



## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

### Aldol-Type Reaction of $\alpha$ -Halo Ketones with $\alpha$ -Ketocarboxylates Mediated by $\text{Sml}_2$ or $\text{Sml}_3$ : Facile Synthesis of $\alpha$ -Hydroxy- $\gamma$ -ketocarboxylates

Tsutomu Arime<sup>a</sup>, Naoki Kato<sup>a</sup>, Fumio Komadate<sup>a</sup>,  
Hiroko Saegusa<sup>a</sup> & Nobuo Mori<sup>a</sup>

<sup>a</sup> Department of Chemistry, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo, 162  
Published online: 23 Sep 2006.

To cite this article: Tsutomu Arime, Naoki Kato, Fumio Komadate, Hiroko Saegusa & Nobuo Mori (1994) Aldol-Type Reaction of  $\alpha$ -Halo Ketones with  $\alpha$ -Ketocarboxylates Mediated by  $\text{Sml}_2$  or  $\text{Sml}_3$ : Facile Synthesis of  $\alpha$ -Hydroxy- $\gamma$ -ketocarboxylates, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:22, 3315-3319, DOI: [10.1080/00397919408010255](https://doi.org/10.1080/00397919408010255)

To link to this article: <http://dx.doi.org/10.1080/00397919408010255>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no

representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

ALDOL-TYPE REACTION OF  $\alpha$ -HALO KETONES WITH  
 $\alpha$ -KETOCARBOXYLATES MEDIATED BY  $\text{SmI}_2$  OR  $\text{SmI}_3$ :  
FACILE SYNTHESIS OF  $\alpha$ -HYDROXY- $\gamma$ -KETOCARBOXYLATES

Tsutomu Arime, Naoki Kato, Fumio Komadate,  
Hiroko Saegusa, and Nobuo Mori\*

Department of Chemistry, Science University of Tokyo,  
Kagurazaka, Shinjuku-ku, Tokyo 162

**Abstract.** The title reaction smoothly proceeds at room temperature to give  $\alpha$ -hydroxy- $\gamma$ -keto esters **3** in good yields, probably via a mechanism involving samarium enolates formed in situ from  $\alpha$ -halo ketones.

$\alpha$ -Halo ketones react with aldehydes in the presence of  $\text{CeI}_3$  to give  $\alpha, \beta$ -unsaturated ketones.<sup>1</sup> Similar reactions leading to unsaturated ketones can be carried out with  $\text{SmI}_2$ ,<sup>2</sup> or  $\text{SmI}_3$ .<sup>3</sup> Using the combination of  $\text{CeCl}_3$ -NaI or  $\text{CeCl}_3$ - $\text{SnCl}_2$ ,  $\beta$ -hydroxy-ketones are obtained with little or no dehydration to unsaturated ketones.<sup>1</sup> These reactions were assumed to proceed via intermediary formation of lanthanoid enolates from  $\alpha$ -

---

\*To whom correspondence should be addressed.

halo ketones. However, ordinary ketones are unreactive or less reactive as enolate electrophiles in the reactions.

We report here an  $\text{SmI}_2$  or  $\text{SmI}_3$  mediated aldol-type reaction of  $\alpha$ -halo ketones **1** with  $\alpha$ -keto esters **2**. This reaction gave  $\alpha$ -hydroxy- $\gamma$ -keto esters **3** in good yields, without dehydration leading to unsaturated keto esters, and any significant side reactions, such as self- or cross couplings, were not observed.

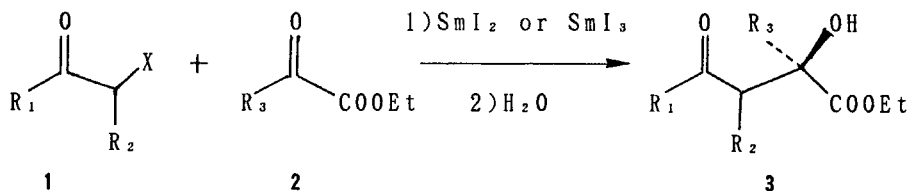


Table 1. The  $\text{SmI}_2$  mediated reaction of  $\alpha$ -halo ketones **1** with  $\alpha$ -keto esters **2**<sup>a)</sup>

Entry	<b>1</b>			<b>2</b>	<b>3</b>
	$\text{R}_1$	$\text{R}_2$	X	$\text{R}_3$	Isolated yield/%
1	Ph	H	Cl	Me	63
2	Ph	H	Br	Me	95
3	Ph	H	Br	Ph	0
4	p- $\text{O}_2\text{N}$ -Ph	H	Br	Me	71
5	p-MeO-Ph	H	Br	Me	99
6	Ph	Me	Br	Me	77(52:48) <sup>b)</sup>
7	Me	H	Br	Me	94
8	-( $\text{CH}_2$ ) <sub>4</sub> -		Br	Me	80(75:25) <sup>b)</sup>

a) Mole ratio of **1** : **2** :  $\text{SmI}_2$  = 1 : 1 : 1.

b) Diastereomer ratio determined by  $^1\text{H}$  NMR.

The reactions with  $\text{SmI}_2$  were performed by the following two different procedures. First, **1** in THF was added to 1 equiv of  $\text{SmI}_2$  in THF. After the initial blue colour turned brownish yellow, **2** in THF was then added. The results thus obtained are summarized in Table 1. All products **3** showed  $^1\text{H}$  NMR, IR and mass spectral data compatible with the structure. Similar results were obtained by an one-step procedure, where a mixture of **1** and **2** was added to  $\text{SmI}_2$ .

In preliminary experiments using  $\text{SmI}_3$ , **3** was obtained in a low yield together with a significant amount of  $\alpha$ -iodo ketone as the major byproduct. But use of an equimolar amount of NaI as an additive was found to suppress the halogen exchange reaction and to increase the yield of **3** by about 10% or more. Thus, all reactions were performed in the presence of NaI by an one-step procedure. The results thus obtained are summarized in Table 2.

The results described above suggest that  $\text{SmI}_2$  or  $\text{SmI}_3$  reacts initially with **1** to form a samarium enolate,  $1^{-3}$  which is the key intermediate for the reactions.

It is apparent from Tables 1 and 2 that  $\text{SmI}_2$  gives better results (shorter reaction time and higher product yield) than those obtained with  $\text{SmI}_3$ -NaI. It is of interest that **2** in which  $\text{R}_3$  is an alkyl group is reactive as an enolate electrophile in the reaction, but **1** with an aryl group is unreactive (Entry 3).

#### Experimental procedure

In the general two-step procedure using  $\text{SmI}_2$ , **1** (1 mmol) in THF (2 ml) was added to a 0.1 M  $\text{SmI}_2$  solution in THF (10 ml) at 0 C under nitrogen atmosphere. After

Table 2. The  $\text{SmI}_2$ -NaI mediated reaction of **1** with **2**<sup>a)</sup>

Entry	<b>1</b>		<b>X</b>	<b>2</b>	<b>3</b>
	$\text{R}_1$	$\text{R}_2$		$\text{R}_3$	Isolated yield/%
1	Ph	H	Cl	Me	44
2	Ph	H	Br	Me	75
3	Ph	H	Br	Ph	0
4	p- $\text{O}_2\text{N}$ -Ph	H	Br	Me	53
5	p-MeO-Ph	H	Br	Me	76
6	Ph	Me	Br	Me	76(58:42) <sup>b)</sup>
7	Me	H	Br	Me	40
8	-( $\text{CH}_2$ ) <sub>4</sub> -		Br	Me	45(70:30) <sup>c)</sup>

a) Mole ratio of  $\text{SmI}_2$  : NaI : **1** : **2** = 1 : 1 : 1 : 1.

b) Diastereomer ratio determined by  $^1\text{H}$  NMR.

c) Ratio of the diastereomers isolated by preparative TLC.

stirring for 2 min until the deep blue color turned brownish yellow, **2** (1 mmol) in THF (2 ml) was then added. The mixture was warmed to room temperature, stirred for 0.5 - 1 h, treated with aqueous 2 M sodium thiosulfate solution (1 ml) and extracted with ether. The extract was washed with brine, dried over magnesium sulfate and evaporated. The residue was subjected to preparative TLC treatment (silica gel, hexane/ether = 1/1).

In the general one-step procedure using  $\text{SmI}_2$ , a solution of **1** (1 mmol) and **2** (1 mmol) in THF (4 ml) was added to a 0.1 M  $\text{SmI}_2$  solution in THF (10 ml) at room temperature, and the mixture was then worked up in a similar manner.

In the general one-step procedure using  $\text{SmI}_2$ ,  $\text{NaI}$  (1 mmol) was added to a 0.1 M  $\text{SmI}_2$  suspension in THF (10 ml). The mixture was stirred for 10 min at room temperature under the air. A solution of 1 (1 mmol) and 2 (1 mmol) in THF (2 ml) was added, and the mixture was stirred for about 12 h until the substrates were consumed, treated with aqueous 2 M sodium thiosulfate solution (ca. 2 ml) and extracted with ether. The extract was worked up in a similar manner.

#### References

- 1) Fukuzawa, S., Tsuruta, T., Fujinami, T. and Sakai, S., J. Chem. Soc., Perkin Trans. 1, 1987, 1473.
- 2) Zhang, Y., Liu, T. and Lin, R., Synth. Commun., 1988, 18, 2003.
- 3) Yu, Y., Lin, R. and Zhang, Y., Tetrahedron Lett., 1993, 34, 4547.

(Received in Japan 22 April 1994)