Synthesis of 4,5-Dihydroisoxazoles Connected by Short Spacers to the Pentafluoro-λ^6-sulfanyl Group

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Abstract: New pentafluoro-λ^6-sulfanyl-containing 4,5-dihydroisoxazoles were synthesized by a convenient and efficient method. These compounds are useful as intermediates in the preparation of pentafluorosulfanyl-containing heterocyclic and polyfunctional compounds.

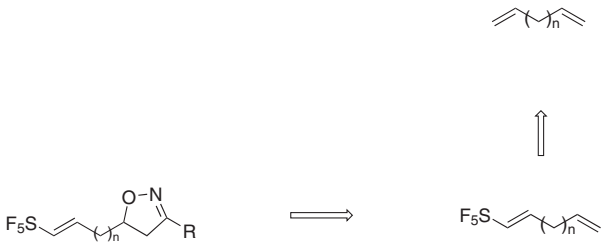
Key words: alkenes, isoxazoles, fluorine, sulfur

In the last several decades, much interest has been devoted to compounds with the pentafluorosulfanyl group.[1–5] Such derivatives may be used in a range of applications, from use as biologically active compounds[3] to energetic materials,[6,7] on the basis of their high electronegativity, high thermal stability, and the bulkiness of the pentafluorosulfanyl group.[2a] At the same time, the methods for the synthesis of heterocyclic compounds with the pentafluorosulfanyl group are still limited.

In continuation of the development of synthetic methods for new organic compounds with the pentafluorosulfanyl substituent,[8] we synthesized some pentafluorosulfanyl-containing derivatives of 4,5-dihydroisoxazoles that had not been described previously. The synthesis of new 4,5-dihydroisoxazoles connected to the pentafluorosulfanyl group through relatively short (C_3, C_4) unsaturated spacers is described here.

Isoxazole derivatives are usually prepared by 1,3-dipolar cycloaddition reactions of nitrile oxides, as illustrated by the retrosynthesis shown in Scheme 1. The nitrile oxides can be generated by dehydration of nitro compounds or by dehydrochlorination of hydroximoyl chlorides with different bases.[9] We have used both approaches for the synthesis of nitrile oxides; pentafluorosulfanyl-substituted alkadienes **1**–**3** and alkenes **4** and **5** have been used as the dipolarophiles (Scheme 2). The retrosynthetic analysis for nitrile oxide addition to alkadienes **1**–**3**, leading to the synthesis of isoxazole derivatives **6**–**9**, **14**, **15**, and **18**–**20** is given in Scheme 1. The 4,5-dihydroisoxazoles with the pentafluorosulfanyl group were constructed by a simple and efficient procedure involving preparation of the dipolarophiles and their reaction with 1,3-dipoles. The dipolarophiles were prepared by photo-induced radical addition of pentafluorosulfanyl chloride to the corresponding alkadienes and dehydrochlorination with potassium hydroxide.[8a]

We first studied 1,3-dipolar cycloaddition reactions of benzonitrile oxide and its 4-fluoro derivative with alkadienes **1**–**3**. As most nitrile oxides are not stable, these species were prepared in situ in the presence of the dipolarophiles.



Scheme 1 Retrosynthesis of (pentafluorosulfanyl)alkenyl-4,5-dihydroisoxazoles to (pentafluorosulfanyl)alkadienes

After analysis of different methods of nitrile oxide synthesis, we decided to use a two-step approach, the first step consisting of aldoxime chlorination by *N*-chlorosuccinimide,[10] and the second step being dehydrochlorination of the resulting hydroximoyl chloride by triethylamine (Scheme 2).[11] The [3+2] cycloaddition of the thus-formed nitrile oxides to dipolarophiles **1**–**3**, **4**, and **5** was performed in diethyl ether at –20 °C to –15 °C. In the optimized procedure, a solution of triethylamine in diethyl ether was added dropwise over two hours to the mixture of arylhydroximoyl chloride and dipolarophile. Dienes **2** and **3** react smoothly with nitrile oxides, leading to 4,5-dihydroisoxazoles **6**–**9** in yields of ca. 80% (Scheme 2). Only the terminal double bond of alkadienes **2** and **3** reacts with benzonitrile oxides; the pentafluorosulfanyl-substituted double bond does not react with nitrile oxides. Moreover, the pentafluorosulfanyl group deactivated both double bonds in conjugated dienes: under the same reaction conditions, 1-pentafluorosulfanylbuta-1,3-diene (**1**) failed to react with benzonitrile oxides**.**

4,5-Dihydroisoxazoles **6**–**9** can be also obtained from alkenes **4** and **5**, obtained by pentafluorosulfanyl chloride addition to the corresponding dienes. 1,3-Dipolar cycloadditions to these alkenes are simple and efficient, giving 4,5-dihydroisoxazoles **10**–**13**, which were isolated as diastereomeric mixtures in isomer ratios of ca. 1:1. Dehydrochlorination of 4,5-dihydroisoxazoles **10**–**13** by potassium carbonate yielded 4,5-dihydroisoxazoles **6**–**9**.

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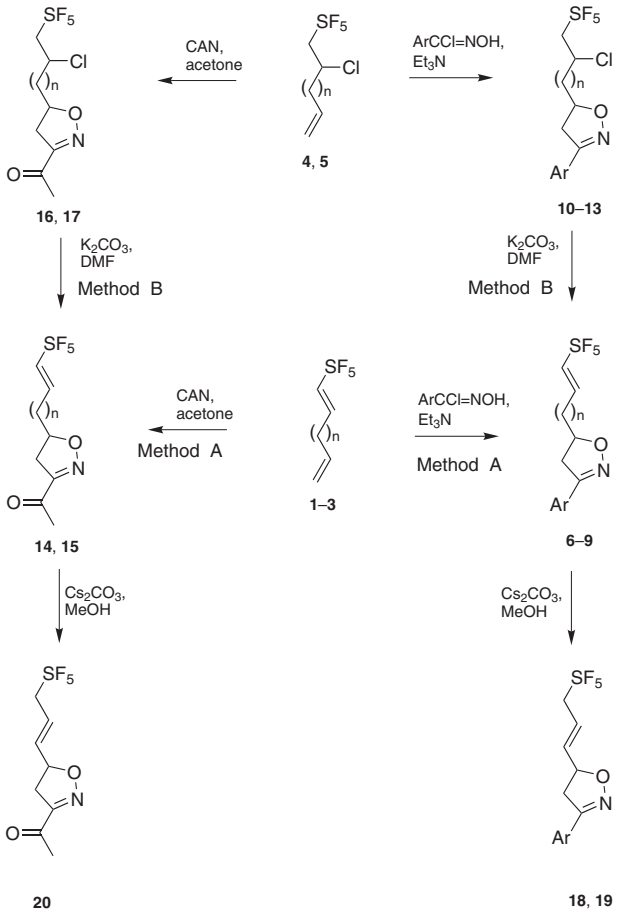
The generation of the nitrile oxide by dehydrochlorination of hydroximoyl chlorides is usually applied to the synthesis of different 3-aryl- and 3-alkylisoxazoles, but is not efficient for the preparation of some other isoxazoles with different functional groups. Therefore, we obtained 3-acetylisoxazoles by another approach, the reactions of dipolarophiles **2**–**5** with an acetone solution of cerium(IV) ammonium nitrate.[12] When alkadienes **2** and **3** were refluxed in acetone with cerium(IV) ammonium nitrate for four hours, 3-acetyl-4,5-dihydroisoxazoles **14** and **15** formed in over 85% yield.



n = 0 (**1**), 1 (**2**, **4**, **6**, **8**, **10**, **12**, **14**, **16**), 2 (**3**, **5**, **7**, **9**, **11**, **13**, **15**, **17**);
Ar = Ph (**6, 7, 10, 11, 18**), *p*-FC_6H_4 (**8**, **9**, **12**, **13**, **19**).

Scheme 2 Synthesis of 3-substituted 5-[(pentafluorosulfanyl)alkyl]-4,5-dihydroisoxazoles from (pentafluorosulfanyl)alkadienes or chloro(pentafluorosulfanyl)alkenes

The possible mechanism consists of reaction of acetone with cerium(IV) ammonium nitrate, followed by in situ transformation of the thus-formed nitroacetone to acetonitrile oxide.[12] This 1,3-dipole adds to dienes **2** and **3**, giving the target isoxazolines **14** and **15**. Adducts **4** and **5** react similarly with this system, giving 4,5-dihydroisoxazoles **16** and **17**.

As we recently reported,[13] treatment of 3-chloro-1-(pentafluorosulfanyl)prop-1-ene with cesium carbonate yielded the product of prototropic rearrangement, 1-chloro-3-(pentafluorosulfanyl)prop-1-ene. By the same methodology, 4,5-dihydroisoxazoles **6**, **8**, and **14** were transformed into 4,5-dihydroisoxazolines **18**–**20** by reaction with cesium carbonate in methanol at room temperature. The yields of the products of prototropic rearrangement were 63–75%.

The structures of isoxazolines **6**–**20** were assigned by ^1H, ^{13}C, and ^{19}F NMR spectroscopic data. The most useful for this purpose was ^{13}C NMR spectroscopy. The coupling constants J_{CF} of the carbon atom connected directly to the pentafluorosulfanyl group as well as J_{CF} of atom C(2) are characteristic for compounds containing the pentafluorosulfanyl substituent: compounds **6**–**9**, **14**, and **15**: $\delta_{C(1)}$ = 146–143, doublet of quintet, $J_{C(1)-F'}$ = 1.6 Hz, $J_{C(1)-F}$ = 20.4 Hz; $\delta_{C(2)}$ = 134–137, quintet, $J_{C(2)-F}$ = 7.5 Hz; compounds **10**–**13**, **16**, and **17**: $\delta_{C(1)}$ = 74–75, doublet of quintet, $J_{C(1)-F'}$ = 1.6 Hz, $J_{C(1)-F}$ = 20.4 Hz; $\delta_{C(2)}$ = 56–55, quintet, $J_{C(2)-F}$ = 7.5 Hz. The carbon atoms in C=N and CHO have chemical shifts δ = 156–158 and 80–81, and appear as singlets. The ^1H NMR spectra contain the following typical multiplets: aromatic protons, protons of vinyl groups, and CHO and CH_2 fragments. The ^{19}F NMR spectra for compounds **6**–**20** showed no significant deviations from the chemical shifts or coupling constants found for other unsaturated or aliphatic derivatives of sulfur hexafluoride. The chemical shifts of the apical fluorine atoms in the SF_5 group were in the range of δ = 140–141, while the basal fluorines were observed at δ = 160–161, with the typical appearance of the AB_4-spin system, J_{AB} = 144–151 Hz.

In summary, we have described an easy and convenient method for the preparation of new, synthetically valuable 4,5-dihydroisoxazoles with pentafluoro-λ^6-sulfanyl groups. In all cases, the double bond connected directly to the pentafluorosulfanyl group failed to react with the nitrile oxides. Studies on this potentially important synthetic methodology are currently in progress. The applications of 1,3-, 1,4-, and 1,5-alkadienes with pentafluoro-λ^6-sulfanyl groups in the synthesis of interesting heterocycles will be reported in the near future.

NMR spectra were recorded on a Bruker CXP-200 spectrometer at 200 MHz (^1H NMR), 188.3 MHz (^{19}F NMR), and 50.3 MHz (^{13}C NMR). Chemical shifts for ^1H NMR and ^{13}C NMR peaks are reported in ppm relative to TMS as internal standard. ^{19}F NMR downfield shifts (δ) are expressed as positive values, relative to external CF_3CO_2H. The starting materials benzaldehyde oxime and CAN were obtained from commercial sources. 4-Fluorobenzaldehyde oxime was prepared by a literature procedure.[11]

5-[3-(Pentafluoro-λ^6-sulfanyl)allyl]-3-phenyl-4,5-dihydroisoxazole (6)

Method A. Alkadiene **2** (0.194 g, 0.001 mol) was dissolved in Et_2O (10 mL). PhCCl=NOH (0.233 g, 0.0015 mol) in Et_2O (5 mL) was added at –40 °C. Et_3N (0.303 g, 0.003 mol) was added dropwise over 1 h. Stirring was continued at –40 °C until the reaction was complete according to TLC (2–3 h). The reaction was then quenched by the addition of sat. NH_4Cl (10 mL) soln. Et_2O extraction, drying with Na_2SO_4, and evaporation of the solvent gave a

dark oil (0.4 g), which was purified by flash chromatography ($CHCl_3$).

Yield: 0.266 g (85%); R_f = 0.44 ($CHCl_3$–hexane, 10:4).

Method B. Compound **10** (6.98 g, 0.02 mol) dissolved in DMF (10 mL) was added to K_2CO_3 (20 g) in DMF (50 mL) in a 100-mL round-bottomed flask equipped with a magnetic stirring bar, dropping funnel, thermometer, and reflux condenser. The mixture was stirred at r.t. for 0.5 h and at 60 °C for 3 h. When the reaction was complete, the mixture was filtered and the DMF was removed under vacuum (35–40 °C, 1.3–2.7 mbar). Isoxazole **6** was isolated by column chromatography (silica gel).

Yield: 5.63 g (90%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.83 (m, 2 H, Ar), 7.59 (m, 3 H, Ar), 6.73 (m, 2 H, CH=CH), 5.02 (m, 1 H, OCH), 3.65 (dd, $J_{H,H}$ = 10.2 Hz, 16.6 Hz, 1 H, CH_2), 3.16 (dd, $J_{H,H}$ = 6.8 Hz, 16.6 Hz, 1 H, CH_2), 2.73 (m, 2 H, CH_2CH=).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 156.80 (s, C=N), 143.40 (d pent, $J_{C,F}$ = 20.1 Hz, 1.5 Hz, F_5SCH=), 134.08 (pent, $J_{C,F}$ = 7.0 Hz, *C*H=CHSF$_5$), 130.81 (s, CH, Ar), 129.49 (s, C, Ar), 129.23 (s, CH, Ar), 127.12 (s, CH, Ar), 79.05 (br s, OCH), 40.09 (s, CH_2), 36.49 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 162.61–159.41 (9 lines, $J_{F–F}$ = 148.50 Hz, 1 F), 140.35 (dm, $J_{F–F}$ = 148.5 Hz, 4 F).

Anal. Calcd for $C_{12}H_{12}F_5NOS$: C, 46.01; H, 3.86; F, 30.32; N, 4.47. Found: C, 46.24; H, 3.90; F, 30.45; N, 4.50.

5-[4-(Pentafluoro-λ^6-sulfanyl)but-3-enyl]-3-phenyl-4,5-dihydroisoxazole (7)

In a procedure analogous to that used for the synthesis of **6** (Method A), **3** (0.208 g, 0.01 mol) was allowed to react with PhCCl=NOH (0.233 g, 0.0015 mol).

Colorless oil; yield: 0.268 g (82%); R_f = 0.34 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70 (m, 2 H, Ar), 7.45 (m, 3 H, Ar), 5.98 (m, 2 H, CH=CH), 4.85 (m, 1 H, OCH), 3.49 (dd, $J_{H,H}$ = 10.6 Hz, 16.6 Hz, 1 H, CH_2), 3.05 (dd, $J_{H,H}$ = 7.6 Hz, 16.6 Hz, 1 H, CH_2), 2.43 (m, 2 H, CH_2CH=), 1.91 (m, 2 H, CH_2CH$_2$).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 156.91 (s, C=N), 141.56 (d pent, $J_{C,F}$ = 19.6 Hz, $J_{C,F}$ = 1.0 Hz, F_5SCH=), 134.33 (pent, $J_{C,F}$ = 7.0 Hz, *C*H=CHSF$_5$), 130.60 (s, CH, Ar), 129.87 (s, C, Ar), 129.18 (s, CH, Ar), 127.03 (s, CH, Ar), 80.24 (s, OCH), 40.57 (s, CH_2), 33.99 (s, CH_2), 27.11 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 163.51–160.32 (9 lines, $J_{F–F}$ = 150.40 Hz, 1 F), 140.60 (dm, $J_{F–F}$ = 150.40 Hz, 4 F).

Anal. Calcd for $C_{13}H_{14}F_5NOS$: C, 47.70; H, 4.31; F, 29.02; N, 4.28. Found: C, 47.58; H, 4.38; F, 29.14; N, 4.40.

3-(4-Fluorophenyl)-5-[3-(pentafluoro-λ^6-sulfanyl)allyl]-4,5-dihydroisoxazole (8)

In a procedure analogous to that used for the synthesis of **6** (Method A), **2** (0.194 g, 0.001 mol) was allowed to react with 4-FC_6H_4CCl=NOH (0.26 g, 0.0015 mol).

Colorless oil; yield: 0.265 g (80%); R_f = 0.4 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.66 (m, 2 H, Ar), 7.12 (m, 2 H, Ar), 6.58 (m, 2 H, CH=CH), 4.94 (m, 1 H, OCH), 3.49 (dd, $J_{H,H}$ = 10.4 Hz, 16.8 Hz, 1 H, CH_2), 3.04 (dd, $J_{H,H}$ = 7.0 Hz, 16.8 Hz, 1 H, CH_2), 2.58 (m, 2 H, CH_2CH=).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 164.28 (d, $J_{C,F}$ = 250.0 Hz, CF, Ar), 155.83 (s, C=N), 143.40 (d pent, $J_{C,F}$ = 19.0 Hz, 1.5 Hz, =CHSF$_5$), 134.01 (pent, $J_{C,F}$ = 7.5 Hz, *C*H=CHSF$_5$), 129.05 (d, $J_{C,F}$ = 8.0 Hz, CH, Ar), 125.80 (d, $J_{C,F}$ = 3.0 Hz, C, Ar), 116.34 (d, $J_{C,F}$ = 22.1 Hz, CH, Ar), 79.15 (s, OCH), 40.07 (s, CH_2), 36.40 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 162.61–159.47 (9 lines, $J_{F–F}$ = 152.0 Hz, 1 F), 140.32 (dm, $J_{F–F}$ = 152.0 Hz, 4 F), –31.84 (m, 1 F).

Anal. Calcd for $C_{12}H_{11}F_6NOS$: C, 43.51; H, 3.35; F, 34.41; N, 4.23. Found: C, 43.42; H, 3.30; F, 34.91; N, 4.11.

3-(4-Fluorophenyl)-5-[4-(pentafluoro-λ^6-sulfanyl)but-3-enyl]-4,5-dihydroisoxazole (9)

In a procedure analogous to that used for the synthesis of **6** (Method A), **3** (0.208 g, 0.01 mol) was allowed to react with 4-FC_6H_4CCl=NOH (0.26 g, 0.0015 mol).

Colorless oil; yield: 0.29 g (84%); R_f = 0.30 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70 (m, 2 H, Ar), 7.14 (m, 2 H, Ar), 6.54 (m, 2 H, CH=CH), 4.79 (m, 1 H, OCH), 3.47 (dd, $J_{H,H}$ = 10.4 Hz, 16.6 Hz, 1 H, CH_2), 3.02 (dd, $J_{H,H}$ = 7.6 Hz, 16.6 Hz, 1 H, CH_2), 2.43 (m, 2 H, CH_2CH=), 1.88 (m, 2 H, CH_2CH$_2$).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 164.20 (d, $J_{C,F}$ = 250.0 Hz, CF, Ar), 155.91 (d, $J_{C,F}$ = 1.0 Hz, C=N), 141.64 (d pent, $J_{C,F}$ = 19.6 Hz, 1.5 Hz, =CHSF$_5$), 138.17 (pent, $J_{C,F}$ = 7.0 Hz, *C*H=CHSF$_5$), 128.98 (d, $J_{C,F}$ = 8.6 Hz, CH, Ar), 126.13 (d, $J_{C,F}$ = 3.5 Hz, C, Ar), 116.33 (d, $J_{C,F}$ = 22.1 Hz, CH, Ar), 80.33 (s, OCH), 40.07 (s, CH_2), 36.40 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 163.30–160.11 (9 lines, $J_{F–F}$ = 154.0 Hz, 1 F), 140.56 (dm, $J_{F–F}$ = 152.0 Hz, 4 F), –31.23 (m, 1 F).

Anal. Calcd for $C_{13}H_{13}F_6NOS$: C, 45.22; H, 3.80; F, 33.01; N, 4.06. Found: C, 45.30; H, 3.83; F, 33.12; N, 4.12.

5-[2-Chloro-3-(pentafluoro-λ^6-sulfanyl)propyl]-3-phenyl-4,5-dihydroisoxazole (10)

In a procedure analogous to that used for the synthesis of **6** (Method A), **4** (0.23 g, 0.001 mol) was allowed to react with PhCCl=NOH (0.233 g, 0.0015 mol).

Colorless oil; yield: 0.313 g (90%); R_f = 0.42 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.71 (m, 2 H, Ar), 7.47 (m, 3 H, Ar), 5.13 (m, 1 H, OCH), 4.81–4.56 (m, 1 H, ClCH), 4.29–3.98 (m, 2 H, CH_2SF_5), 3.66–3.51 (dd, $J_{H,H}$ = 10.4 Hz, 16.8 Hz, 1 H, CH_2), 3.15–3.00 (dd, $J_{H,H}$ = 8.0 Hz, 16.8 Hz, 1 H, CH_2), 2.41–2.28 (m, 2 H, CH_2) (a mixture of diastereomers).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 156.68, 156.58 (s, C=N), 130.43, 130.40 (s, CH, Ar), 129.14, 129.09 (s, C, Ar), 128.84, 128.82 (s, CH, Ar), 126.72 (s, CH, Ar), 77.40, 77.18 (s, OCH), 76.64, 76.60 (d pent, $J_{C,F}$ = 13.7 Hz, 1.5 Hz, F_5SCH_2), 52.84, 52.60 (pent, $J_{C,F}$ = 4.5 Hz, CHCl), 43.32, 42.13 (pent, $J_{C,F}$ = 1.3 Hz, CH_2), 40.51, 40.21 (s, CH_2) (a mixture of diastereomers).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 162.86–159.40 (18 lines, $J_{F–F}$ = 146.0, 148.5 Hz, 1 F), 144.96, 144.13 (dm, $J_{F–F}$ = 146.0, 148.5 Hz, 4 F) (a mixture of diastereomers).

Anal. Calcd for $C_{12}H_{13}ClF_5NOS$: C, 41.21; H, 3.75; F, 27.16; N, 4.01. Found: C, 41.29; H, 3.79; F, 27,28; N, 4.09.

5-[3-Chloro-4-(pentafluoro-λ^6-sulfanyl)butyl]-3-phenyl-4,5-dihydroisoxazole (11)

In a procedure analogous to that used for the synthesis of **6** (Method A), **5** (0.244 g, 0.001 mol) was allowed to react with PhCCl=NOH (0.233 g, 0.0015 mol).

Colorless oil; yield: 0.334 g (92%); R_f = 0.28 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70 (m, 2 H, Ar), 7.45 (m, 3 H, Ar), 4.80 (m, 1 H, OCH), 4.60 (m, 1 H, ClCH), 4.01 (m, 2 H, CH_2SF_5), 3.49 (dd, $J_{H,H}$ = 10.4 Hz, 16.6 Hz, 1 H, CH_2), 3.06 (dd, $J_{H,H}$ = 7.6 Hz, 16.6 Hz, 1 H, CH_2), 2.11–1.85 (m, 4 H, $2CH_2$) (a mixture of diastereomers).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 156.53 (s, C=N), 130.20 (s, CH, Ar), 129.43 (s, C, Ar), 128.78 (s, CH, Ar), 126.64 (s, CH, Ar), 80.46, 79.68 (s, OCH), 76.71, 76.50 (d pent, $J_{C,F}$ = 13.4 Hz, 0.8 Hz, F_5SCH_2), 55.77, 53.34 (pent, $J_{C,F}$ = 4.0 Hz, CHCl), 40.26, 40.08 (s, CH_2), 33.94, 33.23 (pent, $J_{C,F}$ = 1.3 Hz, CH_2-CHCl), 32.25, 31.72 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 162.55–159.44 (9 lines, $J_{F–F}$ = 146.4, 148.5 Hz, 1 F), 144.13 (dm, $J_{F–F}$ = 146.4 Hz, 4 F) (a mixture of diastereomers).

Anal. Calcd for $C_{13}H_{15}ClF_5NOS$: C, 42.92; H, 4.16; F, 26.11; N, 3.85. Found: C, 42.80; H, 4.20; F, 26.23; N, 3.77.

5-[2-Chloro-3-(pentafluoro-λ^6-sulfanyl)propyl]-3-(4-fluorophenyl)-4,5-dihydroisoxazole (12)

In a procedure analogous to that used for the synthesis of **6** (Method A), **4** (0.23 g, 0.001 mol) was allowed to react with 4-FC_6H_4CCl=NOH (0.26 g, 0.0015 mol).

Colorless oil; yield: 0.35 g (95%); R_f = 0.39 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70 (m, 2 H, Ar), 7.15 (m, 2 H, Ar), 5.19–5.09 (m, 1 H, OCH), 4.78–4.58 (m, 1 H, ClCH), 4.25–4.01 (m, 2 H, CH_2SF_5), 3.66–3.51 (dd, $J_{H,H}$ = 10.2 Hz, 16.6 Hz, 1 H, CH_2), 3.13–2.99 (dd, $J_{H,H}$ = 8.0 Hz, 16.6 Hz, 1 H, CH_2), 2.32 (m, 2 H, CH_2) (a mixture of diastereomers).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 163.88 (d, $J_{C,F}$ = 251.0 Hz, CF, Ar), 155.75, 155.66 (d, $J_{C,F}$ = 1.0 Hz, C=N), 128.76, 128.60 (d, $J_{C,F}$ = 8.0 Hz, CH, Ar), 125.46, 125.44 (d, $J_{C,F}$ = 3.5 Hz, C, Ar), 116.15, 115.73 (d, $J_{C,F}$ = 22.1 Hz, CH, Ar), 77.57, 77.34 (s, OCH), 76.61, 76.55 (pent, $J_{C,F}$ = 13.9 Hz, F_5SCH_2), 52.81, 52.55 (pent, $J_{C,F}$ = 4.5 Hz, ClCH), 43.24, 42.06 (s, CH_2), 40.52, 40.23 (s, CH_2) (a mixture of diastereomers).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.82–159.94 (18 lines, $J_{F–F}$ = 144.0, 146.0 Hz, 1 F), 144.69, 143.96 (dm, $J_{F–F}$ = 144.0, 146.0 Hz, 4 F), –32.84 (m, 1 F) (a mixture of diastereomers).

Anal. Calcd for $C_{12}H_{12}ClF_6NOS$: C, 39.19; H, 3.29; F, 31.00; N, 3.81. Found: C, 39.10; H, 3.22; F, 31.12; N, 3.88.

5-[3-Chloro-4-(pentafluoro-λ^6-sulfanyl)butyl]-3-(4-fluorophenyl)-4,5-dihydroisoxazole (13)

In a procedure analogous to that used for the synthesis of **6** (Method A), **5** (0.244 g, 0.001 mol) was allowed to react with 4-FC_6H_4CCl=NOH (0.26 g, 0.0015 mol).

Colorless oil; yield: 0.33 g (93%); R_f = 0.27 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.67 (m, 2 H, Ar), 7.11 (m, 2 H, Ar), 4.79 (m, 1 H, OCH), 4.45 (m, 1 H, ClCH), 4.06 (m, 2 H, CH_2SF_5), 3.46 (dd, $J_{H,H}$ = 10.4 Hz, 16.6 Hz, 1 H, CH_2), 3.02 (dd, $J_{H,H}$ = 8.0 Hz, 16.6 Hz, 1 H, CH_2), 2.10–1.83 (m, 4 H, $2CH_2$) (a mixture of diastereomers).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 163.52 (d, $J_{C,F}$ = 251.0 Hz, CF, Ar), 155.37, 155.35 (d, $J_{C,F}$ = 1.0 Hz, C=N), 128.36 (d, $J_{C,F}$ = 8.1 Hz, CH, Ar), 125.55 (d, $J_{C,F}$ = 3.5 Hz, C, Ar), 115.60 (d, $J_{C,F}$ = 22.1 Hz, CH, Ar), 77.57, 77.34 (s, OCH), 76.61, 76.55 (pent, $J_{C,F}$ = 13.9 Hz, F_5SCH_2), 52.81, 52.55 (pent, $J_{C,F}$ = 4.5 Hz, ClCH), 43.24, 42.06 (s, CH_2), 40.52, 40.23 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.43–159.57 (18 lines, $J_{F–F}$ = 144.7, 146.0 Hz, 1 F), 144.65, 143.56 (dm, $J_{F–F}$ = 144.7, 146.0 Hz, 4 F), –31.44 (m, 1 F) (a mixture of diastereomers).

Anal. Calcd for $C_{13}H_{14}ClF_6NOS$: C, 40.90; H, 3.70; F, 29.86; N, 3.67. Found: C, 40.79; H, 3.75; F, 28.80; N, 3.70.

3-Acetyl-5-[3-(pentafluoro-λ^6-sulfanyl)allyl]-4,5-dihydroisoxazole (14)

Method A. A mixture of diene **2** (0.194 g, 0.001 mol) and CAN (0.558 g, 0.001 mol) in acetone (5 mL) was stirred under reflux for 5 h. The mixture was extracted with Et_2O (3 × 10 mL) and washed with aq $NaHCO_3$ soln (2 × 5 mL), followed by sat. aq NaCl (2 × 5 mL). The ethereal solution was dried over Na_2SO_4 and concentrated under vacuum. The resulting oil was chromatographed (silica gel, $CHCl_3$).

Pale-yellow oil; yield: 0.223 g (80%); R_f = 0.35 ($CHCl_3$).

Method B. In a procedure analogous to that used for the synthesis of **6** (Method B), **16** (3.16 g, 0.02 mol) was allowed to react with K_2CO_3 (20 g).

Yield: 4.85 g (87%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.64–6.39 (m, 2 H, CH=CH), 5.04–4.89 (m, 1 H, OCH), 3.31 (dd, $J_{H,H}$ = 11.0 Hz, 17.6 Hz, 1 H, CH_2), 2.85 (dd, $J_{H,H}$ = 7.4 Hz, 17.6 Hz, 1 H, CH_2), 2.58–2.52 (m, 2 H, CH_2), 2.50 (s, 3 H, CH_3).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 193.10 (s, C=O), 158.30 (s, C=N), 143.80 (d pent, $J_{C,F}$ = 20.2 Hz, 1.6 Hz, =$CHSF_5$), 133.22 (pent, $J_{C,F}$ = 7.6 Hz, CH=$CHSF_5$), 81.96 (s, OCH), 36.94 (s, CH_2), 36.13 (s, CH_2), 26.96 (s, CH_3).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 162.23–159.04 (9 lines, $J_{F–F}$ = 148.52 Hz, 1 F), 140.11 (dm, $J_{F–F}$ = 148.52 Hz, 4 F).

Anal. Calcd for $C_8H_{10}F_5NO_2S$: C, 34.41; H, 3.61; F, 34.02; N, 5.02. Found: C, 34.51; H, 3.67; F, 34.10; N, 5.14.

3-Acetyl-5-[4-(pentafluoro-λ^6-sulfanyl)but-3-enyl]-4,5-dihydroisoxazole (15)

In a procedure analogous to that used for the synthesis of **14** (Method A), **3** (0.208 g, 0.001 mol) was allowed to react with CAN (0.558 g, 0.001 mol).

Colorless oil; yield: 0.205 g (70%); R_f = 0.27 ($CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.51 (m, 2 H, CH=CH), 4.89–4.73 (m, 1 H, OCH), 3.22 (dd, $J_{H,H}$ = 10.8 Hz, 17.4 Hz, 1 H, CH_2), 2.81 (dd, $J_{H,H}$ = 8.2 Hz, 17.4 Hz, 1 H, CH_2), 2.51 (s, 3 H, CH_3), 2.42–2.29 (m, 2 H, CH_2), 1.95–1.77 (m, 2 H, CH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 193.37 (s, C=O), 158.53 (s, C=N), 141.71 (d pent, $J_{C,F}$ = 29.6 Hz, $J_{C,F}$ = 2.0 Hz, =$CHSF_5$), 137.82 (pent, $J_{C,F}$ = 7.5 Hz, CH=$CHSF_5$), 83.42 (s, OCH), 37.35 (s, CH_2), 33.37 (s, CH_2), 26.95 (s, CH_2), 26.83 (s, CH_3).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 163.15–159.96 (9 lines, $J_{F–F}$ = 148.50 Hz, 1 F), 140.48 (dm, $J_{F–F}$ = 148.50 Hz, 4 F).

Anal. Calcd for $C_9H_{12}F_5NO_2S$: C, 36.86; H, 4.12; F, 32.39; N, 4.78. Found: C, 36.96; H, 4.62; F, 32.52; N, 4.88.

3-Acetyl-5-[2-chloro-3-(pentafluoro-λ^6-sulfanyl)propyl]-4,5-dihydroisoxazole (16)

In a procedure analogous to that used for the synthesis of **14** (Method A), **4** (0.23 g, 0.001 mol) was allowed to react with CAN (0.558 g, 0.001 mol).

Colorless oil; yield: 0.19 g (60%); R_f = 0.37 ($CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.29–5.08 (m, 1 H, OCH), 4.78–4.46 (m, 1 H, ClCH), 4.22–3.89 (m, 2 H, CH_2SF_5), 3.35 (dd, $J_{H,H}$ = 10.2 Hz, 17.0 Hz, 1 H, CH_2), 2.82 (dd, $J_{H,H}$ = 7.6 Hz, 17.0 Hz, 1 H, CH_2), 2.52 (s, 3 H, CH_3), 2.40–1.84 (m, 2 H, CH_2) (a mixture of diastereomers).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 193.31, 193.23 (s, C=O), 158.61, 158.42 (s, C=N), 80.99, 80.61 (s, OCH), 76.84, 76.77 (pent,

$J_{C,F}$ = 13.0 Hz, F_5SCH_2), 52.68, 52.59 (pent, $J_{C,F}$ = 4.5 Hz, CHCl), 43.57, 42.25 (s, *C*H_2-CHCl), 37.90, 37.58 (s, CH_2), 27.14, 27.11 (s, CH_3) (a mixture of diastereomers).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.44–159.63 (18 lines, J_{F-F} = 146.6, 148.0 Hz, 1 F), 144.65, 144.03 (dm, J_{F-F} = 146.6, 148.0 Hz, 4 F) (a mixture of diastereomers).

Anal. Calcd for $C_8H_{11}ClF_5NO_2S$: C, 30.44; H, 3.51; F, 30.09; N, 4.44. Found: C, 30.57; H, 3.55; F, 30.12; N, 4.50.

3-Acetyl-5-[3-chloro-4-(pentafluoro-λ^6-sulfanyl)butyl]-4,5-dihydroisoxazole (17)

In a procedure analogous to that used for the synthesis of **14** (Method A), **5** (0.244 g, 0.001 mol) was allowed to react with CAN (0.558 g, 0.001 mol).

Colorless oil; yield: 0.213 g (65%); R_f = 0.3 ($CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.94–4.79 (m, 1 H, OCH), 4.50–4.37 (m, 1 H, ClCH), 4.18–3.85 (m, 2 H, CH_2SF_5), 3.26 (dd, $J_{H,H}$ = 10.4 Hz, 16.8 Hz, 1 H, CH_2), 2.86 (dd, $J_{H,H}$ = 8.0 Hz, 16.8 Hz, 1 H, CH_2), 2.52 (s, 3 H, CH_3), 2.10–1.80 (m, 4 H, CH_2) (a mixture of diastereomers).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 193.48, 193.46 (s, C=O), 158.58, 158.56 (s, C=N), 84.07, 83.36 (s, OCH), 76.84, 76.86 (pent, $J_{C,F}$ = 15.4 Hz, F_5SCH_2), 55.84, 55.46 (pent, $J_{C,F}$ = 4.5 Hz, CHCl), 37.59, 37.63 (s, CH_2), 34.04, 33.40 (s, CH_2), 32.49, 32.06 (s, CH_2), 27.0 (s, CH_3).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.54–159.74 (18 lines, J_{F-F} = 146.0, 148.0 Hz, 1 F), 144.75, 144.34 (dm, J_{F-F} = 146.0, 148.0 Hz, 4 F) (a mixture of diastereomers).

Anal. Calcd for $C_9H_{13}ClF_5NO_2S$: C, 32.99; H, 3.38; F, 28.99; N, 4.27. Found: C, 32.87; H, 3.47; F, 28.84; N, 4.39.

5-[3-(Pentafluoro-λ^6-sulfanyl)prop-1-enyl]-3-phenyl-4,5-dihydroisoxazole (18)

To a soln of **6** (0.939 g, 0.003 mol) in MeOH (10 mL) was added powdered Cs_2CO_3 (0.098 g, 0.0003 mmol) at r.t. and the mixture was stirred for 48 h. The solvent was removed under reduced pressure, and the residual oil was treated with H_2O (5 mL) and then extracted with Et_2O (3 × 30 mL). The combined extracts were dried over Na_2SO_4. After evaporation of the solvent, the residue was isolated by column chromatography (silica gel, $CHCl_3$).

Colorless oil; yield: 0.7 g (75%); *Rf* = 0.32 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70 (m, 2 H, C_6H_5), 7.45 (m, 3 H, Ar), 6.18–5.94 (m, 2 H, HC=CH), 5.33–5.21 (m, 1 H, OCH), 4.35 (ddquin, $J_{H,H}$ = 7.2 Hz, 1.2 Hz, $J_{H,F}$ = 7.4 Hz, 2 H, CH_2SF_5), 3.64 (dd, $J_{H,H}$ = 10.6 Hz, 16.4 Hz, 1 H, CH_2), 3.21 (dd, $J_{H,H}$ = 8.0 Hz, 16.4 Hz, 1 H, CH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 156.79 (s, C=N), 137.72 (s, *C*H=CH), 130.76 (s, CH, Ar), 129.53 (s, C, Ar), 129.23 (s, CH, Ar), 127.16 (s, CH, Ar), 123.06 (pent, $J_{C,F}$ = 4.0 Hz, =*C*HCH_2SF5), 80.61 (s, OCH), 73.20 (pent, $J_{C,F}$ = 15.6 Hz, =*C*HCH_2SF5), 41.04 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.50–158.53 (9 lines, J_{F-F} = 141.00 Hz, 1 F), 142.03 (dm, J_{F-F} = 141.00 Hz, 4 F).

Anal. Calcd for $C_{12}H_{12}F_5NOS$: C, 46.01; H, 3.86; F, 30.32; N, 4.47. Found: C, 46.24; H, 3.90; F, 30.45; N, 4.50.

3-(4-Fluorophenyl)-5-[3-(pentafluoro-λ^6-sulfanyl)prop-1-enyl]-4,5-dihydroisoxazole (19)

In a procedure analogous to that used for the synthesis of **18**, **8** (1.0 g, 0.003 mol) was allowed to react with Cs_2CO_3 (0.098 g, 0.0003 mmol).

Colorless oil; yield: 0.67 g (67%); R_f = 0.3 ($CHCl_3$–hexane, 10:4).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.71 (m, 2 H, FC_6H_4), 7.45 (m, 2 H, FC_6H_4), 6.17–5.93 (m, 2 H, HC=CH), 5.32–5.20 (m, 1 H, OCH), 4.35 (ddquin, $J_{H,H}$ = 7.2 Hz, 1.4 Hz, 7.6 Hz, 2 H, CH_2SF_5), 3.58 (dd, $J_{H,H}$ = 10.8 Hz, 16.6 Hz, 1 H, CH_2), 3.16 (dd, $J_{H,H}$ = 8.0 Hz, 16.6 Hz, 1 H, CH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 164.28 (d, $J_{C,F}$ = 251.0 Hz, CF, Ar), 155.85 (d, $J_{C,F}$ = 1.0 Hz, C=N), 137.57 (pent, $J_{C,F}$ = 1.0 Hz, *C*H=$CHSF_5$), 129.11 (d, $J_{C,F}$ = 8.6 Hz, CH, Ar), 125.84 (d, $J_{C,F}$ = 3.5 Hz, C, Ar), 123.14 (pent, $J_{C,F}$ = 3.5Hz, =*C*HCH_2SF_5), 80.73 (s, OCH), 73.18 (d pent, $J_{C,F}$ = 15.1 Hz, $J_{C,F}$ = 1.0 Hz, CH_2SF_5), 41.05 (s, CH_2).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.41–158.21 (9 lines, J_{F-F} = 141.00 Hz, 1 F), 142.00 (dm, J_{F-F} = 141.00 Hz, 4 F), –32.02 (m, 1 F).

Anal. Calcd for $C_{12}H_{11}F_6NOS$: C, 43.51; H, 3.35; F, 34.41; N, 4.23. Found: C, 43.42; H, 3.30; F, 34.91; N, 4.11.

3-Acetyl-5-[3-(pentafluoro-λ^6-sulfanyl)prop-1-enyl]-4,5-dihydroisoxazole (20)

In a procedure analogous to that used for the synthesis of **18**, **14** (0.837g, 0.003 mol) was allowed to react with Cs_2CO_3 (0.098 g, 0.0003 mmol).

Colorless oil; yield: 0.53 g (63%); R_f = 0.36 ($CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.14–5.85 (m, 2 H, HC=CH), 5.37–5.24 (m, 1 H, OCH), 4.33 (ddquin, $J_{H,H}$ = 7.3 Hz, 1.2 Hz, 7.6 Hz, 2 H, CH_2SF_5), 3.40 (dd, $J_{H,H}$ = 11.2 Hz, 17.4 Hz, 1 H, CH_2), 2.79 (dd, $J_{H,H}$ = 8.6 Hz, 17.4 Hz, 1 H, CH_2), 2.49 (s, 3 H, CH_3).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 193.20 (s, C=O), 158.28 (s, C=N), 136.40 (s, *C*H=$CHCH_2SF_5$), 123.78 (pent, $J_{C,F}$ = 4.5 Hz, =*C*HCH_2SF_5), 83.32 (s, OCH), 72.91 (d pent, $J_{C,F}$ = 15.6 Hz, $J_{C,F}$ = 1.0 Hz, CH_2SF_5), 38.01 (s, CH_2), 27.19 (s, CH_3).

^{19}F NMR (188.3 MHz, $CDCl_3$): δ = 161.81–158.58 (9 lines, J_{F-F} = 144.60 Hz, 1 F), 142.50 (dm, J_{F-F} = 144.60 Hz, 4 F).

Anal. Calcd for $C_8H_{10}F_5NO_2S$: C, 34.41; H, 3.61; F, 34.02; N, 5.02. Found: C, 34.51; H, 3.67; F, 34.10; N, 5.14.

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