Lithium Bis(trimethylsilyl)amide

Compiled by Yong-Hui Liu

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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.

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\text{(TMS)}_2\text{NH} + n-\text{BuLi} \rightarrow \text{LiN(TMS)}_2 + n-\text{BuH}
\]

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-(4S)-isopropyl-2-oxazolidine from (4S)-isopropylpyrazoline in THF using LiHMDS was developed. The product is isolated by deprotonation of (4S)-isopropylpyrazoline 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.\(^5\)
(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 $\text{K}_2\text{CO}_3/\text{Me}_2\text{SO}_4$.\(^6\)

(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 $\beta$-nitroalcohols can be converted into the corresponding nitroimines by the retro-nitroaldol–nitro-Mannich sequence of $\beta$-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/proazaphosphatrane ancillary ligand $\text{P}(i\text{-BuNCH}_2\text{CH}_2)\text{N}$-catalyzed aminations of arylhalides.\(^10\)

(J) 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.\(^11\)

References