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Coupling Reaction of Vinyl Halides with Ketones or Aldehydes Mediated by Samarium Diiodide

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The Barbier- or Grignard-type reaction of vinyl iodides with ketones or aldehydes proceeds on treatment with samarium diiodide in benzene containing hexamethylphosphoric triamide (HMPA) to afford the corresponding coupling compounds (allyl alcohols). The reaction was shown to involve vinyl samariums as an intermediate.

Key words samarium diiodide; vinyl samarium; Barbier reaction; Grignard reaction

Coupling reactions of organohalides with carbonyl compounds by samarium diiodide (SmI_2) have been well established,[1,2] and now are known as the samarium Barbier reaction (SBR) and the samarium Grignard reaction (SGR).[3] The principal advantages of the SBR and SGR in comparison with conventional reactions of magnesium lie in the rapid, mild, and chemoselective reduction of organohalides. In spite of the usefulness of the SBR and SGR, organohalides available in THF, the most common solvent for SmI_2, are virtually restricted to primary and secondary alkyl halides,[1,2] or alkynyl iodides.[4] Since highly reactive carbon radicals arising from aryl or vinyl halides with SmI_2 abstract a hydrogen atom from THF to give the corresponding hydrocarbons, these halides do not undergo coupling with carbonyl compounds in THF.[5] Recently, we found that this hydrogen atom abstraction of reactive radicals can be suppressed by replacement of THF with benzene. Thus the SBR of aryl iodides *via* an aryl radical successfully proceeds by conducting the reaction in benzene-hexamethylphosphoric triamide (HMPA).[6] Alkylidenecarbenoids can be generated from *gem*-dihaloalkenes *via* α-halovinyl radicals by successive single electron reduction with SmI_2 in the benzene-HMPA system.[7] Therefore we expected that a vinyl samarium species could be generated from vinyl halides by the same reaction system. Here we report the SmI_2-mediated coupling reaction of vinyl iodides with ketones or aldehydes conducted in benzene-HMPA (Chart 1).

The reaction of iodomethylenecyclohexane (**1a**, 3 eq) with 1-phenyl-2-hexanone (**2a**, 1 eq) by the procedure for the SBR[3] using 6 eq of SmI_2 in benzene-HMPA (9 : 1) at reflux afforded the *tert*-allylic alcohol (**3**) in 79% yield (Table 1, Run 1).[8,9] Similarly, the SBR of vinyl iodides (**1a**—**d**) and ketones (**2a**, **b**) was found to proceed at both reflux and room temperature in the presence of 10% or 5% HMPA (Runs 1—7). The SmI_2-mediated coupling reaction of **1** and **2** under SGR conditions using the benzene-HMPA system was also found to occur as shown in Table 1, Runs 12—26 (except for Runs 21 and 23).[9] These results indicate the formation of vinyl samariums as an intermediate. In the Grignard procedure, aromatic ketones or aldehydes, which are known to be readily reduced with SmI_2 before coupling with organosamariums,[4,6] as well as aliphatic carbonyl compounds underwent coupling with vinyl samariums (Runs 12—20, 22, 24—26). In general, higher yields were obtained in the SBR than in the SGR.

Vinyl bromides (**1f**, **g**) were also allowed to react under SBR conditions at reflux temperature, although no product was formed under either SBR conditions at room temperature or SGR conditions (Runs 8—11, 27, 28). During either prolonged reaction time at room temperature or the one-hour refluxing required for reduction of vinyl bromides, vinyl samariums formed in these reactions are completely decomposed due to their instability. In order to examine the stability of a vinyl samarium, the iodide **1a**, which is more reactive than vinyl bromides toward SmI_2, was treated with SmI_2 at room temperature for 10 min, 5 h, or 24 h before the addition of **2a**. The yield of **3b** was found to be 77%, 38%, and 4%, respectively (Runs 13—15). Although a single stereoisomer of vinyl iodides (*E*-isomer for **1b**—**e**, *E*- or *Z*-isomer for **1f**) was used, a mixture of stereoisomers was obtained with no stereochemical propensity (Runs 4—10, 20—25). The formation of vinyl radicals, for which the inversion barrier is known to be low,[10] is most likely to be responsible for the stereochemical randomization. Interestingly, when the SGR was conducted with 5% HMPA, the yields of alcohols were very low (Runs 16, 21, 23). Since the SBR with 5% HMPA proceeded with no significant loss of the product (Runs 2, 5), the stability of vinyl samariums may depend on the concentration of HMPA. Further study of the HMPA effect on the SGR is under way.

The generation of vinyl samariums by reduction of vinyl radicals, generated by radical addition (or cyclization) to alkynes in THF-HMPA, has been reported by other groups.[11] However, the attempts made by Molander and Harris to trap the vinyl anion with electrophiles (*e.g.*, acetone) other than D_2O were unsuccessful.[11c] Thus this is the first example, to

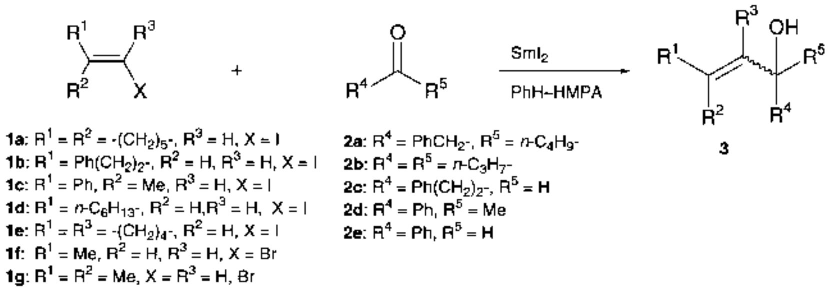

Chart 1

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Table 1. Coupling Reaction of Vinyl Halides with Carbonyl Compounds

Run	Vinyl halide	Carbonyl comp.	Method[a]	Temp.	Time 1[b]	Time 2[b]	HMPA (%)[c]	Yield of **3**[d]	*E*/*Z*[e]
1	**1a**	**2a**	SBR	reflux	2 h	—	10	79%	
2	**1a**	**2a**	SBR	r.t.	2 h	—	5	72%	
3	**1a**	**2b**	SBR	r.t.	1 h	—	10	53%	
4	**1b**	**2a**	SBR	reflux	45 min	—	10	75%	75 : 25
5	**1b**	**2a**	SBR	r.t.	2 h	—	5	71%	44 : 56
6	**1c**	**2a**	SBR	r.t.	1 h	—	10	63%	60 : 40
7	**1d**	**2a**	SBR	reflux	45 min	—	10	86%	40 : 60
8	*E*-**1f**	**2a**	SBR	reflux	1 h	—	10	63%	46 : 54
9	*E*-**1f**	**2a**	SBR	r.t.	15 h	—	10	0%	—
10	*Z*-**1f**	**2a**	SBR	reflux	1 h	—	10	65%	45 : 55
11	**1g**	**2a**	SBR	reflux	30 min	—	10	49%	
12	**1a**	**2a**	SGR	r.t.	10 min	Overnight	10	77%	
13	**1a**	**2a**	SGR	r.t.	10 min	1 h	10	77%[f]	
14	**1a**	**2a**	SGR	r.t.	5 h	1 h	10	38%[f]	
15	**1a**	**2a**	SGR	r.t.	24 h	1 h	10	4%[f]	
16	**1a**	**2a**	SGR	r.t.	5 min	Overnight	5	25%	
17	**1a**	**2c**	SGR	r.t.	10 min	1 h	10	40%	
18	**1a**	**2d**	SGR	r.t.	10 min	1 h	7	53%	
19	**1a**	**2e**	SGR	r.t.	10 min	1 h	7	43%	
20	**1b**	**2a**	SGR	r.t.	5 min	2 h	10	34%	53 : 47
21	**1b**	**2a**	SGR	r.t.	5 min	2 h	5	0%	—
22	**1c**	**2a**	SGR	r.t.	10 min	1 h	10	59%	48 : 52
23	**1c**	**2a**	SGR	r.t.	15 min	1 h	5	trace	—
24	**1c**	**2d**	SGR	r.t.	10 min	1 h	10	49%	58 : 42
25	**1c**	**2e**	SGR	r.t.	10 min	1 h	10	59%	42 : 58
26	**1e**	**2a**	SGR	r.t.	10 min	1 h	10	63%	
27	*E*-**1f**	**2a**	SGR	reflux	5 min	1 h	10	0%	—
28	*E*-**1f**	**2a**	SGR	r.t.	2.5 h	15 h	10	0%	—

a) For SBR and SGR methods, see text. The ratio of **1**/**2**/SmI_2 is 3 : 1 : 6. *b*) In SGR, Time 1 indicates the reaction time of halide and SmI_2, and Time 2 indicates the reaction time after the addition of carbonyl compounds. *c*) 7% HMPA corresponds to about 4 equivalent to SmI_2. *d*) Isolated yield. *e*) Stereochemistries were tentatively assigned by NMR analysis. *f*) Determined by GC.

our knowledge, in which the SmI_2-promoted coupling reaction of vinyl iodides with carbonyl compounds *via* vinyl samariums was achieved under either SBR or SGR conditions.

References and Notes

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3) The abbreviations are used according to the review of ref. 1. For SBR conditions: a mixture of a halide and a carbonyl compound is treated with SmI_2; for SGR: a halide is treated with SmI_2 followed by addition of a carbonyl compound.

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8) For a typical procedure for SBR reaction: To a stirred solution of SmI_2 (0.062 M in benzene containing 10% HMPA , 27.6 ml, 1.70 mmol) was added a mixture of **1a** (189 mg, 0.85 mmol) and **2a** (50 mg, 0.28 mmol) at reflux temperature under nitrogen. After stirring at reflux for 2 h, the mixture was poured into saturated $NaHCO_3$ and extracted with ether. The residue was purified by preparative TLC (hexane : AcOEt = 9 : 1) to give the corresponding allylic alcohol (61.4 mg, 79% yield).

9) When equimolar amounts of **1b** and **2a** were used, the yield of the product was low. Thus we employed the ratio of 1 : 3 : 6 (**2**/**1**/SmI_2) to obtain better yields by generating an excess of vinyl samariums.

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