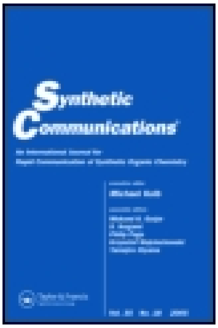

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A Novel Reduction of β-Ketoester with Cp_2TiCl_2A-PrMgBr System

Yongping Yu [a] & Yongmin Zhang [b]
[a] Department of Chemistry, Zhejiang University, Hangzhou, 310027, P. R. China
[b] Department of Chemistry, Hangzhou University, Hangzhou, 310028, P. R. China

To cite this article: Yongping Yu & Yongmin Zhang (1999) A Novel Reduction of β-Ketoester with Cp_2TiCl_2A-PrMgBr System, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:2, 243-247, DOI: 10.1080/00397919908085763

To link to this article: http://dx.doi.org/10.1080/00397919908085763

SYNTHETIC COMMUNICATIONS, 29(2), 243-247 (1999)

A Novel Reduction of β-Ketoester with Cp_2TiCl_2/*i*-PrMgBr System

Yongping Yu[a] and Yongmin Zhang[b]*

[a]Department of Chemistry, Zhejiang University,
Hangzhou, 310027, P. R. China
[b]Department of Chemistry, Hangzhou University,
Hangzhou, 310028, P. R. China

Abstract: β-Ketoesters react with Grignard reagent in the presence of a catalytic amount of Cp_2TiCl_2 to afford the corresponding ketones. A possible mechanism is also proposed.

Sato and his coworkers[1] reported previously that Grignard reagent containing β-H could reduce alkyl ketones, aldehydes and esters to their corresponding alcohols in the presence of a catalytic amount of Cp_2TiCl_2. They also devoloped the Cp_2TiCl_2-catalysed hydromagnesiation reaction of alkynes and this type of reaction has recently become widely used in organic synthesis[2-4]. But aromatic and α,β-unsaturated carbonyl compounds could not be reduced to the corresponding alcohols. We have also described the Cp_2TiCl_2-catalyzed reductions of imines and isocyanates by Grignard reagents.[5-7] Herein we wish to report a novel C-C bond reductive cleavage of β-ketoesters by isopropylmagnesium bromide in the presence of a small amount of

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* To whom the correspondence should be addressed

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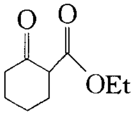
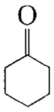
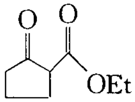
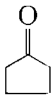
Cp_2TiCl_2 to give corresponding ketones. The results are summarized in Table 1.

$$R^1COCHR^2CO_2R^3 + i\text{-}C_3H_7MgBr \xrightarrow[\text{r. t.}]{10mol\%Cp_2TiCl_2} R^1COCH_2R^2$$

Table 1 Cp_2TiCl_2-catalyzed reduction of β-ketoesters by *i*-PrMgBr

No	Substrate	Product	b. p. (℃/mmHg) (Lit)	Yield[a] (%)
1			41—42/12 (47/15)[8]	71
2			27—28/12 (23—24/10)[8]	69
3	$PhCOCH_2CO_2Et$	$PhCOCH_3$	91—92/8 (67/5)[8]	63
4	$PhCOCH_2CO_2Me$	$PhCOCH_3$		62
5	$PhCH_2COCH_2CO_2Me$	$PhCH_2COCH_3$	83—84/8 (92. 2/10)[8]	58
6	$PhCH_2COCH_2CO_2Et$	$PhCH_2COCH_3$		59
7	$PhCOCHCH_3CO_2Et$	$PhCOCH_2CH_3$	91—92/8 (86. 7/6)[8]	78
8	$PhCOCHCH_3CO_2Me$	$PhCOCH_2CH_3$		73

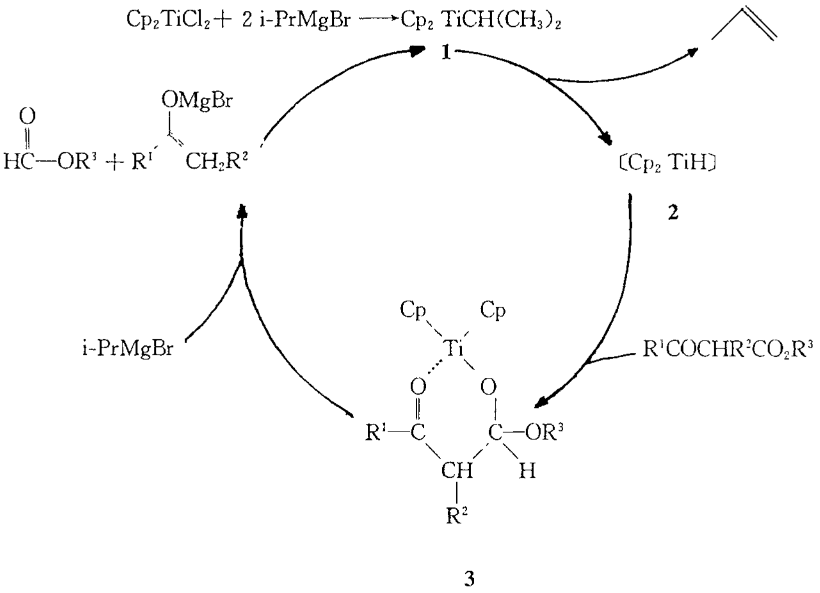
a. Yield of isolated product.

The advantages of this one step dealkoxycarbonylation of β-ketoesters are mild and neutral condition and simple operation.

By analogy with the mechanism proposed for Cp_2TiCl_2-catalyzed reduction of carbonyl compounds,[4] we suggest that the principal intermediate of this catalytic C-C bond cleavage reaction is Cp_2TiH. A presumed mechanism has been described as follows.

As shown in Scheme I, in the first step, isopropylmagnesium bromide reacts with Cp_2TiCl_2 to form the isopropylmagnesium compound **1**. Cp_2TiR is unstable and can easily be decomposed to Cp_2TiH **2**. Cp_2TiH **2** reacts with β-ketoester to form intermediate **3** which is fairly reactive and easily exchange with Grignard reagent at meantime. Then the C-C bond of the imtermediate **3** is cleaved.

Scheme I



Experimental Section

^{1}H NMR spectra were recorded in $CDCl_3$ on JEOL PMX 60 Si spectrometer using TMS as internal standard. IR spectra were obtained on a PE 683 spectrometer (neat). The reaction were performed in a Schlenk type glass apparatus and under a nitrogen atmosphere.

General procedures are as follows: The reaction was performed under nitrogen atmostphere. Isopropylmagnesium bromide in THF (40 ml, 1.0 M) was added to an ether solution of Cp_2TiCl_2 (0.25 g, 1 mmol), and the mixture was stirred for 10 min at room temperature. β-ketoester (10 mmol) in dry ether (10 ml) was slowly added dropwise under nitrogen over about 1 hr. The resulting mixture was stirred for 4 hr at room temperature. The reaction mixture was then acidified with HCl (25 ml, 2 N), extracted with ether (20 ml × 3). The combined ethereal was dried over anhydrous magnesium sulfate. The solvent was evaporated and the crude product was purified by distillation. The products were fully characterized by their ^{1}H NMR and IR spectra, and by their b.p. data.

Acknowledgement

We thank the National Natural Science Foundation of China and the Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences for financial support.

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(Received in Japan 23 March 1998)