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Samarium Iodide-Catalyzed Pinacol Coupling of Carbonyl Compounds

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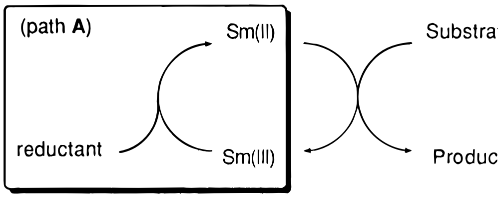
One of the most remarkable developments in recent organic synthesis is the application of divalent samarium compounds as excellent reducing agents.[1] Since the pioneering works by Kagan and Inanaga in the chemistry of samarium(II) iodide (SmI_2), a wide variety of novel types of electron transfer reactions which are far superior to the traditional ones in both efficiency and selectivity have been reported.[1] Unfortunately, almost all of the electron transfer reactions required more than a stoichiometric amount of samarium complexes, except for few examples of hydride transfer reductions such as the Meerwein−Ponndorf−Verley (MPV) reduction[2] and the Tishchenko reaction.[3] This is simply because a catalytic cycle of them has not been established.[4] This limitation strongly decreases the synthetic value of the reactions promoted by low-valent samarium complexes. In this work, we report our preliminary investigation of the establishment of a catalytic cycle of SmI_2 for the reduction of carbonyl compounds.

In order to achieve the catalytic cycle of SmI_2, a reduction pathway of trivalent into divalent samarium species is required (path A in Scheme 1). The previous studies on low-valent samarium-mediated reductions using Sm as a reducing agent[5] and the similar reduction potential between Sm and Mg (−2.41 and −2.37 V, respectively) would offer a possibility that Mg serves as reducing agent of trivalent samarium.[6] Indeed, it was easily found that trivalent samarium salts such as SmI_3, $SmBrI_2$, and $SmClI_2$ underwent the reduction by Mg to provide divalent samarium species.[7] UV-vis spectroscopic analyses clearly indicated the existence of the reduction pathway (Table 1). After the suspension of SmI_3 in THF was treated with Mg, the color change from yellow to dark-blue occurred immediately, and the characteristic absorptions attributed to SmI_2 were observed at 621 and 560 nm (run 1), indicating the formation of SmI_2.[8] It should be noted that the absorptions due to SmI_2 were also detected for reactions employing $SmBrI_2$ and $SmClI_2$ (runs 3 and 4). The decrease of the absorbance compared with the parent SmI_2 solution is probably due to the existence of an equilibrium between SmI_2 and SmI_3, which might be supported by the results that the addition of MgI_2 to a solution of SmI_2 led to the decrease in its absorbance (run 5). These results indicate that the addition of Mg shifts the equilibrium between Sm(II) and Sm(III) toward Sm(II) via Scheme 2.

Scheme 1



The present SmI_2/Mg system could be applied to the pinacol coupling of carbonyl compounds.[9,10] One of the significant points for the successful pinacol coupling under this system is to maintain the concentration of divalent samarium higher than that of carbonyl compounds to avoid the competition between the coupling and the Sm(III)-promoted reactions, such as benzoin condensation and the Tishchenko reaction.[9e] In other words, a fast regeneration of Sm(II) is required. The reduction of initially formed samarium(III) pinacolate is expected to be slower than that of $SmClI_2$ due to the electron-donating alkoxide. Therefore, the use of chlorotrimethylsilane (TMSCl)[11] would transform the samarium(III) pinacolate into its silyl ether along with the formation of $SmClI_2$ to afford the desired reaction pathway. Indeed, the highest yield of the product (66%), comparable with that of the stoichiometric reaction (run 5), was attainable by slow addition of a mixture of benzaldehyde (1 equiv) and TMSCl (1 equiv) to a mixture of SmI_2 (0.1 equiv), TMSCl (0.5 equiv), and an excess of Mg in THF at room temperature (run 1 in Table 2).[12] It is notable that the color of the reaction mixture of dark blue immediately changed into pale

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[1] For recent reviews for the application of low-valent samarium compounds into organic chemistry, see: (a) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. (b) Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press: London, Great Britain, 1994. (c) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (d) Molander, G. A. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, Great Britain, 1991; Vol. 1, Chapter 9, p 251. (e) Inanaga, J. *Yuki Gosei Kagaku* Kyokaishi **1989**, *47*, 200. (f) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573. (g) Kagan, H. B.; Namy, J. L. In *Handbook on the Physics and Chemistry of Rare Earths*; Gschneidner, Jr., K. A., Eyring, L., Eds.; Elsevier Science Publishers: Amsterdam, The Netherlands, 1984; Vol. 6, Chapter 50, p 525.

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[3] (a) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447. (b) Uenishi, J.; Masuda, S.; Wakabayashi, S. *Tetrahedron Lett.* **1991**, *32*, 5097. (c) Yokoo, K.; Mine, N.; Taniguchi, H.; Fujiwara, Y. *J. Organomet. Chem.* **1985**, *279*, C19.

[4] $SmCl_3$-associated electroreductions were reported although it appears to be difficult to conclude that electrochemically formed Sm(II) species work as reducing agents. See: (a) Hébri, H.; Duñach, E.; Périchon, J. *J. Chem. Soc., Chem. Commun.* **1993**, 499. (b) Espanet, B.; Duñach, E.; Périchon, J. *Tetrahedron Lett.* **1992**, *33*, 2485. (c) Hébri, H.; Duñach, E.; Périchon, J. *Synlett* **1992**, 293. (d) Hébri, H.; Duñach, E.; Périchon, J. *Syn. Commun.* **1991**, *21*, 2377. (e) Hébri, H.; Duñach, E.; Heintz, M.; Troupel, M.; Périchon, J. *Synlett* **1991**, 901. (f) Léonard, E.; Duñach, E.; Périchon, J. *J. Chem. Soc., Chem. Commun.* **1989**, 276.

[5] (a) Ogawa, A.; Nanke, T.; Sumino, Y.; Ryu, I.; Sonoda, N. *Chem. Lett.* **1994**, 379. (b) Yanada, R.; Bessho, K.; Yanada, K. *Chem. Lett.* **1994**, 1279. (c) Murakami, M.; Hayashi, M.; Ito, Y. *Synlett.* **1994**, 179. (d) Yoshizawa, T.; Hatajima, T.; Amino, H.; Imamoto, T. *Nihonkagakukaishi* **1993**, 482. (e) Ogawa, A.; Takami, N.; Sekiguchi, M.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 8729.

[6] Sonoda et al. reported that the Sm/SmI_2 system promotes the deoxygenative coupling of amides. They have also shown that this reaction proceeds by using both a catalytic amount of SmI_2 and excess of Mg although any further investigation was not performed. See, ref 5e.

[7] Magnesium metal was activated by vigorous stirring as a usual Grignard technique. SmI_3 and $SmBrI_2$ were prepared by the reaction of SmI_2 with iodine or bromine. $SmClI_2$ was synthesized by the reaction of SmI_2 with 1 equiv of benzyl chloride. The concentration of $SmClI_2$ was not determined in this experiment.

[8] Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.

[9] For examples of SmI_2-mediated pinacol coupling, see: (a) Namy, J. L.; Souppe, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765. (b) Souppe, J.; Danon, L.; Namy, J. L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *250*, 227. (c) Fürstner, A.; Csuk, R.; Rohrer, C.; Weidmann, H. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1729. (d) Shiue, J. S.; Lin, C. C.; Fang, J. M. *Tetrahedron Lett.* **1993**, *34*, 335. (e) Okaue, Y.; Isobe, T. *Mem. Fac. Sci., Kyushu Univ., Ser. C* **1992**, *18*, 179.

[10] For examples of Mg-promoted pinacol coupling reactions, see: (a) Rausch, M. D.; McEwen, W. E.; Kleinberg, J. *Chem. Rev.* **1957**, *57*, 417. (b) Fürstner, A.; Csuk, R.; Rohrer, C.; Weidmann, H. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1729. (c) Csuk, R.; Fürstner, A.; Weidmann, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1802. (d) Adams, R.; Adams, E. W. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, p 459.

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[12] A typical procedure was as follows: To a 0.1 M solution of SmI_2 in dry THF (2 mL) containing 1 mmol of TMSCl and 400 mg of magnesium turnings (Nacalai Tesque) was added dropwise the mixture of carbonyl compound (2 mmol) and TMSCl (2 mmol) over 2 h. After the complete consumption of carbonyl compound, an extractive workup with ether followed by purification (SiO_2 column chromatography) gave the mixture (*dl* and *meso*) of pinacols.

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Table 1. UV-Vis Absorption of the Reaction Mixture of Samarium Salts and Mg in THF[a]

run	conditions	UV-vis[b] λ_{max} (absorbance)
1	SmI_2	620 (0.90), 558 (0.84)
2	$SmI_3 + Mg$	621 (0.43), 560 (0.40)
3	$SmI_2Br + Mg$	620 (0.45), 560 (0.42)
4	$SmI_2Cl + Mg$	621 (0.38), 556 (0.31)
5	$SmI_2 + MgI_2$	620 (0.21), 555 (0.20)

[a] Conditions: samarium salts (0.01 mmol), dry THF (3.5 mL), room temperature. [b] λ_{max} valves are in nanometers (nm).

Scheme 2

$$SmI_2X \quad + \quad Mg \quad \rightleftharpoons \quad SmI_nX_{(2-n)} \quad + \quad MgI_{(2-n)}X_n$$

Table 2. Pinacol Coupling of Benzaldehyde (**1**) under the SmI_2/Mg System

run	SmI_2/TMSCl/**1**/Mg (mmol)	yield[a] (%)
1	0.2/3.0/2.0/16	66
2	0.2/6.0/4.0/16	54
3	0.2/0/2.0/16	14
4	0/3.0/2.0/16	0
5	2.0/3.0/2.0/0	78

[a] Isolated yield.

Scheme 3

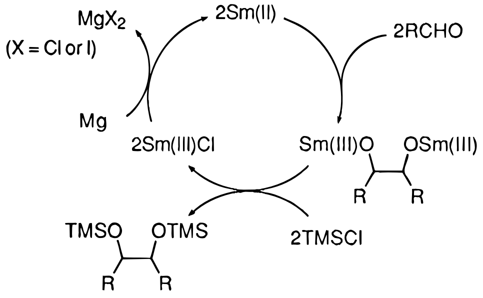

Table 3. Pinacol Coupling of Carbonyl Compounds under the SmI_2/Mg System[a]

run	substrates	yield[b] (%)
1	$PhCH_2CH_2CHO$	57[c]
2	*p*-$CH_3OC_6H_4CHO$	81
3	*p*-$(CH_3)_2NC_6H_4CHO$	76
4	*p*-$CH_3O_2CC_6H_4CHO$	45
5	*p*-CNC_6H_4CHO	23
6	$PhCOCH_3$	68
7	*p*-$CH_3OC_6H_4COCH_3$	76
8	$PhCO(CH_2)_3COPh$	82[d]
9	$PhCH_2CH_2COCH_3$	58[e]

[a] Conditions: SmI_2 (0.2 mmol), TMSCl (3 mmol), substrate (2 mmol), THF (2 mL), room temperature. [b] Isolated yield. [c] Cyclic trimer of hydrocinnamaldehyde was obtained in 36% yield. [d] Only a single isomer (*meso*) was obtained. [e] Reaction time was 48 h; 42% of starting material was recovered.

blue by the addition of a few drops of benzaldehyde/TMSCl and again to dark blue within a few minutes. The formation of benzyl alcohol, benzyl benzoate, and benzoin was not detected, and a bond formation between *para* and carbonyl carbons[9d] did not occur. There was no apparent difference in the diastereoselectivity between the present and the stoichiometric reactions (almost 1:1).[13] A reaction with 5 mol % of SmI_2 also produced the homocoupled product without evident decrease of the yield (run 2). Reaction run in the absence of TMSCl resulted in a complex mixture containing the pinacol, benzyl alcohol, benzoin, benzyl benzoate, and (4-formylphenyl)phenylmethanol[9d] (run 3).

These results cannot prove precisely that SmI_2 serves as a mediator in the reduction system. However, the presence of the catalytic cycle of SmI_2 is suggested by the results as follows. First, the use of other lanthanide salts such as $CeCl_3$, $LaCl_3$, $NbCl_3$, $Yb(OTf)_3$, YbI_3, and $SmCl_3$ gave homocoupled product in low yields (17−19%), whereas these salts and SmI_2 are known to work as Lewis acids. Therefore, the possibility that SmI_2 or trivalent samarium salts only act as a Lewis acid is negligible. Second, no reactions took place in the absence of SmI_2 (run 4), although the TMSCl/Mg system in hexamethylphosphoramide is known to be effective for the pinacol coupling.[14] It rules out the promotion of the pathway by the TMSCl/Mg system. Furthermore, the reduction of Sm(III) into Sm(II) by the Grignard reagent[15] of 4-iodobutyl trimethylsilyl ether can be neglected since no oxidized products of the Grignard reagent (i.e., 1-butanol, 1,8-octandiol) were formed. Third, the reaction without SmI_2 using Mg pretreated with SmI_2 resulted in the recovery of benzaldehyde. This result excludes the possibility that SmI_2 simply activates the Mg surface. Finally, as mentioned above, the recovery of the initial dark blude color proves the regeneration of Sm(II). These observations suggest that Sm(II) serves as the true reducing species. The possible reaction pathway involves the reduction of carbonyl compounds by SmI_2 to give Sm(III) alcoholates followed by silylation of the alcoholates by TMSCl providing the corresponding silyl ether and SmI_2Cl. SmI_2 or SmClI would be regenerated by the electron transfer from Mg (Scheme 3).

Table 3 lists examples of the reductive coupling of carbonyl compounds including aliphatic and aromatic ketones and aldehydes. The aliphatic aldehyde (run 1) as well as aromatic aldehydes (runs 2−5) and ketones (runs 6−8) underwent the pinacol coupling by the SmI_2/Mg system. Although reducible functional groups (ester, cyano) tended to decrease the yield, the present reaction includes a tolerance to methoxy and dimethylamino groups remaining intact under the conditions. Aliphatic ketone was also available in this reduction system to give the corresponding pinacol (run 9). The reaction of 1,5-diphenyl-1,5-pentanedione gave a single isomer (meso) in high yield. The formation of iodotrimethylsilane (TMSI) in situ seems to be negligible since the cleavage of methoxy group by TMSI[16] did not occur.

In summary, we have demonstrated a novel SmI_2-catalyzed reduction system of carbonyl compounds. SmI_2 was found to act as a catalyst in the reduction where trivalent samarium formed is smoothly reduced by Mg to regenerate divalent samarium salts. This method would provide a new route in the field of lanthanide chemistry.

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Supporting Information Available: Detail experimental procedures (3 pages). See any current masthead page for ordering and Internet access instructions.

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(13) The stoichiometric reaction gave 4-iodobutyl trimethylsilyl ether as a byproduct, whereas it was not detected in the catalytic reaction.

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