COMMUNICATIONS

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The Reduction of Carboxylic Acids to Aldehydes by Dichlorobis[π-cyclopentadienyl]titanium-Catalyzed Grignard Reactions

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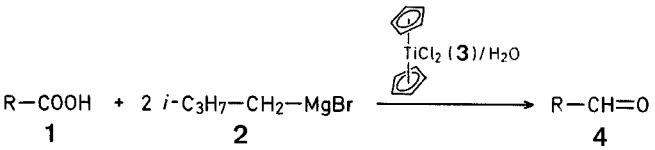
We have recently reported that the course of Grignard reactions with aldehydes[1], ketones[1], or esters[2] is changed drastically on catalysis with dichlorobis[π-cyclopentadienyl]titanium **(3)**. For example, when the reaction of isobutylmagnesium bromide **(2)** with esters was carried out in the presence of 2 mol% of **3**, reduction of esters to primary alcohols became dominant[2]. These findings prompted us to extend the dichlorobis[π-cyclopentadienyl]titanium-catalyzed Grignard reaction to carboxylic acids **1**, which affords tertiary alcohols in the absence of the catalyst[3], in order to determine the full scope of this catalytic system. We initially expected the reaction to proceed in a similar manner to the reaction with esters. However, we obtained some unexpected and synthetically useful results.

Treatment of carboxylic acids **1** with a mixture of 2 mol of isobutylmagnesium bromide **(2)** and catalytic amounts of **3** in ether for 4 h at room temperature under argon followed by hydrolysis afforded the aldehydes **4**.



The results, summarized in the Table, show that yields of aldehydes **4** from alkyl- and aryl-carboxylic acids **1** were fair to good, whereas no aldehydes were obtained from α,β-unsaturated carboxylic acids.

Table. Aldehydes **4** from Carboxylic Acids **1**

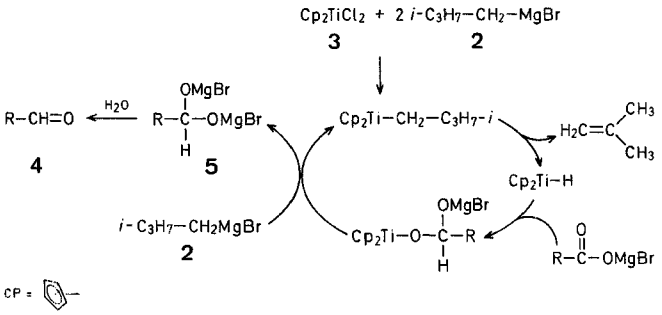
R	Yield [%][a] of **4**	b.p. [°C]/torr	
		found	reported[4]
n-C_6H_{13}	73	156°/760	155°/760
n-C_3H_7—$CH(CH_3)$—	65	125°/760	116°/737
c-C_6H_{11}	59	160°/760	155–158°/760
C_6H_5—CH_2	48	192°/760	193–194°/760
C_6H_5	55[b]	177°/760	178.1°/760
trans-C_6H_5—CH=CH_2	0	—	—

[a] Yield of product isolated by distillation; purity: ≥98% as determined by G.L.C. (PEG 20 M, 5 m).

[b] Benzyl alcohol (14%) also formed. In all other cases the primary alcohol, if detected, was formed in ≤ 1% yield.

Though many methods have been reported for the reduction of carboxylic acid derivatives such as esters, amides, or acyl halides to aldehydes, the only reported methods for straightforward reduction of free carboxylic acids to aldehydes with high selectivity are those using lithium in methylamine[5], thexylborane[6], or bis[4-methylpiperazinyl]aluminum hydride[7]. The present system provides a valuable new methodology for reduction of carboxylic acids **1** to aldehydes **4** and seems to be an attractive alternative to the above reagents.

The mechanism proposed in the following scheme rationalizes the observed catalytic cycle. We have recently found that the complex **5** is stable and affords aldehydes on hydrolysis[8].



Aldehydes 4 from Carboxylic Acids 1 using Isobutylmagnesium Bromide (2) and Dichlorobis[π-cyclopentadienyl]titanium (3); General Procedure:

After stirring a 1.0 molar ether solution of isobutylmagnesium bromide (**2**; 63 ml, 63 mmol) and **3** (75 mg, 0.3 mmol) for 5 min at 0 °C under argon, a carboxylic acid **1** (30 mmol) is added, and the reaction mixture is stirred for 4 h at room temperature. The reaction mixture is then quenched by addition of 4 normal hydrochloric acid (20 ml) and the layers are separated. The aqueous layer is extracted with ether (30 ml). The combined organic layers are dried with magnesium sulfate and then distilled. Identity of the product was confirmed by comparison of I.R. and ^{1}H-N.M.R. spectra and retention times on G.L.C. analysis (PEG 20 M, 5 m) with those of authentic samples.

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