Reaction of secondary amines with 2-(imidazol-1-yl)-perfluoro-5,5-dimethyl-4-ethylidene-2-thiazoline

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Reactions of 2-(imidazol-1-yl)-perfluoro-5,5-dimethyl-4-ethylidene-2-thiazoline with a series of secondary amines in THF resulted in the replacement of the imidazole moiety by the amine moiety.

Key words: nucleophilic substitution and addition, secondary amines, 2-aminosubstituted perftuoro-5,5-dimethyl-4-ethylidene-2-thiazolines.

The recently increasing interest in fluorine-containing heterocyclic compounds is due to the fact that perfluoroalkyl groups and fluorine atoms are capable of enhancing the biological activity of these systems.[1] Among various heterocyclic compounds, derivatives of 2-thiazoline can be specially noted as intermediates in the syntheses of agricultural preparations (for example, see Ref. 2). They can be synthesized starting from internal perfluoroolefins[3] or their derivatives, *e.g.*, perfluoro-3-isothiocyanato-2-methylpent-2-ene.[4,5] The reactions of this compound with O-, S-, and C-nucleophiles afford 2-substituted 2-thiazolines.[6—8] However, its reaction with secondary aliphatic amines results in 2-substituted 6*H*-1,3-thiazines.[9]

The aim of this work was to study the possibility of synthesizing *N*-(perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)amines using this approach. 2-(Imidazol-1-yl)-perfluoro-5,5-dimethyl-4-ethylidene-2-thiazoline (**1**) was chosen as a model compound because this compound is readily accessible and the imidazole can be easily separated from the expected reaction products.

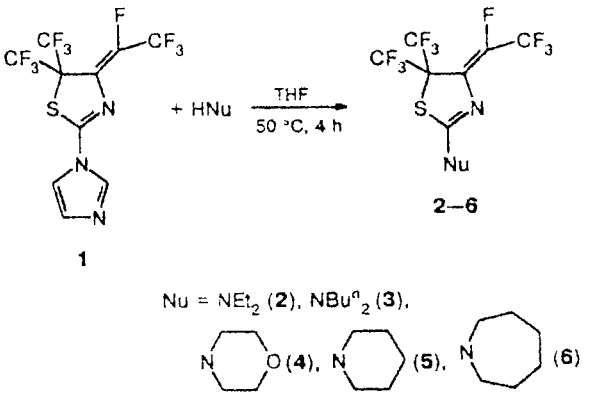
Results and Discussion

The reaction of compound **1** with diethylamine, di-*n*-butylamine, morpholine, piperidine, and azepane in THF (Scheme 1) afforded products of replacement of the imidazole moiety by the secondary amine moiety (compounds **2**—**6**).

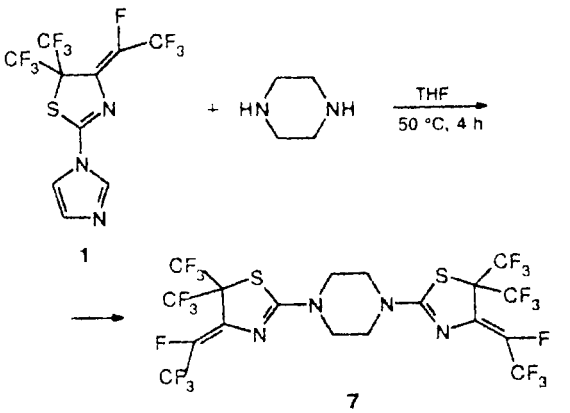
If piperazine was used as a nucleophilic agent (Scheme 2), a bis-substitution product (**7**) was formed.

Initially, the addition of the *N*-nucleophile to the C=N bond of compound **1** to form a zwitter-ion (**8**) (Scheme 3) is likely to take place. Subsequent transformation of **8** to zwitter-ion **9** by proton transfer leads to reaction products **2**—**6** due to the elimination of imida-

Scheme 1



Scheme 2



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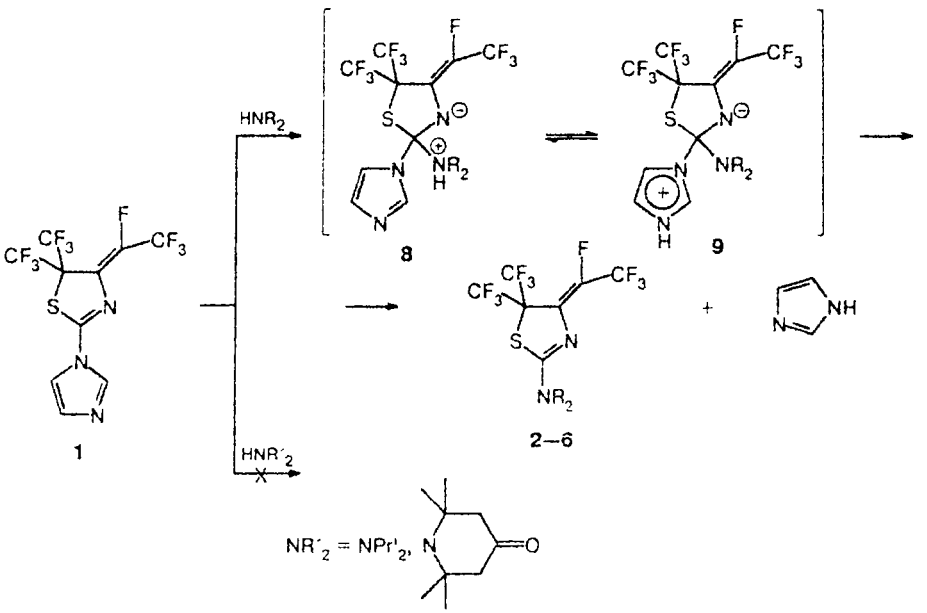
Scheme 3



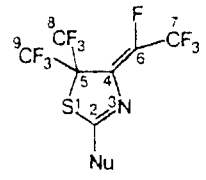
zole. The evidence for the suggested reaction pathway is the fact that compound **1** does not react with diisopropylamine and 2,2,6,6-tetramethylpiperidin-4-one, for which the formation of zwitter-ion **8** is impeded due to steric hindrances.

The structure of compounds **2**—**7** was established by IR, ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy and mass spectrometry, taking into account the published data for compounds of this type.[6] For example, ^{19}F NMR spectra of **2**—**7** contain three signals with the intensity ratio 3 : 6 : 1 (d, J_{F-F} = 8—9 Hz, d, J_{F-F} = 22—23 Hz, and q.sept, J_{F-F} = 22—23 and 8—9 Hz), which implies the *E*-configuration of the C=C bond (Table 1). It should be noted that this configuration for 2-amino-perfluoro-4,4-dimethyl-5-ethylidene-2-thiazoline was confirmed by X-ray structural analysis.[10] The IR spectrum contains an intense absorption band at 1600 cm^{-1}, which characterizes vibrations of atoms at the C=C bond.[11] In addition, a low-intensity absorption band at 1450—1465 cm^{-1}, which can be assigned to vibrations of the C=N bond is present in the IR spectrum.

The analysis of the ^{13}C NMR spectra shows that the signal at δ 161.5—162 (s) corresponds to the C atom in position 2. The signals at δ 139.4—140.4 (qd) and 135.8—137.2 (d) correspond to the C-6 and C-4 atoms of the C=C bond and the signal at δ 120.2 (dq) is assigned to the C-7 atom (the CF_3 group).

Thus, we have performed the synthesis of 2-aminosubstituted derivatives of 2-thiazoline on the basis of replacement of the imidazole moiety at position 2 by the secondary amine moiety.

Table 1. ^{19}F NMR data for 2-thiazolines **2**—**7**[7]



Compound	δ (J_{F-F}/Hz)		
	FC-6 (q.sept)	FC-7 (d)	FC-8, FC-9 (d)
2	9.91 (8, 23)	96.5 (8)	96.1 (23)
3	9.9 (9, 23)	96.4 (9)	95.9 (23)
4	12.6 (8.5, 23)	96.7 (8.5)	95.5 (23)
5	10.2 (9, 23)	96.0 (9)	95.8 (23)
6	9.7 (9, 23)	96.4 (9)	96.0 (23)
7	11.9 (9, 23)	97.8 (9)	97.4 (23)

Experimental

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker WP 200 SY spectrometer (200.5 and 188 MHz, respectively), using $SiMe_4$ and C_6F_6 as the internal standards. IR spectra were obtained on a Specord M-80 spectrometer (CCl_4). Mass spectra were obtained on a VG 707 OE chromato-mass spectrometer (electron ionization energy 70 eV). Compound **1** was obtained by the known procedure.[12]

Reaction of compound 1 with secondary amines. A mixture of compound **1** (5.81 g, 0.02 mol) and Et_2NH (1.095 g, 0.02 mol) in THF (15 mL) was stirred at 50°C for 4 h, poured into water, and extracted with $CHCl_3$. The organic layer was washed with water and dried with $MgSO_4$. The solvent was distilled off and the residue was distilled *in vacuo* to give 3.76 g (64%) of ***N,N*-diethyl-*N*-(perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)amine** (**2**). Some characteristics of this com-

Table 2. Characteristics of compounds **2**—**7**

Compound	Yield (%)	B.p./°C (M.p./°C) *p*/Topp	*m/z*, exp. (*m/z*, calc.)	Found (%) / Calculated			Molecular formula
				C	H	N	
2	64	66—68 / 0.1	392.03990 (392.04050)	33.40 / 33.67	2.64 / 2.57	7.64 / 7.14	$C_{11}H_{10}F_{10}N_2S$
3	68	74—76 / 0.008	448.10247 (448.10310)	40.82 / 40.18	4.06 / 4.05	4.91 / 4.25	$C_{15}H_{18}F_{10}N_2S$
4	66	(66—67)	406.02143 (406.01976)	—	2.58 / 3.07	6.44 / 6.56	$C_{11}H_8F_{10}N_2OS$
5	63	(81—82)	404.03906 (404.04049)	35.12 / 35.64	2.25 / 2.49	7.33 / 6.93	$C_{12}H_{10}F_{10}N_2S$
6	66	98—99 / 0.16	418.05691 (418.05615)	37.00 / 37.32	2.71 / 2.89	7.60 / 6.70	$C_{13}H_{12}F_{10}N_2S$
7	69	(217—218)	723.98370 (723.98710)	29.93 / 29.85	1.16 / 1.11	8.07 / 7.73	$C_{18}H_8F_{20}N_4S_2$

pound are given in Tables 1 and 2. IR, ν/cm^{-1}: 3000 (C—H); 1600 (C=C); 1465 (N=C); 1190—1230 (C—F). MS, *m/z* (I_{rel}(%)): 392 $[M]^+$ (100), 377 $[M-Me]^+$ (13.50), 363 $[M-Et]^+$ (51.34), 349 $[M-NEt]^+$ (70.39), 343 $[M-Et-HF]^+$ (17.07), 329 $[M-NEt-HF]^+$ (23.93), 323 $[M-CF_3]^+$ (30.67), 303 $[M-CF_3-HF]^+$ (10.36), 119 $[C_2F_5]^+$ (1.30), 72 $[NEt_2]^+$ (22.80), 69 $[CF_3]^+$ (10.02), 44 $[HNEt]^+$ (10.63), 29 $[Et]^+$ (26.65). ^1H NMR ($CDCl_3$), δ: 3.42 (q, CH_2) and 1.21 (t, Me). ^{13}C NMR ($CDCl_3$), δ: 162.1 (C-2); 140.4 (C-6, $^1J_{C-F}$ = 249.9, $^2J_{C-F}$ = 38.9 Hz); 137.2 (C-4, $^2J_{C-F}$ = 28.3 Hz); 122.7 (C(8,9), $^1J_{C-F}$ = 284.1 Hz); 120.2 (C-7, $^1J_{C-F}$ = 272.3, $^2J_{C-F}$ = 37.3 Hz); 76.1 (C-5, $^2J_{C-F}$ = 35.2 Hz); 23.9 (C-10); 25.5 (C-11); 18.3 (C-12).

Compounds **3**—**7** were obtained by a similar procedure (see Tables 1 and 2).

***N,N*-Di-*n*-butyl-*N*-(perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)amine (3).** IR, ν/cm^{-1}: 2950 (C—H); 1600 (C=C); 1450 (N=C); 1350 (N—C); 1120—1250 (C—F). MS, *m/z* (I_{rel}(%)): 448 $[M]^+$ (100), 429 $[M-F]^+$ (34.59), 419 $[M-Et]^+$ (23.02), 406 $[M-C_3H_6]^+$ (15.00), 379 $[M-CF_3]^+$ (37.77), 363 $[M-Bu-C_2H_4]^+$ (64.83), 364 $[M-C_4H_8-C_2H_4]^+$ (64.83), 349 $[M-Bu-C_3H_6]^+$ (64.81), 350 $[M-C_4H_8-C_3H_6]^+$ (22.56), 337 $[M-C_2F_5-C_3H_6]^+$ (24.77), 329 $[M-C_2F_5]^+$ (16.32), 323 $[M-CF_3-C_4H_8]^+$ (59.96), 297, 255, 241, 205, 84, 69 $[CF_3]^+$ (5.20), 57 $[Bu]^+$ (61.00), 55 $[C_4H_7]^+$ (28.70), 41 $[MeCN]^+$ (65.75). ^1H NMR ($CDCl_3$), δ: 3.48 and 3.20 (t, NCH_2, 7.0); 1.60 (m, CH_2); 1.30 (m, CH_2); 0.92 (t, Me). ^{13}C NMR ($CDCl_3$), δ: 162.0 (C-2); 139.8 (C-6, $^1J_{C-F}$ = 250.5, $^2J_{C-F}$ = 39.1 Hz); 135.8 (C-4, $^2J_{C-F}$ = 28.1 Hz); 122.8 (C-8, C-9, $^1J_{C-F}$ = 284.1 Hz); 120.2 (C-7, $^1J_{C-F}$ = 272.2, $^2J_{C-F}$ = 37.2 Hz); 75.4 (C-5, $^2J_{C-F}$ = 31.2 Hz); 52.9 (C-10); 50.9 (C-14); 30.6 (C-11); 29.4 (C-15); 19.8 (C-12, C-16); 13.2 (C-13, C-17).

***N*-(Perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)morpholine (4).** The product was distilled *in vacuo* and crystallized from pentane. IR, ν/cm^{-1}: 2980 (C—H); 1600 (C=C); 1450 (N=C); 1350 (N—C); 1180—1240 (C—F). MS, *m/z* (I_{rel}(%)): 406 $[M]^+$ (100), 387 $[M-F]^+$ (23.70), 349 $[M-C_3H_7O]^+$ (29.75), 337 $[M-CF_3]^+$ (16.73), 279, 260, 229, 86, 69 $[CF_3]^+$ (5.42), 56 $[C_3H_6O]^+$ (10.81). ^1H NMR ($CDCl_3$), δ: 3.75 (m, CH_2N), 3.56 (m, CH_2O). ^{13}C NMR ($CDCl_3$), δ: 162.1 (C-2); 140.1 (C-6, $^1J_{C-F}$ = 252.6, $^2J_{C-F}$ = 39.2 Hz); 135.2 (C-4, $^2J_{C-F}$ = 28.5 Hz); 122.5 (C-8, C-9, $^1J_{C-F}$ = 284.4 Hz); 117.0 (C-7, $^1J_{C-F}$ = 272.6, $^2J_{C-F}$ = 37.4 Hz); 74.9 (C-5, $^2J_{C-F}$ = 35.0 Hz); 65.8 (C-10); 48.7 (C-11).

***N*-(Perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)piperidine (5).** The product was distilled *in vacuo* and crystallized from hexane. IR, ν/cm^{-1}: 3000 (C—H); 1600 (C=C); 1445 (N=C); 1350 (N—C); 1190—1250 (C—F). MS, *m/z* (I_{rel}(%)): 404 $[M]^+$ (100), 385 $[M-F]^+$ (23.93), 335 $[M-CF_3]^+$ (14.82), 315 $[M-CF_3-HF]^+$ (12.21), 219, 175, 69 $[CF_3]^+$ (8.55), 55 $[C_4H_7]^+$ (15.29), 41 $[MeCN]^+$ (20.24). ^1H NMR ($CDCl_3$), δ: 3.53 (m, CH_2N, CH_2); 1.68 (m, CH_2). ^{13}C NMR ($CDCl_3$), δ: 162.1 (C-2); 140.4 (C-6, $^1J_{C-F}$ = 249.9, $^2J_{C-F}$ = 38.9 Hz); 137.2 (C-4, $^2J_{C-F}$ = 28.0 Hz); 122.8 (C-8, C-9, $^1J_{C-F}$ = 284.1 Hz); 120.2 (C-7, $^1J_{C-F}$ = 272.3, $^2J_{C-F}$ = 37.3 Hz); 76.1 (C-5, $^2J_{C-F}$ = 35.2 Hz); 23.93 (C-10); 25.5 (C-11); 18.3 (C-12).

***N*-(Perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)azepane (6).** IR, ν/cm^{-1}: 2920, 2850 (C—H); 1600 (C=C); 1450 (C=N); 1315 (C—N); 1150—1250 (C—F). MS, *m/z* (I_{rel}(%)): 418 $[M]^+$ (100), 403 $[M-Me]^+$ (14.80), 399 $[M-F]^+$ (28.59), 389 $[M-N_2-Et]^+$ (5.89), 375 $[M-Pr]^+$ (14.46), 349 $[M-CF_3]^+$ (54.77), 329 $[M-CF_3-HF]^+$ (16.44), 295 $[M-C_6H_9NCN]^+$ (7.79), 279 $[M-CF_3-C_5H_{10}]^+$ (4.95), 260 $[M-CF_3-FC_5H_{10}]^+$ (3.11), 175, 98 $[C_6H_{12}N]^+$ (18.72), 55 $[EtCN]^+$ (28.95), 41 $[MeCN]^+$ (30.86), 69 $[CF_3]^+$ (7.08). ^1H NMR ($CDCl_3$), δ: 3.67 (t, CH_2N); 3.39 (t, CH_2N); 1.77 (m, CH_2); 1.57 (t, CH_2) (signal intensity ratio 1 : 1 : 2 : 2). ^{13}C NMR ($CDCl_3$), δ: 162.1 (C-2); 139.3 (C-6, $^1J_{C-F}$ = 250.0, $^2J_{C-F}$ = 39.1 Hz); 135.9 (C-4, $^2J_{C-F}$ = 28.6 Hz); 122.8 (C-8, C-9, $^1J_{C-F}$ = 284.2 Hz); 120.2 (C-7, $^1J_{C-F}$ = 272.2, $^2J_{C-F}$ = 37.3 Hz); 75.4 (C-5, $^2J_{C-F}$ = 31.2 Hz); 53.0 and 50.9 (C-10); 28.9 and 27.1 (C-11); 26.7 and 26.5 (C-12).

***N,N'*-Bis(perfluoro-5,5-dimethyl-4-ethylidene-2-thiazolin-2-yl)piperazine (7).** The reaction mixture was poured into water, the precipitate that formed was separated, and the product was extracted from the solution with chloroform. The extract and the residue were combined and dried with $CaCl_2$. The solvent was evaporated, and the residue was crystallized from a hexane—chloroform mixture (1 : 4). IR, ν/cm^{-1}: 3000 (C—H); 1600 (C=C); 1450 (C=N); 1315 (C—N); 1150—1250 (C—F). MS, *m/z* (I_{rel}(%)): 724 $[M]^+$ (60.91), 705 $[M-F]^+$ (40.50), 655 $[M-CF_3]^+$ (1.79), 635 $[M-CF_3-HF]^+$ (0.61), 404 $[M-C_7F_{10}NS]^+$ (0.68), 388 $[C_{11}H_8F_{10}N_3S]^+$ (11.35), 362 $[C_{11}H_8F_{10}N_3S-C_2H_4N]^+$ (100), 375 $[C_{11}H_8F_{10}N_3S-Et]^+$ (41.82), 320 $[C_7F_{10}NS]^+$ (16.12), 293 $[C_7F_{10}NS-CH_2=CH]^+$ (18.16), 100 $[CF_2=CF_2]^+$ (1.89), 86 $[C_4H_6N]^+$ (2.64), 69 $[CF_3]^+$ (4.16). ^1H NMR ($CDCl_3$), δ: 3.95 (m, CH_2).

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