while coupling by $Sm\{N[Si(CH_3)_3]_2\}_2$ showed a 5:1 preference for **7b**.

2.3. Reduction of ketimines by Sm(II) reductants

Reduction of **8** by Sm(II) reductants was examined to determine the ability of the more powerful reagents to carry out reduction or reductive coupling of a more sterically congested ketimine. Not only are ketimines more sterically demanding substrates, but they are also typically more difficult to reduce through single electron transfer than aldimines. Table 5 contains the results of reduction of **8** by $SmBr_2$, $Sm\{N[Si(CH_3)_3]_2\}_2$, and $SmI_2/Et_3N/H_2O$. Reduction of **8** by $SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$ provided only reduced product **8c** and no trace of coupling product

Table 4. Reaction of substrate **7** with Sm(II) reductants

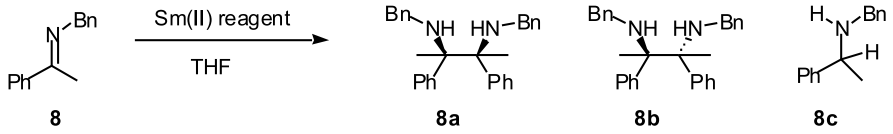


7 **7a** **7b** **7c**

Substrate	R	Sm(II) reagent	Yield of **a** and **b** (**a**:**b**)	Reduced product **c**
7	*m*-$CH_3C_6H_5$	$SmBr_2$ (3.0 equiv.)	20[a] (44:56)	70[a]
7	*m*-$CH_3C_6H_5$	$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	70[b] (15:85)	Trace
7	*m*-$CH_3C_6H_5$	SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	75[b] (46:54)	Trace

[a] Determined by ^1H NMR and GC.
[b] Isolated yield.

Table 5. Reactions of substrate **8** with Sm(II) reductants



Sm(II) reagent	Yield of **8a** and **8b** (**8a**:**8b**)	Reduced product **8c**
$SmBr_2$ (3.0 equiv.)	–	Quantitative[a]
$Sm\{N[Si(CH_3)_3]_2\}_2$ (3.0 equiv.)	–	Quantitative[a]
SmI_2 (1.5 equiv.)/Et_3N (3.0 equiv.)/H_2O (3.75 equiv.)	80[a] (50:50)	20[a]

[a] Determined by ^1H NMR and GC.

was observed. The reaction was quantitative in both cases. Reduction of **8** by $SmI_2/Et_3N/H_2O$ was quantitative and led to 80% of the diamines **8a** and **8b** with the balance being **8c**. While the reaction of **8** with $SmI_2/Et_3N/H_2O$ provides high yield of coupled products, there is no diastereoselectivity in this reaction.

3. Discussion

The goal of this study was to examine and compare the ability of various Sm(II) reductants to reduce or couple substrates containing a C–N double bond. Iminium ions are relatively easy to reduce and a recent report describing the SmI_2-mediated coupling of nitrones with carbonyls suggests that the C=N bond of the nitrone is reduced preferentially to the C=O bond.[13] The perchlorate salt of **1** was used as a prototypical substrate to examine the Sm(II) mediated reduction and reductive coupling of iminium salts. Many of the perchlorate iminium salts we have synthesized in our lab were found to be insoluble in THF and **1** was no exception to this observed trend. To circumvent this, **1** was dissolved in acetonitrile and the Sm(II) substrates in THF were added to the acetonitrile solution. This combination of solvents, reagent and substrates produced a homogeneous solution and reactions were complete within 1 min. The reductive coupling of **1** by SmI_2 and SmI_2–HMPA was clean and quantitative. In both cases good yields of 80% were obtained after column chromatography. Unfortunately the addition of HMPA to SmI_2 had little effect on the diastereoselectivity of the coupling as expected. Examination of $Sm\{N[Si(CH_3)_3]_2\}_2$ in the reaction with **1** provided trace amounts of the *d*/*l* coupled product of **1b**, but unfortunately, it also reduced the acetonitrile co-solvent. Examination of the recent protocol developed by Hilmersson and Dahlen provided both the reduced and coupled product. Interestingly, this more powerful reductant did not reduce the acetonitrile.

Although these results are somewhat disappointing, they do show that SmI_2 alone is a suitable reductant for the coupling of iminium salts. Recent elegant work by Skrydstrup and Riber show that the iminyl radical formed upon reduction of a nitrone (iminium equivalent) can efficiently couple with α,β-unsaturated esters and amides as well.[14]

The next series of experiments focused on the reaction of Sm(II) reagents with aldimines derived from benzaldehyde and benzyl amine **2** or *n*-butyl amine **3**. Reactions of either substrate with $SmBr_2$ or $Sm\{N[Si(CH_3)_3]_2\}_2$ provided good yields of the coupled product, but $SmBr_2$ showed no diastereoselectivity whereas $Sm\{N[Si(CH_3)_3]_2\}_2$ showed a reasonable preference for the anti-coupled product. The reduction of substrates **2** and **3** with $SmI_2/Et_3N/H_2O$ provided reasonable yields of the coupled products, but a considerable amount of the reduced side product was also detected. Unfortunately, this system also showed no diastereoselectivity. Altogether, these results demonstrate that N-substitution has little effect on the yield or diastereoselectivity of the reductive coupling or reduction of the imine. Of the three Sm(II) reagents studied, $Sm\{N[Si(CH_3)_3]_2\}_2$ provided the highest diastereoselectivity.

Substrates **4**–**6** were examined to determine the importance of electronic factors in aldimine reductions. Surprisingly, $Sm\{N[Si(CH_3)_3]_2\}_2$ was ineffective at reducing or coupling these substrates. Use of $SmBr_2$ provided only trace amounts of reduced product even after 12 h. Use of $SmI_2/Et_3N/H_2O$ provided between 65–70% of the coupled diamine products with the balance once again being the reduced amine. Nearly every reaction carried out with $SmI_2/Et_3N/H_2O$ is complete within a few minutes, but the reactions of substrates **4**–**6** took approximately 30–60 min to proceed to completion. Substrates **4** and **5** can be expected to be somewhat more difficult to reduce than the unsubstituted **2**, but **6** should be easier to reduce through single electron transfer from Sm(II).

To further examine the impact of phenyl substitution on aldimines, *meta* substituted substrate **7** was examined. Reactions of **7** proceeded to completion with all of the Sm(II) reagents examined. All of the reactions between **7** and the various Sm(II)-based reagents proceeded in a reasonable amount of time in a manner similar to reactions involving substrate **2**. These results indicate that *para* substitution on the aldimines examined in this study inhibit reduction by Sm(II)-based reagents.

Namy and Machrouhi recently reported that aldimines similar to **5** are efficiently coupled using a combination of SmI_2/NiI_2.[8] Although the role of NiI_2 in this system is unclear, it is quite surprising that $SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$ are incapable of carrying out these reactions at room temperature. Both are known to be strong single electron reductants and their thermodynamic redox potentials are within 100 mV of each other.[16,20] Furthermore, the fact that $SmI_2/Et_3N/H_2O$ reduces these substrates slowly (in comparison to other substrates) suggests that the presence of *para*-substituents influence the rate of reduction. It is interesting that *para* substituted aromatic substrates with both electron donating and electron withdrawing substituents are more difficult to reduce. Mechanistic studies are currently being planned to elucidate the cause of this unexpected result.

Substrate **8** was examined to determine the efficacy of the Sm(II) reagents in ketimine reductions. While all of the reagents examined were capable of reducing **8**, only the combination of $SmI_2/Et_3N/H_2O$ was capable of coupling to provide diamine products **8a** and **8b**. Use of $SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$ provided only reduced **8c**. Reduction of ketimines by $SmBr_2$-HMPA also provide amines exclusively as products.[21] It is unclear at this point whether the reduction proceeds through H-atom abstraction from THF or whether trace amounts of proton from water or solvent impurities are responsible for exclusive amine formation. Nonetheless, these findings suggest that $SmI_2/Et_3N/H_2O$ is the best suited of the reagents examined for reductive coupling of ketimines while $SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$ are best suited for ketimine reduction.

4. Conclusions

The experiments described herein show that SmI_2 is capable of reducing iminium perchlorate **1** to the corresponding diamines **1a** and **1b** with a preference for the *syn* isomer. Use of HMPA or other protocols show no advantage in terms of product stereoselectivity or yield. In the reactions of aldimines **2**, **3** and **7** with Sm(II)-based reductants, $Sm\{N[Si(CH_3)_3]_2\}_2$ showed the best diastereoselectivity in the reductive coupling reaction. For more recalcitrant *para*-substituted aldimines **4–6**, the combination of $SmI_2/Et_3N/H_2O$ was best suited for coupling although little or no diastereoselectivity was observed in the reaction. Reductive coupling of **8** to **8a** and **8b** is best achieved through the use of $SmI_2/Et_3N/H_2O$ while reduction to **8c** is accomplished through the use of $SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$. The results of these experiments are currently being utilized to develop coupling reactions of imines and other functional groups.

5. Experimental

5.1. General

5.1.1. Preparation of (1). Approximately 16.5 g (110 mmol) perchloric acid (70% in water) was added dropwise to a 10.7 g solution of benzyl amine (100.0 mmol) in ice bath. The reaction mixture was stirred overnight, then benzyl amine was added slowly until the solution was slightly basic. The solvent was removed in vacuo to give white solid (17.8 g, 86%). ^{1}H NMR (acetone-d_6): δ 4.51 (s, 2H), 7.42–7.62 (m, 5H). A mixture of 1.0 g (4.8 mmol) of the benzylammonium perchlorate salt, 1.53 g, (14.4 mmol) of benzaldehyde, five drops of diethyl amine, and benzene (70 ml) were heated at reflux with a Dean–Stark trap. After 3 days of reflux, solvent was removed in vacuo and fresh benzene (50 ml×2) was added and distilled off. The brown oily residue was then crystallized in ether at room temperature. The crystallized solid was ground in ether, filtered, and then washed with ether. The white solid was dried under vacuum (1.32 g, 93%). ^{1}H NMR (acetone-d$_6$): δ 5.38 (s, 2H), 7.44–8.27 (m, 10H), 9.51(s, 1H).

5.1.2. Reaction of (1) with Sm(II) reductants. The Sm(II) reagent (1.5 equiv.) was added dropwise to an acetonitrile solution of **1** (0.295 g, 1.0 mmol), under nitrogen atmosphere. The reaction mixture was stirred for additional three hours then saturated ammonium chloride (aq.) was added carefully. Then the solution was extracted with diethyl ether (50 ml×3) and the organic layers were combined then washed with saturated aqueous solution of $Na_2S_2O_3$ (20 ml×2). The organic layer was dried under $MgSO_4$ then the solvent was removed to give the mixture of two diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): **1a**; δ 3.45 (center of AB system, 4H), 3.79 (s, 2H), 7.0–7.5 (m, 20H). **1b**; δ 3.61 (center of AB system, 4H), 3.74 (s, 2H), 7.0–7.5 (m, 20H). **1c**; δ 3.84 (4H, s), 7.0–7.5 (10H, m).

When **1** was reacted with $Sm\{N[Si(CH_3)_3]_2\}_2$, NMR showed only **1b** as a product. Unfortunately **1b** could not be isolated since there were many other side products resulting from reduction of acetonitrile by $Sm\{N[Si(CH_3)_3]_2\}_2$.

For entry 4 in Table 1, SmI_2 and Et_3N, then H_2O was added to the acetonitrile solution of substrate. White precipitate was immediately formed once the addition of H_2O was completed. Then the reaction mixture was worked up as usual and evaporation of solvent gave the mixture of coupled product and reduced product.

5.2. General procedure for synthesis of imines 2–8

To a solution of aldehyde or ketone (50.0 mmol) in CH_2Cl_2 (50 ml) was added 5 g of 4A molecular sieves and benzyl amine (50.0 mmol). The heterogeneous mixture was stirred for an hour then the molecular sieves were filtered off. The filtrate was dried under $MgSO_4$ then the solvent was evaporated in vacuo to give colorless liquid as product (73–97%).

Imine **8** was obtained from acetophenone (20.0 mmol) and benzylamine (20.0 mmol) refluxed in benzene (120 ml) fitted with a Dean–Stark trap overnight. After evaporation of the solvent and drying in vacuo, imine **8** was collected as a slightly yellow oil (70% yield).

5.2.1. Reaction of imines 2–8 with Sm(II) reductants. The Sm(II) reagent was added dropwise to a solution of imine (0.6 mmol) in THF (10 ml), under nitrogen atmosphere. The reaction mixture was stirred for 12 h* then saturated ammonium chloride (10 ml) was added. The reaction mixture was extracted with diethyl ether (50 ml×3) then the organic layers were combined and washed with saturated $Na_2S_2O_3$ solution (10 ml×2). The organic layer was dried under $MgSO_4$ and the solvent was removed in vacuo to give product. *$SmBr_2$ and $Sm\{N[Si(CH_3)_3]_2\}_2$ reductions. When $SmI_2/Et_3N/H_2O$ was used, the reaction was completed within 30 min. ^{1}H NMR (500 MHz, $CDCl_3$): **2a**; δ 3.45 (center of AB system, 4H), 3.79 (s, 2H), 7.0–7.5 (m, 20H). **2b**; δ 3.61 (center of AB system, 4H), 3.74 (s, 2H), 7.0–7.5 (m, 20H). **2c**; δ 3.84 (4H, s), 7.0–7.5 (10H, m). **3a**; δ 0.73–0.76 (t, 6H), 1.03–1.12 (m, 4H), 1.21–1.43 (m, 4H), 2.20–2.30 (m, 4H), 3.72 (s, 2H), 7.00–7.32 (m, 10H). **3b**; δ 0.83–0.86 (t, 6H), 1.21–1.43 (m, 8H), 2.35–2.43 (m, 4H), 3.60 (s, 2H), 7.00–7.32 (m, 10H). **3c**; δ 0.89–0.92 (t, 3H), 1.21–1.51 (m, 4H), 2.62–2.65 (t, 2H), 3.79 (s, 2H), 7.00–7.32 (m, 5H). **4a**; δ 2.31 (s, 6H), 3.46 (center of AB system, 4H), 3.74 (s, 2H), 7.0–7.5 (m, 18H). **4b**; δ 2.41 (s, 6H), 3.60 (center of AB system, 4H), 3.73 (s, 2H), 7.0–7.5 (m, 18H). **4c**; δ 2.38 (s, 3H), 3.81 (s, 2H), 3.84 (s, 2H), 7.0–7.5 (m, 9H). **5a**; δ 3.43 (center of AB system, 4H), 3.67 (s, 2H), 3.89 (s, 6H), 6.78–7.78 (m, 18H). **5b**; δ 3.58 (center of AB system, 4H), 3.65 (s, 2H), 3.84 (s, 6H), 6.78–7.78 (m, 18H). **5c**; δ 3.76 (s, 2H), 3.81 (s, 2H), 3.85 (s, 3H), 7.0–7.5 (m, 9H). **6a**; δ 3.47 (center of AB system, 4H), 3.87 (s, 2H), 7.0–7.6 (m, 18H). **6b**; δ 3.57 (center of AB system, 4H), 3.88 (s, 2H), 7.0–7.6 (m, 18H). **6c**; δ 3.77 (s, 2H), 3.80 (s, 2H), 7.0–7.5 (m, 9H). **7a**; δ 2.40 (s, 6H), 3.45 (center of AB system, 4H), 3.82 (s, 2H), 6.93–7.40 (m, 18H). **7b**; δ 2.29 (s, 3H), 2.40 (s, 3H), 3.62 (center of AB system, 4H), 3.82 (s, 2H), 6.93–7.39 (m, 18H). **7c**; δ 2.39 (s, 3H), 3.82 (s, 2H) 3.85 (s, 2H), 6.93–7.40 (m, 9H). **8a**; δ 1.54 (s, 6H), 3.44 (center of AB system, 4H), 7.0–7.35 (m, 20H). **8b**; δ 1.65 (s, 6H), 3.44 (center of AB system, 4H), 7.0–7.35 (m, 20H). **8c**; 1.39 (d, 3H), 3.64 (center of AB system, 2H), 3.83 (q, 1H), 7.2–7.4 (m, 10H).

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