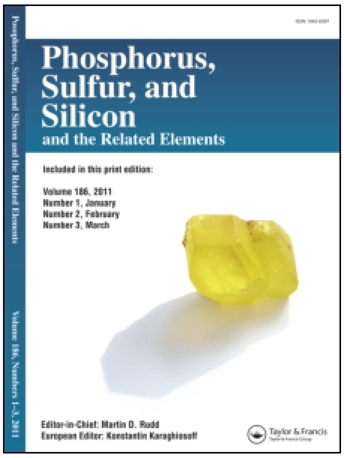


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis and Stereoselective Functionalization of Sulfur-Containing Silyl Heterocycles

Alessandro Degl'Innocenti[a]; Antonella Capperucci[a]; Giulio Castagnoli[a]; Irene Malesci[a]; Tiziano Nocentini[a]
[a] Dipartimento di Chimica Organica, Università di Firenze, Sesto Fiorentino, Italy

To cite this Article Degl'Innocenti, Alessandro , Capperucci, Antonella , Castagnoli, Giulio , Malesci, Irene and Nocentini, Tiziano(2005) 'Synthesis and Stereoselective Functionalization of Sulfur-Containing Silyl Heterocycles', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 5, 1297 — 1302

To link to this Article: DOI: 10.1080/10426500590912222

URL: http://dx.doi.org/10.1080/10426500590912222

Phosphorus, Sulfur, and Silicon, 180:1297–1302, 2005
Copyright © Taylor & Francis Inc.
ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500590912222

Synthesis and Stereoselective Functionalization of Sulfur-Containing Silyl Heterocycles

Antonella Capperucci
Giulio Castagnoli
Alessandro Degl'Innocenti
Irene Malesci
Tiziano Nocentini
Dipartimento di Chimica Organica, Università di Firenze,
Sesto Fiorentino, Italy

2-Silylated five-membered heterocycles can be easily accessed through reaction of bromo(methoxy)methylsilane and dithiols, mercapto amines, and mercapto alcohols. Further reaction of the obtained silylated heterocycles with electrophiles under fluoride ion conditions afford an easy functionalization of such molecules.

Keywords Fluoride ion; organosilanes; stereoselectivity; thiaheterocycles

INTRODUCTION

1,3-Dithiane anions have been extensively used in the past decades as masked acyl carbanions in umpolung reactivity, and have had substantial effects on synthetic organic chemistry.[1] In contrast, treatment with bases of 1,3-dithiolanes has been reported to lead to either deprotonation at C-2 with subsequent cycloelimination to dithiocarboxylate anions and ethylene derivatives[2] or at C-4 to afford products derived from thiocarbonyl derivatives and vinyl thiolate anion.[3] Such behavior prevented the possibility of further functionalization of the dithiolane moiety and consequently its use in umpolung reactivity. Although in fact two examples of functionalization under basic conditions of dithiolanes bearing an electron-withdrawing group are reported in the literature, a general protocol for their functionalization is still lacking.[4]

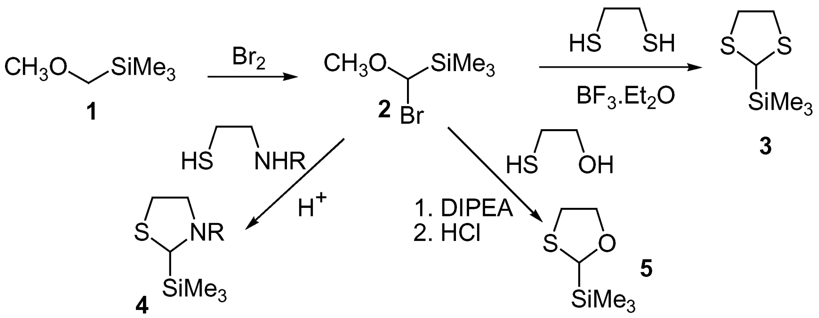
Received July 9, 2004; accepted October 5, 2004.

Address correspondence to Alessandro Degl'Innocenti, Dipartimento di Chimica Organica, Università di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino, Italy. E-mail: alessandro.deglinnocenti@unifi.it

RESULTS AND DISCUSSION

Our interest in the synthesis and the reactivity of organosilanes, in connection with the very mild functionalization conditions of the carbon-silicon bond under fluoride ion catalysis,[5] led us to point our attention to 2-trimethylsilyl-1,3-dithiolane as a possible masked dithiolane anion.

Because direct functionalization of the parent 1,3-dithiolane under basic conditions was prevented, an alternative access to the molecule had to be devised, and we found that a very convenient way to access the molecule was through the reaction of bromo(methoxy)methyltrimethylsilane **2**, easily obtainable by bromination of methoxy methyltrimethylsilane **1** (Scheme 1).[6]



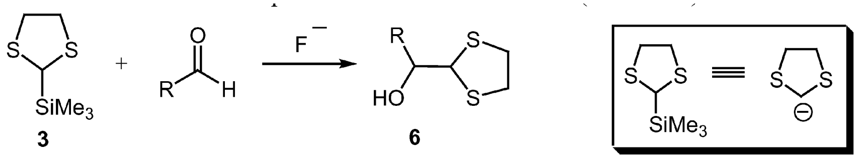
SCHEME 1

Such methodology proved rather interesting for its generality, and can lead to the synthesis, besides silylated dithiolanes **3**, of a wide variety of silylated heterocycles, such as thiazolidines **4**, oxathiolanes **5**, and oxazolidines, thus outlining a general procedure to access silylated five-membered heterocycles (Scheme 1).

Then, taking advantage of the well-known reactivity of organosilanes under fluoride ion catalysis, we evaluated the possibility of dithiolane functionalization in such conditions. Thus, when the silyl dithiolane **3** is treated with aldehydes in the presence of different fluoride ion sources (TBAF, TBAT, TASF), a smooth reaction occurs, leading to the corresponding functionalized α-hydroxy dithiolane **6**, so disclosing the possibility of an effective transfer of a "dithiolane anion" onto electrophiles under mild conditions (Scheme 2).[6]

This reaction appears quite general and occurs with aromatic, heteroaromatic, aliphatic, and α,β-unsaturated aldehydes.

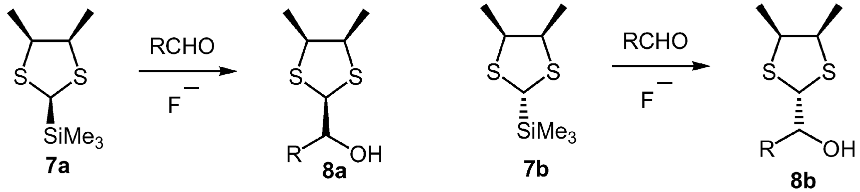
In this context, because fluoride-initiated protodesilylation of organosilanes has been shown to occur with retention of configuration,[7] we became interested in the reactivity of substituted silyldithiolanes.



3 **6**

SCHEME 2

Thus, reaction of *cis* and *trans* 4,5-dimethyl-2-trimethylsilyl-1,3-dithiolanes **7a,b** with benzaldehyde as a typical electrophile, in the presence of TBAF or CsF, afforded, as expected, the corresponding adducts in good yields (Scheme 3),[8] and with complete retention of the configuration of C-2.



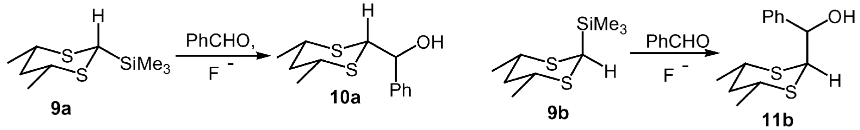
7a **8a** **7b** **8b**

SCHEME 3

These findings disclose a novel example of functionalization of a C—Si to a new C—C bond, with retention of configuration. They appear particularly interesting, taking into account that, with the exception of allylsilanes,[9] there are only a few cases of stereoselective synthetic transformations of sp^3 carbon-silicon bonds to carbon-carbon bonds.

On the other hand, it is firmly established that metallation of 1,3-dithianes[10] and 1,3-diselenanes[11] occurs regioselectively at C-2 at the equatorial rather than the axial hydrogen, and that their metallo derivatives lead, upon reaction with electrophiles, to products bearing the incoming group invariably at the equatorial position, whatever the other substituent eventually present at C-2.

On the contrary, when applied to substituted dithianes, the present methodology again led to the stereoselective synthesis of the axially or equatorially functionalized system (Scheme 4).[8] This result outlines for the first time an axial-oriented substitution on dithiane systems.



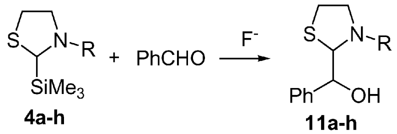
9a **10a** **9b** **11b**

SCHEME 4

These results give further experimental evidence to the notion that these reactions proceed through hypervalent silicon species and not free carbanions.

The obtained results can be extended as well to even more interesting heterocycles such as thiazolidines and oxathiolanes. Despite the utility of the thiazolidine moiety, very few methodologies for the functionalization of position 2 of the heterocyclic ring exist. Only two reports, to the best of our knowledge, deal with such functionalization, and their efficiency seems related to the presence of specific *N*-protecting groups.[12]

Thus we moved to the evaluation of the possible functionalization of the so-obtained silyl thiazolidines, and when compound **4a** was reacted with benzaldehyde, in the presence of the fluoride ion, a smooth reaction occurred, leading to the corresponding functionalized α-hydroxy thiazolidine **11a** in 52% yield, and so disclosed a clean and mild functionalization of the heterocyclic ring and the generation of a novel class of acyl anion synthons (Scheme 5).[13]



	R		R
a	CH_3SO_2	e	PhCH=CHCO
b	p-$CH_3C_6H_4SO_2$	f	BOC
c	CH_3CO	g	Cbz
d	PhCO	h	o-$(CHO)C_6H_4CO$

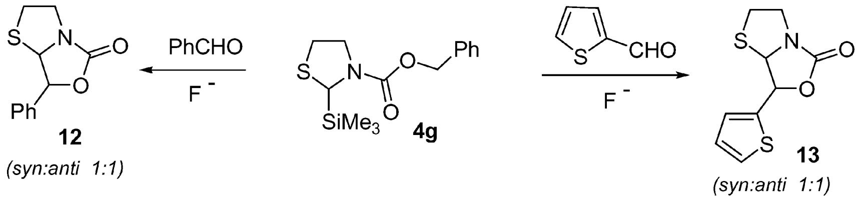
SCHEME 5

The reactivity seemed rather general, and occurred smoothly in the presence of different *N*-protecting groups such as tosyl, mesyl, acetyl, and BOC (*N*-tart-butoxy carbonyl). No reaction was observed when the protecting groups were benzoyl and cinnamoyl, but only the desilylated thiazolidine was recovered from the reaction mixture.

While compounds **4a**,**c** afforded the adducts as mixtures of diastereomers, compound **4b** showed a 20% diastereomeric excess (de), but much more interestingly, the reaction of **4f** both with benzaldehyde and thienylaldehyde afforded, as estimated from the nuclear magnetic resonance (NMR) of the crude reaction mixture, only a single diastereomer, thus evidencing a possible application of the present reaction in diastereoselective synthesis.

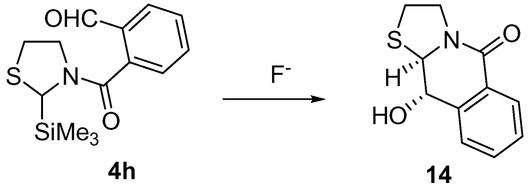
A different behavior was observed when the protecting group was Cbz. In fact, in that case, under the same experimental conditions, a clean cyclization to oxazolidinones **12** and **13** was observed (Scheme 6).[13]

The versatility of the present methodology is further illustrated by another example. When the protecting group itself contains an



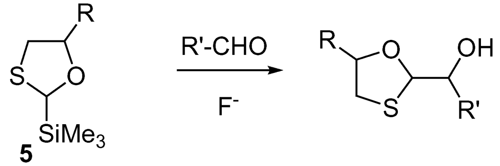
SCHEME 6

electrophilic center, a clean cyclization occurs, leading in good yields to policyclic compounds. Thus, when reacting *N*-*o*-formylbenzoyl-2-trimethylsilylthiazolidine **4h** with fluoride ion, the polycyclic compound **14** can be isolated in very good yield and with an interesting de of 70% (Scheme 7).



SCHEME 7

Finally, differently substituted oxathiolanes **5** can also be efficiently functionalized by taking advantage of the present methodology (Scheme 8).



SCHEME 8

In conclusion, the fluoride ion-based methodology of the carbon-silicon bond functionalization offers a simple and mild strategy for the functionalization of position 2 of a wide series of heterocycles, and opens interesting new perspectives in their synthetic applications.

REFERENCES

[1] D. Seebach, *Synthesis*, **17** (1969); D. Seebach and E. J. Corey, *J. Org. Chem.*, **40,** 231 (1975); P. C. Bulman Page, M. B. van Niel, and J. C. Prodger, *Tetrahedron*, **45,** 7643 (1989).

[2] T. Oida, S. Tanimoto, H. Terao, and M. Okano, *J. Chem. Soc., Perkin Trans. 1,* 1715 (1986).

[3] S. R. Wilson, G. M. Georgiadis, H. N. Khatri, and J. E. Bartmess, *J. Am. Chem. Soc.*, **102,** 3577 (1980); S. R. Wilson, P. Caldera, and M. A. Jester, *J. Org. Chem.*, **47,** 3319 (1982).

[4] H. Paulsen, W. Koebernick, and H. Koebernick, *Tetrahedron Lett.*, **27,** 2297 (1976); M. Yamashita and R. Suemitsu, *J. Chem. Soc., Chem. Commun.*, 691 (1977).

[5] A. Capperucci, A. Degl'Innocenti, P. Metzner, L. Bartoletti, and C. Checcacci, *Phosphorus, Sulfur Silicon Relat. Elem.*, **120–121,** 333–334 (1997); A. Capperucci, A. Degl'Innocenti, and P. Scafato, *Recent Res. Devel. in Synth. Organic Chem.*, **1,** 171–197 (1998); A. Degl'Innocenti and A. Capperucci, *Eur. J. Org. Chem.*, 2171 (2000).

[6] A. Capperucci, A. Degl'Innocenti, and T. Nocentini, *Tetrahedron Lett.*, **42,** 4557 (2001).

[7] See T. H. Chan, P. W. K. Lau, and M. P. Li, *Tetrahedron Lett.*, **27,** 2667 (1976).

[8] A. Capperucci, V. Ceré, A. Degl'Innocenti, T. Nocentini, and S. Pollicino, *Synlett.*, 1447 (2002).

[9] S. E. Denmark and N. G. Almstead, *J. Org. Chem.*, **59,** 5130 (1994); R. Corriu, *Pure Appl. Chem.*, **60,** 99 (1988); T. H. Chan and I. Fleming, *Synthesis*, 761 (1979).

[10] A. A. Hartmann and E. L. Eliel, *J. Am. Chem. Soc.*, **93,** 2572 (1971); E. Eliel, A. G. Abatjoglou, and A. A. Hartmann, *J. Am. Chem. Soc.*, **94,** 4786 (1972); E. L. Eliel, A. A. Hartmann, and A. G. Abatjoglou, *J. Am. Chem. Soc.*, **96,** 1807 (1974); E. L. Eliel, *Tetrahedron*, **30,** 1503 (1974); A. G. Abatjoglou, E. L. Eliel, and L. F. Kuyper, *J. Am. Chem. Soc.*, **99,** 8262 (1977).

[11] A. Krief and L. Defrere, *Tetrahedron Lett.*, **37,** 2667. (1996); A. Krief and L. Defrere, *Tetrahedron Lett.*, **37,** 8011 (1996).

[12] A. I. Meyers, P. D. Edwards, W. F. Rieker, and T. R Bailey, *J. Am. Chem. Soc.*, **106,** 3270 (1984); R. E. Gawley, Q. Zhang, and A. T. McPhail, *Tetrahedron: Asymmetry*, **11,** 2093 (2000).

[13] A. Capperucci, A. Degl'Innocenti, T. Nocentini, A. Mordini, S. Biondi, and F. Dini, *Letters in Organic Chemistry*, **1,** 55–58 (2004).