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·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, tetrahydrodricranone B² and Allopumiliotoxins.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

\[
\text{Ar}-\text{X} + \text{PhB(OH)}₂ \xrightarrow{\text{NiCl₂·6H₂O, K₃PO₄, dioxane, 12 h}} \text{Ar-Ph}
\]

11 examples (6-87%)

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

\[
\text{R}-\text{X} + \text{R'}\text{MgX} \xrightarrow{\text{cat. NiCl₂, 1,3 butadiene}} \text{R-R'}
\]

R = alkyl
R' = alkyl, aryl
8 examples (56-100%)

X = Cl, Br, OTs

(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

\[
\text{R¹-NH}² + \text{CNR}₂ \xrightarrow{10 \text{ mol} \% \text{ NiCl₂, O₂ or air, \ benzene, reflux 1-3 h}} \text{R¹N=C=NR}²
\]

molecular sieves 4 Å or Na₂SO₄

8 examples (48-88%)
(D) Aryl halides are readily homocoupled using a catalytic amount of NiCl$_2$/CrCl$_2$ and bipyridyl-type ligand $\text{1}$ in the presence of manganese at room temperature in good yield.$^{16a}$

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

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

(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 NaBH$_4$/NiCl$_2$.$^8$

References