The structure of 3,5-bis(trifluoromethyl)pyrazole in the gas phase and in the solid state†

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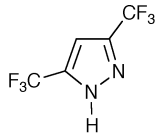
The X-ray molecular structure of the important molecule 3,5-bis(trifluoromethyl)pyrazole has been determined at 120 K and gave crystals belonging to the triclinic $P\bar{1}$ space group. The compound forms tetramers through N–H···N hydrogen bonds and some proton disorder is necessary to explain the geometric features of the monomers. The IR spectra have been recorded in the gas phase (monomers) and in the solid state (tetramers) and analyzed by comparison with the calculated normal frequencies. The use of solid-state NMR spectroscopy combined with *ab initio* GIAO calculations suggests that a certain amount (about 40 ± 10%) of dynamic disorder involving intramolecular proton transfers could be present in the crystal.

We have been interested for several years in the modification of the properties of azoles produced by trifluoromethyl substituents. Thus, we have described the effect of the replacement of a methyl by a trifluoromethyl group on the acid-base properties of pyrazoles.[1] In that work, we discussed, among other pyrazoles, the case of 3,5-bis(trifluoromethyl)pyrazole **1** and reported STO-3G calculations on this compound. The same level of calculations was employed to discuss the flash vacuum pyrolytic behavior of **1**.[2] Its gas-phase structure was determined by electron diffraction (ED) and compared with the STO-3G calculated geometry.[3] The related case of 3,5-bis-(trifluoromethyl)-1,2,4-triazole **2** was published subsequently (thermodynamic properties and MP2/6-31G* calculations).[4] Finally, a review was devoted to trifluoromethylazoles, including **1** and **2**.[5] The recent discovery that Celecoxib, a trifluoromethylpyrazole derivative, is a powerful antirheumatic and antiarthritic drug, makes these compounds even more interesting.[6]

Although compound **1** was used as a ligand as early as 1983–86,[7–10] its great development in organometallic and coordination chemistry started in 1995 and was essentially due to Dias *et al.*[11–19] Other authors like Togni,[20,21] Venanzi,[22] Lalor,[23] Zanello,[24] and Storr[25] and their groups have contributed to this field.



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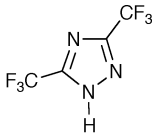

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† *Supplementary material available*: table of calculated and experimental IR frequencies. Conformations of the different monomers. Table of X-ray geometries of different pyrazole derivatives. For direct electronic access see http://www.rsc.org/suppdata/nj/1999/1231/, otherwise available from BLDSC (No. SUP 57664, 8 pp.) or the RSC Library. See Instructions for Authors, 1999, Issue 1 (http://www.rsc.org/njc).

Compound **1** is extraordinarily volatile and previous attempts to determine its X-ray structure at room temperature failed because the crystal evaporates in the chamber upon irradiation.[1] On the other hand, this same volatility facilitated the determination of its gas-phase geometry by electron diffraction (ED).[3] Nevertheless, the knowledge of its solid-state structure remained both a challenge and an interesting problem in relation with the hydrogen-bonded (HB) network of NH-pyrazoles and the possibility to observe proton transfer in the solid state (SSPT). *N*-Unsubstituted pyrazoles form a great variety of supramolecular complexes through N–H···N hydrogen bonds like dimers, trimers, tetramers and catemers, with only the cyclic structures being able to sustain SSPT.[26–29] We report here that the X-ray crystal structure of **1** has been successfully determined at low temperature (120 K). The experimental data, including gas-phase and solid-state IR spectra, are discussed in the light of calculations carried out at the HF/ and DFT B3LYP/6-31G* levels.

Experimental

Calculations

The geometry of 3,5-bis(trifluoromethyl)pyrazole **1** has been fully optimized with the 6-31G* basis set[30] at the HF level of theory and also with a DFT method, B3LYP,[31,32] using the Gaussian 94 package.[33] The minimum nature of the structure obtained has been established by verification of the corresponding frequencies, which are all real. The calculated IR spectrum has been scaled by 0.8929 as recommended in the literature for this level of calculation.[34]

Spectroscopy

IR spectra were recorded on a Perkin–Elmer 983 spectrophotometer. Solid-state spectra were obtained as KBr pellets. A glass cell (10 cm path) equipped with NaCl windows was used to record gas phase spectra: crystalline **1** (a few mg) was

placed in the cell under vacuum and gently heated prior to recording the spectra.

All NMR spectra were recorded at room temperature on a Bruker MSL 300 spectrometer (7.05 Tesla, 300.13 MHz for ^{1}H, 282.40 MHz for ^{19}F, 75.47 MHz for ^{13}C and 30.41 MHz for ^{15}N, 6 mm Chemagnetics CPMAS probe). The chemical shifts of the ^{1}H and ^{13}C spectra are referenced to external solid TSP [sodium 3-(trimethylsilyl)tetradeuteropropionate]. The ^{19}F spectrum is referenced to external CCl_3F. The ^{1}H MAS NMR spectrum was recorded with a standard pulse sequence: 6 μs 90° pulse width, 30 s recycle delay, 125 000 Hz (416.486 ppm) spectral width, 32 scans and 6 kHz spinning rate. The ^{13}C CPMAS spectrum was measured using the usual CP pulse sequence:[35] 8 μs 90° ^{1}H pulse width, 8 ms CP time and 30 s recycle delay, 38 461.538 Hz (509.627 ppm) spectral width, 2225 scans and 6 kHz spinning speed. The ^{19}F spectrum was recorded with a standard pulse sequence: 8 μs 90° pulse width, 5 s recycle delay, 125 000 Hz (442.725 ppm) spectral width, 8 scans and 7 kHz spinning speed. The ^{15}N CPMAS NMR spectrum showed no signal after 12 000 scans.

X-Ray crystallography

The data were collected at 120 K on a STOE imaging plate diffraction system (IPDS), equipped with an Oxford Cryosystems cryostream cooler device and using graphite-monochromated Mo-Kα radiation ($\lambda = 0.710\,73$ Å). Final unit cell parameters were obtained by least-squares refinement of a set of 5000 reflections. Crystal decay was monitored by measuring 200 reflections per image. No fluctuation of the intensity was observed during the course of data collection. A total of 11 260 reflections were collected of which 4150 were unique [R(int) = 0.0754]. The structure was solved by direct methods using SIR92,[36] and refined by full matrix least-squares procedures on F^2 (SHELXL-97).[37] All non-hydrogen atoms were anisotropically refined. All CF_3 groups showed rotational disorder. They were anisotropically refined using ADP with distance and angle restraints in two positions. Occupancy factors were also refined for each F atom. All hydrogen atoms were located on a difference Fourier map and refined with a riding model, except for hydrogen atoms H1a, H1b, H1c and H1d attached to N1a, N1b, N1c, N1d, respectively, which have been refined with a fixed isotropic thermal parameter 20% higher than that of the nitrogen atoms to which they are connected. A weighting scheme {weight $= 1/[\sigma^2(F_o^2) + (0.0919\,P)^2]$ where $P = (F_o^2 + 2\,F_c^2)/3$} has been applied in the last cycles of refinement. Final $R_1 = \Sigma \parallel F_o \mid - \mid F_c \parallel / \Sigma \mid F_o \mid = 0.0573$, $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2 / \Sigma w(F_o^2)^2]^{1/2} = 0.1374$ for 2332 reflections with $F_o > 4\,\sigma(F_o)$, 3253 restraints and 705 parameters ($R_1 = 0.1119$, $wR_2 = 0.1652$ for all data). Drawings have been made with the program ZORTEP[38] with 50% probability thermal ellipsoïds for non-hydrogen atoms.

CCDC reference number 440/151. See http://www.rsc.org/suppdata/nj/1999/1231/ for crystallographic files in .cif format.

Results and discussion

X-Ray molecular structure

Crystal data for $C_{20}H_8N_8F_{24}$, FW 816.34, triclinic, $P\bar{1}$, $a = 8.8547(9)$, $b = 10.1535(10)$, $c = 17.8903(19)$ Å, $\alpha = 90.192(11)°$, $\beta = 94.987(11)°$, $\gamma = 106.811(11)°$, $U = 1533.2(3)$ Å^3, $Z = 2$, $\mu = 0.212$ mm^{-1}. Fig. 1 represents the tetramer (asymmetric unit) with the atom numbering used while Fig. 2 shows the rotational disorder of the CF_3 groups in one molecule. The other monomers are shown in the Electronic Supplementary Information (ESI). All known *N*-unsubstituted (NH) pyrazoles crystallize in four classes as far as the HBs are concerned: catemers (chains), dimers, trimers and tetramers, the last ones being the least common.[39] Compound **1** crystallizes as a tetramer, as only two other NH-pyrazoles are known to do, 3(5)-phenyl-5(3)-methylpyrazole **3** and 3,5-diphenylpyrazole **4**.[40] To discuss the molecular structure of **1** it is better to discuss first the structure of an average monomer and then the conformation of the tetramer (by comparison with those of **3** and **4**). Since there are four independent molecules in the asymmetric unit (each monomer of the tetramer is different), we report in Table 1 the most relevant structural parameters of an average monomer of compound **1**.

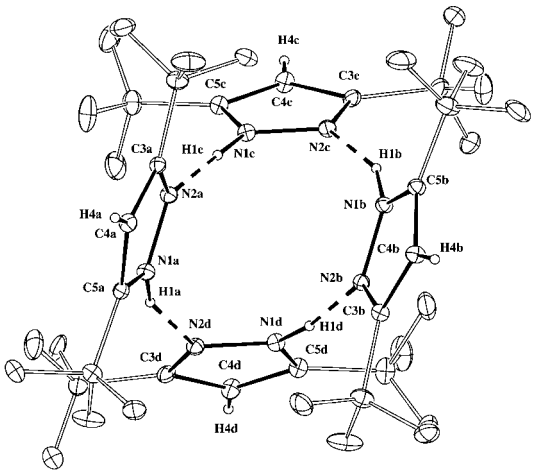


Fig. 1 View of the tetramer with the atom numbering.

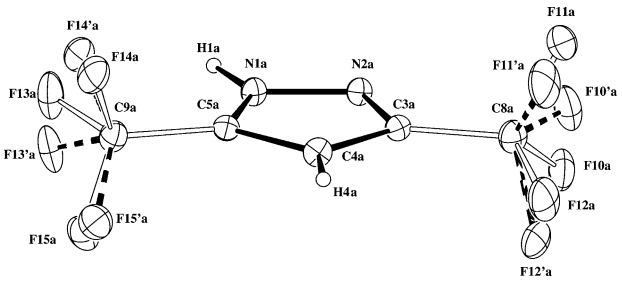
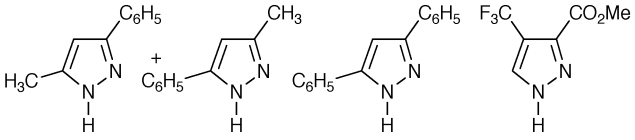


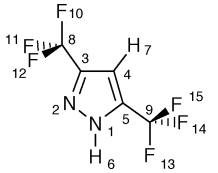
Fig. 2 View of molecule '**a**' of the tetramer showing the rotational disorder of the CF_3 group.

We have found in the Cambridge Structural Database (April 1998 release),[41] 22 compounds corresponding to 55 independent 3,5-bis(trifluoromethyl)pyrazole residues (complete list and details are in the ESI). Since they belong to different types of complexes (many of them being bis- and tris-pyrazolylborates) comparisons are difficult. Bonati has shown that the geometries of pyrazoles are strongly dependent on the substituents on the nitrogen atoms.[42] A principal component analysis (PCA) of the geometries of compound **1** and those of the 22 CSD compounds (average geometries) shows that the first two components represent 90% of the variance. The compounds closest to **1**, in terms of geometry, are CECKEA (ref. 7) and BIXBUF (ref. 8), although compound **1** is closest to Bonati's mean values for a free pyrazole.[42]



3 **4** **5**

Table 1 Calculated (STO-3G and 6-31G*), gas-phase and crystal molecular structure of compound **1**



	STO-3G[1–3]	6-31G*	B3LYP	ED[3]	X-Ray[a]
Bond lengths/Å					
1–2	1.376	1.316	1.337	1.347(14)	1.348
2–3	1.335	1.301	1.334	1.332(22)	1.351
3–4	1.423	1.410	1.411	1.400(12)	1.391
4–5	1.357	1.359	1.380	1.387(20)	1.387
5–1	1.382	1.344	1.361	1.355(19)	1.348
1–6	1.026	0.995	1.011	1.004	—
4–7	1.077	1.069	1.079	1.084	—
3–8	1.549	1.496	1.499	1.515(16)	1.483
5–9	1.548	1.492	1.492	1.490(17)	1.482
8–10	1.374	1.325	1.352	—	1.344
8–11	1.374	1.323	1.350	—	1.368
8–12	1.375	1.315	1.344	1.340(1)	1.327
9–13	1.373	1.315	1.343	—	1.355
9–14	1.373	1.320	1.349	—	1.331
9–15	1.375	1.324	1.355	—	1.320
Bond angles/°					
1–2–3	103.3	105.2	104.1	103.4(9)	107.1
2–3–4	112.5	112.0	112.4	114.3(13)	110.3
3–4–5	105.2	103.2	103.9	102.1(8)	104.0
4–5–1	106.7	107.1	106.5	108.1(12)	109.2
5–1–2	112.3	112.5	113.1	112.1(11)	109.4
5–1–6	127.0	128.0	127.2	125.8	—
6–1–2	120.7	119.5	119.6	122.1	—
3–4–7	127.0	128.6	128.4	131.9	—
5–4–7	127.8	128.2	127.8	126.0	—
2–3–8	120.2	120.8	120.4	118.7(8)	120.1
8–3–4	127.3	127.1	127.2	127.0	129.7
4–5–9	131.9	131.0	131.6	129.2	130.0
9–5–1	121.4	121.8	121.8	122.7(9)	120.8
3–8–10	110.4	110.1	109.9	111.4(5)	111.8
3–8–11	111.5	111.6	111.8	111.4(5)	112.1
3–8–12	111.5	112.2	112.0	111.4(5)	112.4
5–9–13	110.0	111.0	111.2	110.7(5)	111.6
5–9–14	111.3	111.9	112.2	110.7(5)	112.1
5–9–15	111.3	110.5	110.2	110.7(5)	113.4
Torsion angles/°					
2–3–8–10	65.4 [∥ (C)]	−33.4[⊥]	−44.1[⊥/ ∥ (C)]	−44.0(19)[⊥/ ∥ (C)]	−30/0[⊥/ ∥ (N)]
2–3–8–11	−54.9	87.4	76.4	76.0(19)	90/120
2–3–8–12	−174.8	−153.9	−164.4	−164.0(19)	−150/−120
1–5–9–13	−0.1 [∥ (N)]	36.2 [⊥]	148.1	16.0(12)[⊥/ ∥ (N)]	−30/0 [⊥/ ∥ (N)]
1–5–9–14	119.7	−82.9	−91.5	−104.0(12)	90/120
1–5–9–15	−120.0	156.7	27.8 [⊥]	136.0(12)	−150/−120

[a] Average value of the four independent molecules.

The conformation of the tetramers, like those formed by **1**, **3** and **4**, can be described as a "tub". There is an analogy between "molecular" systems derived from benzene and "supramolecular" systems formed by NH-pyrazoles (see Fig. 3). Thus, dimers and trimers form planar (or quasi planar) structures while tetramers, due to angular strain, form tub-shaped structures. This might be relevant for understanding which kind of cyclic structure is the most stable for a given pyrazole.

Theoretical calculations

For compound **1** ($C_5N_2F_6H_2$) there are $3n - 6 = 39$ normal modes. The full calculated and experimental values are provided as ESI. IR studies of pyrazoles with complete assignment of all the normal modes as well as overtones and combination bands have been reported for pyrazole, 1-methylpyrazole and 3,5-dimethylpyrazole.[43] The NH stretching (mode 39: 3497 cm^{-1} in the gas phase) bond is similar to that found for pyrazole itself (3523 cm^{-1} in the gas phase).[44–46] Most bands have a composite origin, but the C_4–H stretching (mode 38: 2921.5 cm^{-1}) and the γ_{NH} (mode 14) bands are quite clean. In the solid state, the main change affects the stretching NH mode that, due to the N–H···N HBs becomes a very broad and complex signal.

The calculated geometries are reported in Table 1 together with the previous STO-3G calculation, the gas-phase ED geometry and the average X-ray geometry. A statistical treatment of these data (correlation matrix) shows that for the bond lengths, the B3LYP/6-31G* geometry is the closest to the ED and X-ray geometries while for the bond angles, the HF/6-31G* geometry is slightly better than the B3LYP/6-31G* version. Assuming that there is no intercept, two equations, one for bond lengths and another for bond angles, relate the X-ray average geometry to the B3LYP/6-31G* geometry:

$$d(\text{Å, X-ray}) = (0.996 \pm 0.003) \cdot d(\text{Å, B3LYP/6-31G*}),$$

$$n = 13, \quad r^2 = 1.000 \quad (1)$$

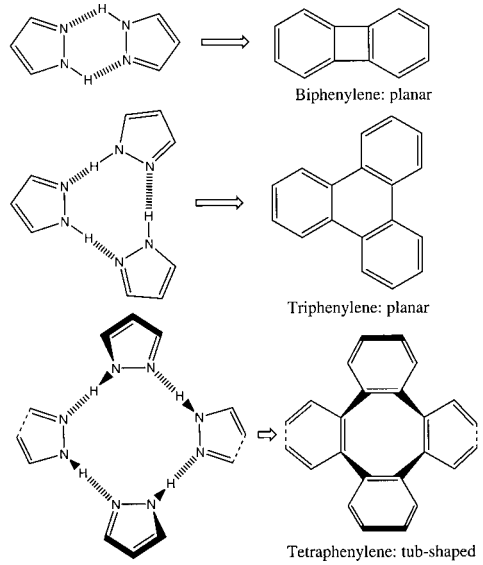


Fig. 3 Correspondance of the supramolecular conformations of dimers, trimers and tetramers with molecular species.

$$\text{Ang}(^\circ, \text{X-ray}) = (1.003 \pm 0.005) \cdot \text{Ang}(^\circ, \text{B3LYP/6-31G*}),$$
$$n = 15, \quad r^2 = 1.000 \quad (2)$$

To discuss the conformation of the trifluoromethyl substituents, it should be remembered that there are two standard situations for an sp^3–sp^2 bond (Fig. 4). These are called "perpendicular" ($\perp$) and "parallel" ($\parallel$) conformations; the latter can have the fluorine atom near a carbon atom (C4) or a near a nitrogen atom (N1 or N2; the N atoms are represented in black in the Newman projection). Note that the $\perp$ and $\parallel$ conformations differ only by 30°, that is a 15° rotation leads to a conformation equidistant from both (right-hand representation in Fig. 4). To simplify the discussion, consider that if the smallest angle (in absolute terms) is close to 0°, the conformation will be $\parallel$ (N), if the smallest angle (in absolute terms) is close to 30°, the conformation will be $\perp$, if the smallest angle (in absolute terms) is close to 60°, the conformation will be $\parallel$ (C) (see Table 1).

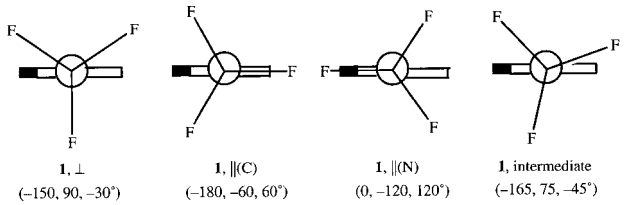


Fig. 4 Standard conformations of the CF_3 groups.

Perpendicular, parallel and in-between conformations are found for the 3-CF_3 and 5-CF_3 groups, depending on the experimental method and on the computational level. The differences in energy between conformers are very low (0.1–0.2 kcal mol^{-1}); consequently, it is safe to consider these groups as free-rotors whose conformation in the crystal will result from close packing. In the solid state, each molecule shows two conformations (**a** and **a′**, **b** and **b′** and so on). In all, there are 16 conformations that can summarized as follows for the 3-CF_3/5-CF_3 groups: **a** [$\perp$/$\parallel$(N)], **a′** [$\parallel$(N)/$\perp$], **b** [intermediate/$\perp$], **b′** [$\perp$/intermediate], **c** [intermediate/intermediate], **c′** [$\perp$/$\perp$], **d** [intermediate/$\perp$] and **d′** [$\perp$/$\perp$]. The intermediate cases (torsion angles ~15°) correspond to situations between $\parallel$(N) and $\perp$. Therefore, the perpendicular and parallel conformations with a fluorine towards a nitrogen predominate in the crystal (see Table 1).

The data on the HB network of compound **1** are summarized in Table 2 with those for two other tetramers, **3** and **4**. Data for another NH-pyrazole bearing a trifluoromethyl group at the 4 position, **5** (a trimer), are also reported. It appears that compound **1** is very similar to compound **4** [while compound **3** has the N–H···N proton midway between both nitrogen atoms and is, for this reason, quite different]. The other CF_3-pyrazole, **5**, has rather different NH and N···H distances. This is almost certainly due to the additional involvement of one (among three available) 3-acetate oxygen in the hydrogen-bonding network.[49]

Annular tautomerism and proton disorder

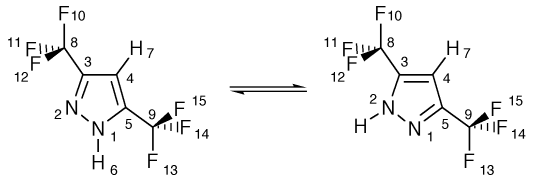
An examination of the residuals corresponding to eqn. (1) and (2) shows that the experimental geometry is intermediate between that calculated and an "inverted B3LYP/6-31G* geometry", that is, a geometry resulting from shifting the NH proton from N1 to N2.

An interpolation of the experimental X-ray geometry between these two B3LYP/6-31G* calculated geometries leads to populations of 0.6 of the N1–H and 0.4 of the N2–H

Table 2 Geometry of N–H···N HBs in *N*-unsubstituted pyrazoles

	N–H/Å	H···N/Å	N···N/Å	N–H···N/°
1a–1d	1.00(5) [N1a–H1a]	1.84(5) [H1a···N2d]	2.806(6) [N1a···N2d]	160(7) [N1a–H1a···N2d]
1d–1b	1.01(5) [N1d–H1d]	1.94(5) [H1d···N2b]	2.941(6) [N1d···N2b]	172(9) [N1d–H1d···N2b]
1b–1c	1.01(5) [N1b–H1b]	1.84(6) [H1b···N2c]	2.799(6) [N1b···N2c]	157(8) [N1b–H1b···N2c]
1c–1a	1.01(5) [N1c–H1c]	1.90(5) [H1c···N2a]	2.913(6) [N1c···N2a]	176(8) [N1c–H1c···N2a]
Average	1.008	1.88	2.865	166
3[a]	1.458(4)	1.458(4)	2.913(1)	176(4)
	1.413(4)	1.413(4)	2.824(5)	175(2)
	1.44(4)	1.41(4)	2.852(5)	178(3)
	1.44(4)	1.41(4)	2.852(5)	178(3)
Average	1.44	1.42	2.860	177
4[b]	1.02	1.90(–)	2.892(3)	154(–)
	1.01	1.90(–)	2.835(3)	154(–)
	1.02	1.92(–)	2.915(3)	165(–)
	1.01	1.87(–)	2.835(3)	156(–)
Average	1.02	1.90	2.869	157
5[c]	0.885	2.031	2.902(5)	168.1
	0.832	2.053	2.874(6)	168.9
	1.005	1.986	2.964(5)	163.8
Average	0.907	2.023	2.913	166.9

[a] 3(5)-Phenyl-5(3)-methylpyrazole (CSD: MEPHPY01; tetramer, four independent molecules).[47] [b] 3,5-Diphenylpyrazole (tetramer, four independent molecules).[48] [c] Methyl-4-trifluoromethylpyrazole-3-carboxylate (CSD: LETCES; trimer, three independent molecules).[49]



tautomers:

$$\text{X-Ray geometry} = (0.60 \pm 0.04)\cdot(\text{B3LYP/6-31G* normal}) + (0.40 \pm 0.04)\cdot(\text{B3LYP/6-31G* inverted}),\quad n = 28,\ r^2 = 1.000 \quad (3)$$

Despite the fact that the X-ray data were collected at 120 K and that the refinement properly converged with low residual electron density, only hydrogen atoms belonging to the major "normal" tautomer (*ca.* 60% according to the interpolation) have been located. Nevertheless, all our previous experience suggests that the interpolation method using heavy atoms is at least as reliable as the direct location of N–H protons in the case of disorder.[50,51] The geometric parameters most sensitive to tautomerism are the internal angles on the nitrogen atoms.[42,52] We have collected in Table 3 the data corresponding to pyrazole itself (a catemer with localized protons) and to **1**. The population (in %) of the "normal" tautomer (for instance, that with the proton on N1) is given by $\%(N1) = 100(\Delta N + \Delta N_0)/2\Delta N_0$, where ΔN_0 is the maximum difference between the angles on N1 and N2 (100% population). Assuming that $\Delta N_0(\mathbf{1}) = (8.8 \pm 0.2)^\circ$, then the percentage of the "normal" tautomer is about 63.1 ± 0.3, which is in acceptable agreement with the previous estimation [eqn. (3)].

For "symmetrical" pyrazoles, that is those having identical substituents at positions 3 (R^3) and 5 (R^5), the theoretical tautomer ratio is 50 : 50. This only truly happens in the gas phase for the isolated monomer; in condensed phases, the equilibrium is more or less perturbed by intermolecular interactions. Although this is particularly true for the solid state, in practice most cases of proton disorder correspond to mixtures that cannot be distinguished from the ideal 50 : 50 ratio.[26–29,39,40] On the other hand, "asymmetrical" pyrazoles, $R^3 \neq R^5$, crystallize in only one tautomeric form, which can be different depending on the solvent.

It remains to be determined whether this disorder is static or dynamic: *N*-unsubstituted pyrazoles show both kinds of disorder, which can be differentiated only by solid-state NMR spectroscopy.[55] A series of NMR experiments were carried out with a sample of **1** in natural abundance.

The ^{1}H NMR spectrum (Fig. 5) shows the signals for H4 at 6.51 ppm (in $CDCl_3$ solution: 6.86 ppm)[1] and for the NH at 14.2 ppm, strongly deshielded by the hydrogen bonds. The fact that the NH signal is much broader than that of H4 might be a first indication of dynamic disorder. The ^{19}F NMR spectrum of **1** (Fig. 5) shows a single line at −63.8 ppm, typical for trifluoromethylpyrazoles: compound **1** in solution, −62.4 ppm;[5] 1-substituted-3,5-bis(trifluoromethyl)pyrazoles,

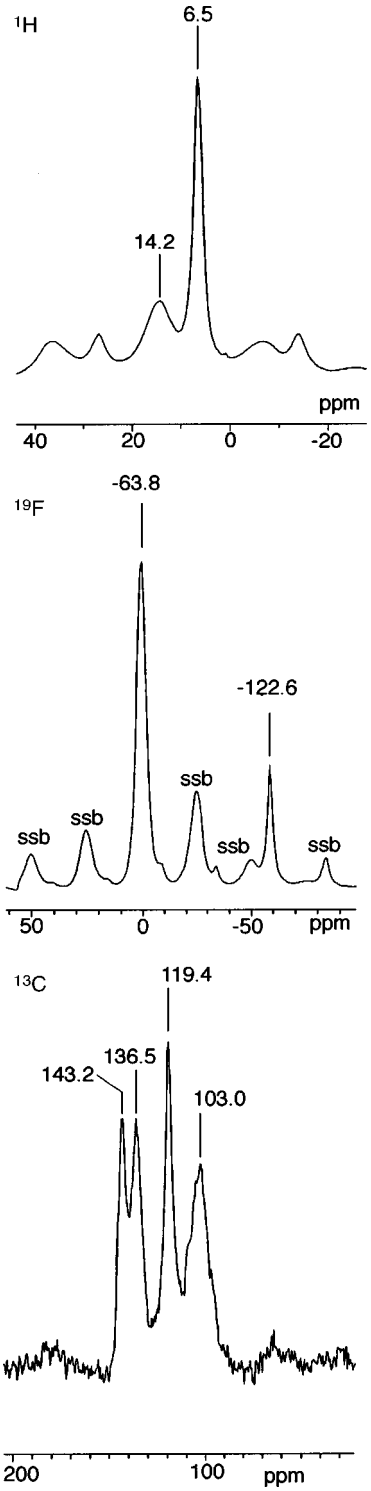


Fig. 5 ^{1}H, ^{19}F and ^{13}C MAS NMR spectra of compound **1**. In the ^{19}F spectrum the signal at −122.6 ppm does not arise from compound **1**.

Table 3 Values of the internal angles (in °) at N1 and N2 in *N*-unsubstituted pyrazoles

Substituents	Phase	Method	N1	N2	ΔN	Ref.
None	—	6-31G*	112.8	104.9	7.9	53
None	Gas	MW at RT	113.1(3)	104.1(3)	9.0	52
None	Crystal	X-ray at 108 K	113.0(5)	103.7(5)	9.3	54
3,5-CF_3	—	6-31G*	112.5	105.2	7.3	This work
3,5-CF_3	—	B3LYP/6-31G*	113.1	104.1	9.0	This work
3,5-CF_3	Gas	ED at RT	112.1(11)	103.4(9)	8.7	3
3,5-CF_3	—	X-ray at 120 K	109.4[a]	107.1[a]	2.3	This work

[a] Average values of the four independent molecules.

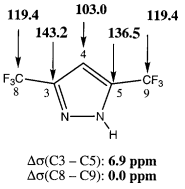


Fig. 6 ^{13}C NMR experimental δ values for compound **1** in the solid state (see Fig. 5, ^{13}C); the experimental δ values in DMSO-d^6 are: C3 and C5, 138.2; C4, 104.7; C8 and C9, 120.6 ppm. The GIAO calculated absolute shieldings (σ values) are: C3, 57.52; C5, 67.19 [$\Delta\sigma$(C5 − C3) = 9.67]; C4, 99.96; C8, 96.38; C9, 97.45 ppm [$\Delta\sigma$(C9 − C8) = 1.07 ppm].

−64.1 (3-CF_3) and −60.8 ppm (5-CF_3);[5] the difference in chemical shifts between the 3- and 5-CF_3 groups in the ^{19}F NMR spectrum is, however, too small to conclude that the single line at −63.8 ppm is due to coalescence and not to a lack of resolution. Since we could not observe a ^{15}N NMR signal even after 12 000 scans with the unlabelled compound, the most interesting information is contained in the ^{13}C CPMAS NMR spectrum (Fig. 5).

To discuss this spectrum we have carried out GIAO-type calculations[56–58] using the RHF/6-31G* optimized geometry. The results concerning ^{13}C absolute shieldings (σ) are summarized in Fig. 6 (GIAO calculations for ^{19}F shieldings yield a $\Delta\sigma$ of 0.9 ppm for 3- and 5-CF_3 groups). To verify that theoretically calculated absolute shieldings can be used to estimate ΔC_0 for a given pyrazole, we carried out GIAO/RHF/6-31G* calculations on 3,5-dimethylpyrazole, a compound for which we have carefully measured ΔC_0 (8.2 ppm);[28,29] the calculated shieldings (54.92 and 63.71 ppm for C3 and C5, respectively) correspond to 8.8 ppm, in good agreement with the experiment. Therefore, the experimental result (Figs. 5 and 6) showing a ΔC_0 of only 6.7 ppm must correspond to the average spectrum of rapidly exchanging pyrazole tautomers, that is, to a dynamic disorder in the crystal. The populations of both tautomers cannot be the same (otherwise, a single line would be observed at coalescence) but it would be hazardous to calculate the populations by interpolation.

To conclude, the great volatility of compound **1** is not related to weaker HBs as judged from their geometry. This compound crystallizes as a tetramer. A certain amount of proton disorder, probably dynamic, is suggested by the analysis of solid-state NMR spectra.

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