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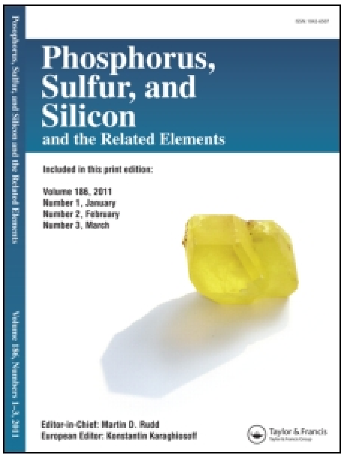

## Phosphorus, Sulfur, and Silicon and the Related Elements

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# HMDST as Useful Tool in Organic Synthesis: A Further Step in the Delivery of Sulfur Functionalities

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# HMDST as Useful Tool in Organic Synthesis: A Further Step in the Delivery of Sulfur Functionalities

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*Bis(trimethylsilyl)sulfide (HMDST) was demostrated to be a very efficient reagent in the delivery of sulfur functionalities, allowing us to synthesize a wide range of thiocarbonyl compounds. The most reactive derivatives were trapped with suitable dienes, leading to the synthesis of different heterocyclic molecules with an high degree of chemo- and regioselectivity. Recently, the mildness of this methodology also allowed us to obtain particularly reactive thiooxocompounds, such as thioformylsilanes, $\alpha,\beta$-unsaturated thioaldehydes, thioketones, thioacylsilanes, and thioacylstannanes.*

**Keywords** Cycloadditions; heterocycles; silyl sulfides; thiocarbonyl componds

## INTRODUCTION

Organic sulfur compounds represent an important class of molecules, because they are able to participate in many chemical and biological processes. Moreover, in the past years, the chemistry of organic derivatives containing both a sulfur and a silicon moiety has grown because of the particular reactivity of such functionalities.[1]

In fact, silyl sulfides, formally similar to thiols, are able to show a particular reactive behavior and are useful intermediates in searching for alternative strategies and for the development of novel sulfurated molecules, the outcome of the process being related to the structure of the silyl sulfide used.

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## RESULTS AND DISCUSSION

In this vein, in the past several years we have been interested in the reactivity of a particular silyl sulfide, bis(trimethylsilyl)sulfide (hexamethyldisilathiane, HMDST), which has been demonstrated to be a versatile reagent in the delivery of sulfur functionalities onto organic molecules.[2]

In particular, hexamethyldisilathiane is able to afford, through a direct thionation of a wide series of carbonyl compounds, the corresponding thiooxoderivatives.

Treatment in fact of acylsilanes[3] (or their benzotriazole derivatives), aldehydes,[4] and ketones[5] of different nature with HMDST and a suitable catalyst ($CoCl_2$ or TfOTMS) obtained the related thiocarbonyl compounds, with a high degree of chemo- and stereoselectivity,[4] depending on the nature of the catalyst and on the amount of HMDST used.

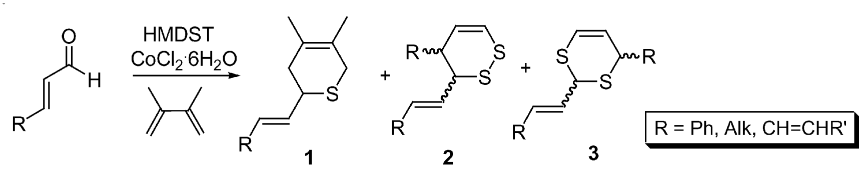
The versatility and the mildness of the HMDST-based thionation procedure has been evidenced by obtaining labile classes of thiocarbonyl compounds, such as monomeric aminothioaldehydes of furan, benzofuran, thiophene, and benzothiophene,[6] and azido-thioaldehydes.[7]

Depending on the reaction conditions, a fine-tuning of the reactivity of HMDST with azido-aldehydes made it possible to achieve a selective reduction of $-N_3$ moiety to amino group,[8] to afford amines without any reaction of the formyl group or in the presence of a suitable catalyst, such as HCl, the azido group itself can act as efficient trapping agent, thus leading to different fused isothiazole ring systems.[9]

More recently, bis(trimethylsilyl)sulfide was demonstrated to be able to obtain particularly reactive thiocarbonyl derivatives, such as thioformylsilanes[10] and $\alpha,\beta$-acetylenic thiooxocompounds.[11]

In this context, a deeper investigation recently led to the synthesis of $\alpha,\beta$-ethylenic thiocarbonyls: treatment of several $\beta$-substituted $\alpha,\beta$-unsaturated aldehydes with HMDST in the presence of $CoCl_2{\cdot}6H_2O$ and 2,3-dimethylbutadiene as trapping agent afforded the expected 3,6-dihydro-2*H*-thiopyran cycloadducts **1**, together with variable amounts of products arising from self-dimerization of the so-formed $\alpha,\beta$-ethylenic thioaldehydes (Scheme 1). These compounds, for their peculiar structure, can behave as heterodienes and heterodienophiles in Diels–Alder cycloadditions, thus affording regioisomeric 1,2- (**2**) and 1,3-dithiins (**3**), formed respectively through a head-to-head and a head-to-tail cycloaddition, as a mixture of *cis* and *trans* stereoisomers.

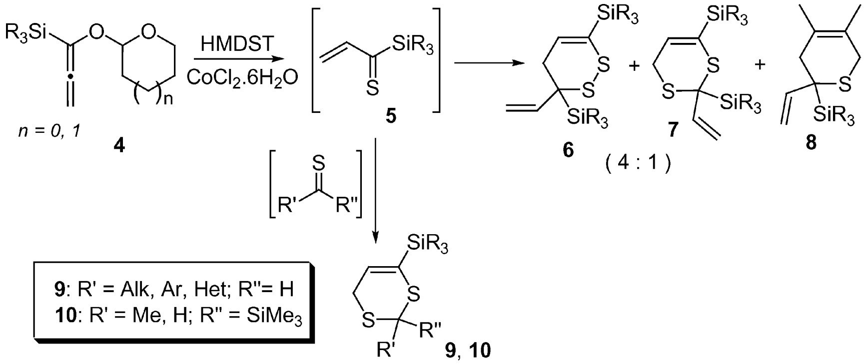
As already observed in the synthesis of $\alpha,\beta$-acetylenic thiooxoderivatives, $\beta$-protection was necessary in order to avoid conjugated addition of HMDST on the enonic framework.



**SCHEME 1**

As far as thioacylsilanes can be considered synthetic equivalents of thioladehydes, we wondered whether the described methodology could also be used for obtaining $\alpha,\beta$-ethylenic thioacylsilanes. Direct treatment of the parent propenoylsilanes with HMDST, under catalytic conditions, showed again the aforementioned 1,4-addition on the unsaturated system.

Thus we had to devise different access to such molecules, and, as far as propenoylsilanes are obtained from allenes, we performed the reaction on the silylated allenes **4** with HMDST and 2,3-dimethylbutadiene, and indeed in these conditions we were able to synthesize thiopropenoylsilanes **5** as silylated 1,2- (**6**) and 1,3-dithiins (**7**), arising from a self-dimerization process (Scheme 2).[12]



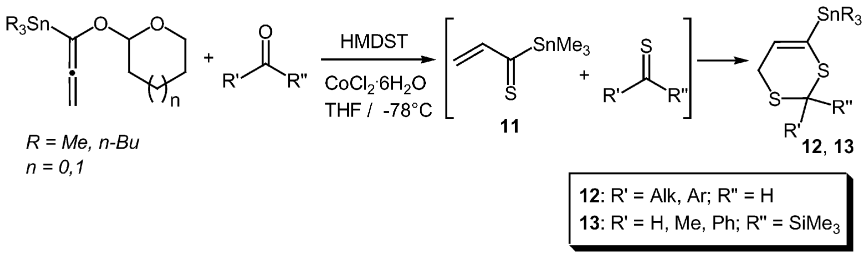
**SCHEME 2**

It is interesting to note that, as opposed to $\alpha,\beta$-unsaturated thioaldehydes, the presence of the silyl group decreases the formation of the adduct **8** with the diene (<5%), and the cycloaddition showed a high degree of regioselectivity, with 1,2-dithiins formed predominantly, thus evidencing the importance of the silyl moiety in driving the regiochemical outcome of the reaction. It should be noted that cycloaddition the related thioacrolein afforded 1,3-dithiin as the predominant isomer.[13]

Furthermore, the so-generated thiopropenoylsilanes behave also as very reactive heterodienes, being able to trap *in situ* generated thioacylsilanes and thioaldehydes (Scheme 2),[14] including aliphatic thioaldehydes, compounds that are known to be rather reluctant to act as heterodienophiles under catalytic conditions.[15]

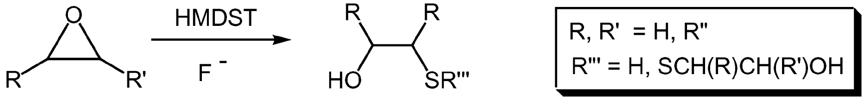
It is worthwhile noting that this result represents the first example of cycloaddition of two different thiooxo compounds, and that in all these reactions a regiochemical control was achieved, in that the 1,3-adduct (**9**, **10**) (the major regioisomer) formed and no trace of 1,2-isomer was evidenced in the crude reaction mixtures. An exception is the reaction of thiobenzaldehyde, in which variable amounts of 6-phenyl-3-silyl-1,2-dithiin isomer has been recovered from the reaction mixtures.

Very recently, HMDST has also been shown able to afford for the first time the synthesis of a new class of thiocarbonyl compounds, like thiopropenoylstannanes **11**, an unexplored series of stannylated derivatives capable of acting as very efficient thiabutadienes with *in situ* generated thioaldehydes and thioacylsilanes of different nature, leading to novel and interesting class of 1,3-dithiin systems **12** and **13**.[16]



**SCHEME 3**

Finally, as a further proof of the versatility of hexamethyldisilathiane, its reaction with different epoxides afforded a mild and regioselective ring opening of such small ring heterocycles, allowing us to obtain substituted $\beta$-hydroxy thiols or disulfides, depending on the reactional conditions (Scheme 4).



**SCHEME 4**

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