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# Samarium/*N*-bromosuccinimide-induced reductive dimerization of carbonyl compounds

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**Abstract**—Stereoselective reductive coupling of carbonyl compounds has been achieved using samarium/*N*-bromosuccinimide in methanol. The combination of these agents has proved a powerful addition to the arsenal of samarium-based reductants currently utilized.

The reductive coupling of carbonyl compounds to give pinacols is an important reaction for the formation of vicinally functionalized C–C bonds.[1] Titanium reagents,[2] cerium reagents,[3] samarium diiodide,[4] and ytterbium metal[5] were effective for this purpose in certain cases. There is increasing attention given to performing a wide variety of synthetic reactions by a direct reaction of metals. Samarium metal is well suited to overcome the drawbacks of dissolving metal reduction because of its ready availability and low cost.[6] It is stable in air, and has a strong reducing power, similar to that of magnesium. The operational simplicity of using samarium metal in various chemical reactions has been demonstrated in our recent publications.[7]

Reductive coupling of carbonyl compounds to pinacols using samarium–iodine in methanol and samarium/iodine–titanium isopropoxide was achieved.[8] A bivalent salt free samarium bis (trifluoromethanesulfonate) complex was used for intermolecular pinacol coupling reactions of aromatic ketones to diols with high diastereoselectivity (*dl* isomer was predominantly formed).[9] Diastereoselective pinacol coupling alkyl aryl ketones with samarium in the presence of trimethylsilyl chloride was accomplished.[8] Sm/$Et_2AlI$ was used for the reductive coupling of carbonyl compounds.[10] Based on these reports in this area, we became interested further in this reaction. In this letter, we report a facile and convenient reductive dimerization of carbonyl compounds by samarium metal in the presence of *N*-bromosuccinimide. The reducing ability of samarium-mediated reactions has been modified by the use of several additives.[8–10] However, the use of *N*-bromosuccinimide as an additive in the samarium-induced chemistry has not been investigated. In principle, Sm/NBS-induced reaction has advantages over the traditional methods since this study avoids the tedious preparation of samarium dibromide.

The reaction of Sm/NBS toward various carbonyl compounds has been investigated using methanol as solvent. At the beginning of our study, several acetophenone derivatives were selected for the dimerization reaction by samarium/NBS-induced reactions (**1** to **2**). Interestingly, the yield of the reduction product **3** was very low (Scheme 1, Table 1). The rate of reaction was fast and the isolated yield of the product was high. Aromatic aldehyde **4** and aliphatic ketones **7** and **10** underwent smooth pinacol coupling under this condition. Notably, the existing methods failed to produce dimeric products when aliphatic ketones were used as the substrates.

The steric crowding has posed no problem in the dimer formation when the reaction was performed using Sm/NBS in methanol. For example, when benzophenone (**13**) was used as the substrate, the reductive coupling product **14** was formed exclusively in 69% yield. Fluorene **15** resulted in a mixture of the dimerized product

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*Keywords*: Samarium; *N*-Bromosuccinimide; Reductive coupling; Electron transfer.

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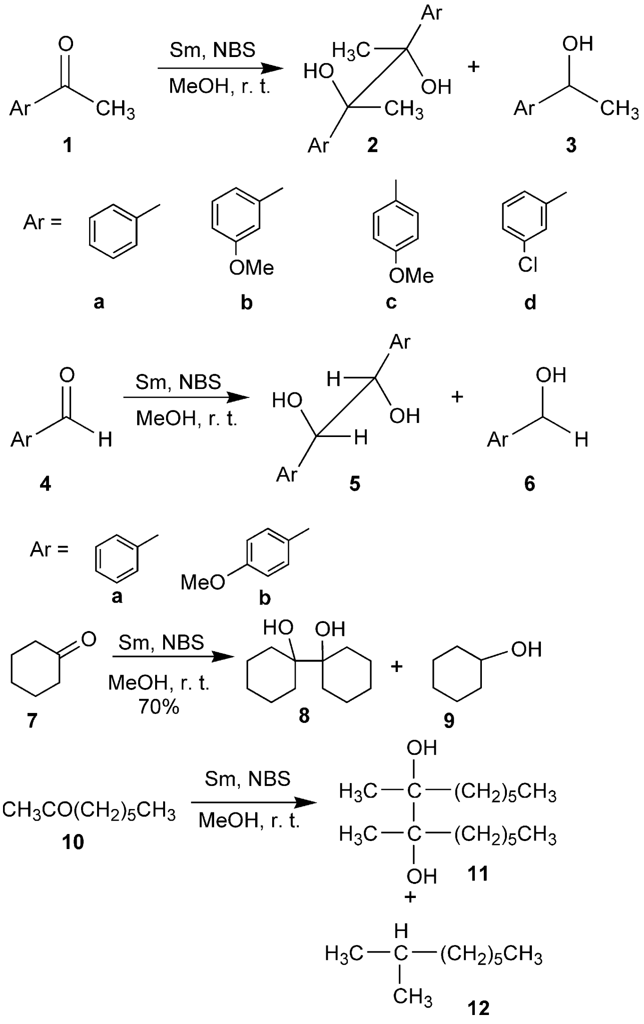


Scheme 1.

**Table 1.** Reductive dimerization of carbonyl compounds with Sm/NBS in methanol

| Entry | Carbonyl compounds | Diol (yield %) | *dl:meso* | Alcohol (yield %) | Time (h) |
|---|---|---|---|---|---|
| 1 | **1a** | **2a** (79) | 70:30 | — | 0.5 |
| 2 | **1b** | **2b** (69) | 70:28 | — | 0.5 |
| 3 | **1c** | **2c** (68) | 70:30 | **3c** (11) | 0.5 |
| 4 | **1d** | **2d** (60) | 70:30 | **3d** (9) | 0.5 |
| 5 | **4a** | **5a** (75) | 75:25 | **6a** (5) | 0.5 |
| 6 | **4b** | **5b** (75) | 75:25 | **6b** (5) | 0.5 |
| 7 | **7** | **8** (70) | — | **9** (10) | 0.5 |
| 8 | **10** | **11** (69) | — | **12** (10) | 0.5 |
| 9 | **13a** | **14a** (69) | — | — | 3 |
| 10 | **13b** | **14b** (69) | — | — | 3 |
| 11 | **15** | **16** (63) | — | **17** (10) | 3 |

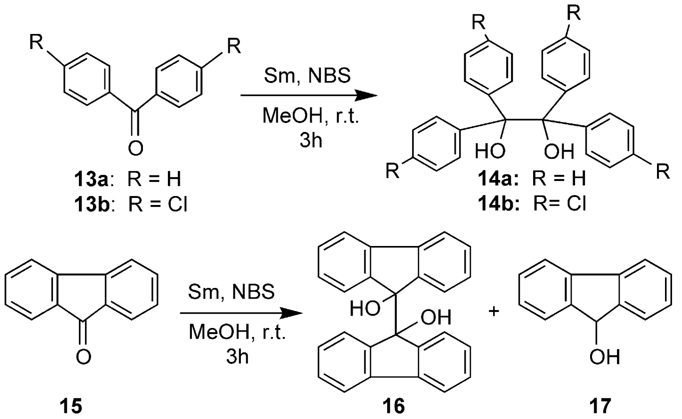
**16** (63%) along with **17**. Using many of the conditions described in the literature, such dimerization could not be achieved in satisfactory yield (Scheme 2).

The distinct advantages of the reductive dimerization of carbonyl compounds for the synthesis of the diols reported herein over other methods included a very short reaction time, fewer by-products, and an overall high yield. For example, redistilled chlorotrimethylsilane/Sm (stored under an inert atmosphere and molecular sieves) afforded product in a nonstereoselective manner. The yield of the Sm/$Et_2AlI$-indued reaction was moderate with low diastereoselectivity. Samarium/$I_2$ produced 24% undesired products. Some of the problems were solved using samarium diiodide in the presence of HMPA.[11] However, HMPA is toxic and carcinogenic. The most important solution, however, was the discovery of samarium dibromide-mediated reactions.[12] The reported preparation of samarium dibromide is complex, which required heating a mixture of anhydrous samarium tribromide in the presence of hydrogen gas at 740 °C. Samarium dibromide could not be obtained by the reaction of samarium metal with 1,2-dibromoethane. Kagan and co-workers discovered a better method for the preparation of samarium dibromide by reducing samarium trioxide with lithium dispersion in THF.[12] However, the whole experimental procedure needed a considerable amount of time and required a number of reagents. In contrast, our method by reacting samarium metal with NBS in the presence of methanol is very simple. We believe the reactive species is samarium dibromide on the basis of the color of the solution. Our hypothesis is further supported by the fact that reaction of samarium tribromide with acetophenone failed completely to achieve any detectable amount of dimeric product. Addition of samarium metal to this solution, however, afforded an identical mixture of products with an identical stereoselectivity. This indicates the formation of samarium dibromide in the medium by the reduction of samarium tribromide with samarium metal in methanol.

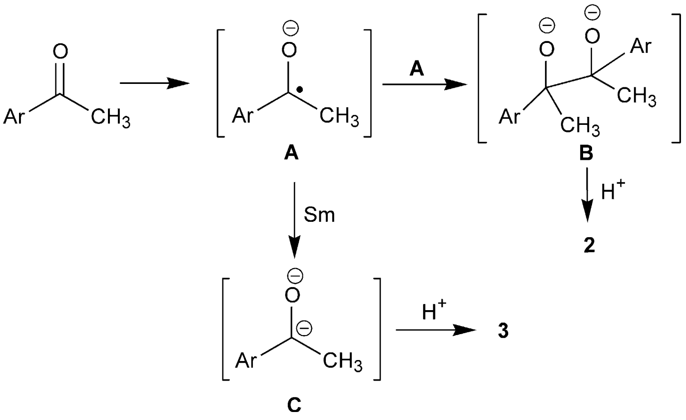
Given the nature of the products, the most probable mechanism would be a reaction very similar to our samarium–iodine induced reduction reaction of the imines.[7b] Single electron transfer to the unsaturated carbon–oxygen bond may generate the ion radical **A** and because of the stability of the benzylic radical, a self-coupling process, **A** to **B** may be feasible. If the reaction follows **A** to **B** path, a pinacol type of compound **2** maybe formed. Further electron transfer to the ion radical **A** would generate a dianion **C**, which on protonation by methanol would generate alcohol **3** (Scheme 3).

While many of the existing methods failed to achieve dimerization of aliphatic ketones, successive dimerization of these types of ketones with Sm/NBS system deserves special attention. The stability of the ion radical **A** is very crucial for an effective dimerization. In aromatic systems, such a radical is much more stable compared to the aliphatic systems. It is apparent that the combination of Sm/NBS in methanol generates a powerful reducing system. This system, in turn, is capable of the reductive dimerization of aliphatic ketones in spite of less stability of this kind of ion radical compared with the aromatic system.[12] Interestingly, using a similar method, benzophenone (**13**) could not be dimerized.[12] But, our present method works well with benzophenone and other related sterically congested ketones.

In conclusion, we have developed a simple Sm/NBS-induced methodology of reductive coupling of different



Scheme 2.



Scheme 3.

types of carbonyl compounds to produce the corresponding diols in good yield and excellent selectivity. This study has established that NBS is an outstanding promoter in samarium-induced chemistry. The ready availability, cost, and easy handling procedure associated with this present Sm/NBS makes this method attractive.[13]

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13. Representative experimental procedure: A mixture of acetophenone **1a** (0.1 g, 0.83 mmol), samarium metal (0.375 g, 2.49 mmol), and NBS (0.06 g, 0.49 mmol) in MeOH (5 mL) was stirred at room temperature under argon and the reaction monitored by TLC. After the ketone was consumed (30 min), the reaction mixture was diluted with $CH_2Cl_2$, 0.5 mL saturated $NaHCO_3$ solution added, and passed through a pad of Celite. The filtrate was dried ($Na_2SO_4$), concentrated, and residue subjected to silica gel chromatography. The diol **2a** was obtained in 79% yield as a mixture of diastereomers (*dl*:*meso* = 70:30).