

Stereoselective Reductive Coupling of Carbonyl Compounds by a Sm/Et₂AlI System

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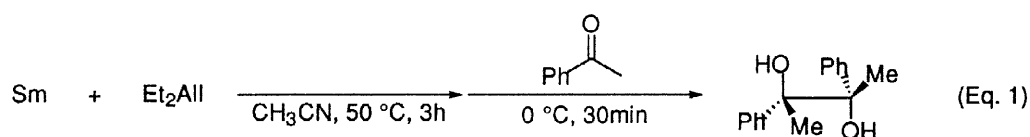
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Abstract: A new method for generation of the samarium (II) species by the reaction of samarium metal with diethylaluminum iodide (Et₂AlI) under mild conditions has been developed. Divalent samarium species generated *in situ* from a Sm/Et₂AlI system caused the reductive coupling of aromatic ketones with moderate stereoselectivity to afford corresponding *dl*-vic-diols in moderate yields. © 1998 Elsevier Science Ltd. All rights reserved.

The reductive coupling of aldehydes and ketones to glycols (pinacol coupling) is a powerful method for constructing carbon-carbon bonds,¹ and it can be accomplished with reagents such as Mg metal² or various low-valent complexes of Ti,³ Zr,⁴ V,⁵ Nb,^{5b,6} Sn,⁷ Sm⁸ or Ce.⁹ Recently, the stereochemistry of pinacol coupling has been of great interest due to the creation of two new adjacent stereocenters during the same stage. Although numerous reports on the stereoselective intramolecular pinacol couplings have appeared,^{1e,10} the intermolecular coupling is fairly uncommon.^{3a,3b,11} In particular, there are few reports on highly stereoselective intramolecular reductive coupling of carbonyl compounds using a low-valent samarium species, which is an excellent reagent of pinacol coupling of carbonyl compounds.^{12,13}

We have recently disclosed that the samarium (II) species was easily prepared by the treatment of metallic samarium with organohalosilanes, R_nSiX_{4-n} (X=Br and I), under ambient conditions.¹⁴ In this Sm/R_nSiX_{4-n} system, the reactivity of the low valent samarium species was affected by the organohalosilanes used (e.g., yield of hydrobenzoin, reductive coupling product of benzaldehyde,^{14a,14b} and the selectivity of the azo, nitroso, azoxy, and amino products, during the reduction of aromatic nitro compounds^{14c}). From these results on the reactions using the Sm/R_nSiX_{4-n} system, it is interesting to note that the use of other organometallic reagents instead of organohalosilanes may cause some exchange during the reactions.

In the course of our studies on the development of new preparative methods of the divalent samarium species, we found that the dark green solution similar to the THF solution of SmI₂ obtained by Kagan's method could be easily prepared by the reaction of metallic samarium with diethylaluminum iodide (Et₂AlI) (1). From the studies of the utility of this samarium species in organic reactions, we found that the reductive dimerization of ketones proceeded with high stereoselectivity (Eq. 1).



In a representative procedure the samarium (II) species was easily generated as follows: samarium powder (75 mg, 0.5 mmol) and acetonitrile (2.5 mL) were placed in a three-necked flask. A toluene solution of diethylaluminum iodide (1.5 mL of a 1.0 M solution, 1.5 mmol) was slowly added at 0 °C, and the mixture was stirred at 50 °C for 3 h under a nitrogen atmosphere. The samarium metal was gradually dissolved, and the color of the solution changed to dark green. When acetophenone (60 mg, 0.5 mmol) (2) was added to the resulting dark green solution at 0 °C, 2,3-diphenylbutane-2,3-diol (3) was formed in 61 % yield with high stereoselectivity (*dl* : *meso* = 4.5 : 1.0) (Run 3 in Table 1).¹⁵ The yield and stereoselectivity of the diol 3 were markedly affected by the reaction temperature (Runs 2-5).¹⁶ The maximum yield was obtained at 0 °C, while higher temperatures (25 and 50 °C) led to a decrease in the yield of 3 due to the formation of various byproducts. The highest stereoselectivity was observed at 50 °C (Run 5). The ratio of the organoaluminum reagent to the samarium metal also affected the yield of 3 (Runs 1, 3 and 6). When the samarium species generated from the samarium metal and two equivalents amount of Et₂AlI were reacted with 2, pinacolic product 3 was formed in an unsatisfactory yield (Run 1). In the case of the Sm/Et₂AlI (1/4 mmol) reagent, the color of the solution changed to yellow which is the characteristic color of Sm(III), and the yield of the coupling product decreased (Run 6).

The results of the reactions of various carbonyl compounds with the divalent samarium species generated *in situ* from Sm/Et₂AlI are shown in Table 2. In the reaction of 4-methylacetophenone, a decrease in the

Table 1. Reductive Coupling of Acetophenone by Sm/Et₂AlI Reagent under Various Reaction Conditions.

Run	Sm/Et ₂ AlI mmol / mmol	Temp/°C	Yield/% ^a	Selectivity ^b <i>dl</i> / <i>meso</i>
1	0.5 / 1.0	0	28 %	—
2	0.5 / 1.5	-40	52 %	1.6 : 1.0
3	0.5 / 1.5	0	61 %	4.5 : 1.0
4	0.5 / 1.5	25	30 %	5.3 : 1.0
5	0.5 / 1.5	50	27 %	5.6 : 1.0
6	0.5 / 2.0	0	18 %	—

^a Isolated yield. ^b Determined by ¹H NMR.

Table 2. Reductive Coupling of Various Carbonyl Compounds by Sm/Et₂AlI Reagent^a

Run	Substrate	Yield/% ^b	Selectivity ^c <i>dl</i> / <i>meso</i>	Run	Substrate	Yield/% ^b	Selectivity ^c <i>dl</i> / <i>meso</i>
1	X = 4-CH ₃	63	3.8 : 1.0	5		43	1.2 : 1.0
2 ^d	X = 4-Cl	60	1.3 : 1.0	6 ^e		trace	—
3 ^d	X = 4-OCH ₃	71	4.8 : 1.0	7		68	1.0 : 1.3
4	X = 2-CH ₃	45	14.1 : 1.0				

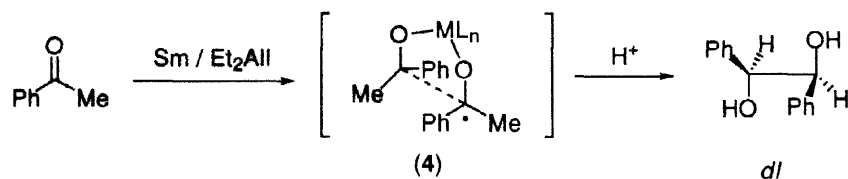
^a Carbonyl compound (0.5 mmol) was reacted with Sm (0.5 mmol) species generated *in situ* from Sm (0.5 mmol)/Et₂AlI (1.5 mmol) at 0 °C for 30 min. ^b Isolated yield. ^c Determined by ¹H NMR.

^d Sm (0.75 mmol)/Et₂AlI (2.25 mmol) was used. ^e The reaction was carried out for 24 h.

stereoselectivity was not observed; however, the substitution of a chloro or methoxy group for hydrogen in the *para* position reduced the stereoselectivity of the products (Runs 1-3). In the case of 2-methylacetophenone, the highest *dl* selectivity was obtained (*dl* : *meso* = 14.1 : 1.0) (Run 4). However, non-aryl ketones such as 2-pentanone did not couple at an appreciable rate (5% after 24 h) (Run 6). The reaction of aromatic aldehydes such as benzaldehyde with the samarium (II) species under the same reaction conditions as that of acetophenone led to a mixture of stereoisomers (*dl* : *meso* = 1.0 : 1.3) in 68 % yield (Run 7).

Although we can not explain the reason for the high stereoselectivity at the present time, the stereoselectivity has been rationalized by considering the chelation model **4** in which samarium or aluminum is coordinated to both oxygen atoms (Scheme 1).¹⁸

Scheme 1



The results described in this paper show that the Sm/Et₂AlI system is not only a new generation method of the Sm (II) species but also a useful method for the highly stereoselective pinacol coupling of ketones. Further application of this reaction system in organic reactions is now in progress.

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