The MgCl$_2$–Et$_3$N Base System: A Useful Reagent in Organic Synthesis

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Introduction

The combination of MgCl$_2$ and Et$_3$N is a considerably stronger base than Et$_3$N alone. This base system has been used for a variety of base-induced reactions such as: $\alpha$-carboxylation of ketones,$^1$ condensation,$^2$ acylation of malonate derivatives,$^3,4$ phosphonoacetes,$^5,6$ anti-aldol$^7$ and imine aldol$^8$ reactions, ortho-formylation of phenols,$^9$ and Mannich reactions.$^{10}$ Moreover, this base system was used in Dieckman-type cyclizations$^{11}$ and also for the preparation of $\beta$-ketoamides by the condensation of ketones and isocyanates.$^{12}$

Abstracts

(A) $\alpha$-Carboxylation of ketones with carbon dioxide in the presence of MgCl$_2$–Et$_3$N followed by reaction with methyl vinyl ketone (MVK) yielded the Michael adducts in 42–75% yields or the Robinson adducts in 56–70% yields. This method reduced the polymerization of MVK usually observed under strong basic conditions.$^1$

(B) $\alpha,\beta$-Unsaturated cyano esters were prepared by the condensation of aryl aldehydes with ethyl cyanoacetate in the presence of MgCl$_2$–Et$_3$N as catalyst.$^7$

(C) Acylation of diethyl malonate with an acid chloride using MgCl$_2$–Et$_3$N as base gave adducts in excellent yields. This method was also used for the preparation of $\beta$-oxo esters from ethyl malonate mono potassium salt and acid chlorides in 92–99% yields.$^3$

(D) Acylation of (acylamino)malonate with MgCl$_2$–Et$_3$N as base afforded $\alpha$-acyl $\beta$-keto esters in good to excellent yields with a variety of acid chlorides.$^4$
(E) Acylation of triethyl α-fluorophosphonoacetate with 2.2 equivalents of a benzoyl chloride in dry toluene and in the presence of MgCl₂–Et₃N afforded the diacylated adduct, which was deacylated in aqueous ethyl acetate and in the presence of SiO₂ to α-fluoro-β-keto esters. Good to excellent yields (78–94%) were obtained.⁵

(F) Acylation of diethyl phosphonoacetic acid in the presence of MgCl₂–Et₃N as base gave β-keto phosphonates in 40–90% yields.⁶

(G) In 2002 Evans and co-workers used MgCl₂–Et₃N in anti-aldol reactions of chiral N-acyloxazolidinones in the presence of chlorotrimethylsilane. The adducts were formed with high diastereoselectivity (dr up to 32:1). The reactions are operationally simple and can be run without rigorous exclusion of water.

(H) Stereoselective imine aldol reactions of N-cyclohexylimine with aromatic aldehydes in the presence of MgCl₂–Et₃N were reported recently by Hayashi et al. High yields of products were obtained consisting essentially of the erythro isomer.

(I) A combination of MgCl₂–Et₃N was used as base in the ortho-formylation of phenols by Skattebøl and co-workers. The reaction gave higher yields (70–99%) and fewer byproducts compared to most other methods.

(J) Phenols react with Eschenmoser’s salt in the presence of the MgCl₂–Et₃N as base, affording exclusively ortho-substituted benzylamines in high yields (66–98%).¹⁰

References
