

Thiophilic Allylation of Dithioesters and Trithiocarbonates

*Antonella Capperucci^a, Alessandro Degl'Innocenti^{a,b}, M. Cristiana Ferrara^a, Bianca F. Bonini^c,
Germana Mazzanti^c, Paolo Zani^c and Alfredo Ricci^{c,d}.*

^a*Dipartimento di Chimica Organica dell'Università, via G. Capponi 9, 50121 Firenze, Italy.*

^b*Dipartimento di Chimica, via N. Sauro 85, 85100 Potenza, Italy.*

^c*Dipartimento di Chimica Organica "A. Mangini", viale Risorgimento 4, 40136 Bologna, Italy.*

^d*Centro C.N.R. sulla Chimica e la Struttura dei Composti Eterociclici, via G. Capponi 9, 50121
Firenze, Italy.*

Abstract: Reaction of dithioesters and trithiocarbonates with silylated nucleophiles under fluoride ion conditions affords a novel example of silyl mediated regiochemical control in the thiophilic functionalization.

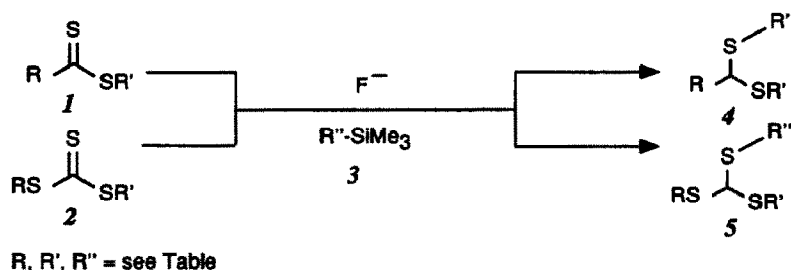
Thiocarbonyl compounds have recently emerged as useful synthetic intermediates, which have been demonstrated to play an important role in the synthesis of complex natural products¹.

Reactions of different organometallic species with thiocarbonyl compounds have been deeply investigated and have been shown to proceed both in a carbophilic or a thiophilic fashion. Although anyway a complex pattern appears in the reactions of thioketones with lithium or Grignard reagents², a more straightforward reactional behaviour has been encountered in the reactions of organometallic derivatives with dithioesters. Upon reaction of saturated Grignard reagents³ or PhLi² with these compounds a thiophilic attack is obtained, while the use of unsaturated Grignard reagents leads to products deriving from a carbophilic attack, which Thuillier and Masson⁴ have elegantly shown to occur, unlike thioketones⁵, through a direct carbophilic pathway.

We recently disclosed a novel fluoride ion induced reaction of allylsilanes with thioketones, that afforded in rather mild conditions, products deriving from thiophilic addition, thus showing a novel regiochemical control through the use of these organometallic compounds⁶. We were then interested in evaluating the effect of different heteroatoms on the C=S in this kind of regiochemical control.

We report in this communication on the reactivity of different allylsilanes and benzylsilane with some heterosubstituted thiocarbonyl derivatives, such as dithioesters and trithiocarbonates.

Upon reacting for instance different dithioesters *I* (R = Ph, biphenyl; R' = Ph, Et, Allyl) with



allylsilanes **3** in the presence of fluoride ion (see Table), a very clean reaction occurs, and the corresponding bis-sulfides **4** are isolated⁷. A limitation of this behaviour is found for ethyl dithioacetate, which in the same conditions affords a complex reaction mixture probably due to the presence of hydrogens α to the thiocarbonyl group.

Besides confirming the inversion of the regiochemistry of addition already observed in the case of thioketones⁶, these results outline a completely different reactional pathway to that observed with allylic Grignard reagents, pointing out how the use of allylsilanes then allows a direct access to allylic bis-sulfides.

This kind of reaction is not limited to dithioesters, but can be conveniently performed on both linear or cyclic trithiocarbonates such as **2a** and **2b**, thus offering a new entry to allylic tris-sulfides **5**.

It is interesting to note that products deriving from nucleophilic substitution of R'S- moiety⁸ in dithioesters have never been observed.

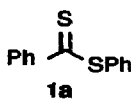
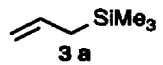
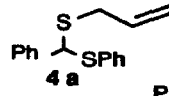
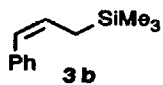
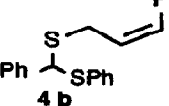
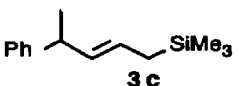
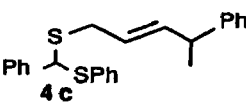
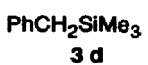
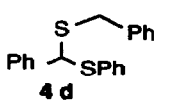
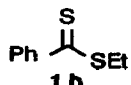
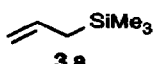
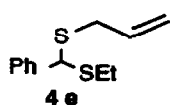
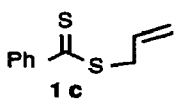
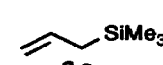
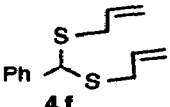
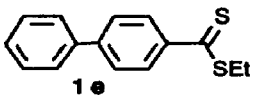
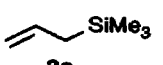
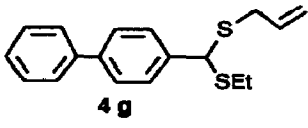
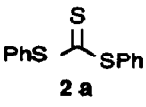
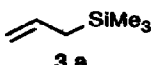
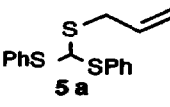
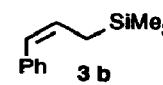
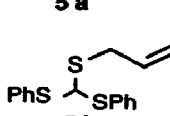
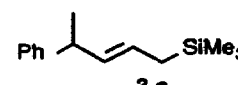
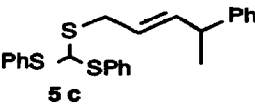
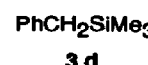
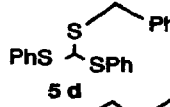
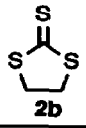
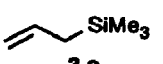
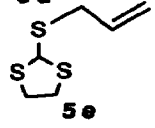
Both anhydrous TBAF or TASF may be conveniently employed in these reactions, the former requiring the use of DMF as the solvent at room temperature, while the latter can be used, if required, in THF also at much lower temperatures.

These results show that the actual nature of the starting compounds does not affect this kind of reactivity. Allylsilanes attack from the less hindered site; in fact no product deriving from allyl shift has ever been isolated from the reaction mixtures, even though this possibility cannot be ruled out by using different regioisomeric allylsilanes⁹ and also no trace of isomerization of the double bond was observed¹⁰.

It is interesting to observe that the same regiochemical control can be achieved when reacting silyl derivatives of a different nature, such as benzylsilane. Even though, in fact, the use of benzyl magnesium bromide in reactions of dithioesters or trithiocarbonates leads again to products deriving from a direct carbophilic attack⁴, the reaction with benzylsilane leads smoothly to the synthesis of the corresponding benzyl sulfide¹¹.

In conclusion, the use of silylated nucleophiles such as allylsilanes and benzylsilane allows a novel regiochemical control in the addition reaction of organometallic species to thiocarbonyl compounds. Further work on different organosilanes is now currently under way in our laboratories.

Table. Reactions of dithioesters and trithiocarbonates with allyl and benzyl silanes.

Thiocarbonyl	Silyl derivative	Catalyst	Product ^a	Yield (%) ^b
		TBAF ^c		50
		TBAF ^c		45
		TBAF ^c		41
		TBAF ^c		54
		TBAF ^c		72
		TBAF ^c		61
		TBAF ^c		78
		TBAF ^c TASF ^d		69 51
		TBAF ^c TASF ^d		66 55
		TBAF ^c		60
		TBAF ^c		67
		TBAF ^c		71

^a All products showed spectroscopic and analytical data consistent with the assigned structure.
^b Refers to chromatographically pure material. ^c DMF, r.t. ^d THF, -78 C.

References and notes

1. Vedejs, E.; Reid, J.G. *J. Org. Chem.* **1987**, *52*, 4269. Vedejs, E.; Fedde, C.L.; Schwartz, C.E. *J. Am. Chem. Soc.* **1984**, *106*, 4617. Tamaru, Y.; Harada, T.; Yoshida, Z.-I; *J. Am. Chem. Soc.* **1980**, *102*, 2932 and references cited therein. Ireland, R.; Brown, F.R. *J. Org. Chem.* **1980**, *45*, 1868. Roth, M.; Dubs, P.; Gotschi, E.; Eschenmoser, A. *Helv. Chim. Acta* **1971**, *54*, 710. Duus, F. in Reid, D.H. "Organic Compounds of Sulfur, Selenium and Tellurium", vol. 3, p. 219; The Chemical Society, London, 1975.
2. Beak, P.; Yamamoto, J.; Upton, C.J. *J. Org. Chem.*, **1975**, *40*, 3052 and references cited therein. Paquer, D. *Bull. Soc. Chim. Fr.* **1975**, 1439 and references cited therein.
3. Leger, L.; Saquet, M. *Bull. Soc. Chim. Fr.*, **1975**, 657.
4. Masson, S.; Saquet, M.; Thuillier, A. *Tetrahedron* **1977**, *33*, 2949.
5. Rautenstrauch, V. *Helv. Chim. Acta* **1974**, *57*, 496. Metzner, P.; Vialle, A.; Vibet, A. *Tetrahedron Lett.* **1976**, 4295.
6. Capperucci, A.; Ferrara, M.; Degl'Innocenti, A.; Bonini, B.F.; Mazzanti, G.; Zani, P.; Ricci, A. *Synlett* **1992**, *17*, 880.
7. Typical procedure. A solution of anhydrous TBAF (75 mg, 0.287 mmol) prepared according to Majetich¹² in 2 mL of dry DMF, containing 300 mg of activated molecular sieves¹³, is treated with a solution of 50 mg (0.22 mmol) of phenyldithiobenzoate *1a* and 32 mg (0.28 mmol) of allylsilane *3a* in 2 mL of DMF. The mixture is stirred overnight, quenched with aqueous NH₄Cl and the crude material obtained purified by tlc elution (petroleum ether/CH₂Cl₂ 4:1) to afford 30 mg of pure *4a* (50%). ¹H NMR (CDCl₃) δ (ppm): 3.20 (d, 2H), 5.08 (m, 1H), 5.14 (m, 1H), 5.18 (s, 1H), 5.87 (m, 1H), 7.20-7.55 (m, 10H). MS *m/z* (%): 272 (M⁺, 20), 271 (52), 135 (100).
8. Reactions of dithioesters with organocuprates afford the double addition products with loss of the -SR moiety: Bertz, S.H.; Dabbagh, G.; Williams, L.M. *J. Org. Chem.* **1985**, *50*, 4414.
9. An experiment performed using a more hindered allylsilane, such as *E*-2-trimethylsilyl-non-3-ene, to check whether in such conditions allyl shift could be observed, afforded no reaction with dithioesters.
10. The absence of double bond *E/Z* isomerization in these reactions seems to point out a more or less concerted process.
11. Following the previously described procedure 57 mg (0.22 mmol) of diphenyltrithiocarbonate *2a* and 47 mg (0.28 mmol) of benzyltrimethylsilane *3d*, dissolved in 2 mL of anhydrous DMF, were added to a solution of 75 mg (0.287 mmol) of anhydrous TBAF in 2 mL of DMF to afford the corresponding sulfide *5d* (87%, after tlc purification). ¹H NMR (CDCl₃) δ (ppm): 3.97 (s, 2H), 4.92 (s, 1H), 7.26-7.39 (m, 11H), 7.48-7.53 (m, 4H).
12. Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745.
13. Activated molecular sieves have been proved to be inert in the fluoride ion induced reaction of allylsilanes¹².