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REVIEW ARTICLE

HMDS (Hexamethyldisilazane) in Organic Synthesis [2020 Onwards]

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Abstract: HMDS is renowned as a versatile organosilicon reagent for Michael-aldol processes and also as a silylation, amination, and amidation agent due to its strong silylating activity, gentle reaction conditions, and compatibility with a wide range of functional groups. But in heterocyclic chemistry, it also shows great promise. The breaking of the N-Si bond provides a convenient source of nitrogen (*e.g.,* in multicomponent reactions), and the trimethylsilane moiety can be engaged in the synthesis of heterocycles *via* multiple pathways (*e.g.,* as a cyclization promoter). HMDS has been widely used in a variety of fields, including organic synthesis, electrochemistry, film preparation, photolithography, and coating processes. HMDS is also a useful reagent for dehydration and ammonolysis in the synthesis of amides, imides, and nitrogen-containing heterocycles. In the pharmaceutical and fine chemical industries, HMDS improves reaction selectivity, increases product yields, and simplifies purification processes. Additionally, its use in catalyst-assisted transformations and microwave-assisted organic reactions has improved its utility in modern green and sustainable chemistry strategies. Its volatility and ease of removal have also contributed to its relevance for lab- and industrial-scale synthesis. Though HMDS has benefits, it is moisture-sensitive, combustible, and requires safety precautions. Overall, HMDS is a crucial reagent in modern organic synthesis, finding extensive use in the synthesis of intricate organic compounds and sophisticated functional materials. In this mini-review, representative applications of HMDS in organic synthesis are critically and comprehensively reviewed from 2020 forward to date with mechanistic insights. The merits and demerits of specific HMDS-mediated synthetic organic transformations are also discussed.

Keywords: HMDS (Hexamethyldisilazane), carbon-carbon bond formations, carbon-heteroatom bond formations, heteroatom-heteroatom bond formations, cyclization, silylation, amination and deprotection.

1. INTRODUCTION

Bis(trimethylsilyl)amine, also called hexamethyldisilazane, HMDS, is an organosilicon chemical with molecular formula [(CH3)3Si]2NH (**I**, Fig. **1**) [1]. The molecule is a derivative of ammonia with two hydrogen atoms substituted by trimethylsilyl groups. An electron diffraction investigation demonstrates that the silicon-nitrogen bond length (173.5 pm) and Si-N-Si bond angle (125.5o) are identical to those in disilazane (where methyl groups are substituted by hydrogen atoms), indicating that steric considerations are not a factor in regulating angles in this situation [2]. This colourless liquid is a reagent and a precursor to bases widely used in organic synthesis and organometallic chemistry. HMDS is an inexpensive, stable, and versatile reagent in chemical synthesis. It is primarily used for the efficient, moderate trimethylsilylation of hydroxyl, amino, and thiol compounds, often yielding ammonia as the only by-product [3]. Although HMDS has poor reactivity and therefore conventionally requires high temperatures, it is now routinely activated by catalysts such as iodine or acidic silica to enable rapid, high-yield reactions.

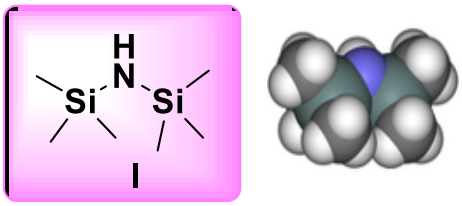


Fig. (1). Structure of Hexamethyldisilazane (HMDS)(**I**). *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

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