PREPARATION OF NEW THIOCARBANION SPECIES BEARING THIAZOLINYL AND BENZOTHIAZOLYL GROUPS AND REACTIONS WITH CARBONYL COMPOUNDS

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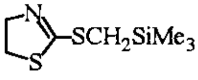
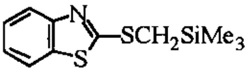
Abstract-----2-Trimethylsilylmethylthiothiazoline (**1**) reacted with aromatic aldehydes in the presence of cesium fluoride or tris(dimethylamino)sulfur(trimethylsilyl)difluoride (TASF) to give 2-heteroarylthioethanol (**4**) or thiiran (**5**) derivatives in good yields. The reactions of 2-trimethylsilylmethylthiobenzothiazole (**2**) with aromatic aldehydes are also discussed.

The α-thiocarbanions[1] are readily prepared by the fluoride ion-promoted desilylation of trimethylsilylmethyl sulfides under mild conditions and can be conveniently applied to obtain various 1,3-dipolar reagents such as thiocarbonyl ylides[2] and related chemical species.[3] The active species generated by desilylation is very susceptible to the action of substituted groups, particularly the heterocyclic substituted group, on the sulfur atom, so that is may behave as a only thio-carbanion or have 1,3-dipolar character. 2-Trimethylsilylmethylthiothiazoline (1)[4,5] was recently shown to react with hetero dipolarophiles to give thiiran derivatives through the formal 1,3-dipolar cycloaddition reaction.[2d] 2-Timethylsilylmethylthiopyridine reacted with carbonyl compounds to give 2–pyridylthioethanol derivatives in the presence of cesium fluoride in good yields.[6]



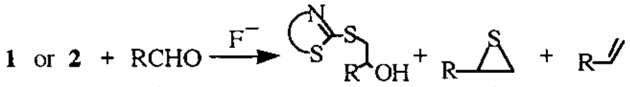
1



2

We reinvestigated the reactions of **1** with aldehydes using TASF instead of cesium fluoride as the fluoride ion source to obtain the corresponding 2–heteroarythioethanol compounds. We also examined the reactions of 2-trimethylsilylmethylthiobenzothiazole (**2**)[7] with carbonyl compounds in the presence of cesium fluoride in acetonitrile. At the start of this study,[8] the reactions of **1** and **2** with carbonyl compounds in the presence of fluoride ions were carefully studied. The reaction of **1** with 2.0 equivalents of aromatic aldehydes (**3**) in the presence of 1.2 equivalents of cesium fluoride in acetonitrile proceeded at room temperature for 45 h to yield the corresponding thiirans (**6a-e**).[9] The results are listed in Table 1 (Entries 1-5). When compound (**1**) reacted with **3** using an equivalent amount of TASF in THF at room temperature for 3 h, the corresponding 2-thiazolinylthioethanol derivatives (**4a-d**) were obtained in good yields as shown in Table 1 (Entries 6-10).

Table 1. Reactions of 1 and 2 with Aldehydes (3) Promoted by A Fluoride Ion

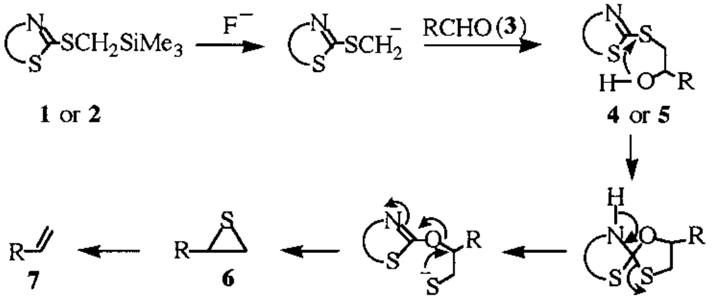


3 **4** or **5** **6** **7**

Entry	Heterocycle	R (**3**)	Conditions[a]	Yield (%) 4 or 5	6	7
1	**1**	C_6H_5 (**3a**)	**A**		40 (**6a**)	
2	**1**	4-MeC_6H_4 (**3b**)	**A**		21 (**6b**)	
3	**1**	4-$MeOC_6H_4$ (**3c**)	**A**		38 (**6c**)	
4	**1**	4-$C_6H_5C_6H_4$ (**3d**)	**A**		75 (**6d**)	
5	**1**	1-naphthyl (**3e**)	**A**		59 (**6e**)	
6	**1**	**3a**	**B**	90[b] (**4a**)		
7	**1**	**3b**	**B**	100[b] (**4b**)		
8	**1**	**3c**	**B**	81[b] (**4c**)		
9	**1**	**3d**	**B**	80 (**4d**)		
10	**1**	4-NCC_6H_4 (**3f**)	**B**	70[b] (**4e**)	20[b] (**6f**)	10 (**7**)
11	**2**	**3a**	**A**	24 (**5a**)	23 (**6a**)	
12	**2**	**3d**	**A**	21 (**5b**)		
13	**2**	**3e**	**A**		43 (**6e**)	
14	**2**	4-$O_2NC_6H_4$ (**3g**)	**A**	68 (**5c**)		
15	**2**	**3a**	**B**	39 (**5a**)		
16	**2**	**3d**	**B**	31 (**5b**)		
17	**2**	**3g**	**B**	39 (**5c**)		

[a] Conditions **A**: CsF (1.2 equiv.), MeCN, room temperature, 45 h;
B: TASF (1 equiv.), THF, room temperature, 3 h.
[b] Determined by ^{1}H-nmr.

These arylthioethanols (**4**) were converted into the correponding thiiran derivatives (**6**) with prolonged reaction time under same reaction conditions. The formation of thiiran may be considered to occur in a step-wise manner *via* 2-heteroarylthioethanol (Scheme 1). Compound (**2**) also reacted with aromatic aldehydes in the presence of cesium fluoride at room temperature giving the corresponding 2-benzothiazolylthioethanols (**5a-e**)[10] and thiirans (**6a, e, f**) as shown in Table 1 (Entries 11-14). The 2-benzothiazolylthiocarbanion species was obtained by treating with TASF in THF. It reacted with benzaldehyde derivatives to give the corresponding **5a-c**. The yields were less than those as shown in Table (Entries 15-17). The formation of the carbanion from **1** using TBAF (tetrabutylammonium fluoride) in THF did not occurr. These results are very different from those previously reported for reactions of 2-pyridylthiocarbanion with carbonyl compounds to give only thioethanol derivatives.[6]



Scheme 1

A typical experimental procedure is as follows: A solution of benzaldehyde (**3a**) (0.106 g, 1.0 mmol), **1** (0.103 g, 0.5 mmol), and TASF (0.5 ml, 0.5 mmol) in THF (3ml) was stirred at room temperature for 3 hr under an argon atmosphere. After evaporating of the solvent, the residue was chromatographed by silica gel (Kieselgel 60, hexane-CH_2Cl_2 1:1) to give 2-(thiazolin-2-yl)thio-1-phenylethanol (0.108 mg, 90%).[11]

In conclusion, 2-trimethylsilylmethylthio-thiazoline (**1**) and -benzothiazole (**2**)[12] are not only precursors of thiocarbanions[13] under mild conditions but also new reagents for the synthesis of 2-heteroarylthioethanol and thiiran derivatives. New methods are being sought for obtaining heteroarylthiocarbanions using a various heterocyclic systems with the sulfur atoms.

REFERNCES AND NOTES

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4. 2-Trimethylsilylmethylthiothiazoline (**1**) was prepared by reaction of 2-mercaptothiazoline with chloromethyltrimethylsilane in the presence of sodium hydroxide and sodium iodide in ethanol under reflux for 1 h in 66% yield. Compound (**2**) was synthesized from 2-mercaptobenzothiazole and chloromethyltrimethylsilane in 74% yield in manner similar to the preparation of **1**.
5. **1**: bp 145°C (19 mmHg). ^{1}H-nmr ($CDCl_3$) δ 0.16 (s, 9H), 2.82 (s, 2H), 3.36 (t, J = 6.5 Hz, 2H), 4.23 (t, J = 6.5 Hz, 2H); ir (neat) ν max cm^{-1} 2961, 1572, 1245, 964, 849; ms *m/z* (%) 205 (M$^+$, 11), 190 (100), 158 (7), 133 (4), 116 (9), 73 (51).
6. S. Kohra, H. Ueda, and Y. Tominaga, *Heterocycles*, 1993, **36**, 1497.
7. **2**: bp 152°C (5 mmHg). ^{1}H-nmr ($CDCl_3$) δ 0.19 (s, 9H), 2.60 (s, 2H), 7.20-7.80 (m, 4H); ir (neat) ν max cm^{-1} 2957, 1424, 1251, 847, 758; ms *m/z* (%) 253 (M$^+$, 10), 238 (27), 158 (7), 86 (64), 84 (100), 73 (19), 47,(27).
8. Fluoride ions promoted the protodesilylation of **1** to afford 2-methylthiothiazoline in 95 % yield.
9. **6d**: ^{1}H-nmr ($CDCl_3$) δ 2.69 (dd, J = 1.5 and 5.5 Hz, 1H), 2.89 (dd, J = 1.5 and 6.6 Hz, 1H), 3.93 (dd, J = 2.9 and 5.7 Hz, 1H), 7.20-7.64 (m, 9H); ir (neat) ν max cm^{-1} 1483, 839, 760, 687, 600; Ms *m/z* (%) 213 (M$^+$, 14), 188 (7), 180 (100), 165 (16), 152 (17), 76 (9); HR-ms Calcd for $C_{14}H_{12}S$ = 212.066. Found 212.066.

   Compounds (**6**) were fully characterized by ^{1}H-nmr (90 MHz), ir, and HR-ms
10. **5b**: ^{1}H-nmr ($CDCl_3$) δ 3.71(dd, J = 2.6 and 3.4 Hz, 2H), 5.10 (bs, 1H), 5.24 (dd, J = 5.8 and 6.9 Hz, 1H), 7.20-7.84 (m, 13H); ir (KBr) ν max cm^{-1} 3400, 1421, 1057, 998, 747; ms *m/z* (%) 363 (M$^+$, 6); HR-ms Calcd for $C_{21}H_{17}S$ = 363.075. Found 363.076.

    Compounds (**5**) and (**7**) were fully characterized by ^{1}H-nmr(90 MHz), ir, and HR-ms.
11. **4a**: ^{1}H-nmr ($CDCl_3$) δ 3.17-3.63 (4H, m, S-CH_2-, S-CH_2-), 4.19 (2H, t, J = 4.0 Hz, N-CH_2-), 5.04 (1H, t, J = 3.0 Hz, CH(OH)), 7.25-7.65 (5H, m, aromatic-H).
12. Protodesilylation of **2** by TBAF in THF did not occurred.
13. 2-Benzothiazolylthiocarbanion cannot be generated by the lithiation of 2-methylthiobenzothiazole with *n*-butyllithium: K. Hirai and Y. Kishida, *Heterocycles*, 1974, **2**, 185.

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