The MgCl₂–Et₃N Base System: A Useful Reagent in Organic Synthesis

Compiled by Hany Fakhry Anwar

Hany Fakhry Anwar was born in Cairo, Egypt, in 1979. He received his B.Sc. in chemistry (2001) and his M.Sc. in organic chemistry (2005) from Cairo University. Currently, he is in the final stage of his Ph.D. thesis under the supervision of Associate Professor Trond Vidar Hansen at the School of Pharmacy, Department of Pharmaceutical Chemistry, Oslo University. His research interests focus on the synthesis of heterocyclic compounds and natural products.

School of Pharmacy, Department of Pharmaceutical Chemistry, University of Oslo, P. O. Box 1068, Blindern, N-0316 Oslo, Norway
E-mail: hany.anwar@farmasi.uio.no

Introduction

The combination of MgCl₂ and Et₃N is a considerably stronger base than Et₃N alone. This base system has been used for a variety of base-induced reactions such as: α-carboxylation of ketones, condensation, acylation of malonate derivatives, phosphonoacetates, anti-aldol reactions, ortho-formylation of phenols, and Mannich reactions. Moreover, this base system was used in Dieckmann-type cyclizations and also for the preparation of β-ketoamides by the condensation of ketenes and isocyanates.

Abstracts

(A) α-Carboxylation of ketones with carbon dioxide in the presence of MgCl₂–Et₃N 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.

(B) α,β-Unsaturated cyano esters were prepared by the condensation of aryl aldehydes with ethyl cyanoacetate in the presence of MgCl₂–Et₃N as catalyst.

(C) Acylation of diethyl malonate with an acid chloride using MgCl₂–Et₃N 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.

(D) Acylation of (acylamino)malonate with MgCl₂–Et₃N as base afforded α-acyl β-keto esters in good to excellent yields with a variety of acid chlorides.
(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.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 MgCl₂–Et₃N were reported recently by Hayashi et al.8 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.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 MgCl₂–Et₃N as base, affording exclusively ortho-substituted benzylamines in high yields (66–98%).10

References