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Synthesis of new silylated sulfur-containing heterocycles through thionation of bis(acylsilanes)

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Abstract—The thionation of bis(acylsilanes) with spacers of variable size with hexamethyldisilathiane under cobalt(II) chloride or trimethylsilyl triflate catalysis affords 2,5-bis(trialkylsilyl)-thiophenes, 2,6-bis(trialkylsilyl)-4*H*-thiopyrans and 2,7-bis(trialkylsilyl)-4,5-dihydrothiepine generally along with a minor amount of the corresponding oxo analogue. The synthesis of both symmetrical and unsymmetrical bis(trialkylsilyl) derivatives was achieved.

Acylsilanes are well known compounds that have been shown to be useful intermediates in synthetic organic chemistry.[1] They participate in regio- and stereoselective processes that allow the synthesis of a number of polyfunctionalized molecules. Preparation of silyl enolethers, diastereoselective aldol condensations, the synthesis of β-hydroxysilanes and the stereoselective synthesis of vinylsilanes are just a few examples of their valuable reactivity. On the other hand, bis(acylsilanes) have been less investigated, and only very recently have they been demonstrated as being very useful compounds,[2] able to participate in a number of interesting reactions, such as cyclization reactions via intramolecular aldol condensation and cyclodehydration[2b,c,3] or formation of elaborated silyl organofluorine compounds.[4]

Moreover, the corresponding sulfurated derivatives, thioacylsilanes, are known as useful building blocks for polyfunctionalized molecules.[5] In fact, besides being synthetic equivalents of thioaldehydes through a simple protodesilylation reaction, thioacylsilanes combine in their structure the high reactivity of the carbon–sulfur double bond towards nucleophiles, electrophiles and cycloaddition reactions, together with the peculiar reactivity of organosilanes, thus leading to various compounds containing the Si–C–S unit.[5,6]

Enethiolizable thioacylsilanes have been thoroughly investigated[7] and, inter alia, they have been shown to lead to 2-silyl thiacycloalkenes or *Z*-α-silyl sulfides, which are precursors of thioannulated cyclopentenes and thiofunctionalized enones, thus disclosing a general access to differently silylated sulfur heterocycles of variable ring size.

In this context, we became interested in the evaluation of the possibility of devising a general access to a new class of thioacylsilanes, namely bis(thioacylsilanes), through direct thionation of bis(acylsilanes), and in this connection the hexamethyldisilathiane (HMDST)-based thionation procedure that proved, due to its mildness, to be quite efficient in thionating labile molecules such as α,β-unsaturated acylsilanes and stannanes,[8] seemed well suited for such a transformation.

Thus we reacted 1,5-bis(acylsilane) **1a** with HMDST in the presence of $CoCl_2{\cdot}6H_2O$ and 2,3-dimethyl-1,3-butadiene as trapping agent, but no trace of the cycloadduct of the thioacylsilane was evident in the crude mixture. Nonetheless, a clean reaction was observed,

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Keywords: acylsilanes; thionation; thiopirans; dihydrothiepines.

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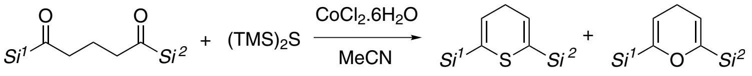


1a : $Si^1=Si^2=t\text{-}BuMe_2Si$

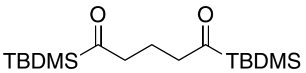
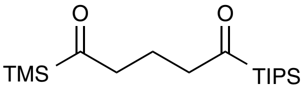
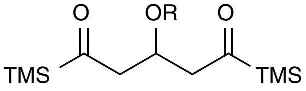
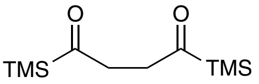
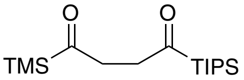
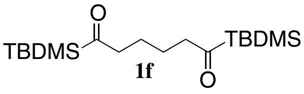
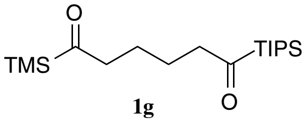
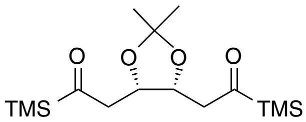
1b : $Si^1=Me_3Si$
$Si^2=i\text{-}Pr_3Si$

2a, 2b **3a, 3b**

Scheme 1.

affording one main product (63%), which was characterized as 2,6-bis(*tert*-butyldimethylsilyl)-4*H*-thiopyran **2a**,[9] together with a very minor amount (6%) of 2,6-bis(*tert*-butyldimethylsilyl)-4*H*-pyran **3a** (Scheme 1). Compound **3a** has already been obtained by treatment of bis(acylsilane) **1a** with acid.[3b]

Table 1. Thionation of bis(acylsilanes)

Entry	Bis(acylsilane)	Catalyst	Product	Yield[a,b] (%)
1	 **1a**	$CoCl_2{\cdot}6H_2O$	**2a**	63[c]
2	 **1b**	$CoCl_2{\cdot}6H_2O$	**2b**	75[d]
3	 **1c** (R=H) **1c'** (R=Ac)	$CoCl_2{\cdot}6H_2O$	—	—
4	 **1d**	$CoCl_2{\cdot}6H_2O$	**4d**	61[e]
5	 **1e**	$CoCl_2{\cdot}6H_2O$	**4e**	48[f]
6	 **1f**	TfOTMS	**6f**	57
7	 **1g**	TfOTMS	**6g**	51[g]
8	 **1h**	$CoCl_2{\cdot}6H_2O$ TfOTMS	—	—

[a] Yield of isolated product.

[b] All compounds showed spectroscopic and analytical data consistent with the assigned structure.

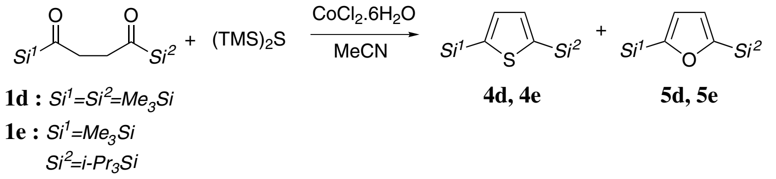
[c] Pyran **3a** (6%) was isolated.

[d] Pyran **3b** (2%) was detected.

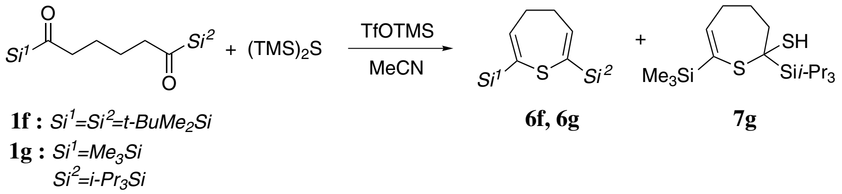
[e] Furan **5d** (13%) was isolated.

[f] Furan **5e** (43%) was obtained.

[g] Thiol **7g** (27%) was obtained.



Scheme 2.



Scheme 3.

This result allows the hypothesis that the formation of such unreported silylated sulfur heterocycles can be achieved by intramolecular cyclization of the enethiol form of the thioacylsilane on the other C=X group ($X = S$ or O), followed by dehydration or hydrogen sulfide elimination, and this behavior may be ascribed to the presence of the silyl group, which favors enethiolization of alkyl thiones bearing a hydrogen atom at the α-carbon.[10]

With the aim of evaluating the generality of such a reaction as a potential general route for the synthesis of sulfurated heterocycles of variable ring size, we tried it with various bis(acylsilanes) bearing either different silylated groups or different lengths of carbon chain between them including also β-hydroxy-substituted bis(acylsilanes). The results so obtained are summarized in Table 1. The bis(acylsilanes) reacted smoothly under the present conditions, and the reaction appears to be general.

The unsymmetrical substituted bis(acylsilane) **1b** led to 2,6-bis(trialkylsilyl)-4*H*-thiopyran **2b** (75%) (Scheme 1). Also in this case traces (2%) of the corresponding 2,6-bis(trialkylsilyl)-4*H*-pyran **3b** were detected.[3b]

In both of the above reactions an aldol-like intermediate, 2,6-bis(trialkylsilyl)-3,4-dihydro-2*H*-thiopyran-2-thiol, was observed in very small amounts (2–3%) after purification of the crude product.

When the hydroxy-substituted bis(acylsilane) **1c** was treated under the same conditions, only a complex mixture of unidentified products was obtained. Reaction of the acetyl protected derivative **1c′** did not afford any trace of the desired bis(thioacylsilane), even under different experimental conditions.

This type of reaction is not limited to the thionation of 1,5-bis(acylsilanes) but can be efficiently extended to 1,4-bis(acylsilanes) **1d** and **1e**, allowing in this case the isolation of 2,5-bis(trialkylsilyl)thiophenes **4d**[11] and **4e** (Scheme 2), together with 2,5-bis(trialkylsilyl)furans **5d** and **5e**.[3b] It is worth noting that the silyl-thiophene **4e** has not previously been described in the literature.

On the other hand, when bis(acylsilanes) with a four-methylene chain linker, such as the 1,6-bis(acylsilanes) **1f** and **1g**, were used under the same conditions, the reaction did not afford the expected thionation or cyclization derived products, and unreacted starting compounds were recovered. We therefore used the stronger catalyst TfOTMS to promote the reaction and indeed under these conditions the 2,7-bis(*tert*-butyldimethylsilyl)-4,5-dihydrothiepine **6f** was isolated in good yield by treating 1,6-bis(acylsilane) **1f** with HMDST (Scheme 3).[12]

When the unsymmetrical 1,6-bis(acylsilane) **1g** was reacted under the same conditions, again the related silyl thiepine **6g** was obtained (Scheme 3), together with the aldol-like intermediate product, 2-triisopropyl-7-trimethylsilyl-2,3,4,5-tetrahydro-thiepine-2-thiol **7g** (27%), thus providing a method for synthesizing this kind of molecule.[13]

Moreover, when 3,4-dihydroxy-1,6-bis(trimethylsilyl)-acylsilane, protected as the acetonide **1h**, was treated with HMDST and either TfOTMS or $CoCl_2·6H_2O$, no formation of the thionated compounds was observed, the reaction leading only to decomposition of the starting bis(acylsilane) in the case of triflate, and to an unidentified mixture of compounds with cobalt(II) chloride.

In conclusion, thionation of bis(acylsilanes) with HMDST affords a general route to bis-silylated thiaheterocycles of variable size, with both symmetrical and unsymmetrical trialkylsilyl substitution being possible.

Acknowledgements

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9. Typical procedure: To a solution of 1,5-bis(acylsilane) **1a** (50 mg, 0.15 mmol) in CH_3CN (0.35 mL) was added under a N_2 atmosphere HMDST (0.127 mL, 0.60 mmol) and a solution of $CoCl_2{\cdot}6H_2O$ (71 mg, 0.30 mmol) in CH_3CN (1.1 mL). The reaction mixture was stirred at rt overnight (the reaction was monitored by TLC) and was then diluted with diethyl ether, washed with water and brine and dried over Na_2SO_4. The solvent was evaporated and the products were separated by preparative TLC (hexanes/diethyl ether 200:1) to give **2a** (31 mg, 63%) and **3a** (3 mg, 6%). Data for **2a**: ^1H NMR (200 MHz, $CDCl_3$) δ (ppm): 0.12 (12H, s), 0.90 (18H, s), 2.67 (2H, t, $J = 4.6$ Hz), 5.99 (2H, t, $J = 4.6$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): −5.8, 17.1, 26.8, 29.4, 129.2, 134.9. MS [EI] m/z (%): 326 (M^+, 5), 269 (30), 211 (90), 155 (24), 73 (100). IR (film) ν (cm^{-1}): 2955, 1648, 1470, 1250. Calcd for $C_{17}H_{34}SSi_2$: C, 62.50; H, 10.49. Found: C, 62.31; H, 10.73.
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12. Typical procedure: To a solution of 1,6-bis(acylsilane) **1f** (50 mg, 0.15 mmol) in CH_3CN (0.5 mL) were added, under an inert atmosphere, HMDST (0.127 mL, 0.60 mmol) and TfOTMS (0.012 mL, 0.06 mmol). The mixture was stirred at rt overnight (the progress of the reaction was followed by GC/MS). After dilution with diethyl ether, the organic phase was washed with water and brine and dried over Na_2SO_4. The solvent was evaporated and the product was separated by preparative TLC (hexanes/diethyl ether 200:1) to give **6f** (29 mg, 57%). ^1H NMR (200 MHz, $CDCl_3$) δ (ppm): 0.10 (12H, s), 0.92 (18H, s), 2.53–2.61 (4H, m), 6.24–6.30 (2H, m). ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): −5.6, 17.1, 26.9, 30.6, 135.8, 141.8. MS [EI] m/z (%): 340 (M^+, 11), 283 (51), 163 (26), 73 (100). IR (film) ν (cm^{-1}): 2954, 1584, 1470, 1248. Calcd for $C_{18}H_{36}SSi_2$: C, 63.45; H, 10.65. Found: C, 63.29; H, 10.80.
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