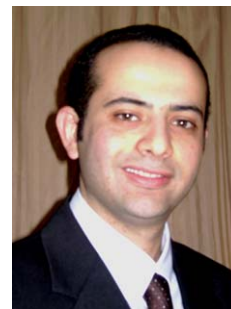


SYNLETT Spotlight 292

The $\text{MgCl}_2\text{-Et}_3\text{N}$ Base System: A Useful Reagent in Organic Synthesis

Compiled by Hany Fakhry Anwar



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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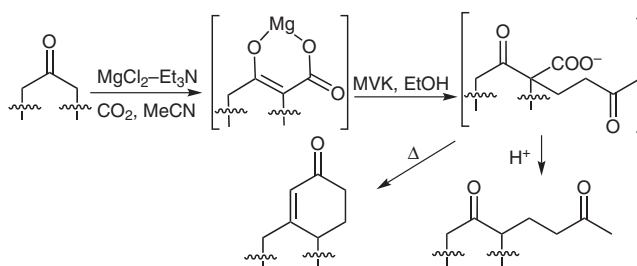
Introduction

The combination of MgCl_2 and Et_3N is a considerably stronger base than Et_3N alone. This base system has been used for a variety of base-induced reactions such as: α -carboxylation of ketones,¹ condensation,² acylation of

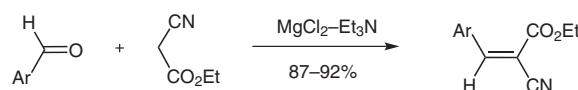
malonate derivatives,^{3,4} phosphonoacetes,^{5,6} *anti*-aldol⁷ and imine aldol⁸ reactions, *ortho*-formylation of phenols,⁹ and Mannich reactions.¹⁰ Moreover, this base system was used in Dieckman-type cyclizations¹¹ and also for the preparation of β -ketoamides by the condensation of ketenes and isocyanates.¹²

Abstracts

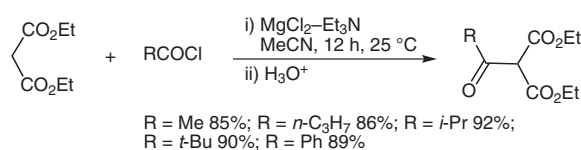
(A) α -Carboxylation of ketones with carbon dioxide in the presence of $\text{MgCl}_2\text{-Et}_3\text{N}$ followed by reaction with methyl vinyl ketone (MVK) yielded the Michael adducts in 42–75% yields or the Robinson adducts in 56–70% yields. This method reduced the polymerization of MVK usually observed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



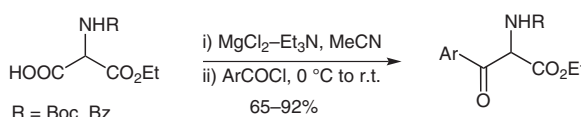
(B) α,β -Unsaturated cyano esters were prepared by the condensation of aryl aldehydes with ethyl cyanoacetate in the presence of $\text{MgCl}_2\text{-Et}_3\text{N}$ as catalyst.²



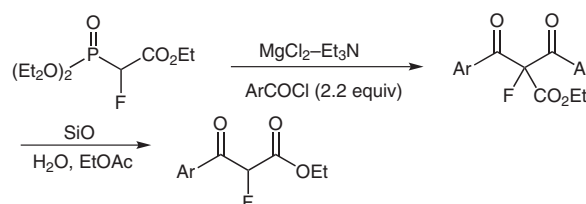
(C) Acylation of diethyl malonate with an acid chloride using $\text{MgCl}_2\text{-Et}_3\text{N}$ as base gave adducts in excellent yields. This method was also used for the preparation of β -oxo esters from ethyl malonate mono potassium salt and acid chlorides in 92–99% yields.³



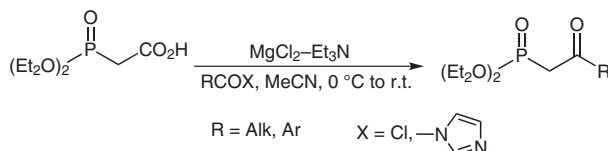
(D) Acylation of (acylamino)malonate with $\text{MgCl}_2\text{-Et}_3\text{N}$ as base afforded α -acyl β -keto esters in good to excellent yields with a variety of acid chlorides.⁴



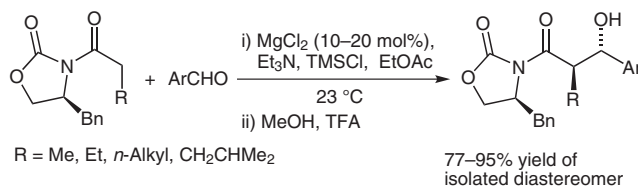
(E) Acylation of triethyl α -fluorophosphonoacetate with 2.2 equivalents of a benzoyl chloride in dry toluene and in the presence of $\text{MgCl}_2\text{-Et}_3\text{N}$ afforded the diacylated adduct, which was deacylated in aqueous ethyl acetate and in the presence of SiO_2 to α -fluoro- β -keto esters. Good to excellent yields (78–94%) were obtained.⁵



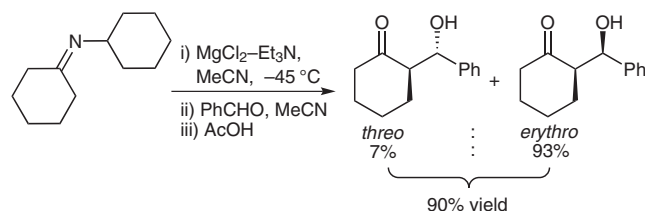
(F) Acylation of diethyl phosphonoacetic acid in the presence of $\text{MgCl}_2\text{-Et}_3\text{N}$ as base gave β -keto phosphonates in 40–90% yields.⁶



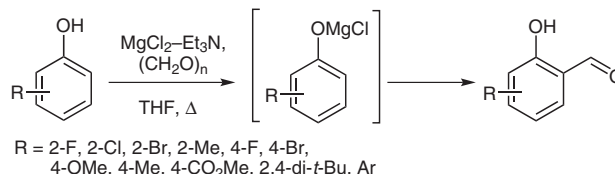
(G) In 2002 Evans and co-workers used $\text{MgCl}_2\text{-Et}_3\text{N}$ in *anti*-aldol reactions of chiral *N*-acyloxazolidinones in the presence of chlorotrimethylsilane.⁷ The adducts were formed with high diastereoselectivity (dr up to 32:1). The reactions are operationally simple and can be run without rigorous exclusion of water.



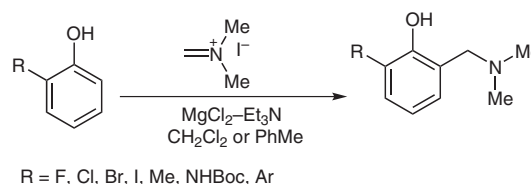
(H) Stereoselective imine aldol reactions of *N*-cyclohexylimine with aromatic aldehydes in the presence of $\text{MgCl}_2\text{-Et}_3\text{N}$ were reported recently by Hayashi et al.⁸ High yields of products were obtained consisting essentially of the *erythro* isomer.



(I) A combination of $\text{MgCl}_2\text{-Et}_3\text{N}$ was used as base in the *ortho*-formylation of phenols by Skattebøl and co-workers.⁹ 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 $\text{MgCl}_2\text{-Et}_3\text{N}$ as base, affording exclusively *ortho*-substituted benzylamines in high yields (66–98%).¹⁰



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