

SYNLETT Spotlight 58

NiCl₂ and NiCl₂ · 6H₂O: A very Useful Mild Lewis Acid in Organic Synthesis

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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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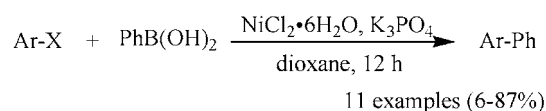
Introduction

Lewis acids are very useful reagents in organic synthesis. The classical Lewis acids currently used include BF₃·OEt₂, ZnCl₂, SnCl₂, TiCl₄ and many others. Nickel chloride can be also added to this list. NiCl₂ is a mild Lewis acid that promotes a wide variety of organic transformations in aqueous medium or organic solvent and may be used either catalytically or stoichiometrically. NiCl₂ was also used in a key step in the synthesis of bi-benzopyran-4-ol,¹ tetrahydrodicranenone B² and Allo-

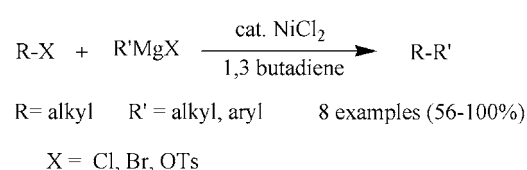
pumiliotoxins.³ NiCl₂ is a selective reductive agent when used with hydrides such as LiAlH₄ and NaBH₄. In fact, the mixture of NiCl₂ and NaBH₄ is used to prepare nickel boride,⁴ a reducing agent for many functional groups: azide,⁵ nitrile,⁶ NO bond,⁷ alkene⁸ and haloalkane.⁹ NiCl₂ was used in the regioselective rearrangement of dienols,¹⁰ ring-opening of epoxide,¹¹ nickel(II)/chromium(II) chloride-mediated addition to aldehydes or ketones,^{2,3} Suzuki cross-coupling,¹² Biginelli reaction,¹³ reductive Heck-like reactions,¹⁴ nickel-catalyzed cross-coupling reaction of Grignard reagents¹⁵ and homo-coupling reactions.¹⁶

Abstract

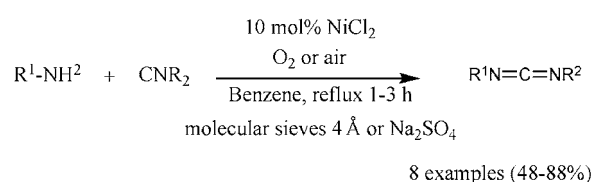
(A) Suzuki cross-coupling with ArBr and ArI can be carried out with PhB(OH)₂ in good yields using NiCl₂·6H₂O as a catalyst precursor.¹²



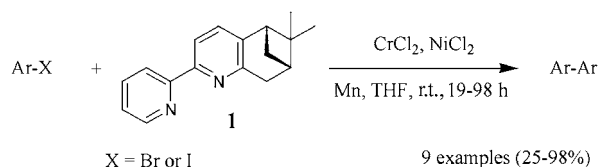
(B) NiCl₂-(1,3-butadiene) catalyzes the cross-coupling reaction of alkyl chlorides, bromides, and tosylates with Grignard reagents under mild conditions.¹⁵



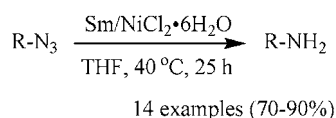
(C) A general and convenient preparation of unsymmetrical *N,N'*-carbodiimides was achieved by the nickel(II)-catalyzed reaction of isocyanides with primary amines using molecular oxygen as an oxidant.¹⁷



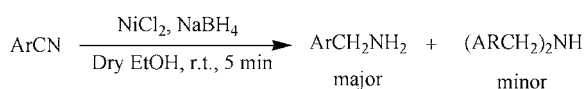
(D) Aryl halides are readily homocoupled using a catalytic amount of $\text{NiCl}_2/\text{CrCl}_2$ and bipyridyl-type ligand **1** in the presence of manganese at room temperature in good yield.^{16a}



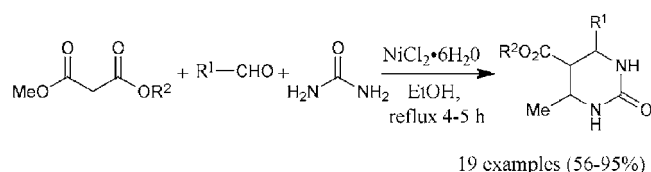
(E) Azides are efficiently reduced to the corresponding amines with $\text{Sm}/\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ in excellent yields under mild conditions.¹⁸



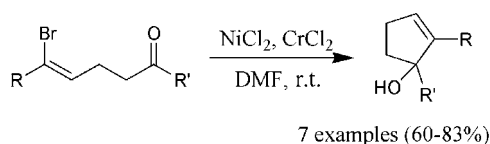
(F) Nitriles are rapidly reduced to primary amines with nickel boride at room temperature.⁶



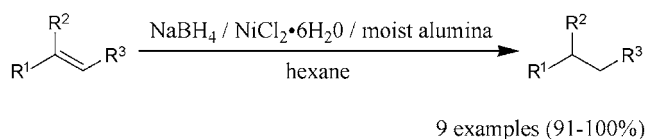
(F) A Biginelli reaction was efficiently used for the synthesis of 3,4-dihydropyrimidinones from aldehydes, β -keto esters and urea in ethanol, using $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$.¹³



(G) An intramolecular Nozaki–Kishi cyclization was efficiently employed in the cyclization of *Z*-vinyl bromides to the corresponding cyclopentenols in good yields.²



(H) In the presence of moist alumina, aliphatic and aromatic alkenes were hydrogenated quantitatively to alkanes under mild conditions with $\text{NaBH}_4/\text{NiCl}_2$.⁸



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