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Structure and tautomerism of 4-bromo substituted 1*H*-pyrazoles

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Abstract—The tautomerism in the solid state and in solution of five 4-bromo-1*H*-pyrazoles has been studied by multinuclear magnetic resonance spectroscopy and, for one of them, by X-ray crystallography (3,4-dibromo-5-phenyl-1*H*-pyrazole). When there is a bromine atom at position 3(5), in all cases, the tautomer present in the solid state is the 3-bromo one. In solution, the same tautomer is the major one. DFT calculations justify the predominance of 3-bromo tautomers over 5-bromo ones and provide some useful chemical shifts obtained through GIAO calculations.

1. Introduction

3(5),4-Dibromopyrazoles unsubstituted at position 1 (N*H*-pyrazoles), **I**, are prepared by the two traditional methods represented in Scheme 1.[1–3] From pyrazolinones **II** through 3(5)-bromo-1*H*-pyrazoles **III** or by perbromination of pyrazoles **IV**. The first method we have used to prepare the 3(5)-methyl derivative **I** (R^1=CH_3).[4] The second one was discovered by Hüttel and co-workers and lead, when R^1=H, to 3,4,5-tribromo-1*H*-pyrazole **I** (R^1=Br).[5–9] This last compound was used to prepare novel scorpionate ligands devoid of C–H bonds.[10]

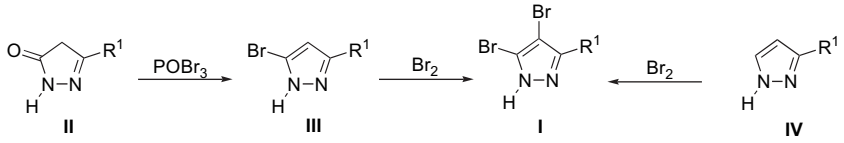
In search of new polybrominated pyrazoles useful in forming complexes through the corresponding polypyrazolylborates,[11] we describe here a series of five 4-bromopyrazoles **1**–**5** (Scheme 2). The present investigation on tautomerism of these bromopyrazoles[12] will provide general criteria to be used for the establishment of polypyrazolylborates structure.

Of the five compounds in Scheme 2, 4-bromo-3(5)-methyl-5(3)-phenyl-1*H*-pyrazole **1** is well known having been described several times, including its X-ray structure (Refcode: LIYGOP).[13] It is interesting to briefly summarize the structure and solid-state properties of **1** since this compound can serve as a model for the remaining four ones.[14–17] Compound **1** crystallizes in a tetramer formed by both tautomers in a **1a1b1a1b** disposition. The N*H* protons are disordered and the situation corresponds to a mixture of the two situations of Scheme 3. In general, the annular tautomerism of 3(5)-substituted-N*H*-pyrazoles has been the subject of many studies,[18] but that concerning 3(5)-bromo-1*H*-pyrazoles is still unreported and is the object of the present paper to explore it.

2. Results and discussion

2.1. X-ray molecular structure of 3,4-dibromo-5-phenyl-1*H*-pyrazole (2a)

This compound crystallizes forming also a tetramer with S_4 symmetry (see Fig. 2) as predicted by our model for pyrazoles bearing phenyl or bromo substituents at both positions



Scheme 1. Synthesis of *N*-unsubstituted dibromopyrazoles.

Keywords: Bromopyrazoles; Tautomerism: X-ray structure; Solid-state NMR; DFT calculations; GIAO calculations.
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✠ Dr. S. Trofimenko passed away on Monday, February 26, 2007.

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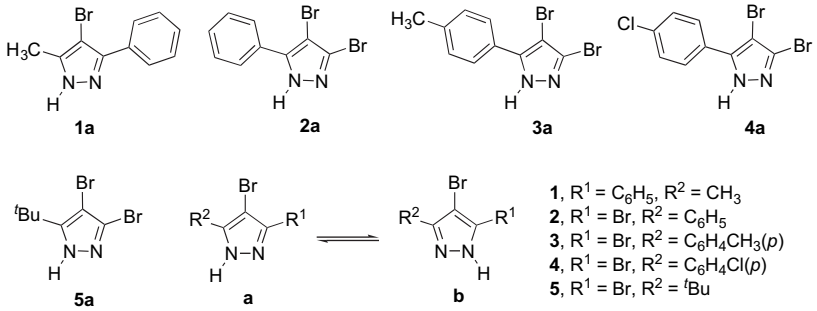
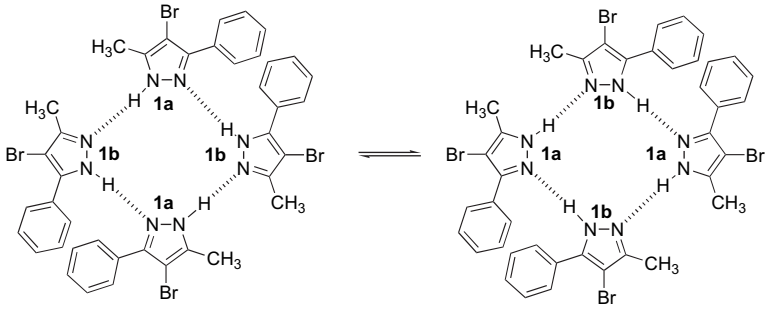
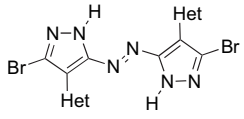


Scheme 2. The five pyrazoles of the present study and their tautomerism.



Scheme 3. The tautomerism of 4-bromo-3(5)-methyl-5(3)-phenyl-1*H*-pyrazole **1** in the solid state.

3 and 5.[15,17] The tautomer present is **2a** (Fig. 1). This is the second example of a 3(5)-bromo-1*H*-pyrazole whose structure has been determined. The other example, also a 3-bromo tautomer, has the dimeric azo structure **6** (Refcode: WEJHOI).[13]



6 (WEJHOI)

A search in the CSD[13] for 4-bromo-1*H*-pyrazoles yields the structures reported in Scheme 4.

It has been shown that the secondary structure of N*H*-pyrazoles corresponds to two main structural motives: trimers and catemers for small substituents at positions 3 and 5 and dimers and tetramers for large substituents at positions 3 and 5.[15–17] The substituent at position 4 increases the apparent size of substituents R^3 and R^5 by a buttressing effect thereby diminishing the accessible surface to the nitrogen atoms involved in the hydrogen bonds.[17] The sum of the molar refractivities, MR, of the substituents in positions 3 and 5 allows to predict the secondary structure:[15] less than 2.6 for trimers and catemers and larger than 2.6 for dimers and tetramers (taking into account the 4-bromo buttressing effect).[17] The data of Scheme 4 are in agreement with this rule.

2.2. NMR study in the solid state (CPMAS)

We have reported in Table 1 the ^{13}C and ^{15}N NMR data concerning compounds **1**–**5** in solution and in the solid state. We will first discuss the solid-state results because in crystals most pyrazoles exist as a single tautomer (100% of **a** or

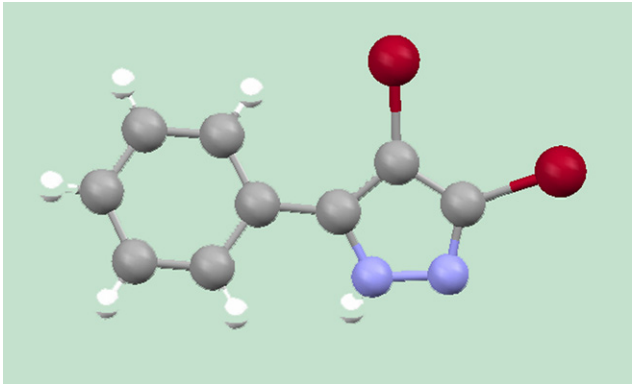


Figure 1. A view of 3,4-dibromo-5-phenyl-1*H*-pyrazole (**2a**).

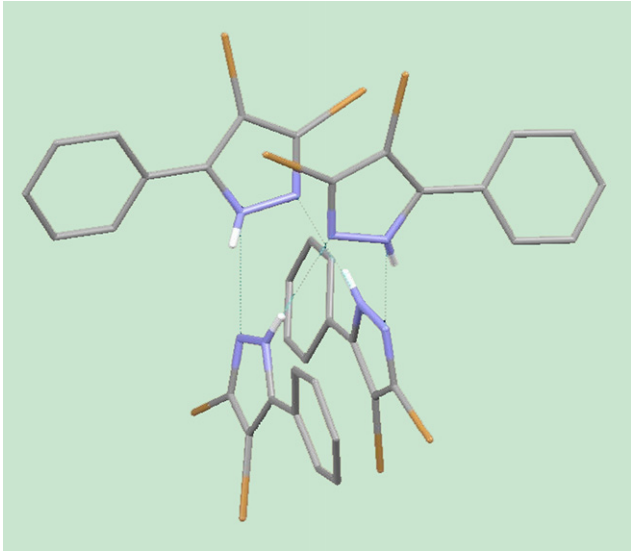
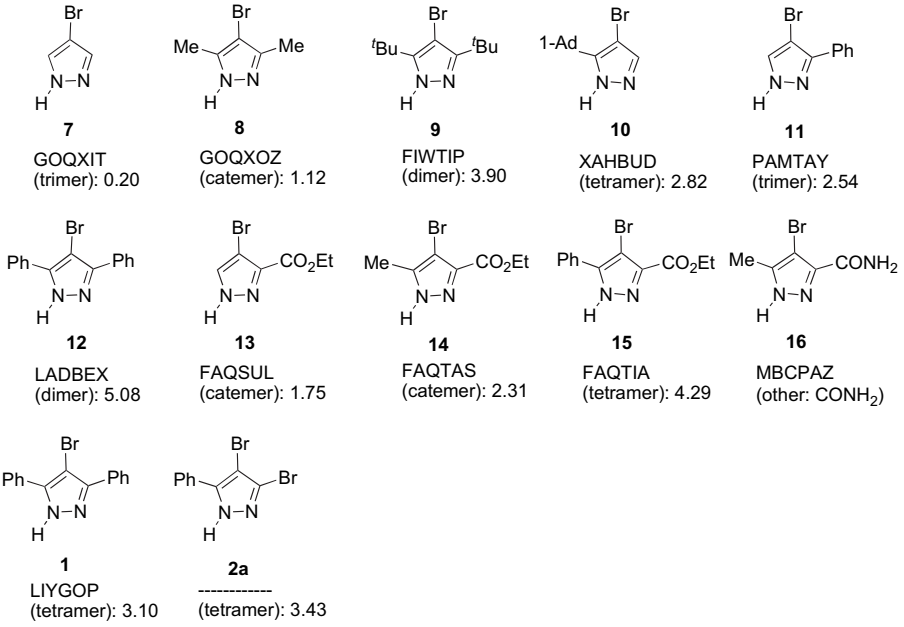


Figure 2. A view of the tetramer $(\mathbf{2a})_4$.



Scheme 4. N–H···N hydrogen-bond motifs and sum of molar refractivities ($\Sigma MR_{3,5}$)[15] of 4-bromo-1*H*-pyrazoles. The presence of a $CONH_2$ substituent gives rise to a different HB pattern.

100% of **b**), compound **1** being one of the rare exceptions although there are exactly 50% of **a** and 50% of **b**. Assignments are based on standard 2D techniques in solution (see Section 4) and comparison with other pyrazoles.[19,20] Particularly useful has been a paper of Holzer et al. describing many simple polybromo-substituted pyrazoles.[21]

The solid-state ^{13}C NMR chemical shifts of compound **1**, a tetramer **1a1b1a1b**, have been already reported.[14] Here we confirm the dynamic nature of the situation depicted in Scheme 3: the solid-state proton transfer (SSPT) occurs within the tetramer (the four C3 and C5 carbon atoms appear at 142.7 ppm). The ^{15}N signals are too far apart (−176 and −98 ppm) for coalescence to occur at 300 K, and only broadening is observed.

Since the X-ray structure has been determined and since there is no polymorphism (we have used the same sample for crystallography—Fig. 1—and CPMAS NMR) the solid-state chemical shifts of pyrazole **2** must correspond to tautomer **2a**. To demonstrate that all the other 3(5)-bromo-1*H*-pyrazoles are also **a** tautomers, we need to examine the data summarized in Scheme 5.

The ^{13}C signals of compounds **2**–**5** are neither splitted (two tautomers) nor broad (save the carbon atoms linked to the bromine) thereby excluding an SSPT as found in **1**. Therefore, only one tautomer is present and by internal comparison, if **2** is a 3-Br tautomer so are the other aryl derivatives, **3** and **4**. A comparison with 4-bromo-3,5-diphenyl-1*H*-pyrazole **19** confirms that signals at 137–140 ppm correspond to a C5-aryl atom. The signal of C3–Br has not been observed for pyrazoles **2**–**4**, they are expected at about 127 ppm (see **20** and **22** in Scheme 5) and are probably under the signals of the 5-aryl substituent. If they were 5-bromo derivatives, the C–Br signal would appear near 115 ppm (see **21** and **22** in Scheme 5), a zone devoid of interferences where nothing was observed. A *tert*-butyl substituent shifted the signal of the carbon where it is bonded by about 20 ppm and it does not affect the opposite signal.[19] We have calculated the expected chemical shifts for tautomers **5a** and **5b** from those of **21** and **22**, and since the effect of the N-methylation is small,[19] there is no doubt that the tautomer present in the solid state is **5a**.

The ^{15}N signals are in the expected range,[20] some splittings are observed (N2 of **4a**, N1 and N2 of **5a**) probably due to the proximity of the bromine atoms. N2 atoms resonate at about −95 ppm for **3a** and **4a** and about −103 ppm for **2a** and **5a**. The first ones should be dimers (for **19**, also a dimer,[15a] N2 appears at −90.5 ppm —Scheme 5) and the second ones tetramers (see the X-ray structure of **2a**) according to what we had already found that in dimers the N2 signal is shifted about 10 ppm.[15b] In **2a**, **3a**, and **4a** such conclusions are supported by the differences in ^{15}N chemical shifts, $\Delta\delta$ for N2, between solid state and solution[15b,c] the HB motifs have the following values of $\Delta\delta$ for N2: dimers around 8 ppm and tetramers around 19 ppm. However, the $\Delta\delta$ in **5a**, about 12 ppm is not so clear.

2.3. NMR study in solution and the problem of tautomerism of bromo-1*H*-pyrazoles

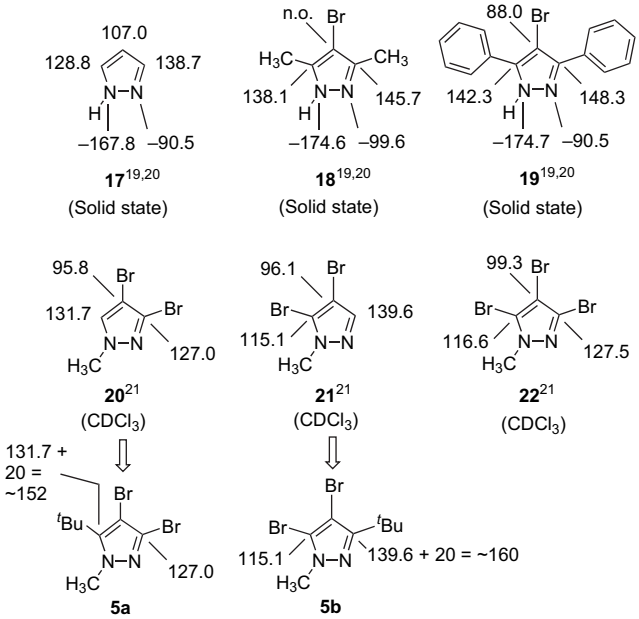
Integration in ^1H NMR (see Section 4) shows that compound **1** in DMSO-d_6 at 300 K is a mixture of 75% **1a**–25% **1b** while in THF-d_8 at 191 K it is 65% **1a**–35% **1b**. For the remaining pyrazoles, only one series of signals is observed in DMSO-d_6 at 300 K and in THF-d_8 at 200 K. Therefore, only a tautomer is present in solution or, at least, very predominant. By simple comparison with the CPMAS data, the conclusion that all of them are 3-bromo derivatives **a** prevails. The rule that the most abundant tautomer in solution coincides with that found in the crystal is again verified.[18,22]

Even that from the ^{13}C NMR chemical shifts and the gs-HMQC and gs-HMBC spectra there is no doubt about

Table 1. ^{13}C and ^{15}N chemical shifts (δ, ppm) of pyrazoles **1–5** (THF-d_8, DMSO-d_6, and CPMAS) and ^{1}J (^{15}N–^{1}H) in hertz

Compd	Solv.	Taut.	C3	C4–Br	C5	Substituent	N(H)1	N2
1	THF, 191 K	**a**	C–Ph: 148.4	91.5	C–Me: 139.8	Ph: 134.2 (*ipso*), 127.9 (*ortho*), 129.2 (*meta*), 130.0 (*para*); 10.3 (5-Me)	−180.3, ^{1}J=−106.1	−89.6
		b	C–Me: 148.8	92.4	C–Ph: 140.3	3-Me: 13.0; Ph: 129.7 (*ipso*), 127.6 (*ortho*), 128.7 (*meta*), 130.0 (*para*)	−186.1, ^{1}J=−107.7	−87.1
1	DMSO, 300 K	**a**	C–Ph: 147.1	90.4	C–Me: 138.8	Ph: 132.7 (*ipso*), 126.9 (*ortho*), 128.4 (*meta*), 127.8 (*para*); 9.8 (5-Me)		
		b	C–Me: 147.2	91.4	C–Ph: 139.0	3-Me: 12.2; Ph: 128.4 (*ipso*), 126.9 (*ortho*), 128.8 (*meta*), 128.7 (*para*)		
1	CPMAS, 300 K	**a**	C–Ph: 142.7 (vbr s)	83.8 (vbr s)	C–Me: 142.7 (vbr s)	Ph: 130.5 (*ipso*), 125.7 (*ortho*), 127.3 (*meta*), 127.3 (*para*); 5-Me: 10.5;	−176	−98
		b	C–Me: 142.7 (vbr s)	83.8 (vbr s)	C–Ph: 142.7 (vbr s)	3-Me: 11.7; Ph: 130.5 (*ipso*), 125.7 (*ortho*), 127.3 (*meta*), 127.3 (*para*)		
2	DMSO, 300 K	**a**	C–Br: nd	93.5	C–Ph: 141.6	Ph: 127.1 (*ipso*), 127.1 (*ortho*), 128.9 (*meta*), 129.4 (*para*)		
2	THF, 219 K	**a**	C–Br: 130.6	94.8	C–Ph: 142.5	Ph: 129.2 (*ipso*), 128.0 (*ortho*), 130.1 (*meta*), 130.4 (*para*)	−177.7, ^{1}J=106.1	−83.8
2	CPMAS, 300 K	**a**	C–Br: nd	93.9 (vbr s)	C–Ph: 140.1	Ph: 126.1 (*ipso*), 126.1 (*ortho*), 129.1 (*meta*), 129.1 (*para*)	−175.9	−102.0
3	DMSO, 300 K	**a**	C–Br: nd	93.2	C–*p*-MePh: 141.6	*p*-MePh: 125.0 (*ipso*), 127.0 (*ortho*), 129.4 (*meta*), 139.0 (*para*), Me: 20.8		
3	THF, 200 K	**a**	C–Br: 130.6	94.4	C–*p*-MePh: 142.4	*p*-MePh: 126.3 (*ipso*), 127.9 (*ortho*), 130.7 (*meta*), 140.4 (*para*), Me: 21.6	−179.9, ^{1}J=104.6	−86.5
3	CPMAS, 300 K	**a**	C–Br: nd	89.6 (vbr s)	C–*p*-MePh: 138.6	*p*-MePh: 122.9 (*ipso*), 124.5 (*ortho*), 129.2 (*meta*), 138.6 (*para*), Me: 22.4	−177.4	−95.0
4	THF, 300 K	**a**	C–Br: 130.6	C–Br: 95.2	C–*p*-ClPh: 141.8	*p*-ClPh: 128.2 (*ipso*), 129.7 (*ortho*), 130.1 (*meta*), 136.0 (*para*)		
4	THF, 219 K	**a**	C–Br: 130.7	C–Br: 95.2	C–*p*-ClPh: 141.4	*p*-ClPh: 127.9 (*ipso*), 129.8 (*ortho*), 130.3 (*meta*), 135.9 (*para*)	−177.3, ^{1}J=−105.3	−83.2
4	DMSO, 300 K	**a**	C–Br: nd	C–Br: 93.9	C–*p*-ClPh: 140.8	*p*-ClPh: 126.9 (*ipso*), 128.9 (*ortho*), 129.0 (*meta*), 134.1 (*para*)		
4	CPMAS 300 K	**a**	C–Br: nd	95.5 (vbr s)	C–*p*-ClPh: 137.5	*p*-ClPh: 125.0 (*ipso*), 129.4 (*ortho*), 127.2 (*meta*), 132.7 (*para*)	−176.2	−93.4, −95.0
5	THF, 300 K	**a**	C–Br: 130.5	93.3	C–*t*-Bu: 150.7	*t*-Bu: 33.2 (C), 28.7 (Me)		
5	THF, 200 K	**a**	C–Br: 130.7	93.3	C–*t*-Bu: 149.8	*t*-Bu: 33.0 (C), 28.1 (Me)	−177.9, ^{1}J=−105.2	−89.9
5	DMSO, 300 K	**a**	C–Br: nd	91.7	C–*t*-Bu: 149.8	*t*-Bu: 32.0 (C), 28.1 (Me)		
5	CPMAS, 300 K	**a**	C–Br: 124.5 (vbr s)	89.1 (vbr s)	C–*t*-Bu: 150.8	*t*-Bu: 32.9 (C), 27.6, 28.1, 28.4, 29.1 (Me)	−169.3, −170.3, −171.3, −172.0	−101.4, −102.3, −102.9, −103.7

vbr s=very broad signal; nd=not detected.



Scheme 5. ^{13}C and ^{15}N chemical shifts of related pyrazoles.

the structure of the most predominant tautomer in each case, we decided to confirm it by doing some NOESY experiments. These experiments show a NOE effect between the N*H* and the *ortho*-aryl or the *tert*-butyl protons for each studied compound. In Figure 3 we have

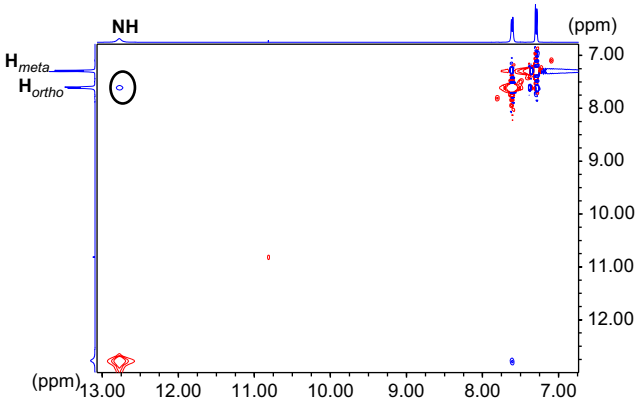


Figure 3. NOESY spectrum at 300 K of 3(5),4-dibromo-5(3)-*p*-tolyl-1*H*-pyrazole (**3**).

reproduced the NOESY spectrum of compound **3** as an example.

2.4. Computational study

We have carried DFT calculations at the B3LYP/6-311++G** level of the energies (Table 2) and absolute shieldings (Table 3) of a series of simple bromo-1*H*-pyrazoles including the effect of DMSO solvent as a continuum (PCM).

Table 2. Energetic results, absolute values in hartree and relative values in kJ mol^{-1}

Pyrazole	Vacuum	E_{rel}	PCM-DMSO	E_{rel}
17	−226.2660	—	−226.2785	—
3-Bromo	−2799.8057	0.00	−2799.8190	0.00
5-Bromo	−2799.8040	4.43	−2799.8149	10.83
3,4-Dibromo	−5373.3412	0.00	−5373.3542	0.00
4,5-Dibromo	−5373.3403	2.53	−5373.3506	9.38
3,4,5-Tribromo	−7946.8773	—	−7946.8874	—

Table 3. Calculated NMR chemical shifts (δ^{13}C=174.0−0.941 σ^{13}C −17.6; δ^{15}N=−141.7−0.978 σ^{15}N)

Pyrazole	C-3	C-4	C-5	N-1	N-2
17	138.2	104.5	128.1	−173.1	−79.8
3-Bromo	125.5	108.0	130.4	−173.7	−79.4
5-Bromo	140.0	108.6	112.4	−168.7	−72.2
3,4-Dibromo	126.6	96.6	131.7	−174.4	−76.6
4,5-Dibromo	140.9	96.7	114.0	−168.8	−71.6
3,4,5-Tribromo	128.3	98.8	116.3	−170.2	−72.1

It appears that the 3-bromo tautomers are more stable than the 5-bromo ones and that the predominance increases considerably in DMSO.

We have calculated (GIAO/B3LYP/6-311++G**) the absolute shieldings of the six N*H*-pyrazoles in Table 2 both in vacuum and in DMSO (PCM model). We have transformed these σ into chemical shifts using linear equations and some experimental values from Refs. 19–21. The intercepts should be similar to the references: for ^{13}C, σTMS=184.7 ppm and for ^{15}N, $\sigma MeNO_2$=−154.4 ppm at the same level). In the case of carbon atoms bearing a Br substituent we have had to include a correction of −17.6 ppm (statistically calculated) to fit the experimental values. We have already noted that calculations at the level used are unable to reproduce CBr atoms.[23]

The predicted ^{15}N chemical shifts for the 3,4-dibromo derivative are similar to those found in THF-d_8 at low temperature for **4a** (219 K) and **5a** (200 K).

3. Conclusions

As a general and useful rule it can be stated that 3(5),4-dibromo-1*H*-pyrazoles crystallize as 3,4-dibromo tautomers, the same forms that predominate in solution.

4. Experimental

4.1. General

The starting pyrazoles 3(5)-methyl-5(3)-phenyl-1*H*-pyrazole,[24,25] 3(5)-*p*-chlorophenyl-1*H*-pyrazole,[26] 3(5)-phenyl-1*H*-pyrazole,[24,27] 3(5)-*p*-tolyl-1*H*-pyrazole,[28] and 3(5)-*tert*-butyl-1*H*-pyrazole[27,29,30] were prepared by the literature methods. Melting points were determined with a Thermo-Galen hot stage microscope and are given uncorrected.

4.2. 4-Monobromination of 3-substituted pyrazoles

The pyrazole was dissolved in methanol, and few drops of concentrated hydrochloric acid were added. This was followed by the dropwise addition of 1 equiv of bromine. After the addition was complete, the solution was stirred for 1 h, and was then poured into a large amount of water with excess ammonia. The precipitated solid was filtered off, and extracted with methylene chloride. The extracts were filtered through a short layer of alumina, and the filtrate was evaporated to dryness. Further purification was via recrystallization from toluene/heptane.

4.2.1. 4-Bromo-3(5)-methyl-5(3)-phenyl-1*H*-pyrazole (1). Yield 91%, mp 106–108 °C. Lit. mp 97 °C.[22] Calcd for $C_{10}H_9BrN_2$: C 50.6; H 3.8; N 11.8%. Found: C 50.3; H 4.0; N 11.6%. NMR (δ, ppm): THF-d_8 191 K, **1a** (65%) 2.30 (CH_3), 7.92 (*ortho*, ^3J=7.4 Hz), 7.42 (*meta*, ^3J=7.4 Hz), 7.33 (*para*, ^3J=7.3 Hz), 12.67 (NH); **1b** (35%) 2.22 (CH_3), 7.75 (*ortho*, ^3J=7.5 Hz), 7.53 (*meta*, ^3J=7.5 Hz), 7.44 (*para*, ^3J=7.0 Hz), 12.77 (NH); DMSO-d_6 300 K, **1a** (75%) 2.24 (CH_3), 7.77 (*ortho*, ^3J=7.4 Hz), 7.43 (*meta*), 7.35 (*para*), 13.13 (NH); **1b** (25%) 2.18 (CH_3), 7.70 (*ortho*, ^3J=6.5 Hz), 7.48 (*meta*), 7.41 (*para*), 13.24 (NH).

4.3. 4,5-Dibromination of 3-substituted pyrazoles

The appropriate pyrazole was dissolved in methanol, containing 3 equiv of sodium hydroxide. Two equivalents of bromine were slowly added dropwise to this solution. After completion of the addition, the solution was stirred for another hour, and was then added slowly to a large amount water, containing excess hydrochloric acid. The precipitated product was filtered off, and was partially air-dried. It was then taken up in ethyl acetate, which allowed for the separation of the remaining aqueous layer. The organic phase was passed through a short layer of alumina, and the elute was evaporated to dryness.

4.3.1. 3(5),4-Dibromo-5(3)-phenyl-1*H*-pyrazole (2). Yield 83%, mp 130–132 °C. Calcd for $C_9H_6Br_2N_2$: C 35.7; H 1.99; N 9.27%. Found: C 35.5; H 2.05; N 9.02%. NMR (δ, ppm): DMSO-d_6 300 K, 7.72 (*ortho*, ^3J=7.1 Hz), 7.54 (*meta*, ^3J=7.3 Hz), 7.48 (*para*, ^3J=7.2 Hz), 13.94 (NH); THF-d_8 300 K, 7.72 (*ortho*, ^3J=6.8 Hz), 7.48 (*meta*, ^3J=7.3 Hz), 7.42 (*para*, ^3J=7.1 Hz), 12.83 (NH); THF-d_8 219 K, 7.76 (*ortho*, ^3J=7.3 Hz), 7.55 (*meta*, ^3J=7.5 Hz), 7.48 (*para*, ^3J=7.4 Hz), 13.26 (NH).

4.3.2. 3(5),4-Dibromo-5(3)-*p*-tolyl-1*H*-pyrazole (3). Yield 76%, mp 171–173 °C. Calcd for $C_{10}H_8Br_2N_2$: C 38.0; H 2.53; N 8.86. Found: C 37.7; H 2.71; N 8.67%. NMR (δ,

ppm): DMSO-d_6 300 K, 7.61 (*ortho*, ^3J=8.1 Hz), 7.33 (*meta*, ^3J=8.1 Hz), 2.36 (CH_3), 13.90 (NH); THF-d_8 300 K, 7.61 (*ortho*, ^3J=7.8 Hz), 7.30 (*meta*, ^3J=7.9 Hz), 2.38 (CH_3), 12.79 (NH); THF-d_8 200 K, 7.66 (*ortho*, ^3J=8.1 Hz), 7.38 (*meta*, ^3J=8.1 Hz), 2.40 (CH_3), 13.27 (NH).

4.3.3. 3(5),4-Dibromo-5(3)-*p*-chlorophenyl-1*H*-pyrazole (4). Yield 85%, mp 200–202 °C. Calcd for $C_9H_5Br_2ClN_2$: C 32.1; H 1.5; N 8.31. Found: C 31.8; H 1.7; N 8.03%. NMR (δ, ppm): $CDCl_3$ 300 K, 7.62 (*ortho*, ^3J=8.6 Hz, ^4J=1.8 Hz), 7.47 (*meta*, ^4J=1.8 Hz), 10.85 (NH); THF-d_8 300 K, 7.74 (*ortho*, ^3J=8.6 Hz, ^4J=2.2 Hz), 7.52 (*meta*, ^4J=2.2 Hz), 12.93 (NH); THF-d_8 200 K, 7.80 (*ortho*, ^3J=8.6 Hz), 7.33 (*meta*, ^3J=8.1 Hz), 13.90 (NH); DMSO-d_6 300 K, 7.75 (*ortho*, ^3J=8.6 Hz, ^4J=2.2 Hz), 7.62 (*meta*, ^4J=2.2 Hz), 14.02 (NH).

4.3.4. 3(5),4-Dibromo-5(3)-*tert*-butyl-1*H*-pyrazole (5). Yield 74%, mp 225–226 °C. Calcd for $C_7H_{10}Br_2N_2$: C 29.82; H 3.57; N 9.93%. Found: C 29.5; H 3.82; N 9.58%. NMR (δ, ppm): THF-d_8 300 K, 1.40 (*t*-Bu), 12.23 (NH); THF-d_8 200 K, 1.40 (*t*-Bu), 12.63 (NH); DMSO-d_6 300 K, 1.34 (*t*-Bu), 13.14 (NH).

4.4. X-ray crystallographic analysis

A crystal was selected and mounted on a glass fiber with epoxy cement. Diffraction data were collected on a Bruker-AXS APEX CCD diffractometer with Mo Kα radiation (λ=0.71073 Å). The data-set was treated with SADABS absorption correction T_{min}/T_{max}=0.4031. Unit-cell parameters, tetragonal, a=9.6515(10) Å, c=21.725(5) Å, V=2023.8(5) Å^3, were determined by sampling three different sections of the Ewald sphere. The unit-cell parameters and systematic absences in the diffraction data were uniquely consistent for the reported space group $P\text{-}42_1c$ (no. 114). The structure was solved by direct methods and completed by difference Fourier synthesis. The absolute structure parameter refined to nil indicating that the true hand of the data was determined. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atom H1 was located from the difference map and refined with an isotropic parameter constrained as 0.20 U_{eq} of the nitrogen atom N1. The phenyl hydrogen atoms were treated as idealized contributions. Structure factors and anomalous dispersion coefficients are contained in SHELXTL 6.12 program library (G. Sheldrick, 2001; Siemens XRD, Madison, WI). Selected data: $C_9H_6Br_2N_2$, M=301.98, T=298(2) K, Z=8, D_{calcd}=1.982 g/cm^3, μ=7.964 mm^{-1}, $F(000)$=1152, reflections collected=22,137, unique reflections=2455, R_{int}=0.0511, refined parameters=122, GoF (F^2)=1.040, $R_1[I>2\sigma]$=0.0485, wR_2 (all data)=0.1080. The supplementary crystallographic data for this paper have been deposited under reference number CCDC 640197. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html; or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk.

4.5. NMR measurements

4.5.1. Solution. The spectra were recorded on a Bruker DRX 400 (9.4 T, 400.13 MHz for ^{1}H, 100.62 MHz for ^{13}C and 40.56 MHz for ^{15}N) spectrometer with a 5-mm inverse-detection H-X probe equipped with a z-gradient coil. Chemical shifts (δ in ppm) are given from internal solvents, DMSO-d_6 2.49 for ^{1}H and 39.5 for ^{13}C, THF-d_8 3.58 for ^{1}H and 67.6 for ^{13}C, and for ^{15}N, nitromethane (0.00) was used as an external reference. Typical parameters for ^{1}H NMR spectra were spectral width 5050–6265 Hz, pulse width 7.5 μs and resolution 0.31–0.38 Hz per point. Typical parameters for ^{13}C NMR spectra were spectral width 20,576 Hz, pulse width 10.6 μs and resolution 0.63 Hz per point; WALTZ-16 was used for broadband proton decoupling; the FIDS were multiplied by an exponential weighting (lb=1 Hz) before Fourier transformation. NOESY spectra were acquired at 300 K in the phase-sensitive mode with mixing times of 0.9–1.4 s. Inverse proton detected heteronuclear shift correlation spectra, (^{1}H–^{13}C) gs-HMQC, (^{1}H–^{13}C) gs-HMBC, and (^{1}H–^{15}N) gs-HMBC, were acquired and processed using standard Bruker NMR software and in non-phase-sensitive mode and were carried out to assign the ^{1}H, ^{13}C and ^{15}N signals. Gradient selection was achieved through a 5% sine truncated shaped pulse gradient of 1 ms. Variable temperature: a Bruker BVT3000 temperature unit was used to control the temperature and an exchanger to reach low temperatures. To avoid problems at low temperatures caused by air moisture, pure nitrogen was used as cooling gas stream.

4.5.2. Solid state. ^{13}C (100.73 MHz) and ^{15}N (40.60 MHz) CPMAS NMR spectra were obtained on a Bruker WB 400 spectrometer at 300 K using a 4-mm DVT probehead. Samples were carefully packed in a 4-mm diameter cylindrical zirconia rotor with Kel-F end-caps. Operating conditions involved 3.2 μs 90° ^{1}H pulses and decoupling field strength of 78.1 kHz by TPPM sequence. ^{13}C spectra were originally referenced to a glycine sample and then the chemical shifts were recalculated to the Me_4Si (for the carbonyl atom δ (glycine)=176.1 ppm) and ^{15}N spectra to $^{15}NH_4Cl$ and then converted to nitromethane scale using the relationship: δ ^{15}N(nitromethane)=δ ^{15}N(ammonium chloride)—338.1 ppm. The typical acquisition parameters for ^{13}C CPMAS were: spectral width, 40 kHz; recycle delay, 5 s for **5**, 35 s for **3**, and 60 s for **1**, **2**, and **4**; acquisition time, 30 ms; contact time, 2 ms; and spin rate, 12 kHz. In order to distinguish protonated and unprotonated carbon atoms, the NQS (Non-Quaternary Suppression) experiment by conventional cross-polarization was recorded; before the acquisition the decoupler is switched off for a very short time period of 25 μs. And for ^{15}N CPMAS were: spectral width, 40 kHz; recycle delay, 5 s for **5**, 35 s for **3**, and 60 s for **1**, **2**, and **4**; acquisition time, 35 ms; contact time, 7 ms; and spin rate, 6 kHz.

4.6. Theoretical calculations

All calculations were carried out using the B3LYP hybrid functional[31] with geometry optimization and frequencies at the B3LYP/6-31G*[32] level and a further optimization at the B3LYP/6-311++G** level.[33] Frequency analyses were carried out at the same level used in the geometry optimizations, and the nature of the stationary points was determined in each case according to the appropriate number of negative eigenvalues of the Hessian matrix. DMSO solvent effects were taken into account throughout this study using the polarized continuum model (PCM)[34] as implemented in

Gaussian 03.[35] Using the B3LYP/6-311++G** optimized geometries, we have calculated the GIAO absolute shieldings (see Supplementary data).[36]

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.06.007.

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