SYNLETT Spotlight 58

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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

Compiled by Philippe Labrie

P. Labrie was born in 1977, received his BSc degree in Chemistry (2000) from Laval University, Québec, Canada. Currently he is doing a PhD under the tutelage of Dr. René C.-Gaudreault, Laval University, Québec, Canada and Dr. Suman Rakhit, MCR Research Inc, Toronto, Ontario, Canada. His present research interest is the development of anticancer agents and inhibitors of P-glycoprotein. He is also investigating the application of Michael-type addition of arylboronic acids to enones derived from carbohydrates.

Department of Chemistry, Université Laval, Québec G1K 7P4, Canada

E-mail: plabrie16@hotmail.com

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 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

References

- (1) Lin, G.-q.; Hong, R. *J. Org. Chem.* **2001**, *66*, 2877.
- (2) Trost, B. M.; Pinkerton, A. B. *J. Org. Chem.* **2001**, *66*, 7714.
- (3) (a) Aoyagi, S.; Wang, T.-C.; Kibayashi, C. *J. Am. Chem. Soc.* **1993**, *115*, 11393. (b) Halterman, R. L.; Zhu, C. *Tetrahedron Lett.* **1999**, *40*, 7445.
- (4) Dhawan, D.; Grover, S. K. *Synth. Commun.* **1992**, *22*, 2405.
- (5) Jefford, C. W.; Jaggi, D.; Bernardinelli, G.; Boukouvalas, J. *Tetrahedron Lett.* **1987**, *28*, 4041.
- (6) Khurana, J. M.; Kukreja, G. *Synth. Commun.* **2002**, *32*, 1265.
- (7) Rowley, M.; Tsukamoto, M. *J. Am. Chem. Soc.* **1989**, *111*, 2735.
- (8) Yakabe, S.; Hirano, M.; Morimoto, T. *Tetrahedron Lett.* **2000**, *41*, 6795.
- (9) Tabaei, S.-M. H.; Pittman, C. U. Jr; Mead, K. T. *J. Org. Chem.* **1992**, *57*, 6669.
- (10) (a) Kyler, K. S.; Watt, D. S. *J. Am. Chem. Soc.* **1983**, *105*, 619. (b) Kyler, K. S.; Bashir-Hashemi, A.; Watt, D. S. *J. Org. Chem.* **1984**, *49*, 1084.
- (11) Mukaiyama, T.; Soga, T.; Takenoshita, H. *Chem. Lett.* **1989**, 997.
- (12) Zim, D.; Monteiro, A. L. *Tetrahedron Lett.* **2002**, *43*, 4009.
- (13) Lu, J.; Bai, Y. *Synthesis* **2002**, 466.
- (14) Tufariello, J. J.; Meckler, H.; Pushpananda, K.; Senaratne, A. *Tetrahedron* **1985**, *41*, 3447.
- (15) Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222.
- (16) (a) Chen, C. *Synlett* **2000**, *10*, 1490. (b) Kotora, M.; Matsumura, H.; Takahashi, T. *Chem. Lett.* **2000**, *3*, 236.
- (17) Kiyoi, T.; Seko, N.; Yoshino, K.; Itot, Y. *J. Org. Chem.* **1993**, *58*, 5118.
- (18) Wu, H.; Chen, R.; Zhang, Y. *Synth. Commun.* **2002**, *32*, 189.