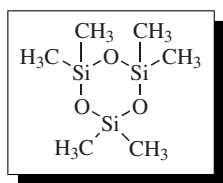


Hexamethylcyclotrisiloxane



[541-05-9]

C₆H₁₈O₃Si₃

(MW 222.46)

(reagent for the preparation of dimethylsilanols,¹ trapping of in-situ-generated silanones,² silylenes,³ silyl azides,⁴ silanethiones,⁵ and derivatives)

Physical Data: mp 64–64.5 °C; bp 133–134 °C.

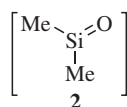
Solubility: soluble in most organic solvents.

Form Supplied in: white, crystalline solid.

Purification: sublimation: 55 °C at 55 mmHg.

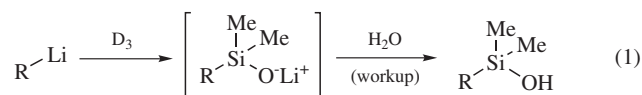
Handling, Storage, and Precautions: hexamethylcyclotrisiloxane is a stable, crystalline solid that can be stored in a bottle without precaution for air and moisture exposure.

Introduction. Hexamethylcyclotrisiloxane, (**1**), (D₃) is the simplest member of a series of cyclic oligodimethylsiloxanes, primarily used as synthetic equivalents for the reactive intermediate dimethylsilanone (**2**). This characteristic is responsible for its extensive application in polymer chemistry.⁶ However, its use in synthetic chemistry can be traced to a 1970 report in which Lee and co-workers attempted to induce the anionic polymerization of D₃ with *n*-butyllithium¹. To their surprise, rather than the expected⁷ PDMS (polydimethylsilicone) polymer, they obtained an 82% yield of *n*-butyldimethylsilanol. This reaction has been shown to be general for alkyl-, alkenyl-, aryl-, and heteroaryl-lithium reagents, resulting in the production of many organic dimethylsilanols. Hexamethylcyclotrisiloxane has also been exploited as an efficient trapping reagent for a variety of short-lived intermediates, including silanones and silyenes. The ability of D₃ to intercept these reactive species has been attributed to its rigid, planar structure,⁸ and the resultant release of strain from ring expansion.



Preparation of Substituted Dimethylsilanols: General Considerations. In 1993, Sieburth and co-workers reported the preparation and use of dimethyl- and diphenylsilanols as coordinating, directing groups for the lithiation of adjacent aryl C–H bonds.⁹ Since that time, the use of silanols has increased dramatically, with applications ranging from coordination chemistry to natural product synthesis.^{10–12} Considering the increased awareness of silanols, together with the facility of their preparation, there are remarkably few substituted dimethylsilanols reported as reagents in organic synthesis. Despite their limited number, the utility of dimethylsilanols as synthetic reagents has increased because of their role as effective donors in the palladium-catalyzed, cross-coupling reactions with aryl- and alkenyl halides and

pseudohalides.¹³ Many of the organodimethylsilanols used for this process have been prepared from the combination of D_3 with organolithium reagents to afford substituted dimethylsilanols in good to excellent yields (eq 1). There are no examples in the literature describing the combination of other organometallic species, such as Grignard reagents, with D_3 to provide dimethylsilanols. However, Sieburth and co-workers describe the reaction of *n*-butylmagnesium bromide with hexaphenylcyclotrisiloxane to provide *n*-butyldiphenylsilanol in 27% yield.¹⁴ In comparison, the combination of *n*-butyllithium and hexaphenylcyclotrisiloxane under the same conditions afforded the 91% yield of the desired silanol product.

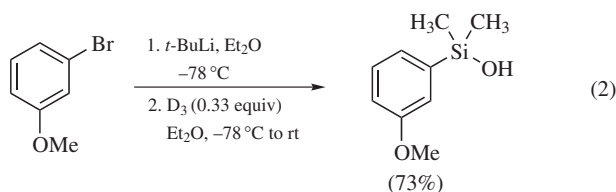


R = 1° alkyl-, alkenyl-,
alkynyl-, aryl-, heteroaryl-

Although D_3 is less reactive than other silicon electrophiles, such as dichlorodimethylsilane and chlorodimethylsilane, it is more useful because it affords fewer by-products and is less prone to undesirable reaction pathways. One of the major problems associated with the preparation and isolation of silanols is their tendency to dehydratively dimerize to form disiloxanes.¹⁵ This dimerization has been shown to be rapid under either strongly basic or acidic conditions.¹⁶ Hydrolysis of the chlorosilane resulting from the reaction of an organolithium reagent with dichlorodimethylsilane generates significant amounts of HCl and therefore requires careful monitoring of the pH of the reaction solution to prevent disiloxane formation. In contrast, the neutralization of the lithium silanolate generated in the reaction with D_3 is less problematic. Another advantage of D_3 is the selective formation of the organodimethylsilanol whereas with, e.g., chlorodimethylsilane or dimethyldichlorosilane, double addition to provide a tetraorganosilane is a common problem.¹⁷

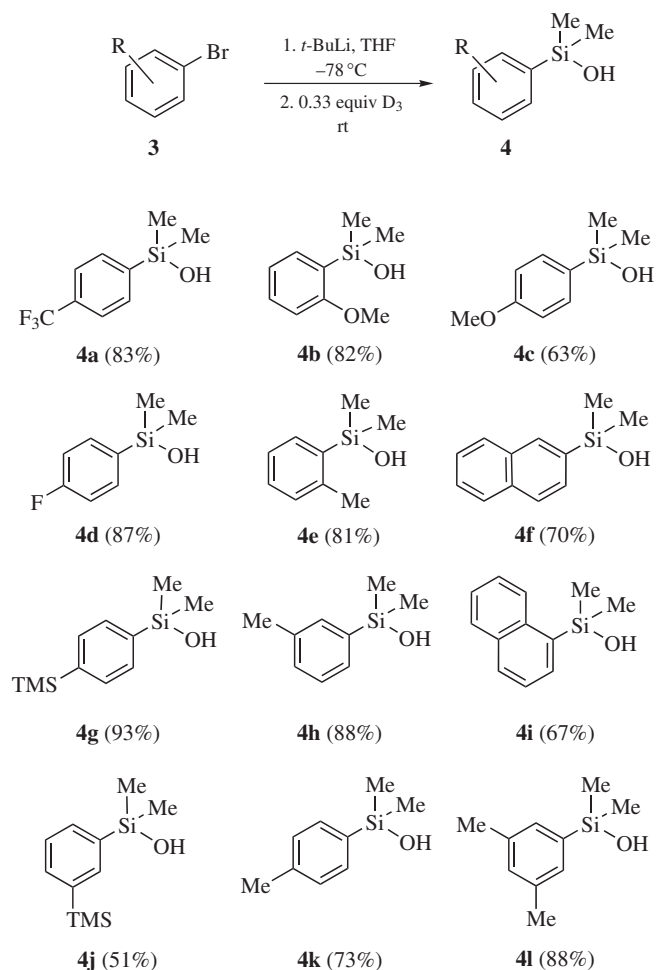
Organolithium Reagents from Halogen-metal Exchange.

Although the reaction of polydimethylsiloxane and methyl lithium to provide lithium trimethylsilanolate had been known for some time,¹⁸ Lee and co-workers were the first to use a defined cyclic dimethylsiloxane, D_3 , with *n*-butyllithium to prepare *n*-butyldimethylsilanol.¹ Later, Sieburth combined D_3 with an aryllithium reagent, generated by lithium-halogen exchange, to prepare an aryldimethylsilanol (eq 2).⁹ In each of these reactions the 3/1 stoichiometry of the organolithium reagent to D_3 is used as all three dimethylsilanone units are available.



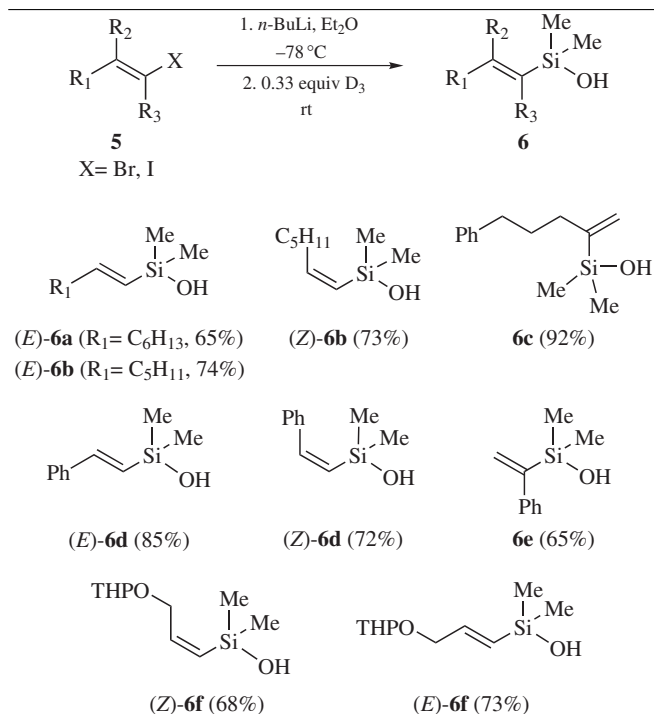
Many different aryldimethylsilanols have been prepared from the corresponding aryl bromides. Electron-poor (**4a**, **d**), electron-rich (**4b**, **e**), and moderately encumbered (**4e**, **i**, **l**) aryl bromides are excellent substrates for the silanol preparation (Scheme 1).^{19–22} Trimethylsilyl-substituted aryl bromides are also competent and

provide dimethylsilanols **4g** and **4j**. These aryldimethylsilanols are useful as donors in the palladium-catalyzed Heck-type²⁰ and cross-coupling reactions.^{19,21}



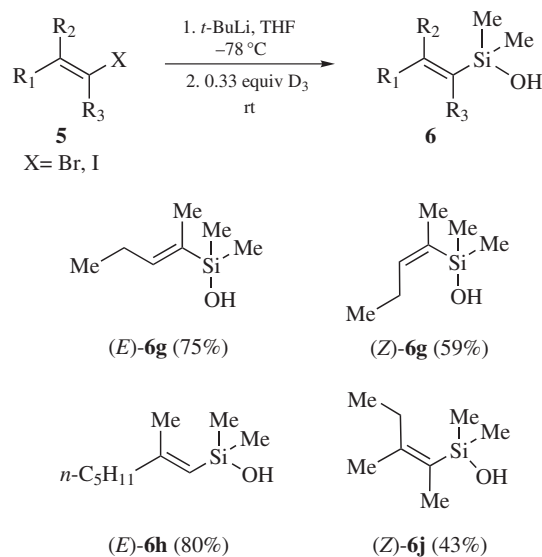
Scheme 1 Substituted aryldimethylsilanols

Similarly, alkenyllithium reagents derived from lithium-halogen exchange of the corresponding bromides react with D₃ to provide alkenylsilanols in good to excellent yields. Geometrically defined, 1-alkenyldimethylsilanols (Scheme 2, **6a, b**)^{23–25} have been prepared, as well as the *E*- and *Z*- β -styrylsilanols (**6d**).^{23,26} In addition, the dimethylsilanol can be installed in the 2-position of the alkene (**6c, e**).^{23,27} Alkenyldimethylsilanols incorporating heteroatom functionality are prepared in comparable yields (**6f**).²⁵



Scheme 2 Simple alkenyldimethylsilanols

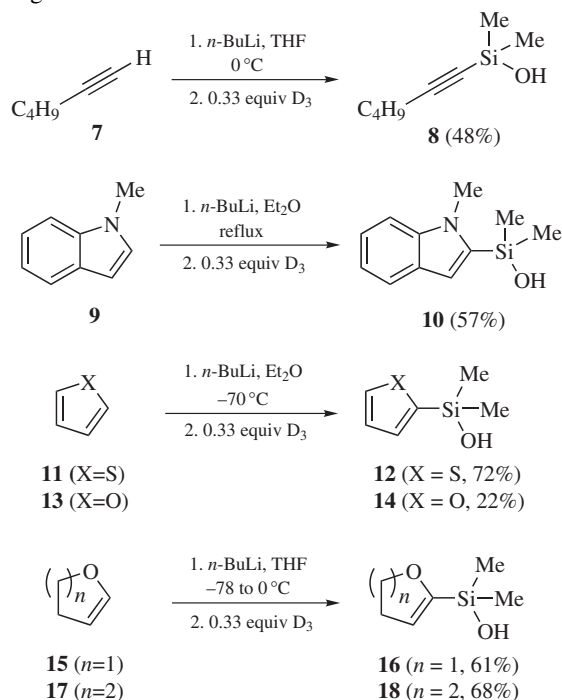
A series of tri- and tetrasubstituted alkenyl dimethylsilanols were prepared to study the substituent effects on the stereochemical outcome of a subsequent cross-coupling reaction.²⁸ The products were obtained in high geometrical purity by the combination of D_3 and the geometrically defined alkenyllithium reagents generated by bromine–lithium exchange with *t*-butyllithium (Scheme 3).



Scheme 3 Highly substituted alkenyldimethylsilanols

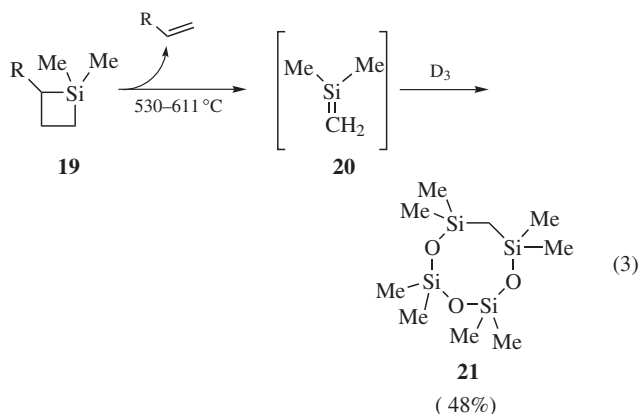
Organolithium Reagents from Direct Deprotonation. Organolithium reagents prepared via lithium–halogen exchange require either installation of the halide or commercially available, halogenated substrates. Alternatively, substrates that can be deprotonated directly with reliable site selectivity provide organolithium reagents that have also been used in combination with

D₃ to provide dimethylsilanols. Such carbon acidic substrates include alkynes²³ and heterocycles, which have produced the corresponding dimethylsilanols in good yields (Scheme 4).^{23,29,30} The preparation and use of indolyl-2-dimethylsilanol (**10**) is noteworthy because it is considerably more stable than the corresponding boronic acid.²⁹

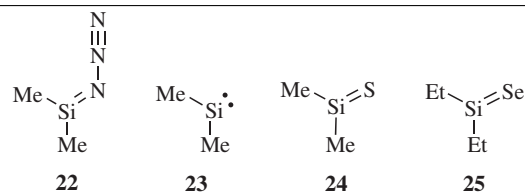


Scheme 4 Substituted dimethylsilanols derived from direct lithiation

Miscellaneous Reactions. Highly reactive silicon intermediates, such as dimethylsilanone and dimethylsilylene can be trapped with D₃. The facility with which D₃ intercepts such reactive intermediates is ascribed to the relief of strain in the planar cyclotrisiloxane ring. Upon insertion of a silylene or silanone, the ring expands from six- to eight-membered and alleviates the nonbonding interactions among the methyl groups. For example, the thermolysis of silacyclobutanes such as **19** generates a dimethylsilylene (**20**) that can be trapped with D₃ to form silacycle **21**, which is expanded by one Si–C unit (eq 3).³



Similarly, dimethylsilyl azide (**22**),⁴ dimethylsilene (**23**),³¹ dimethylsilanethione (**24**),⁵ and diethylsilaslanone (**25**)³² have also been trapped using D₃ (Scheme 5).



Scheme 5 Highly reactive unsaturated silicon species

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Scott E. Denmark & Christopher R. Butler
University of Illinois, Urbana, IL, USA