Carbon–Carbon Bond Formation between α-Halogenoketones and Aldehydes Promoted by Cerium(III) Iodide or Cerium(III) Chloride–Sodium Iodide

Shin-ichi Fukuzawa,* Tatsuo Fujinami, and Shizuyoshi Sakai

Department of Applied Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu 432, Japan

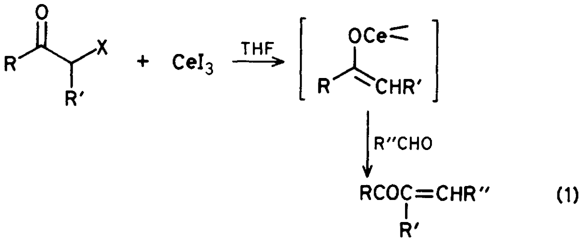
α-Halogenoketones react with aldehydes to form α,β-unsaturated ketones accompanied by dehalogenation in the presence of cerium(III) iodide, but the use of cerium(III) chloride–sodium iodide results in the formation of β-keto alcohols.

Recently the use of lanthanide salts in organic synthesis has been of interest. Several synthetically useful organic reactions using trivalent lanthanide salts have been reported.[1] In the hydrodehalogenation of α-halogenoketones with cerium(III) sulphate and sodium iodide[1b] cerium enolate was assumed to be formed as an intermediate in the reaction, which was carried out in aqueous tetrahydrofuran (THF). It was thought that if a non-aqueous solvent was employed instead, the reactivity of the cerium enolate could be examined.[2,3] Indeed, when α-halogenoketones were treated with cerium(III) iodide (CeI_3) prepared *in situ* from cerium metal and iodine,[4] followed by addition of aldehydes in dry THF, an aldol-like

Table 1. The reaction between α-halogenoketones and aldehydes in the presence of CeI_3.[a]

α-Halogenoketone	Aldehyde	Product(s)	Yield/%[b]
$PhCOCH_2Br$	$MeCHO$[c]	$PhCOCH{=}CHMe$[d]	95
	$EtCHO$[c]	$PhCOCH{=}CHEt$[d]	95
	$PhCHO$	$PhCOCH{=}CHPh$[d]	98
	$\overline{OCH{=}CHCH{=}C}CHO$	$PhCOCH{=}CH\overline{C{=}CHCH{=}CHO}$	98
	$MeCH{=}CHCHO$	$PhCOCH{=}CHCH{=}CHMe$	95
	$PhCH{=}CHCHO$	$PhCOCH{=}CHCH{=}CHPh$	95
	$Me_2C{=}CHCH_2C(Me){=}CHCHO$	$PhCOCH{=}CHC{=}C(Me)CH_2CH_2CH{=}CMe_2$	90
	$EtCHO$[c,e]	$PhCOCH_2CH(OH)Et$	80
		$PhCOCH{=}CHEt$	10
	$\overline{OCH{=}CHCH{=}C}CHO$[e]	$PhCOCH_2C(OH)H\overline{C{=}CHCH{=}CHO}$	85
		$PhCOCH{=}CH\overline{C{=}CHCH{=}CHO}$	10
$MeCOCH_2Cl$	$PhCHO$	$MeCOCH{=}CHPh$	80
$\overline{COCH_2CH_2CH_2CH_2C}HCl$	$PhCHO$	$\overline{COCH_2CH_2CH_2CH_2C}{=}CHPh$	70
$\overline{COCH_2CH_2CH_2CH_2C}HBr$	$PhCHO$	$\overline{COCH_2CH_2CH_2CH_2C}{=}CHPh$	90
$\overline{COCH_2CH_2CH_2CH_2C}HBr$	$PhCHO$[e]	$\overline{COCH_2CH_2CH_2CH_2C}HCH(OH)Ph$	80

[a] A mixture of α-halogenoketone (2 mmol), aldehyde (2 mmol), and CeI_3 (2 mmol) in THF was stirred at room temperature for 1 h. [b] Isolated yield. [c] 4 mmol aldehyde was used. [d] Predominantly *trans*. [e] $CeCl_3$ (2 mmol) and NaI (6 mmol) were used instead of CeI_3.



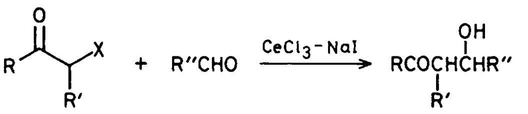
(1)

reaction occurred under mild conditions, α,β-unsaturated ketones being obtained, equation (1). This is the first example of the generation and reaction of a cerium enolate that does not use a metal exchange procedure.[3]

In a typical reaction, phenacyl bromide (2 mmol) was added to a THF (5 ml) solution of CeI_3 (2 mmol). Benzaldehyde (2 mmol) was then added at room temperature. The resulting mixture was stirred for 1 h, and then quenched with aqueous sodium thiosulphate and extracted with chloroform. After drying over $MgSO_4$ and evaporation of the solvent, the crude product was purified by column chromatography on silica gel. The product was determined to be chalcone by ^1H n.m.r. and i.r. The reaction occurs with other aldehydes also to give α,β-unsaturated ketones in high yields. With α,β-unsaturated aldehydes such as cinnamaldehyde and crotonaldehyde, the carbonyl carbon was attacked initially, followed by dehydration to give buta-1,3-dienyl ketones in excellent yields. Other α-halogenoketones such as 1-chloroacetone, 2-chlorocyclohexanone, and 2-bromocyclohexanone reacted similarly with aldehydes to form α,β-unsaturated ketones. Typical results are summarized in Table 1.

When the reaction was quenched with deuterium oxide, deuteriated acetophenone ($PhCOCH_2D$) was isolated from the reaction with phenacyl bromide. This indicates that the first step in the reaction is debromination and the reacting species is the cerium enolate.

In these reactions C–C bond formation and subsequent dehydration occurs in one pot. In contrast, the use of



(2)

cerium(III) chloride ($CeCl_3$)–sodium iodide (NaI) instead of CeI_3 resulted mainly in the production of β-keto alcohols, with only a little subsequent dehydration, equation (2). These results are also shown in Table 1. This type of reaction is analogous to the reaction of other metal enolates.[3] Thus, different products are obtained using CeI_3 or $CeCl_3$–NaI.†

Received, 27th February 1985; Com. 270

References

1 For recent examples see, (a) P. Girard and H. B. Kagan, *Tetrahedron Lett.*, 1975, 4513; J.-L. Luche and A. L. Gemal, *J. Chem. Soc., Chem. Commun.*, 1978, 976; (b) T.-L. Ho, *Synth. Commun.*, 1979, 241; (c) M. Ouertani, P. Girard, and H. B. Kagan, *Tetrahedron Lett.*, 1982, **23**, 4315. J. L. Namy, J. Soupe, J. Collins, and H. B. Kagan, *J. Org. Chem.*, 1984, **49**, 2045.

2 Preparation of cerium enolate by a metal exchange reaction between lithium enolate and $CeCl_3$ has been reported: T. Imamoto, T. Kusumoto, and M. Yokoyama, *Tetrahedron Lett.*, 1983, **24**, 5233.

3 The preparation of aluminium enolate from α-halogenocarbonyl compounds is known, which reacts with some carbonyl compounds to give β-keto alcohols: K. Maruoka, S. Hashimoto, Y. Kitagawa, H. Yamamoto, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 3301; N. Tsuboniwa, S. Matsubara, Y. Morizawa, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 1984, **25**, 2569.

4 J. L. Namy, P. Girard, and H. B. Kagan, *Nouv. J. Chim.*, 1977, **1**, 5.

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† We also showed that β-keto alcohols can be converted into α,β-unsaturated ketones by CeI_3 in THF. This suggests that the β-keto alcohol is formed first, with CeI_3 then working as a dehydrating agent.