**SYNLETT Spotlight 348**

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

**Lithium Bis(trimethylsilyl)amide**

Compiled by Yong-Hui Liu

Yong-Hui Liu was born in 1986 at Langfang, Hebei Province, P. R. of China. He graduated from the Xuchang University in 2009 and received his B.Sc. degree in Chemistry. Presently he is working as a postgraduate towards his M.Sc. under the supervision of Professor Zhan-Hui Zhang at the Hebei Normal University. His research interest is focused on the development of new synthetic methodologies of heterocyclic compounds.

The College of Chemistry & Material Science, Hebei Normal University, Shijiazhuang 050016, P. R. of China

E-mail: liu_yonghui1986@163.com

**Introduction**

Lithium bis(trimethylsilyl)amide (LiHMDS) is a colorless solid, which is soluble in a variety of organic solvents suitable for reactive compounds, such as organometallic substances or substituted metal amides. The compound melts at 71–72 °C.\(^1\) It is unstable in air and catches fire when compressed, but it is stable in an atmosphere of nitrogen. Reactions with a variety of nonmetallic halides give lithium halides and hexamethyldisilazyl derivatives.

**Abstracts**

(A) B. Li et al.\(^2\) reported an efficient and catalyst-free procedure for the synthesis of 2-[4-(4-cyanophenoxy)phenyl]-1H-indole-6-carboximidamide hydrochloride salt from 2-[4-(4-cyanophenoxy)phenyl] indole-6-carbonitrile by treatment with LiHMDS using THF as solvent at room temperature.

(B) A new method for preparing 2-lithio-(4\(^S\))-isopropyl-2-oxazolide from (4\(^S\))-isopropylloxazoline in THF using LiHMDS was developed. The product is isolated by deprotonation of (4\(^S\))-isopropyl oxazoline with LiHMDS followed by removal of the volatile materials.\(^3\)

(C) Petersen and co-workers\(^4\) reported that 1 was treated with LiHMDS in THF at room temperature to produce 2 in a yield of >90%. Under same conditions, only lower yield of 2 was obtained using pyridine, DBU, acetylide or KO\(_t\)-Bu.

(D) The preparation of the regioisomeric 3-amino-5-substituted-1,2,4-thiadiazoles can be attained by treatment of the 3-bromo-5-substituted-1,2,4-thiadiazoles with LiHMDS in THF.\(^5\)
LiHMDS has been employed in the preparation of enone 3 in two steps via deprotonating the acetate and NHCbz groups to induce a Dieckmann cyclization, followed by methylation with K$_2$CO$_3$/Me$_2$SO$_4$.

Ruediger et al. found that treatment of protected epoxide 4 with LiHMDS in THF at reflux temperature formed the allylic alcohol 5 exclusively. However, when 4 was treated with lithium di-n-propylamide the unexpected allylic alcohol 6 was obtained.

Lee et al. reported that 7 underwent cyclization by treatment with LiHMDS in THF to give 8.

A series of β-nitroalcohols can be converted into the corresponding nitroimines by the retro-nitroaldol–nitro-Mannich sequence of β-nitroalcohols with LiHMDS. In this reaction, LiHMDS behaved not only as base, but also as reactant.

LiHMDS behaved as a sterically hindered non-nucleophilic base in Pd/proazaphosphatrane ancillary ligand P(i-BuNCH$_2$CH$_2$)$_3$N-catalyzed aminations of arylhalide.

In addition to the above cases, LiHMDS can also be applied for the preparation of the bis(ethylene) complex (pypyrH)RhCl(C$_2$H$_4$)$_2$ by the treatment of (pypyrH)–RhCl(C$_2$H$_4$)$_2$ in benzene at ambient temperature.

References