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

Compiled by Philippe Labrie

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Introduction

Lewis acids are very useful reagents in organic synthesis. The classical Lewis acids currently used include BF₃·ΟEt₂, 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 tetrahydrodricranenone 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,¹² 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 NiCl2/CrCl2 and bipyridyl-type ligand 1 in the presence of manganese at room temperature in good yield.\(^{16a}\)

\[
\text{Ar-X} \quad + \quad \begin{array}{c}
\text{C} \text{O} \text{C} \\
\text{N} \\
\text{N} \\
\end{array} \quad \text{NiCl}_2 \quad \text{CrCl}_2 \\
\text{Mn, THF, rt, 19-98 h} \quad \text{Ar-Ar}
\]

9 examples (25-98%)

(E) Azides are efficiently reduced to the corresponding amines with Sm/NiCl2·6H2O in excellent yields under mild conditions.\(^{18}\)

\[
\begin{align*}
\text{R-N}_3 & \xrightarrow{\text{Sm/NiCl}_2\cdot 6\text{H}_2\text{O}} \text{R-NH}_2 \\
\text{THF, 40 oC, 25 h} & \\
14 \text{ examples (70-90%)}
\end{align*}
\]

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

\[
\begin{align*}
\text{ArCN} & \xrightarrow{\text{NiCl}_2, \text{NaBH}_4} \text{ArCH}_2\text{NH}_2 + \text{(ARCH}_2\text{NH)}_2 \\
\text{Dry EtOH, r.t., 5 min} & \\
7 \text{ examples (60-83%)}
\end{align*}
\]

(F) A Biginelli reaction was efficiently used for the synthesis of 3,4-dihydropyrimidinones from aldehydes, β-keto esters and urea in ethanol, using NiCl2·6H2O.\(^{13}\)

(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 NaBH4/NiCl2.\(^{8}\)

9 examples (91-100%)

References