

A New Reformatsky Type Reaction *Via* Cadmium Salt In Aqueous Media

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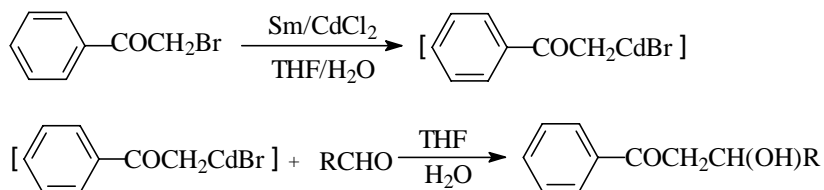
Abstract: In the presence of cadmium (II) chloride-metallic samarium, α -bromoacetophenone reacts with aldehydes in THF–H₂O under mild conditions to give β -hydroxy ketones in good yields.

Keywords: Synthesis, samarium, Reformatsky-type reaction, β -hydroxy ketone.

The aldol condensation is one of the most important reactions for forming carbon-carbon bonds¹. It is known that the intermolecular Reformatsky type reaction of α -halogeno ketones with carbonyl compounds is a method for the preparation of β -hydroxy ketones². After decades of stagnation, considerable progress has been achieved by continuously increasing the reactivity of the zinc, by application of various other metal salts, and by the activation of the whole reaction system. All these reactions are carried out in organic solvents through a six-electron cyclic transition state³. For example, these Reformatsky-type reactions can be mediated by zinc powder⁴, tin-aluminum couple⁵, aluminum-bismuth salt⁶.

Here, we wish to report a new method for the synthesis of β -hydroxy ketone mediated by Sm/CdCl₂ in THF–H₂O media. The active metallic cadmium is produced by samarium and cadmium chloride. α -bromoacetophenone and cadmium could react with aliphatic aldehydes and aromatic aldehydes to give β -hydroxy ketones in good yields. Cadmium-catalyzed reaction to give α,β -unsaturated esters have been reported⁷. Our interests in applying cadmium to organic synthesis have led us to investigate cadmium induced Reformatsky-type reaction in aqueous media.

Scheme 1



The reaction was suggested to proceed as **Scheme 1**. The results were summarized in **Table 1**. Study on the reaction shows that β -hydroxyketones can hardly be obtained without H₂O, it may be the results of cadmium chloride dissolved poorly in the THF. Under a nitrogen atmosphere, the yield is much higher than in the air. Unfortunately, α -bromoacetophenone can not react with ketones under the same conditions.

Table 1

Entry	R	T/t (°C/h)	Yield(%)*
a	C ₆ H ₅	55/16	69
a**	C ₆ H ₅	55/16	30
b	<i>p</i> -ClC ₆ H ₄	60/16	74
c	<i>p</i> -MeC ₆ H ₄	60/20	60
d	<i>m</i> -ClC ₆ H ₄	55/16	75
e	C ₆ H ₅ CH=CH	60/16	63
f	4,5-(OCH ₂ O)-C ₆ H ₃	55/24	55
g	<i>p</i> -MeOC ₆ H ₄	60/20	58
h	<i>n</i> -C ₃ H ₇	55/16	69
i	<i>n</i> -C ₄ H ₉	55/16	67
j	<i>n</i> -C ₆ H ₁₃	55/16	70

*Isolated yields based on aldehydes ** under air.

General procedure: Under a nitrogen atmosphere, samarium powder (1.5mmol, 0.23g), cadmium chloride (1.5mmol, 0.28g), α -bromoacetophenone (2mmol, 0.4g), THF (8ml) and H₂O (1ml) were placed in a three-necked reaction flask, then aldehydes (1mmol) were added to the system. The mixture was stirred for the time indicated in **Table 1**. Then hydrochloric acid (0.1mol/L, 3ml) was added and the mixture was extracted with diethyl ether (2×20ml). The extracts were washed with brine. After being dried over anhydrous MgSO₄, the solvent was evaporated under reduced pressure. The pure product was separated from the residue through preparative TLC on silica gel with hexane-ethyl acetate as eluent.

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