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Alkylation of 1-phenyl-3,5-disubstituted pyrazoles with polyfluorinated aliphatic aldehydes Properties of 1-phenyl-4-(1-hydroxypolyfluoroalkyl)pyrazole derivatives

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Abstract

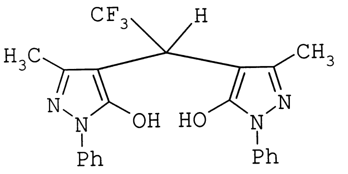
Polyfluorinated aliphatic aldehydes react with 1-phenyl-3-methylpyrazole-5-one, 1-phenyl-3-methyl-5-amino (*N*,*N*-dimethylamino-methylenamino)pyrazole and 1-phenyl-3-aminopyrazole-5-one at room temperature in the absence of catalyst with formation of 4-(1-hydroxypolyfluoroalkyl)pyrazoles. Dehydration of 4-(1-hydroxypolyfluoroalkyl)pyrazoles with morpholinosulfur trifluoride generates 4-polyfluoroalkylidenepyrazoles, which are active dienophiles and react with 2,3-dimethylbutadiene and cyclopentadiene forming spirocyclic pyrazole derivatives. © 2000 Elsevier Science S.A. All rights reserved.

Keywords: Pyrazole; Alkylation; Polyfluorinated aliphatic aldehyde

1. Introduction

Poly- and perfluoroalkyl derivatives of aromatic and heteroaromatic compounds are intensively studied [1–5]. One of the possible approaches to the synthesis of these compounds consists in interaction of perfluoroketones [6] or aldehydes [2] with aromatic or heteroaromatic derivatives. Polyfluorinated tertiary or secondary alcohols containing aryl or heteroaryl substituent in the α-position, are formed in these reactions. Compounds of this type are used for synthesis of substances with analgesic and antinociceptive activity [7,8].

The reactions of perfluoroaldehydes with heteroaromatic compounds have been studied on the example of 3-pyridyllithium [2]. The thermal condensation of 1-phenyl-3-methylpyrazole-5-one with the hydrate of trifluoroacetic aldehyde is known among other heteroaromatic compounds. 1,1-bis-(1-phenyl-3-methyl-5-hydroxypyrazole-4-yl)-2,2,2-trifluoroethane (**1**) (see Section 2.2) is formed in this example [9].



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2. Results and discussion

2.1. Interaction of 1-phenyl-3,5-disubstituted pyrazoles with polyfluorinated aldehydes

We have found that the aldehydes (**2a, b**) react with such electron rich heteroaromatic compounds as 1-phenyl-3,5-disubstituted pyrazoles (**3a–d**) at room temperature and in the absence of catalysts or condensing agents forming heterocyclic products alkylated on the 4-position. The 1-phenyl-3,5-disubstituted-4-(1-hydroxypolyfluoroalkyl)pyrazoles (**4a–e**) were accordingly obtained. Up to 17% of compound (**1**) has been formed also when the pyrazole (**3a**) interacts with trifluoroacetic aldehyde.

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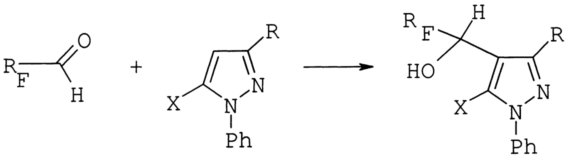
The compounds (**4a, b**) have been obtained also by reaction of 1-phenyl-3-methylpyrazole-5-one with the ethylhemiacetal of trifluoroacetic aldehyde or 1,1,2,2,3,3,4,4-octafluoropentanal hydrate. These processes occur at room temperature over 1–5 days, whereas reactions of the 1-phenyl-3-methylpyrazole-5-one with aldehydes (**2a, b**) are complete in 2–5 h.

The nature of the substituent in a 5-position of the heterocycle (**3**) influences the path of the reaction. 1-Phenyl-3-methylpyrazole, 1-phenyl-3,5-dimethylpyrazole and 1-phenyl-3-methyl-5-ethoxypyrazole cannot be alkylated with aldehyde (**2b**) even on long heating in the presence of $BF_3{\cdot}OEt_2$ catalyst. Only polymerization of aldehyde (**2b**) is observed in that case.

IR and NMR spectroscopic data have proved the structure of the compounds (**4a–e**).

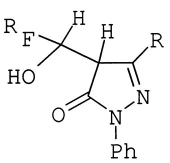

2a,b 3a-d 4a-e

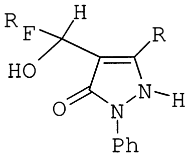
2 R_F= CF_3 (**a**), $(CF_2)_4H$ (**b**);

3 R = CH_3, X = OH (**a**), NH_2 (**b**), N=CHN $(CH_3)_2$ (**c**); R = NH_2, X = OH (**d**);

4 R_F = CF_3, R = CH_3, X = OH (**a**); R_F = $(CF_2)_4$ H, R = CH_3, X = OH (**b**), X = NH_2 (**c**), X = N=CHN $(CH_3)_2$ (**d**); R_F = $(CF_2)_4$, R = NH_2, X = OH (**e**).

The absorption of OH groups in 3200–3400 cm^{-1} region and absence of signals of carbonyl groups of possible isomers (**5a, b, e**) and (**5′a, b, e**) is observed in the IR spectra of compounds (**4a, b, e**). Only one set of signals of ^1H and ^{19}F nuclei is present in the ^1H and ^{19}F NMR spectra of DMSO-d_6, CD_3CN, CH_3OH solutions of compounds (**4a, b, e**). That testifies the absence (within sensitivity of the method) of possible isomers (**5a, b, e**). There are no signals of connected proton nuclei of the heterocycle in the ^{13}C NMR spectrum of the solution of compound (**4a**) in DMSO-d_6 recorded with application of APT technique [10]. That proves the structure of compound (**4a**) and also testifies the absence of another possible product of alkylation on the second nitrogen atom of the pyrazole cycle (**6**).

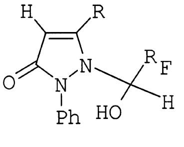

5a,b,e


5'a,b,e

5 R_F = CF_3, R = CH_3 (**a**); R_F = $(CF_2)_4H$, R = CH_3 (**b**), R = NH_2 (**e**);

5′ R = CF_3, R = CH_3 (**a**); R = $(CF_2)_4H$, R = CH_3 (**b**), R = NH_2 (**e**).

It would be possible to expect the formation of half-aminales (**7**) and (**8**) as the products of addition of aminogroup to a molecule of aldehyde in the case of the pyrazoles (**3b, d**). However, the alkylated pyrazoles (**4c, e**) are not changed in boiling methanol in the presence of hydrochloric acid. Such behavior is not characteristic of half-aminales of perfluoroaldehydes which are easily hydrolyzed under these conditions [11].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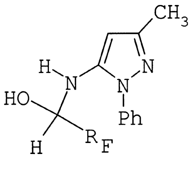
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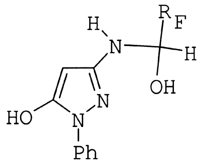
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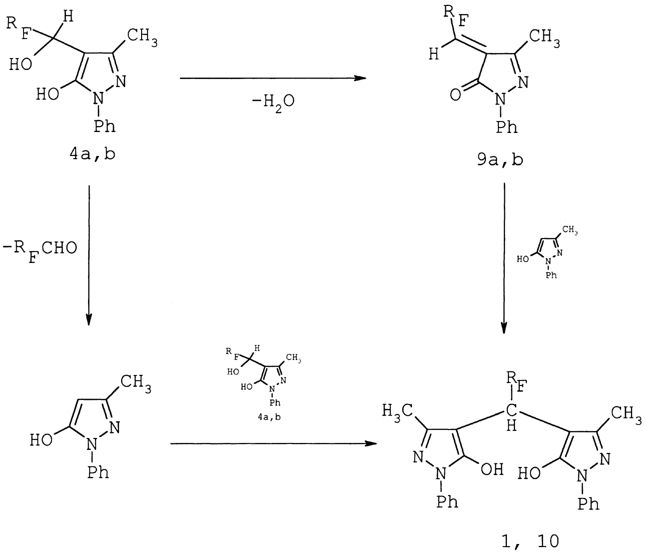
The compounds (**4a–e**) are high melting, colorless, crystalline and soluble in polar organic solvents. They are the first representatives of pyrazoles containing 1-hydroxypolyfluoroalkyl substituents. It is necessary to note that much attention has been paid to investigation of other heterocycles, obtained by more difficult methods, containing similar substituents, over recent years. The 1-hydroxypolyfluoroalkyl derivatives of pyridine [2,3], quinoline, pyrimidine [4], thiophene and furan [5] have been studied. We have investigated some chemical properties of the compounds (**4a, b**) with the purpose to obtain new fluorine containing derivatives of pyrazoles.

2.2. Thermal transformations of 1-phenyl-3-methyl-4-(1-hydroxypolyfluoroalkyl)-5-hydroxypyrazoles



1 R_F = CF_3;

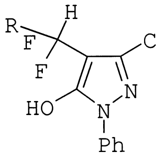
4 R_F = CF_3 (**a**), R_F = $(CF_2)_4H$ (**b**);

9 R_F = CF_3 (**a**), R_F = $(CF_2)_4H$ (**b**);

10 R_F = $(CF_2)_4H$.

Pyrazoles (**4a, b**) have been transformed into 1,1-bis-(1-phenyl-3-methyl-5-hydroxypyrazole-4-yl)-2,2,2-trifluoroethane (**1**) and 1,1-bis-(1-phenyl-3-methyl-5-hydroxypyrazole-4-yl)-2,2,3,3,4,4,5,5-octafluoropentane (**10**) on heating to 130°C for a long time. It is possible to propose two mechanisms for course of this process. The 1-phenyl-3-methyl-5-hydroxypyrazole is formed by eliminating a molecule of aldehyde (**2a**) or (**2b**) from a molecule of pyrazole (**4a**) or (**4b**). This then interacts with another molecule of pyrazole (**4a**) or (**4b**) or with a molecule of 4-polyfluoroalkylidenepyrazole (**9a**) or (**9b**), that can be formed by elimination of a molecule of water from a molecule of pyrazole (**4a**) or (**4b**). Compound (**10**) has been obtained by interaction of 4-polyfluoroalkylidenepyrazole (**9b**) with 1-phenyl-3-methyl-5-hydroxypyrazole.

2.3. Dehydration of 1-phenyl-3-methyl-4-(1-hydroxypolyfluoroalkyl)-5-hydroxypyrazoles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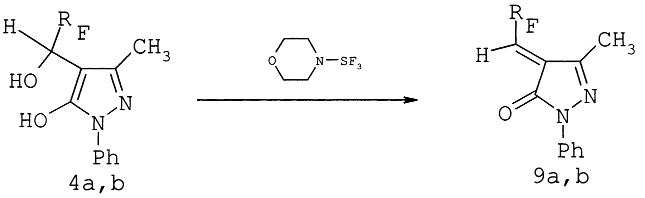
The corresponding 4-fluoroalkylpyrazoles (**11**) are not formed by reactions of compounds (**4a, b**) with morpholinosulfur trifluoride. Only 4-polyfluoroakylydenepyrazoles (**9a, b**) are obtained as the products of dehydration. It was not possible to isolate 4-trifluoroethylidenepyrazole-5-one (**9a**) from the reaction mixture because of its decomposition. It was identified as the cycloadduct with diene (**12a**). Compound (**9b**) is a red crystalline product, which is soluble in non-polar organic solvents in contrast to the precursor (**4b**). The process of dehydration is stereospecific as the presence of a single set of signals in spectrum ^{19}F NMR of reaction mixture indicates that only one of two possible geometrical isomers of compound (**9b**) has been formed.

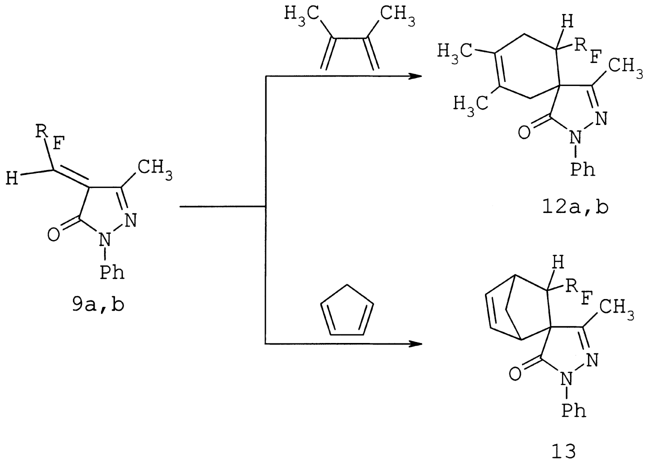


4 $R_F = CF_3$ (**a**), $R_F = (CF_2)_4H$;
9 $R_F = CF_3$ (**a**), $R_F = (CF_2)_4H$.

2.4. Reactions of 1-phenyl-3-methyl-4-polyfluoroalkylidenepyrazole-5-ones

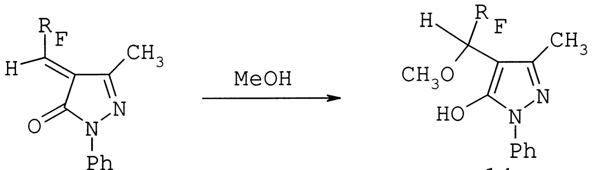
The presence of the polyfluoroalkyl substituent at the exocyclic carbon at the double bond of compounds (**9a, b**) increases its activity in reactions with dienes. The products of Diels–Alder reactions with 2,3-dimethylbutadiene and cyclopentadiene are spirocyclic compounds (**12a, b**) and (**13**) formed when reaction is carried out at room temperature and in the absence of catalysts. The product of reaction of unstable compound (**9a**) with 2,3-dimethylbutadiene had been obtained when this diene was added directly to the reaction mixture of compound (**4a**) and morpholinosulfur trifluoride. It should be noted that intramolecular Diels–Alder reactions of the unfluorinated α-oxoalkylidenes of a pyrazole have been published recently. But they proceed under rather harsh conditions and α-oxoalkylidenes behave as dienes [12].

The presence of four chiral atoms of carbon in a molecule of compound (**13**) causes complication in the ^{1}H and ^{19}F NMR spectra. Comparison of integrated intensities of the signals gives the conclusion that there occurs more than 80% formation of one of six possible pairs of diastereomers. The formation of only one pair of diastereomers has been observed in the case of compounds (**12a, b**).

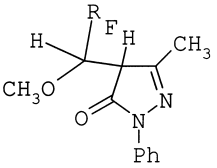


9 $R_F = CF_3$ (**a**), $R_F = (CF_2)_4H$ (**b**);
12 $R_F = CF_3$ (**a**), $R_F = (CF_2)_4H$ (**b**);
13 $R_F = (CF_2)_4H$.

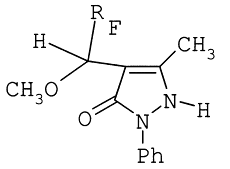
Compound (**9b**) easily adds a molecule of methanol forming the corresponding 4-(1-methoxypolyfluoroalkyl)-pyrazole (**14**). The signal of the proton for the 4-position of pyrazole nucleus is absent from the ^{1}H NMR spectrum of compound (**14**) recorded in $CDCl_3$. The characteristic carbonyl group IR absorption is absent in a KBr disc indicating the presence of this compound in the 5-hydroxy form (**14**), instead of in the form of pyrazole-5-ones (**15a**) or (**15′a**).



9b 14



15a



15'a

3. Experimental

IR spectra were measured on a UR-10 spectrometer; ^1H, ^{19}F, ^{13}C NMR spectra were recorded on Varian-VXR (^1H: 300 MHz, ^{19}F: 282 MHz, ^{13}C: 75 MHz) using TMS as internal standard for ^1H and ^{13}C NMR spectra, and C_6F_6 (−162.9 ppm) as internal standard for ^{19}F NMR spectra. Purification of products was by column chromatography on silica gel, the eluent used was $CHCl_3$/MeO = 9/1. Analysis and spectroscopic data are given in Tables 1 and 2.

*3.1. Synthesis of 4-(1-hydroxy-2,2,2-trifluoroethyl)pyrazole (**4a**) and 4-(1-hydroxy-2,2,3,3,4,4,5,5-octafluoropentyl)pyrazoles (**4b–e**)*

1. Trifluoroacetic aldehyde (8.67 mmol) was obtained by heating at 90°C of ethylhemiacetal of trifluoroacetic aldehyde (17.23 mmol) with a mixture of P_2O_5 (1 g) and 98% H_2SO_4 (4 ml) and condensed at −70°C. Then it was passed for 10 min into a stirred suspension of pyrazole (**3a**) (6.63 mmol) in chloroform (10 ml) at −40°C. The mixture was stirred at −20°C for 1 h and then heated up to 20°C and stirred for 15 h. The precipitate containing compound (**4a**) and 17% of compound (**1**), judging from its solution in DMSO ^{19}F NMR spectrum, was filtered. It was washed with boiling chloroform (20 ml) to remove compound (**1**).
2. The ethylhemiacetal of trifluoroacetic aldehyde (4 mmol) at 20°C was added to a suspension of equimolar amounts of pyrazole (**3a**) in chloroform (10 ml). The mixture was maintained at 20°C for 5 days and compound (**4a**) was filtered off.
3. A solution of aldehyde (**2b**) (3.1 mmol) in chloroform (5 ml) at 20°C was added to a stirred suspension of pyrazole (**3a**) or (**3b–d**) (3.0 mmol) in chloroform (5 ml). The mixture was stirred at 20°C for 24 h and then the compounds (**4b, c, e**) were filtered off. In the case of compound (**4d**), chloroform was removed in vacuo (20 torr), the oily residue was treated with *n*-hexane (5 ml) and pyrazole (**4d**) was filtered off.
4. The hydrate of aldehyde (**2b**) (6.76 mmol) at 20°C was added to a stirred suspension of equimolar amounts of pyrazole (**3a**) in chloroform (10 ml). The mixture was stirred for 24 h and compound (**4b**) was filtered off.

*3.2. Thermolysis of 1-phenyl-3-methyl-4-(1-hydroxy-2,2,2-trifluoroethyl)-5-hydroxypyrazole (**4a**) and 1-phenyl-3-methyl-4-(1-hydroxy-2,2,3,3,4,4,5,5-octafluoropentyl)-5-hydroxypyrazole (**4b**)*

1. Pyrazole (**4a**) or (**4b**) (5 mmol) was heated at 130°C for 5 h. Compound (**1**) was recrystallized from methanol; compound (**10**) was washed with *n*-hexane (5 ml).
2. The mixture of 1-phenyl-3-methyl-5-hydroxypyrazole (4 mmol) and of equimolar amounts of 1-phenyl-3-methyl-4-(2,2,3,3,4,4,5,5-octafluoropentylidene)pyrazole-5-one (**9b**) was heated at 130°C for 5 h then compound (**10**) was washed with *n*-hexane (5 ml).

Table 1
Yields, melting points and analytical data for compounds **1**, **4a–e**, **9b**, **10**, **12a**, **b**, **13**, **14**

N	Melting point (°C)	Yield (%)	Found (%)			Formula	Calculated (%)		
			C	H	N		C	H	N
1	279–281	34	–	–	–	–	–	–	–
4a	118–120	(i) 34[b], (ii) 14[b]	52.77	4.18	10.42	$C_{12}H_{11}F_3N_2O_2$	52.94	4.07	10.29
4b	82–85	(iii) 91[b], (iv) 75[b]	44.54	3.04	6.90	$C_{15}H_{12}F_8N_2O_2$	44.57	2.99	6.93
4c	147–148	78	44.64	3.28	10.40	$C_{15}H_{13}F_8N_3O$	44.68	3.25	10.42
4d	88–91	90	47.23	4.05	12.17	$C_{18}H_{18}F_8N_4O$	47.17	3.96	12.22
4e[a]	168–169	70	41.46	2.67	10.30	$C_{14}H_{11}F_8N_3O_2$	41.49	2.74	10.37
9b	38–41	62	46.50	2.78	7.18	$C_{15}H_{10}F_8N_2O$	46.65	2.61	7.25
10	122–123	(i) 24[b], (ii) 75[b]	53.51	3.61	10.02	$C_{25}H_{20}F_8N_4O_2$	53.58	3.60	10.00
12a	Oil	26	64.27	5.49	8.35	$C_{18}H_{19}F_3N_2O$	64.28	5.69	8.33
12b	26–27	72	53.72	4.32	6.05	$C_{21}H_{20}F_8N_2O$	53.85	4.30	5.98
13	Oil	53	53.06	3.77	6.29	$C_{20}H_{16}F_8N_2O$	53.10	3.57	6.19
14	57–59	56	45.92	3.60	6.70	$C_{16}H_{14}N_2O_2F_8$	45.94	3.37	6.70

[a] ES mass spectroscopy $M^+ = 405$.

[b] See Section 3.

Table 2
IR and NMR spectral characteristics of compounds **1**, **4a–e**, **9b**, **10**, **12a**, **b**, **13**, **14**

N	^{1}H NMR, δ (ppm), J (Hz)	^{19}F NMR, δ (ppm), J (Hz)	IR, ν (cm^{-1}), in range 3400–950 cm^{-1}
1	(DMSO-d$_6$): 2.27 (6H, s, CH$_3$); 4.34 (1H, q, CHCF$_3$, $^3J_{HF} = 10.5$); 7.26 (2H, t, Ar); 7.44 (4H, t, Ar); 7.67 (4H, d, Ar); 14.73 (2H, w.s, OH)	(DMSO): −67.47 (d, $^3J_{HF} = 10.2$)	(Kbr): 3100, 2950, 1615, 1590, 1510, 1470, 1420, 1380, 1330, 1290, 1260, 1170, 1140, 1110, 1065, 1130
4a	(DMSO-d$_6$): 2.24 (3H, s, CH$_3$); 5.06 (1H, m, CH); 6.53 (1H, s, OH); 7.24 (1H, t, Ar); 7.45 (2H, t, Ar); 7.69 (2H, d, Ar); 11.32 (1H, w.s, OH) (DMSO-d$_6$)[a]: 17.78; 50.86 (q, $^2J_{CF} = 32.5$); 107.35; 112.50; 112.93 (q, $^1J_{CF} = 282.6$); 116.12; 124.79; 135.33	(DMSO): −77.00 (s); (CH$_3$OH): −77.50 (d, $^3J_{HF} = 5.6$)	(KBr): 3300, 3100, 2940, 2820, 1615, 1580, 1510, 1460, 1430, 1390, 1365, 1305, 1275, 1230, 1180, 1130, 990, 960
4b	(DMSO-d$_6$): 2.26 (3H, s, CH$_3$); 5.24 (1H, d, CH); 6.48 (1H, s, OH); 7.01 (1H, t.t, CF$_2$H, $^2J_{HF} = 50.5$, $^3J_{HF} = 5.1$); 7.24 (1H, t, Ar); 7.46 (2H, t, Ar); 7.69 (2H, d, Ar)	(CH$_3$OH): −137.39 (2F, d, $^2J_{HF} = 50.5$); −130.45, −128.92 (2F, $^2J_{AB} = 287.6$); −123.77, −116.31 (2F, $^2J_{AB} = 279.4$); −123.62, −122.41 (2F, $^2J_{AB} = 318.0$)	(KBr): 3200–2600, 1615, 1580, 1510, 1470, 1420, 1385, 1370, 1320, 1290, 1180, 1140, 1090, 1050
4c	(DMSO-d$_6$): 2.21 (3H, s, CH$_3$); 5.20 (1H, m, CH); 5.27 (2H, s, NH$_2$); 6.53 (1H, d, OH); 7.02 (1H, t.t, CF$_2$H, $^2J_{HF} = 50.6$, $^3J_{HF} = 5.4$); 7.32 (1H, t, Ar); 7.48 (2H, t, Ar); 7.54 (2H, d, Ar)	(CH$_3$OH): −137.34 (2F, d, $^2J_{HF} = 50.2$); −130.48, −128.61 (2F, $^2J_{AB} = 285.9$); −122.27, −123.50 (2F, $^2J_{AB} = 300.0$); −124.39, −115.67 (2F, $^2J_{AB} = 281.1$)	(KBr): 3500, 3410, 3150, 2950, 2890, 2750, 1620, 1580, 1540, 1510, 1460, 1410, 1370, 1350, 1340, 1310, 1290, 1240, 1180, 1130, 1100, 1055, 1010, 980
4d	(C$_6$D$_6$): 1.84 (3H, s, CH$_3$); 2.36 (6H, s, 2CH$_3$); 5.12 (1H, d, CH); 5.71 (1H, t.t, CF$_2$H, $^2J_{HF} = 51.9$, $^3J_{HF} = 5.4$); 6.20 (1H, s, OH); 6.84 (1H, s, CH); 6.95 (1H, t, Ar); 7.16 (2H, t, Ar); 7.80 (2H, d, Ar)	(Toluene): −137.51 (d), −136.91 (d) (2F, $^2J_{HF} = 44.5$, $^2J_{AB} = 296.3$); −132.37, −128.53 (2F, $^2J_{AB} = 288.7$); −125.07, −113.48 (2F, $^2J_{AB} = 277.7$); −124.89, −124.43 (2F, $^2J_{AB} = 285.6$)	(KBr): 3200, 3000, 2980, 2940, 2750, 1650, 1605, 1565, 1510, 1490, 1440, 1390, 1310, 1260, 1220, 1180, 1120, 1090, 1080, 1065, 1040, 1020, 1000
4e	(CD$_3$CN): 3.54 (2H, s, NH$_2$); 5.17 (1H, s, OH); 5.96 (1H, m, CH); 6.22 (1H, d, OH); 6.43 (1H, t.t, CF$_2$H, $^2J_{HF} = 51.6$, $^3J_{HF} = 5.4$); 7.13 (1H, t, Ar); 7.38 (2H, t, Ar); 7.88 (2H, d, Ar)	(CH$_3$CN): −137.45 (2F, d, $^2J_{HF} = 51.4$); −129.57, −128.99 (2F, $^2J_{AB} = 289.3$); −126.53, −121.82 (2F, $^2J_{AB} = 276.3$); −123.07, −122.58 (2F, $^2J_{AB} = 292.9$)	(KBr): 3390, 3275, 3110, 2990, 2910, 2760, 1670, 1620, 1575, 1500, 1470, 1455, 1420, 1380, 1360, 1350, 1300, 1240, 1225, 1190, 1140, 1105, 1080, 1040, 970, 960
9b	(C$_6$D$_6$): 1.90 (3H, t, CH$_3$, $^5J_{HH} = 2.7$); 5.10 (1H, t, CF$_2$H, $^2J_{HF} = 51.0$, $^3J_{HF} = 5.7$); 6.58 (1H, t, CHCF$_2$, $^3J_{HF} = 15.9$); 6.97 (1H, t, Ar); 7.21 (2H, t, Ar); 8.11 (2H, d, Ar)	(*n*-hexane): −137.49 (2F, d, $^2J_{HF} = 51.4$); −129.57 (2F, s); −124.67 (2F, s); −105.93 (2F, s)	(KBr): 3100, 2950, 2880, 1730, 1675, 1610, 1510, 1470, 1450, 1420, 1355, 1325, 1180, 1130, 1090, 1060, 1040, 1010, 1000, 960
10	(DMSO-d$_6$): 2.27 (6H, s, 2CH$_3$); 4.31 (1H, t, CHCF$_2$, $^3J_{HF} = 19.5$); 6.96 (1H, t.t, CF$_2$H, $^2J_{HF} = 50.4$); 7.27 (2H, t, Ar); 7.47 (4H, t, Ar); 7.71 (4H, d, Ar); 14.56 (2H, w.s, 2OH)	(CH$_3$OH): −137.23 (2F, d, $^2J_{HF} = 49.7$); −129.02 (2F, s); −121.41 (2F, s); −107.59 (2F, s)	(KBr): 3100, 2940, 1610, 1590, 1510, 1470, 1420, 1380, 1290, 1180, 1130, 1050, 1030
12a	(C$_6$D$_6$): 1.20−2.45 (13H, Alk); 2.81 (1H, m, CH); 6.94 (1H, t, Ar); 7.21 (2H, t, Ar); 8.38 (2H, d, Ar)	(CHCl$_3$): −70.35 (d, $^3J_{HF} = 7.9$)	(Film): 3080, 3010, 2930, 2870, 1720, 1610, 1510, 1460,1440, 1410, 1375, 1355, 1325, 1305, 1265, 1240, 1235, 1175, 1150, 1120, 1090, 1040, 1015
12b	(C$_6$D$_6$): 1.19−2.45 (13H, Alk); 3.14 (1H, m, CH); 5.14 (1H, t.t, CF$_2$H, $^2J_{HF} = 51.3$, $^3J_{HF} = 5.1$); 6.94 (1H, t, Ar); 7.21 (2H, t, Ar); 8.39 (2H, d, Ar)	(CHCl$_3$): −139.23 (d), −137.43 (d) (2F, $^2J_{HF} = 54.2$, $^2J_{AB} = 307.6$); −131.94, −130.34 (2F, $^2J_{AB} = 289.8$), −124.19, −123.08 (2F, $^2J_{AB} = 293.8$); −118.65, −110.49 (2F, $^3J_{HA} = 11.7$, $^3J_{HB} = 25.4$, $^2J_{AB} = 276.3$)	(Film): 3080, 3010, 2940, 2880, 1720, 1605, 1510, 1460, 1440, 1410, 1375, 1360, 1325, 1300, 1280, 1180, 1140, 1080, 1050, 1020, 1005, 950
13	(C$_6$D$_6$): 1.02–2.93 (7H, Alk); 3.59 (1H, d.d, CH); 5.08 (1H, t.t, CF$_2$H, $^2J_{HF} = 51.6$, $^3J_{HF} = 5.1$); 5.75 (1H, m, CH); 6.00 (1H, m, CH); 6.94 (1H, t, Ar); 7.21 (2H, t, Ar); 8.34 (2H, d, Ar)	(C$_6$D$_6$): −136.77 (2F, d, $^2J_{HF} = 51.4$); −129.74, −129.16 (2F, $^2J_{AB} = 291.0$); −123.22, −122.74 (2F, $^2J_{AB} = 300.3$); −109.56, −104.72 (2F, $^2J_{AB} = 274.3$)	(KBr): 2980, 1720, 1605, 1510, 1420, 1370, 1310, 1290, 1180, 1135, 1050
14	(CDCl$_3$): 2.18 (3H, s, CH$_3$); 3.21 (3H, s, OCH$_3$); 4.73 (1H, d.d, CHCF$_2$); 6.05 (1H, t.t, CF$_2$H, $^2J_{HF} = 51.9$, $^3J_{HF} = 5.4$); 7.15 (1H, t, Ar); 7.24 (2H, t, Ar); 7.48 (2H, d, Ar)	(CDCl$_3$): −138.69 (2F, d, $^2J_{HF} = 54.7$); −132.77, −131.23 (2F, $^2J_{AB} = 287.8$); −126.23, −125.02 (2F, $^2J_{AB} = 295.2$); −125.30, −117.77 (2F, $^2J_{AB} = 285.6$)	(KBr): 3100, 3050, 1630, 1580, 1510, 1470, 1420, 1370, 1315, 1285, 1235, 1180, 1140, 1070, 1045, 985, 955

[a] ^{13}C NMR, δ (ppm), J (Hz).

*3.3. Synthesis of 1-phenyl-3-methyl-4-(2,2,3,3,4,4,5,5-octafluoropentylidene)pyrazole-5-one (**9b**)*

Morpholinosulfur trifluoride [13] (7.2 mmol) was added to a stirred suspension of pyrazole (**4b**) (6 mmol) in dichloromethane (30 ml) at 0°C. The obtained red solution was stirred at 0°C for 30 min and then heated up to 20°C. The solution was filtered from an insignificant amount of residue after 6 h, washed with 3 × 50 ml of water and dried over Na_2SO_4. The solvent was removed in vacuo (20 torr) and the oily residue was treated with *n*-hexane (20 ml). The red solution was filtered from insoluble residue and *n*-hexane was removed in vacuo (20 torr). Compound (**9b**) crystallizes on storage at 20°C over 24 h.

*3.4. Synthesis of spiro[(1-phenyl-3-methylpyrazole-5-one)-4,5′-(1′,2′-dimethyl-4′-trifluoromethyl-cyclohexene)] (**12a**), spiro[(1-phenyl-3-methyl-pyrazole-5-one)-4,5′-(1′,2′-dimethyl-4′-(1,1,2,2,3,3,4,4-octafluorobutyl)cyclohexene)] (**12b**), spiro-[(1-phenyl-3-methylpyrazole-5-one)-4,5′-(6′-(1,1,2,2,3,3,4,4-octafluorobutyl)bicyclo[2.2.1]hept-2-ene)] (**13**)*

1. Diene (Aldrich) (1.26 mmol) was added to the solution of equimolar amounts of 1-phenyl-3-methyl-4-(2,2,3,3,4,4,5,5-octafluoropentylidene)pyrazole-5-one (**9b**) in chloroform (8 ml). The solvent was removed in vacuo (20 torr) over 24 h. The oily residue was purified by column chromatography (see Section 3).
2. Morpholinosulfur trifluoride (7.38 mmol) was added to a stirred suspension of pyrazole (**4a**) (5.68 mmol) in chloroform (20 ml) at 0°C. The obtained red solution was stirred at 0°C for 30 min and then heated to 20°C. The mixture was stirred at 20°C for 20 min and then 2,3-dimethylbutadiene (Aldrich) (8.52 mmol) was added. The solution was filtered from an insignificant amount of residue after 4 h, washed with 3 × 50 ml of water and dried over Na_2SO_4. The solvent was removed in vacuo (20 torr) and the oily residue was purified by column chromatography (see Section 3).

*3.5. Synthesis of 1-phenyl-3-methyl-4-(1-methoxy-2,2,3,3,4,4,5,5-octafluoropentyl)-5-hydroxypyrazole (**14**)*

1-Phenyl-3-methyl-4-(2,2,3,3,4,4,5,5-octafluoropentylidene)pyrazole-5-one (1.34 mmol) was dissolved in methanol (15 ml). The solvent was removed in vacuo (20 torr) for 6 h and the oily residue was purified by column chromatography (see Section 3).

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