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Lithium Bis(trimethylsilyl)amide

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

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.

The preparation of lithium bis(trimethylsilyl)amide must be performed in an atmosphere of dry nitrogen. The pentane containing *n*-butyllithium is added slowly to a stirred solution of hexamethyldisilazane (Scheme 1). The reaction mixture is boiled for 30 minutes, and evaporate the solvents. LiHMDS is obtained as colorless crystals.

Scheme 1

Abstracts

(A) B. Li et al.² reported an efficient and catalyst-free procedure for the synthesis of 2-[4-(4-cyanophenoxy)phenyl]-1*H*-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-oxazolidine 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-workers⁴ 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 *KOt*-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

(E) 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_2CO_3/Me_2SO_4 .⁶

(F) 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.⁷

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

(H) 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 reagent.⁹

(I) LiHMDS behaved as a sterically hindered non-nucleophilic base in Pd/proazaphosphatane ancillary ligand $P(i-BuNCH_2CH_2)_3N$ -catalyzed aminations of arylhalide.¹⁰

(J) In addition to the above cases, LiHMDS can also be applied for the preparation of the bis(ethylene) complex $(pypyrH)RhCl(C_2H_4)_2$ by the treatment of $(pypyrH)-RhCl(C_2H_4)_2$ in benzene at ambient temperature.¹¹

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