Tetrahedron Letters,Vol.24,No.28,pp 2901-2904,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

REACTIONS OF 2-TRIMETHYLSILYLTHIAZOLE WITH ACYL CHLORIDES AND ALDEHYDES
SYNTHESIS OF NEW THIAZOL-2-YL DERIVATIVES

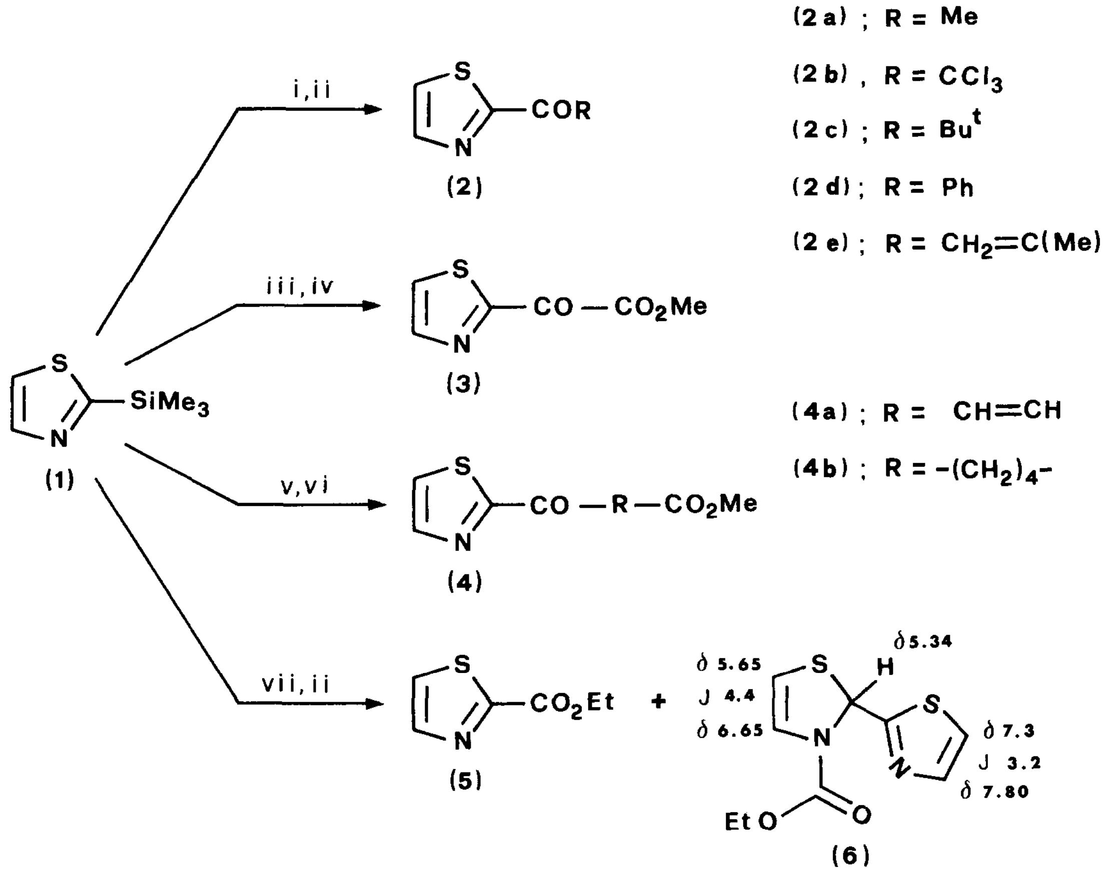
Alessandro Medici, Giancarlo Fantin, Marco Fogagnolo, and Alessandro Dondoni*

Laboratory of Organic Chemistry, Faculty of Sciences, University of Ferrara,
Ferrara, Italy

Summary : 2-Trimethylsilylthiazole (1) undergoes *ipso*-substitution of the silyl group with various acyl chlorides and ethyl chloroformate affording 2-acylthiazoles (2)-(5) but adds by the carbon-silicon bond to the carbonyl group of aldehydes yielding thiazol-2-yl-trimethylsiloxy-methane derivatives (7).

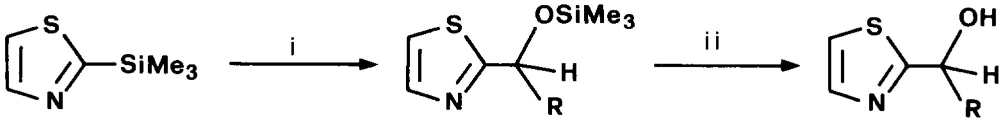
We reported earlier that thiazol-2-yl-silanes reacted with ketenes to produce high yields of the corresponding thiazolyl-siloxy-ethylenes (silyl enol ethers) which were eventually hydrolysed to 2-acylthiazoles.[1] We now describe the reactions of 2-trimethylsilylthiazole (1) with other *C*-electrophiles, namely acyl chlorides and aldehydes, which appear specific of this silylthiazole and constitute a new approach toward the carbon-carbon bond formation at C-2 of the thiazole ring.

Treating solutions of 2-silylthiazole[1] (1) (0.1-0.05 M) in methylene dichloride at room temperature with two mol. equiv. of various acyl chlorides (Scheme 1), followed by quenching with aqueous sodium bicarbonate, gave[2] the corresponding 2-acylthiazoles[3] (2) in very good yields. On the other hand, low yields of (2) (10-15 %) resulted from reactions carried out with one mol. equiv. of acyl chloride. Similarly, the reactions between (1) and dicarboxylic acid dichlorides, followed by quenching with basic methanol, afforded the corresponding thiazolylketoesters (3) and (4). The *E*-configuration about the carbon-carbon double bond of fumaric acid chloride was retained in the product (4a) (J_{HH} = 15.8 Hz). The reaction of (1) with ethyl chloroformate was solvent dependent. In benzene, the main product was the thiazolyl ethylcarboxylate (5) (62 %, m.p. 47-49°C) accompanied by compound (6) (15 %, m.p. 35-39°C) constituted by a C-2 to C-2 bond between an *N*-ethoxycarbonylthiazoline molecule and one of 1,3-thiazole. The adduct (6) was the only product isolated (43 %) when the reaction was carried out in methylene dichloride as a solvent.



Scheme 1. Reagents and Conditions : i, 2 equiv. RCOCl, CH_2Cl_2, 3 h; ii, aq. $NaHCO_3$; iii, 2 equiv. $(COCl)_2$, C_6H_6, 2 h; iv, MeOH-Et_3N; v, 2 equiv. $R(COCl)_2$, CH_2Cl_2, 3 h; vi, $NaHCO_3$ in MeOH-H_2O; vii, 2 equiv. EtOCOCl, CH_2Cl_2 or C_6H_6,20 h.

2-Silylthiazole (1) reacted with aldehydes by a 1,2-addition mode to the carbonyl group (Scheme 2). Treating (1) with one mol. equiv. of benzaldehyde or i-butyraldehyde in the absence of solvent at room temperature gave in virtually quantitative yields the 2-(α-trimethylsiloxy)-alkylthiazoles[5] (7a) and (7b) which readily underwent acid-catalysed desilylation to the corresponding hydroxyalkylthiazoles[5] (8). Similarly, the reaction between (1) and acrolein gave exclusively the 2-(α-trimethylsiloxy)-allylthiazole[5] (7c), thus showing the selectivity of the reaction in favour of the 1,2-addition to the carbonyl group over the conjugate 1,4-addition across the α,β-enone system. On the other hand, ketones such as acetone and methyl vinyl ketone, resulted inert toward (1) under the same or more vigorous conditions (12 h reflux).



(1) (7) (8)

(7a), (8a) ; R = Ph

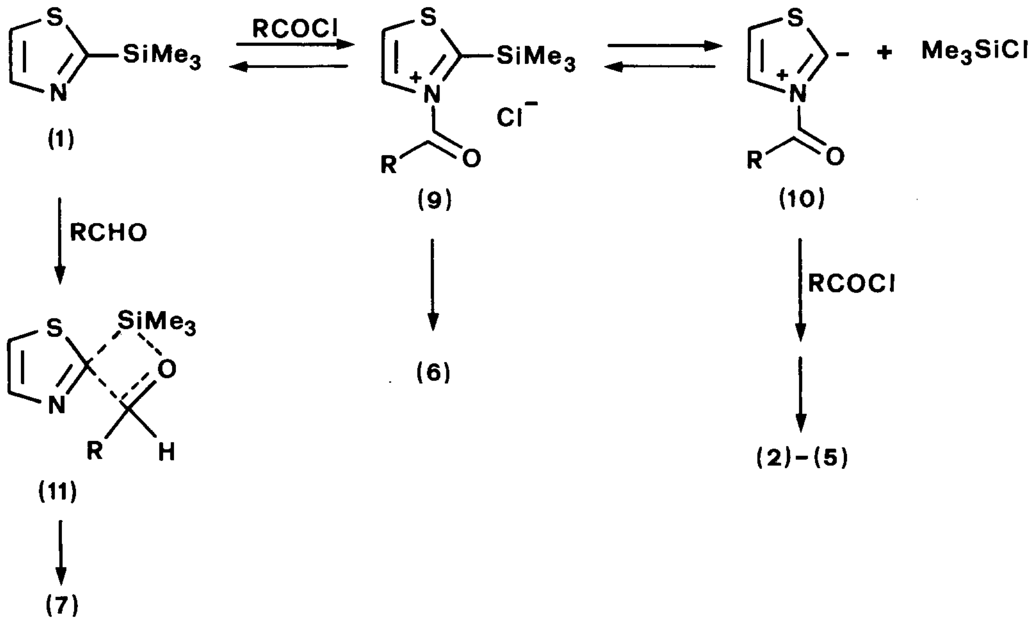
(7b), (8b) ; R = Me$_2$CH

(7c) ; R = CH$_2$=CH

Scheme 2. Reagents and Conditions : i, 1 equiv. RCHO, neat,1-4 h; ii, MeOH-HCl 5%.

We believe that the reactions of (1)with acyl chlorides involve the *N*-acylthiazolium ylide[6,7] (10) as a key intermediate whose formation from (1) is favoured *inter alia* by the assistance of the chloride ion in the desilylation process. In agreement with this hypothesis are the substantial increase of yields with the increase of the initial amount of acyl chloride with respect to (1), and the lack of reaction between (1) and the week electrophile diethyl carbonate under the original or more vigorous conditions. While products (2)-(5)are formed from (10) plus a molecule of acyl chloride, the adduct (6) should arise from the attack of (9) on (10) in competition with the relatively poor electrophile ethyl chloroformate. This alternative route is preferred in methylene dichloride because the polar solvent increases the amount of the salt (9) among the various species in equilibrium. On the other hand, the reactions of (1) with aldehydes are likely to occur through a four-centre transition state or intermediate[1] (11) which allows the internal transfer of the SiMe$_3$ group from carbon to oxygen to give the observed 1,2-adduct (7).

The reactions described appeared to be specific processes of 2-trimethylsilylthiazole (1) since the 4- and 5-trimethylsilyl derivatives resulted inert with both acyl chlorides and aldehydes[8] even under more vigorous conditions.



REFERENCES AND NOTES

1. A. Medici, P. Pedrini, and A. Dondoni, J. Chem. Soc., Chem. Commun., 1981, 655.
2. All new compounds were characterized by elemental analyses (C,H,N) and spectral data (^{1}H NMR, IR, MS). B.p.'s and m.p.'s (after crystallization from *n*-hexane) were uncorrected. Yields were based on isolated products.
3. (2a), 89 %, b.p. 98-102 °C at 15 mm Hg; (2b), 84 %, m.p. 61-64 °C; (2c), 84 %, oil; (2d), 70 %, m.p. 42-46 °C; (2e), 62 %, b.p. 51-53 °C at 1 mm Hg.
4. (3), 76 %, m.p. 26-29 °C; (4a), 44 %, m.p. 92-95 °C; (4b), 74 %, b.p. 85-87°C at 15 mm Hg.
5. (7a), 95 %, b.p. 132-134 °C at 15 mm Hg; (8a), 98 %, m.p. 107-109 °C; (7b), 90 %, b.p. 101-102 °C at 20 mm Hg; (8b), 98 %, b.p. 115-116 °C at15 mm Hg; (7c), 76 %, oil.
6. An identical type of intermediate is proposed for the reaction of 1,3-thiazole with ketenes to give 2-acylthiazoles : A. Medici, G. Fantin, M. Fogagnolo, P. Pedrini, and A. Dondoni, J. Org. Chem., submitted for publication.
7. R. Breslow and McNelis, J. Am. Chem. Soc., 81, 3080 (1959); P. Haake, L.P. Bausher, W. B. Miller, ibid., 91, 1113 (1969); P. Haake, Tetrahedron Lett., 22, 2939 (1981); H. Kwart and G. King, 'd-Orbitals in the Chemistry of Silicon, Phosphorus, and Sulfur', Springer-Verlag, Berlin-Heidelberg, 1977, p. 84.
8. The 1,2-addition of 5-trimethylsilylthiazole to benzaldehyde has been achieved in the presence of KF and 18-Crown 6.

(Received in UK 29 April 1983)