Acylation of fluorine-containing spiro[cyclopropane-1-pyrazolines] and dehydrohalogenation of the resulting adducts

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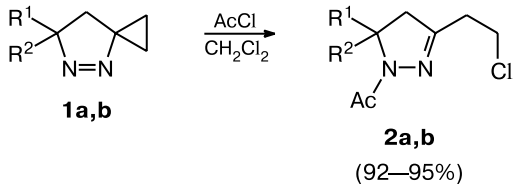
Acylation of 6-(1-fluorovinyl)-6-methyl- and 6-(2,2,3,3-tetrafluorocyclobutyl)-4,5-diazaspiro[2.4]hept-4-enes with acetyl chloride proceeds as electrophilic addition to the N(5) atom and is accompanied by opening of the cyclopropane ring to give 1-acetyl-3-(2-chloroethyl)-5-(1-fluorovinyl)-5-methyl- and 1-acetyl-3-(2-chloroethyl)-5-(2,2,3,3-tetrafluorocyclobutyl)-4,5-dihydropyrazoles, respectively. Under the same conditions, acylation of 6-(2,3,3-trifluorocyclobut-1-enyl)-4,5-diazaspiro[2.4]hept-4-ene is not regioselective. The (2-chloroethyl)pyrazolines obtained undergo dehydrochlorination into vinylpyrazolines in the presence of an excess of MeONa in MeOH. The reaction of 4-acetyl-6-(2,3,3-trifluorocyclobut-1-enyl)-4,5-diazaspiro[2.4]hept-5-ene with MeONa results in selective replacement of the F atom at the double bond by a methoxy group.

Key words: fluorine-containing spiro[cyclopropane-1-pyrazolines], acylation, acetyl chloride, cyclopropane ring opening, dehydrochlorination, NMR spectra.

The study of the effect of fluorine-containing groups on the reactivities of heterocycles is of interest both from the theoretical standpoint and for the possible synthesis of new fluorine-containing synthetic intermediates. Recently,[1,2] we have obtained spiro[cyclopropanepyrazolines] with fluoroalkyl and fluorocycloalkyl substituents in the heterocycle. The presence of a conjugated azocyclopropane fragment makes them interesting objects, *e.g.*, for investigation of the direction of an electrophilic attack. It is known[3,4] that acylation of some spiro[cyclopropanepyrazolines] proceeds regioselectively as 1,5-addition to the azocyclopropane fragment, with opening of the cyclopropane ring. To estimate the reactivities of spiro[cyclopropanepyrazolines] containing fluorinated substituents in the heterocycle, here we studied acylation of the earlier[1,2] synthesized 6-(1-fluorovinyl)-6-methyl- (**1a**), 6-(2,2,3,3-tetrafluorocyclobutyl)- (**1b**), and 6-(2,3,3-trifluorocyclobut-1-enyl)-4,5-diazaspiro[2.4]hept-4-enes (**1c**) and dehydrohalogenation of the resulting *N*-acyl-3-(2-chloroethyl)pyrazolines.

It turned out that the reaction of compound **1a** with acetyl chloride in CH_2Cl_2, as in the case of analogous but nonfluorinated compounds studied previously,[3,4] proceeds regioselectively at the azocyclopropane fragment to give *N*-acetyl-3-(2-chloroethyl)pyrazoline **2a** in ~92% yield (Scheme 1). The reaction of AcCl with one of the diastereomeric tetrafluorocyclobutylpyrazolines **1b** occurs in a similar fashion affording the corresponding product **2b** in ~97% yield. In this reaction, we used the minor isomer of starting pyrazoline **1b** prepared by 1,3-dipolar cycloaddition of the *in situ* generated diazocyclopropane to 1,1,2,2-tetrafluoro-3-vinylcyclobutane[2] and additionally purified by column chromatography on Al_2O_3.

Scheme 1



R^1 = CH_2=CF, R^2 = Me (**a**); R^1 = 2,2,3,3-tetrafluorocyclobutyl, R^2 = H (**b**)

The ^{1}H NMR spectra of the compounds obtained contain signals characteristic of the 2-chloroethyl substituent (δ 2.8 and 3.8, vicinal J = 6.5—7.0 Hz) and signals for the nonequivalent protons at the C(4) atom (geminal J = 18—19 Hz). The ^{13}C NMR spectra show, along with signals for the proton-bearing C atoms, low-field signals for the C=N (δ 153—156) and C=O groups (δ 168—170).

Acylation of compound **1c** is nonselective, yielding not only (2-chloroethyl)-2-pyrazoline **2c** as the result of the opening of the cyclopropane ring but also 1-acetylspiro[cyclopropane-1,5′-(2-pyrazoline)] **3** (Scheme 2). This reaction is similar to the acylation of 5-vinyl-

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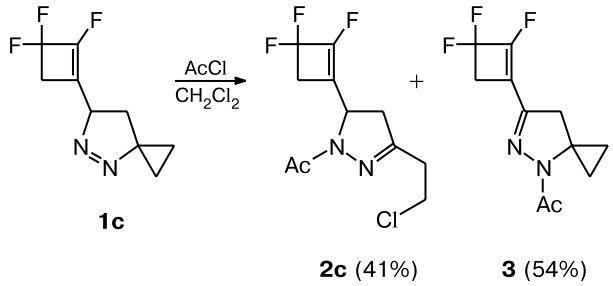
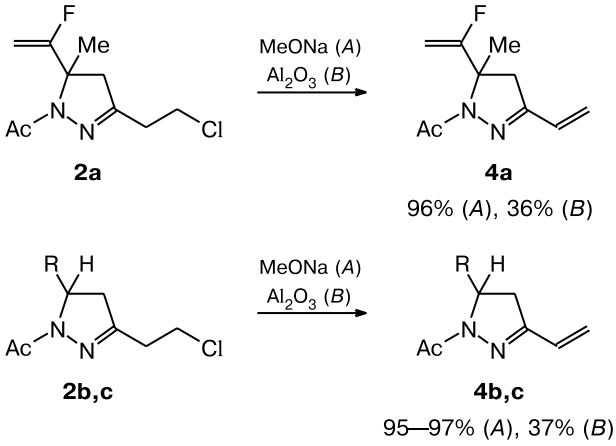
spiro[cyclopropane-1,3′-(1-pyrazoline)], which also affords products with both the opened and retained cyclopropane ring.[5] Acetylpyrazolines **2c** and **3** were isolated by preparative TLC on silica gel in 41 and 54% yields, respectively. Compound **3** is formed through addition of the acetyl fragment to the N atom adjoining the cyclopropane ring and elimination of the methine proton from the heterocycle. This partial change in the direction of the electrophilic attack (in contrast to spiro[cyclopropanepyrazolines] **1a,b**) is probably due to the possibility of the formation of 2-pyrazoline **3** with conjugated double bonds.

Scheme 2



When treated with a double to triple excess of MeONa in MeOH, (2-chloroethyl)pyrazolines **2a—c** underwent virtually complete dehydrochlorination into vinylpyrazolines **4a—c** (Scheme 3, method *A*). In this case, nucleophilic substitution of the methoxy group for the Cl atom occurs only slightly, in contrast to, *e.g.*, partial transformation of (2-bromoethyl)pyrazole into (2-methoxyethyl)pyrazole in the presence of MeONa in MeOH.[6]

Scheme 3

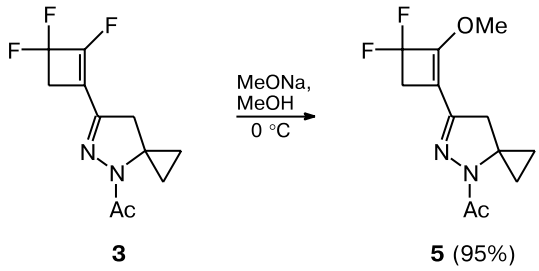


R = 2,2,3,3-tetrafluorocyclobutyl (**b**),
2,3,3-trifluorocyclobut-1-enyl (**c**)

Partial dehydrochlorination of (2-chloroethyl)pyrazolines **2a—c** into vinylpyrazolines **4a—c** also occurred upon application of their solutions in CH_2Cl_2 to the surface of neutral Al_2O_3 (see Scheme 3, method *B*). However, after ~12 h, the extent of dehydrochlorination stopped at the ratio of **2** : **4** ≈ 1.7 : 1. Apparently, pyrazolines **4a—c** cannot be obtained in high yields under these conditions because of reversible dehydrohalogenation/hydrohalogenation at the sorbent surface. The observed phenomena seem to be analogous to the earlier[7,8] reported dehydrohalogenation of 1,2-dihaloethanes into 2-haloethenes at the surface of anhydrous Fe, Al, and Ru halides.

When trifluorocyclobutenylpyrazoline **3** was treated with MeONa in MeOH, the F atom at the double bond was replaced nearly quantitatively by a methoxy group (Scheme 4).

Scheme 4



The structure of methoxy derivative **5** was confirmed by spectroscopic data. For instance, its ^1H and ^{13}C NMR spectra contain signals for the methoxy group at δ 3.90 and 57.8, respectively. In addition, the ^{19}F NMR spectrum of this compound shows no signal for the F atom at the double bond, while the signal for the CF_2 group is retained (δ −105.2).

Apparently, this reaction occurs as 1,4-addition—elimination accelerated by the presence of the polarized conjugated azadiene fragment. For comparison, note that pyrazoline **2c** containing no similar fragment did not undergo such a transformation. Examples of formal nucleophilic substitution for the F atom at the double bond in fluorinated cyclobutenes have been documented.[9,10]

Our investigation demonstrated that spiro[cyclopropanepyrazolines] with fluorine-containing substituents behave in acetylation reactions like most nonfluorinated analogs. Depending on the nature of the substituent in position 5 of the heterocycle, they react either selectively at the azocyclopropane system to give 1,5-adducts or, if the substituent is unsaturated, at different N atoms to give products with both the opened and retained cyclopropane ring. In the former case, selective dehydrochlorination of the resulting 3-(2-chloroethyl)-2-pyrazolines into unsaturated derivatives (*e.g.*, 3,5-divinyl-2-pyrazolines) is also of certain interest.

Experimental

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AC-200 spectrometer (200, 50.3, and 188.3 MHz, respectively) in $CDCl_3$ with 0.05% Me_4Si as the internal standard; ^{19}F chemical shifts are referenced to CCl_3F. Mass spectra were recorded on a Finnigan MAT INCOS-50 instrument (EI, 70 eV) with an RSL-200 capillary column (30 m long) or by direct inlet probe. Melting points were determined in capillaries on a Kofler hot stage. Preparative TLC was performed with Merck silica gel 60 (0.040—0.063 mm) or plates (20×20 cm) with a 1.5-mm fixed layer of alumina 60. Starting 6-(1-fluorovinyl)-6-methyl- (**1a**),[1] 6-(2,2,3,3-tetrafluorocyclobutyl)- (**1b**),[2] and 6-(2,3,3-trifluorocyclobut-1-enyl)-4,5-diazaspiro[2.4]hept-4-enes (**1c**)[2] were prepared according to the known procedures. The minor diastereomer[2] of compound **1b** was additionally purified by column chromatography on Al_2O_3 in heptane—ether (5 : 1).

Acylation of 4,5-diazaspiro[2.4]hept-4-enes 1a—c (general procedure). A cooled solution of AcCl (1 mmol) in CH_2Cl_2 (0.5 mL) was added at 0 to 5 °C over three to four minutes to a stirred solution of 4,5-diazaspirohept-4-ene **1a—c** (1 mmol) in CH_2Cl_2 (1.5 mL). The reaction mixture was stirred for 20 to 30 min and concentrated *in vacuo*. The yellowish residue was analyzed by ^{1}H and ^{19}F NMR spectroscopy and then purified or separated (for starting reagent **1c**) by preparative TLC on SiO_2.

1-Acetyl-3-(2-chloroethyl)-5-(1-fluorovinyl)-5-methyl-4,5-dihydropyrazole (2a) was obtained as a yellowish oily liquid from compound **1a** (155 mg) and AcCl (78 mg) and purified on SiO_2 in hexane—ether (4 : 5). The yield of compound **2a** was 214 mg (92%), R_f 0.54. Found (%): C, 51.41; H, 5.94; Cl, 15.07; N, 12.15. $C_{10}H_{14}ClFN_2O$. Calculated (%): C, 51.62; H, 6.06; Cl, 15.24; N, 12.04. MS, *m/z* (I_{rel} (%)): 232 (4), 234 (1) $[M]^+$; 217 (1); 192 (3); 190 (10); 175 (25); 43 (100). ^{1}H NMR, δ: 1.70 (d, 3 H, Me, $J_{H,F}$ = 1.0 Hz); 2.25 (s, 3 H, Ac); 2.76, 3.19 (both ddd, 1 H each, C(4)H_2, ^2J = 18.5 Hz, J = 2.4 Hz, J = 1.0 Hz); 2.78 (tdd, 2 H, α-CH_2, ^3J = 6.9 Hz, J = 2.3 Hz, J = 1.0 Hz); 3.76 (t, 2 H, CH_2Cl, ^3J = 6.9 Hz); 4.50 (dd, 1 H, *trans*-CF=CH_2, $J_{H,F}$ = 49.3 Hz, ^2J = 3.6 Hz); 4.73 (dd, 1 H, *cis*-CF=CH_2, $J_{H,F}$ = 17.3 Hz, ^2J = 3.6 Hz). ^{13}C NMR, δ: 21.9 (d, Me, $^3J_{C,F}$ = 3.4 Hz); 22.6 (s, CO<u>Me</u>); 32.9 (s, α-CH_2); 40.2 (s, CH_2Cl); 48.7 (s, C(4)); 64.1 (d, C(5), $^2J_{C,F}$ = 26.8 Hz); 90.2 (d, =CH_2, $^2J_{C,F}$ = 19.6 Hz); 152.8 (s, C(5)); 163.7 (d, CF, $^1J_{C,F}$ = 259 Hz); 168.5 (s, C=O). ^{19}F NMR, δ: −110.3 (br.dd, $J_{H,F}$ = 49.3 Hz, $J_{H,F}$ = 17.3 Hz).

1-Acetyl-3-(2-chloroethyl)-5-(2,2,3,3-tetrafluorocyclobutyl)-4,5-dihydropyrazole (2b) was obtained as a yellowish viscous liquid from compound **1b** (222 mg) and AcCl (78 mg) and purified on SiO_2 in heptane—ether (1 : 4). The yield of compound **2b** was 282 mg (94%), R_f 0.60. Found (%): C, 43.69; H, 4.32; Cl, 11.60; N, 9.41. $C_{11}H_{13}ClF_4N_2O$. Calculated (%): C, 43.94; H, 4.36; Cl, 11.79; N, 9.32. MS, *m/z* (I_{rel} (%)): 300 (11), 302 (4) $[M]^+$; 260 (15); 258 (50); 209 (20); 131 (100); 95 (47); 43 (93). ^{1}H NMR, δ: 2.26 (s, 3 H, Me); 2.32, 2.54 (both m, 1 H each, CH_2CF_2); 2.78 (dd, 1 H, H_a(4), ^2J = 19.0 Hz, ^3J = 5.5 Hz); 2.84 (br.d, 2 H, α-CH_2, ^3J = 6.6 Hz); 3.15 (dd, 1 H, H_b(4), ^2J = 19.0 Hz, ^3J = 11.5 Hz); 3.54 (m, 1 H, $CHCF_2$); 3.79 (t, 2 H, CH_2Cl, ^3J = 6.6 Hz); 4.83 (m, 1 H, H(5)). ^{13}C NMR, δ: 21.9 (s, Me); 30.1 (dddd, C(4′), $^2J_{C,F}$ = 33.7 Hz, $^2J_{C,F}$ = 22.0 Hz, $^3J_{C,F}$ = 11.7 Hz, $^3J_{C,F}$ = 1.4 Hz); 32.9 (s, α-CH_2); 37.8 (br.s, C(4)); 40.5 (s, CH_2Cl); 41.1 (dddd, C(3′), $^2J_{C,F}$ = 31.9 Hz, $^2J_{C,F}$ = 22.0 Hz, $^3J_{C,F}$ = 9.9 Hz, $^3J_{C,F}$ = 3.5 Hz); 52.3 (s, C(5)); 116.8 (ddt, CF_2, $^1J_{C,F}$ = 296 Hz, $^1J_{C,F}$ = 284 Hz, $^2J_{C,F}$ = 25.6 Hz); 118.1 (ddt, CF_2, $^1J_{C,F}$ = 301 Hz, $^1J_{C,F}$ = 287 Hz, $^2J_{C,F}$ = 26.5 Hz); 155.8 (s, C(3)); 169.8 (s, C=O). ^{19}F NMR, δ: −106.7, −129.0 (both br.d, CF_2, J = 212 Hz); −111.2, −118.0 (both br.d, CF_2, ^2J = 210 Hz).

1-Acetyl-3-(2-chloroethyl)-5-(2,3,3-trifluorocyclobut-1-enyl)-4,5-dihydropyrazole (2c) and 4-acetyl-6-(2,3,3-trifluorocyclobut-1-enyl)-4,5-diazaspiro[2.4]hept-5-ene (3). A yellowish oily residue (135 mg) was obtained from pyrazoline **1c** (103 mg, ~0.5 mmol) and AcCl (40 mg, ~0.5 mmol). Separation of the residue by preparative TLC on SiO_2 in heptane—ether (1 : 2) gave compounds **2c** (58 mg, 41%) and **3** (67 mg, 54%). <u>Compound **2c**</u>. R_f 0.27. Found (%): C, 47.00; H, 4.19; N, 10.09. $C_{11}H_{12}ClF_3N_2O$. Calculated (%): C, 47.07; H, 4.31; N, 9.98. ^{1}H NMR, δ: 2.29 (s, 3 H, Me); 2.62 (dt, 2 H, CH_2 of the cyclobutene, $J_{H,F}$ = 12.2 Hz, $J_{H,F}$ = 3.0 Hz); 2.85 (t, 2 H, CH_2, J = 6.4 Hz); 2.92 (dd, 1 H, H_a(4), ^2J = 17.7 Hz, ^3J = 5.1 Hz); 3.21 (dd, 1 H, H_b(4), ^2J = 17.7 Hz, ^3J = 11.6 Hz); 3.79 (t, 2 H, CH_2Cl, J = 6.4 Hz); 5.14 (m, 1 H, H(5)). ^{13}C NMR, δ: 21.5 (s, Me); 33.0 (s, CH_2); 37.6 (dt, C(4′), $^2J_{C,F}$ = 22.7 Hz, $^3J_{C,F}$ = 17.4 Hz); 39.5 (s, C(4)); 40.2 (s, CH_2Cl); 50.1 (q, C(5), $J_{C,F}$ = 3.7 Hz); 118.0 (dt, C(3′), $^1J_{C,F}$ = 275 Hz, $^2J_{C,F}$ = 25.0 Hz); 124.6 (dt, C(1′), $^2J_{C,F}$ = 17.0 Hz, $^3J_{C,F}$ = 8.0 Hz); 140.1 (dt, C(2′), $^1J_{C,F}$ = 345 Hz, $^2J_{C,F}$ = 26.0 Hz); 155.1 (s, C(3)); 169.0 (s, C=O). ^{19}F NMR, δ: −110.5 (br.s, 2 F, CF_2); −105.9 (br.s, 1 F, CF). <u>Compound **3**</u>. R_f 0.65. Found (%): C, 53.92; H, 4.48; N, 11.66. $C_{11}H_{11}F_3N_2O$. Calculated (%): C, 54.10; H, 4.54; N, 11.47. MS, *m/z* (I_{rel} (%)): 244 $[M]^+$ (43), 217 (28), 149 (27), 111 (19), 95 (15), 85 (16), 69 (24), 55 (42), 43 (100). ^{1}H NMR, δ: 0.71 (m, 2 H, H(1) and H(2) oriented from the N atom of the heterocycle); 2.13 (m, 2 H, H(1) and H(2) oriented toward the N atom of the heterocycle); 2.24 (s, 3 H, Me); 2.91 (dt, 2 H, H(4′), $^3J_{H,F}$ = 12.0 Hz, $^4J_{H,F}$ = 3.3 Hz); 3.23 (br.s, 2 H, H(7)). ^{13}C NMR, δ: 11.4 (s, C(1), C(2)); 23.1 (s, Me); 36.6 (dt, C(4′), $^3J_{C,F}$ = 17.0 Hz, $^2J_{C,F}$ = 23.0 Hz); 42.9 (s, C(7)); 44.8 (s, C(3)); 117.7 (dt, C(1′), $^2J_{C,F}$ = 18.0 Hz, $^3J_{C,F}$ = 6.5 Hz); 118.6 (dt, C(3′), $^1J_{C,F}$ = 275 Hz, $^2J_{C,F}$ = 26.0 Hz); 142.5 (dt, C(2′), $^1J_{C,F}$ = 357 Hz, $^2J_{C,F}$ = 27.0 Hz); 143.1 (dt, C(5), $^3J_{C,F}$ = 7.0 Hz, $^4J_{C,F}$ = 3.2 Hz); 169.7 (s, C=O). ^{19}F NMR, δ: −110.5 (br.s, 2 F, CF_2); −105.9 (br.s, 1 F, CF).

Dehydrochlorination of 1-acetyl-3-(2-chloroethyl)-4,5-dihydropyrazoles 2a—c (general procedure). ***A.*** Sodium methoxide (27—32 mg, 0.5—0.6 mmol) in MeOH (1.5 mL) was added at −20 °C to a solution of compound **2a—c** (0.2 mmol) in MeOH (0.5 mL). The reaction mixture was left at this temperature for 8 to 12 h. Then the solvent was removed *in vacuo*, two drops of water were added, and the residue was treated with CH_2Cl_2 (2×2 mL). The solution was passed through a thin layer of silica gel and concentrated to give individual 3-vinyl-4,5-dihydropyrazoles **4a—c** in 95 to 97% yields.

B. A solution of compound **2a—c** (0.1 mmol) in ether (2 mL) was applied to neutral Al_2O_3 (bulk volume ~2 mL), hermetically closed, and left for 12 h. Then the substances were washed out of the sorbent with ether (10 mL) and the solvent was removed *in vacuo*. The reaction mixtures contained dehydrochlorination products **4a—c** (35—38%) and the starting pyrazolines **2a—c** (62—65%) (^{1}H NMR data). When the reaction mixture was kept on Al_2O_3 for a longer period of time (24—30 h), the ratio of the reaction products and the starting 3-(2-chloroethyl)pyrazolines remained virtually unchanged.

1-Acetyl-5-(1-fluorovinyl)-5-methyl-3-vinyl-4,5-dihydropyrazole (4a). Found (%): C, 61.35; H, 6.85; N, 14.21. $C_{10}H_{13}FN_2O$. Calculated (%): C, 61.21; H, 6.68; N, 14.28. MS, *m/z* (I_{rel} (%)): 196 $[M]^+$ (15), 170 (5), 154 (26), 139 (47), 119 (14), 109 (46), 43 (100). ^{1}H NMR, δ: 1.72 (d, 3 H, Me, J = 1.0 Hz); 2.30 (s, 3 H, COMe); 2.87, 3.32 (both d, 1 H each, C(4)H$_2$, ^2J = 17.0 Hz); 4.63 (dd, 1 H, *trans*-CF=CH, $J_{H,F}$ = 49.0 Hz, ^2J = 4.0 Hz); 4.78 (dd, 1 H, *cis*-CF=CH, $J_{H,F}$ = 17.6 Hz, ^2J = 4.0 Hz); 5.48 (br.d, 1 H, =CH$_2$, J_{trans} = 17.5 Hz); 5.61 (br.d, 1 H, =CH$_2$, J_{cis} = 10.7 Hz); 6.62 (dd, 1 H, =CH, J_{trans} = 17.5 Hz, J_{cis} = 10.7 Hz). ^{13}C NMR, δ: 22.3 (d, Me, $^3J_{C,F}$ = 2.5 Hz); 22.8 (s, CO<u>Me</u>); 44.8 (s, C(4)); 64.6 (d, C(5), $^2J_{C,F}$ = 29.0 Hz); 90.4 (d, =CH$_2$, $^2J_{C,F}$ = 19.8 Hz); 122.3 (s, =CH$_2$); 129.5 (s, =CH); 152.7 (s, C(3)); 163.5 (d, =CF, $^1J_{C,F}$ = 260 Hz); 169.2 (s, C=O). ^{19}F NMR, δ: −110.2 (br.dd, $J_{H,F}$ = 49.0 Hz, $J_{H,F}$ = 17.6 Hz).

1-Acetyl-5-(2,2,3,3-tetrafluorocyclobutyl)-3-vinyl-4,5-dihydropyrazole (4b). Found (%): C, 50.18; H, 4.53; N, 10.48. $C_{11}H_{12}F_4N_2O$. Calculated (%): C, 50.00; H, 4.58; N, 10.60. MS, *m/z* (I_{rel} (%)): 264 $[M]^+$ (19), 222 (64), 131 (12), 95 (100), 77 (10), 43 (72). ^{1}H NMR, δ: 2.21, 2.53 (both m, 1 H each, C(4′)H$_2$); 2.31 (s, 3 H, Me); 2.84 (br.dd, 1 H, H$_a$(4), ^2J = 18.3 Hz, ^3J = 5.5 Hz); 3.21 (dd, 1 H, H$_b$(4), ^2J = 18.3 Hz, ^3J = 11.5 Hz); 3.62 (m, 1 H, H(3′)); 4.86 (m, 1 H, H(5)); 5.63 (m, 2 H, =CH$_2$); 6.62 (dd, 1 H, =CH, J_{trans} = 17.8 Hz, J_{cis} = 10.8 Hz). ^{13}C NMR, δ: 22.1 (s, Me); 30.1 (ddt, C(4′), $^2J_{C,F}$ = 34.1 Hz, $^2J_{C,F}$ = 23.3 Hz, $^3J_{C,F}$ = 10.8 Hz); 33.7 (d, C(5), $J_{C,F}$ = 1.3 Hz); 41.0 (dddd, C(3′), $^2J_{C,F}$ = 30.5 Hz, $^2J_{C,F}$ = 19.7 Hz, $^3J_{C,F}$ = 10.8 Hz, $^3J_{C,F}$ = 3.6 Hz); 52.8 (s, C(4)); 116.9 (ddt, CF$_2$, $^1J_{C,F}$ = 294 Hz, $^1J_{C,F}$ = 284 Hz, $^2J_{C,F}$ = 25.1 Hz); 118.2 (ddt, CF$_2$, $^1J_{C,F}$ = 302 Hz, $^1J_{C,F}$ = 287 Hz, $^2J_{C,F}$ = 26.9 Hz); 123.6 (s, =CH$_2$); 129.2 (s, =CH); 155.4 (s, C(3)); 170.1 (s, C=O). ^{19}F NMR, δ: −128.5, −107.0 (both br.d, 1 F each, CF$_2$, J = 212 Hz); −117.5, −111.3 (both br.d, 1 F each, CF$_2$, J = 208 Hz).

1-Acetyl-5-(2,3,3-trifluorocyclobut-1-enyl)-3-vinyl-4,5-dihydropyrazole (4c). Found (%): C, 54.43; H, 4.62; N, 11.26. $C_{11}H_{11}F_3N_2O$. Calculated (%): C, 54.10; H, 4.54; N, 11.47. MS, *m/z* (I_{rel} (%)): 244 $[M]^+$ (10), 202 (30), 183 (2), 137 (4), 95 (39), 84 (23), 43 (100). ^{1}H NMR, δ: 2.32 (s, 3 H, Me); 2.63 (m, 2 H, C(4′)H$_2$); 3.02 (dd, 1 H, H$_a$(4), ^2J = 17.5 Hz, ^3J = 5.8 Hz); 3.30 (dd, 1 H, H$_b$(4), ^2J = 17.5 Hz, ^3J = 9.5 Hz); 5.18 (m, 1 H, H(5)); 5.58, 5.70 (both br.d, 1 H each, =CH$_2$, J_{trans} = 18.0 Hz, J_{cis} = 11.1 Hz); 6.65 (dd, 1 H, =CH, J_{trans} = 18.0 Hz, J_{cis} = 11.1 Hz). ^{13}C NMR, δ: 21.9 (s, Me); 35.4 (s, C(4)); 37.6 (dt, C(4′), $^2J_{C,F}$ = 22.7 Hz, $^3J_{C,F}$ = 17.0 Hz); 50.1 (dd, C(5), $^3J_{C,F}$ = 7.1 Hz, $^4J_{C,F}$ = 3.6 Hz); 123.4 (s, =CH$_2$); 124.4 (dt, C(1′), $^2J_{C,F}$ = 25.6 Hz, $^3J_{C,F}$ = 6.5 Hz); 124.5 (dt, C(3′), $^1J_{C,F}$ = 339 Hz, $^2J_{C,F}$ = 31.0 Hz); 129.0 (s, =CH); 140.1 (dt, C(2′), $^1J_{C,F}$ = 345 Hz, $^2J_{C,F}$ = 32.0 Hz); 154.9 (s, C(3)); 169.1 (s, C=O). ^{19}F NMR, δ: −112.6 (br.s, 1 F, CF); −111.2 (br.s, 2 F, CF$_2$).

4-Acetyl-6-(3,3-difluoro-2-methoxycyclobut-1-enyl)-4,5-diazaspiro[2.4]hept-5-ene (5). Sodium methoxide (27 mg, 0.5 mmol) in MeOH was added at −5 °C to a solution of compound **3** (49 mg, 0.2 mmol) in MeOH (1 mL). The reaction mixture was stirred at 0 °C for 3 h, concentrated, washed with CH_2Cl_2 (3 mL), and passed through a ~1-cm layer of silica gel, which was then additionally washed with CH_2Cl_2 (3 mL). Removal of the solvent gave compound **5** (48.6 mg, 95%) as colorless crystals, m.p. 60—62 °C. Found (%): C, 56.38; H, 5.40; N, 10.82. $C_{12}H_{14}F_2N_2O_2$. Calculated (%): C, 56.25; H, 5.51; N, 10.93. MS, *m/z* (I_{rel} (%)): 256 $[M]^+$ (60), 214 (100), 199 (91), 185 (10), 171 (17), 151 (7), 121 (10), 111 (41). ^{1}H NMR, δ: 0.69 (m, 2 H, H(1) and H(2) oriented from the N atom of the heterocycle); 2.13 (m, 2 H, H(1) and H(2) oriented toward the N atom of the heterocycle); 2.21 (s, 3 H, Me); 2.89 (t, 2 H, H(4′), $^3J_{H,F}$ = 3.3 Hz); 3.18 (br.s, 2 H, H(7)); 3.90 (s, 3 H, OMe). ^{13}C NMR, δ: 11.4 (s, C(1), C(2)); 23.3 (s, CO<u>Me</u>); 37.8 (t, C(4′), $^2J_{C,F}$ = 22.5 Hz); 43.8 (s, C(7)); 44.4 (s, C(3)); 57.8 (s, OMe); 110.6 (t, C(1′), $^3J_{C,F}$ = 19.3 Hz); 120.0 (t, C(3′), $^1J_{C,F}$ = 278 Hz); 146.2 (t, C(6), $^4J_{C,F}$ = 3.7 Hz); 146.9 (t, C(2′), $^2J_{C,F}$ = 20.6 Hz); 169.5 (s, C=O). ^{19}F NMR, δ: −105.1 (br.s).

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