

## SYNLETT Spotlight 192

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

## Al–NiCl<sub>2</sub>·6H<sub>2</sub>O: A Mild and Efficient System for Selective Reduction of Functional Groups in Organic Synthesis

Compiled by B. Rama Raju

B. Rama Raju was born at Pathara, Orissa in India. He received his B.Sc. in Chemistry (Hons) from Khallikote (Autonomous) College, India. He completed his M.Sc. at Berhampur University, Orissa, in 2001. Currently he is pursuing his Ph.D. under the tutelage of Dr. Anil K. Saikia, Department of Chemistry, Indian Institute of Technology, Guwahati, India. His research interests include the development of new synthetic methodologies, incorporation of fluorine in organic molecules and their applications, and the synthesis of biologically active molecules.

Department of Chemistry, Indian Institute of Technology  
Guwahati, Guwahati 781039, India  
E-mail: bachu@iitg.ernet.in



### Introduction

The most common broad-spectrum reducing agents are metal hydrides like LiAlH<sub>4</sub>, NaBH<sub>4</sub>, DIBAL-H, and 9-BBN. Apart from this, some hydrogenation catalysts have been investigated in order to find conditions under which a given group will be reduced chemoselectively.<sup>1</sup> Metal-metal-salt binary systems such as Al–NiCl<sub>2</sub>·6H<sub>2</sub>O·THF,<sup>2</sup> Al–SbCl<sub>3</sub> or Zn–SbCl<sub>3</sub>,<sup>3</sup> Fe–NiCl<sub>2</sub>·6H<sub>2</sub>O·THF,<sup>4</sup> or Sm–

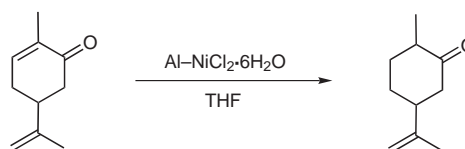
NiCl<sub>2</sub>·6H<sub>2</sub>O·THF<sup>5</sup> have long been used as reducing agents for many functional groups.

Reagents based on aluminum find wide application in organic synthesis.<sup>6</sup> The Al–NiCl<sub>2</sub>·6H<sub>2</sub>O system is a highlight in current organic chemistry due to its selectivity, mild reaction conditions, easy handling, low cost, and convenient isolation process.

### Abstracts

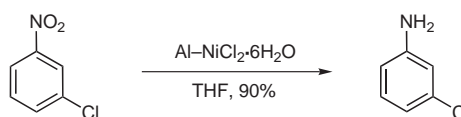
#### (A) Chemoselective reduction of $\alpha$ -enones:

$\alpha,\beta$ -Unsaturated carbonyl compounds give saturated ketones upon treatment with Al–NiCl<sub>2</sub>·6H<sub>2</sub>O. Aromatic aldehydes and ketones are smoothly reduced to the corresponding alcohols. Isolated double bonds, esters, aliphatic aldehydes, and ketones remain unaffected by this reagent.<sup>7</sup>



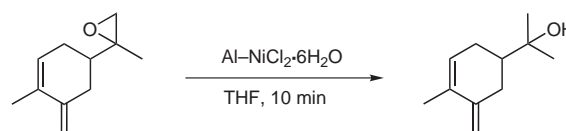
#### (B) Reduction of nitroarenes to amines:

Sarmah et al. showed that aromatic nitro compounds are reduced to the corresponding amines efficiently under neutral and mild conditions. Short reaction times and a simple work-up procedure make this a versatile reagent.<sup>8</sup>



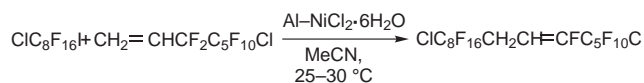
#### (C) Conversion of oxiranes into alcohols:

Ring opening of the oxiranes takes place from the less hindered side of the epoxides, thereby giving the highest-substituted alcohols. An exception is the case of styrene oxide, where 1-phenylethanol is the major product.  $\alpha,\beta$ -Epoxy ketones remain unaffected under these reaction conditions.<sup>2</sup>



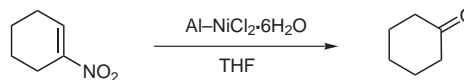
## (D) Addition to electron-deficient alkenes:

The Al–NiCl<sub>2</sub>·6H<sub>2</sub>O redox couple promotes the addition of per(poly)fluoroalkyl iodides to per(poly)fluoroalkyl-substituted ethenes, giving the corresponding addition–elimination products in moderate yields.<sup>9</sup>

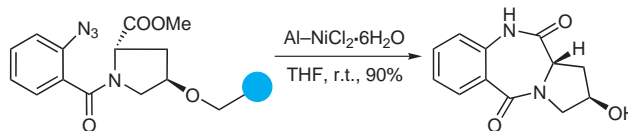


## (E) Conversion of nitroolefins into carbonyl compounds:

Saturated ketones can be obtained from nitroolefins in mild reaction conditions with Al–NiCl<sub>2</sub>·6H<sub>2</sub>O.<sup>10</sup>

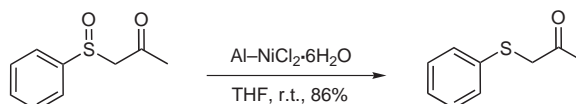


(F) Synthesis towards pyrrolo[2,1-c][1,4]benzodiazepines (PBD): Employing Al–NiCl<sub>2</sub>·6H<sub>2</sub>O, many heterocyclic compounds like PBDs and dilactams can be synthesized via solid-phase reductive cyclization of nitro and azido compounds.<sup>11</sup>



## (G) Facile reduction of sulfoxides to sulfides:

Sulfoxides can be reduced to the corresponding sulfides within short periods of time in high yields. Interestingly, ketones are not reduced under these reaction conditions.<sup>12</sup>



## References

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