Category

Key words

reagent

carbon dioxide organolithium

Grignard reagent

Metal-Mediated Synthesis

J. WU, X. YANG, Z. HE, X. MAO, T. A. HATTON,* T. F. JAMISON* (MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, USA)

Continuous Flow Synthesis of Ketons from Carbon Dioxide and Organolithium or Grignard Reagents *Angew. Chem. Int. Ed.* **2014**, *53*, 8416–8420.

Ketones from Carbon Dioxide and Organolithium or Grignard Reagents

$$\begin{array}{c|c} & & & \\ II & \\ II & \\ O & \\ \end{array}$$

$$\begin{array}{c|c} & & & \\ R^1 \text{Li } (0.4 - 1 \text{ equiv}) \\ \hline \text{or } R^2 \text{MgBr } (1 \text{ equiv}) \\ \end{array}$$

$$\begin{array}{c|c} & & & \\ R^{1-2} \text{CO}_2 \text{Li} \\ \hline \end{array}$$

$$\begin{array}{c|c} & & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$$\begin{array}{c|c} & & \\ \hline & & \\ \end{array}$$

$R^{1-2} = Alk, HetAr$

Selected examples:

Significance: The authors report two complementary continuous flow systems using either stoichiometric amounts or an excess of CO₂ for the preparation of ketones. Starting from organolithium or Grignard reagents, the described synthesis shows significant advantages over conventional batch conditions in suppressing undesired symmetric ketone and tertiary alcohol byproducts.

Comment: The observation that in this reaction organolithium reagents are more reactive in ${\rm Et_2O}$ than in THF is unprecedented. Furthermore, by integrating an in-line generation of organolithium or organomagnesium species, a telescoped one-flow process capable of preparing ketones in a modular fashion from simple precursors has been established.

SYNFACTS Contributors: Paul Knochel, Thomas Klatt Synfacts 2014, 10(11), 1191 Published online: 20.10.2014

 $\textbf{DOI:}\ 10.1055/s\text{-}0034\text{-}1379343;\ \textbf{Reg-No.:}\ P13314SF$