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# Thiosilanes in Sulfur Chemistry: A General Approach to Silyl Thiaheterocycles and Their Use in Stereoselective Synthesis

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ABSTRACT: *2-Silyl five-membered sulfurated heterocycles can be efficiently accessed through reaction of bromo(methoxy)methyl trimethylsilane with suitable β-substituted mercaptans HS-$CH_2CH_2$-XH, leading to the formation of 2-silyl-1,3-dithiols, 2-silyl-1,3-thiazolidines, and 2-silyl-1,3-oxathiolanes. β-Mercaptoalcohols are obtained through regioselective ring opening of epoxides with bis(trimethylsilyl)sulfide (HMDST). In a similar way, thiiranes and aziridines react with HMDST, leading to the formation of 1,2-dithiols and β-aminothiols. Fluoride ion induced functionalization of the pentaatomic heterocycles smoothly affords the transfer of the heterocyclic ring on electrophiles, thus showing these silyl derivatives as a new class of acyl anion equivalents. When stereodefined compounds are reacted, the stereoinformation is transferred from the carbon–silicon to the newly formed carbon–carbon bond.* © 2007 Wiley Periodicals, Inc. Heteroatom Chem 18:516–526, 2007; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20345

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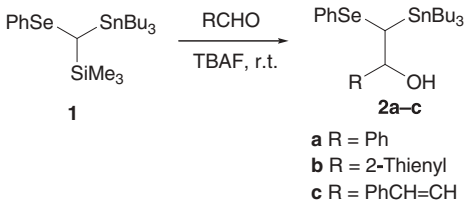
## *INTRODUCTION*

Sulfur-containing five-membered heterocycles are very interesting molecules for their applications in synthetic organic chemistry and also for their properties as biologically active compounds. Moreover, in recent years, the chemistry of organosilicon compounds has witnessed an unbelievable growth as a consequence of the critical role played in many chemical transformations. Extensive investigations have been carried out over the years and have outlined their tolerance for other functional groups and their versatility as intermediates in organic synthesis.

Thus, reagents and methods based on organosilicon chemistry are an area of increasing interest in organic synthesis. Organosilanes, in fact, together with some other organometallic compounds, such as Sn, Cu, B, Al, and Zn derivatives, represent alternative and very useful reagents, which have led to the development of alternative strategies with respect to the organoalkali or Grignard derivatives, providing, through their particular behavior, the development of novel methodologies. The utility of such organometallic reagents is mainly due to their behavior as "non-basic organometallics," thus being compatible with functional groups that are labile under strong basic conditions.

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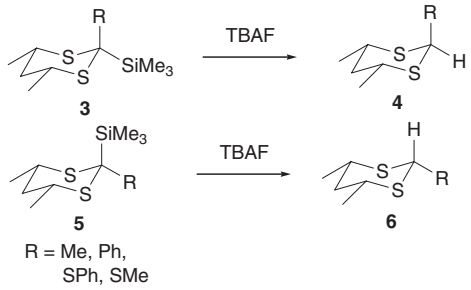



SCHEME 2

The use of organosilanes has led to synthesize molecules hardly accessible with the classical metalation procedures. In this context, silylated sulfur-containing heterocycles have recently found interesting applications, thus offering the opportunity to develop new and alternative synthetic strategies [1].

## *RESULTS*

Organosilanes are generally characterized by a particular reactivity, related to the properties of the C—Si bond, that has led to synthetic achievements unobtainable through the classical organic procedures. Some selected examples are represented, for instance, by the reaction of trifluoromethyllithium with carbonyl compounds that do not afford the desired 1,2-addition product [2]. When, on the contrary, trifluoromethylsilane was reacted with carbonyl derivatives, the wanted trifluoromethyl adduct was isolated as its silyl ether [3]. In a similar way, perfluoroketene dithioacetals do not react with lithium ester enolates, but such lack of reactivity was overcome by using α-silyl acetates, thus leading to the formation of the nucleophilic substitution product [4].

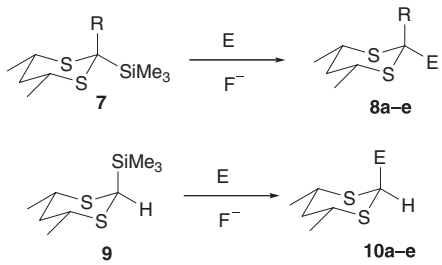
We also recently found that fluoride-catalyzed reaction of α-tributylstannyl-(phenylseleno)methyltrimethylsilane **1** with aldehydes led to a smooth transfer of **1** onto the electrophile (Scheme 1), affording the formation of α-hydroxy compounds **2a–c**. This reaction thus showed that **1** can act as the synthetic equivalent of an α-tributylstannyl-(phenylseleno)methyl anion, a species that cannot be obtained through metalation, where a tin–lithium exchange occurs [5].

Furthermore, some examples of functionalization of a C—Si bond to a new C—C bond with retention of configuration have been reported. In fact, with the exception of allylsilanes [6], there are only a few cases of stereoselective transformations of $sp^3$ carbon–silicon bonds to carbon–carbon bonds. Such examples include conversions of C—Si bonds of epoxysilanes to C—C bonds upon reaction with aldehydes [7], stereoselective insertion into strained bonds [8], palladium-catalyzed conversions of chiral trifluoro benzyl silanes to chiral diaryl silanes [9], diastereoselective intramolecular reaction of a benzyl silane [10], the retention of configuration in the desilylative hydroxymethylation of α-silyl sulfides [11], and, more recently, the reactivity of chiral benzyl silanes [12] and silylated aziridines [13] with aldehydes.

On the basis of these results, we then moved to the evaluation of the reactivity of different hetero-substituted silyl nucleophiles, such as 2-silyl sulfurated heterocycles.

A recent investigation of the fluoride ion induced protodesilylation of sterically defined silyl dithianes disclosed a novel example of protodesilylation with retention of configuration [14]. Thus, for instance, *cis* **3** and *trans* **5** 2-silyl-2-substituted-4,6-dimethyl dithianes, when subjected to fluoride-induced desilylation with TBAF, reacted smoothly to afford the corresponding 2-substituted-4,6-dimethyl dithianes **4** and **6**, respectively, in good yields, with clean retention of configuration (Scheme 2).

Besides protodesilylation, the more synthetically useful carbodesilylation reactions were then examined with the aim to check whether the stereoconservative behavior could be extended also to the formation of a new C—C bond. Thus, different stereochemically defined silyl dithianes **7** and **9** (Scheme 3) were reacted with electrophiles, showing




SCHEME 3

**TABLE 1** Stereoselective Functionalization of Silyl Dithianes **7**

| *Entry* | *R* | *E* | *Product* | *Yield (%)* |
|---|---|---|---|---|
| 1 | H | $CH_3I$ | **8a** | 31 |
| 2 | H | PhCHO | **8b** | 72 |
| 3 | H | $C_6H_{11}CHO$ | **8c** | 56 |
| 4 | H | 2-furyl CHO | **8d** | 76 |
| 5 | $SiMe_3$ | $CH_3I$ | **8e** | 59 |

an interesting stereoconservative functionalization, leading to the corresponding adducts **8** and **10** in good yields (Tables 1 and 2, respectively) [1,15].

While anyway the functionalization of the equatorial substituted dithianes **7** appears quite obvious (Table 1), nonetheless disclosing an alternative and mild procedure to functionalize such molecules, reactions of the trans diastereomer **9** yielded the products **10** (Table 2) in which the electrophile is unequivocally positioned in the axial position, showing that the configuration is still retained from the C—Si to the newly formed C—C bond, and may suggest the presence of a hypervalent silicon species and not of a free carbanion. Such results outlined for the first time a successful selective functionalization of the axial position of such compounds. It is in fact reported that metalation of 1,3-dithianes [16] and 4,6-disubstituted-1,3-dithianes [17] occurs regioselectively at C-2 and that their carbanions, upon reaction with electrophiles, invariably led to products showing the incoming group at the equatorial position, irrespective of the stereochemistry of the starting dithianes.

## *DISCUSSION*

It is well known that 1,3-dithiane anions have been extensively used in the last decades as masked acyl carbanions in umpolung reactivity, being very useful intermediates in a number of organic processes [18]. Nonetheless, although several methods for their unmasking have been reported [19], they still suffer from the generally harsh conditions of their unblocking. On the other hand, dithiolanes, thiazolidines, and oxathiolanes have been reported to be unmasked under milder conditions, thus possibly showing an application of such molecules in the generation of formyl and acyl anions equivalents. Unfortunately, such heterocycles suffer generally difficulties in their functionalization under strong basic conditions.

**TABLE 2** Stereoselective Functionalization of *trans* Silyl Dithiane **9**

| *Entry* | *E* | *Product* | *Yield (%)* |
|---|---|---|---|
| 1 | $CH_3I$ | **10a** | 26 |
| 2 | PhCHO | **10b** | 63 |
| 3 | $C_6H_{11}CHO$ | **10c** | 47 |
| 4 | 2-furyl CHO | **10d** | 70 |
| 5 | *p*-$CH_3O$ $C_6H_4$ CHO | **10e** | 56 |

1,3-Dithiolane anions, for instance, upon treatment with bases, have been reported to undergo either deprotonation at C-2 [20a] or at C-4 [20b,c], with subsequent cycloreversion in both the cases. Only few examples of functionalization under basic conditions of dithiolanes are reported in the literature, thus evidencing the still present need for a general protocol for their functionalization [21].

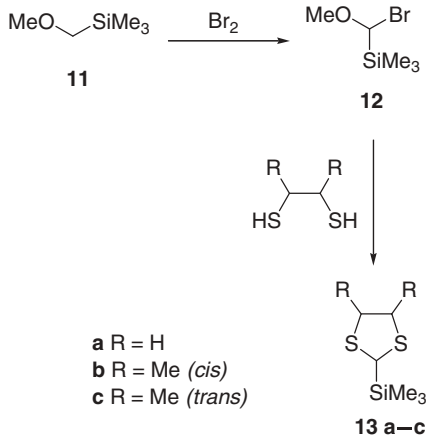
Thiazolidines are also reported to be metalated, but only in the presence of specific nitrogen-protecting groups [22].

Thus, taking advantage of the previously described results in the reactivity of dithianes, which seem to occur via a pentacoordinated silicon species, and not a free carbanion, we envisaged that the functionalization of the C—Si bond in five-membered silyl-heterocyclic systems could possibly lead to the solution of such problem and to the development of a novel and general functionalization methodology for such labile heterocycles.

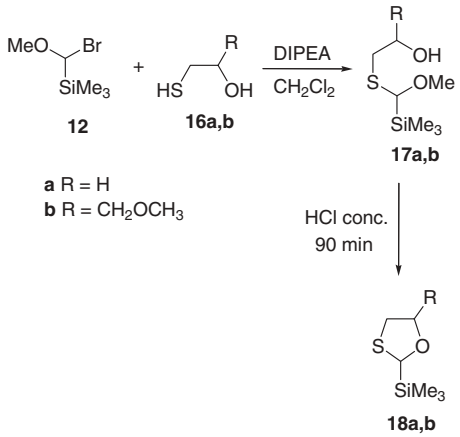
In this context, direct access through metalation to five-membered silyl heterocycles appeared difficult or even impossible, and thus an alternative access to such molecules had to be devised.

We found that a general access to silyl dithiolanes and, more generally, to five-membered ring silylated heterocycles could be envisaged through the reaction of bifunctional molecules, such as 1,2-dithiols, 1,2-amino thiols, and 1,2-mercapto alcohols with formyl trimethylsilane. Difficulties in the generation and handling of such labile molecule [23] led to the search for a possible synthetic equivalent of such a compound, and we envisaged in bromo(methoxy)methyl trimethylsilane **12** the reagent of choice. Such a molecule, in fact, can be obtained in quantitative yield by treating the commercially available methoxy methyl trimethylsilane **11** with bromine [24] and subsequent one pot treatment with the suitable mercaptan (Scheme 4) [25].

Thus, for instance, when 1,2-ethanedithiol was reacted with bromo methoxy derivative **12**, the corresponding 2-trimethylsilyl-1,3-dithiolane **13a** was obtained in good yield (Scheme 4). Such a reaction then evidenced the ability of **12** to act as a real synthetic equivalent of formyl silane and opened the way to a possible general route to access a wide variety of silyl heterocycles.




SCHEME 4

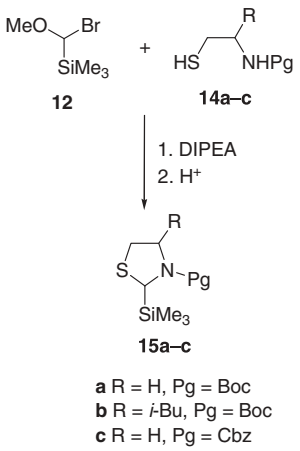



SCHEME 6

In a similar way, by reacting *meso*-butane-2,3-dithiol, both *cis* **13b** and *trans* **13c** diastereoisomers of *meso*-4,5-dimethyl-2-trimethylsilyl-1,3-dithiolane were isolated (Scheme 4).

Then, with the aim to seek for the generality of the present reaction, we decided to test different bifunctional molecules. We took into consideration the possible access to silyl thiazolidines, and then we reacted **12** in situ with N-protected 1,2-aminoethanethiols **14a,c** to afford smoothly 2-silyl-*N*-protected 1,3-thiazolidines **15a** and **15c** (Scheme 5).

Moreover, when *N*-Boc-protected 2-amino-4-methylpentane-1-thiol **14b** was reacted, the substituted 4-isobutyl *N*-Boc-2-silyl thiazolidine **15b** was obtained as an equimolar mixture of cis and trans isomers (Scheme 5).




SCHEME 5

As a further step, we wanted to verify the possible generalization to another interesting heterocyclic system, such as silyl oxathiolane, and thus freshly prepared bromo(methoxy)methyltrimethylsilane **12** was reacted in situ with β-mercaptoethanol **16a** at room temperature, in the presence of DIPEA (diisopropylethylamine) and stirred overnight (Scheme 6), but this time the intermediate compound **17a** was obtained (Scheme 6).

In order to achieve the cyclization to the desired oxathiolane, we had to devise a slightly different synthetic approach with respect to that used for the synthesis of silyl-1,3-dithiolanes.

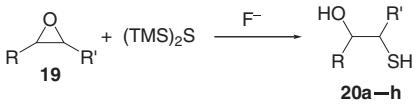
The reaction was repeated under the same conditions and, after stirring overnight in the presence of DIPEA, concentrated HCl was added in the same flask and the mixture was stirred for 1 h 30 min to obtain the wanted 2-trimethylsilyl-1,3-oxathiolane **18a** (Scheme 6).

Because of the instability of these heterocycles under acidic conditions, the treatment with HCl must not be longer than 1 h 30 min, in order to avoid fragmentation of the oxathiolane ring.

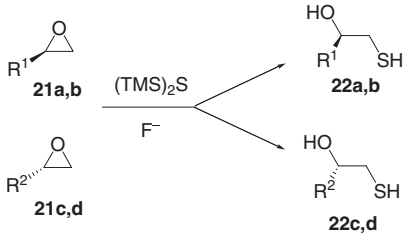
2-Trimethylsilyl-5-(methoxymethyl)-1,3-oxathiolane **18b** was obtained similarly, as a mixture of diastereoisomers (6:1), by reacting **12** with 1-mercapto-3-methoxypropan-2-ol **16b** (Scheme 6).

Nonetheless, it is clear that the generality of this procedure is strictly related to the availability of the required starting bifunctionalized molecules, namely 1,2-dithiols, 1,2-amino thiols, and 1,2-mercapto alcohols.

In this context, we recently found that a direct and easy access to β-mercapto alcohols was obtained in the reactivity of a particular silyl sulfide, bis(trimethylsilyl)sulfide (HMDST), which over the years proved a very versatile reagent in the delivery




SCHEME 7




**a** $R^1$ = *R*-(–)-Ph
**b** $R^1$ = *S*-(+)-$CH_2OMe$
**c** $R^2$ = *R*-(+)-$CH_2OBn$
**d** $R^2$ = *S*-(+)-2-(*S*-2-oxiranyl)-*N*-Cbz-pyrrolidine

SCHEME 8

of sulfurated moieties [26], with ring-strained heterocycles, such as oxiranes, thiiranes, and aziridines.

It is well known that the ring opening of epoxides with nucleophiles represents a very versatile chemical transformation to access a wide range of functionalized molecules [27].

In particular, reactions with sulfur nucleophiles offer the opportunity to access different interesting sulfurated molecules [28]. Thiosilanes [29] and silane thiols [30] have been used as nucleophiles with oxiranes, even if not always a regiocontrolled reaction was achieved.

Thus, reaction of differently substituted epoxides **19** with HMDST and TBAF as catalyst afforded a mild ring opening of the heterocyclic ring (Scheme 7), leading to the formation of various β-mercaptoalcohols **20a–h** in high yields (Table 3), arising from a regioselective attack of the silyl sulfide on the less hindered side of the oxirane [31].

This procedure can be applied as well to chiral epoxides **21a–d**, thus affording a regioselective and enantioconservative access to chiral β-mercaptoalcohols **22a–d** (Scheme 8).

Also aziridines **23a–c** and episulfides **23d–f**, upon treatment with bis(trimethylsilyl)sulfide and TBAF as catalyst, lead to the formation of 1,2-mercaptoamines **24a–c** and 1,2-dithiols **24d–f**, respectively (Scheme 9), together with variable amounts of the corresponding disulfides [1]. The reaction proved to be regioselective in these cases too, the HMDST-induced ring-opening occurring on the less substituted side of the heterocyclic ring.

A number of ring-opening reactions of aziridines have been reported, either with carbon- and heteroatom-containing nucleophiles [32], and the reaction with sulfurated reagents represents an interesting procedure for obtaining β-amino sulfides [33]. Examples of acid- or base-catalyzed ring openings have been described [34]. Recently, silylated nucleophiles, as trimethylsilyl cyanide, trimethylsilyl azide, and trimethylsilyl halides, were reported to attack aziridines under Lewis Acid catalysis, with high regioselectivity.

On the contrary, to the best of our knowledge, only few examples have been described on the ring opening of thiiranes, probably due to their easy polymerization and tendency to be desulfurized. Generally such reactions are reported under Lewis Acid catalysis [35] and represent a very useful method to obtain sulfurated heterocyclic systems [36].

This approach then affords an easy access to a variety of functionalized mercaptans, precursors for the synthesis of five-membered silylated heterocycles.

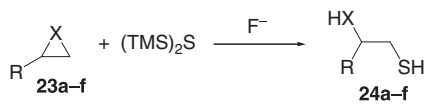
**TABLE 3** Direct Synthesis of β-Mercaptoalcohols **20**

| *Entry* | *R* | *R'* | *Product* | *Yield (%)* |
|---|---|---|---|---|
| 1 | Me | H | **20a** | 65 |
| 2 | Ph | H | **20b** | 95[a] |
| 3 | *i*-$PrOCH_2$ | H | **20c** | 72[b] |
| 4 | $AllOCH_2$ | H | **20d** | 87 |
| 5 | $ClCH_2$ | H | **20e** | 40 |
| 6 | $CH_2$=CH | H | **20f** | 80 |
| 7 | $CH_3$ | $CH_3$ | **20g** | 55 |
| 8 | Cyclohexyl | | **20h** | 90 |

[a]4.6% of the regioisomer.
[b]2.5% of the regioisomer.

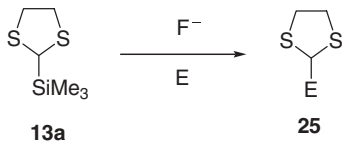
## *Functionalization of 2-Silyl-1,3-heterocycles*

The development of a general and reliable method to access a variety of silyl heterocycles then opened the way to a thorough investigation of their chemistry.




**a** X = NTs; R = Me
**b** X = NTs; R = $^i$Pr
**c** X = NTs; R = $^t$Bu
**d** X = S; R = Me
**e** X = S; R = Ph
**f** X = S; R = $CH_2OBn$

SCHEME 9




**13a** **25**

SCHEME 10

As already mentioned, simple 1,3-dithiolanes when deprotonated at position 2 or 4 suffer from cycloreversion [20] and only few examples of metalation are reported, with specific substituents on position 2 [21].

Thus, the obtained 2-silyl dithiolane **13a** was treated with electrophiles in the presence of different fluoride ion sources (TBAF, TBAT, TASF) and a smooth reaction occurred, leading to the corresponding functionalized dithiolane **25** (together with minor amount of desilylated dithiolane), so disclosing the possibility of an effective transfer of a "dithiolane anion" onto electrophiles under mild conditions (Scheme 10) [37]. These results showed that, under the present conditions, **25** can be considered as a masked dithiolane anion.

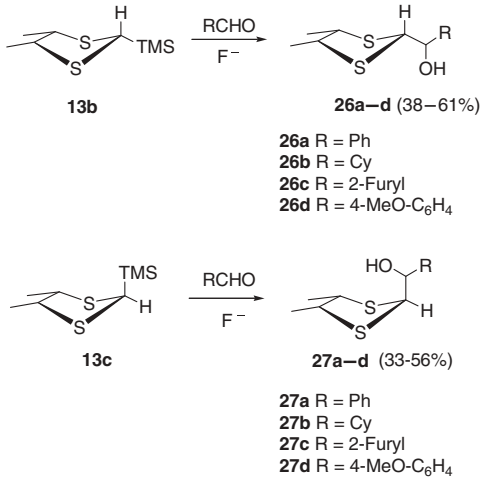
This reactivity may be conveniently performed with aromatic, heteroaromatic, aliphatic, and α, β-unsaturated aldehydes (Table 4, entries 1–6), affording in all cases protected α-hydroxy aldehydes. Reactive halo derivatives, such as allyl bromide and methyl vinyl ketone, will undergo reaction as well (Table 4, entries 7,8). With α,β-unsaturated aldehydes only 1,2-adducts have been isolated, whereas reaction with methyl vinyl ketone afforded a 3:1 mixture of 1,2- and 1,4-adducts.

As a further step of the present investigation, the stereochemical outcome of the reaction was considered. Thus, both *cis* and *trans* 4,5-dimethyl-2-trimethylsilyl-1,3-dithiolanes **13b** and **13c** were obtained from *meso*-2,3-butanedithiol with bromo(methoxy)methyl trimethylsilane **12** in a 1:3

**TABLE 4** Reactivity of 2-Silyl Dithiolane **13a**

| *Entry* | *E* | *Yield (%)* |
|---|---|---|
| 1 | Ph CHO | 79 |
| 2 | 4-Br-$C_6H_4$ CHO | 78 |
| 3 | 2-Thienyl CHO | 83 |
| 4 | N-Me-pyrroylCHO | 12 |
| 5 | PhCH=CHCHO | 81 |
| 6 | $PrCH_2CHO$ | 80 |
| 7 | $CH_2$=$CHCOCH_3$ | 30[a] |
| 8 | $CH_2$=$CHCH_2Br$ | 30 |

[a]3:1 mixture of 1,2- and 1,4-adducts.

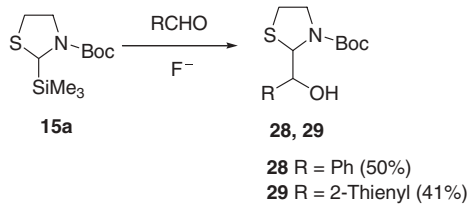



SCHEME 11

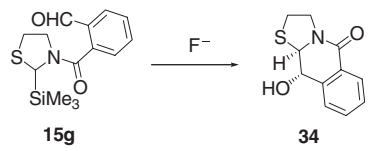
ratio. After chromatographic separation, fluoride ion induced reaction of the two isomers with aldehydes as typical electrophiles was performed, leading to the corresponding adducts **26** and **27** in good yields (Scheme 11) [15]. A representative series of aldehydes was reacted (aromatic, heteroaromatic, and aliphatic) showing in all cases complete retention of the configuration of C-2 and then outlining that the stereoconservative behavior observed in the dithiane series holds also for the dithiolane one.

Our interest in this kind of functionalization was then focused on the thiazolidine series. The thiazolidine ring system derives special importance from the fact that it is an integral part of medicinally important compounds like penicillins [38] and some antiradiation drugs [39]. Substituted thiazolidine derivatives represent important key intermediates for the synthesis of pharmacologically active drugs [40]. Thiazolidines are also relevant in food chemistry, as far as they are incorporated in flavor-enhancing additives [41], and their synthetic utility is shown by their use as blocking groups [42] and as intermediates in the synthesis of aldehydes [43] and aminoethane thiols [44].

Despite the utility of the thiazolidine moiety, still very few methodologies for the functionalization of position 2 of the heterocyclic ring exist. Only few reports, in fact, to the best of our knowledge, deal with such functionalization, and its efficiency seems related to the presence of specific N-protecting groups. Meyers et al. report efficient metalation of the thiazolidine ring when on the nitrogen atom a *tert*-butylformamidine group is present [22a], whereas, more recently, Gawley and Toru have reported an interesting functionalization of *N*−Boc substituted




SCHEME 12




SCHEME 14

thiazolidines [22b–d], showing their possible use as chiral acyl anion synthons.

Thus, *N*-Boc-2-silyl-thiazolidine **15a** was smoothly reacted in the presence of TBAF and aldehydes, leading to the formation of a series of α-hydroxy 1,3-thiazolidines **28** and **29** (Scheme 12) [45].

In order to try a generalization of this behavior and to verify whether such functionalization could be dependent on a specific nitrogen-protecting group, different N-protected thiazolidines **15d–f** were reacted with aldehydes (Scheme 13).

The reaction appears rather general, being also efficient in the presence of mesyl, tosyl, and acetyl substituents, leading to the α-hydroxy adducts **30–33** as a mixture of diastereoisomers. Only in the cases of *N*-benzoyl and *N*-cinnamoyl thiazolidines no reaction was observed, but only the desilylated thiazolidine was recovered from the reaction mixture.

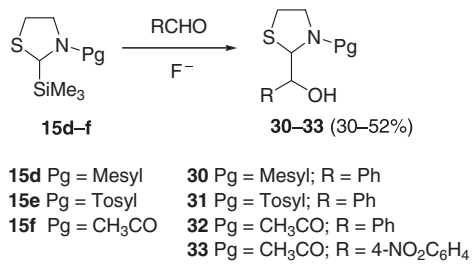
A particular behavior was observed when an electrophilic center is contained in the protecting group. When in fact *N*-(*o*-formyl)benzoyl-2-trimethylsilyl-thiazolidine **15g** was reacted with PhCHO and TBAF (Scheme 14), no reaction with benzaldehyde was observed, but the polycyclic compound **34** was isolated in good yield, arising from an intramolecular cyclization. As evidenced by the X-ray crystallographic structure, an interesting diastereomeric excess of 70% (anti-isomer) was obtained. Such a reaction then discloses the route to an easy and diastereoselective access to polycyclic derivatives with a possible biological activity.

A further example of the versatility of such methodology was evidenced when the protecting group was Cbz [46]. In fact, when *N*-Cbz protected 2-trimethylsilyl-1,3-thiazolidine **15c** was reacted at room temperature with benzaldehyde, under fluoride ion catalysis (Scheme 15), the oxazolidinone **35a** was isolated as the sole product, probably arising from an intramolecular attack by the alcoholate intermediate **36** on the Cbz carbonyl carbon, no trace of the expected α-hydroxy adduct being observed.

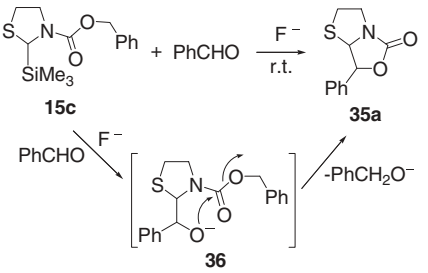
A similar result was also obtained with *p*-fluorobenzaldehyde, butyraldehyde, and cyclohexanecarbaldehyde, which afforded the cyclic compounds, together with variable amounts of desilylated thiazolidine.

An analogous behavior was indeed reported by Gawley and coworkers in the reaction of *N*-Boc 2-lithio-4-isopropyl-1,3-thiazolidine, which led to the formation of oxazolidinones with aliphatic aldehydes, while on the contrary the reaction with benzaldehyde afforded only the open chain adduct [22b].

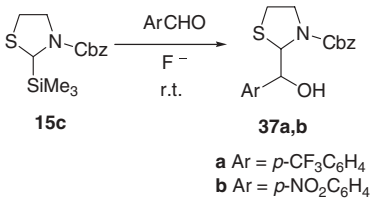
In order to generalize such behavior, thiazolidine **15c** was reacted under the same conditions with *p*-trifluoromethylbenzaldehyde and *p*-nitrobenzaldehyde, but such reactivity showed not to be univocal (Scheme 16). This time in fact the homologated α-hydroxy protected thiazolidines **37a,b** were isolated as predominant products as 1:1 mixture of diastereoisomers.




SCHEME 13




SCHEME 15




SCHEME 16

On the contrary, 2-thienyl-aldehyde and *p*-anisaldehyde under the same reaction conditions gave mixtures of both products **35c,d** and **37c,d** (65:35, respectively) (Scheme 17). It is interesting to note that the open chain adducts **37c,d** were isolated as single diastereoisomers.

The reaction of silyl thiazolidine **15c** with aldehydes and TBAF was then performed at different temperatures, and the reactivity appeared clearly to be a function of the temperature and the nature of the aldehyde. Higher temperatures were shown to favor ring cyclization, whereas lower ones led predominantly to the formation of open chain adducts. Results are summarized in Table 5.

Interestingly the open chain adducts were isolated as single isomers with an *anti* configuration, whereas the fused oxazolidinones were obtained as mixture of *syn/anti* isomers, the ratio depending on the temperature and the aldehyde [46]. This may suggest a kinetic resolution of the two initially formed *syn/anti* isomeric thiazolidine alcoholates, the *syn* adduct being shown to undergo cyclization faster that the *anti* isomer.

As a further step of this kind of investigation, the stereochemical aspect was taken into consideration and the reactivity of different substituted thiazolidines was considered.

**TABLE 5** Reaction of Thiazolidine **15c** with Aldehydes

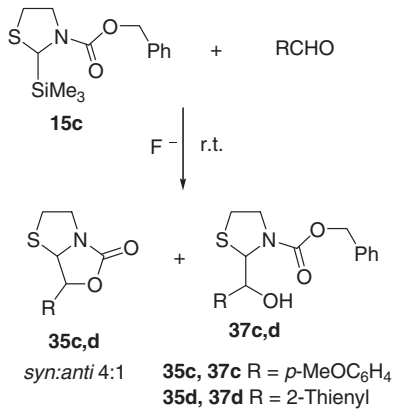
| *Entry* | *Aldehyde* | **35** | **37** | *T* | *Yield (%)* |
|---|---|---|---|---|---|
| 1 | PhCHO | 100 | 0 | rt[a] | 68 |
| | | 65 | 35 | 0°C | 60 |
| 2 | *p*-$FC_6H_4CHO$ | 100 | 0 | rt | 61 |
| | | 65 | 35 | 0°C | 68 |
| 3 | *n*-$C_3H_7CHO$ | 100 | 0 | rt | 32 |
| | | 65 | 35 | 0°C | 31 |
| 4 | Cy-CHO | 100 | 0 | rt | 28 |
| | | 65 | 35 | 0°C | 31 |
| 5 | *p*-$CF_3$-$C_6H_4CHO$ | 0 | 100 | rt | 37 |
| | | 65 | 35 | 35°C | 42 |
| 6 | *p*-$NO_2$-$C_6H_4CHO$ | 0 | 100 | rt | 30 |
| | | 65 | 35 | 35°C | 32 |
| 7 | 2-ThienylCHO | 65 | 35 | rt | 43 |
| | | 30 | 70 | 0°C | 46 |
| | | 100 | 0 | 35°C | 51 |
| | | 0 | 100 | −20°C | 48 |
| 8 | *p*-$MeOC_6H_4CHO$ | 65 | 35 | rt | 40 |
| | | 100 | 0 | −20°C | 41 |

[a]rt = Room temperature.

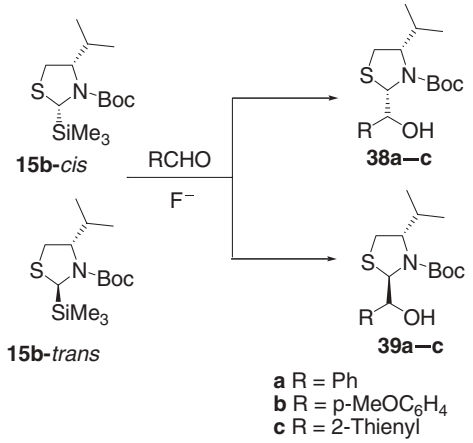
Thus, after chromatographic separation, **15b**-*cis* and **15b**-*trans* isomers of 4-(isopropyl)-*N*-Boc-2-trimethylsilyl thiazolidine were obtained as enantiopure compounds, and then reacted with aldehydes, to afford the expected products **38** and **39**, as equimolar mixture of diastereomers (Scheme 18) [1]. No diastereoselectivity is then obtained, but the functionalization occurs with retention of configuration of the starting C—Si bond, thus affording mixture of enantiopure diastereomers.

## *Silyl 1,3-Oxathiolanes*

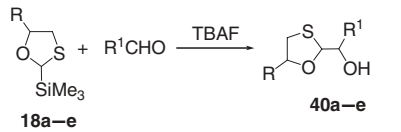
We moved then to the evaluation of the chemical behavior of 2-trimethylsilyl-1,3-oxathiolanes. Oxathioacetals are important compounds as far as, together with acetals and dithioacetals, represent the




SCHEME 17




SCHEME 18




**18a—e** **40a—e**

**a** R = H; $R^1$ = Ph
**b** R = (5*R*)-$MeOCH_2$ ; $R^1$ = *p*-F-$C_6H_4$
**c** R = H; $R^1$ = 2-Thienyl
**d** R = Me; $R^1$ = Ph
**e** R = Ph; $R^1$ = Ph

**SCHEME 19**

most commonly used protecting groups for carbonyl compounds [47].

Moreover, they can be employed as acyl anion equivalents in umpolung reactivity [47], and substituted chiral derivatives have been used in diastereoselective reactions.

The use of oxathioacetals is in addition more convenient than the corresponding acetals or dithioacetals, being more stable than *O*,*O*-acetals in acidic conditions and easier to deprotect with respect to *S*,*S*-acetals [19].

1,3-Oxathiolanes are very interesting compounds as well, and several methods are reported for their synthesis. Usual procedures involve the use of carbonyl compounds and 1,2-mercaptoalcohols under suitable catalytic conditions [47,48].

In addition, this heterocyclic ring is contained in several pharmacologically active molecules [49]. Thus, the previously obtained 2-silyl oxathiolanes **18** were reacted with different aldehydes in the presence of TBAF, leading to the formation of α-hydroxy oxathiolanes **40** (Scheme 19) [25].

No appreciable diastereoselection was evidenced, but a stereoconservative functionalization was obtained when chiral oxathiolanes were used.

The functionalization seemed rather general and occurred with different aromatic and heteroaromatic aldehydes, leading to the synthesis of a representative number of α-hydroxy adducts. No reaction was observed with nonenolizable aliphatic aldehydes, but only the desilylated oxathiolane [50].

## *CONCLUSIONS*

Organosilicon compounds have found in recent years increasing applications in the search for new synthetic methodologies, and in this context fluoride ion induced reactivity of a carbon–silicon bond has since long time been used in the generation of nucleophilic species. Application of these concepts to a series of sulfur-containing silyl heterocycles has led to the development of a simple and mild protocol for their not always obvious functionalization. Thus, for instance, while 1,3-dithiolanes under strong basic conditions undergo ring fragmentation, silyl dithiolane can be efficiently functionalized, disclosing a new synthetic equivalent of a dithiolane anion. Similarly, different heterocycles such as 2-trimethylsilyl-1,3-thiazolidines and 2-trimethylsilyl-1,3-oxathiolanes can be efficiently functionalized under similar conditions, disclosing new classes of potential formyl and acyl anion synthons. An interesting feature of such reactivity appears the stereoconservative behavior, which allows, when reacting stereodefined molecules, to transfer the stereoinformation to the corresponding products.

A particular behavior was found when thiazolidines, with specific protecting groups on nitrogen, were reacted under fluoride ion catalysis, leading to the formation of open chain adducts or polycyclic compounds, according to the reaction conditions, with interesting degrees of diastereoselectivity.

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