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MeOH or H₂O as efficient additive to switch the reactivity of allylSmBr towards carbonyl compounds

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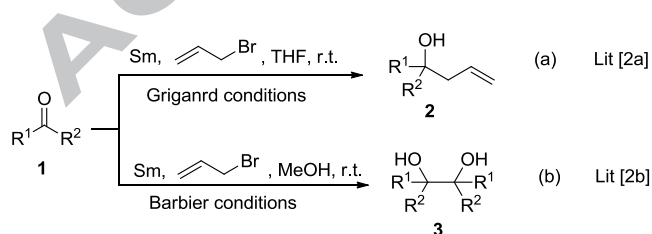
ABSTRACT

A variety of carbonyl compounds were treated by allylSmBr (allylSmBr) with MeOH as the cosolvent to have further insights on the previously reported reductive coupling of aryl ketones mediated by Sm/alkyl halide/MeOH. The results demonstrate that the real reducing species in Sm/alkyl halide/MeOH system should be allylSmBr, and MeOH has elegantly switched the reactivity of allylSmBr from being nucleophilic to being good reductive coupling reagent. Besides, H₂O was also found to be a useful additive to realize the pinacol coupling of aliphatic aldehydes and ketones promoted by allylSmBr.

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1. Introduction

The reaction between Sm and allylic bromide has been known to generate allylic samarium bromide (allylSmBr) in THF, which is an organosamarium reagent and proved to be highly nucleophilic.¹ Grignard reaction took place when the carbonyl compounds were treated by the species affording homoallylic alcohols in good to excellent yields (Scheme 1 (a)).^{2a} Interestingly, Banik group reported that aromatic ketones when treated by Sm/allylic bromide in MeOH (Barbier reaction condition) afforded the diols in moderate yields (Scheme 1 (b)).^{2b} It is noteworthy that reductive coupling occurred instead of the normal Barbier reaction.



Scheme 1. Reactions of carbonyl compounds with Sm, and allylic bromide under Grignard or Barbier conditions

Apparently, the existence of a reducing species should account for the latter pinacol coupling. The study carried out by Banik group excluded the generation of samarium dibromide under the condition, but the mechanism still remains unclear. Based on our recent study³ on the reactivity of allylSmBr, whose reducing ability was greatly enhanced by using HMPA as the additive, and the work by Zhang's group, who have achieved the reductive dehalogenation^{4a} and deoxygenation^{4b} using allylSmBr

with a small amount of MeOH or diethyl phosphate as additive. It seems plausible that the real reducing species is allylSmBr and methanol could tune the reactivity of allylSmBr towards the coupling reactions that yield pinacol products. To prove the proposal, allylSmBr was prepared according to standard procedure in THF and a variety of cosolvents including MeOH was added to the mixture before the carbonyl compound was introduced. Benzaldehyde was used as the model substrate and the results are shown in Table 1.

Table 1. The effects of a variety of additives on the reactivity of allylSmBr towards benzaldehyde^a

Entry	Additive	Yield(%) ^b of 3a	Yield(%) ^b of 2a
1	MeOH (5ml)	50	32
2	MeOH (10ml)	86	trace
3	MeOH (20ml)	69	— ^c
4	EtOH (10ml)	51	26
5	<i>i</i> -PrOH (10ml)	45	41
6	<i>t</i> -BuOH (10ml)	52	34

7	<i>n</i> -BuOH (10ml)	10	48
8	Pyridine (10ml)	trace	52
9	Et ₃ N (10ml)	trace	57

^a Reaction conditions: substrate 1.0 mmol, Sm 2.5 mmol, allylBr 1.4 mmol, additive in dry THF 10 mL under N₂ at the room temperature.

^b Isolated yield

^c Not detected.

When MeOH (5 mL) was used as the cosolvent, it was satisfying to find benzaldehyde afforded the desired diols **3a** in 50% yield (Table 1, entry 1). Since the homoallylic alcohol **4a** was still formed in a significant ratio (32%), the dosage of MeOH was increased. When 10 mL of MeOH was attempted, Gratifyingly, the yield of **2a** was improved to 86% (Table 1, entry 2). However, further increase of MeOH dosage led to incomplete reaction and decreased yield (Table 1, entry 3). In contrast, the influences of other cosolvents such as EtOH, ^tBuOH, Pyridine and Et₃N did not show comparable results.






At this stage, it is reasonable to conclude that the real reducing species in the reactions reported by Banik was allylSmBr. MeOH should function as a donor ligand and also is a suitable proton source to Sm(II)⁵ thus switching the reactivity of allylSmBr from being nucleophilic to good SET reagent to facilitate the coupling reaction.

The generality of the reaction was also examined⁶ (table 2). Aromatic aldehydes could afford the diols **3a-3i** in good to excellent yields with trace amounts of the alcohol **4** being detected (Table 2, entries 1-9). Both electron-withdrawing and electron-donating groups were tolerated, including the hydroxyl (entry 9). 2-Furaldehyde also underwent the coupling smoothly (entry 10). Aryl ketones and diaryl ketones afforded satisfying yields of the diols (entry 11-16) wherein the simple reduction affording benzhydrols **4** was inevitable in some cases. For aliphatic ketones and aldehydes, poor or even no yield of the diol **3** could be obtained and **4** became the major products (entry 17-18).

In recent years, H₂O has been well documented as an additive to SmI₂.⁷ Considering the similarity between the two reagents, H₂O was then attempted as additive to allylSmBr here for the coupling reaction of aliphatic carbonyl compounds. Although H₂O has been reported to greatly enhance the reducing power of SmI₂,⁷ this simple molecule as an additive to switch the reactivity of allylSmBr is not known partly because the organosamarium reagents were usually believed to be moisture sensitive. Tentatively, only 1.0 equiv. of H₂O was first added (Table 3, entry 1). It is encouraging to find allylSmBr did tolerate the existence of H₂O to some extent and afforded the diol **3q** in 43% yield. Increase of the H₂O dosage to 2 equiv. resulted in incomplete consumption of the starting materials

indicating the detrimental effect of excess H₂O. Finally, 1.4 equiv. of H₂O was found to give useful yields of **3q** (62%). Cyclopentanone and *n*-nonyl aldehyde afforded the corresponding diols in similar yields (entries 4 and 5). Investigation has also been carried out to see if H₂O as the additive could improve the reductive coupling of **1j**, **1l** and **1n**, since with MeOH as the cosolvents, these substrates afforded significant amounts of addition products. As shown in Table 3, very little improvement could be observed for 2-furaldehyde **1j** (Table 3, entry 6 vs Table 2, entry 10). For **1l**, however, significant improvement was achieved. **1l** afforded the diols **3l** in 91% yield and no addition product could be detected under allylSmBr/H₂O conditions (Table 3, entry 7 vs Table 2, entry 12). Substrates **1n** afforded simple alcohol **4n** as the only product in 98% yield under allylSmBr/H₂O conditions and the addition product was not detected (Table 3, entry 7 vs Table 2, entry 14).

Table 3. Influences of H₂O on the reactivity of allylSmBr towards aliphatic carbonyl compounds^a


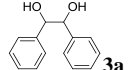
Entry	Substrates 1	Additive	Yield(%) ^b of 3	Yield(%) ^b of 2
1		H ₂ O (1.0 equiv.)	3q , 43	2q , 38
2	1q	H ₂ O (2.0 equiv.)	3q , 48	- ^c
3	1q	H ₂ O (1.4 equiv.)	3q , 62	2q , 20
4	<i>n</i> -C ₈ H ₁₇ CHO 1r	H ₂ O (1.4 equiv.)	3r , 67	2r , 15
5		H ₂ O (1.4 equiv.)	3s , 61	2s , 17
6		H ₂ O (1.4 equiv.)	3j , 71	2j , 11
7		H ₂ O (1.4 equiv.)	3l , 91	2l , trace
8		H ₂ O (1.4 equiv.)	3n , trace	4n , 98

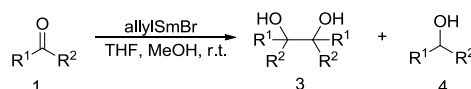
^a Reaction conditions: substrate 1.0 mmol, Sm 2.5 mmol, allylBr 1.4 mmol, additive in dry THF 10 mL under N₂ at the room temperature.

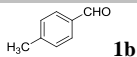
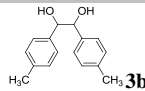
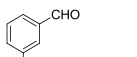
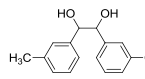
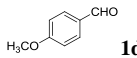
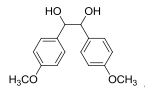
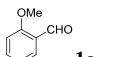
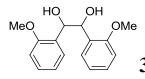
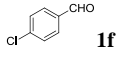
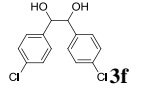
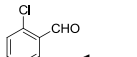
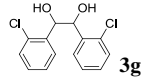
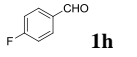
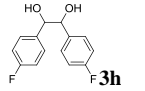
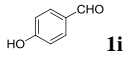
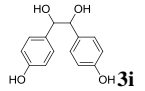
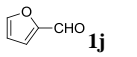
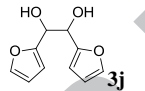
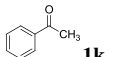
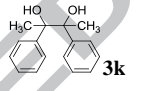
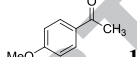
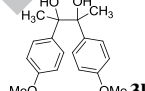
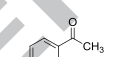
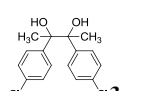
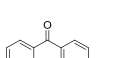
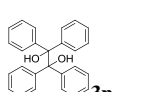
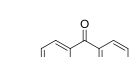
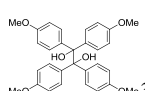
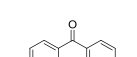
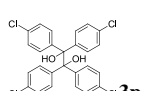
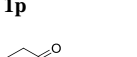
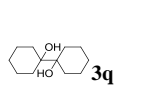
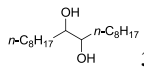
^b Isolated yield

^c Not detected. Incomplete consumption of **1q**.

Table 2. Reductive coupling of aldehydes and ketones with allylSmBr^a

Entry	Substrates 1	Products 3	Yield (%) of 3 ^b	dl : meso	Yield (%) of 4 ^b
1			86	41:59	trace



2	 1b	 3b	78	47:53	trace
3	 1c	 3c	82	47:53	trace
4	 1d	 3d	85	71:29	trace
5	 1e	 3e	65	53:47	trace
6	 1f	 3f	86	47:53	trace
7	 1g	 3g	55	53:47	trace
8	 1h	 3h	73	49:51	trace
9	 1i	 3i	81	77:23	trace
10	 1j	 3j	67	57:43	12
11	 1k	 3k	80	56:44	trace
12	 1l	 3l	73	72:28	26
13	 1m	 3m	84	62:38	trace
14	 1n	 3n	70	-	21
15	 1o	 3o	92	-	-
16	 1p	 3p	75	-	11
17	 1q	 3q	40	-	36
18	$n\text{-C}_8\text{H}_{17}\text{CHO}$ 1r	 3r	trace	-	77

^a Reaction condition: substrate 1.0 mmol, Sm 2.5 mmol, allylBr 1.4 mmol, MeOH 10 ml in dry THF 10 mL under N₂ at the room temperature.

^b Isolated yields.

In conclusion, allylSmBr-induced reductive coupling of carbonyl compounds has been developed. MeOH and H₂O were found to be effective additive being able to switch the reactivity of allylSmBr. Thus the highly nucleophilic allylSmBr could function as good reductive coupling or reducing reagent in their presence. Since MeOH and H₂O are greener additives than HMPA,^{8, 3a-b} the reactivity of allylSmBr switched by these additives is worthy of further study so as to find more interesting applications in organic synthesis.

Acknowledgments

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Supplementary data

Supplementary data (the spectral data and the ¹H NMR, ¹³C NMR spectra of **3**) associated with this article can be found in the online version.

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 - General Procedure for the pinacol coupling of aldehydes and ketones to form the diols (3)*. An oven-dried 50 mL two-necked flask containing finely powdered samarium (0.375 g, 2.5 mmol) was evacuated and backfilled with N₂ for three times. Under a positive pressure of nitrogen, a solution of allylBr (0.12 mL, 1.4 mmol) in dry THF (10 mL) was added via a syringe, and then added a grain of iodine. The mixture was allowed to stir at room temperature for 1 h (the mixture was deep purple). MeOH or H₂O was then added followed by addition of a solution of aldehydes or ketones (1 mmol) in dry THF (1 mL) via a syringe. The reaction mixture was stirred at room temperature until the completion of the reaction (monitored by TLC). The reaction was quenched by a sat. potassium sodium tartrate solution (5 mL). The mixture was extracted by ethyl acetate (3 × 15 mL). The combined extracts were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (200–300 mesh) using petroleum/EtOAc (10/1, v : v) as eluent to afford the corresponding product **3**.
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Title:

MeOH or H₂O as efficient additive to switch the reactivity of allylSmBr towards carbonyl compounds

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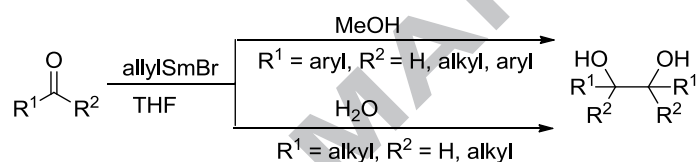
Graphical

Abstract

MeOH or H₂O as efficient additive to switch the reactivity of allylSmBr towards carbonyl compounds

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Highlights

- The real reducing species in Sm/alkyl halide/MeOH system should be allylSmBr.
- MeOH switched allylSmBr from a nucleophile to good reductive coupling reagent.
- H₂O was useful additive to realize the coupling of aliphatic carbonyl compounds.
- AllylSmBr switched by greener additive is hopeful to find more applications.