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Aldol-Type Reaction of α-Halo Ketones with α-Ketocarboxylates Mediated by SmI_2 or SmI_3: Facile Synthesis of α-Hydroxy-γ-ketocarboxylates

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ALDOL-TYPE REACTION OF α-HALO KETONES WITH α-KETOCARBOXYLATES MEDIATED BY SmI_2 OR SmI_3: FACILE SYNTHESIS OF α-HYDROXY-γ-KETOCARBOXYLATES

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

α-Halo ketones react with aldehydes in the presence of CeI_3 to give α,β-unsaturated ketones.[1] Similar reactions leading to unsaturated ketones can be carried out with SmI_2[2] or SmI_3.[3] Using the combination of $CeCl_3$-NaI or $CeCl_3$-$SnCl_2$, β-hydroxy-ketones are obtained with little or no dehydration to unsaturated ketones.[1] These reactions were assumed to proceed via intermediary formation of lanthanoid enolates from α-

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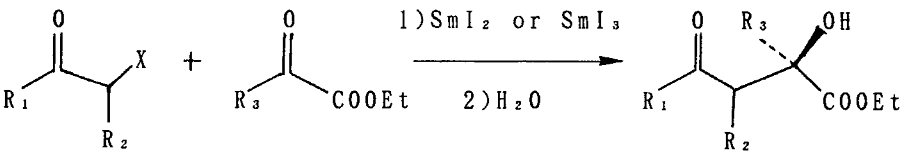
halo ketones. However, ordinary ketones are unreactive or less reactive as enolate electrophiles in the reactions.

We report here an SmI_2 or SmI_3 mediated aldol-type reaction of α-halo ketones **1** with α-keto esters **2**. This reaction gave α-hydroxy-γ-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.



1 **2** **3**

Table 1. The SmI_2 mediated reaction of α-halo ketones **1** with α-keto esters **2**[a]

Entry	**1** R_1	R_2	X	**2** R_3	**3** Isolated yield/%
1	Ph	H	Cl	Me	63
2	Ph	H	Br	Me	95
3	Ph	H	Br	Ph	0
4	p-O_2N-Ph	H	Br	Me	71
5	p-MeO-Ph	H	Br	Me	99
6	Ph	Me	Br	Me	77(52:48)[b]
7	Me	H	Br	Me	94
8	-$(CH_2)_4$-		Br	Me	80(75:25)[b]

a) Mole ratio of **1** : **2** : SmI_2 = 1 : 1 : 1.
b) Diastereomer ratio determined by ^1H NMR.

The reactions with SmI_2 were performed by the following two different procedures. First, **1** in THF was added to 1 equiv of 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 ^1H 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 SmI_2.

In preliminary experiments using SmI_3, **3** was obtained in a low yield together with a significant amount of α-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 SmI_2 or 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 SmI_2 gives better results(shorter reaction time and higher product yield) than those obtained with SmI_3-NaI. It is of interest that **2** in which 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 SmI_2, **1**(1 mmol) in THF (2 ml) was added to a 0.1 M SmI_2 solution in THF (10 ml) at 0 C under nitrogen atmosphere. After

Table 2. The SmI_3-NaI mediated reaction of **1** with **2**[a]

Entry	**1**			**2**	**3**
	R_1	R_2	X	R_3	Isolated yield/%
1	Ph	H	Cl	Me	44
2	Ph	H	Br	Me	75
3	Ph	H	Br	Ph	0
4	p-O_2N-Ph	H	Br	Me	53
5	p-MeO-Ph	H	Br	Me	76
6	Ph	Me	Br	Me	76(58:42)[b]
7	Me	H	Br	Me	40
8	-$(CH_2)_4$-		Br	Me	45(70:30)[c]

a) Mole ratio of SmI_3 : NaI : **1** : **2** = 1 : 1 : 1 : 1.
b) Diastereomer ratio determined by ^{1}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 SmI_2, a solution of **1**(1 mmol) and **2**(1 mmol) in THF (4 ml) was added to a 0.1 M 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 SmI_3, NaI(1 mmol) was added to a 0.1 M SmI_3 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.

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