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A FACILE AND CONVENIENT SYNTHETIC METHOD FOR 2-BIS(TRIFLUOROACETYL)METHYLENE- AND 2-TRIFLUORO-ACETYLMETHYLENE-2,3-DIHYDRO-3-METHYLTHIAZOLES

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Abstract – 2,3-Dimethylthiazolium iodides (**1**) reacted easily with trifluoroacetic anhydride in the presence of pyridine to give 2-bis(trifluoroacetyl)methylene-2,3-dihydro-3-methylthiazoles (**2**) in excellent yields. Deacylation of **2** proceeded readily in moderate to high yields by acid catalyst such as silica gel and aqueous hydrochloric acid to afford the corresponding 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (**3**), which were smoothly reconverted into diacylated compounds (**2**) with trifluoroacetic anhydride. The highly poralized structure of **2** was also briefly discussed.

INTRODUCTION

Thiazole and thiazoline rings are important heterocyclic systems because of being applicable to the creation of useful biologically active substances as medicinal and agricultural chemicals. In medicinal scientific fields, some typical histamine H_2 receptor antagonists, which are well-known agents for peptic ulcer, are composed of a thiazole ring as an essential unit.[1-4] Third generation cephalosporins, which have a 2-(2-aminothiazol-4-yl)acetamido moiety as a 7β-side chain, have a broad spectrum of activity and

This paper is dedicated to Professor Dr. Ekkehard Winterfeldt on the occasion of his 75th birthday.

have a 2-(2-aminothiazol-4-yl)acetamido moiety as a 7β-side chain, have a broad spectrum of activity and further increased activity against gram-negative organisms.[5-8] In addition, most of fourth generation cephalosporins having a greater resistance to β-lactamases than the third generations also have a 7-(2-aminothiazol-4-yl)acetamido system.[7,8] Treatment with above medicines has been widely recommended as first-line treatment up to now in clinical practice. In common with these thiazole-containing medicines, chemical modification of thiazole ring has been attempted vigorously in agricultural scientific fields. For example, a fundamental approach to herbicides using new thiazolyliden-ketonitriles as suitable structure has been carried out since they have inhibitory activity of photosystem II.[9] In that study, it has been reported that 3-oxo-4-phenyl-2-[4-phenyl-3*H*-thiazol-(2*E*)-ylidene]butyronitrile possessed especially high activity of inhibition of photosystem II, and suggested that the thiazole-thiazoline tautomerism would contribute to the inhibition of photosynthetic electron flow.

Besides, much attention in recent years has been focused on the development of new methodologies for the syntheses of many kinds of fluorine-containing heterocycles, since these compounds are now widely recognized as important organic materials showing specific functions as well as interesting biological activities.[10-13]

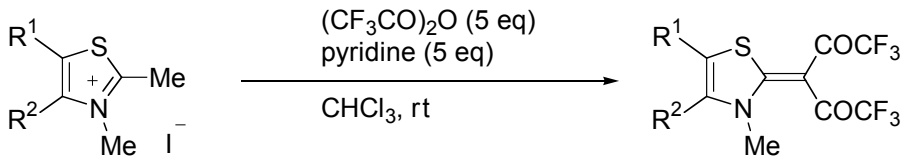
In the course of our investigations on the synthesis of various trifluoroacetylated olefins by the electrophilic substitutions[14-18,23] of olefinic hydrogens and the nucleophilic substitutions[15,19-23] at olefinic carbons, it was found that ketene dithioacetals[14] and orthoacetates[15] reacted with trifluoroacetic anhydride quite easily to afford the corresponding β-trifluoroacetylated ketene *S*,*S*- and *O*,*O*-acetals, respectively, and that these acylated compounds cleanly underwent nucleophilic *O*-*N* and *S*-*N* exchange reactions[21,23] with various aliphatic and aromatic amines to give β-trifluoroacetylated ketene *S*,*N*-, *O*,*N*-, and *N*,*N*-acetals.

In continuation of our extensive studies on the synthesis of trifluoroacetylated ketene acetals and their analogues, we here report an efficient synthetic method for new cyclic β-trifluoroacetylated ketene *S*,*N*-acetals, 2-bis(trifluoroacetyl)methylene- and 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (**2** and **3**), from 2,3-dimethylthiazolium iodides (**1**) with trifluoroacetic anhydride by improving the previously reported method.[24] Moreover, the highly poralized structure of diacylated compounds (**2**) is also described.

RESULTS AND DISCUSSION

We examined the reaction of 3-methylthiazolium iodides (**1**) with trifluoroacetic anhydride (Scheme 1 and Table 1). Reaction of 4,5-unsubstituted thiazolium iodides (**1a**) with 5 times molar amounts of trifluoroacetic anhydride in the presence of pyridine in chloroform easily proceeded at room temperature within 4 h to give 2-bis(trifluoroacetyl)methylene-2,3-dihydro-3-methylthiazole (**2a**) in 80% yield (entry

1). 4-Methyl-, 5-methyl-, and 5-chlorothiazolium iodides (**1b**,**c**,**f**) also exhibited the same reactivity with 4,5-unsubstituted thiazolium iodides (**1a**) to afford the corresponding 2-bis(trifluoroacetyl)methylene-2,3-dihydro-3-methylthiazoles (**2b,c,f**) in high yields (entries 2, 3, and 6). However, in the cases of 4,5-dimethyl- and 5-ethoxythiazolium iodides (**1d,e**), prolongation of the reaction time or/and large excess (10 times molar) amounts of the reagents were necessary to complete the reaction (entries 4 and 5). Previously, Bailey et al. reported the reaction, as the sole example of thiazolium salts, of 2,3-dimethylbenzo[*d*]thiazolium iodide with trifluoroacetic anhydride (10 eq) in the presence of pyridine (9 eq) for 15 min at 0 °C without solvent to give 2-bis(trifluoroacetyl)methylene-2,3-dihydro-3-methylbenzo[*d*]thiazole in a low yield (45%).[24] In contrast to this, the significant improvement of product yields would be achieved by the present method using chloroform as a solvent.



1a-f **2a-f**

Scheme 1

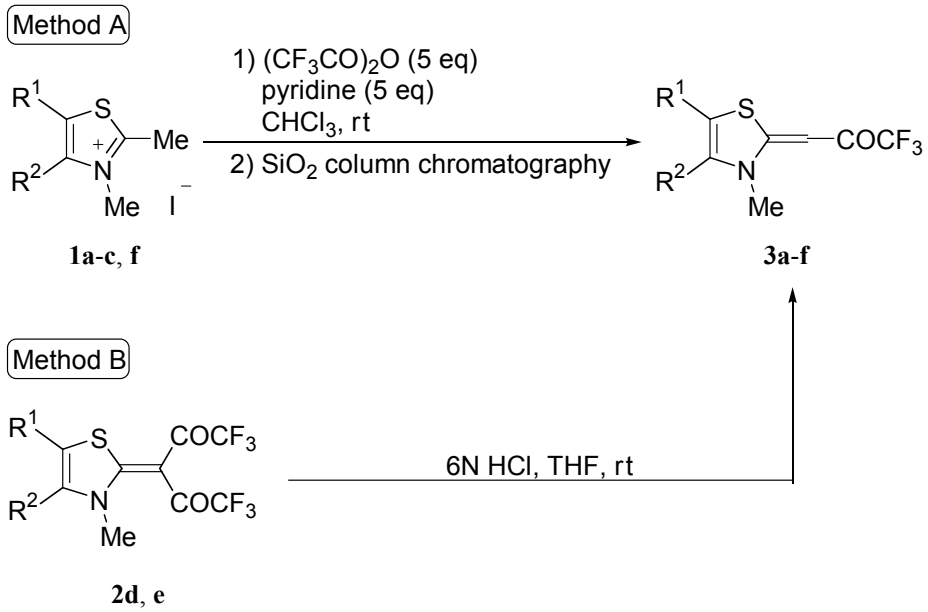
Table 1. Bis(trifluoroacetylation) of 2-methylthiazolium iodides (**1a-f**).

Entry	Substrate	R^1	R^2	Time (h)	Product	Yield (%)[a]
1	**1a**	H	H	4	**2a**	80
2	**1b**	H	Me	4	**2b**	84
3	**1c**	Me	H	4	**2c**	92
4[b]	**1d**	Me	Me	17	**2d**	89
5	**1e**	EtO	H	21	**2e**	70
6	**1f**	Cl	H	4	**2f**	91

[a] Isolated yields.
[b] Molar ratio, [**1d**] / [$(CF_3CO)_2O$] / [pyridine] = 1 / 10 / 10.

Acid-catalyzed deacylation of **2a**-**f** proceeded quite easily at room temperature to afford the corresponding 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (**3a**-**f**) in moderate to high yields (Scheme 2 and Table 2). 4,5-Unsubstituted, 4-methyl, 5-methyl, and 5-chloro derivatives (**3a**-**c** and **3f**) could be quite easily synthesized merely by submitting the crude products (**2a**-**c** and **2f**), prepared by bis(trifluoroacetylation) of **1a**-**c** and **1f**, to column chromatography on silica gel (entries 1-3 and 6, Method A). Deacylation of 4,5-dimethyl and 5-ethoxy derivatives (**2d**, **e**) did not take place merely by passing them through silica gel column. Treatment of **2d** and **2e** with 6N hydrochloric acid at room temperature for 4 h in tetrahydrofuran led to successful deacylation to give **3d** and **3e**,

respectively (entries 4 and 5, Method B).



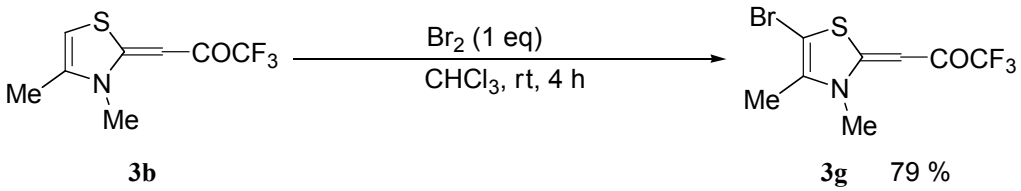
Scheme 2

Table 2. Synthesis of monoacylated compounds (**3a-f**)

Entry	Substrate	R^1	R^2	Method[a]	Time (h)	Product	Yield (%)[b]
1	**1a**	H	H	A	4	**3a**	65
2	**1b**	H	Me	A	43	**3b**	87
3	**1c**	Me	H	A	4	**3c**	72
4	**2d**	Me	Me	B	4	**3d**	84
5	**2e**	EtO	H	B	4	**3e**	88
6	**1f**	Cl	H	A	23	**3f**	91

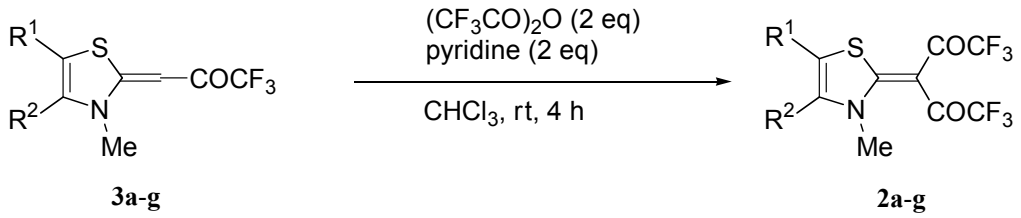
[a] Method A: SiO_2 column chromatography, Method B: 6N HCl.
[b] Isolated yields.

Next, we tried to synthesize 5-bromo-4-methyl derivative (**3g**) by bromination of 4-methyl one (**3b**) as depicted in Scheme 3. Regioselective bromination of **3b** with an equimolar amount of bromine proceeded quite easily and cleanly at room temperature for 4 h in chloroform to give the desired **3g** as a sole product in 79% yield without any formation of by-products brominated at other positions.



Scheme 3

In addition we tried the transformation of monoacylated **3a**-**g** to diacylated **2a**-**g**, specially to prepare bis(trifluoroacetylated) 5-bromo-4-methyl derivative (**2g**). The desired diacylation was successfully performed by treatment of **3a**-**g** with 2 times molar amounts of trifluoroacetic anhydride and pyridine in chloroform for 4 h to afford the corresponding **2a**-**g** in excellent yields (Scheme 4 and Table 3).



3a-g **2a-g**

Scheme 4

Table 3. Bis(trifluoroacetylation) of monoacylated compounds (**3a-g**)

Entry	Substrate	R^1	R^2	Product	Yield (%)[a]
1	**3a**	H	H	**2a**	97
2	**3b**	H	Me	**2b**	97
3	**3c**	Me	H	**2c**	91
4	**3d**	Me	Me	**2d**	96
5	**3e**	EtO	H	**2e**	91
6	**3f**	Cl	H	**2f**	97
7	**3g**	Br	Me	**2g**	98

[a] Isolated yields.

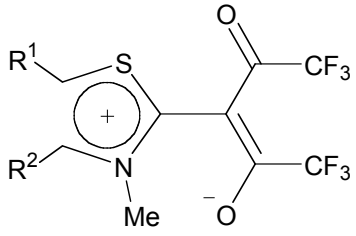
The selected ^{1}H NMR chemical shifts for thiazolium iodides (**1**), bis(trifluoroacetylated) derivatives (**2**), and mono(trifluoroacetylated) ones (**3**) are summarized in Table 4. Interestingly, the signals of H-4 (8.23 ppm) and H-5 (8.00 ppm) for **2a** (diacyl) appeared in much lower field than those (H-4: 7.28 ppm, H-5: 6.80 ppm) for **3a** (monoacyl) and were very close to those (H-4: 8.25 ppm, H-5: 7.98 ppm) for **1a** (thiazolium). The ^{1}H NMR spectra of other compounds (**1b**,**c**,**e**,**f**, **2b**,**c**,**e**,**f**, and **3b**,**c**,**e**,**f**) showed a marked tendency similar to those of **1a**, **2a**, and **3a**. IR spectra for diacylated derivatives (**2a**-**g**) showed an absorption in the range of 1641-1669 cm^{-1} (ν C=O). This band was absent for monoacylated derivatives (**3a**-**g**). These suggest that the aromatization of thiazoline to thiazolium takes place for diacylated derivatives (**2**) to form the inner thiazolium salts (**2'**) which have the highly polarized structure bearing an isolated trifluoroacetyl group as depicted in Figure 1 (resonance contribution from a zwitter ionic structure).

Finally we examined some reactions of **2b** with amines in order to prove the highly polarized structure of **2** from the standpoint of the reactivity. Reaction of **2b** with *N*,*N*'-diethylethylenediamine didn't take place in refluxing acetonitrile for 16 h and 80% of the substrate (**2b**) was recovered unchanged.

Table 4. The selected ^{1}H NMR chemical shifts of **1-3** in $CDCl_3$/DMSO-d_6 (2/1) [δ, ppm]

Compound	H-4	H-5	CH_3-3	CH_3-4	CH_3-5
1a	8.25[a]	7.98[a]	4.02[a]	-	-
2a	8.23	8.00	3.87	-	-
3a	7.28	6.80	3.66	-	-
1b	-	7.72	3.99	2.58	-
2b	-	7.75	3.68	2.59	-
3b	-	6.48	3.54	2.33	-
1c	8.12	-	4.10	-	2.52
2c	7.97	-	3.78	-	2.56
3c	6.95	-	3.59	-	2.29
1d	-	-	3.98	2.47	2.47
2d	-	-	3.67	2.49	2.49
3d	-	-	3.51	2.22	2.22
1e	8.03	-	4.20	-	-
2e	7.65	-	3.74	-	-
3e	6.70	-	3.54	-	-
1f	8.44	-	4.05	-	-
2f	8.27	-	3.71	-	-
3f	7.27	-	3.62	-	-
2g	-	-	3.76	2.57	-
3g	-	-	3.64	2.34	-

[a] Measured in DMSO-d_6.



2'

Figure 1

Benzylamine reacted with **2b** in refluxing acetonitrile for 41 h to afford *N*-benzyl-2,2,2-trifluoroacetamide quantitatively with deacylated product (**3b**) in 94% yield. Thus, in both cases, neither nucleophilic *S*-*N* nor *N*-*N* exchange reaction occurred at the olefinic carbon atom in this new cyclic β-trifluoroacetylated ketene *S*,*N*-acetal system. This is undoubtedly due to the highly polarized thiazolium structure (**2'**) for **2b** in which there is a considerable *C*-*C* single-bond character on the exomethylene moiety.

In conclusion, the present method provides a simple and efficient access to various 2-bis(trifluoroacetyl)methylene- and 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles which are not easily obtained by other methods. Evaluation of biological activities for **2a-g** and **3a-g** is now under way.

EXPERIMENTAL

General procedure for bis(trifluoroacetylation) of 2-methylthiazolium iodides (1).

To an ice-cooled mixture of **1**[25,26] (2 mmol) and pyridine (0.791 g, 10 mmol) was added dropwise a solution of trifluoroacetic anhydride (2.10 g, 10 mmol) in dry $CHCl_3$ (3 mL) with continuous stirring (in the case of **1d**, each 20 mmol of pyridine and trifluoroacetic anhydride was used). After stirring for 4 - 21 h at ambient temperature, the mixture was dissolved in CH_2Cl_2 (50 mL). The whole mixture was washed with aq. Na_2CO_3 and dried over Na_2SO_4. Removal of the solvent and pyridine under vacuum afforded 2-bis(trifluoroacetyl)methylene-2,3-dihydro-3-methylthiazoles (**2a**-**f**).

1,1,1,5,5,5-Hexafluoro-3-(3-methyl-3*H*-thiazol-2-ylidene)pentane-2,4-dione (2a): mp 98-99 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 3H, CH_3), 7.72 (d, *J*= 4.0 Hz, 1H, SCH=C), 7.92 (d, *J*= 4.0 Hz, 1H, NCH=C); IR (KBr) 1641, 1597, 1547 cm^{-1}.

3-(3,4-Dimethyl-3*H*-thiazol-2-ylidene)-1,1,1,5,5,5-hexafluoropentane-2,4-dione (2b): mp 133-134 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.57 (s, 3H, CCH_3), 3.70 (s, 3H, NCH_3), 7.45 (s, 1H, CH); IR (KBr) 1658, 1580 cm^{-1}. Anal. Calcd for $C_{10}H_7F_6NO_2S$: C, 37.62; H, 2.21; N, 4.39; F, 35.71. Found: C, 37.54; H, 2.04; N, 4.53; F, 35.75.

3-(3,5-Dimethyl-3*H*-thiazol-2-ylidene)-1,1,1,5,5,5-hexafluoropentane-2,4-dione (2c): mp 128-129 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.59 (s, 3H, CCH_3), 3.81 (s, 3H, NCH_3), 7.75 (s, 1H, CH); IR (KBr) 1654, 1580 cm^{-1}.

1,1,1,5,5,5-Hexafluoro-3-(3,4,5-trimethyl-3*H*-thiazol-2-ylidene)pentane-2,4-dione (2d): mp 173-174 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$/DMSO-d_6 = 2/1) δ 2.49 (s, 6H, CCH_3), 3.67 (s, 3H, NCH_3); IR (KBr) 1664, 1591 cm^{-1}. Anal. Calcd for $C_{11}H_9F_6NO_2S$: C, 39.65; H, 2.72; N, 4.20; F, 34.21. Found: C, 39.93; H, 2.61; N, 4.04; F, 34.06.

3-(5-Ethoxy-3-methyl-3*H*-thiazol-2-ylidene)-1,1,1,5,5,5-hexafluoropentane-2,4-dione (2e): mp 96-97 °C (crude product); ^{1}H NMR ($CDCl_3$) δ 1.49 (t, *J*= 6.8 Hz, 3H, $CH_2C\underline{H}_3$), 3.76 (s, 3H, NCH_3), 4.23 (q, *J*= 6.8 Hz, 2H, CH_2), 7.40 (s, 1H, CH); IR (KBr) 1659, 1600, 1576 cm^{-1}.

3-(5-Chloro-3-methyl-3*H*-thiazol-2-ylidene)-1,1,1,5,5,5-hexafluoropentane-2,4-dione (2f): mp (decomp) 91-93 °C (crude product); ^{1}H NMR ($CDCl_3$) δ 3.72 (s, 3H, CH_3), 7.54 (s, 1H, CH); IR (KBr) 1669, 1589, 1554 cm^{-1}.

Synthesis of 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (3a-c,f): Method A.

To an ice-cooled mixture of **1** (2 mmol) and pyridine (0.791 g, 10 mmol) was added dropwise a solution of trifluoroacetic anhydride (2.10 g, 10 mmol) in dry $CHCl_3$ (3 mL) with continuous stirring. After stirring for 4 - 43 h at ambient temperature, the mixture was dissolved in CH_2Cl_2 (50 mL). The whole mixture was washed with aq. Na_2CO_3 and then with dil. HCl, and dried over Na_2SO_4. Evaporation of the solvent and fractionation of a residue by silica gel column chromatography (CH_2Cl_2) afforded 2-

trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (**3a**-**c**,**f**).

Synthesis of 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (3d,e): Method B.

To a solution of **2** (0.710 mmol) dissolved in THF (4 mL) was added 6 N HCl (8 mL). After stirring for 4 h at ambient temperature, the mixture was extracted with CH_2Cl_2 (50 mL). The organic layer was washed with water and dried over Na_2SO_4, and the solvent was evaporated to give 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (**3d**,**e**).

1,1,1-Trifluoro-3-(3-methyl-3*H*-thiazol-2-ylidene)propan-2-one (3a): mp 175-176 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 3H, CH_3), 5.95 (s, 1H, $CHCOCF_3$), 6.66 (d, *J*= 4.2 Hz, 1H, SCH=C), 6.84 (d, *J*= 4.2 Hz, 1H, NCH=C); IR (KBr) 1581, 1527 cm^{-1}. Anal. Calcd for $C_7H_6F_3NOS$: C, 40.19; H, 2.89; N, 6.70; F, 27.25. Found: C, 40.46; H, 2.88; N, 6.90; F, 27.05.

3-(3,4-Dimethyl-3*H*-thiazol-2-ylidene)-1,1,1-trifluoropropan-2-one (3b): mp 175-176 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3H, CCH_3), 3.48 (s, 3H, NCH_3), 5.87 (s, 1H, $CHCOCF_3$), 6.28 (s, 1H, SCH=C); IR (KBr) 1582, 1522 cm^{-1}. Anal. Calcd for $C_8H_8F_3NOS$: C, 43.05; H, 3.61. Found: C, 43.33; H, 3.46.

3-(3,5-Dimethyl-3*H*-thiazol-2-ylidene)-1,1,1-trifluoropropan-2-one (3c): mp 173-174 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3H, CCH_3), 3.53 (s, 3H, NCH_3), 5.82 (s, 1H, $CHCOCF_3$), 6.67 (s, 1H, NCH=C); IR (KBr) 1580, 1520 cm^{-1}. Anal. Calcd for $C_8H_8F_3NOS$: C, 43.05; H, 3.61; N, 6.27; F, 25.53. Found: C, 42.91; H, 3.48; N, 6.30; F, 25.32.

1,1,1-Trifluoro-3-(3,4,5-trimethyl-3*H*-thiazol-2-ylidene)propan-2-one (3d): mp 155-156 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.16 (s, 6H, CCH_3), 3.42 (s, 3H, NCH_3), 5.75 (s, 1H, CH); IR (KBr) 1580, 1511 cm^{-1}.

3-(5-Ethoxy-3-methyl-3*H*-thiazol-2-ylidene)-1,1,1-trifluoropropan-2-one (3e): mp 145-146 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 1.40 (t, *J*= 6.0 Hz, 3H, $CH_2C\underline{H}_3$), 3.48 (s, 3H, NCH_3), 4.00 (q, *J*= 6.0 Hz, 2H, CH_2), 5.77 (s, 1H, $CHCOCF_3$), 6.33 (s, 1H, NCH=C); IR (KBr) 1609, 1563, 1534 cm^{-1}. Anal. Calcd for $C_9H_{10}F_3NO_2S$: C, 42.69; H, 3.98; N, 5.53; F, 22.51. Found: C, 42.40; H, 3.73; N, 5.41; F, 22.21.

3-(5-Chloro-3-methyl-3*H*-thiazol-2-ylidene)-1,1,1-trifluoropropan-2-one (3f): mp 154-155 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 3.56 (s, 3H, NCH_3), 5.95 (s, 1H, $CHCOCF_3$), 6.83 (s, 1H, NCH=C); IR (KBr) 1581, 1567, 1528, 1511 cm^{-1}. Anal. Calcd for $C_7H_5ClF_3NOS$: C, 34.51; H, 2.07; N, 5.75; F, 23.39; Cl, 14.55. Found: C, 34.92; H, 1.99; N, 5.78; F, 23.12; Cl, 14.20.

Synthesis of 3-(5-bromo-3,4-dimethyl-3*H*-thiazol-2-ylidene)-1,1,1-trifluoropropan-2-one (3g).

To a stirred solution of **3b** (304 mg, 1.36 mmol) in $CHCl_3$ (10 mL) was added dropwise Br_2 (227 mg, 1.42 mmol) and the mixture was stirred for 4 h at ambient temperature. After evaporation of the solvent, purification of a residue by silica gel column chromatography (benzene) afforded **3g** (325 mg, 79%).

3g: mp (decomp) 154-155 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3H, CCH_3), 3.49 (s, 3H, NCH_3), 5.95 (s, 1H, CH); IR (KBr) 1600, 1581, 1527, 1518 cm^{-1}. Anal. Calcd for $C_8H_7BrF_3NOS$: C, 31.80; H, 2.34; N, 4.64; F, 18.87; Br, 26.45. Found: C, 31.94; H, 2.46; N, 4.59; F, 18.75; Br, 26.14.

General procedure for bis(trifluoroacetylation) of 2-trifluoroacetylmethylene-2,3-dihydro-3-methylthiazoles (3).

To an ice-cooled mixture of **3** (1 mmol) and pyridine (158 mg, 2 mmol) was added dropwise a solution of trifluoroacetic anhydride (420 mg, 2 mmol) in dry $CHCl_3$ (4 mL) with continuous stirring. After stirring for 4 h at ambient temperature, the mixture was dissolved in CH_2Cl_2 (50 mL). The whole mixture was washed with aq. Na_2CO_3 and dried over Na_2SO_4. Removal of the solvent and pyridine under vacuum gave 2-bis(trifluoroacetyl)methylene-2,3-dihydro-3-methylthiazole (**2a**-**g**).

3-(5-Bromo-3,4-dimethyl-3*H*-thiazol-2-ylidene)-1,1,1,5,5,5-hexafluoropentane-2,4-dione (2g): mp (decomp) 178-179 °C (hexane-benzene); ^{1}H NMR ($CDCl_3$) δ 2.51 (s, 3H, CCH_3), 3.67 (s, 3H, NCH_3); IR (KBr) 1668, 1588, 1550 cm^{-1}. Anal. Calcd for $C_{10}H_6BrF_6NO_2S$: C, 30.17; H, 1.52; N, 3.52; F, 28.63; Br, 20.07. Found: C, 30.17; H, 1.49; N, 3.52; F, 28.25; Br, 19.93.

Reaction of 2b with *N*,*N*'-diethylethylenediamine.

To a stirred solution of **2b** (180 mg, 0.56 mmol) in MeCN (4 mL) was added *N*,*N*'-diethylethylenediamine (67 mg, 0.58 mmol) and the mixture was refluxed for 16 h. Evaporation of the solvent gave **2b** (144 mg, 80% recovery).

Reaction of 2b with benzylamine.

To a stirred solution of **2b** (101 mg, 0.32 mmol) in MeCN (4 mL) was added benzylamine (119 mg, 1.11 mmol) and the mixture was refluxed for 41 h. After evaporation of the solvent, a residue was fractionated by silica gel column chromatography. Elution with benzene afforded slightly contaminated benzyltrifluoroacetamide (69 mg) and that with CH_2Cl_2 gave **3b** (67 mg, 94%).

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