

SYNLETT Spotlight 385

Hexamethyldisilane

Compiled by Audrey Giros



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

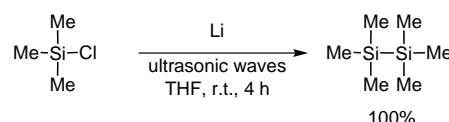
Audrey Giros was born in 1984 in Conflans Ste Honorine, France. She graduated from the National Polytechnic School of Chemical Engineering and Technology of Toulouse in 2009 and received in the same year her M.Sc. degree in organic chemistry. She is currently working under the supervision of Dr. Luis Blanco and Dr. Sandrine Deloisy. Her Ph.D. research project focuses on organosilicon chemistry for the total synthesis of a sila-analogue of testosterone. She is developing methodologies for the synthesis of a silicon-silicon bond-containing molecules and their use in various reactions such as functionalization or cyclization.

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Introduction

Hexamethyldisilane ($\text{Me}_3\text{SiSiMe}_3$, CAS: 1450-14-2) is a hygroscopic colorless and odorless liquid which absorbs in the far UV region.¹ In organic chemistry it is often used as an alternative of chlorotrimethylsilane or hexamethyldisilazane silylating agents. Hexamethyldisilane also promotes reduction and can act as a co-catalyst. It was recently revealed to be a key reagent in the anomerization of carbohydrates. Additionally, hexamethyldisilane can be a valuable starting material for the synthesis of sila-substituted organic and biologically active molecules. In

the semiconductor industry this oligoorganosilane is employed as a precursor in the Chemical Vapor Deposition process.² Hexamethyldisilane is commercially available, but it can be easily synthesized by reaction of chlorotrimethylsilane with an alkali metal in organic solvents (Scheme 1).³ This method is particularly efficient and cheap.⁴

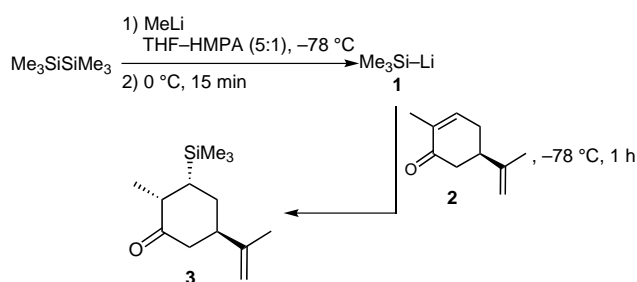


Scheme 1 Efficient preparation of hexamethyldisilane in laboratory

Abstracts

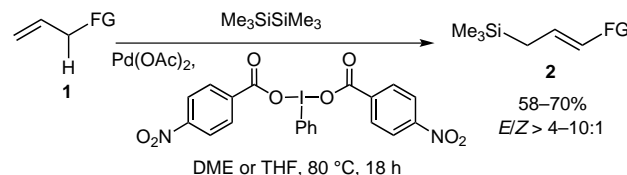
(A) Hexamethyldisilane as a Source of Trimethylsilylanion:

In the stereoselective synthesis of 3-trimethylsilyldihydrocarvone developed by Blay et al., hexamethyldisilane is used as a precursor of the nucleophilic species **1**.⁵ The Michael addition of Me_3SiLi on (*R*)-(-)-carvone **2** proceeds in a very high yield (91%). This optimized procedure for the cleavage of a Si-Si bond is carried out under inert atmosphere, using hexamethylphosphoric triamide (HMPA) in a specific proportion with three temperature ranges.⁶



(B) New C-C and C-Bond Activation:

Rhodium-catalyzed silylation of the C-CN bond from aryl nitriles⁷ and palladium-catalyzed allylic C-H silylation⁸ have been performed with hexamethyldisilane assistance. From the allylic substrates **1**, excellent regio- and good stereoselectivities were observed with a high level of functional group tolerance.



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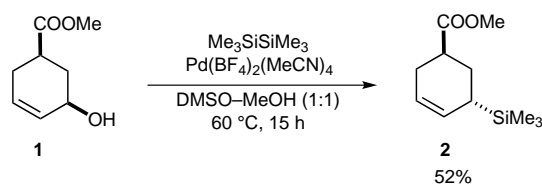
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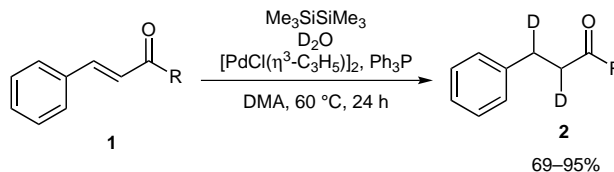
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(C) *A Useful Allylic C–OH Activation:*

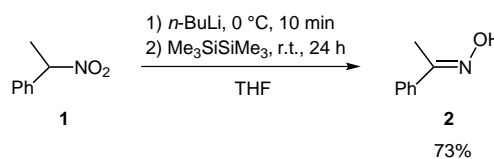
Szabó and co-workers described an inexpensive procedure for the regioselective synthesis of allylsilanes from allylic alcohols under palladium catalysis.⁹ With hexamethyldisilane, the silylation proceeds smoothly under mild conditions (50–60 °C, without an inert atmosphere, no addition of acid or additive). Diverse functional groups (hydroxy-, methoxy- and nitrophenyl, ether and ester) and cyclic scaffolds like **1** are tolerated.

(D) *Hexamethyldisilane as Co-Catalyst:*

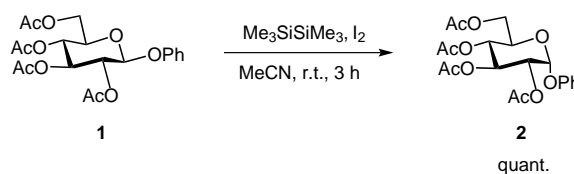
Hexamethyldisilane promotes reduction of alkynes¹⁰ and enones **1**,¹¹ desulfonation¹² and Mizoroki–Heck-type coupling of aryl nitriles to vinylsilanes.¹³ In these metal-catalyzed reactions, the disilane acts as a co-catalyst in generating the active catalytic species or by regenerating palladium or rhodium catalysts.

(E) *Hexamethyldisilane as a Reducing Agent:*

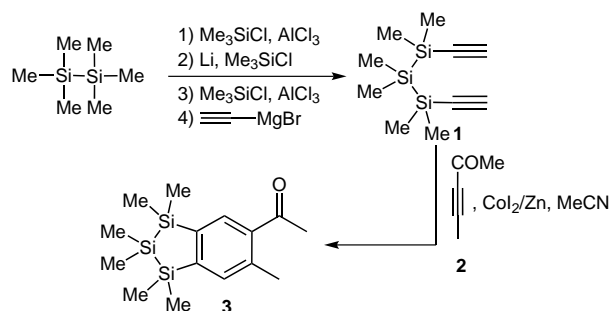
Under mild conditions nitroalkanes can be mono-deoxygenated to ketoximes by treatment of the corresponding nitronate anions with hexamethyldisilane.¹⁴ The cleaved disilane reacts as a ‘counterattack reagent’ by successive nucleophilic attacks of the resulting Me_3Si^- and Me_2SiO^- species. Bis(trimethylsilyl)ether is generated as side product. For instance, *N*-(phenylethylidene)hydroxylamine **2** is formed in good yield (73%).

(F) *Hexamethyldisilane/I₂ as a Precursor of TMSI:*

Malik et al. demonstrated that the hexamethyldisilane–iodine system mediated the anomerization of alkyl glycoside in quantitative yield.¹⁵ Indeed the in situ formation of Me_3SiI species leads to the anomerization step by ring opening of a silylated carbohydrate intermediate.

(G) *Hexamethyldisilane as a Silicon Backbone:*

Starting from hexamethyldisilane, Tacke and co-workers build silicon analogues of biologically active molecules.¹⁶ The odorant 1,2,3-trisilaindane **3** is synthesized via a multistep procedure including two chlorodemethylation steps to prepare a dichlorotrisilane intermediate. Subsequent nucleophilic substitutions with ethynylmagnesium bromide lead to a trisiladiyne **1** which is engaged in a cobalt-catalyzed cycloaddition with the pent-3-yn-2-one **2**. It is noteworthy the trisila-phantolide derivative **3** displays a creamy-lactonic odor in contrast with the musk odor of its carbon analogue.



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