

SYNLETT Spotlight 350

Hexamethyldisilazane

Compiled by Xiang Deng^{a,b}



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

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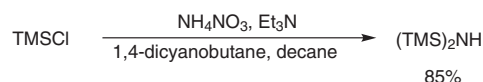
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Introduction

Hexamethyldisilazane (HMDS) is a colorless liquid with an ammonia odor. It is a versatile silylating agent, which can react with alcohols, acids, amines, thiols, phenols, amides, thioamides, sulfonamides, and enolizable ketones. Ammonia, the by-product of the reaction, can be readily removed from the reaction medium. In the past few years, applications of hexamethyldisilazane have been quite extensive, especially in the field of organic synthesis, manufactures of medicines and industry. Hexamethyldisilazane is used as valuable raw material for antisclerotic and antineoplastic drugs as well as synthetic

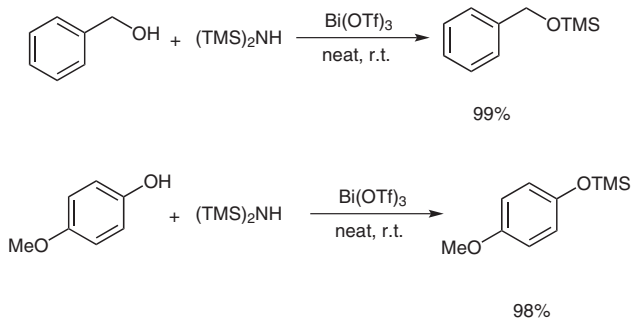
antibiotics, such as amikacin, ftorafur, parmidin, penicillin, etc. It is usually used as a surface treatment agent for diatomite, silica, and titanium powder. Further, it is used as a cohesive aid for light-etching agents in semiconductor industry. It can be used in prime treatment for hard-coatings on plastics and in the syntheses of cross-linked resins. In general, hexamethyldisilazane is commercially available and can also be easily prepared according to the reported procedures¹ (Scheme 1).



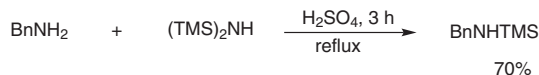
Scheme 1

Abstract

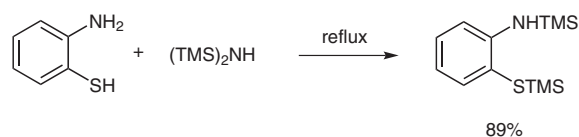
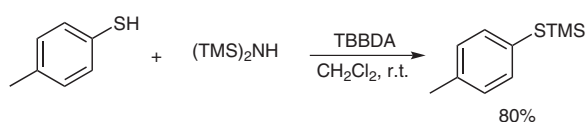
(A) Hexamethyldisilazane, as an inexpensive and easy available compound, has been used for the preparation of trimethylsilyl ethers from hydroxyl compounds. The main drawback is its poor silylating power, which needs forceful condition and long reaction time. A variety of catalysts have been reported for the activation of HMDS in the literature. Kadam and Kim have demonstrated that Bi(OTf)₃ is a highly efficient chemoselective catalyst for silylation of alcohols and phenols under solvent-free conditions.²



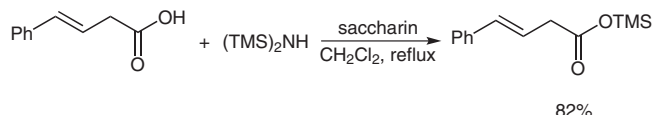
(B) As an efficient silylating reagent, hexamethyldisilazane can also react with amines to synthesize a series of silylating compounds. The (trimethylsilyl)phenethylamine compounds were prepared from starting phenethylamine with hexamethyldisilazane in the presence of a catalytic amount of sulfuric acid in good yields (70%).³



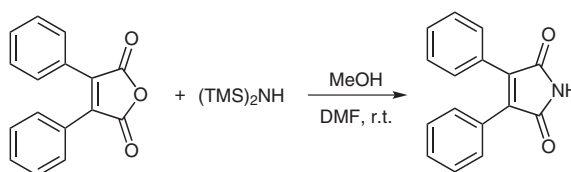
(C) Ghorbani-Vaghei et al.^{4a} described a new method for the silylation of thiols with hexamethyldisilazane in the presence *N,N,N',N'*-tetrabromobenzene-1,3-disulfonamide (TBBDA) to give the corresponding trimethylsilyl sulfides in good yields. Risto et al. reported that both amine and thiol groups of 2-aminothiophenol could be converted simultaneously into the corresponding silylation groups by using hexamethyldisilazane.^{4b}



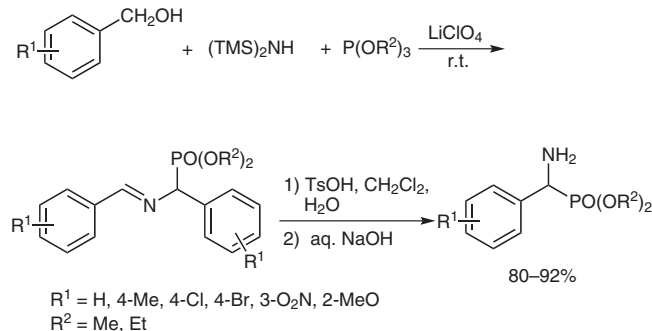
(D) (*E*)-Trimethylsilyl-4-phenyl-3-butenic acid was successfully synthesized from (*E*)-4-phenyl-3-butenic acid by reaction with hexamethyldisilazane in the presence of a catalytic amount of saccharin.⁵



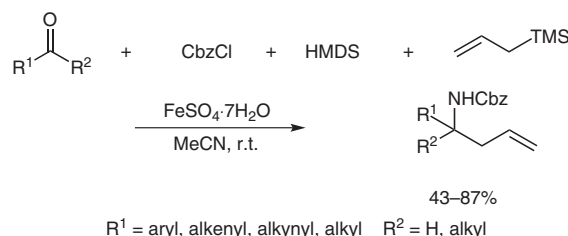
(E) Hexamethyldisilazane acts as a nitrogen source in the synthesis of heterocycles. Moon and co-workers⁶ have reported that 1*H*-furan-2,5-dione was easily converted into 1*H*-pyrrole-2,5-dione after treatment with hexamethyldisilazane.



(F) Azzi et al.⁷ have successfully extended the use of HMDS as a source of ammonia for the one-pot synthesis of α -amino phosphonates in high yields under solvent-free conditions mediated by solid LiClO₄. The present procedure provides a novel, very mild and green methodology for the preparation of primary α -amino phosphonates under neutral reaction conditions.



(G) Song et al.⁸ reported an efficient catalytic four-component reaction of carbonyl compounds, benzyl chloroformate (CbzCl), HMDS, and allyltrimethylsilane to produce Cbz-protected homoallylic amines in the presence of iron(II) sulfate heptahydrate, an inexpensive and environmentally friendly catalyst. This protocol not only presents a novel four-component synthesis of Cbz-protected homoallylic amines, but also adds a synthetically useful entry into the catalysis with iron(II) salts.



References

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