

SYNLETT Spotlight 348

Lithium Bis(trimethylsilyl)amide

Compiled by Yong-Hui Liu

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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.

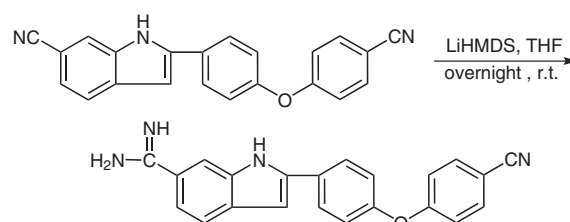
The preparation of lithium bis(trimethylsilyl)amide must be performed in an atmosphere of dry nitrogen. The pentane containing *n*-butyllithium is added slowly to a stirred solution of hexamethyldisilazane (Scheme 1). The reaction mixture is boiled for 30 minutes, and evaporate the solvents. LiHMDS is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



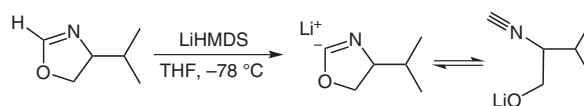
Scheme 1

Abstracts

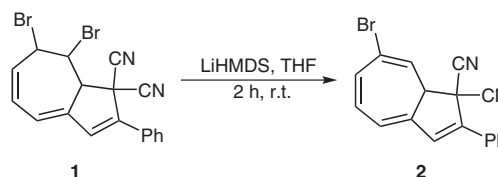
(A) B. Li et al.² reported an efficient and catalyst-free procedure for the synthesis of 2-[4-(4-cyanophenoxy)phenyl]-1*H*-indole-6-carboximidamide hydrochloride salt from 2-[4-(4-cyanophenoxy)phenyl]indole-6-carbonitrile by treatment with LiHMDS using THF as solvent at room temperature.



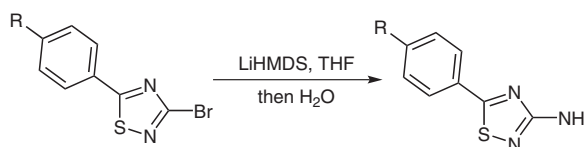
(B) A new method for preparing 2-lithio-(4*S*)-isopropyl-2-oxazoline from (4*S*)-isopropyl-2-oxazoline in THF using LiHMDS was developed. The product is isolated by deprotonation of (4*S*)-isopropyl-2-oxazoline with LiHMDS followed by removal of the volatile materials.³



(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



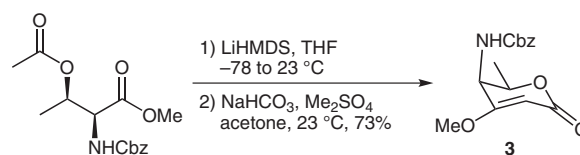
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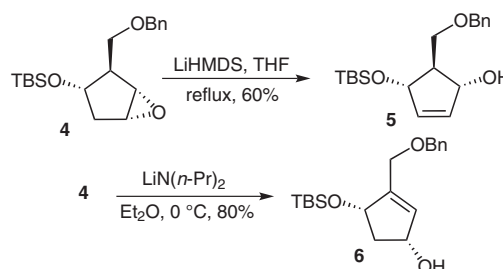
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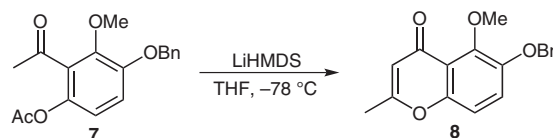
(E) LiHMDS has been employed in the preparation of enone **3** in two steps via deprotonating the acetate and NHCbz groups to induce a Dieckmann cyclization, followed by methylation with $\text{K}_2\text{CO}_3/\text{Me}_2\text{SO}_4$.⁶



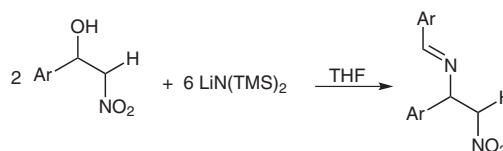
(F) Ruediger et al. found that treatment of protected epoxide **4** with LiHMDS in THF at reflux temperature formed the allylic alcohol **5** exclusively. However, when **4** was treated with lithium di-*n*-propylamide the unexpected allylic alcohol **6** was obtained.⁷



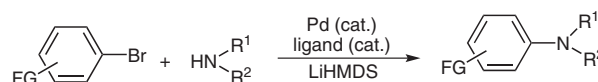
(G) Lee et al. reported that **7** underwent cyclization by treatment with LiHMDS in THF to give **8**.⁸



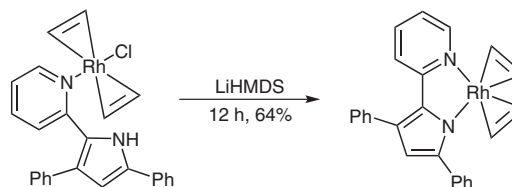
(H) A series of β -nitroalcohols can be converted into the corresponding nitroimines by the retro-nitroaldol–nitro-Mannich sequence of β -nitroalcohols with LiHMDS. In this reaction, LiHMDS behaved not only as base, but also as reagent.⁹



(I) LiHMDS behaved as a sterically hindered non-nucleophilic base in Pd/proazaphosphatrane ancillary ligand $\text{P}(i\text{-BuNCH}_2\text{CH}_2)_3\text{N}$ -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 $(\text{pypyrH})\text{RhCl}(\text{C}_2\text{H}_4)_2$ by the treatment of $(\text{pypyrH})\text{-RhCl}(\text{C}_2\text{H}_4)_2$ in benzene at ambient temperature.¹¹



References

- (1) Amonoo-Neizer, E. H.; Shaw, R. A.; Skovlin, D. O.; Smith, B. C. *Inorg. Synth.* **1966**, *8*, 19.
- (2) Li, B.; Pai, R.; Cardinale, S. C.; Butler, M. M.; Peet, N. P.; Moir, D. T.; Bavari, S.; Bowlin, T. L. *J. Med. Chem.* **2010**, *53*, 2264.
- (3) Baird, B.; Pawlikowski, A. V.; Su, J.; Wiench, J. W.; Pruski, M.; Sadow, A. D. *Inorg. Chem.* **2008**, *47*, 10208.
- (4) Petersen, M. Å.; Broman, S. L.; Kadziola, A.; Kilså, K.; Nielsen, M. B. *Eur. J. Org. Chem.* **2009**, 2733.
- (5) Wehn, P. M.; Harrington, P. E.; Eksterowicz, J. E. *Org. Lett.* **2009**, *11*, 5666.
- (6) Pragani, R.; Stallforth, P.; Seeberger, P. H. *Org. Lett.* **2010**, *12*, 1624.
- (7) Ruediger, E.; Martel, A.; Meanwell, N.; Solomon, C.; Turmel, B. *Tetrahedron Lett.* **2004**, *45*, 739.
- (8) Lee, C.; Lee, J. M.; Lee, N. R.; Kim, D. E.; Jeong, Y. J.; Chong, Y. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4538.
- (9) Tanaka, S.; Kochi, K.; Ito, H.; Mukawa, J.; Kishikawa, K.; Yamamoto, M.; Kohmoto, S. *Synth. Commun.* **2009**, *39*, 868.
- (10) Urganekar, S.; Verkade, J. G. *Adv. Synth. Catal.* **2004**, *346*, 611.
- (11) McBee, J. L.; Escalada, J.; Tilley, T. D. *J. Am. Chem. Soc.* **2009**, *131*, 12703.