Synlett
Spotlight 348

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. 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. 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)-isopropylloxazoline in THF using LiHMDS was developed. The product is isolated by deprotonation of (4S)-isopropylloxazoline with LiHMDS followed by removal of the volatile materials.

(C) Petersen and co-workers 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 regiosomeric 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.
(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 K₂CO₃/Me₂SO₄.

(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.

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

(I) LiHMDS behaved as a sterically hindered non-nucleophilic base in Pd/proazaphosphatrane ancillary ligand P(i-BuNCH₂CH₂)₃N-catalyzed aminations of arylhalide.

(J) In addition to the above cases, LiHMDS can also be applied for the preparation of the bis(ethylene) complex (pypyrH)RhCl(C₂H₄)₂ by the treatment of (pypyrH)–RhCl(C₂H₄)₂ in benzene at ambient temperature.

References