MgBr$_2$·OEt$_2$ – A Versatile Reagent in Organic Synthesis

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Introduction

Use of magnesium(II) species as Lewis acid catalysts for various functional group transformations is well documented. Of these, magnesium halides are the most useful. Readiness availability and ease of preparation prompted the frequent use of MgBr$_2$·OEt$_2$ in various organic transformations. The oxophilic and coordinating nature of MgBr$_2$·OEt$_2$ has been demonstrated through its use as a bidentate chelating Lewis acid in a number of chelation-controlled reactions such as cycloadditions, asymmetric aldol reactions, rearrangements, radical additions, hydrogen transfer reactions, stereoselective reductions, and anomerizations. MgBr$_2$·OEt$_2$ is commercially available as a grey solid (mp >300 °C, fp 35 °C). It can be readily prepared by reacting a slight excess of magnesium turnings with 1,2-dibromoethane in anhydrous diethyl ether. The solution can be stored at room temperature for several months and the solid can be stored in a vacuum desiccator for indefinite periods without any loss of activity.

Abstracts

(A) Condensation of 2,5-dimethoxy-2,5-dihydrofuran with ethyl vinyl ether in the presence of a catalytic amount of MgBr$_2$·OEt$_2$ resulted in 2-furylacetaldehyde diethyl acetal in 50% yield. The reaction is a formal acetal and ethyl vinyl ether condensation followed by aromatization. The protocol has been employed in the synthesis of various 2-(2-furo)tetrahydrofuranic or -pyranic moieties in good yields.

(B) A mild and practical N-acylation of amides was possible by the dual activation of both amides and acid anhydrides with MgBr$_2$·OEt$_2$. The method was applicable to amides that can undergo O-acylation and are susceptible to racemization or O,N-acyl migrations.

(C) We have recently reported a mild method for the formation of cyclic siloxanes by the exchange of the Li counterion of an intermediate alkoxide with Mg, using excess MgBr$_2$·OEt$_2$. The reaction may formally be considered to be a semi-Brook rearrangement.

(D) MgBr$_2$·OEt$_2$, in combination with Bu$_3$SnH, was effective in a chelation-controlled reductive opening of methoxybenzylidene acetals. The reaction offers a mild and efficient method for selective mono-MPM ether protection of diols. High conversions, regioselectivity and tolerance to functional groups make this a very useful protocol in natural product synthesis.

(E) MgBr$_2$·OEt$_2$ effected deprotection of aliphatic SEM ethers under extremely mild and high yielding conditions in the presence of other sensitive groups like acetones, TBS and TIPS ethers and O-silylated cyanohydrins. A variety of functionalities including alcohols, esters, benzyl groups, dithianes, and methoxy acetals are tolerated.
(F) The MgBr₂·OEt₂-Me₂S system was used for a mild and chemoselective deprotection of p-methoxybenzyl (PMB) ethers in the presence of 1,3-diene, 2-butyldimethylsilyl (TBDMS) ether, benzoate, benzyl ether, and acetonides. The method is especially effective for 1,3-diene systems that tend to isomerize rapidly when other protocols are employed.

(G) A stereodivergent opening of the oxirane ring with MgBr₂·OEt₂ was recently described. While MgBr₂·OEt₂ alone resulted in the syn-anti product in high yields.

(H) The efficacy of MgBr₂·OEt₂ as a chelating Lewis acid in highly diastereoselective addition of nucleophiles to Cr(CO)₃-complexed aryl aldehydes was recently demonstrated by us. The results indicated that MgBr₂·OEt₂ can form an effective seven-membered chelate.

(I) MgBr₂·OEt₂ could afford 3-hydroxyazetidines by a highly regio- and stereoselective cyclization of 2,3-epoxy amines.

References


