Samarium(II) Triflate as a New Reagent for the Grignard-Type Carbonyl Addition Reaction

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On treatment of a THF solution of $Sm(OTf)_3$ with 1 equiv of an organolithium or organomagnesium reagent at ambient temperature, the purple or deep green solution of the divalent samarium triflate [$Sm(OTf)_2$] was readily obtained. For this preparation, *s*-BuLi was the most effective as was evidenced by the reduction of 2-phenylethyl iodide in the presence of HMPA. The $Sm(OTf)_2$ reagent mediated the Grignard-type reaction effectively in THF/HMPA; alkylation and allylation of ketones or aldehydes with alkyl, allyl, or benzyl halides proceeded *via* organosamarium intermediates. Diastereoselectivity of the samarium−Grignard reaction was examined using 2-methylcyclohexanone, 4-*tert*-butylcyclohexanone, and 2-phenylpropanal and was found to be higher in each case than that with SmI_2. With 2-methylcyclohexanone, for example, $Sm(OTf)_2$ gave the greatest ratio of *axial* alcohol:*equatorial* alcohol = 99:1, and SmI_2 gave a ratio of 91:9. Halides containing an ester or a silyl group were reactive in the Reformatsky- or Peterson-type reaction, respectively, using the $Sm(OTf)_2$ reagent.

In the past decade, samarium(II) diiodide (SmI_2) has been proven to be a useful and essential reagent for reduction of organic functional groups and for carbon−carbon bond formation.[1] Typical examples are the reduction of carbonyl compounds and Barbier-type reactions. However, SmI_2 occasionally induces ring opening of the solvent tetrahydrofuran (THF).[2] Other divalent samarium compounds are of interest with respect to their reducing ability for organic functional groups and stereocontrolled carbon−carbon bond-forming reactions. For example, samarium(II) dibromide reduces ketones[3a] and aromatic esters[3b] to give dimerization products. Samarocene, dicyclopentadienylsamarium[4] which is prepared by the reaction of SmI_2 with cyclopentadienylsodium, is an efficient reagent for the Barbier-type reactions where it affords the stable organosamarium intermediates including allylic and benzylic samariums.[4] We have been interested in the divalent derivatives of lanthanides for selective organic synthesis. In our preliminary communication, we succeeded in the preparation of divalent samarium(II) triflate [$Sm(OTf)_2$] by treatment of samarium(III) triflate [$Sm(OTf)_3$] with *s*-BuLi in THF.[5]

Organolanthanide triflates prepared from organolithium compounds and trivalent lanthanide triflates are one of the useful reagents for selective organic synthesis. Thus, reagents have been reacted with amides to produce unsymmetrical ketones without contamination by the tertiary alcohols[6] and react in highly diastereoselective fashion with chiral ketones.[7] However, synthetic utilities are limited because certain organolithium compounds are not easily available. We present here an alternative method of preparation of organolanthanide triflates by reduction of alkyl halides with a divalent lanthanide triflate, i.e., $Sm(OTf)_2$ or $Yb(OTf)_2$. We also demonstrate that the $Sm(OTf)_2$-mediated Grignard-type carbonyl addition is highly stereoselective and unique in its reactivity.

Results and Discussion

Preparation of $Sm(OTf)_2$ and Simple Reduction of the Alkyl Halide. On treatment of a THF solution of $Sm(OTf)_3$ with 1 equiv of an organolithium or organomagnesium reagent at ambient temperature, the purple or deep green solution of the divalent samarium triflate [$Sm(OTf)_2$][8] was readily obtained.[9] Generation of the Sm(II) species was unsuccessful in the presence of hexamethylphosphoric triamide (HMPA), a pale orange solution being formed. We first surveyed which organometallic reagent was most effective for preparing Sm(II) species in the simple reduction of 2-phenylethyl iodide into ethylbenzene as a probe reaction. To the THF solution of Sm(II) species obtained by the procedure described above was added HMPA followed by addition of 2-phenylethyl iodide and *tert*-butyl alcohol, and then the mixture was stirred at room temperature for 1 h,

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(1) Reviews: (a) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29 *Comprehensive Organic Synthesis*; Trost B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, pp 251−282. *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: Chichester, 1995; pp 4428−4432. (b) Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press: London, 1994.

(2) (a) Soupe, J.; Namy, J.-L.; Kagan, H. B. *Tetrahedron Lett.* **1984**, *25*, 2869. (b) Namy, J-L.; Colomb, M.; Kagan, H. B. *Tetrahedron Lett.* **1994**, *35*, 1723.

(3) (a) Lebrun,A.; Namy, J.-L.; Kagan,H. B. *Tetrahedron Lett.* **1993**, *34*, 2311. (b) Yoshizawa, T.; Hatajima, T.; Amano, H.; Imamoto, T. *Nippon Kagaku Kaishi* **1993**, 482.

(4) (a) Namy, J. L.; Collins, J.; Zhang, J.; Kagan, H. B. *J. Organomet. Chem.* **1987**, *328*, 81. (b) Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *39*, 6097. (c) Collin, J.; Namy, J.-L.; Dallemer, F.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 3118. (d) Bied, C.; Collin, J.; Kagan, H. B. *Tetrahedron* **1992**, *48*, 3877.

(5) Fukuzawa, S.; Tsuchimoto, T.; Kanai, T. *Chem. Lett.* **1994**, 1981.

(6) (a) Collins, S; Hong, Y. *Tetrahedron Lett.* **1987**, *38*, 4391. (b) Collins, S.; Hong, Y.; Hoover, G. J.; Veit, J. R. *J. Org. Chem.* **1990**, *55*, 3565.

(7) Molander, G. A.; Burkhardt, E. R.; Weinig, P. *J. Org. Chem.* **1990**, *55*, 4990.

(8) This formula may not represent the correct structure of Sm(II) species. "$Sm(OTf)_2$" probably forms a complex with LiOTf and THF.

(9) Imamoto et al. reported the generation of samarium(II) halides by treatment of samarium(III) halides with butyllithium. Imamoto, T.; Kusumoto, T.; Yokoyama, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1042. See also ref 3.

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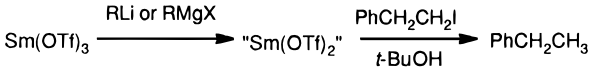
Table 1. Reduction of 2-Phenylethyl Iodide with Sm(II) Species Generated by the Reaction of $Sm(OTf)_3$ with Organometallic Reagents[a]



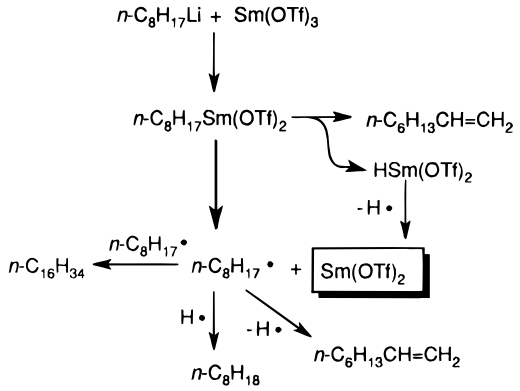
run	organometallic reagent	yield of ethylbenzene,[b] %
1	MeLi	23
2	*n*-BuLi	63
3	*s*-BuLi	88
4	*t*-BuLi	32
5	PhLi	0
6	EtMgBr	81
7	*n*-BuMgBr	68
8	*s*-BuMgCl	73
9	*t*-BuMgCl	45

[a] $PhCH_2CH_2I$ (0.9 mmol), *t*-BuOH (1.0 mmol), $Sm(OTf)_3$ (2.0 mmol), organometallic reagent (2.0 mmol), THF (5.0 mL), HMPA (1.0 mL). [b] Determined by GLC.

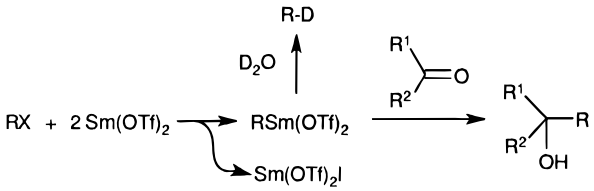
during which time the purple color faded. Table 1 demonstrates that *s*-BuLi was superior to other organometallic reagents in the preparation of Sm(II) species among the organometallic reagents tested: *n*-BuLi, EtMgBr, *n*-BuMgBr, and *s*-BuMgCl were moderately effective, but MeLi, PhLi, *t*-BuLi, and *t*-BuMgCl were not suitable for generating Sm(II) species. We chose *s*-BuLi as a reducing agent for preparing $Sm(OTf)_2$. On the other hand, EtMgBr was revealed to be effective in the preparation of $Sm(OTf)_2$ for the pinacol coupling reaction as reported independently by Inanaga et al.[10] Iodometric titration of Sm(II) obtained by the reduction of $Sm(OTf)_3$ with *s*-BuLi revealed that the concentration of the divalent samarium was within a range of 0.086−0.091 mol/L.[11,12] This result was consistent with that obtained by the reduction of 2-phenylethyl iodide. THF was the choice of solvent in the preparation of the samarium(II) species with *s*-BuLi. The use of other solvents was less satisfactory: The yield of reduction of 2-phenylethyl iodide in a solvent/HMPA is given; tetrahydropyran (78%), dimethoxyethane (63%), diethyl ether (15%), cyclohexane (2%), and toluene (3%). Ytterbium(II) triflate could be prepared from $Yb(OTf)_3$ by a similar procedure, and its reactivity was compared to that of $Sm(OTf)_2$ in the following Grignard-type reaction.

The question arises as to how the divalent samarium species are generated by the reaction of the trivalent samarium with an alkyllithium. Reaction of alkyllithium with $Sm(OTf)_3$ at −78 °C gives a clear homogeneous solution, a trivalent organosamarium species being formed.[6,7] When the solution temperature is allowed to warm to room temperature, the solution becomes purple

Scheme 1



Scheme 2



which indicates the generation of divalent samarium. After hydrolysis of a $Sm(OTf)_2$ solution prepared with *s*-BuLi, careful analysis by GC/MS revealed the presence of 3,4-dimethylhexane which must have resulted from the homo-coupling of *s*-BuLi. Because it is difficult to detect smaller molecules such as butane and butenes, we prepared the $Sm(OTf)_2$ solution with 1-octyllithium instead of *s*-BuLi and analyzed the hydrolyzed solution (Scheme 1). GC/MS analysis showed the production of hexadecane (20−25%), octane (35−40%), and 1-octene (30−35%). These results suggest that a trivalent organosamarium compound should be produced in the initial step of the reaction, and it would then undergo both radical cleavage and/or β-hydride elimination processes[13] to give the divalent samarium species.[14]

Samarium−Grignard Reaction of Simple Halides with Ketones and Aldehydes. We investigated the Grignard-type reaction of simple organic halides with acetophenone or acetone. We routinely conducted the reaction by the "samarium−Grignard" procedure that has been defined by Curran;[15] the reaction was performed by addition of the organic halide to the Sm(II) in THF/HMPA solution followed by addition of a ketone or an aldehyde (Scheme 2). When the reaction was carried out by the "samarium−Barbier" procedure, i.e., simultaneous addition of the halide and the ketone to Sm(II),[15] the yield of the alcohols decreased and a considerable amount of pinacol coupling products was formed. One molar amount of the halide and a half molar amount of the ketone were employed for one molar amount of $Sm(OTf)_2$. Table 2 summarizes the results of the reaction. The Grignard-type reaction with propyl, butyl, dodecyl, or 2-phenylethyl iodide proceeded smoothly at room temperature to produce the corresponding adducts with ketones in good

(10) Inanaga et al. independently reported the pinacol coupling reaction with $Sm(OTf)_2$ prepared from $Sm(OTf)_3$ and EtMgBr. Hanamoto, T.; Sugimoto,Y.; Sugino, A.; Inanaga, J. *Synlett* **1994**, 377.

(11) (a) Evans, D. F.; Fazakerley, G. V.; Phillips, R. F. *J. Chem. Soc. A* **1971**, 1931. (b) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. (c) Girard, P.; Kagan, H. B. *Nouv. J. Chim.* **1981**, *5*, 479. (d) Imamoto, T.; Ono, M. *Chem. Lett.* **1987**, 501.

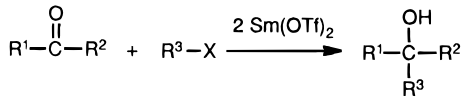
(12) The possibility of simultaneous titration of the unreacted *s*-BuLi during the iodometric titration of Sm(II) species would be ruled out by following reasons. First, we titrated $Sm(OTf)_2$ solution more than 1 h after treatment of $Sm(OTf)_3$ with *s*-BuLi during which time the unreacted *s*-BuLi is not alive any longer because a maximum lifetime of *s*-BuLi in THF at 20 °C is about 1 h (*Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: Chichester, 1995; pp 907−914). Second, treatment of cyclohexanone with $Sm(OTf)_2$ gave cyclohexanol and the pinacol as reduction products, but no alkylated product was detected;[5] this suggests the absence of *s*-BuLi. On the other hand, on treatment of cyclohexanone with a mixture of $Sm(OTf)_2$ and *s*-BuLi (1 eqiuv to cyclohexanone), the alkylated product was produced in addition to the reduction products.

(13) Elimination of β-hydrogen of σ-bonded organolanthanide compounds have been reported. (a) Evans, W. J.; Meadows, J. H.; Wayda, A. L; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1982**, *104*, 2008; **1982**, *104*, 2015. (b) Yokoo, K.; Mine, N.; Taniguchi, H.; Fujiwara, Y. *J. Organomet. Chem.* **1985**, *279*, C19.

(14) The similar results were obtained by Inanaga et al. See ref 10.

(15) (a) Curran D. P.; Totleben, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 6050. (b) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943.

Table 2. Grignard-Type Reaction of Alkyl Halides with Carbonyl Compounds Mediated by $Sm(OTf)_2$[a]



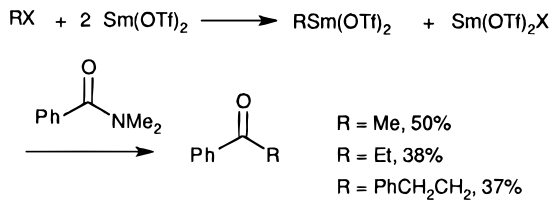
run	carbonyl compound	alkyl halide	% yield of adduct [b]
1	acetophenone	MeI	56
2		EtI	84
3		*n*-PrI	86
4		*n*-BuI	90
5[c,d]			51
6		*n*-BuBr	63
7		*i*-PrBr	74
8		c-C_6H_{11}Br	67
9[e]	acetone	*n*-$C_{12}H_{25}$	86
10[e]		$PhCH_2CH_2I$	67
11	cyclohexanone	*n*-BuI	87
12[c,d]			32
13	2-octanone		77
14	2,4-dimethyl-3-pentanone		84
15	*β*-tetralone		62
16	2-cyclohexen-1-one		85[f]
17	benzalacetone		82[f]
18	octanal		67
19	benzaldehyde		84
20	acetophenone	CH_2=$CHCH_2I$	67
21[d]			82
22[c,d]			92
23	benzaldehyde		60
24	cyclohexanone		65
25[e]	acetone	$PhCH_2Br$	58
26[d,e]			95
27	cyclohexanone		56

[a] Unless otherwise noted, alkylation was carried out by using an alkyl halide, a carbonyl compound, $Sm(OTf)_3$, and *s*-BuLi (0.9:0.5:2.0:2.0 molar ratio) by the Grignard procedure at room temperature for 1 h in THF/HMPA (5.0 mL/1.0 mL). [b] Determined by GLC based on a carbonyl compound. [c] $Yb(OTf)_2$ was used instead of $Sm(OTf)_2$ using 2.0 mL of HMPA. [d] The reaction was carried out by the Barbier procedure. [e] The molar ratio of acetone: alkyl halide = 2.0:0.9. [f] 1,2-Adduct only.

yields (runs 3−10). Quenching with D_2O instead of the addition of a ketone provided a deuterated alkane, demonstrating that the reduction of alkyl iodide with $Sm(OTf)_2$ should give an organosamarium intermediate. Worthy of note is that a $Sm(OTf)_2$-mediated samarium−Grignard reaction with methyl or ethyl iodide was reproducible and gave the corresponding adduct in good yield (runs 1−2). This results contrasts sharply to the results obtained in the SmI_2-mediated samarium−Grignard reaction with methyl iodide, which is not reproducible, and with the analogous reaction with ethyl iodide, which gives a poor yield[15] although the samarium−Barbier reaction with methyl iodide on ketones gave good yields.[11b] A possible explanation of this difference could be that the expected "organosamarium species" prepared with $Sm(OTf)_2$ is more stable than the organosamarium species prepared with SmI_2. When bromides were used instead of iodides, lower yields of adducts resulted. The reaction with secondary halides such as isopropyl bromide and cyclohexyl bromide similarly proceeded to afford the corresponding alcohols in good yields (runs 6−8). Secondary iodides gave a complex mixture of products. Thus, secondary bromides appear to be preferable to a secondary iodides for synthetic applications.

The reaction of butyl iodide/Sm(II) with several carbonyl compounds is summarized in runs 11−19 of Table 2. With ketones and aldehydes which were examined, the reaction proceeded smoothly to afford the adducts in good yields. Both a sterically hindered ketone (2,4-dimethyl-3-pentanone in run 14) and an enolizable ketone (*β*-tetralone in run 15) afforded the corresponding alcohols in moderate yields. With α-enones such as 2-cyclohexen-1-one and benzalacetone, the reaction was 1,2-regioselective (runs 16−17). These results were similar to those obtained in the reaction of organolanthanide reagents, e.g., organocerium reagents, with such carbonyl compounds.[16] $Yb(OTf)_2$ also mediated the reaction of organic halides with ketones, but only the Barbier procedure gave acceptable yields (runs 5 and 12); the Grignard procedure resulted in 5−10% yield of the product probably due to slow metal−halogen exchange and instability of the generated organoytterbium species.

Scheme 3



Organolanthanum triflates have been reported to react with amides to give asymmetrical ketones in high yield.[6] "The organosamarium reagent" prepared by the reaction of the alkyl iodide with $Sm(OTf)_2$ also reacted with benzamides to afford alkyl phenyl ketones in moderate yields: alkyl = CH_3 (50%), C_2H_5 (38%), and 2-phenylethyl (37%) (Scheme 3).

Reaction with Allylic and Benzylic Halides. Treatment of allyl iodide with $Sm(OTf)_2$ provided the "allylsamarium reagent".[16c,17] Trapping this reagent with ketones gave the corresponding homoallylic alcohols in good yields. Considering that SmI_2 induces the Wurtz-type coupling of allyl halides in the absence of ketones or aldehydes, the success in generating the allylsamarium species was unexpected, as pointed out.[11b,15] We also succeeded in preparation of the stable "benzylsamarium reagent" from benzyl bromide. The reagent was added to acetone under the same conditions which were used for the allyl case. The results of these reactions are shown in runs 20−27 of Table 2.

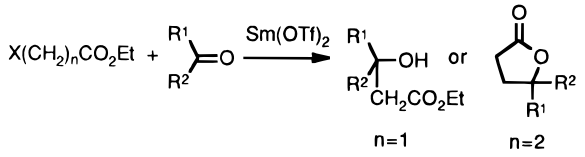
Samarium−Reformatsky and −Peterson Reaction. The samarium−Grignard reaction is also applicable to functionalized halides. When α- or *β*-halo esters were employed in the $Sm(OTf)_2$-mediated reaction with carbonyl compounds, *β*-hydroxy esters or *γ*-lactones were, respectively, obtained in good yields, the ester group being unaffected in the reaction.[11b,18] We call this reaction the samarium−Reformatsky reaction. The results are shown in Table 3. Each reaction probably involves the samarium enolate or homoenolate. When $Sm(OTf)_2$ was applied to the reaction of (iodomethyl)-trimethylsilane with ketones and aldehydes, methyl-

(16) (a) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904. (b) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392. (c) Fukuzawa, S.; Sakai, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3308.

(17) Soupe, J.; Danon, L.; Namy, J.-L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *250*, 227.

(18) (a) Otsubo, K.; Kawamura, K.; Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1987**, 1487. (b) Tabuchi, T.; Kawamura, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3889. (c) Fukuzawa, S.; Sumimoto, N.; Fujinami, T.; Sakai, S. *J. Org. Chem.* **1990**, *55*, 1628.

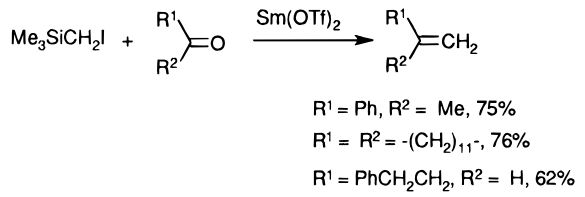
Table 3. Reformatsky-Type Reaction with Carbonyl Compounds[a]



run	RX	carbonyl compounds	type of product	yield,[b] %
1[c]	$BrCH_2CO_2Et$	acetophenone	β-hydroxy ester	71
2[c]	$BrCH_2CO_2Et$	cyclohexanone	β-hydroxy ester	81
3	$BrCH(CH_3)CO_2Et$	benzaldehyde	β-hydroxy ester	67
4	$ICH_2CH_2CO_2Et$	acetophenone	γ-lactone	85
5	$ICH_2CH_2CO_2Et$	cyclohexanone	γ-lactone	81

[a] Reaction was carried out by using a halo ester, a ketone, $Sm(OTf)_3$, and *s*-BuLi (0.5:0.5:2.0:2.0 molar ratio) by the Grignard procedure at room temperature for 1 h in THF/HMPA (5.0 mL/1.0 mL). [b] Isolated yield. [c] The reaction was carried out by the Barbier procedure.

Scheme 4



enenation of the carbonyl proceeded smoothly (Scheme 4). We call this reaction the samarium−Peterson reaction.[19]

Stereochemistry of the Samarium−Grignard Reaction. Molander et al. have demonstrated that the methylytterbium reagent prepared from methyllithium and $Yb(OTf)_3$ reacts with 2-methylcyclohexanone with a highly selective equatorial attack.[7] The stereochemical aspects of the lanthanide−Grignard reaction of substituted cyclohexanones using $Sm(OTf)_2$, $Yb(OTf)_2$, SmI_2, or YbI_2 are summarized in Table 4. The "methylsamarium reagent" prepared from methyl iodide and $Sm(OTf)_2$ showed high diastereoselectivity in the addition reaction with 2-methylcyclohexanone in a good yield, the ratio of *axial* alcohol to *equatorial* alcohol being 96:4 (run 1).[20] The stereoselectivity of the methyl addition to the ketone using SmI_2, YbI_2, or $Yb(OTf)_2$ turned out to be lower (*axial* alcohol:*equatorial* alcohol = 89−80:11−20). The "(2-phenylethyl)samarium reagent" prepared from 2-phenylethyl iodide with $Sm(OTf)_2$ also accomplished a diastereoselective reaction with 2-methylcyclohexanone (Scheme 5). The selectivity of 99:1 was higher than that with SmI_2.[15] The reaction using $Yb(OTf)_2$ and YbI_2 gave similarly high diastereoselectivity, but low yields. Stereoselective addition was observed also in the reaction with 4-*tert*-butylcyclohexanone using $Sm(OTf)_2$ (*axial* alcohol:*equatorial* alcohol = 81−75:19−25) (Table 4, runs 12−15). On the other hand, according to earlier reports, the SmI_2-mediated alkylation of 4-*tert*-butylcyclohexanone gave the *axial* alcohol with 70:30 at the best ratio.[15]

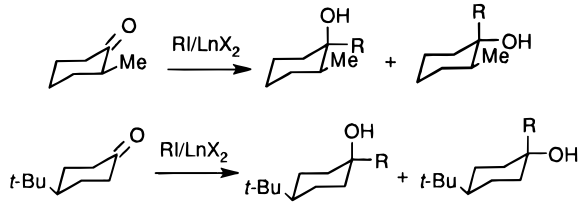
The stereochemical outcome of the samarium−Grignard reaction of 2-phenypropanal with $Sm(OTf)_2$ was studied in regard to the ratio of Cram to *anti*-Cram

Table 4. Stereochemistry of the Reaction of Alkyl Halides with Ketones[a]

run	ketone	R in RI	LnX_2	% yield of adduct[b]	ratio[c] (*ax* : *eq*)
					
1		Me	$Sm(OTf)_2$	72	96 : 4
2[d, e]			$Yb(OTf)_2$	38	87 : 13
3			SmI_2	20	80 : 20
4[d, f]			SmI_2	79	89 : 11
5[d, e]			YbI_2	93	93 : 7
6		$PhCH_2CH_2$	$Sm(OTf)_2$	80	99 : 1
7[d, e]			$Yb(OTf)_2$	36	99 : 1
8[f]			SmI_2	88	91 : 9
9[d, e]			YbI_2	52	99 : 1
10		$CH_2=CHCH_2$	$Sm(OTf)_2$	68	73 : 27
11[d]			SmI_2	78	72 : 28
					
12		Me	$Sm(OTf)_2$	75	75 : 25
13[d, f]			SmI_2	64	70 : 30
14		$PhCH_2CH_2$	$Sm(OTf)_2$	78	81 : 19
15[f]			SmI_2	81	62 : 38

[a] Unless otherwise noted, alkylation was carried out by using an alkyl halide, a ketone, and LnX_2 (0.9:0.5:2.0 molar ratio) by the Grignard procedure at room temperature for 1 h in THF/HMPA (5.0 mL/1.0 mL). [b] Determined by GLC based on a ketone. [c] Isomer ratio was determined by GLC using a capillary column DB-WAX-25N (J&W Scientific). [d] The reaction was carried out by the Barbier procedure. [e] 2.0 mL of HMPA was used. [f] Ref 15.

Scheme 5



selectivity.[21] Results summarized in Table 5 demonstrate that $Sm(OTf)_2$ always afforded higher Cram selectivity than SmI_2 in the reaction with each alkyl iodide examined: the use of $Sm(OTf)_2$ gave 90:10 in the reaction with methyl iodide, whereas SmI_2 gave 73:27 (runs 1−3). The Cram selectivity with $Sm(OTf)_2$ was higher than that with MeMgX and MeLi[21] and was as high as that with bulky methyl organometallic reagents such as $MeYb(OTf)_2$[7] and $MeTi(OR)_3$.[22]

Conclusion. The new samarium reagent, $Sm(OTf)_2$, was readily prepared by the reduction of $Sm(OTf)_3$ with *s*-BuLi in THF. This reagent reduces alkyl halides to produce the "organosamarium triflate" [23] that adds to a

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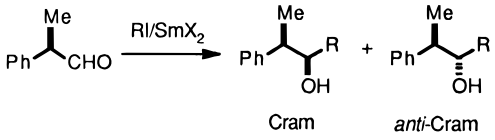
(21) (a) Nogradi, M. *Stereoselective Synthesis*; VCH: Weinheim, 1995; Chapter 5 and references cited therein. (b) Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588.

(22) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer-Verlag: Berlin, 1986.

(23) Organosamarium reagent prepared from $RX/Sm(OTf)_2$ behaves differently from that prepared from RX/SmI_2 or $RLi/Sm(OTf)_3$. The differences between the various approaches may be the result of species, LiOTf, SmI_nOTf_{3-n} etc., interacting with the organosamarium reagent.

Table 5. Cram/*anti*-Cram Selectivity in the Alkylation of 2-Phenylpropanal[a]



run	alkyl halide	SmX_2	yield of adduct,[b] %	Cram:*anti*-Cram[c]
1	MeI	$Sm(OTf)_2$	69	86:14
2[d]		SmI_2	88	73:27
3[g]		$Sm(OTf)_2$	60	90:10
4[d]	CH_2I_2	$Sm(OTf)_2$	85	92:8[f]
5[d,e]		SmI_2	91	92:8[f]
6	*n*-BuI	$Sm(OTf)_2$	76	90:10
7[g]		$Sm(OTf)_2$	67	92:8
8		SmI_2	84	85:15
9[g]		SmI_2	79	88:12

[a] Unless otherwise noted, alkylation was carried out by using an alkyl halide, an aldehyde, and SmX_2 (0.9:0.5:2.0 molar ratio) by the Grignard procedure at room temperature for 1 h in THF/HMPA (5.0 mL/1.0 mL). [b] Determined by GLC based on the aldehyde. [c] The isomer ratio was determined by GLC using a capillary column DB-WAX-25N (J&W Scientific). [d] The reaction was carried out by the Barbier procedure. [e] Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3891. [f] Yield and stereochemistry were determined after reduction of the iodomethyl group to the methyl group. [g] The aldehyde was added to the mixture of RI and SmX_2 at −78 °C.

variety of carbonyl compounds with higher diastereoselectivity than does the organosamarium species derived from SmI_2. Thus, $Sm(OTf)_2$ should be a promising reagent for selective organic synthesis.

Experimental Section

General. ^1H and ^{13}C NMR spectra were measured from $CDCl_3$ solutions. The chemical shifts are reported in δ units downfield from the internal reference, Me_4Si. GC/MS analyses were performed on a capillary column (DB-5-30N-STD, J&W Scientific, 0.25 mm, 30 m) (helium as carrier gas). High-resolution mass spectra were taken at the Institute of Physical and Chemical Research, Wako, Saitama, Japan. Column chromatographies on SiO_2 were performed with Merck silica gel 60. Elemental analyses were carried out in the microanalytical laboratory of Chuo University.

Materials. Samarium(III) trifluoromethanesulfonate was prepared from samarium oxide (Nippon Yttrium Co., Ltd, 99.9%) and trifluoromethanesulfonic acid in water: the resulting hydrate was dried by heating under vacuum at 200 °C for 48 h.[24] Butyllithium (1.6 M, hexane solution), *s*-butyllithium (1.0 M, cyclohexane solution), *tert*-butyllithium (1.0 M, cyclohexane solution), and Grignard reagents (1.0 M, THF solution) were purchased from Kanto Chemicals and used after titration.[25] THF was distilled under nitrogen from sodium benzophenone ketyl just prior to use. HMPA was purchased from Aldrich and distilled from CaH_2 and kept over 4A molecular sieves under nitrogen. The THF solution of SmI_2 or YbI_2 was prepared from samarium or ytterbium metal (Nippon Yttrium Co., Ltd, 99.9%) and 1,2-diiodoethane as described in the literature.[11b] Authentic samples for GC/MS analyses were prepared by the reaction of carbonyl compounds with Grignard reagents. All organic compounds were commercially available and used without purification unless otherwise noted.

Caution: $Sm(OTf)_3$ is quite hygroscopic and must be strictly dried before use. Preparation of divalent samarium [$Sm(OTf)_2$] was unsuccessful if a slight amount of moisture was present as a contaminant.

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(25) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

Preparation of $Sm(OTf)_2$ Solution. Under a nitrogen atmosphere, Sm $(OTf)_3$ (1.2 g, 2.0 mmol) was placed in a 50-mL Schlenk tube and equipped with a septum inlet. The tube was heated at 200 °C in vacuo for 2 h. After the tube had been cooled down to room temperature, a magnetic stirring bar was placed in the flask, which was flushed with nitrogen. THF (5 mL) was added by a syringe through the rubber septum with stirring. The mixture was stirred at room temperature for 1 h, and a cyclohexane solution (2.0 mL) of *s*-BuLi (1.0 M, 2.0 mL, 2.0 mmol) was injected slowly into the suspension at −20 °C. The solution was allowed to warm to 0 °C and to room temperature over a period of 1 h during which time a purple solution of the divalent samarium triflate was obtained. Concentration of the divalent samarium was titrated to be 1.8 mmol by iodometry.[11]

Simple Reduction of 2-Phenylethyl Iodide with $Sm(OTf)_2$. To the THF solution of $Sm(OTf)_2$, prepared as described above, was added HMPA (1.0 mL) with stirring at room temperature, and then a mixture of 2-phenylethyl iodide (209 mg, 0.90 mmol) and *tert*-butyl alcohol (70 mg, 1.0 mmol) was added to the reagent solution. The mixture was stirred at room temperature for 1 h until the purple color of the solution faded. The solution was hydrolyzed with diluted HCl. The organic phase was separated, and the aqueous phase was extracted with diethyl ether. The combined organic extracts were washed with brine and dried ($MgSO_4$). GC/MS analysis revealed the presence of ethylbenzene, the quantity of which was determined using an internal standard (84 mg, 0.79 mmol, 88%).

Samarium−Grignard Reaction of Alkyl Halides with Carbonyl Compounds Using $Sm(OTf)_2$. The following provides a typical procedure for the reaction of alkyl halides with carbonyl compounds. To the THF (5 mL)/HMPA (1.0 mL) solution of $Sm(OTf)_2$ (1.8 mmol) was added butyl iodide (166 mg, 0.90 mmol) at room temperature. The solution was stirred at room temperature for 1 h during which time the purple color of the solution faded. Acetophenone (60 mg, 0.50 mmol) was then added to the resulting solution, and the reaction mixture was stirred for 1 h and quenched with dilute HCl. The organic phase was separated, and the aqueous phase was extracted with diethyl ether. The combined organic extracts were washed with brine and dried ($MgSO_4$). GC/MS analysis revealed the presence of 2-phenyl-2-hexaol, the quantity of which was determined to be 0.45 mmol, 90% using naphthalene as an internal standard. Evaporation of the solvent left a pale yellow residue which was subjected to column chromatography on silica gel; hexane/ether (1/1) eluted the alcohol.

The Barbier Procedure for the Reaction of Alkyl Halides with Carbonyl Compounds by Divalent Lanthanide (LnX_2). The following provides the typical Barbier procedure for the reaction of organic halides with carbonyl compounds. To the THF/HMPA solution of LnX_2 (2.0 mmol) was added a mixture of allyl iodide (152 mg, 0.90 mmol) and acetophenone (60 mg, 0.50 mmol). The resulting mixture was stirred at room temperature for 1 h. The solution was hydrolyzed with dilute HCl. The organic phase was separated, and the aqueous phase was extracted with diethyl ether. The combined organic extracts were washed with brine and dried ($MgSO_4$). GC/MS analysis revealed the presence of 2-phenyl-4-penten-2-ol, the quantity of which was determined using naphthalene as an internal standard.

3-Methyl-2-phenyl-2-butanol. The title compound was prepared by the reaction of isopropyl bromide with acetophenone. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.80 (d, 3H, J = 6.8 Hz), 0.89 (d, 3H, J = 6.8 Hz), 1.52 (s, 3H), 1.66 (s, 1H, OH), 2.02 (oct, 1H, J = 6.8 Hz), 7.2−7.4 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 17.1, 17.3, 26.5, 38.5, 76.6, 125.2, 126.3, 127.7, 147.7. HRMS (EI) m/z calcd for $C_{11}H_{16}O$ 164.1201, found 164.1200 (M^+). IR (neat) 3466, 2971, 1446, 1372, 1029 cm^{-1}.

2-Methyl-2-tetradecanol. The title compound was prepared by the reaction of 1-iodododecane with acetone. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, J = 7.1 Hz), 1.21 (s, 6H), 1.25−1.51 (m, 22H), 2.28 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 13.8, 22.5, 24.2, 28.8, 29.3, 29.5, 29.6, 30.1, 31.8, 43.8, 70.2. HRMS (EI) m/z calcd for $C_{15}H_{30}$ ($M^+ - H_2O$) 210.2347, found 210.2350.

Anal. Calcd for $C_{15}H_{32}O$: C, 78.87; H, 14.12. Found: C, 78.72; H, 13.90. IR (neat) 3366, 2924, 2853, 1466, 1376 cm^{-1}.

5-Dodecanol. The title compound was prepared by the reaction of butyl iodide with octanal. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.89 (t, 3H, $J = 7.1$ Hz), 0.91 (t, 3H, $J = 7.1$ Hz), 1.2−1.6 (m, 18 H), 1.65 (s, 1H, OH), 3.60 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 14.0, 22.6, 22.7, 25.6, 27.8, 29.2, 29.6, 31.8, 37.1, 37.4, 71.9. HRMS (EI) m/z calcd for $C_{12}H_{26}O$ (M^+) 186.1984, found 186.1981. IR (neat) 3341, 2956, 2927, 2857, 1465, 1041 cm^{-1}.

2-Methyl-3-(2′-propyl)-3-heptanol. The title compound was prepared by the reaction of butyl iodide with 2,4-dimethyl-3-pentanone. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.9−1.5 (m, 21H), 1.93 (sept, 2H, $J = 6.8$ Hz). ^{13}C NMR ($CDCl_3$) δ 13.9, 17.0, 17.4, 23.7, 26.4, 33.7. HRMS (EI) m/z calcd for $C_{11}H_{22}$ ($M^+ - H_2O$) 154.1721, found 154.1720. IR (neat) 3489, 2958, 1467, 1132 cm^{-1}.

1,3-Diphenyl-1-propanone. The title compound was prepared by the reaction of 2-phenylethyl iodide with *N*,*N*-dimethylbenzamide. Mp 67−69 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 3.08 (t, 2H, $J = 8.1$ Hz), 3.31 (t, 2H, $J = 8.1$ Hz), 7.2−7.6 (m, 8H). ^{13}C NMR ($CDCl_3$) δ 30.1, 40.4, 126.1, 128.0, 128.4, 128.5, 128.6, 133.0, 136.8, 141.3, 199.2. Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.51; H, 6.83. IR (KBr) 1681 cm^{-1}.

1-[(Ethoxycarbonyl)methyl]cyclohexanol.[26] The title compound was prepared by the reaction of ethyl bromoacetate with cyclohexanone. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.2−1.8 (m, 15H), 2.47 (s, 2H), 3.4 (br s, 1H), 4.17, (q, 2H). ^{13}C NMR ($CDCl_3$) δ 14.1, 21.9, 25.5, 37.4, 45.2, 60.5, 69.9, 172.8. HRMS (EI) m/z calcd for $C_{10}H_{18}O_3$ (M^+)186.1256, found 186.1261. IR (neat) 3522, 2933, 1715, 1194, 1029 cm^{-1}.

Methylenecyclododecane. The title compound was prepared by the reaction of (iodomethyl)trimethylsilane with cyclododecanone. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.2−2.0 (m, 22H), 4.72 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 22.7, 23.3, 23.8, 24.2, 24.5, 33.1, 110.4, 147.1. HRMS (EI) m/z calcd for $C_{13}H_{24}$ (M^+) 180.1878, found 180.1881. IR (neat) 2930, 2861, 1643 cm^{-1}.

Registry Numbers (supplied by author): 2-Phenyl-2-propanol, 617-94-7; 2-phenyl-2-butanol, 1565-75-9; 2-phenyl-2-pentanol, 4383-18-0; 2-phenyl-2-hexanol, 4396-98-9; 2-methyl-4-phenyl-2-butanol, 103-05-9; 1-cyclohexyl-1-phenylethanol, 4352-39-0; 1-butyl-1-cylohexanol, 5445-30-7; 5-methyl-5-undecanol, 21078-80-8; 1-phenyl-1-pentanol, 583-03-9; 1-butyl-2-cyclohexen-1-ol, 88116-46-5; 3-methyl-1-phenyl-1-hepten-3-ol, 91671-45-3; 2-butyl-1,2,3,4-tetrahydro-2-naphthol, 91671-46-4; 2-phenyl-4-penten-2-ol, 4743-74-2; 1-phenyl-3-buten-1-ol, 936-58-3; 1-(2-propenyl)-1-cyclohexanol, 1123-34-8; 1-benzyl-1-cyclohexanol, 1944-01-0; 2-methyl-1-phenyl-2-propanol, 100-86-7; *trans*-1,2-dimethyl-1-cyclohexanol, 19879-12-0; *cis*-1,2-dimethyl-1-cyclohexanol, 19879-11-9; 2-methyl-1-(2′-phenylethyl)-1-cyclohexanol, 108686-39-1;2-methyl-1-(2′-phenylethyl)-1-cyclohexanol, 142041-26-7; *trans*-4-*tert*-butyl-1-methyl-1-cyclohexanol, 16980-55-5; *cis*-4-*tert*-butyl-1-methyl-1-cyclohexanol, 16980-56-6; *cis*-4-*tert*-butyl-1-(2′-phenylethyl)-1-cyclohexanol, 142041-15-4; *trans*-4-*tert*-butyl-1-(2′-phenylethyl)-1-cyclohexanol, 142041-25-6; *trans*-2-methyl-1-(2′-propenyl)-1-cyclohexanol, 24580-51-6; (*R*,*R*)-3-phenyl-2-butanol, 1502-79-0; (*R*,*S*)-3-phenyl-2-butanol, 1502-80-3; (*R*,*R*)-2-phenyl-3-heptanol, 96929-99-6; (*R*,*S*)-2-phenyl-3-heptanol, 96930-05-1 acetophenone, 98-86-2; propiophenone, 93-55-0; ethyl 3-hydroxy-3-phenylbutanoate, 2293-60-9; (*R*,*S*)-ethyl 3-hydroxy-2-methyl-3-phenylpropionate, 17226-81-2; (*R*,*R*)-ethyl 3-hydroxy-2-methyl-3-phenylpropionate, 17226-82-3; 4-methyl-4-phenyl-γ-butyrolactone, 21303-80-0; 1-oxaspiro[4.5]decane-2-one, 699-61-6, α-methylstyrene, 98-83-9; 4-phenyl-1-butene, 768-56-9.

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Supporting Information Available: Copies of ^1H spectra of all known and new compounds (35 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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