

SYNLETT Spotlight 88

MgBr₂·OEt₂ – A Versatile Reagent in Organic Synthesis

Compiled by Suresh Kumar Tipparaju



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

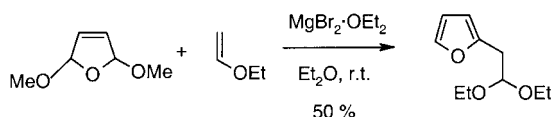
Use of magnesium(II) species as Lewis acid catalysts for various functional group transformations is well documented.¹ Of these, magnesium halides are the most useful. Ready availability and ease of preparation prompted the frequent use of MgBr₂·OEt₂ in various organic transformations. The oxophilic and coordinating nature of MgBr₂·OEt₂ has been demonstrated through its use as a bidentate chelating Lewis acid in a number of chelation-controlled reactions such as cycloadditions,² asymmetric aldol reactions,³ rearrangements,⁴ radical additions,^{5,6}

hydrogen transfer reactions,⁷ stereoselective reductions,⁸ and anomerizations.⁹

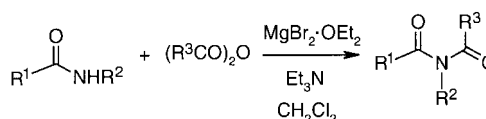
MgBr₂·OEt₂ is commercially available as a grey solid (mp >300 °C, fp 35 °C). It can be readily prepared by reacting a slight excess of magnesium turnings with 1,2-dibromoethane in anhydrous diethyl ether.¹⁰ The solution can be stored at room temperature for several months and the solid can be stored in a vacuum desiccator for indefinite periods without any loss of activity.

Abstracts

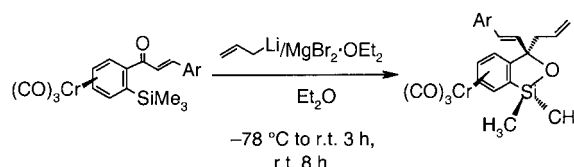
(A) Condensation of 2,5-dimethoxy-2,5-dihydrofuran with ethyl vinyl ether in the presence of a catalytic amount of MgBr₂·OEt₂ resulted in 2-furylacetaldehyde diethyl acetal in 50% yield. The reaction is a formal acetal and ethyl vinyl ether condensation followed by aromatization. The protocol has been employed in the synthesis of various 2-(2-furo)tetrahydrofuranic or -pyranic moieties in good yields.¹¹



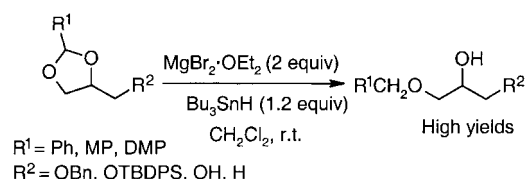
(B) A mild and practical N-acylation of amides was possible by the dual activation of both amides and acid anhydrides with MgBr₂·OEt₂.¹² The method was applicable to amides that can undergo O-acylation and are susceptible to racemization or O,N-acyl migrations.



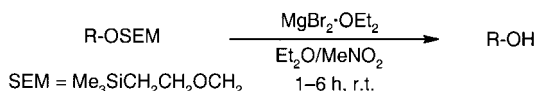
(C) We have recently reported a mild method for the formation of cyclic siloxanes by the exchange of the Li counterion of an intermediate alkoxide with Mg, using excess MgBr₂·OEt₂.¹³ The reaction may formally be considered to be a *semi*-Brook rearrangement.



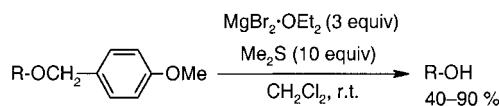
(D) MgBr₂·OEt₂, in combination with Bu₃SnH, was effective in a chelation-controlled reductive opening of methoxybenzylidene acetals.¹⁴ The reaction offers a mild and efficient method for selective mono-MPM ether protection of diols. High conversions, regioselectivity and tolerance to functional groups make this a very useful protocol in natural product synthesis.



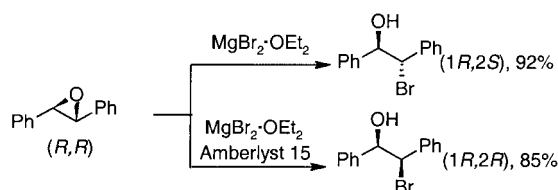
(E) MgBr₂·OEt₂ effected deprotection of aliphatic SEM ethers under extremely mild and high yielding conditions in the presence of other sensitive groups like acetonides, TBS and TIPS ethers and O-silylated cyanohydrins.¹⁵ A variety of functionalities including alcohols, esters, benzyl groups, dithianes, and methoxy acetals are tolerated.



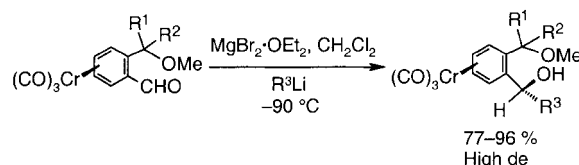
(F) The $\text{MgBr}_2 \cdot \text{OEt}_2$ - Me_2S system was used for a mild and chemo-selective deprotection of *p*-methoxybenzyl (PMB) ethers in the presence of 1,3-diene, *t*-butyldimethylsilyl (TBDMS) ether, benzoate, benzyl ether, and acetonides.¹⁶ The method is especially effective for 1,3-diene systems that tend to isomerize rapidly when other protocols are employed.¹⁷



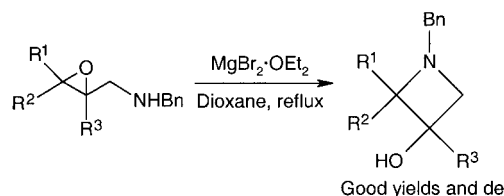
(G) A stereodivergent opening of the oxirane ring with $\text{MgBr}_2 \cdot \text{OEt}_2$ was recently described.¹⁸ While $\text{MgBr}_2 \cdot \text{OEt}_2$ alone resulted in the *anti*-bromohydrin in high diastereomeric excess, use of $\text{MgBr}_2 \cdot \text{OEt}_2$ /Amberlyst 15 gave the *syn*-product in high yields.



(H) The efficacy of $\text{MgBr}_2 \cdot \text{OEt}_2$ as a chelating Lewis acid in highly diastereoselective addition of nucleophiles¹⁹ to $\text{Cr}(\text{CO})_3$ -complexed aryl aldehydes was recently demonstrated by us.^{19a} The results indicated that $\text{MgBr}_2 \cdot \text{OEt}_2$ can form an effective seven-membered chelate.



(I) $\text{MgBr}_2 \cdot \text{OEt}_2$ could afford 3-hydroxyazetidines by a highly regio- and stereoselective cyclization of 2,3-epoxy amines.²⁰



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