

SYNLETT Spotlight 379

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

Lithium Naphthalenide

Compiled by Jian-Wu Gao

Jian-Wu Gao was born in Xingtai, Hebei Province (P. R. of China) in 1981. He graduated from Hebei Chemical and Pharmaceutical Vocational Technology College in 2002. Thereafter, he spent five years working at Pharmaron in Beijing, P. R. of China. Presently he is working towards his M.Sc. degree under the supervision of Professor Zhan-Hui Zhang at the Hebei Normal University. His current interests are the development of new methods for the synthesis of biologically active heterocyclic compounds.

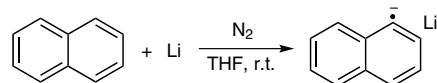
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Introduction

During the last three decades, the use of lithium naphthalenide (LN) as a reductant in organic synthesis has increased considerably. It has been used for the reductive cleavage of benzyl ethers,¹ *N,N,N',N'*-tetramethylphosphorodiamidates,² and chlorinated aryloxyalkanoic acids.³ It was found to be a useful reagent for the removal of sulfide and sulfone.⁴ In addition, LN-induced reductive decyanation,⁵ alkylation,⁶ and dehalogenation⁷ are also readily accomplished.

Lithium naphthalenide can be dissolved in ether, benzene, and tetrahydrofuran, and can be stored in solution up to several days. But it must be protected from air and moisture and can react with protic solvents and tetrahydrofuran at elevated temperatures.⁸ It can be conveniently prepared as a stable stock solution by mixing equal parts of freshly cut lithium metal and naphthalene in tetrahydrofuran at room temperature.⁹

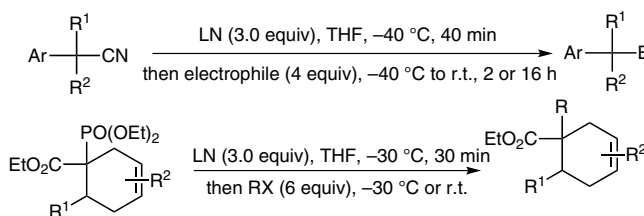


Scheme 1

Abstracts

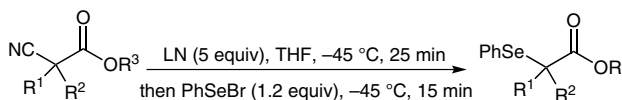
(A) Reductive Alkylations:

Tsao and co-workers reported that LN could induce reductive alkylation/addition reactions of aryl-, pyridyl-, and 2-thienyl-substituted dialkylacetonitriles. Upon treatment with LN in THF, both aryl and pyridyl precursors could undergo the reductive decyanation smoothly, and the in situ generated carbanions could be readily trapped by alkyl halides, ketones, aldehydes, or even oxygen to afford a wide range of highly substituted aromatic and heteroaromatic derivatives.¹⁰ Furthermore, the phosphono groups could also be easily removed by reduction with LN and in situ generated enolates could be readily trapped with a variety of alkylating agents to allow for the installation of an alkyl group to the quaternary carbon centers.¹¹



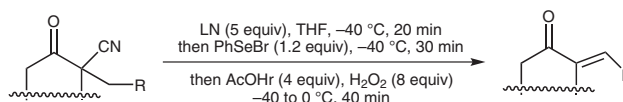
(B) Reductive α -Selenenylation of α,α -Dialkyl- α -cyanoacetates:

Ko and co-workers have found that α,α -dialkyl- α -cyanoacetates were readily reduced with LN to give the corresponding ester enolates, and the ester enolates could be readily trapped by phenylselenenyl bromide to obtain various highly substituted α -(phenylselenenyl)acetates.¹²

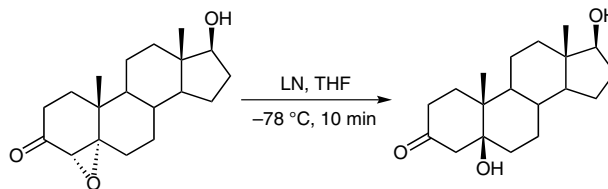


(C) *One-Pot Conversion of α -Cyanoacetates into α,β -Unsaturated Esters:*

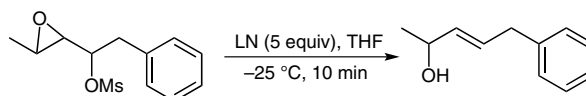
Zhu and co-workers have developed a highly efficient and completely regiocontrolled procedure for the synthesis of α -phenylseleno ketones starting from readily available α -cyano ketones making use of the LN-induced reductive selenenylation. Moreover, α -phenylseleno thus formed without isolation upon subsequent treatment with hydrogen peroxide and acetic acid, could be further converted into the corresponding α,β -unsaturated ketones with high regioselectivity.¹³

(D) *Reductive Cleavage of α,β -Epoxy Ketones:*

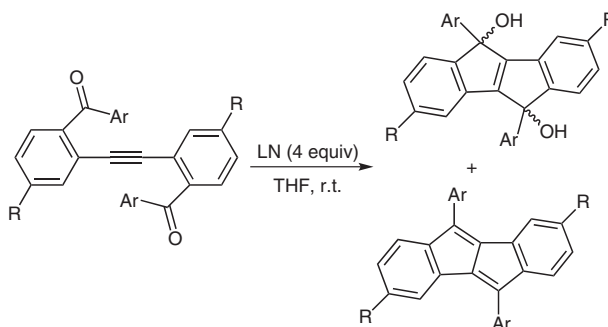
LN is also used as a mild and efficient reagent for the reductive of α,β -epoxy ketones to give the corresponding β -hydroxy ketones.¹⁴

(E) *Reductive Elimination of Epoxy Mesylates:*

Wu et al. have found that LN can serve as a mild reducing agent for reductive elimination of epoxy mesylates into the transpositioned allylic alcohol.¹⁵ The reaction conditions displayed a high tolerance for the substrate bearing a phenyl group.

(F) *Reductive Double Cyclization of Bis(arylcarbonyl)diphenylacetylenes:*

In addition to the above cases, LN can also be applied as a reductant for intramolecular reductive double cyclization of bis(arylcarbonyl)diphenylacetylenes. The reaction proceeded in THF at room temperature to produce the *trans* and *cis* isomers of hydroxymethylene-bridged stilbenes and dibenzo[*a,e*]pentalenes.¹⁶



References

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