

2-(TRIMETHYLSILYL)- AND 2-(TRIMETHYLSTANNYL)- Δ^2 -THIAZOLINES: SYNTHETIC ASPECTS AND REACTIVITY

Olga Bortolini, Giancarlo Fantin, Marco Fogagnolo, Alessandro Medici*,
and Paola Pedrini

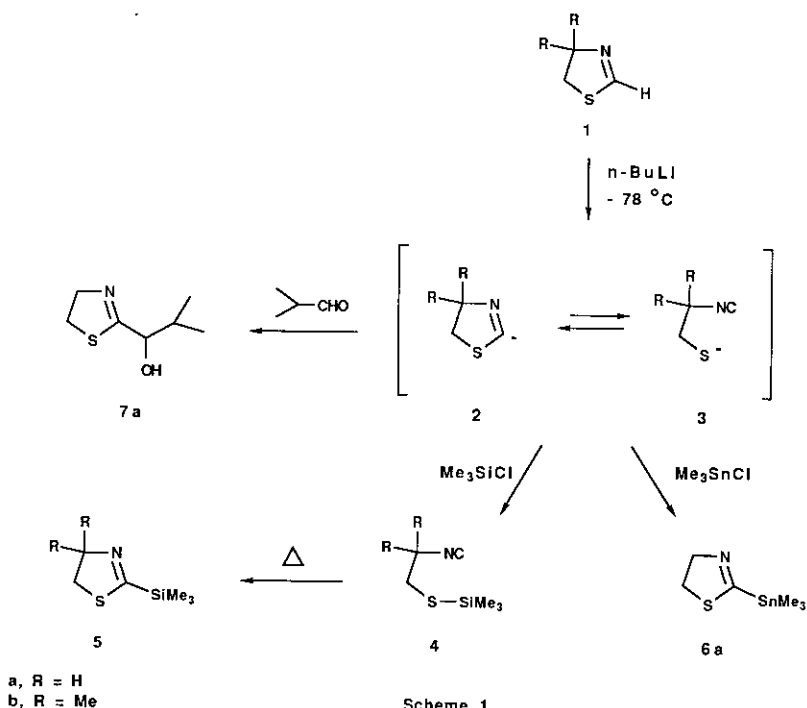
Dipartimento di Chimica, Università di Ferrara, 44100 Ferrara, Italy

Abstract- The synthesis of 2-(trimethylsilyl)- and 2-(trimethylstannyl)- Δ^2 -thiazolines is reported. The reactivity of the title compounds toward various electrophiles is also discussed.

In previous papers we described the synthesis of 2-trimethylsilyl- and 2-trimethylstannyl-thiazoles¹ and oxazoles.² The reactivity of these metallated compounds toward different electrophiles demonstrates their synthetic utility in new carbon-carbon bond formation.³

Studies on Δ^2 -oxazolines were carried out in parallel to those on oxazoles. Attempts to prepare the corresponding 2-(trimethylsilyl)- and 2-(trimethylstannyl)oxazolines by lithiation and quenching with trimethylsilyl or trimethyltin chloride gave the expected stannyl derivative but failed in the obtainment of the silyl compound.^{2c}

We have now extended this methodology to the synthesis of 2-(trimethylsilyl)- and 2-(trimethylstannyl)- Δ^2 -thiazolines. Reaction of thiazoline (1)⁴ with 1.1 equivalents of *n*-BuLi at -78 °C in ether produces an equilibrium mixture of the C₂-anion (2) and the open-chain α -isocyano thioenolate (3), as shown in Scheme 1. A similar behaviour has been previously reported for Δ^2 -oxazolines and oxazoles under the identical experimental conditions.^{2a,2c} The species in equilibrium can be trapped by appropriate electrophiles. The crude α -isocyano silyl thioenol ether (4)⁵ (90% yield, nmr) was formed on treatment of the equilibrium mixture with 1 equivalent of trimethylsilyl chloride. The 2-(trimethylstannyl)- Δ^2 -thiazoline (6a)⁶ (44% yield) or 2-(hydroxyisobutyl)- Δ^2 -thiazoline (7a)⁷ (27% yield) were obtained by quenching the 2 $\rightleftharpoons$ 3 mixture with 1 equivalent of trimethyltin chloride or 2 equivalents of isobutyraldehyde, respectively. Distillation of the α -isocyano silyl thioenol ethers (4) (oil bath at 120 °C) gave the 2-(trimethylsilyl)thiazolines (5a, 42% and 5b, 53%).⁸ The same procedure, i.e. the thermal conversion of the silyl isocyanide into the silyl azole, has been successfully applied in the preparation of 2-(trimethylsilyl)oxazoles but it was unfeasible with Δ^2 -oxazolines.^{2c} Although this isomerization should be disfavoured in both cases due to the relative O-Si vs. C-Si bond strengths, the cyclization to 2-(trimethylsilyl)oxazoles appears to be assisted by the aromaticity.³ In our case, however, the absence of the aromaticity in the resulting product is balanced by the easier insertion of the isonitrile into the S-Si bond.^{2a,3}



Scheme 1

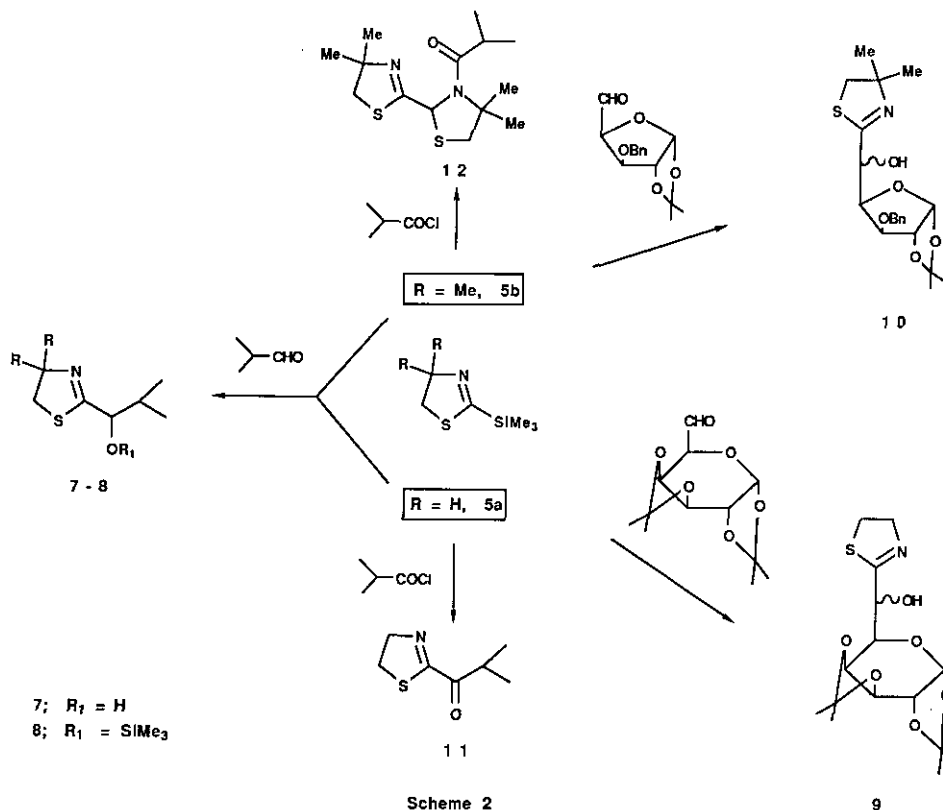
The synthetic utility of **5** has been examined with two different electrophiles which both gave the 2-thiazoline derivatives by substitution of the SiMe_3 group (see Scheme 2). Treatment of **5** with two equivalents of isobutyraldehyde (neat) produced the silyl ethers (**8**), one of which was isolated and fully characterized.⁹ Upon reaction with 1 equivalent of 1 M solution of tetra-*n*-butylammonium fluoride (TBAF-THF) the compounds (**8**) gave the corresponding alcohols (**7**)¹⁰ (**7a**, 35%; **7b**, 50%).

In addition to this we have explored the possibility of obtaining an asymmetric control on this reaction by using chiral aldehydes. The reaction of **5a** with 1,2,3,4-di-*O*-isopropylidene- α -*D*-galactohexodialdo-1,5-pyranose¹¹ (1 equivalent in benzene) produced the corresponding alcohol (**9**)¹² (50% yield, $ds \geq 95\%$), while **5b** with 1,2-*O*-isopropylidene-3-*O*-benzyl- α -*D*-xylopentodialdofuranose¹³ gave the alcohol (**10**)¹⁴ (30% yield, $ds = 85\%$).¹⁵

The reaction of **5** with isobutyryl chloride gave rise to different adducts, depending on the substituents of the thiazoline ring. In particular, the silylthiazoline (**5a**) with 2 equivalents of the mentioned chloride in benzene gave the 2-acyl derivative (**11**) in 50% yield.¹⁶ The same reaction carried out on **5b** in the absence of solvent for 7 days at room temperature produced the compound (**12**) in 30% yield.¹⁷ A similar condensation reaction has also been reported with 1,3-thiazoles.¹⁸

The reactivity of 2-(trimethylstannyl)- Δ^2 -thiazoline (**6a**) has been investigated in respect to palladium-catalyzed cross-coupling reaction, methodology recently employed for the arylation of heterocycles.^{2c} The reaction of **6a** with 1 equivalent of 2-bromothiophene or 3-bromoquinoline in benzene in the presence of catalytic amounts of $\text{Pd}(\text{PPh}_3)_4$ at 80°C resulted in a progressive decomposition of the stannyl derivative without production of the corresponding cross-coupling adduct. Extension of this reaction to different alkyl or aryl halides is now in progress in our

laboratories.



ACKNOWLEDGMENTS

We thank the Ministero P.I. (Rome) for financial support and Professor A. Dondoni for helpful discussion.

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- 3 A. Dondoni, G. Fantin, M. Fogagnolo, A. Mastellari, A. Medici, E. Negrini, and P. Pedrini, *Gazz. Chim. Ital.*, **1987**, 118, 211 and references therein.
- 4 Thiazoline 1a (H. Wenker, *J. Am. Chem. Soc.*, **1935**, 57, 1079): bp 139-140°C; 1H -nmr (80 MHz, $CDCl_3$) δ 3.20 (dt, $J = 1.0$ and 9.0 Hz, 2 H), 4.22 (ddt, $J = 1.0$, 2.4 and 9.0 Hz, 2 H), 7.84 (t, $J = 2.4$ Hz, 1 H). Thiazoline 1b was prepared in 30% yield by treatment of 4,4-dimethyl-

- Δ^2 -oxazoline with P_2S_5 according to literature: A. I. Meyers, *J. Org. Chem.*, **1960**, 25, 1147. Physical and spectral data: bp 145-148° C (lit 61° C/45 Torr; J. Laduranty, F. Barbott, and L. Miginiac, *J. Organomet. Chem.*, **1987**, 335, 283); 1H -nmr (80 MHz, $CDCl_3$) δ 1.37 (s, 6 H), 3.02 (s, 2 H), 7.67 (s, 1 H).
- 5 Compound **4a** (R = H): ir (film) 2120, 1670, 1250 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.35 (s, 9 H), 2.75 (br t, J = 7.0 Hz, 2 H), 3.50 (t, J = 7.0 Hz, 2 H). Compound **4b** (R = Me): ir (film) 2115, 1675, 1250 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.35 (s, 9 H), 1.50 (m, 6 H), 2.70 (m, 2 H).
- 6 Compound **6a**: bp 108-110 °C (18 mmHg); ir (film) 1570, 1250, 1190 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.37 (s, 9 H), 3.02 (t, J = 9.0 Hz, 2 H), 4.35 (t, J = 9.0 Hz, 2 H).
- 7 Compound **7a**: oil; ir (film) 3260 (broad), 1620 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.87 (d, J = 12.4 Hz, 3 H), 1.05 (d, J = 12.4 Hz, 3 H), 1.95 (m, 1 H), 3.37 (t, J = 8.6 Hz, 2 H), 4.25 (m, 3 H); ms m/z 159 (M^+).
- 8 Compound **5a**: bp 86-87° C (18 mmHg); ir (film) 1570, 1250 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.27 (s, 9 H), 2.80 (t, J = 9.0 Hz, 2 H), 4.39 (t, J = 9.0 Hz, 2 H). Compound **5b**: bp 95-97° C (18 mmHg); ir (film) 1570, 1250 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.33 (s, 9 H), 1.42 (s, 6 H), 2.94 (s, 2 H).
- 9 Compound **8a**: oil; ir (film) 1620 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.12 (s, 9 H), 0.87 (d, J = 7.0 Hz, 3 H), 0.95 (d, J = 7.0 Hz, 3 H), 1.90 (m, 1 H), 3.17 (m, 2 H), 4.25 (m, 3 H); ms m/z 231 (M^+).
- 10 Compound **7a**: see ref. 6. Compound **7b**: mp 77-79 °C; ir ($CHCl_3$) 1655 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 0.95 (d, J = 11.0 Hz, 3 H), 1.02 (d, J = 11.0 Hz, 3 H), 1.37 (s, 3 H), 1.42 (s, 3 H), 1.92 (m, 1 H), 3.17 (s, 2 H), 3.32 (br s, 1 H), 4.22 (d, J = 4.0 Hz, 1 H).
- 11 G. B. Howarth, D. G. Lance, W. A. Szarek, and J. K. N. Jones, *Can. J. Chem.*, **1969**, 47, 75.
- 12 Compound **9**: syrup; 1H -nmr (80 MHz, $CDCl_3$) δ 1.32 (s, 3 H), 1.37 (s, 3 H), 1.49 (s, 3 H), 1.52 (s, 3 H), 3.35 (t, J = 8.4 Hz, 2 H), 3.77-4.73 (m, 8 H), 5.53 (d, J = 5.0 Hz, 1 H); ms m/z 345 (M^+).
- 13 M. L. Wolfrom and S. Hanessian, *J. Org. Chem.*, **1962**, 27, 1800.
- 14 Compound **10**: syrup; 1H -nmr (80 MHz, $CDCl_3$) δ 1.30 (s, 6 H), 1.32 (s, 3 H), 1.35 (s, 3 H), 3.07 (s, 2 H), 3.93-4.90 (m, 7 H), 6.00 (d, J = 4.0 Hz, 1 H), 7.32 (s, 5 H); ms m/z 393 (M^+).
- 15 Diastereomeric ratios (ds) have been obtained from nmr spectra. The absolute configuration of **9** and **10** has not been established, however, an anti configuration may be proposed on the basis on the Felkin-Anh open-chain model for asymmetric induction: M. Cherest, H. Felkin, and N. Prudent, *Tetrahedron Lett.*, **1968**, 2099 and N. T. Anh, *Top. Curr. Chem.*, **1980**, 88, 145.
- 16 Compound **11**: oil; ir (film) 1700, 1590 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 1.16 (d, J = 6.8 Hz, 6 H), 3.31 (t, J = 9.0 Hz, 2 H), 3.54 (m, 1 H), 4.52 (t, J = 9.0 Hz, 2 H); ms m/z 157 (M^+).
- 17 Compound **12**: mp 70-72° C; ir ($CHCl_3$) 2960, 2920, 1645 cm^{-1} ; 1H -nmr (80 MHz, $CDCl_3$) δ 1.05 (d, J = 7.0 Hz, 3 H), 1.15 (d, J = 7.0 Hz, 3 H), 1.33 (s, 3 H), 1.40 (s, 3 H), 1.55 (s, 3 H), 1.75 (s, 3 H), 2.30-3.55 (m, 5 H), 5.60 (s, 1 H); ms m/z 300 (M^+).
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Received, 2nd April, 1990