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

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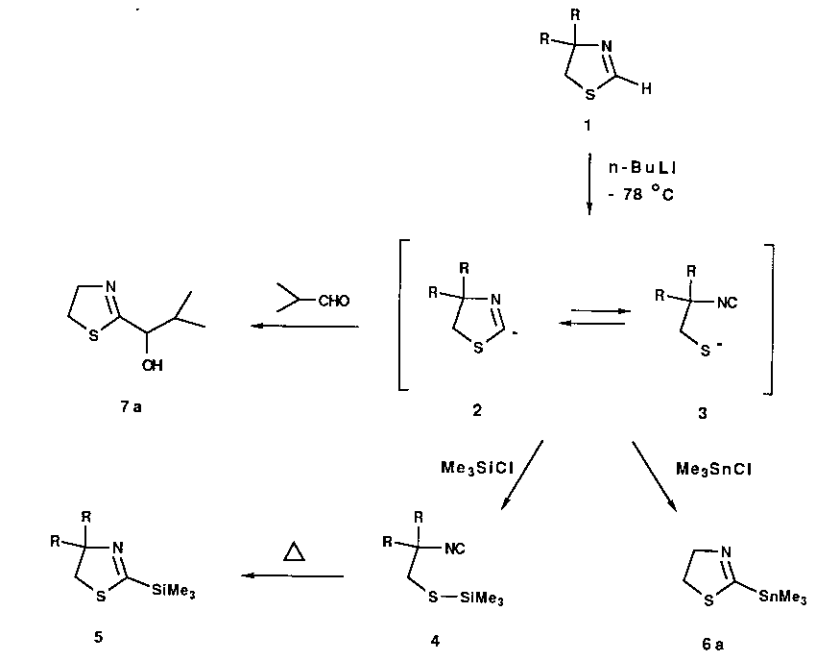
Abstract- The synthesis of 2-(trimethylsilyl)- and 2-(trimethylstannyl)- Δ^2-thiazolines is reported. The reactivity of the title compounds toward various electrophiles is also discussed.

In previous papers we described the synthesis of 2-trimethylsilyl- and 2-trimethylstannyl-thiazoles[1] 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 C_2-anion (**2**) and the open-chain α-isocyano thioenolate (**3**), as shown in Scheme 1. A similar behaviour has been previuosly 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** ⇌ **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

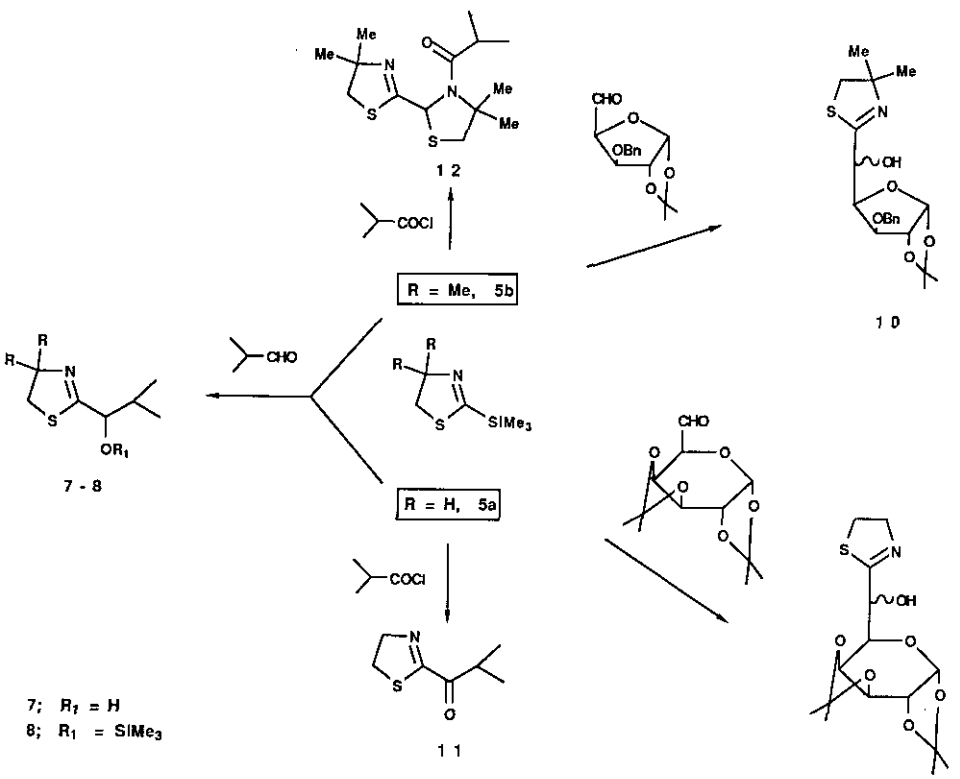
The synthetic utility of 5 has been examined with two different electrophiles which both gave the 2-thiazoline derivatives by substitution of the $SiMe_3$ group (see Scheme 2). Treatment of 5 with two equivalents of isobutyraldehyde (neat) produced the silyl ethers (**8**), one of which was isolated 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-galacto-hexodialdo-1,5-pyranose[11] (1 equivalent in benzene) produced the corresponding alcohol (**9**)[12] (50% yield, ds ≥ 95%), while **5b** with 1,2-O-isopropylidene-3-O-benzyl- α -D-xylo-pentodialdofuranose[13] 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 $Pd(PPh_3)_4$ 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.



Scheme 2

ACKNOWLEDGMENTS

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2 **2a.** A. Dondoni, T. Dall'Occo, G. Fantin, M. Fogagnolo, A. Medici, and P. Pedrini, J.Chem.Soc., Chem. Commun., **1984**, 258. **2b.** A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, and P. Pedrini, J. Org. Chem., **1987**, 52, 3413. **2c.** A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, and P. Pedrini, Synthesis, **1987**, 693.

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4 Thiazoline **1a** (H. Wenker, J. Am. Chem. Soc., **1935**, 57, 1079): bp 139-140°C; ^{1}H-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); ^{1}H-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}; ^{1}H-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}; ^{1}H-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}; ^{1}H-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}; ^{1}H-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}; ^{1}H-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}; ^{1}H-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}; ^{1}H-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}; ^{1}H-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; ^{1}H-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; ^{1}H-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}; ^{1}H-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}; ^{1}H-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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