Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 2831–2835

TETRAHEDRON LETTERS

An easy access to α,β-unsaturated thioacylsilanes: a useful route to silylated 1,2-dithiins

Antonella Capperucci,* Alessandro Degl'Innocenti,* Simona Biondi, Tiziano Nocentini and Giuseppe Rinaudo

Dipartimento di Chimica Organica, ICCOM, via della Lastruccia 13, I-50019 Sesto Fiorentino (FI), Italy

Received 17 December 2002; revised 10 February 2003; accepted 17 February 2003

Abstract—Treatment of different silylated allenes with hexamethyldisilathiane (HMDST) in the presence of $CoCl_2 \cdot 6H_2O$ affords an easy and high yielding access to α,β-unsaturated thioacylsilanes, which undergo a self-dimerization reaction to afford polyfunctionalized 1,2-dithiins as the major products.

Acylsilanes are well-known compounds that have been shown to be useful as 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 enol-ethers,[2] diastereoselective aldol condensations,[3] the synthesis of β-hydroxysilanes[4] and the stereoselective synthesis of vinylsilanes[5] are just a few examples of their valuable reactivity.

The presence of a double bond together with the acylsilane moiety provides an expansion of acylsilane synthetic potentialities, and opens the way to the possible construction of novel and more versatile synthons.

In this context, ethylenic and acetylenic acylsilanes[6] have recently emerged as versatile intermediates, due to the high reactivity of the unsaturated moiety: such compounds may in fact participate in $TiCl_4$ promoted allylations,[7] 1,4-additions with silylated nucleophiles[8] or act as dienophiles in Diels–Alder reactions,[6] and [1,3]-dipolar cycloadditions.[9] [3+2] Annulations with allenylsilanes[9] and with ketone enolates[10] have also been reported, together with [3+4] annulations with α,β-unsaturated methyl ketone enolates.[11]

On the other hand, thiocarbonyl containing molecules have recently experienced an increasing interest in modern organic synthesis, due to the fact that such compounds have shown to be as key intermediates in the synthesis of molecules with high biological activity, and relevant complexity.[12]

In this context, thioacylsilanes appeared as very attractive molecules, because they couple the high reactivity of the carbon–sulfur double bond with the peculiar reactivity of organosilanes, thus enabling the synthesis of various products containing the Si–C–S unit. Moreover, thioacylsilanes can serve as synthetic equivalents of thioaldehydes through a simple protodesilylation reaction.

Thioacylsilanes have been widely investigated by the Bonini group,[13] and can be accessed, among the various methods described in the literature, through the acid-catalyzed reaction of acylsilanes with hydrogen sulfide,[13a] or through the $CoCl_2 \cdot 6H_2O$ catalyzed reaction of bis(trimethylsilyl)sulfide (HMDST).[14] Nevertheless such procedures cannot be applied to the synthesis of α,β-unsaturated thioacylsilanes, and in general, α,β-unsaturated thiocarbonyls have always been difficult to synthetize directly, this often being due to competing Michael additions. Some success has been obtained in the case of ethylenic β-substituted parent carbonyls,[15] or in the presence of a stabilizing group.[16]

Our long dating interest in the chemistry of acylsilanes,[1a,17] and, more recently, in the synthesis of thiocarbonyl containing compounds,[15c,18] led us recently to uncover a simple and general access to a particular class of thioacylsilanes, namely acetylenic thioacylsilanes, through our recently developed hexamethyldisilathiane based thionation procedure[18d] of carbonyl compounds, which, due to its intrinsic mildness, proved to be well suited for the synthesis of such compounds.

* Corresponding authors. Tel.: +39-055-457-3551; fax: +39-055-457-3531; e-mail: alessandro.deglinnocenti@unifi.it

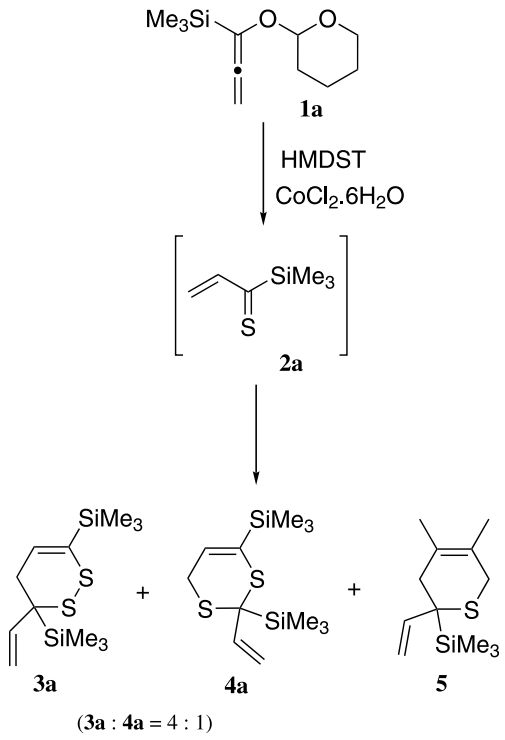
0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00445-3

We were then attracted by the possibility of creating a general access also to another class of difficult to obtain thioacylsilanes, ethylenic thioacylsilanes. As expected, the HMDST based thionation procedure, when applied directly to the parent α,β-unsaturated acylsilanes, showed again the already mentioned limitations.

Thus we had to devise a different access to such molecules, and we reasoned that, being unsaturated acylsilanes obtainable through the hydrolysis of the corresponding silylated allenes, the same reaction could hold in the presence of HMDST to afford the wanted α,β-ethylenic silyl thioketones.

Thus, we reacted 1-trimethylsilyl-1-tetrahydropyranyl-1,2-propadiene **1a** with HMDST in the presence of $CoCl_2 \cdot 6H_2O$ and 2,3-dimethyl-1,3-butadiene[19] (Scheme 1), and we were quite pleased to recover from the reaction mixture compounds **3a** and **4a** (in the ratio **3a**:**4a** = 4:1), together with a small amount of **5** (<5%), thus evidencing the formation of the thiopropenoylsilane intermediate **2a**, which undergoes preferably self-dimerization reactions, thus confirming the tendency of such molecules to behave as thiabutadienes with reactive dienophiles in hetero Diels–Alder reactions.[20]

Nevertheless, this reaction proved that allenes can be efficiently used as precursors of unsubstituted unsaturated thioacylsilanes. Furthermore, although thiopropenoylsilane can be considered a synthetic equivalent of thioacrolein, the regiochemical outcome of the present reaction proved to be quite different, affording as the predominant compound the head-to-head dimer **3a** instead of the 1,3-dithiin **4a**, usually obtained as the largely predominant isomer upon generation of thioacrolein.[15e] This result is rather interesting if we take into account that the biological importance of the disulfide bridge is widely recognized, being one of the two major covalent linkages between amino acids in polypeptides and proteins.[15e]



Scheme 1.

This methodology then opens a useful route to polyfunctionalized 1,2-dithiins. Furthermore, the presence in the obtained molecules of both the allylsilane and the vinylsilane moieties envisages the possibility of further selective functionalization.

The reaction proved quite general, occurring smoothly with several differently silylated allenes, as summarized in Table 1. In the case of the triphenyl substituted allene **1g**, no traces of the self-dimerization compound were found, but only oligomers, this is probably due to the very large steric hindrance of the silyl moiety.

Worth noting is the very high regioselectivity observed in these cycloadditions, being 1,2-dithiins formed predominantly (Table 1, entries 1, 2 and 4) or exclusively (Table 1, entries 3, 5–8). Thus, the ratio **3**:**4** was 80:20 for the trimethylsilyl allene **1a**, 97:3 for **1b** and 98:2 for **1d**. On the other hand, no traces of compound **4** were found in the reactions of allenes **1c** and **1f–h**.

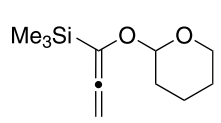
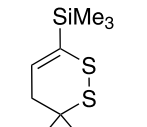
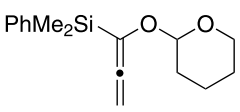
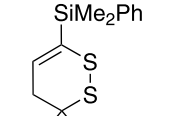
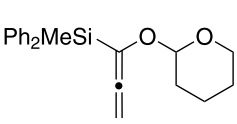
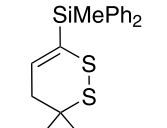
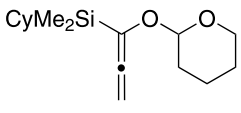
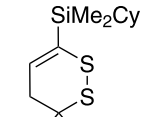
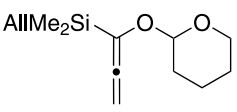
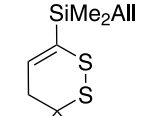
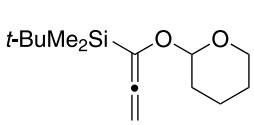
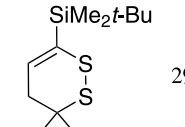
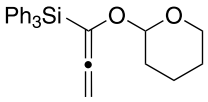
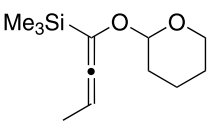
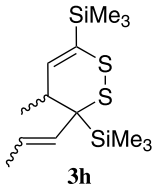
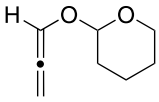
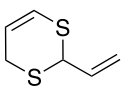
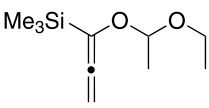
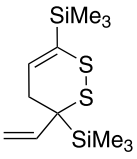
Interestingly, when the reaction was performed on compound **1i**, again the formation of the self-dimerization products was observed, but this time the ratio 1,2-dithiin:1,3-dithiin (ca. 1:6, respectively) was quite similar to what was observed by other authors,[15e] thus evidencing the importance of the silyl moiety in driving the regiochemical outcome of the reaction. It is also noteworthy that in the case of allene **1e** the allylsilane moiety is not involved at all, thus giving further proof of the mildness and versatility of such procedure.

In contrast to the observations of Segi[15e] and other authors,[20] our ethylenic thioacylsilanes did not react as thiabutadienes in hetero Diels–Alder reactions with different alkenes: thus in fact, upon generating silyl thioketones in the presence of norbornadiene, maleic anhydride or vinyl ethers, no traces of the corresponding adducts were obtained.

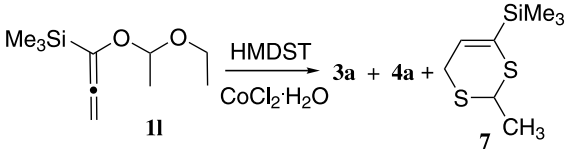
Another interesting observation was made in the reaction of compound **1l** in which, besides the expected self-dimerization products **3a** and **4a**, compound **7** was also found,[21] which seems to arise from a [4+2] cycloaddition reaction of propenoylthioacylsilane **2a** with the in situ formed thioacetaldehyde (Scheme 2).

This result proves quite interesting and represents the first example of a cycloaddition reaction between two different thiocarbonyl compounds, one behaving as a 4π diene and the other as a 2π dienophile. Furthermore, taking into consideration that alkanethials are quite

Table 1. Thionation of silylated allenes

Entry	Allene	Product	Yield[a,b] (%)
1	 **1a**	 **3a**	65[c]
2	 **1b**	 **3b**	59[d]
3	 **1c**	 **3c**	36
4	 **1d**	 **3d**	42[d]
5	 **1e**	 **3e**	45
6	 **1f**	 **3a**	29
7	 **1g**	— [e]	—
8	 **1h**	 **3h**	57[f]
9	 **1i**	 **6**	64[g]
10	 **1l**	 **3a**	57[d,h]

[a]Yield of isolated product.
[b]All compounds showed spectroscopical and analytical data consistent with the assigned structure.
[c]16% of 1,3-dithiin **4a** was isolated.
[d]2-3% of the corresponding 1,3-dithiin (**4**) was detected in the crude.
[e]Oligomers of thiopropenoyltriphenylsilane were isolated.
[f]A mixture of stereoisomers was obtained.
[g]1,2-dithiin was obtained as minor regioisomer (ca.10%). Yield determin ed by ^{1}H NMR.
[h]1,3-dithiin **7** was isolated (30%).



Scheme 2.

reluctant to Diels–Alder reactions,[18a] it outlines the very good qualities of propenoylthioacylsilane as a very powerful diene.

In conclusion, we have devised a general methodology for the synthesis of thiopropenoylsilanes, which afford upon self-dimerization a general and regioselective access to silylated 1,2-dithiins.

Acknowledgements

The authors gratefully acknowledge Mrs Brunella Innocenti for carrying out elemental analyses.

References

1. (a) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647; (b) Bulman-Page, P. C.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147; (c) Cirillo, P. F.; Panek, J. S. *Org. Prep. Proc. Int.* **1992**, *24*, 553; (d) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A. *J. Organomet. Chem.* **1998**, *567*, 181.
2. Ager, D. *J. Chem. Soc. Rev.* **1982**, *11*, 493.
3. Schinzer, D. *Synthesis* **1989**, 179.
4. Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981; p. 274.
5. Soderquist, J. A.; Anderson, C. L. *Tetrahedron Lett.* **1988**, *29*, 2425.
6. (a) Hassner, A.; Soderquist, J. A. *J. Organomet. Chem.* **1977**, *131*, C1; (b) Soderquist, J. A.; Hassner, A. *J. Am. Chem. Soc.* **1980**, *102*, 1577; (c) Reich, H. J.; Kelly, M. J. *J. Am. Chem. Soc.* **1982**, *104*, 1119; (d) Reich, H. J.; Kelly, M. J.; Olson, R. E.; Holtan, R. C. *Tetrahedron* **1983**, *39*, 949; (e) Reich, H. J.; Eisenhart, E. K.; Olson, R. E.; Kelly, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 7791; (f) Nowick, J. S.; Danheiser, R. L. *J. Org. Chem.* **1989**, *54*, 2798; (g) Tius, M. A.; Stergiades, I. A. *J. Org. Chem.* **1999**, *64*, 7547 and references cited therein.
7. Danheiser, R. L.; Fink, D. M. *Tetrahedron Lett.* **1985**, *26*, 2509.
8. (a) Ricci, A.; Degl'Innocenti, A.; Borselli, G.; Reginato, G. *Tetrahedron Lett.* **1987**, *28*, 4093; (b) Degl'Innocenti, A.; Capperucci, A.; Mordini, A.; Ricci, A.; Reginato, G. *Tetrahedron Lett.* **1992**, *33*, 1507.
9. Danheiser, R. L.; Fink, D. M. *Tetrahedron Lett.* **1985**, *26*, 2513.
10. (a) Takeda, K.; Fujisawa, M.; Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc.* **1993**, *115*, 9351; (b) Takeda, K.; Nakajima, A.; Yoshii, E. *Synlett* **1997**, 255.
11. (a) Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E. *J. Am. Chem. Soc.* **1995**, *117*, 6400; (b) Takeda, K.; Nakajima, A.; Takeda, M.; Okamoto, Y.; Sato, T.; Yoshii, E.; Koizumi, T.; Shiro, M. *J. Am. Chem. Soc.* **1998**, *120*, 4947.
12. (a) Ireland, R. E.; Brown, F. R., Jr. *J. Org. Chem.* **1980**, *45*, 1868; (b) Tamaru, Y.; Harada, T.; Yoshida, Z.-I. *J. Am. Chem. Soc.* **1980**, *102*, 2392; (c) Vedejs, E.; Wittemberger, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 4357 and references cited therein; (d) Ichimori, K.; Stuehr, D. J.; Atkinson, R. N.; King, S. B. *J. Med. Chem.* **1999**, *42*, 1842 and references cited therein.
13. (a) Bonini, B. F.; Fochi, M. *Rev. Heteroat. Chem.* **1997**, *16*, 47 and references cited therein; (b) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A.; Varchi, G. *Tetrahedron Lett.* **1999**, *40*, 6473; (c) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A.; Tomasulo, M.; Varchi, G. *J. Organomet. Chem.* **2001**, *637–639*, 407.
14. (a) Ricci, A.; Degl'Innocenti, A.; Capperucci, A.; Reginato, G. *J. Org. Chem.* **1989**, *54*, 19; (b) Degl'Innocenti, A.; Scafato, P.; Capperucci, A.; Bartoletti, L.; Spezzacatena, C.; Ruzziconi, R. *Synlett* **1997**, 361; (c) Degl'Innocenti, A.; Capperucci, A.; Oniciu, D. C.; Katritzky, A. R. *J. Org. Chem.* **2000**, *65*, 9206.
15. (a) Metzner, P.; Vialle, J. *Bull. Soc. Chim. Fr.* **1972**, 3138 and references cited therein; (b) Usov, V. A.; Korchevin, N. A.; Tselin, Y. S.; Voronkov, M. G. *Zh. Org. Khim.* **1975**, *11*, 410; (c) Degl'Innocenti, A.; Capperucci, A.; Mordini, A.; Reginato, G.; Ricci, A.; Cerreta, F. *Tetrahedron Lett.* **1993**, *34*, 873; (d) Briard, E.; Dat, Y.; Levillain, J.; Ripoll, J.-L. *Tetrahedron Lett.* **1997**, *38*, 8707; (e) Li, G. M.; Niu, S.; Segi, M.; Tanaka, K.; Nakajima, T.; Zingaro, R. A.; Reibenspies, J. H.; Hall, M. B. *J. Org. Chem.* **2000**, *65*, 6601 and references cited therein.
16. (a) Muraoka, M.; Yamamoto, T.; Enomoto, K. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1241 and references cited therein; (b) Kim, B. S.; Kim, K. *J. Org. Chem.* **2000**, *65*, 3690.
17. Capperucci, A.; Degl'Innocenti, A.; Dondoli, P.; Nocentini, T.; Reginato, G.; Ricci, A. *Tetrahedron* **2001**, *57*, 6267 and references cited therein.
18. (a) Capperucci, A.; Degl'Innocenti, A.; Ricci, A.; Mordini, A.; Reginato, G. *J. Org. Chem.* **1991**, *56*, 7323; (b) Capperucci, A.; Degl'Innocenti, A.; Scafato, P.; Spagnolo, P. *Chem. Lett.* **1995**, 147; (c) Degl'Innocenti, A.; Capperucci, A.; Scafato, P.; Mecca, T.; Reginato, G.; Mordini, A. *Synlett* **1999**, 1739; (d) Degl'Innocenti, A.; Capperucci, A. *Eur. J. Org. Chem.* **2000**, 2171.
19. *Typical procedure*: A solution of 50 mg (0.24 mmol) of allene **1a** in 1 ml of CH_3CN was added under N_2 atmosphere with 98 μl (0.47 mmol) of HMDST and a solution of $CoCl_2 \cdot 6H_2O$ (57 mg, 0.24 mmol) in 1.5 ml of CH_3CN. The mixture was stirred at rt overnight, then diluted with diethyl ether, washed with water and dried over Na_2SO_4. Evaporation of the solvent afforded the crude product, which after purification on TLC (hexanes:diethyl ether, 30:1) gave 45 mg of **3a** (65%) and 11 mg of **4a** (16%). Isomer **3a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 0.11 (9H, s), 0.13 (9H, s), 2.34 (1H, dd, $J=5.8$ Hz, $J=19.4$ Hz), 2.66 (1H, dd, $J=2.2$ Hz, $J=19.4$ Hz), 4.80 (1H, d, $J=17.2$ Hz), 5.21 (1H, d, $J=10.2$ Hz), 5.87 (1H, dd, $J=17.2$ Hz, $J=10.2$ Hz), 6.17 (1H, dd, $J=2.2$ Hz, $J=5.8$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): −4.3, −1.8, 21.8, 27.9, 114.2, 116.5, 129.5, 137.9. MS m/z (%): 288 (1, M^+), 256 (1), 215 (1), 183 (2), 167 (5), 144 (1), 142 (1), 91 (3), 73 (100), 71 (3), 59 (5). Calcd for $C_{12}H_{24}S_2Si_2$: C, 49.94; H, 8.38. Found: C, 49.67; H, 8.57. Isomer **4a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 0.17 (9H, s), 0.19 (9H, s), 2.96 (1H, dd, $J=6.6$ Hz, $J=16.8$ Hz), 3.13 (1H, dd, $J=2.8$ Hz, $J=16.8$ Hz), 5.08 (1H, dd, $J=1.6$ Hz, $J=17.6$ Hz), 5.21 (1H, dd, $J=1.6$ Hz, $J=10.2$ Hz), 5.80 (1H, dd, $J=17.6$ Hz, $J=10.2$ Hz), 6.14 (1H, dd, $J=2.8$ Hz, $J=6.6$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): −4.3, −1.8, 21.8, 27.9, 116.5, 123.1, 134.9, 137.9. MS m/z (%): 288 (1, M^+), 256 (1), 183 (2), 167 (2), 144 (1), 92 (6), 84 (100), 73 (31), 59 (5). Calcd for $C_{12}H_{24}S_2Si_2$: C, 49.94; H, 8.38. Found: C, 49.70; H, 8.42.
20. (a) Karakasa, T.; Yamaguchi, H.; Motoki, S. *J. Org. Chem.* **1980**, *45*, 927; (b) Bock, H.; Mahmand, S.; Hirabayashi, T.; Semkow, A. *J. Am. Chem. Soc.* **1982**, *104*, 312; (c) Schaumann, E.; Ruther, G. *Tetrahedron Lett.* **1985**, 5265; (d) Glass, R. S.; Farooqui, F.; Sabahi, M.; Ehler, K. W. *J. Org. Chem.* **1989**, *54*, 1092; (e) Block, E.;

Zhao, S. H. *Tetrahedron Lett*. **1990**, *31*, 5003; (f) Marchand, A.; Mauger, D.; Guignant, A.; Pradère, J.-P. *Tetrahedron: Asymmetry* **1995**, *6*, 853; (g) Bell, A. S.; Fishwick, C. W. G.; Redd, J. E. *Tetrahedron Lett*. **1996**, *37*, 123; (h) Saito, T.; Nagashima, M.; Karakasa, T.; Motoki, S. *J. Chem. Soc., Chem. Commun*. **1999**, 1001.

21. Compound **7**: ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 0.15 (9H, s), 1.61 (3H, d, $J=7.0$ Hz), 3.29 (1H, dd, $J=17.6$ Hz, $J=6.2$ Hz), 3.56 (1H, dd, $J=17.6$ Hz, $J=3.2$ Hz), 4.21 (1H, q, $J=7.0$ Hz), 6.13 (1H, dd, $J=6.2$ Hz, $J=3.2$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): −1.8, 21.2, 28.7, 39.7, 122.1, 136.9. MS m/z (%): 204 (1, M^+), 189 (1), 144 (8), 116 (2), 91 (3), 73 (100), 71 (5), 59 (8). Calcd for $C_8H_{16}S_2Si$: C, 47.00; H, 7.89. Found: C, 46.77; H, 8.06.