



Samarium-mediated Barbier reaction of carbonyl compounds

Manas K. Basu and Bimal K. Banik*

*The University of Texas, M. D. Anderson Cancer Center, Department of Molecular Pathology, Box 89,
1515 Holcombe Boulevard, Houston, TX 77030, USA*

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Abstract—Samarium metal in the presence of catalytic amounts of iodine was found to be effective for the Barbier reaction of carbonyl compounds. © 2000 Elsevier Science Ltd. All rights reserved.

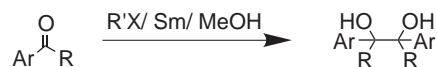
The development of Barbier-type of carbon–carbon bond formations offers tremendous opportunities in synthetic organic chemistry.¹ Significant advances in this type of reaction have been developed. The metals being used include primarily Sn,² Zn,³ Mg,⁴ Bi,⁵ and Cd.¹ The main drawbacks of these metals are long reaction times and only reactive halides are found to be effective. Indium in aqueous solution has shown considerable promise in the addition of unsaturated halides to the carbonyl groups.⁶ Kagan et al.⁷ have demonstrated and favorably compared samarium diiodide-mediated Barbier reaction of aldehydes and ketones with the other available methods. The method using samarium diiodide is excellent, but the commercially-available reagent is expensive, and is also moisture- and air-sensitive. As an alternative, this reagent can be prepared in situ in an inert atmosphere under very stringent conditions.

The use of samarium metal in synthetic organic chemistry is rapidly increasing because of its several advantages (availability, stability and cost) over the widely-used single-electron transfer reagent, samarium diiodide.^{8–12} Yanada has studied extensively various reactions mediated by samarium metal in conjunction with different types of Lewis acids.⁹ We have demonstrated a facile reduction of a nitro group by this metal in the presence of catalytic amounts of iodine and solid ammonium chloride.¹⁰ We have also used samarium–iodine for the reduction of imines.¹¹ During the course of these studies, we discovered a pinacol type of coupling of ketones in the presence of samarium and alkyl halides using methanol as the solvent.¹² Thus, our initial attempts to achieve a Barbier type of reaction have culminated in a simple method of dimerization of ketones (Scheme 1).

Recognizing the importance of Barbier reaction^{1–7} in organic synthesis, we have continued to examine this reaction in detail. This paper describes the successful realization of Barbier-type reactions for a wide variety of aldehydes and ketones by samarium metal and catalytic amounts of iodine.

Reaction of acetophenone with allyl bromide in the presence of samarium–catalytic amounts of iodine in tetrahydrofuran as the solvent produced the unsaturated alcohol as the major product (Table 1, entry 1). Analyses of the crude reaction mixtures revealed the presence of small amounts of pinacol-type compounds (10%). Encouraged by this result, we performed similar reactions with other substrates and the results are represented in Table 1. Reaction of allyl bromide with acetophenone under identical conditions using methanol as the solvent afforded the dimeric compounds with no traces of the addition products. On the other hand, the reaction failed to produce any desired compound when acetonitrile was used as the solvent. This indicated that the nature of the solvent controlled the formation of the product in the samarium-induced reduction reaction.



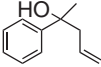


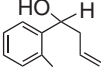


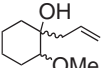


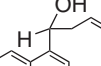


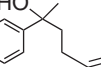
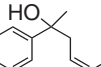


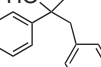


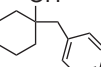


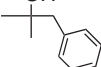

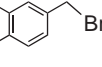
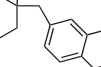

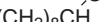


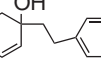


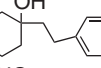


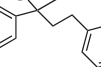
It can be seen from Table 1 that allyl bromide, benzyl bromide and naphthyl bromide produced products in good yield (entries 1–10). 2-Phenyl ethyl iodide gave products in relatively low yield (entries 11–13). However, allyl chloride failed to undergo a Barbier-type reaction under identical conditions. In general, no elimination of the resulting alcohols was observed. How-



Scheme 1.

* Corresponding author.

Table 1. Barbier reaction of aldehydes and ketones in the presence of samarium metal and catalytic amounts of iodine in THF

Entries	Carbonyl Compounds	Halides	Products	Time (min)	Yield (%)
1				20	80
2				20	70
3				20	70 ^a
4				20	90
5				120	20
					40
6				30	64
7				30	52
8				30	52
9				30	56
10	CH ₃ (CH ₂) ₈ CHO			20	81
11				20	31
12				20	42
13				20	45

a: A mixture of *trans*-allyl ether and *cis*-allyl ether (60:40) was obtained (For a related study, see: Yasuda, M.; Fujibayashi, T.; Baba, A. *J. Org. Chem.* **1998**, 63, 6401).

ever, an isomerization of the double bond was noted when homoallyl bromide was used as the halide.

Samarium metal was used previously for the Barbier reaction in the presence of trimethyl silyl bromide and trimethyl silyl chloride–sodium iodide with a single substrate.¹³ The reactive species was claimed to be bivalent samarium cation, although no justification was provided and the structure of the bivalent samarium equivalent was not confirmed. In addition, this method

required freshly-distilled silyl chloride and a reflux temperature. In contrast, our method has a much wider application, requires only samarium and catalytic amounts of iodine and can be carried out at room temperature.

Recently, a trivalent samarium cation was proposed to be the reactive species when imines were allylated or alkylated by samarium metal and catalytic amounts of iodine.¹⁴ The yield of the desired product from the

reaction of imines and benzyl bromide was low and dibenzyl was found to be the major product from the reaction.¹⁵ However, addition of benzyl bromide to the ketones by following our method afforded the benzyl alcohol in an excellent yield, a small portion of which was dimerized (entries 6–10). Thus, the involvement of trivalent samarium species in this type of addition reactions remains a question. Our study indicates that pre-generated bivalent or trivalent samarium species is not required for the Barbier addition of halides to carbonyl compounds. We believe the formation of an activated samarium-R reagent attacks the carbonyl group in THF solution. Further studies are needed to define the critical role of solvents in the samarium-induced addition and dimerization of carbonyl compounds in the presence of halides.

In comparison to all of the previous reports, the present method is rapid, convenient and cost-saving. In conclusion, we have demonstrated a general method for Barbier-type addition reactions of aldehydes and ketones in excellent yields at room temperature.¹⁶

Acknowledgements

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- Typical procedure: Alkyl halide (1.50 mmol) was added dropwise to samarium (1.50 mmol) (preactivated by heating with 0.05 mmol of iodine) in 4.0 mL dry THF under an argon atmosphere at room temperature. A dark blue or purple color was generated within 2–5 min. The carbonyl compound (0.5 mmol) was added dropwise while slowly maintaining the blue color of the reaction mixture. The reaction mixture was stirred for 10–30 min and then was quenched with 0.1N hydrochloric acid. The resulting mixtures were extracted with CH₂Cl₂, dried over sodium sulfate and evaporated to dryness. Finally, the product was purified by column chromatography.