Milata Viktor (Orcid ID: 0000-0001-8986-1752)

Mass spectrometrical and quantum-chemical study of pentafluorophenylhydrazones.

Dušan Bortňák[a], Daniel Pecher[d], Daniel Végh[a], Martin Breza[b], Peter Mikuš[c], Viktor Milata[a]

[a]Department of Organic Chemistry; [b]Department of Physical Chemistry, Faculty of Chemical and Food Technology, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovakia

[c]Department of Pharmaceutical Analysis and Nuclear Pharmacy, Faculty of Pharmacy, Comenius University in Bratislava, Odbojárov 10, SK-832 32 Bratislava, Slovakia

[d]Toxicological and Antidoping Center, Faculty of Pharmacy, Comenius University in Bratislava, Odbojárov 10, SK-832 32 Bratislava, Slovakia

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ABSTRACT

Twenty-one pentafluorphenylhydrazones have been analyzed by means of tandem mass spectrometry (ESI MS/MS) conditions to compare their fragmentations with those ones obtained from quantum-chemical calculations of the hydrazone moiety depending on the substitution from the aldehyde site. The hydrazone N – N bond of is disrupted under such conditions and therefore these results are in accordance with the facts that an electron rich particle, such as an anion and or radical in a solution, can cause this disruption and simultaneous defluorination in para-position of the hydrazone part of the molecule.

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1 INTRODUCTION

Hydrazones are very useful intermediates in organic synthesis [1] for their possible broad application[2]. In continuation of our previous work (synthetic exploitation of pentafluorophenylhydrazine), where we demonstrated its different reactivity in comparison to phenylhydrazine with 3-oxo-2-ethoxymethylenebutanenitrile [3] or its reactions with various β,β-activated enolethers [4] or in Clauson-Kaas Reaction [5], we decided to study nucleophilic substitution of the azide anion with various pentafluorophenylhydrazones **1** listed in Table 1 (Fig. 1):

Poly/perfluorinated aromatics are very frequently used substrates for numerous nucleophiles like azides ([5-8], nitromethane [9-11], cyanide anion ([12], or other nucleophiles [13]. They are employed as a principal step in the building of selective substituted (hetero)aromatics. We have prepared a set of pentafluorophenylhydrazones and started to study the planned reaction with the azide anion. Because preliminary results were very repugnant, we decided to extend the set of the studied compounds to twenty-one derivatives. Our set included the sterically hindered alkyl-substituted derivative **1u**, variously substituted phenylderivatives with electron-withdrawing (**1i**, **1j**), activated (**1a**, **1b**) or strongly activated (**1c**-**1h**) derivatives and electron-rich five-membered heterocycles with diene (furane derivatives **1r**-**1t**) with less (**1k**) or more aromatic character (thiophene derivatives **1l** – **1q**) bearing different substituents in positions 5-, but also 4- (**1q**, **1m**) and finally bithiophene derivatives **1n**, **1p** where we have prepared also the corresponding hydrazone from the deuterated aldehyde **1o** for special study.

2 MATERIALS AND METHODS

All NMR spectra were obtained using an INOVA NMR 300 MHz spectrometer (operating frequencies of 300 MHz (^{1}H), 75 MHz (^{13}C) and 282 MHz (^{19}F)) equipped by an inverse triple resonance probe and a standard tuneable X/H probe with the possibility to tune the high frequency channel to the resonance frequency of ^{19}F. Tetramethylsilane was used for the calculation of the ^{1}H and ^{13}C chemical shift scales and correctly referenced using the (residual) solvent signals (2.50 and 39.52 ppm for DMSO, 7.26 and 77.00 ppm for chloroform). $CFCl_3$ was used for the calculation of the ^{19}F chemical shift scale; in order to correctly reference the ^{19}F chemical shift scale an automatic referencing mechanism exploiting the ^{2}H signal of the deuterated solvent was used.

2.1 Synthesis

The synthesis of the pentafluorophenylhydrazones **1**, published previously in ref. [17], was properly modified (Scheme 1). The synthesis is based on the condensation of the ethanolic solution of pentafluorophenylhydrazine with an ethanolic solution of appropriate aldehyde and with a catalytic amount of hydrochloric acid according to the following scheme:

Particular products were sufficiently pure for the synthesis, but before the mass spectra analysis the samples were purified by recrystallisation or column chromatography (the yield of **1r** is low due to its lower stability in acidic media while other furane derivatives have stabilizing substituents; the given result is obtained after chromatography). Majority of used aldehydes were obtained from Merck / Sigma-Aldrich® and pentafluorophenylhydrazine has been obtained from Flurochem®. New

compounds are presented with their physico-chemical properties, for known compounds only unpublished characteristics are presented (Table 2).

General procedure for the preparation of pentafluorophenylhydrazones **1**

To the solution of the corresponding aldehyde in ethanol we have added the ethanolic solution of the pentafluorophenylhydrazine according to the amounts given in Table 2. To this mixture a catalytic amount of concentrated hydrochloric acid was added (approximately 3-5 drops). The reaction mixture has been refluxed for 8 hours (under TLC + UV control). The solvent was evaporated under reduced pressure and the residue has been crystallized from ethanol to obtain the pentafluorophenylhydrazone **1.**

1-Benzylidene-2-(perfluorophenyl)hydrazine (1a)

White crystalline matter.

1-(2-methylbenzylidene)-2-(perfluorophenyl)hydrazine (1b)

White crystalline matter. ^{1}H NMR (300 MHz, dmso) δ 10.27 (s, 1H), 8.41 (s, 1H), 7.68 (m, 1H), 7.22 (m, 3H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, dmso) δ 141.3, 137.8 (d,tt, *J*= 244, 14, 5 Hz) 137.1 (dm, *J*= 244H) 135.7, 133.5 (dtt *J*=242, 20, 5 Hz) 132.6, 130.8, 128.6, 126.0, 125.4, 121 (t *J*=11Hz) 19.2.

1-((4-bromo-5-methylthiophen-2-yl)methylene)-2-(perfluorophenyl)hydrazine (1m)

Brown crystalline matter. ^{1}H NMR (300 MHz, dmso) δ 10.37 (s, 1H), 8.17 (s, 1H), 7.23 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, dmso) δ 137.7 (dm *J*=245 Hz), 137.3 (dm *J*=246 Hz) 137.2, 136.0, 135.0, 133,9 (dm *J*= 247Hz) 129.9, 120.8 (m) 108.7, 14.6.

(E)-1-((5-nitrofuran-2-yl)methylene)-2-(perfluorophenyl)hydrazine (1s)

Orange crystalline matter. ^{1}H NMR (300 MHz, dmso) δ 10.95 (s, 1H), 8.03 (s, 1H), 7.75 (d, *J* = 3.9 Hz, 1H), 7.03 (d, *J* = 4.0 Hz, 1H). ^{13}C NMR (75 MHz, dmso) δ 152.7, 151.3, 138.2 (dm *J*= 245 Hz) 137.7 (dm *J*=247 Hz) 135,1 (dm *J*= 245 Hz) 129.4, 119,8 (m) 115.2, 112.5.

2.2 LC-Q-TOF MS/MS conditions

Liquid chromatography high-resolution tandem mass spectrometry (LC-MS/MS) analyses were performed on an LC Agilent Infinity System (Agilent Technologies, Santa Clara, CA, USA) equipped with a gradient pump (1260 Bin Pump VL), an automatic injector (1260 HiPals), and a column thermostat (1290 TCC). The LC was performed using the Zorbax Extend-C18 column, 2.1x50 mm, 1.7µm (Agilent Technologies, Santa Clara, CA, USA) column with a mixture of acetonitrile and 0.1% aqueous solution of formic acid as mobile phases. Gradient elution was used with the linear gradient from 5 to 95% of acetonitrile in 10 minutes. The flow rate was of 400 µL/min.
The LC system was coupled with a quadrupole time-of-flight mass spectrometer (6520 Accurate Mass Q-TOF LC/MS - Agilent Technologies, Santa Clara, CA, USA) which was equipped with an electrospray ionization source operated in positive ionization mode. All measurements were performed with the following MS parameters: drying gas temperature 360°C, drying gas flow 12 L.min^{-1}, nebulizing gas pressure 60 psi, ESI source voltage 3500 V, fragmentor voltage 100 V, skimmer voltage 65 V, collision gas N_2. The system was calibrated before analysis to an external standard and internal calibration during the analysis using a reference solution was used as well. The data were scanned

over the mass range *m/z* = 50 - 1000. MS/MS fragmentation was done applying collision energy of 10, 20, and 40 eV, respectively.
All compounds were dissolved in the acetonitrile-water mixture (1:1, V/V) resulting in solutions with concentrations of 1 mg/mL, which were used for the LC-MS/MS analysis (injection volume 1.0 µL). The obtained *m/z* of $[M+H]^+$ adducts of the analyzed compounds were compared to the theoretical *m/z* values of these adducts calculated by MassHunter software and the mass deviations in ppm were calculated $[(m/z_{theor.}-m/z_{obtained})/m/z_{theor.} \times 10^6]$. All mass deviations were lower than 5 ppm. The fragmentation spectra of each compound obtained by applying all of the above-mentioned collision energies were also recorded, and the tentative molecular formulas were calculated for the most abundant fragments (MassHunter Workstation Software Version B.06.00).

2.3 Computational methods

Geometries of the neutral compounds A under study and of their AH^+ cations protonated at heteroatom sites in their singlet ground states were optimized at the DFT level of theory using the B3LYP hybrid functional [21]. Dunning's correlation consistent cc-pVDZ basis sets were used for all atoms [22]. Stability of the optimized structures was tested by vibrational analysis (no imaginary vibrations). All calculations were performed using Gaussian16 software [23]. MOLDRAW software was used for geometry manipulation and visualisation purposes. [24]. If the conformational changes due to protonation cause sufficient bond elongation, these bonds are weakened and hence are more likely to cleave. [25]. Therefore the bond elongation after protonation

$$\Delta d = d(AH^+) - d(A) \quad (1)$$

where A and AH^+ are the neutral molecule and its protonated cation, respectively, seem to be a good prediction parameter for MS fragmentation. However, quantum chemistry alone cannot predict the collision energies appropriate for fragmentation[26].

3 RESULTS AND DISSCUSION

In this structure-fragmentation correlation study, we have used mass spectrometry for both confirming molecular mass and elemental composition of investigated ions (due to complications with elemental analysis of fluorinated compounds), as well as for the study of the title compounds in deep vacuum. Mass spectrometry can be a versatile tool for study of energies of the bonds in the molecule under deep vacuum conditions, e.g. without any stabilizing influences like solvatation, dipole-dipole interaction etc., and, of course, without the influence of any anion/nucleophile. [27] From this point of view, we can consider the influence of the strong electron-withdrawing effect of the pentafluorophenyl nucleus onto -NH-N=CH- fragment substituted from the opposite side with alkyl, aryl, electron-rich five-membered heteroaryl nuclei bearing various substituents in different positions. Such hydrazones **1** were prepared from logical components, but their chemical reaction with azide or cyanide anion, respectively gave surprisingly unexpected products, 2,3,5,6-tetrafluorophenylaniline and corresponding nitrile [17]. Thus, breaking of the NH-N= is the crucial moment to study the behaviour of the title molecules. For this reason we have used tandem mass spectrometry technique applied to the molecular ion: even though we have recorded fragmentations of this molecular ion applying multiple collision energies, for comparison we

considered only the lowest one, e.g. 10 eV to gently influence studied molecules and thus finding the softest bond(s) in the molecule. A representative MS/MS spectrum (collision energy of 10 eV) of one of the studied compounds is presented in Fig. 2. Abundancies of the individual fragments obtained by MS/MS analysis are summarized in the Table 3. The relative abundancies were calculated as the ratio of absolute abundance of the fragment and the sum of abundancies of all observed masses with abundance >1.00% of the most abundant mass). (Fig. 2):

Fig. 2: ESI MS/MS spectrum of **1r**

Strong electron-withdrawing effect of the penta/tetrafluorophenyl substituent is causing polarization of N-N bond. The nitrogen of this bond, which is bounded by the stronger double bond with the carbon atom is in conjugation with (hetero)aromatic nucleus. Therefore, the fragmentation of most of the derivatives **1** results in Ar-CH(D)N ion and ion C_6F_5NH with m/z 182,0026 (path B, Scheme 2):

At the same time a parallel fragmentation (Table 3) based on the dehydrofluorination (path A) or double dehydrofluorination (path AA) of the protonated species during ionization occurs. This scheme is applied for unsubstituted phenyl derivative **1a** and slightly activated (2-methylphenyl) derivatives **1b**. Other mesomerically strongly activated arylderivatives (**1c**-**1h**) have common feature that ion m/z 182 is observed only in low abundancies and only one dehydrofluorination occurrs – path A (with the exception of 2,4-dihydroxyderivative **1e** displaying follow-up dehydrocyanation of the ion m/z 182 and the presence of path AA). For **1d**, **1h** the ion M – 182 (Ar-CH(D)=N) undergoes dehydrocyanation less (**1d**) or more (**1h**) intensively. In the trimethoxyderivative **1g** the demethylation of the M – 182 ion m/z 180 and following demethoxylation to ion m/z 149 (relative abundance 2.57%) is present.

Deactivated arylderivatives (**1i**, **1j**) produce the ion m/z 182 with parallel (dehydro)fluorination and following denitration (m/z 266; relative abundance 6.96 %) or demethoxycarbonylation (m/z 267; relative abundance 7.91 %).

Arylsubstituted pentafluorophenylhydrazones were supplemented with electron-rich five-membered heterocycles with various substituents (**1k**-**1t**). 1-Methylpyrrol-2-yl derivative **1k** does not produced the ion m/z 182, but M – 182 = 108 is sufficiently intensive (relative abundance 32.13 %). Besides the path A the dehydrocyanation of the parent ion (m/z 263; relative abundance 15.73 %) parallelly occurs. Thiophene derivative **1l** fragments through both path A and B, while its 5-methyl-4-bromo analogue **1m** does not displayed ion m/z 182. Dithiophene derivatives **1n** – **1p** display only the ion M – 182. In the case of deuterated analogue **1o** the fragmentation confirms the fact that no deuterium is migrated between the fragments. The 5-Nitrothienyl derivative **1q** behaves differently: besides the fragmentation path B, the typical fragmentation for the nitrocompounds, e.g. M – 16 (deoxygenation; relative abundance 7.01 %), followed by (M – 16) – 30 (removal NO; relative abundance) and final defluorination to the ion m/z 272 (relative abundance 1.54 %) occurs parallelly. Interesting is also the third fragmentation path to m/z 272 (relative abundance 3.47 %) which represents the elimination of H_2ONS fragment from the molecular ion. Unlike the aromatic

thiophene derivatives, the furane ones have higher diene character. The parent furane derivative **1r** displays paths B, A and AA with following decarbonylation or denitrogenation of ions m/z 257 (path A) or 237 (path AA), respectively. The 5-Nitrofurane derivative **1s** undergoes path B and also produces the ion m/z 247 (after the release of O_2N-CH=O fragment similar to thiophene; relative abundance 10.73 %). This ion is defluorinated or should eliminate C_4H_3N to m/z 182 by the path parallel to the path B. The 5-(4-Bromophenyl)furane derivative **1t** undergoes fragmentation similar to activating arylderivatives and does not produce the ion m/z 182, but produces an ion M – 182 = 251. Alternatively, it undergoes decyanation (m/z 405; relative abundance 2.12 %) followed by debromination to the ion m/z 325 (relative abundance 0.46 %).

The aromatic nucleus from aldehyde part of the title pentafluorophenylhydrazones derivatives **1a-1t** produces the Ar-CH(D)N ion and the C_6F_5NH ion with m/z 182,0026 (path B). This is supported by the fact that non-aromatic aldehyde derivative of 2,2-dimethylpropanal **1u** produces the ion with m/z 197 ($C_6H_2F_5N_2$; relative abundance 11.97 %) which gives the ion m/z 182 after elimination of NH. In this case, also an elimination of HCN is occurring with the resulting ion m/z 155 (C_5F_5; relative abundance 0.42 %). Path A displays no ion, but path AA gives the ion m/z 227.

Studied aromatic and heteroaromatic derivatives of pentafluorophenylhydrazones **1** present one principal fragmentation occurring after breaking the N – N bond of the hydrazone bridge, which is not typical for aliphatic analogues. This fact confirms our experimental results of the reaction of the title pentafluorophenylhydrazones with anions which give us similar products and also parallel nucleophilic substitution of the fluorine atom in position 4 [17].

To confirm the presence of fluorine atoms in the molecules we also measured ^{19}F NMR spectra and performed HRMS instead of elemental analysis. Because some compounds prepared previously by us have not been yet published with ^{19}F NMR spectra, they are displayed in Table 4.

3.2 Quantum chemical calculations-fragmentation correlation

The protonation at F atoms in meta- and para- positions leads usually to C-F bond breaking and a simple HF removal. This is connected with up to 0.05 Å changes in bridge bonds. Protonated F atoms in ortho- positions can be moreover replaced by H atoms and for the realated HF splitting is taken the H atom from the -NH- bridge site. The protonation of other heteroatoms is connected with lower bridge bonds changes than of the F atoms. Nitro group N atoms are not protonated and the H atom is shifted to the neighboring aromatic C atoms. Analogously for the Br atom in **1m** the proton is shifted to the bridge –N= site.

The greatest N-N bond elongation is connected with the protonation at the bridge –NH- site (Table 5) whereas the neighboring –N= site protonation has much lower bond-length consequences (Table 6). Our results indicate that the N-N bond splitting is more probable than of the neigboring N_H-C_{PhF} bond to the fluorinated benzene ring (maybe except **1g**). An alternative C(H)-N bridge bond break is even much less probable and breaking the C(H) bond to an aromatic carbon atom of the R substituent is highly improbable.

4 CONCLUSIONS

Twenty-one pentafluorophenylhydrazones have been prepared to study their reaction with the azide anion which provided an unexpected decay to nitrile and 2,3,5,6-tetrafluoroaniline. Therefore, we studied energies and bond dissociation of these molecules in the gaseous phase under strong dilution (ESI MS/MS). We have found that the N – N bond of the hydrazone is disrupted under such conditions (fragment C_6F_5NH = 182.0026 and corresponding (protonated) nitrile = M – 182.0026 are produced). These results are in accordance with the facts that electron-rich particles, such as an anion or a radical in a solution, can cause this disruption and simultaneous mono/double de(hydro)fluorination in para-position of the hydrazone residuum of the molecule.

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ORCID

Viktor Milata 0000-0001-8986-1752

Martin Breza 0000-009-5995-0279

Daniel Pecher 0000-0002-9284-1493

Dušan Bortňák 0000-0003-4140-9163

Daniel Végh 0000-0003-3945-7107

Peter Mikuš 0000-0001-5755-9970

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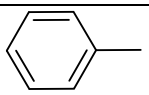
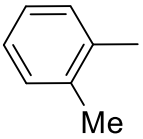
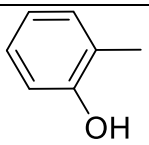
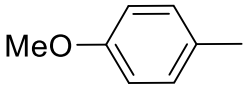
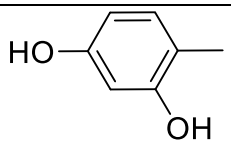
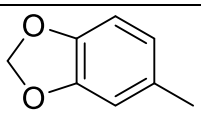
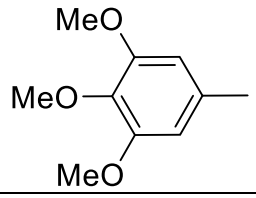
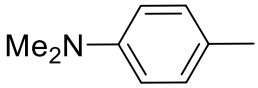
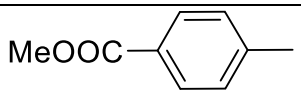
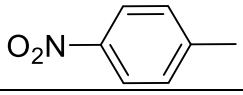
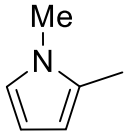
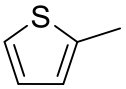
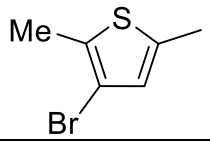
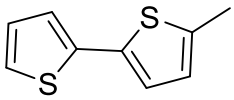
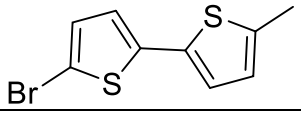
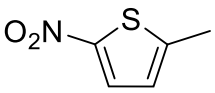
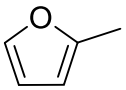
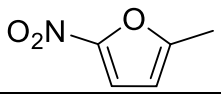
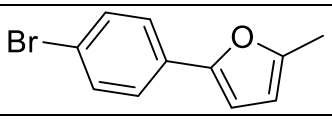
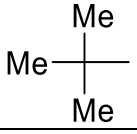
[27] F. Tureček, "The Basics of Gas-Phase Ion Chemistry ," *Chem. Listy*, vol. 114, no. 2, pp. 89–95, 2020.

Table 1: List of prepared and studied compounds

Entry	Substituent R		Ref.
1a	phenyl		[14]
1b	2-methylphenyl		
1c	2-hydroxyphenyl		[15]
1d	4-methoxyphenyl		[16]
1e	2,4-dihydroxyphenyl		[17] [16]
1f	benzo[d][1,3]dioxol-5-yl		[17]

1g	3,4,5-trimethoxyphenyl		[16]
1h	4-(*N*,*N*-dimethylamino)phenyl		[17]
1i	4-(methoxycarbonyl)phenyl		[17]
1j	4-nitrophenyl		[16]
1k	1-methylpyrrol-2-yl		[18]
1l	thiophene-2-yl		[19]
1m	4-bromo-5-methylthiophene-2-yl		
1n	2,2´-bithiophene-5-yl		[19]
1o	2,2´-bithiophene-5-yl	* like above	[17]
1p	5´-bromo-2,2´-bithiophene-5-yl		[17]
1q	5-nitrothiophene-2-yl		[17]
1r	fur-2-yl		[20]
1s	5-nitrofuran-2-yl		
1t	5-(4-bromophenyl)furan-2-yl		[17]
1u	tert-butyl		[17]

* appropriate deuterated aldehyde has been used

Table 2: Reaction conditions of the pentafluorophenylhydrazine with the corresponding aldehyde

Compd.	$C_6F_5NHNH_2$ (g/mmol/ml of EtOH)	Adehyde (g/mmol/ml of EtOH)	Yield (%)	Note
a	1.866/9.42/20	1.000/9.42/5	42	**a**
b	1.649/8.32/20	1.000/8.32/5	72	**a**
c	1.622/8.19/20	1.000/8.19/5	92	**a**
d	1.455/7.34/20	1.000/7.34/5	40	a
e	1.434/7.24/20	1.000/7.24/30	35	a
f	1.319/6.66/15	1.000/6.66/45	74	a
g	1.010/5.10/10	1.000/5.10/20	89	a
h	1.328/6.70/15	1.000/6.70/35	81	a
i	1.207/6.09/15	1.000/6.09/25	98	a
j	1.311/6.62/15	1.000/6.62/20	71	a
k	1.815/9.17/20	1.000/9.17/5	27	b
l	1.766/8.91/20	1.000/8.91/5	64	a
m	0.966/4.88/10	1.000/4.88/20	60	a
n	1.020/5.15/10	1.000/5.15/20	88	a
o	0.202/1.0/5	0.200/1.0/5	91	a
p	0.725/3.66/10	1.000/3.66/20	73	a
q	1.260/6.36/15	1.000/6.36/15	85	a
r	2.062/10.41/20	1.000/10.41/5	8	b
s	1.404/7.09/15	1.000/7.09/15	63	a
t	0.789/3.98/10	1.000/3.98/20	quant.	a
u	0.500/2.52	0.197/2.29	quant.	c

a – crystallized from ethanol, b – chromatographed (silicagel 60 μm/toluene), c – use of $BF_3.Et_2O$

Table 3: Reaction conditions of the pentafluorophenylhydrazine with corresponding aldehyde

Compound	Parent ion		Path B				Path A		Path AA	
	$[M + H]^+$		Ar - CH(D)N		C_6F_5NH		M - HF		M - 2H2F	
	Abund.	Rel. abund. (%)	Abund.	Rel. abund. (%)	Abund.	Rel. abund. (%)	Abund.	Rel. abund. (%)	Abund.	Rel. abund. (%)
1a	20833.06	*38.74*	5900.51	*10.97*	5806.4	*10.80*	15404.27	*28.65*	1807.99	*3.36*
1b	51635.26	*39.78*	18821.76	*14.50*	8127.54	*6.26*	29787.80	*22.95*	3259.04	*2.51*
1c	12843.76	*42.20*	4161.70	*13.67*	635.31	*2.09*	4060.58	*13.34*	124.17	*<1.00*
1d	87434.15	*46.83*	47257.29	*25.31*	1613.35	*<1.00*	12518.16	*6.70*	1256.99	*<1.00*
1e	342298.83	*46.07*	319676.31	*43.03*	2170.82	*<1.00*	32142.01	*4.33*	2508.32	*<1.00*
1f	26053.20	*34.67*	41399.39	*55.09*	298.98	*<1.00*	1766.25	*2.35*	183.78	*<1.00*
1g	4438.53	*19.91*	15339.22	*68.81*	-	-	35.34	*<1.00*	-	-
1h	118604	*48.57*	78782.41	*32.26*	-	-	472.66	*<1.00*	-	-
1i	73120.42	*43.61*	10276.04	*6.13*	19689.77	*11.74*	25255.53	*15.06*	1600.34	*<1.00*
1j	624.26	*30.90*	23.69	*1.17*	924.87	*45.79*	138.41	*6.85*	-	-
1k	23685.28	*33.02*	23048.71	*32.13*	-	-	1174.82	*1.64*	299.14	*<1.00*
1l	43715.87	*39.40*	12732.14	*11.47*	10763.67	*9.70*	30654.95	*27.63*	3503.35	*3.16*
1m	33104.12	*59.05*	5690.99	*10.15*	1477.27	*2.64*	3616.37	*6.45*	238.54	*<1.00*
1n	5102.1	*21.80*	12540.21	*53.58*	-	-	-	-	-	-
1o	29229	*27.48*	76064.96	*71.52*	-	-	-	-	-	-
1p	15776.78	*16.77*	72453.63	*77.00*	-	-	-	-	-	-
1q	3194.46	*29.46*	130.21	*1.20*	4718.92	*43.51*	559.41	*5.16*	-	-
1r	66408.09	*38.37*	23735.24	*13.71*	17662.57	*10.20*	29901.7	*17.28*	2324.50	*1.34*
1s	409.88	*20.40*	17.85	*<1.00*	948.61	*47.22*	39.63	*1.97*	-	-
1t	22088.22	*34.50*	29777.69	*46.51*	2052.96	*3.21*	875.35	*<1.00*	-	-

1u	131484.93	*34.34*	53404.20	*13.95*	36698.1	*9.58*	15670.14	*4.09*	7697.99	*2.01*

Table 4. ^{19}F NMR spectra of selected compounds 1

Compound	δ (^{19}F NMR)	Compound	δ (^{19}F NMR)
1b	-156.20 (d, *J* = 24.9 Hz, 2F), -164.47 (td, *J* = 23.9, 4.0 Hz, 2F), -170.75 (tt, *J* = 23.3, 6.0 Hz, 1F)	**1j**	-155.23 (m, 2F), -164.04 (td, *J* = 22.3, 3.3 Hz, 2F), -168.55 (tt, *J* = 23.3, 4.9 Hz, 1F)
1c	-156,84 (m, 2F), -164.16 (m, 2F), -170.50 (tt, *J* = 23.3, 5.9 Hz, 1F)	**1m**	-155.75 (m, 2F), -164.33 (m, 2F), -169.73 (m, 1F).
1d	δ -156.00 (dd, *J* = 19.9, 4.6 Hz,2F), -164.53 (td, *J* = 23.2, 4.1 Hz, 2F), -170.81 (tt, *J* = 23.3, 6.1 Hz, 1F)	**1r**	-155.48 (dd, *J* = 19.0, 4.0 Hz, 2F), -164.36 (td, *J* = 21.8, 2.8 Hz, 2F), -169.68 (tt, *J* = 23.3, 5.6 Hz 1F)
1g	-155.61 (m, 2F), -164.32 (m, 2F), -170.05 (m, 1F)	**1s**	-154.48 (d, *J* = 23.4 Hz, 2F), -163.80 (td, *J* = 22.5, 3.7 Hz, 2F), -167.08 (t, *J* = 23.1 Hz, 1F)

Table 5. Relevant bond-length changes, Δd [Å] (Eq. (1)), for the protonation at the bridge –NH- site

Entry	C_R-C_H	C_H-N	N-N_H	N_H-C_{PhF}
1a	-0.015	0.007	0.131	0.076
1b	-0.016	0.009	0.132	0.077
1c	-0.025	0.016	0.109	0.075
1d	-0.032	0.022	0.064	0.055
1f	-0.023	0.013	0.126	0.079
1g	-0.027	0.015	0.126	0.128
1h	-0.030	0.020	0.120	0.082
1j	-0.006	0.002	0.139	0.073
1l	-0.021	0.011	0.128	0.078
1m	-0.021	0.012	0.133	0.075
1q	-0.011	0.004	0.138	0.073
1s	-0.012	0.004	0.138	0.073

Table 6. Relevant bond-length changes, Δd [Å] (Eq. (1)), for the protonation at the bridge –N= site

Entry	C_R-C_H	C_H-N	N-N_H	N_H-C_{PhF}
1a	-0.027	0.019	0.038	0.037
1b	-0.028	0.019	0.038	0.040
1c	-0.021	0.015	0.024	0.033
1d	-0.062	0.044	0.012	0.022
1f	-0.038	0.026	0.044	0.041
1g	-0.045	0.030	0.048	0.091
1h	-0.050	0.036	0.047	0.044
1j	-0.020	0.016	0.037	0.032
1l	-0.035	0.023	0.041	0.039
1m	-0.033	0.023	0.042	0.038
1q	-0.025	0.018	0.041	0.031
1s	-0.024	0.018	0.040	0.030

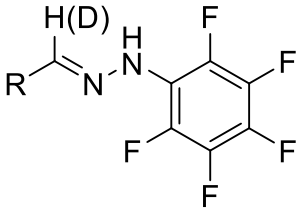


Fig. 1: Title pentafluorophenylhydrazones **1**

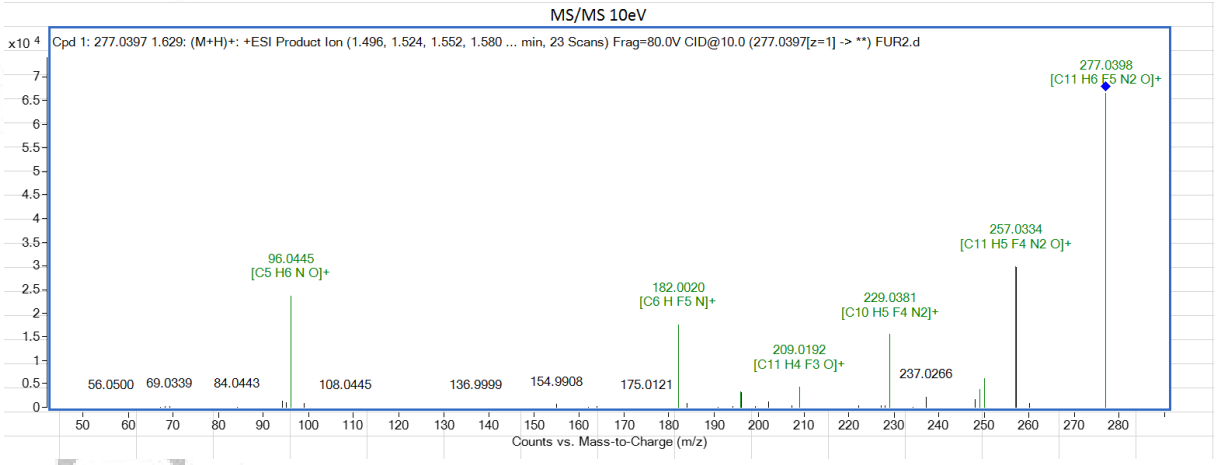
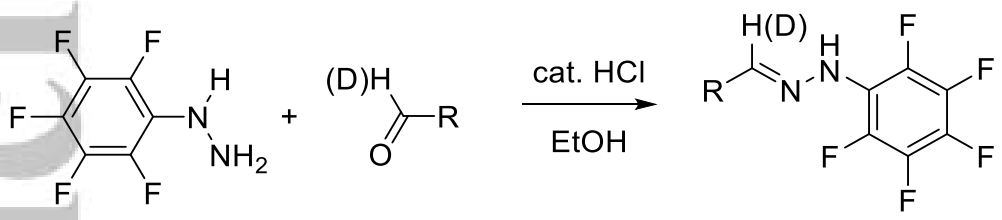


Fig. 2: ESI MS/MS spectrum of **1r**

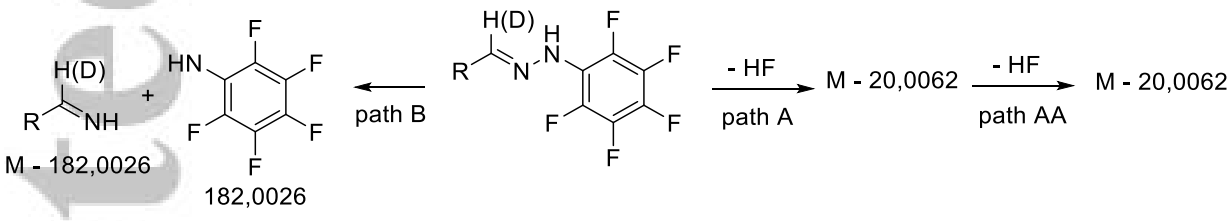
Scheme 1



1

Scheme 1: Preparation of the pentafluorophenylhydrazones **1**

Scheme 2



1

Scheme 2: Fragmentation scheme of pentafluorophenylhydrazones **1**