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BARBIER-TYPE REACTIONS OF ARYL HALIDES WITH KETONES MEDIATED BY SAMARIUM DIIODIDE

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Barbier-type reaction of aryl halides with ketones took place on treatment with samarium diiodide in benzene containing 10 % hexamethylphosphoric triamide (HMPA). The reaction involves an aryl samarium as an intermediate.

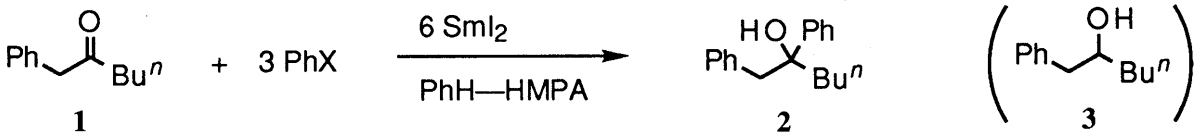
KEYWORDS samarium diiodide; aryl samarium; Barbier reaction; *tert*-alcohol

Inter- and intramolecular Barbier-type reactions between alkyl halides and ketones mediated by samarium diiodide (SmI_2) in tetrahydrofuran (THF) have been well established.[1, 2] However, the coupling reaction of aryl halides with ketones does not proceed at all under similar conditions, since aryl radicals generated from aryl halides with SmI_2 abstract hydrogen atom from THF faster than they couple with ketones mediated by SmI_2.[3] Here we report SmI_2-mediated Barbier-type arylation of ketones conducted in benzene–HMPA.

Recently we have found that benzene is a more efficient solvent than THF for the generation of alkylidenecarbenes from *gem*-dibromoalkenes *via* α-bromovinyl radicals by the reduction with SmI_2 in the presence of HMPA, since the rate of hydrogen atom abstraction by the radicals from solvent leading to the formation of hydrogenative debromination products decreases by replacement of THF with benzene.[4] Therefore, we expected for Barbier-type reaction that the hydrogen atom transfer from solvent to aryl radicals generated by the reduction of aryl halides with SmI_2 would also be suppressed by using benzene–HMPA as a solvent system.

The reaction of halobenzenes with benzyl butyl ketone (**1**) to afford the phenylated *tert*-alcohol (**2**) is summarized in Table I. Addition of a mixture of benzyl butyl ketone (1.0 eq) and excess amount of iodobenzene (3.0 eq) dissolved in benzene to a solution of SmI_2 (6.0 eq) in benzene containing 10 % HMPA

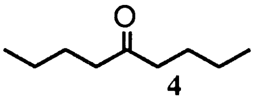
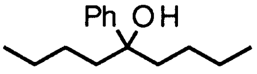
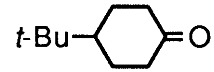
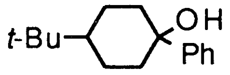
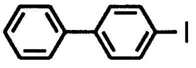
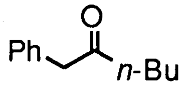
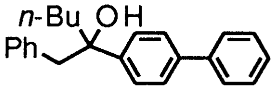
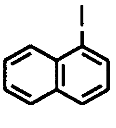
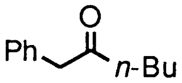
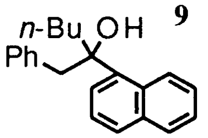
Table I. Reaction of Halobenzenes with Benzyl Butyl Ketone (**1**)



Entry	Halobenzene	Conditions	Yield (**2**, %)[a]	Recovery (**1**, %)[a]	**3**, %[a]
1	PhI	rt, 10 min	74	0	0
2	PhBr	rt, 10 min	28	44	7
3	PhBr	rt, 3 h	66	11	12
4	PhCl	rt, 10 min	0	72	6
5	PhCl	rt, 5 h	3	0	77
6	PhCl	reflux, 3 h	8	35	26

a) Isolated yield.

Table II. Barbier-Type Reaction of Aryl Iodides with Ketones

Entry	Aryl Halide	Ketone	Product	Yield (%)[a]
1	PhI	 **4**	 **5**	48
2	PhI	 **6**	 **7**	58[b]
3	 **8**	 **1**	 **9**	60[c]
4	 **10**	 **1**	 **11**	26[d]

a) Isolated yield. b) Ratio of axial alcohol to equatorial alcohol is 53 / 47. c) 29 % of **1** was recovered. d) 61 % of **1** was recovered.

afforded **2** in 74 % yield (entry 1).[5] Bromobenzene was also allowed to react with **1** by elongation of reaction time until the disappearance of deep purple color of SmI_2 (entry 2, 3), whereas chlorobenzene was found to be unsuitable substrates for the present reaction (entry 4—6). 1-Phenylhexan-2-ol (**3**) probably formed from the ketone (**1**) by the reduction with SmI_2 was detected in both chloro- and bromobenzene.[6] Similar reactions of aryl iodides with ketones proceeded at room temperature within 10 min, and gave addition products in moderate yield (Table II). Unlike the alkylation or the allylation of 4-*t*-butylcyclohexanone (**6**) mediated by SmI_2 in THF, where equatorial attack predominated,[1a, 7b] no substantial stereoselectivity was observed in the case of phenylation of **6** in benzene (entry 2). It is probably due to steric effects that **11** is obtained in low yield from α-iodonaphthalene (entry 4).

In the reaction of alkyl halides with ketones promoted by SmI_2 in THF, a coupling mechanism between a ketyl radical and an alkyl radical has been proposed.[1b, 2b] In our reaction, however, the ketone (**1**) completely disappeared within 10 min in the reaction by use of iodobenzene, whereas large amounts of **1** remained unchanged in the case of chloro- or bromobenzene under the same conditions (Table I, entry 1, 2, 4). If the reaction rate of a ketone with SmI_2 is independent of the halides to be used, it seems to be difficult to rationalize this observation by the formation of ketyl radicals. Curran and his co-workers have demonstrated that SmI_2-promoted Barbier reaction of alkyl halides with ketones conducted in THF–HMPA will proceed by an organometallic addition mechanism.[7, 8] Thus, we carried out the following experiment:

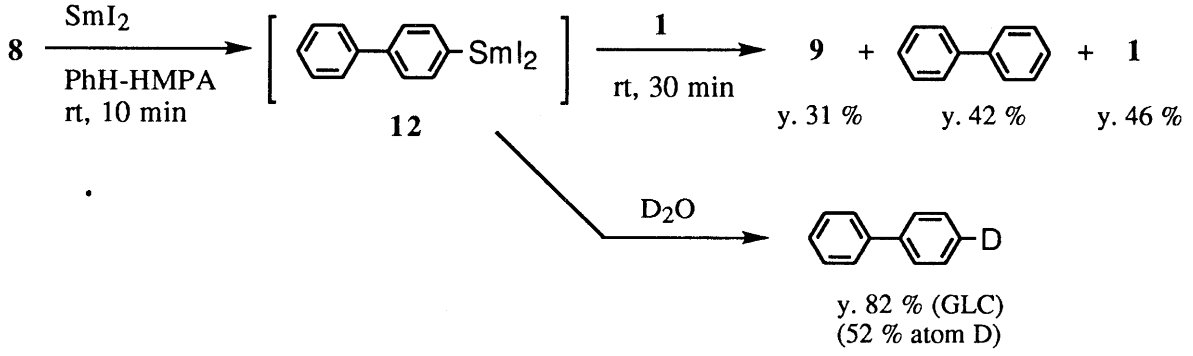


Chart 1

iodobiphenyl (**8**, 1.2 eq) was treated with SmI$_2$ (2.4 eq) in benzene–HMPA for 10 min at room temperature; the deep purple color of SmI$_2$ changed to a brownish yellow toward the end of the addition of the iodide, followed by addition of ketone (**1**, 1.0 eq). Biphenyl-adduct (**9**) was produced in 31 % yield along with biphenyl (42 %) and unchanged **1** (46 %) as illustrated in Chart 1. Treatment of the reaction mixture with deuterium oxide instead of ketone gave 82 % biphenyl, which was 52 % deuterium labeled (determined by NMR), and no detectable amount of quaterphenyl was expected to be formed by biphenyl radical coupling.9) Although a significant decrease in the yield of **9** compared with the result of Table II entry 3 may indicate the possibility of an alternative pathway involving addition of phenyl radical to the ketone,10) the results of Chart 1 clearly indicate that the present reaction involves arylsamarium species as one of the important intermediates.

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5) In order to reduce a halobenzene to its anion twice equimolar of SmI$_2$ is necessary. Thus, the ratio of SmI$_2$ to halobenzene is 2 : 1.
6) Recently, it has been found that the reduction of ketones with SmI$_2$ is accelerated by the addition of water. Therefore, it is possible to consider that the formation of **3** is attributed to water added in quenching process, see: E. Hasegawa, D. P. Curran, *J. Org. Chem.*, **58**, 5008 (1993).
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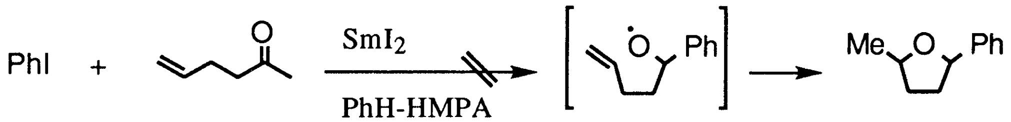
9) Since low solubility of quaterphenyl to the solvent would cause to be difficult to detect it, similar reaction using iodobenzene instead of iodobiphenyl was also carried out. As the results, only 3 % yield of biphenyl was detected by GLC.
10) Similar mechanism has been considered by Kagan.1d) We attempted the reaction of iodobenzene with 5-hexen-2-one. If the radical addition mechanism will be involved, unstable alkoxy radical formed by addition of phenyl radical would spontaneously cyclize to lead to methyl tetrahydrofuran derivative.11) However, a complex mixture of products was obtained and no cyclized product was detected.



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