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Diastereoselective Pinacol Coupling of Alkyl Aryl Ketones with Rare Earth Metals in the Presence of Chlorosilanes

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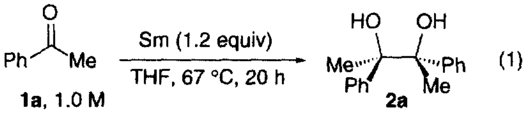
Abstract: *Rare earth metals (Ln) are found to act as useful reducing agents for the pinacol coupling reaction of alkyl aryl ketones in the presence of chlorosilanes. Although the hitherto known pinacol coupling reaction using rare earth reducing agents generally exhibits very low diastereoselectivities, the present pinacol coupling by use of a Ln/R_3SiCl system usually indicates higher diastereoselectivities. In particular, a Yb/Me_3SiCl system attains the diastereoselective pinacol coupling of primary alkyl aryl ketones with the dl/meso ratio of 8/2~9/1.* © 1999 Elsevier Science Ltd. All rights reserved.

The chemistry of lanthanoid compounds has been growing in recent years, because of the many synthetic applications of lanthanoid compounds. Among these, the reduction and reductive transformations using divalent lanthanoid halides such as SmI_2 have been developed greatly. Compared with divalent lanthanoid compounds, however, the use of zero-valent lanthanoid metals in organic synthesis has been limited to several excellent works, which include the reductive transformations of carbonyl compounds with Yb,[1] the cyclopropanation with Sm/CH_2I_2,[2] and the reduction using Ce.[3] Although the combination of chlorosilanes and zero-valent metals such as Na, Li, Mg, Zn, *etc.* is widely known to be effective for reductive transformations of carbonyl compounds,[4] only very limited examples of the systems consisting of rare earth metals and halosilanes are known hitherto.[5] Recently, we have developed a novel diastereoselective pinacol coupling of aliphatic aldehydes using low-valent vanadium (or titanium) catalysts and chlorosilanes.[6] This prompted us to examine the pinacol coupling using Ln metals and Me_3SiCl. In contrast to very low diastereoselectivity observed in the hitherto known systems of rare earth metals and chlorosilanes,[5c] the present Ln/R_3SiCl system, especially Yb/Me_3SiCl, was found to indicate the higher diastereoselectivities.

When the reduction of acetophenone (**1a**) with samarium metal and Me_3SiCl was conducted under THF reflux, the corresponding pinacol (**2a**) was obtained in 69% yield with moderate diastereoselectivity (eq 1). Irradiation with ultrasounds slightly increased the yield of **2a** (75%). In the absence of Me_3SiCl, however, both the yield and diastereoselectivity decreased drastically. Moreover, the reaction in the absence of Me_3SiCl without sonication afforded **2a** in only 6% yield. These results suggest that Me_3SiCl plays an important role in both the reducing ability and selectivity of this pinacol coupling.



(1)

Me_3SiCl (1.2 equiv)	69% [*dl*/meso = 75/25]
Me_3SiCl (1.2 equiv), •)))	75% [*dl*/meso = 75/25]
•))), without Me_3SiCl	19% [*dl*/meso = 54/46]

Table 1 indicates the results of the pinacol coupling of **1a** using some other rare earth metals in place of Sm. Interestingly, a variety of rare earth metals effected the reductive coupling of **1a** successfully in the presence of Me_3SiCl. Among them, Yb metal indicated the excellent diastereoselectivity (*dl*/meso = 89/11). The diastereoselectivity was influenced by the bulkiness of chlorosilanes employed. In the case of Yb, for example, the diastereoselectivity decreased when $Me_2PhSiCl$ was used instead of Me_3SiCl (85%, *dl*/meso = 78/22).

Table 1. Pinacol Coupling of **1a** Using Ln–Me_3SiCl^a

Ln	Yield[b] (%)	*dl*/meso[c]	Ln	Yield[b] (%)	*dl*/meso[c]
Ce	84	74/26	Dy	87	75/25
Pr	78	74/26	Tm	85	70/30
Nd	77	76/24	Yb	80	89/11
Gd	85	74/26	Lu	47	63/37

[a] Reductive coupling of acetophenone (2.0 mmol) with Ln (2.4 mmol) and Me_3SiCl (2.4 mmol) was conducted upon irradiation with ultrasound at 67 °C for 20 h in THF (2 mL). [b] Isolated yield. [c] Determined by ^1H NMR.

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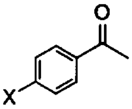
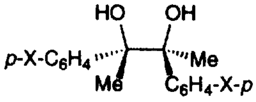
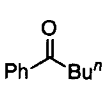
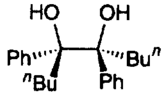
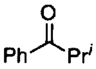
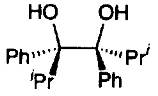
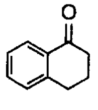
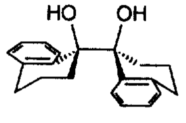
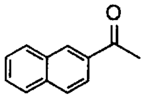
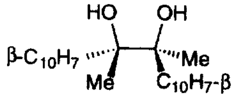
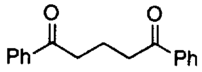
Table 2 represents the results of the pinacol coupling of several alkyl aryl ketones. In general, the pinacol coupling of primary alkyl aryl ketones proceeded with high diastereoselectivity (entries 1, 3, and 6), whereas, in the case of secondary alkyl aryl ketones such as isopropyl phenyl ketone, the diastereoselectivity was lost entirely (entry 4). Cyclic ketones such as 1-tetralone also underwent diastereoselective pinacol coupling in good yield (entry 5). Interestingly, the pinacol coupling of 1,3-dibenzoylpropane took place intramolecularly, giving the corresponding *meso*-diol selectively (entry 7). In contrast to aromatic ketones, the attempted pinacol coupling of aliphatic ketones such as 2-octanone with Yb/Me$_3$SiCl resulted in the recovery of the starting ketone. On the other hand, the reduction of aromatic aldehydes such as benzaldehyde by Yb/Me$_3$SiCl provided the corresponding 1,2-diol and 1,3-dioxolane in 49% and 7%, respectively, with very low diastereoselectivity (*dl*/meso = 56/44).

In conclusion, the pinacol coupling of alkyl aryl ketones has been revealed to take place diastereoselectively by the combination of ytterbium metal and Me$_3$SiCl.[7] This method is interesting in terms of the high diastereoselectivity, because the hitherto known pinacol coupling using low-valent lanthanoid reagents generally indicated the lower diastereoselectivity.[8,9]

Table 2. Reductive Coupling with Yb-Me$_3$SiCl^a

Entry	Ketone	Yield (%)^b [*dl*/meso]
		
1	X = Cl	80 [82/18]
2	MeO	87 [69/31]
3		 66^c [85/15]
4		 57^c [49/51]
5		 80 [82/18]
6		 76 [74/26]
7^d		 92 [0/100]

^{a}Reductive coupling of ketone (1.0 mmol) with Yb (1.2 mmol) and Me$_3$SiCl (1.2 mmol) was conducted at 67 °C for 20 h in THF (5 mL). ^{b}Isolated yield. ^{c}NMR yield. ^{d}1,3-Dibenzoylpropane (0.5 mmol).

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7. To get insight into the mechanism, the pinacol coupling was examined in the solution prepared by the reaction of Yb with Me$_3$SiCl in THF, followed by removal of the insoluble solid (which was probably Yb metal and/or YbCl$_2$). However, the desired pinacol coupling did not proceed at all, suggesting that the pinacol coupling may occur on the surface of the solid.
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