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2-Trimethylsilyl-1,3-dithiolane as a masked dithiolane anion

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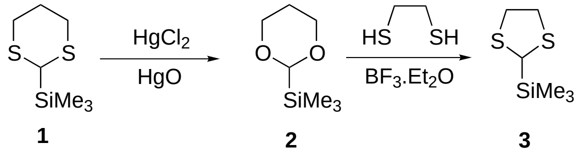
Abstract—2-Trimethylsilyl-1,3-dithiolane, easily obtainable through transthioacetalization of corresponding silylated acetals, can be efficiently reacted, under fluoride-ion catalysis, with different organic electrophiles, leading to a general and mild functionalization protocol. This reactivity discloses the ability of compound **3** to act as a masked dithiolane anion. © 2001 Elsevier Science Ltd. All rights reserved.

1,3-Dithiane anions have been extensively used in the last decades as masked acyl carbanions in umpolung reactivity, and have had substantial impact on synthetic organic chemistry.[1] In contrast, 1,3-dithiolanes, upon treatment with bases, have been reported to undergo 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] thus preventing the possibility of further functionalization of the dithiolane moiety and consequently their 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, there is still the need for a general protocol for their functionalization.[4]

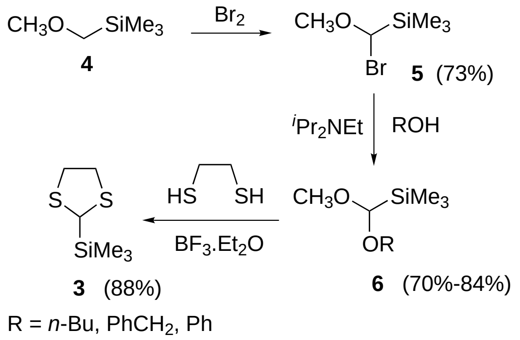
Our interest in the synthesis and the reactivity of organosilanes, in connection with the very mild functionalization conditions of the carbon–silicon bond under fluoride-ion catalysis,[5] led us to point our attention to 2-trimethylsilyl-1,3-dithiolane, as a possible masked dithiolane anion.

Direct functionalization of the parent 1,3-dithiolane under basic conditions being prevented, an alternative access to such molecule had to be devised. We envisaged the transthioacetalization reaction of 2-trimethylsilyl-1,3-dioxane **2**, in turn obtained by reaction of the silyl dithiane **1** with 1,3-propanediol in the presence of Hg^{2+} salts, with ethanedithiol, under BF_3 catalysis[6] as a possible way to access dithiolane **3** (Scheme 1). This procedure was indeed able to afford for the first time the desired molecule, albeit in an unsatisfactory yield, due to the poor conversion of the silyl dithiane **1** into the corresponding silylated 1,3-dioxane **2**.

To overcome these problems an alternative procedure has been devised, through bromination of methoxymethyltrimethylsilane **4**,[7] followed by reaction with alcohols or phenols, to afford the open chain acetals **6**, which can then be efficiently subjected to $BF_3 \cdot Et_2O$-catalyzed transthioacetalization to the desired compound (Scheme 2).[8]



Scheme 1.



Scheme 2.

Keywords: organosilanes; dithiolanes; fluoride-ion catalysis; hydroxyaldehydes.

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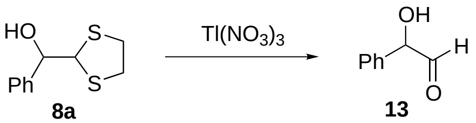
Then, taking advantage of the well-known reactivity of organosilanes under fluoride-ion catalysis, we evaluated the possibility of dithiolane functionalization in such conditions.

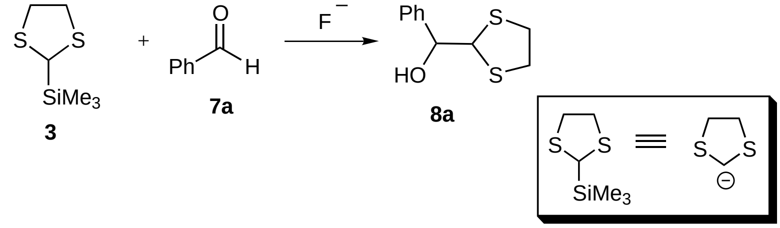
Thus, when the silyl dithiolane **3** is treated with benzaldehyde in the presence of different sources of fluoride ion (TBAF, TBAT, TASF), a smooth reaction occurs, leading to the corresponding functionalized α-hydroxy dithiolane **8a** (together with desilylated dithiolane, ca. 20%), so disclosing the possibility of an effective transfer of a 'dithiolane anion' onto electrophiles under mild conditions (Scheme 3).[9] This reactivity appears not to be restricted to benzaldehyde **7a**, but may be conveniently extended to aliphatic **7g**, heteroaromatic **7c**,**d** and α,β-unsaturated aldehydes **7e**,**f**, affording in all cases protected α-hydroxy aldehydes. The low yields observed for **7d** may be attributed to steric hindrance of the *N*-methyl group. Reactive halo derivatives such as allyl bromide **11** and methyl vinyl ketone **9** will undergo reaction as well. With α,β-unsaturated aldehydes **7e** and **7f** only 1,2-adducts have been isolated, whereas reaction with methyl vinyl ketone **9** afforded a 3:1 mixture of 1,2- and 1,4-adducts (**10a** and **10b**, respectively). Examples of this reactivity are summarized in Table 1.

Furthermore, the hydroxydithiolanes obtained can be easily and efficiently transformed into hydroxy aldehydes **13** upon treatment with $Tl(NO_3)_3$, as shown in Scheme 4,[10] thus disclosing a novel synthetic route to an interesting class of compounds.



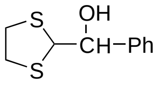
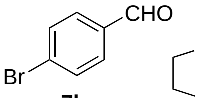
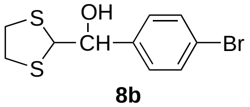
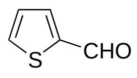
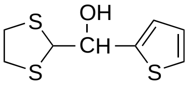
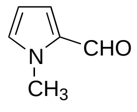
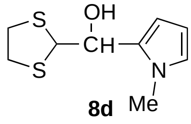
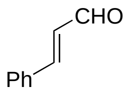
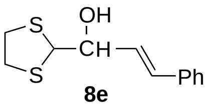
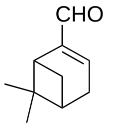
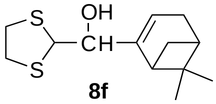
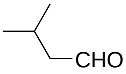
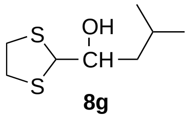
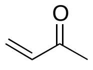
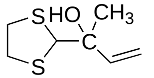
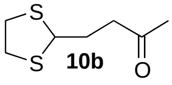
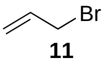
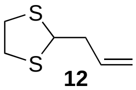
8a **13**

Scheme 4.



Scheme 3.

Table 1.

Aldehyde	Product	Yield (%)[a,b]
Ph-CHO **7a**	 **8a**	79
 **7b**	 **8b**	78
 **7c**	 **8c**	83
 **7d**	 **8d**	12
 **7e**	 **8e**	81
 **7f**	 **8f**	24
 **7g**	 **8g**	80
 **9**	 **10a**  **10b**	30[c]
 **11**	 **12**	30

[a] Yields refer to chromatographically pure material. [b] All spectroscopic and analytical data were consistent with the assigned structure. [c] 3 : 1 mixture of 1,2 : 1,4 adducts.

In conclusion we have presented a novel protocol for the generation of unreported 2-trimethylsilyl-1,3-dithiolane **3**, whose fluoride-ion-catalyzed reactivity allows the development of an efficient and mild protocol for the general functionalization of the dithiolane moiety. These results show that, under the present conditions, **3** can behave as a masked dithiolane anion. Further work in this direction is currently underway in our laboratory.

References

1. (a) Seebach, D. *Synthesis* **1969**, 17; (b) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231; (c) Bulman Page, P. C.; van Niel, M. B.; Prodger, J. C. *Tetrahedron* **1989**, *45*, 7643.
2. Oida, T.; Tanimoto, S.; Terao, H.; Okano, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1715.
3. (a) Wilson, S. R.; Georgiadis, G. M.; Khatri, H. N.; Bartmess, J. E. *J. Am. Chem. Soc.* **1980**, *102*, 3577; (b) Wilson, S. R.; Caldera, P.; Jester, M. A. *J. Org. Chem.* **1982**, *47*, 3319.
4. (a) Paulsen, H.; Koebernick, W.; Koebernick, H. *Tetrahedron Lett.* **1976**, *27*, 2297; (b) Yamashita, M.; Suemitsu, R. *J. Chem. Soc., Chem. Commun.* **1977**, 691.
5. (a) Capperucci, A.; Degl'Innocenti, A.; Metzner, P.; Bartoletti, L.; Checcacci, C. *Phosphorus Sulfur Silicon* **1997**, *120–121*, 333–334; (b) Capperucci, A.; Degl'Innocenti, A.; Scafato, P. *Recent Res. Devel. Synth. Org. Chem.* **1998**, *1*, 171–197; (c) Degl'Innocenti, A.; Capperucci, A. *Eur. J. Org. Chem.* **2000**, 2171.
6. *Spectroscopic data of 2-trimethylsilyl-1,3-dithiolane **3***: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.18 (s, 9H), 3.06–3.29 (m, 4H), 3.53 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ −2.3, 37.6, 39.4. MS *m*/*z* (%): 178 (M^+, 51), 150 (74), 135 (98), 105 (84), 91 (34), 77 (68), 75 (69), 73 (100), 59 (88).
7. Christiansen, M. L.; Benneche, T.; Undheim, K. *Acta Chem. Scand. Ser. B* **1987**, *40*, 536.
8. Recent results show that **3** can also be efficiently obtained from **5** under basic conditions.
9. *Typical procedure:* To a solution of 88 mg (0.28 mmol) of anhydrous TBAF (dried over 250 mg of activated molecular sieves 4 Å, following Majetich's procedure[11]), in 1.5 mL of dry DMF, a solution of benzaldehyde (0.28 mmol, 28 μL) and 2-trimethylsilyl-1,3-dithiolane (50 mg, 0.28 mmol) in 1 ml of dry DMF was added at room temperature, under an inert atmosphere. The reaction was monitored by GC/MS, then the mixture was diluted with diethyl ether, washed with water, brine and dried over Na_2SO_4. Purification by TLC (hexanes/ethyl acetate 5:1) afforded 47 mg of pure product **8a** (79%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.14–3.32 (m, 4H), 4.62 (d, 1H, $J=7.0$ Hz), 4.79 (d, 1H, $J=7.0$ Hz), 7.30–7.46 (m, 5H). MS *m*/*z* (%): 135 (M^+−77, 0.5), 107 (18), 105 (100), 79 (15), 77 (22). Reaction with TBAT as catalyst gave comparable results.
10. *Typical procedure*. To a solution of (1,3-dithiolane-2-yl)-phenyl methanol **8a** (15 mg, 0.071 mmol) in 0.5 ml of THF was added at room temperature, under an inert atmosphere, 31 mg (0.071 mmol) of $Tl(NO_3)_3 \cdot 3H_2O$ in 1 mL of methanol. After 5 min a white precipitate was formed, then the reaction mixture was treated with diethyl ether, washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvent afforded 7.2 mg of product **13** (75%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.24 (s, 1H), 7.31–7.43 (m, 5H), 9.64 (s, 1H). MS *m*/*z* (%): 136 (M^+, 3), 105 (91), 77 (100), 51 (73). Upon standing, partial dimerization of the α-hydroxyaldehyde was observed. ^{1}H NMR of the dimer ($CDCl_3$): δ 4.30 (d, 2H, $J=6.4$ Hz), 4.62 (d, 2H, $J=6.4$ Hz), 7.28–7.40 (m, 10).
11. Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745.