Spirodioxolane Intermediates in the Reaction of 2-(Trimethylsilyl)thiazole with Aldehydes. Support for the 2-Ylide Mechanism

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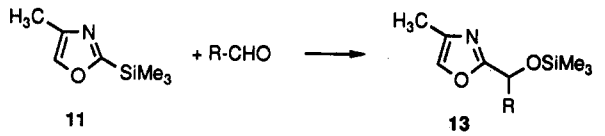
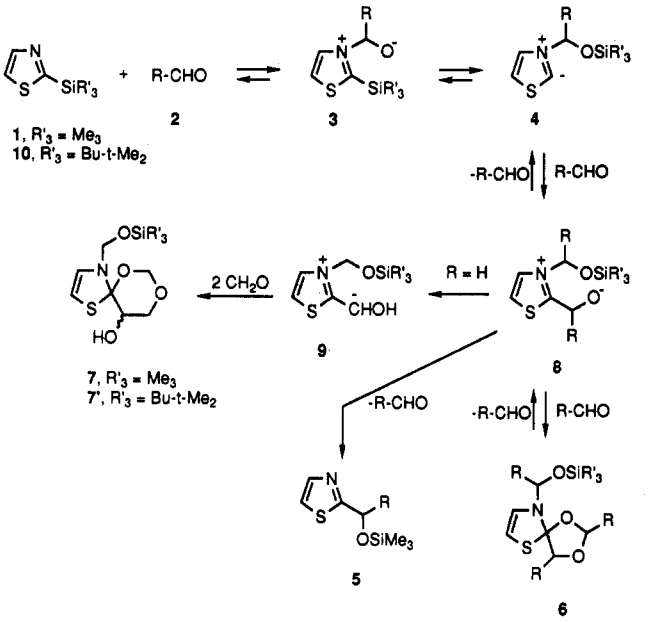
Received October 29, 1992

In recent years one of us reported very facile and uncatalyzed replacement of the silyl group of 2-(trimethylsilyl)thiazole (2-TST, 1) by various carbon electrophiles such as ketenes, acyl chlorides, aldehydes,[3] and heteroaryl cations[4] to give the corresponding 2-substituted thiazoles in good yields.[5] As well as being interesting in relation to thiazole chemistry,[6] the reaction of 1 with aldehydes (Scheme I) has proved to be a key process in synthetic methodologies directed toward the preparation of polyhydroxylated carbon chains.[7] The 2-[(silyloxy)methyl]-thiazole **5** which forms in this reaction is essentially the result of insertion of the carbonyl of the aldehyde into the C–Si bond of 1. A multistep mechanism via a thiazolium 2-ylide **4** has been proposed[3,5,7] for this reaction. A possible route to **4** involves quaternization of the nitrogen of 1 by a molecule of aldehyde to give betaine **3**, followed by silyl group migration. It was suggested that the ready cleavage of the carbon–silicon bond in **3** is assisted by the formation of the oxygen-silicon bond (intramolecular catalysis). There are other chemical[8] and biochemical[9] processes where a thiazolium 2-ylide has been assumed as an intermediate. A similar carbodesilylation reaction, presumably via a 2-ylide intermediate as well, has been reported[10] for 2-(trimethylsilyl)-4-methyloxazole (2-TSMO, 11) and aldehydes to give the corresponding 2-[(silyloxy)methyl]oxazoles **13**. We now report a study



11 **13**

Scheme I



of the kinetics of reactions of 2-TST, 1, 2-(*tert*-butyldimethylsilyl)thiazole (2-TBST, **10**) and 2-(trimethylsilyl)-4-methyloxazole (2-TSMO, 11) with various aldehydes and the identification of reaction intermediates which support the above mechanism.

Results and Discussion

The reaction of 1 with aldehydes **2a–k** was followed using NMR spectroscopy and rate constants evaluated based on NMR intensities are listed in Table I. The rate of reaction with aliphatic aldehydes decreased in the order of increasing size of the substituent, R, being essentially instantaneous with formaldehyde (**2a**) and very slow with pivalaldehyde (**2e**). In the aromatic series, reactivity decreased with decreasing electron withdrawal by substituents (all para), from *p*-nitrobenzaldehyde (**2f**) to *p*-anisaldehyde (**2k**). Logarithms of rate constants in Table I correlate satisfactorily ($r = 0.961$) with Hammett σ-parameters[11] for **2f–k**, with $\rho = 2.0$. Secondary reactions, including apparent benzoin and hemiacetal formation, were seen for the more reactive aromatic aldehydes, particularly for **2f–h**. For fast-reacting aliphatic aldehydes, stable intermediates were observed whose formation was immediate from formaldehyde (**2a**), rapid with acetaldehyde (**2b**), and slow from isobutyraldehyde (**2c**). Figure 1, showing a profile of the acetaldehyde reaction, is a classic two-step example indicating a stable intermediate on the path to product. The intermediate appeared by NMR to be a 1:3 adduct between 2-TST and the aldehyde having a spiro[thiazoline-2,4′-dioxolane] structure **6**. Intermediates were not detected in kinetic studies involving aldehydes **2d–k**. Products from most of these reactions were isolated and characterized as documented in the experimental section.

With formaldehyde (**2a**) only one intermediate stereoisomer (**6a**, Table II) was formed whereas with acetaldehyde (**2b**) six or more stereoisomers were present, in unequal amounts, which could not be fully characterized

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0022-3263/93/1958-3196$04.00/0

Table I. Kinetics of the Reaction of 2-TST (1) with Aldehydes in CH_2Cl_2 at 25 °C

aldehyde (RCHO)	R	$[2]_0/[1]_0$	10^3k^a	max concn of 6 (min)
2a	H			immediate (−78 °C)
2b	Me	5.0	44.	5
2c	*i*Pr	1.8	9.5	30
2d	*s*Bu	1.8	5.5	*b*
2e	*t*Bu	2.9	0.2	*b*
2f	PhNO$_2$-*p*	5.3	62.	*b*
2g	PhCN-*p*	5.0	15.	*b*
2h	PhCF$_3$-*p*	4.6	13.	*b*
2i	PhBr-*p*	1.05	4.6	*b*
2j	Ph	3.1	2.9	*b*
2k	PhOMe-*p*	2.6	0.2	*b*

[a] Rate constants for reaction assumed first order in both 1 and 2, in L/mol per min. [b] Not detected.

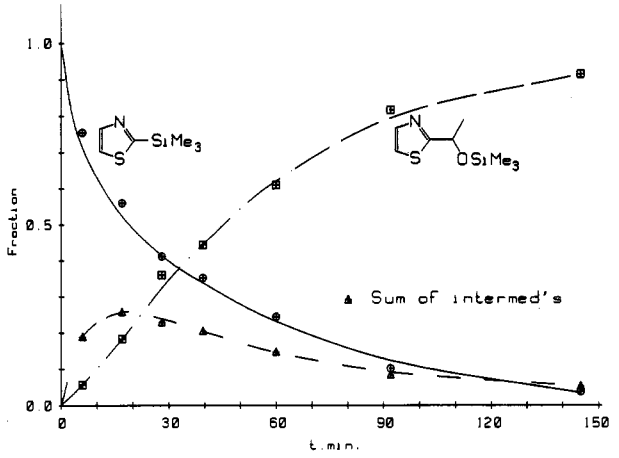

Figure 1. 2-TST + acetaldehyde reaction profile at 25 °C.

spectroscopically. Isobutyraldehyde (**2c**) showed a low concentration of mostly a single 1:3 stereoisomer (**6c**, Table II) at room temperature. Slowing this reaction (−25 °C) allowed observation of an initial mixture of several stereoisomers, but with time **6c** predominated (>70%) and could be thoroughly characterized. To define its relative stereochemistry, measurements of nuclear Overhauser enhancements in **6c** were performed. Mutual enhancements between the 2′-H and 5′-H (Figure 2) indicate a cis configuration of the isopropyl groups on the dioxolane ring. Furthermore, NOE enhancements between the 6-H and both dioxolane ring hydrogens place all three protons in close proximity in one or more conformations of **6c**. Upon aging reaction mixtures for suitable periods, the 1:3 adducts **6b** and **6c** afforded the corresponding 2-[(silyloxy)methyl]thiazoles **5b** and **5c**, whereas **6a** gave a complex mixture of oxymethylated products. Details of NMR structural characterization of unisolable intermediates appear at the end of this section.

Reaction of formaldehyde with an excess of 2-TSMO (**11**) was very slow below −80 °C in contrast to the immediate disappearance caused by **1**. Near −70 °C buildup of the 1:3 adduct **12a** proceeded gradually, allowing its full spectroscopic characterization (Table II); the half-life of **12a** was a little more than 2 h. Rates were compared for reactions of **1** and **11** with acetaldehyde at 25 °C; the second order rate constant for **11** was 3.7×10^{-4} L/mol per min, about 1/100 that for 2-TST, **1**. The silyloxazole concentration had dropped by half after 24 h to produce a very complex mixture. Spectra at this point exhibited features consistent with the presence of several stereoisomers of **12b**, but also revealed numerous additional ^{13}C signals. It proved impossible to isolate identifiable products from this reaction even though products derived from **11** and other aldehydes have been reported.[10] Nevertheless, a 100-fold reduction of acetaldehyde reactivity toward the oxazole supports a similar mechanism since it parallels reduction of basicity by 2 orders of magnitude for oxazoles vs thiazoles as a class.[12]

The foregoing indicates a dependence of the reaction rate on the ability of the aldehyde to interact with **1** to give 1:3 adducts **6**, in a process strongly inhibited by bulky substituents in aliphatic aldehydes and by electron-releasing groups in aromatic ones. On the assumption that the formation of **6** occurs by initial electrophilic attack of the aldehyde at the nitrogen of **1** followed by silyl group migration (Scheme I) we hoped that the replacement of the trimethylsilyl group of 2-TST with the bulkier *tert*-butyldimethylsilyl of 2-TBST, **10**, would allow us to detect earlier intermediates in the reaction pathway. Formaldehyde indeed reacted far more slowly with **10** than with **1**. Gradual diminution of **2a** in the presence of a large excess of **10** could be followed at −50 °C, accompanied by formation of 1:3 adduct **6** (R = H, R′$_3$ = *t*-BuMe$_2$). Overnight aging near −25 °C of this adduct afforded a 1:4 product which was characterized through its ^1H and ^{13}C NMR spectra as the spiro[thiazoline-2,4′-dioxane] **7′** (Figure 3). The simple C$_2$-[(silyloxy)methyl]thiazole was not detected. The analogous 1:4 adduct **7** appeared to form as a minor component accompanying **6a** in a very dilute formaldehyde solution when diluted **1** was allowed to mix diffusionally in an NMR tube near −50 °C. Although no information on the early stages of the reaction was provided, these results corroborate earlier observations[13] on the sluggish reactivity of **10** with aldehydes and the superior synthetic utility of 2-TST (**1**).

These observations provide considerable insight into the multistep mechanism[3] of the reaction of 2-TST (**1**) with aldehydes **2**. The reaction appears to proceed through a reversibly accessible spirodioxolane intermediate **6** (Scheme I) whose concentration depends on the substituents R′ and R in both **1** and **2**. Reaction retardation for bulky aliphatic aldehydes and acceleration for electron-poor aromatic ones, as well as the reduced reactivity of oxazole analog **11**, are consistent with an electrophilic attack on nitrogen in **1** to give the betaine **3**. The direct conversion of **3** to **6** is unlikely whereas this can be easily rationalized to occur via the 2-ylide **4** and its capture by two molecules of aldehyde. Hence, the formation of **6** supports the postulated 2-ylide **4** as a key intermediate in this reaction. Conversion of **6** to the final product **5** probably proceeds through further reversible steps involving loss of two molecules of aldehyde with intermittent transfer of the silyl group from the N-alkyl to the C-alkyl moiety. The less extensively investigated reaction of 2-TSMO (**11**) appears to follow the same mechanism. The silyl group exchange occurs readily in the trimethylsilyl case while it becomes very slow for the bulky *tert*-butyldimethylsilyl group.[14] In this case, the intermediate **8** rearranges to **9** (arbitrarily shown as the charge-separated resonance hybrid to illustrate its reactivity as an activated

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(13) It has been previously reported (refs 3,5b) that 2-TBST failed to react with isobutyraldehyde and benzaldehyde.

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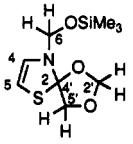
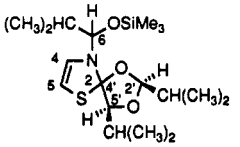
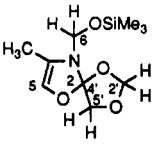
Table II. Selected Chemical Shifts (ppm) and Coupling Constants (Hz) of Adducts 6a, 6c, and 12a



6a



6c



12a

	6a		6c		12a	
position	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
2		109.2		116.0		119.5
4	6.04, d, 4.7	127.6, ddt, 182, 8, 5	6.11, d, 4.9	124.0, ddd, 182, 8, 4		120.3
5	5.18, d, 4.6	89.4, dd, 193, 9	5.24, d, 4.9	90.4, dd, 191, 9	5.92, q, 1.5	121.6
6	4.48, 3.76, AB, J = 10.8	69.8, dd, 155, 157	4.69, d, 5.1	83.1, dm, ^1J = 149	4.65, AB, J = 11.2	65.7
2′	5.16, 4.84, AB, $\|J\| < 1$	94.3, ddd, 170, 166, 7	4.93, d, 4.5	107.7, dm, ^1J = 163	5.09, 4.94, AB, $\|J\| < 1$	93.9
5′	4.49, 3.80, AB, J = 10.3	72.3, ddd, 157, 149, 6	3.35, d, 9.4	87.6, dm, ^1J = 145[a]	4.07, 3.80, AB, J = 10.8	69.8
CH_3					1.77, d, 1.5	7.9

[a] The low-field component of this doublet was obscured due to overlap; ±2 Hz.

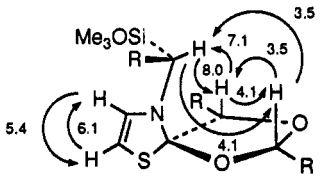


Figure 2. ^{1}H NMR analysis of **6c**: Results of NOE experiments (% signal enhancement) in CD_2Cl_2 at −25 °C.

aldehyde[8a,9a]) which is then trapped by two molecules of aldehyde to give the stable spiro[thiazoline-2,4′-dioxane] **7′**. The carbonyl umpolung as shown in the conversion of **8** to **9** has been postulated in other chemical[8] and biochemical[9] transformations involving thiazolium salts.

In conclusion, a rationale for the formation of the adduct **6** via the *N*-[(silyloxy)methyl]thiazolium 2-ylide **4** is given. Recent ab initio calculations[15] support this reaction pathway although they indicate that the betaine **3** is not required as an intermediate to **4**. It is worth noting that the thiazolium 2-ylide **4** should be a quite accessible intermediate due to stabilization of the negative charge by the adjacent sulfur atom (α-sulfur effect).[16] The oxygen atom of **11** apparently allows 2-ylide formation as well,[10] based on the formation of **12a**. An ylide mechanism has also recently been proposed for the uncatalyzed reaction of 2-(trimethylsilyl)pyridine with aldehydes.[17]

NMR Structural Characterization of Unisolable Intermediates. Although **6a** was not isolated, and would no doubt prove impossible to isolate, spectroscopic evidence lends great confidence in its structure as shown.[18] The following points strongly support the structure of **6a** (see Table II). Proton NMR shows four essentially isolated AB or AX patterns, one due to the now significantly shielded 2*H*-thiazoline protons (J = 4.7). Differential shieldings of 2 ppm or more compared to 2-TST are strongly indicative of dearomatization of the ring. Carbon-13 NMR shows six carbons in addition to the $SiMe_3$ group, of which one has no attached proton, two bear just one (the thiazoline types), and three are methylene carbons. The ^{13}C chemical shift of $C_{2'}$, 94.4 ppm, is almost identical to 94.3 reported for 4,4-dimethyl-1,3-dioxolane.[19] Values of $^1J_{C-H}$ of 166.0 and 169.9 Hz for $C_{2'}$ as well as 149 and 157 Hz for $C_{4'}$ compare well with 165 and 149 Hz, respectively, in 1,3-dioxolane.[20] Proton chemical shifts of 4.84 and 5.16 ppm at C2′ compare with the pairs 5.00, 5.17; 4.93, 5.07; and 4.89, 5.09 in three 4-substituted 1,3-dioxolanes.[21] The small value of $^2J_{H-H}$ at $C_{2'}$, 0.8 Hz, falls in the range given for 4-methyl-1,3-dioxolane: 0.0–0.8 Hz, solvent dependent.[22] At $C_{5'}$, $^2J_{H-H}$ is 10.3 Hz, compared to (−)8.5 to 9.0 Hz in some 4-substituted 1,3-dioxolanes.[23] The structure of **12a** was assigned based on comparisons with **6a**.

Spectroscopic evidence also strongly supports the structure of **7′** as that shown in Figure 3. Proton NMR shows a nearly "first order" system of eight coupled spins plus an isolated "AB" proton pair. Computational analysis was performed, using Fortran programs revised from those of Swalen and Reilly[24] for use on a personal computer, to fit 41 calculated transitions of an 8-spin network to 38 resolved frequencies from protons of the 4-thiazoline and hydroxy-1,3-dioxane rings of **7′**. Average deviation for the fit was less than 0.1 Hz. The (silyloxy)methyl group contains the two isolated protons. Proton shifts and spin couplings are presented in Figure 3. The shift of the hydroxyl hydrogen was temperature dependent; $\Delta\delta/\Delta T$ = 0.007 ppm/°C, confirming it as an active hydrogen (OH/NH) type. The ^{13}C NMR spectrum of **7′** shows seven carbon types besides those of the TBS group. One is without any proton, three bear one each, and three are methylenes, based on one-bond spin splittings (see Figure 3). The carbon chemical shift of $C_{2'}$, 87.4 ppm, corresponds to 95.4 ppm observed for C_2 in 1,3-dioxane.[25] With no γ-axial substituent, the unsubstituted dioxane would be expected to exhibit less shielding at C_2 by as much as 9 ppm, while a γ-equatorial substituent should exert a small

(15) Calculations indicate that formation of the 2-ylide may occur by attack of the aldehyde on nitrogen with concerted migration of the silyl group (Wu, Y.-D.; Houk, K. N.; Dondoni, A. *J. Org. Chem.*, submitted).

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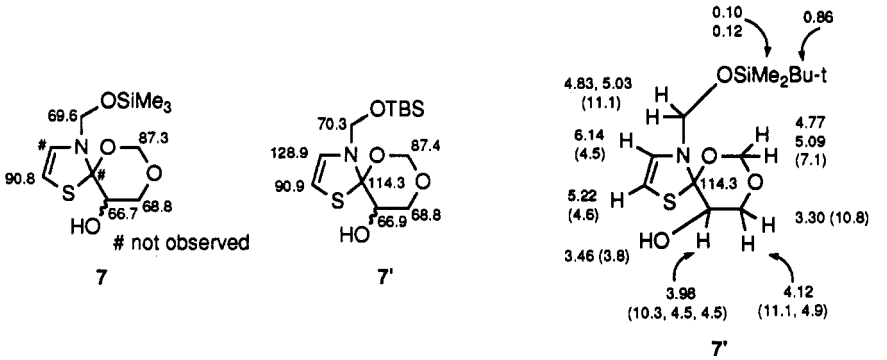

Figure 3. ^{13}C Data (δ) of 7 (−50 °C, left) and 7′ (−30 °C, center) and ^{1}H NMR data (δ, J) of 7′ (−30 °C, right), all in CD_2Cl_2.

Table III

RCHO	R	quantity of 2 (mmol)	vol of 1, μL	soln vol, mL (est)	$[2]_0$
2b	Me	13.8 mg (0.313)	10	0.53	0.59
2c	*i*-Pr	50 μL (0.551)	50	0.60	0.92
2d	*s*-Bu	60 μL (0.560)	50	0.66	0.85
2e	*t*-Bu	100 μL (0.921)	50	0.60	1.53
2f	$PhNO_2$-*p*	100.9 mg (0.668)	20	0.59	1.13
2g	PhCN-*p*	82.4 mg (0.628)	20	0.56	1.12
2h	$PhCF_3$-*p*	100 μL (0.732)	25	0.68	1.08
2i	PhBr-*p*	61.0 mg (0.330)	50	0.59	0.56
2j	Ph	100 μL (0.984)	50	0.60	1.64
2k	PhOMe-*p*	100 μL (0.821)	51	0.60	0.83

(<1 ppm) shielding influence;[26] a net of 8 ppm shielding in 7′ compared to that for 1,3-dioxane is fully consistent with the structure. Spin couplings, $^{1}J_{C-H}$ = 161.5 and 171.6 Hz at C_2, are close to 158 and 166 Hz reported for 5-*tert*-butyl-1,3-dioxane.[27] Geminal H–H couplings of (−)6.95 at $C_{2'}$ and (−)11.4 at $C_{6'}$ are comparable to $|J|$ values of 6 and 11 Hz reported for *trans*-4,5-dimethyl-1,3-dioxane.[28] The long-range coupling of 1.3 Hz in 7′ between one hydrogen at $C_{2'}$ and one at $C_{6'}$ corresponds to 1.5 Hz reported between H_{2e} and H_{6e} of 4-phenyl-1,3-dioxane.[29] Finally, in the thiazoline ring, essentially identical proton and ^{13}C shifts as well as C–H couplings strongly support identical environments in 7′ and **6**.

Experimental Section

General. NMR spectra (^{1}H, ^{13}C) were obtained using Bruker WM-250 or AM-400 spectrometers with methylene chloride-d_2 (MSD Isotopes) used as solvent, lock, and reference: δ_H = 5.32 ($CHDCl_2$), δ_C = 53.8 (CD_2Cl_2). Sample temperature was controlled at 25 °C for most experiments; formaldehyde studies were at various temperatures from −30 °C to below −80 °C. Nuclear Overhauser effect measurements for the isobutyraldehyde reaction were obtained at −25 °C. Liquid aldehydes were not dried; CD_2Cl_2 was stored over 3-Å molecular sieves. The solvent was not degassed, but all solutions were prepared under a stream of nitrogen. Quantities of aldehydes, RCHO, and 2-TST in kinetic experiments were as tabulated in Table III.

Materials. All aldehydes were obtained from commercial sources, and except for formaldehyde and *p*-bromobenzaldehyde were used as supplied. Formaldehyde solutions were prepared by vigorous heating of solid paraformaldehyde (MC&B) in a closed tube and driving the gas produced through a pipette immersed in cold solvent (dry ice/ethanol bath). Formaldehyde concentration was not measured but was evidently very low; based on NMR intensities the highest reached was estimated as 3 mol % in CD_2Cl_2. About 3–4% of the benzyl alcohol was indicated in the *p*-bromobenzaldehyde; this was reduced below 1% by slurrying and decanting with hexanes (3×). Commercial 2-TST, **1**, (Fluka) contained some 5–6% free thiazole which appeared inert in the systems studied. Preparation of 2-TSMO, **11**, was as described previously.[10]

2-(*tert*-Butyldimethylsilyl)thiazole (2-TBST, 10). *N*-Butyllithium (6.5 mL of 1.6 N in hexane, 10.4 mmol) was added to thiazole (Aldrich) (851 mg, 10.0 mmol) in dry THF (20 mL) under N_2 with cooling in a dry ice/acetone bath such that the temperature did not exceed −70 °C. After stirring 15 min at −75 °C, *tert*-butyldimethylsilyl triflate (Aldrich) (2.645 g, 10.0 mmol) was added dropwise, maintaining the temperature at less than −75 °C. The solution was stirred in the dry ice bath overnight, gradually warming to room temperature after the bath evaporated. The solution was diluted with hexane (20 mL), washed with 3% $NaHCO_3$ (50 mL), dried (Na_2SO_4), and concentrated and the residue chromatographed on silica gel eluting with 20:1 hexane/ethyl acetate giving 858 mg of light yellow oil. Kugelrohr distillation (bp 60–65 °C/0.1 mm) gave 699 mg (35%) of colorless liquid: ^{1}H NMR ($CDCl_3$) δ 0.40 (s, $SiMe_2$), 0.97 (s, CMe_3), 7.53 (d, 3,5-H), 8.15 (d, 3,4-H); ^{13}C NMR ($CDCl_3$) δ −5.4 ($SiMe_2$), 16.9 (CSi), 26.2 (Me_3), 121.3 (5-C), 145.7 (4-C); the 2-C signal was not detected.

Kinetics. Rate constants in Table I were obtained by least-squares fit of rate data to the integrated second-order rate equation for 1:1 stoichiometry,[30] using commercial software[31] and a personal computer:

$$kt = \frac{1}{a_0 - s_0} \ln \frac{s_0(a_0 - x)}{a_0(s_0 - x)}$$

where x represents concentration reacted; a_0 and s_0 are, respectively, initial aldehyde and 2-TST concentrations. Results of pseudo-first-order treatment in cases with a large excess of aldehyde differed little. Only acetaldehyde showed significant levels (>10%) of 1:3 intermediates in kinetic runs. The rate constant calculated for 1:3 stoichiometry, just for points measured during the first hour of reaction, was 27% larger than that for 1:1. Although rate constants are somewhat approximate due to the difficulty of accurate solution volume measurements and to uncertainties in NMR intensities, they nevertheless illustrate relative reactivities among the various aldehydes.

Hammett parameters were fit to the equation:

$$\log k = \rho\sigma + \log k_0$$

using the same software[31] as for kinetic data fits. σ values are from ref 11. We obtained ρ = 2.0 and $k_0 = 1.3 \times 10^{-3}$ (from intercept) with r = 0.9614.

Product Analysis. General Procedure: A solution of the aldehyde **2** (1 mmol) and 2-TST (**1**) (1.5 equiv) in 5 mL of dichloromethane was stirred at room temperature until the aldehyde disappeared completely on TLC (24 h for aliphatic aldehydes; 96 h for aromatic ones). Reactions of **2d** and **2h** were also carried out with 10 equiv of 2-TST. The solvent was

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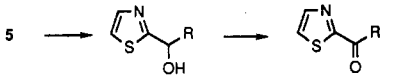
evaporated under reduced pressure and the crude residue treated with Bu_4NF (1.1 equiv, 1.1 M solution in THF). The mixture was stirred at room temperature for 1 h, treated with water, and extracted with Et_2O. The combined organic phases were dried (Na_2SO_4), and the solvent was evaporated to give[32] the corresponding 2-(α-hydroxyalkyl)thiazole (alcohol) **14** or 2-aroylthiazole (ketone) **15**. Pure compounds were obtained by column chromatography (CC) on silica gel with the indicated mixture of solvents. Alcohols **14c** (R = *i*-Pr) and **14j** (R = Ph) have already been described.[3] No products were isolated from the reactions of **2a** and **2e**. New compounds were characterized as follows:

Alcohol 14b (R = Me): CC, 80:20 Et_2O–hexane, 96%, oil; ^1H NMR ($CDCl_3$) δ 1.63 (d, 3 H, J = 6.8 Hz), 3.80 (bs, 1 H, exch D_2O), 5.15 (q, 1 H, J = 6.8 Hz), 7.29 (d, 1 H, J = 3.1 Hz), 7.71 (d, 1 H, J = 3.1 Hz). Anal. Calcd for C_5H_7NOS: C, 46.49; H, 5.46; N, 10.84. Found: C, 46.68; H, 5.75; N, 10.69.

Alcohol 14d (R = *sec*-Bu): CC, 60:40 Et_2O–hexane, (55% with 1.5 equiv of **1**; 85% with 10 equiv of **1**), 70:30 mixture of diastereomers, oil; ^1H NMR (d_6-DMSO) major isomer δ 0.74 (d, 3 H, J = 7.1 Hz), 0.90 (t, 3 H, J = 7.4 Hz), 4.74 (d, 1 H, J = 4.1 Hz), 7.55 (d, 1 H, J = 3.4 Hz), 7.70 (d, 1 H, J = 3.4 Hz); minor isomer δ 0.82 (t, 3 H, J = 7.4 Hz), 0.83 (d, 3 H, J = 7.1 Hz), 4.67 (d, 1 H, J = 4.9 Hz), 7.57 (d, 1 H, J = 3.4 Hz), 7.70 (d, 1 H, J = 3.4 Hz); both isomers δ 1.08–1.24 (m, 1 H), 1.36–1.54 (m, 1 H), 1.76–1.92 (m, 1 H), 6.0 (bs, 1 H, exch D_2O). Anal. Calcd for $C_8H_{13}NOS$: C, 56.13; H, 7.65; N, 8.18. Found: C, 56.34; H, 7.80; N, 7.97.

(32) Depending upon the substituent R, 2-(α-hydroxyalkyl)thiazoles **14** are converted to 2-acylthiazoles **15** during the workup (see ref 3a).



14 **15**

Ketone 15f (R = $PhNO_2$-*p*): CC, 30:70 Et_2O–hexane), 81%; mp 114–116 °C; ^1H NMR ($CDCl_3$) δ 7.83 (d, 1 H, J = 3.1 Hz), 8.15 (d, 1 H, J = 3.1 Hz), 8.35–8.40 (m, 2 H), 8.64–8.70 (m, 2 H). Anal. Calcd for $C_{10}H_6N_2O_3S$: C, 51.28; H, 2.58; N, 11.96. Found: C, 51.01; H, 2.60; N, 12.01.

Ketone 15g (R = PhCN-*p*): CC, 25:75 Et_2O–hexane, 60%; mp 104–105 °C; ^1H NMR ($CDCl_3$) δ 7.81 (d, 1 H, J = 3.1 Hz), 7.81–7.86 (m, 2 H), 8.13 (d, 1 H, J = 3.1 Hz), 8.57–8.63 (m, 2 H). Anal. Calcd for $C_{11}H_6N_2OS$: C, 61.67; H, 2.82; N, 13.07. Found: C, 61.80; H, 3.01; N, 13.25.

Ketone 15h (R = $PhCF_3$-*p*): CC, 20:80 Et_2O–hexane), (50% with 1.5 equiv of **1**, 98% with 10 equiv of **1**), oil; ^1H NMR ($CDCl_3$) δ 7.78 (d, 1 H, J = 3.1 Hz), 7.76–7.82 (m, 2 H), 8.12 (d, 1 H, J = 3.1 Hz), 8.56–8.62 (m, 2 H). Anal. Calcd for $C_{11}H_6F_3NOS$: C, 51.34; H, 2.35; N, 5.44. Found: C, 51.46; H, 2.53; N, 5.63.

Ketone 15i (R = PhBr-*p*): CC, 10:90 Et_2O–hexane, 58%, oil; ^1H NMR ($CDCl_3$) δ 7.65–7.69 (m, 2 H), 7.75 (d, 1 H, J = 3.1 Hz), 8.10 (d, 1 H, J = 3.1 Hz), 8.37–8.43 (m, 2 H). Anal. Calcd for $C_{10}H_6BrNOS$: C, 44.81; H, 2.25; N, 5.22. Found: C, 44.56; H, 2.01; N, 5.35.

Alcohol 14k (R = PhOMe-*p*): CC, 60:40 Et_2O–hexane), 60%, mp 99–101 °C; ^1H NMR ($CDCl_3$) δ 3.80 (s, 3 H), 3.99 (bs, 1 H, exch D_2O), 6.01 (s, 1 H), 6.86–6.95 (m, 2 H), 7.29 (d, 1 H, J = 3.1 Hz), 7.34–7.43 (m, 2 H), 7.70 (d, 1 H, J = 3.1 Hz). Anal. Calcd for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33. Found: C, 59.59; H, 5.16; N, 6.14.

Acknowledgment. We thank Merck colleagues Dr. J. E. Lynch for the preparation of 2-TBST (**10**), Dr. M. W. Baum for performing preliminary NMR studies, and Mr. R. A. Reamer for assisting with NOE experiments. Drs. D. Perrone and A. Marra of the University of Ferrara are thanked for isolation and characterization of alcohol and ketone products of aldehydes and 2-TST.