HETEROCYCLIZATION REACTIONS WITH α,β-UNSATURATED FLUORINE-CONTAINING ISOTHIOCYANATES: REACTIONS OF PERFLUORO-2-METHYL-2-PENTEN-3-YL ISOTHIOCYANATE WITH ENAMINES[1]

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Dedicated to Professor Rolf Huisgen on the occasion of his 75th birthday

Abstract - A one-step synthesis of polyfluorinated 4,5-dihydro- and 2,5-dihydro-1,3-thiazoles starting from perfluoro-2-methyl-2-penten-3-yl isothiocyanate and enamines is described. The formation of 4,5-dihydro-1,3-thiazoles proceeds stereospecifically with respect to the exocyclic CC double bond.

INTRODUCTION

Nitrogen- and sulfur-containing polyfluorinated heterocycles are available *via* Thorpe-type cyclization reactions[2,3] from polyfluoro-α,β-unsaturated thiocyanates.[4,5] We now report that their thermodynamically more stable isomers, namely the perfluoro-α,β-unsaturated isothiocyanates, likewise, are excellently suited for the synthesis of various polyfluorinated nitrogen- and sulfur-containing heterocycles *via* intramolecular heterocyclization reactions.

Only one representative of this class of compounds – the perfluoro-2-methyl-1-propen-1-yl isothiocyanate – has been described so far.[6] The preparative potential as perfluorinated building

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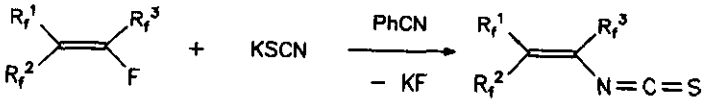
block for heterocyclic synthesis has not yet been exploited, although the regioselective introduction of short-chain perfluoroalkyl groups into target molecules is of current interest. Perfluoroalkyl groups in strategical positions of organic molecules may modify reactivity,[7] selectivity in chemical reactions,[8] biological activity,[9] and material properties[10] profoundly.

RESULTS AND DISCUSSION

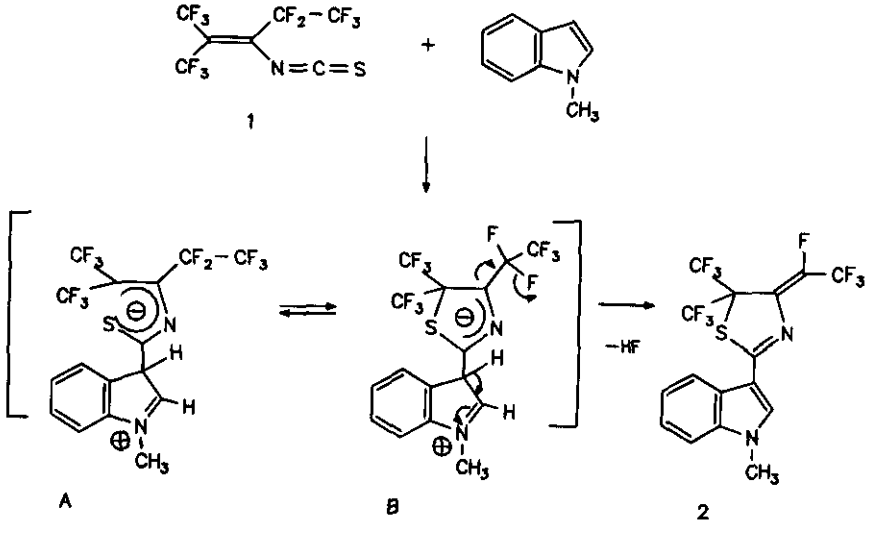
Unfluorinated α,β-unsaturated isothiocyanates represent valuable, highly versatile educts for heterocyclic synthesis. However, they can not be prepared by conventional methods.[11] In contrast, perfluoro-α,β-unsaturated isothiocyanates are perfectly stable compounds, accessible in high yields on direct substitution of fluorine in perfluoroolefins by rhodanide[5,6] (Scheme 1). The ambident anion exclusively attacks perfluoroolefins by its nitrogen terminus. This selectivity



Scheme 1

can be readily explained by the HSAB concept.[12] In the present paper we describe a new, preparatively simple access to partially fluorinated thiazole derivatives, starting from perfluoro-α,β-unsaturated isothiocyanates and enamines.

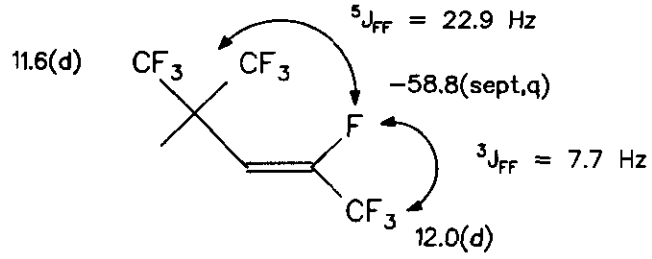
Construction of heterocycles from unfluorinated isothiocyanates and enamines is well documented,[11,13] but in the case of fluoro-substituted α,β-unsaturated isothiocyanates of type 1 additional functionalities are present, namely a highly electrophilic CC double bond, capable for



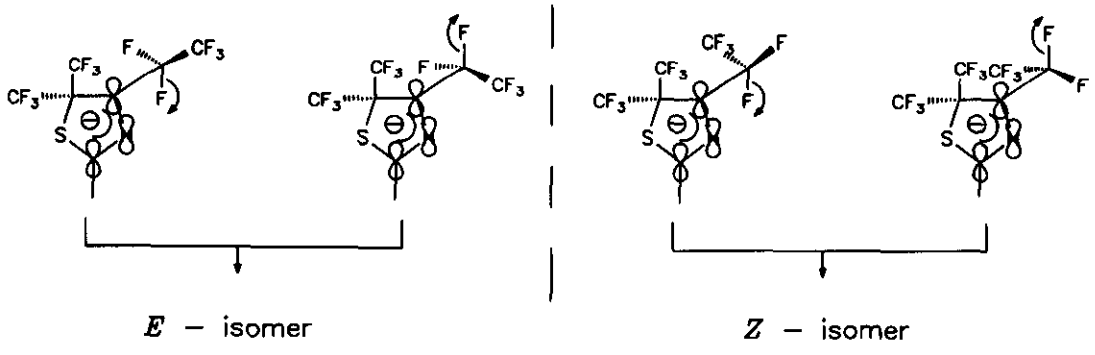
Scheme 2

nucleophilic attack, and mobile fluorine atoms in allylic position, enlarging the preparative potential of this class of compounds considerably.

When perfluoro-2-methyl-2-penten-3-yl isothiocyanate (**1**) is treated with 1-methylindole, compound (**2**) can be isolated in 78% yield (Scheme 2). The large coupling constant of $^{5}J_{FF}$= 22.9 Hz reveals that the $C(CF_3)_2$ group and the single fluorine are placed *cis* in respect to the CC double bond Therefore, the exocyclic CC double bond formed by fluoride elimination exclusively exhibits *E*-configuration. Likewise, the exocyclic CC double bond of 2-amino-perfluoro-4,4-dimethyl-4,5-dihydro-5-ethylidene-1,3-thiazole obtained on reaction of perfluoro-2-methyl-2-penten-3-yl thiocyanate - an isomer of **1** - and ammonia is *E*-configurated.[2]



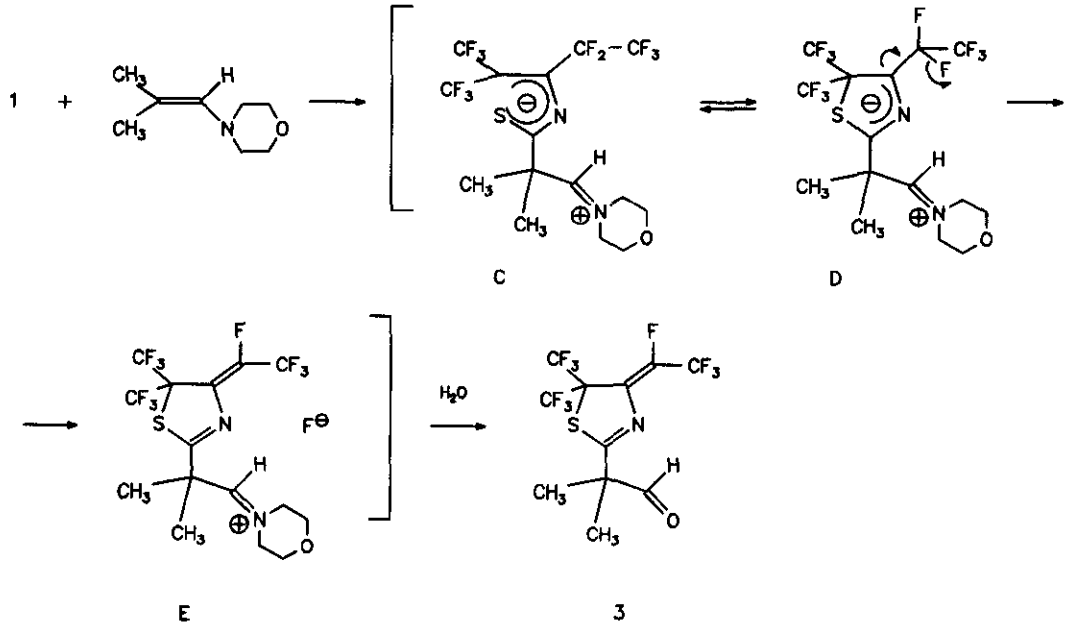
The conformers of the 4-pentafluoroethyl-1-thia-3-azacyclopentenyl anion (**B**), formed on 1,5-electrocyclization of the 1-thia-3-azapentadienyl anion (**A**), providing the *E*-olefin on fluoride elimination are energetically much more favored (Scheme 3), since the sterically demanding groups $C(CF_3)_2$ and CF_3 are occupying positions which guarantee maximum distance form each other [14]



Scheme 3

The discussion about the size of a trifluoromethyl group remains still a controversial issue.[15] The van der Waals radii of a trifluoromethyl group and of a methyl group are 2.7 Å / 2.0 Å, whereas the van der Waals volumes are 42.6 $Å^3$ and 16.8 $Å^3$ respectively. Therefore, the sterical demand of a trifluoromethyl group seems to be close to that of an isopropyl group. The stereoselectivity observed in the above reaction is in agreement with these findings.

The final step of the reaction sequence **1** → → **2** is a deprotonation with rearomatization of the indole system.



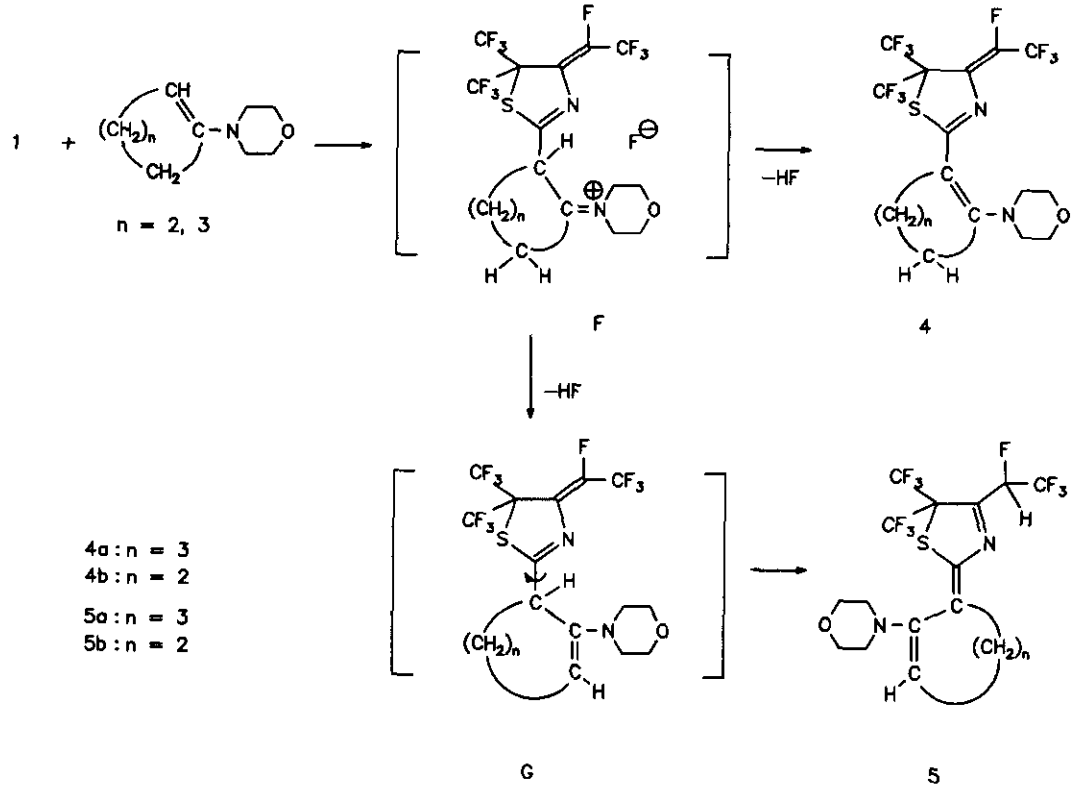
Scheme 4

When **1** is reacted with 2-methyl-1-morpholino-1-propene (Scheme 4), the iminium salt **E** formed *via* 1,5-electrocyclization and fluoride elimination from the zwitterionic primary adduct **C** was not isolated Hydrolysis of the iminium salt results in the formation of a stable carbonyl compound (**3**), which itself represents an interesting fluoro-containing building block for heterocyclic chemistry.[16]

When 1-morpholino-1-cyclohexene is introduced into the above reaction (Scheme 5), depending on the molar ratio of the starting materials and the reaction conditions applied, compound (**4a**) or mixtures of **4a** and **5a** are formed (Table 1).

Isomer (**4a**) is obtained in nearly quantitative yield under acidic conditions, when equimolar amounts of the enamine (solution in ether) are added slowly to a stirred solution of **1** in ether at 0 °C On the contrary, under basic conditions, when a solution of **1** in ether is added to a stirred solution of two equivalents of the corresponding enamine in ether in a temperature range of -5 – 0 °C a mixture of **4a** and **5a** is formed in a 13:87 ratio. Attempts to isomerize compounds **4a** → **5a** and **5a** → **4a** in the presence of acids or bases failed. Therefore, we conclude that **4a** and **5a** are formed *via* a common intermediate, namely the iminium salt **F**, which has two options for stabilization *via* deprotonation.

At low temperatures, in the absence of an excess of the enamine isomer (**4a**) is formed from the iminium salt **F** by loss of the more acidic α-proton. In the presence of an excess of the enamine, abstraction of the proton in α'-position of the iminium moiety **F**, which is lower in acidity



Scheme 5

Table 1.

Isomer ratio **4a/5a** under different reaction conditions

ratio of 1 : enamine	solvent	t °C	**4a** (%)	**5a** (%)
1 : 2	-----	20	92	8
1 · 2	hexane	30 - 35	69	31
1 . 2	MeCN	0 - 2	84	16
1 2	Et_2O	-5 - 0	13	87
1 1	Et_2O	-5 - 0	100	--

but sterically easier to attack, competes with the abstraction of the α-proton. The intermediate **G** formed by this procedure is unstable under the reaction conditions applied, and spontaneously undergoes a 1,5-prototropic shift to give the fully conjugated system (**5a**). Prototropic rearrangements in similar trifluoromethyl substituted species are well documented.[17]

It should be noted that in the case of 1-morpholino-1-cyclopentene under similar reaction condi-

tions as summarized in Table 1 only isomer (**4b**) is formed. We explain the different experimental results with the different CH acidity of the α- and α'-protons of the iminium salts **F** of cyclohexanone and cyclopentanone,[18] which are intermediates of the reaction.

X-RAY DIFFRACTION STUDIES OF COMPOUNDS (4b) AND (5a)

Unequivocal evidence for the structures (**4b**) and (**5a**) was provided by X-ray structure analyses. The *E*-configuration of the exocyclic CC double bond of compounds (**4**) identified by ^{19}F Nmr spectroscopy was confirmed. The stereochemistry of the exocyclic CC double bond of compound (**5a**), which we were unable to determine on the basis of the spectroscopic data available, was shown to be *Z*. Molecular structures of compounds (**4b**) and (**5a**) are shown in Figures 1 and 2

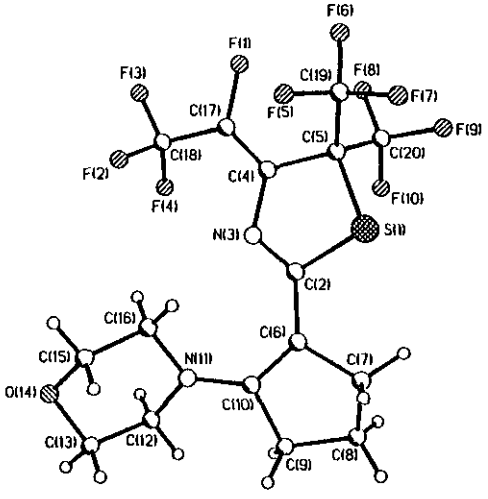


Figure 1. Molecular structure of compound (**4b**)

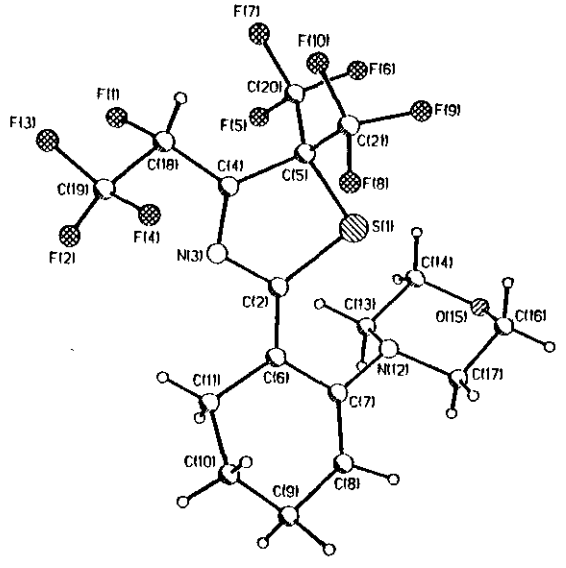


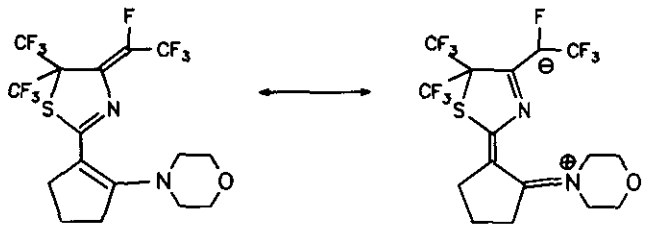
Figure 2 Molecular structure of compound (**5a**)

The thiazoline ring in **5a** adopts almost planar conformation. However, the heterocycle in **4b** exhibits significant envelope-type distortion, the folding angle along the S(1)...C(4) line being equal to 13.5°.

The most interesting feature of molecule (**4b**) is its extended conjugated π-system C(17)C(4)N(3) C(2)C(6)C(10)N(11), which involves three pairs of π-electrons and the lone pair of the N(11) atom. The existence of the conjugation is manifested by the overall planarity of the system. The torsion angles C(17)C(4)N(3)C(2), C(4)N(3)C(2)C(6), N(3)C(2)C(6)C(10) being equal to 172.4°, 175.1° and

5.7°, respectively. The somewhat larger C(2)C(6)C(10)N(11) torsion angle of 31.0° would not exclude the retention of the essential part of conjugation energy between the C(6)=C(10) double bond and the lone pair of the N(11) atom. Another important geometrical consequence of the extensive conjugation is a distinct redistribution of bond lengths, *viz.* the elongation of the formal double bonds [C(6)=C(10) (1.404(2) Å) and C(2)=N(3) (1.306(3) Å)] and the shortening of the formal single bonds [C(4)-N(3) (1.383(2) Å), C(2)-C(6) (1.415(3) Å), and C(10)-N(11) (1.332(2) Å)] as compared to the corresponding standard values for C=C, C-C, C=N and C-N bonds [1.330, 1.542, 1.279, 1.468 Å].[19]

The efficiency of the conjugation in molecule (**4b**) is enhanced by the opposite sense of the electron-donor properties of the groups present at both ends of the conjugated system, namely by the electron-releasing capacity of N(11) on the one hand, and the electron-withdrawing effect of the =CF-CF_3 group, on the other. Such an efficiently conjugated system, as present in molecule (**4b**), in fact may be treated as a superposition of the two resonance structures (**4b**) and (**4b'**) (Scheme 6)



4b **4b'**

Scheme 6

It is noteworthy, that the different position of the amine substituent relative to the endocyclic C=C bond in **5a** makes an effective participation of its lone pair with the conjugated chain impossible, which is obviously reflected in the bond lengths, exhibiting only a very slight degree of π-bond delocalization.

All other geometrical characteristics of molecules (**4b**) and (**5a**) are unexceptional.[2] The cyclopentene and cyclohexene rings in **4b** and **5a** have typical envelope and chair conformations [atom C(8) in **4b** is displaced from the mean plane C(7)C(6)C(10)C(9) by 0.396(3) Å; atom C(11) in **5a** is displaced from the mean plane C(6)C(7)C(8)C(9)C(10) by 0.61(1) Å]. The morpholine rings in both structures adopt as typical for such rings chair conformation. It is also noteworthy, that in molecule (**4b**) with the long conjugated chain the environment at the morpholine N atom is somewhat more flattened than that in **5a**, the endocyclic torsion angles around the C-N bonds being C(16)N(11)C(12)C(13) 48.4°, C(15)C(16)N(11)C(12) 48.5° and C(17)N(12)C(13)C(14) 57.4°, C(16)C(17)N(12)C(13) 57.6° in **4b** and **5a**, whereas the rest of the torsion angles in morpholine rings are close to 60° and span almost the same ranges from 54.7 - 62.8° and 57.3 - 61.1° in **4b** and **5a**, respectively.

EXPERIMENTAL

Materials and methods:

The ^{1}H Nmr spectra were obtained with Bruker AC-250 (250.1 MHz), Bruker WM-250 (250.1 MHz) and Bruker AM-360 (360.1 MHz) spectrometers, ^{13}C Nmr spectra - with Bruker AM-360 (90.6 MHz), Bruker AC-250 (62.9 MHz) and Bruker AC-200 (50.3 MHz) spectrometers. As reference standard, TMS was used. Chemical shifts are referenced internally to solvent peaks ($CDCl_3$ ^{1}H: 7.24 ppm, ^{13}C: 77.00 ppm; $(CD_3)_2CO$ ^{13}C: 28.00 ppm). ^{19}F Nmr were recorded on Bruker AC-250 (235.3 MHz) and Bruker AC-200 (188.7 MHz) spectrometers (CF_3COOH as external standard). Ir spectra were recorded on Perkin-Elmer 257 and Perkin-Elmer 1600 FT-IR spectrophotometers. Mass spectra were measured on a M112S Finnigan MAT instrument operating in the EI mode at 70 eV, m/z values, proposed assignment and relative intensity (%) for ^{32}S isotope are listed. Isolation of compound (**5a**) was performed by column chromatography on SiO_2 (silica gel 60, 0.063 - 0.200 mm, 70 - 230 mesh ASTM for column chromatography, pH = 6.5-7.5).

X-ray Diffraction studies of single crystals of **4b** and **5a** were carried out with 4-circle diffractometers (173 and 188 K, Syntex $P2_1$ and Siemens P3/PC instruments, Mo K_α-radiation, graphite monochromators, O/2O scan, $2O < 56$ and 52^{o} for **4b** and **5a**, respectively).[20] Crystals of **4b** and **5a** are monoclinic, at 173 and 188 K: a = 13.792(3) and 10.372(3) Å, b = 8.949(2) and 9.031(3) Å, c = 14.835(3) and 21.791(7) Å, β = 95.77(3)° and 98.56(2)°, V = 1822(1) and 2018(1) $Å^3$, d_{calc} = 1.470 and 1.601 g/cm^3, Z = 4, space group $P2_1/n$ and $P2_1/c$ for **4b** and **5a**, respectively.

The structures were solved by a direct method and refined in anisotropic-isotropic (H-atoms; for 5 H-atoms bound to carbons included in calculated positions with the common refined U_{iso} = 0.068(7) $Å^2$) approximation; absorption corrections were not applied. The final refinement converged to R = 0.031 and 0.075, R_w = 0.041 and = 0.074 for 2545 and 1621 observed independent reflections with $I > 3\sigma(I)$ for **4b** and **5a**, respectively. All calculations were carried out with a PC/AT computer using the SHELXTL PLUS programs (PC version).[21]

Perfluoro-2-methyl-2-penten-3-yl isothiocyanate (1)

32.28 g (107.6 mmol, 20 ml) of perfluoro-2-methyl-2-pentene was added dropwise to a stirred suspension of 11.0 g (113.3 mmol) of dry KSCN in 70 ml of abs. benzonitrile at 5-10 °C. The mixture was warmed up to room temperature and stirred for additional 2 h. The volatile products were distilled off at 20-40 °C/1 mm Hg into a trap cooled to -78 °C. The lower layer of the trap was separated and distilled to give 30.52 g (93%) of **1**, bp 52 °C/71 mm Hg;[5] 3.19 g starting material were recovered from the trap (-78 °C). ^{13}C Nmr ($CDCl_3$): δ = 110.15 (tq, $^{1}J_{CF}$= 265.4, $^{2}J_{CF}$= 41.1, $\underline{C}F_2CF_3$), 118.06 (qt, $^{1}J_{CF}$= 287.8, $^{2}J_{CF}$= 35.3, $CF_2\underline{C}F_3$), 119.88 (q, $^{1}J_{CF}$= 274.5, *trans*-$\underline{C}F_3$-C=C-CF_2), 120.47 (q, $^{1}J_{CF}$= 277.6, *cis*-$\underline{C}F_3$-C=C-CF_2), 122.83 [sept, $^{2}J_{CF}$= 32.3, $(CF_3)_2\underline{C}$], 133.26 (t, $^{2}J_{CF}$= 32.8, C=$\underline{C}$-CF_2), 143.78 (N=$\underline{C}$=S).

2-(1-Methylindol-3-yl)-perfluoro-4,5-dihydro-5,5-dimethyl-4-ethylidene-1,3-thiazole (2)

After adding at room temperature 2.65 g (7.81 mmol) of **1** in 5 ml of abs. toluene dropwise to a stir-

red solution of 2.05 g (15.63 mmol, 2 ml) 1-methylindole in 30 ml of abs. toluene, the mixture was heated up to 60 °C for 8 h. The mixture was washed with H_2O and extracted with ether. The organic layer was separated, dried ($MgSO_4$), and evaporated to dryness. The residue was washed with small amounts of hexanes and filtered. Yield: 2.76 (78%) **2**, mp 184-185.5 °C (after recrystallization from hexanes). Ir (KBr): ν_{max} (cm^{-1}) = 1679, 1614, 1568, 1471. ^1H Nmr ($CDCl_3$) δ = 3.86 (s, 3H, CH_3), 7.36 (m, 3H, aromatic H), 7.58 (s, 1H, aromatic H), 8.26 (m, 1H, aromatic H). ^{13}C Nmr (acetone-d_6): δ = 32.2 (CH_3), 71.56 [sept d, $^2J_{CF}$= 31.3, $^3J_{CF}$= 4.0, $(CF_3)_2\underline{C}$], 106.92, 109.95, 120.45, 122.14, 123.20, 124.43, 136.75, 137.18 (indole C), 118.64 (qd, $^1J_{CF}$= 273.1, $^2J_{CF}$= 37.8, =CF-$\underline{C}F_3$), 121.90 [q, $^1J_{CF}$= 284.3, $(\underline{C}F_3)_2C$], 137.59 (dq, $^2J_{CF}$= 25.7, $^3J_{CF}$= 2.4, N-$\underline{C}$=CF-CF_3), 142.46 (dq, $^1J_{CF}$= 262.6, $^2J_{CF}$= 39.4, =$\underline{C}$F-CF_3), 161.88 (dq, $^4J_{CF}$= 10.4, $^5J_{CF}$= 1.6, S-$\underline{C}$=N). ^{19}F Nmr ($CDCl_3$): δ = -58.8 (sept q, $^5J_{FF}$= 22.9, $^3J_{FF}$= 7.7, 1F, =$\underline{C}F$-CF_3), 11.6 [d, $^5J_{FF}$= 22.9, 6F, $(\underline{C}F_3)_2C$], 12.0 (d, $^3J_{FF}$= 7.7, 3F, =CF-$\underline{C}F_3$). Anal. Calcd for $C_{16}H_8N_2F_{10}S$: C, 42.68; H, 1.79; N, 6.22. Found. C, 42.68; H, 1.90, N, 6.23.

2-Methyl-2-(perfluoro-4,5-dihydro-5,5-dimethyl-4-ethylidene-1,3-thiazol-2-yl)propanal (3)

4.30 g (12.7 mmol) of **1** was added dropwise to 1.79 g (12.7 mmol) of 2-methyl-1-morpholino-1-propene at 10-15 °C. Stirring was continued for 24 h 15 ml of H_2O, 1 ml of conc. HCl were added with stirring. After 10 min the organic layer was separated, 5 ml of CH_2Cl_2 and 20 ml of H_2O were added with stirring. Then the organic layer was separated, dried ($MgSO_4$), and distilled. Yield. 3.33 g (67%) **3**, bp 72-76 °C/16 mm Hg. Ir (film): ν_{max} (cm^{-1}) = 1735, 1685, 1588. ^1H Nmr ($CDCl_3$): δ = 1.45 (s, 6H, 2x CH_3), 9.56 (s, 1H, CH=O). ^{13}C Nmr ($CDCl_3$): δ = 21.25 [$C(\underline{C}H_3)_2$], 53.12 [$\underline{C}(CH_3)_2$], 72.85 [sept d, $^2J_{CF}$ = 32.0, $^3J_{CF}$= 4.4, $\underline{C}(CF_3)_2$], 118.60 (qd, $^1J_{CF}$= 274.7, $^2J_{CF}$= 37.1, =CF-$\underline{C}F_3$), 122.50 [q, $^1J_{CF}$= 284.3, $C(\underline{C}F_3)_2$], 136.53 (dq, $^2J_{CF}$= 28.3, $^3J_{CF}$= 2.7, N-$\underline{C}$=CF-CF_3), 148.14 (dq, $^1J_{CF}$= 273.6, $^2J_{CF}$= 40.2, =$\underline{C}$F-CF_3), 177.73 (dq, $^4J_{CF}$= 11.8, $^5J_{CF}$= 2.0, S-$\underline{C}$=N), 197.30 ($\underline{C}$H=O) ^{19}F Nmr ($CDCl_3$): δ = -51.1 (sept q, $^5J_{FF}$= 24.2, $^3J_{FF}$= 8.9, 1F, =$\underline{C}F$-CF_3), 10.9 [d, $^5J_{FF}$= 24.2, 6F, $(\underline{C}F_3)_2C$], 11.2 (d, $^3J_{FF}$= 8.9, 3F, =CF-$\underline{C}F_3$) Anal. Calcd for $C_{11}H_7NOF_{10}S$: C, 33.78; H, 1.80; N, 3.58. Found: C, 33.96; H, 1.96; N, 3.71.

2-(2-Morpholino-1-cyclohexenyl)perfluoro-4,5-dihydro-5,5-dimethyl-4-ethylidene-1,3-thiazole (4a)

To a stirred solution of 2.50 g (7.4 mmol) **1** in 50 ml of abs. ether, 1.23 g (7.4 mmol) of 1-morpholino-1-cyclohexene in 5 ml of abs. ether was dropped at -5 — 0 °C. After 3 h at 0 °C, the reaction mixture was slowly warmed up to room temperature, stirred for additional 15 h, and evaporated to dryness in vacuo. The residue was dried in a vacuum desiccator over KOH. Yield: 3.13 g (87%) **4a**, mp 165-166 °C (after recrystallization from methanol). Ir (KBr): ν_{max} (cm^{-1}) = 1670, 1635, 1540. ^1H Nmr ($CDCl_3$): δ = 1.63 (m, 4H, $CH_2\underline{C}H_2$), 2.23 (m, 2H, CH_2), 2.45 (m, 2H, CH_2), 2.76 (m, 4H, 2x NCH_2), 3.86 (m, 4H, 2x OCH_2). ^{13}C Nmr ($CDCl_3$): δ = 21.91 ($\underline{C}H_2$), 22.17 ($\underline{C}H_2$), 22.78 ($\underline{C}H_2$), 26.34 ($\underline{C}H_2$), 51.14 (2x $N\underline{C}H_2$), 65.78 (2x $O\underline{C}H_2$), 69.35 [sept, $^2J_{CF}$= 29.8 $(CF_3)_2\underline{C}$], 118.98 (qd, $^1J_{CF}$= 274.4, $^2J_{CF}$= 37.5, =CF-$\underline{C}F_3$), 123.0 [q, $^1J_{CF}$= 282.6, $(\underline{C}F_3)_2C$], 127.05 (N-C=$\underline{C}$-CH_2), 135.73 (dq, $^2J_{CF}$= 28.0, $^3J_{CF}$= 2.3, N-$\underline{C}$=CF-CF_3), 145.95 (dq, $^1J_{CF}$= 269.2, $^2J_{CF}$= 39.3, =$\underline{C}$F-CF_3), 160.05 (d, $^6J_{CF}$= 2.62, N-$\underline{C}$=C-CH_2), 166.96 (dq, $^4J_{CF}$= 12.0, $^5J_{CF}$= 1.7, S-$\underline{C}$=N) ^{19}F Nmr ($CDCl_3$): δ = -54.8 (sept q, $^5J_{FF}$= 21.4, $^3J_{FF}$= 5.8, 1F, =$\underline{C}F$-CF_3), 11.72 [d, $^5J_{FF}$ = 21.4, 6F, $(\underline{C}F_3)_2C$],

12.02 (d, $^{3}J_{FF}$ = 5.8, 3F, =CF-C$\underline{F}_3$). Anal. Calcd for $C_{17}H_{16}N_2OF_{10}S$: C, 41.98; H, 3.32; N, 5 76. Found: C, 42.00; H, 3.26; N, 5.77.

2-(2-Morpholino-1-cyclopentenyl)perfluoro-5,5-dimethyl-4,5-dihydro-4-ethylidene-1,3-thiazole (4b)

2.12 g (6.3 mmol) of **1** was added dropwise to 1.92 g (12.5 mmol) of 1-morpholino-1-cyclopentene with stirring, maintaining a temperature of 20 °C When the exothermic reaction ceased, the mixture was stirred additional 30 min, then 20 ml of H_2O were added. The precipitate was filtered, washed with H_2O and dried on air at ambient temperature for 15 h. Yield: 2.83 g (96%) **4b**, mp 129-130 °C (after recrystallization from methanol). Ir (KBr): ν_{max} (cm^{-1}) = 1662, 1572, 1503. ^{1}H Nmr (CCl_4): δ = 1.59 (m, 2H, CH_2), 2.32 (t, $^{3}J_{HH}$= 7.4, 2H, CH_2), 2.41 (t, $^{3}J_{HH}$= 7.4, 2H, CH_2), 3.12 (m, 4H, 2x NCH_2), 3.33 (m, 4H, 2x OCH_2). ^{13}C Nmr ($CDCl_3$): δ = 20.48 ($\underline{C}H_2$), 34 40 ($\underline{C}H_2$), 35.47 ($\underline{C}H_2$), 51.37 (2x $N\underline{C}H_2$), 66.72 (2x $O\underline{C}H_2$), 71.77 [septd, $^{2}J_{CF}$= 31.32, $^{3}J_{CF}$= 4 8, $(CF_3)_2\underline{C}$], 100.83 (N-C=$\underline{C}$-CH_2), 119.67 (qd, $^{1}J_{CF}$= 273.1, $^{2}J_{CF}$= 37.8, =CF-$\underline{C}F_3$), 122.71 [q, $^{1}J_{CF}$= 282.7, $(\underline{C}F_3)_2$C], 141.98 (dq, $^{1}J_{CF}$= 260.2, $^{2}J_{CF}$= 39.4, =$\underline{C}$F-CF_3), 138.12 (dq, $^{2}J_{CF}$= 28.1, $^{3}J_{CF}$= 2 4, N-$\underline{C}$=CF-CF_3), 163.49 (d, $^{6}J_{CF}$= 2.41, N-$\underline{C}$=C-CH_2), 164.20 (dq, $^{4}J_{CF}$= 9.6, $^{5}J_{CF}$= 1 6, S-$\underline{C}$=N) ^{19}F Nmr (CCl_4): δ = -62.5 (sept q, $^{5}J_{FF}$= 24.0, $^{3}J_{FF}$= 9.0, 1F, =C$\underline{F}$-CF_3), 11.77 [d, $^{5}J_{FF}$= 24.0, 6F, $(C\underline{F}_3)_2$C], 12.34 (d, $^{3}J_{FF}$= 9.0, 3F, =CF-C$\underline{F}_3$). Anal. Calcd for $C_{16}H_{14}N_2OF_{10}S$: C, 40.68; H, 2 99; N, 5.93. Found: C, 40.73; H 3.05; N 5.89.

2-(2-Morpholino-2-cyclohexene-1-ylidene)-2,5-dihydro-4-(1,2,2,2-tetrafluoroethyl)-5,5-bis(trifluoromethyl)-1,3-thiazole (5a)

A solution of 2.49 g (7.3 mmol) **1** in 5 ml of abs. ether was added dropwise with stirring to a solution of 2.46 g (14.7 mmol) of 1-morpholino-1-cyclohexene in 5 ml of abs. ether at -5 – 0 °C. After completion of the addition, the mixture was stirred for 15 min, warmed up slowly to room temperature, and stirred additional 30 min. Then 30 ml of H_2O were added, the organic layer was separated and evaporated to dryness. Then H_2O was added and the precipitate was collected, washed with a mixture of H_2O/CH_3OH and dried. The crude material 2.46 g (69%) consisted of 13% **4a** and 87% **5a** (^{19}F Nmr analysis). For analytical data 0.53 g (90%) **5a**, mp 93-94 °C. were isolated from 0.68 g of the isomeric mixture by column chromatography on 100 g of silica gel (eluant: hexanes/ethyl acetate 8:1). Ir (KBr): ν_{max} (cm^{-1}) = 1600, 1535. ^{1}H Nmr ($CDCl_3$): δ = 1 70 (m, 2H, CH_2), 2.27 (m, 2H, CH_2), 2.74 (m, 6H, 2x NCH_2, CH_2), 3.84 (m, 4H, 2x OCH_2), 5 51 (dq, 1H, $^{2}J_{HF}$= 44.7, $^{3}J_{HF}$= 5.3, C$\underline{H}$F-CF_3), 5.76 (m, 1H, =C$\underline{H}$). ^{13}C Nmr ($CDCl_3$): δ = 22.43 ($\underline{C}H_2$), 25.85 ($\underline{C}H_2$), 28.91 ($\underline{C}H_2$), 52.75 (d, $^{8}J_{CF}$= 4.32, 2x $N\underline{C}H_2$), 65.95 (2x $O\underline{C}H_2$), 76.03 [sept, $^{2}J_{CF}$= 29.31, $\underline{C}(CF_3)_2$], 82.38 (d q, $^{1}J_{CF}$= 193.1, $^{2}J_{CF}$= 35.7, $\underline{C}$HF-CF_3), 121.09 (qd, $^{1}J_{CF}$= 282.6, $^{2}J_{CF}$= 27.7, CHF-$\underline{C}F_3$), 122.21 (q, $^{1}J_{CF}$= 283.1, $\underline{C}F_3$), 122.37 (q, $^{1}J_{CF}$ = 287.1, $\underline{C}F_3$), 124.07 (d, $^{7}J_{CF}$= 2.0, N-C=$\underline{C}$H), 137.43 (d, $^{5}J_{CF}$= 5.0, S-C=$\underline{C}$), 138.85 (d, $^{6}J_{CF}$= 4.5, C=$\underline{C}$-N), 146.57 (d, $^{4}J_{CF}$= 2.5, S-$\underline{C}$-N), 147.48 (d, $^{2}J_{CF}$= 15.6, =$\underline{C}$-CHF). ^{19}F Nmr ($CDCl_3$): δ = -112.1 (d with additional multicoupling, $^{2}J_{FH}$= 44.7, 1F, CH$\underline{F}$-CF_3), 2.45 (d with additional multicoupling, $^{3}J_{FF}$= 14.9, 3F, CHF-C$\underline{F}_3$), 11.33 (m, 3F, C$\underline{F}_3$), 11.48 (q, $^{4}J_{FF}$= 9.4, 3F, C$\underline{F}_3$). Ms (m/z): 486 [M]$^+$ (1.68); 417 [M-CF_3]$^+$ (1.85); 388 [$C_{12}H_8F_{10}NS$]$^+$ (7.30); 373 [M-CF_3CS]$^+$ (77.37); 279 [M-3CF_3]$^+$ (4.91); 251 [C_6F_7NS]$^+$ (1.71); 207 [C_5F_7N]$^+$ (1.59); 147 [$C_{10}H_{13}N$]$^+$ (100.00); 135 [$C_9H_{13}N$]$^+$ (40.13); 119 [C_4F_3N]$^+$ (24.26); 77 [C_6H_5]$^+$

(15.33); 28 $[N_2]^+$ (10.18). Anal. Calcd for $C_{17}H_{16}N_2OF_{10}S$: C, 41.98; H, 3.32; N, 5.76. Found: C, 42.07; H, 3.36; N, 5.77.

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