The Unusual Properties of 5-Methyl-4,5,6,7-tetrahydro-1*H*-indazole in the Solid State

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Abstract: The crystal structure of the title compound was determined by X-ray analysis at 200 K. Three independent molecules form a trimer joined by strong and linear N–H···N hydrogen bonds. There is another centrosymmetrically related trimer in the unit cell. Both tautomers (1*H* and 2*H*) are present in each trimer. Disorder of the N*H* protons involved in the N–H···N hydrogen bonds has been observed. Solid-state ^{13}C CPMAS NMR was used to establish the dynamic nature of the N*H*-proton disorder, the title compound being the first example of proton transfer in a tautomeric mixture of pyrazoles with an equilibrium constant other than 1.

Keywords
crystal structure · NMR spectroscopy · proton transfer · pyrazoles · tautomerism

Introduction

Compound **1**, although it should be named 5-methyl-4,5,6,7-tetrahydro-1*H*-indazole, has to be considered structurally as a tetramethylene-substituted pyrazole. The reason is that N*H*-indazoles are always 1*H* tautomers,[1–3] while N*H*-pyrazoles of this kind are mixtures of both tautomers **1a** and **1b** (Figure 1).[4] Tautomerism involving only annular nitrogen atoms, that is, atoms pertaining to the ring, is called "annular tautomerism".[1]

Compound **1** was prepared from 4-methylcyclohexanone in two steps and was obtained in the racemic form with respect to C(5).[5] Its crystallization is expected to yield a racemic compound since spontaneous resolution is a relatively rare phenomenon.[6] Thus four entities are possible for this compound (eight if one considers that owing to conformational flexibility of the six-membered ring, the methyl group can be axial or equatorial).

To understand why the structure of **1** in the solid state is unusual we have to summarize the present knowledge of the structure of N*H*-pyrazoles in this state, knowledge which is mainly based on X-ray crystallography and CPMAS NMR spectroscopy. Two kinds of N*H*-pyrazoles **2** have to be considered, depending on whether the substituents at positions 3 and 5 (R^3 and R^5) are identical (including the hydrogen as a substituent) or different. Compound **1** belongs to this latter group,

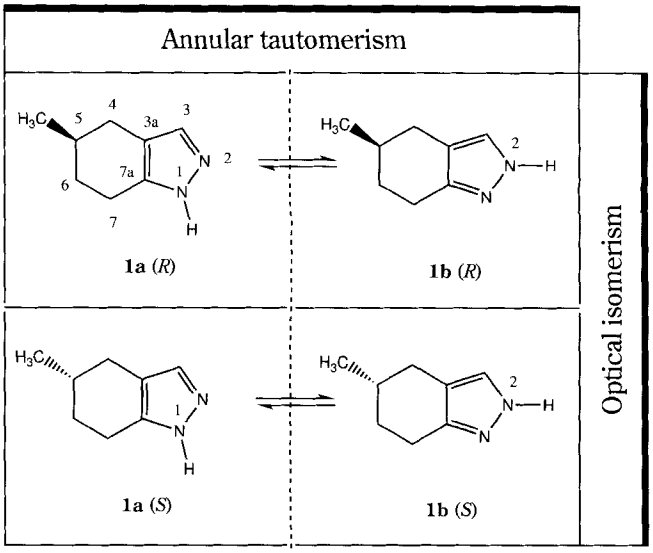

Fig. 1. Isomers of compound **1**.

the polymethylene chain $CH_2-CH(CH_3)-CH_2-CH_2$ being a special class of 4,5- (**2a**) and 3,4-disubstituted pyrazole **2b** (Scheme 1). We have summarized all the available information in Table 1 (the geometry of these and other pyrazoles has been discussed elsewhere).[25]

Regarding annular tautomerism, the thermodynamic aspects (position of the equilibrium) and the kinetic ones (proton transfer) should be distinguished. The problem of determining and discussing the equilibrium constant occurs only for the asymmetric pyrazoles. In solution and in the gas phase, asymmetric N*H*-pyrazoles exist as a mixture of tautomers **2a** and **2b** with

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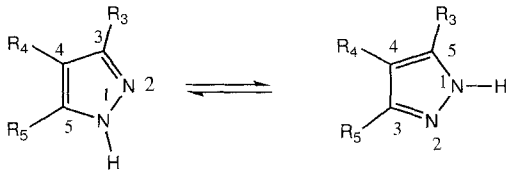


2a **2b**

Scheme 1.

Table 1. Structure of N*H*-pyrazoles in the solid state [a].

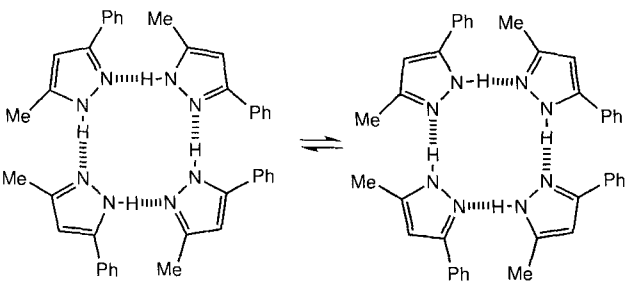
	Asymmetric, $R^3 \neq R^5$	Symmetric, $R^3 = R^5$
Cyclic dimers	**3**, R^3 = Me, R^4 = NO_2, R^5 = H [7]	**4**, $R^3 = R^5$ = Ph, R^4 = Br [8] **5**, $R^3 = R^5$ = Ph, R^4 = NO_2 [9] **6**, $R^3 = R^5$ = Bu^t, R^4 = H [10] **7**, $R^3 = R^5$ = Bu^t, R^4 = NO_2 [9]
Cyclic trimers	**8**, R^3 = H, R^4 = NO_2, R^5 = Me [7] **10**, R^3 = Ph, R^4 = Br, R^5 = H [11] **12**, Campho[*c*]pyrazole [14] **14**, R^3 = CO_2Me, R^4 = CF_3, R^5 = H [16]	**9**, $R^3 = R^5$ = H, R^4 = NO_2 [9] **11**, $R^3 = R^5$ = Me, R^4 = H [12,13] **13**, $R^3 = R^5$ = H, R^4 = Br [15]
Cyclic tetramers	**15**, R^3 = Ph(Me), R^5 = Me(Ph), R^4 = H [17–19]	**16**, $R^3 = R^5$ = Ph, R^4 = H [8]
Catamers	**17**, R^3 = N_3, R^4 = Ph, R^5 = H [20]	**18**, $R^3 = R^5 = R^4$ = H [21–23] **19**, $R^3 = R^5$ = Me, R^4 = NO_2 [24]

[a] Reference numbers are given in square brackets.

equilibrium constants which depend on the nature of R^3 and R^5 but are never very different from unity.[26, 27] In the solid state, on the other hand, there is only one tautomer present: compounds **3**, **8** (desmotropy), **10**, **12** (the 2*H* tautomer probably resulting from the Mills–Nixon effect),[4] **14** and **17**. The only exception is 3(5)-phenyl-5(3)-methylpyrazole (**15**), a cyclic tetramer formed by two 3-phenyl-5-methyl and two 3-methyl-5-phenyl tautomers.

As for the kinetic aspect of proton transfer along the intermolecular hydrogen bond, the necessary conditions for its observation are: i) the pyrazole must be symmetric; ii) the structure should be cyclic, that is, only the compounds **4**, **5**, **6**, **7**, **9**, **11**, **13** and **16** present the required structural characteristics. Here again the exception is compound **15**, where a quadruple proton transfer transforms a tetramer ($2\times$**2a** $+2\times$**2b**) into another tetramer ($2\times$**2b** $+2\times$**2a**) of the same energy, as in Scheme 2.

In summary, for asymmetric N*H*-pyrazoles one should expect either only one tautomer (dimers, trimers, tetramers and catamers) or both tautomers in a 1:1 ratio present in a cyclic, even structure ($n = 2$ dimers or $n = 4$ tetramers).



2 x **2a** + 2 x **2b** 2 x **2b** + 2 x **2a**

Scheme 2.

Results and Discussion

X-ray crystallography: The main geometrical characteristics of the molecular and crystal structure of compound **1** are reported in Table 2. The three independent molecules of the title compound form trimers in which the 1*H* tautomer, the molecules labelled as **A** and **B** in Figure 2, and the 2*H* tautomer, the molecule labelled **C**, are present. The pyrazole rings of the three

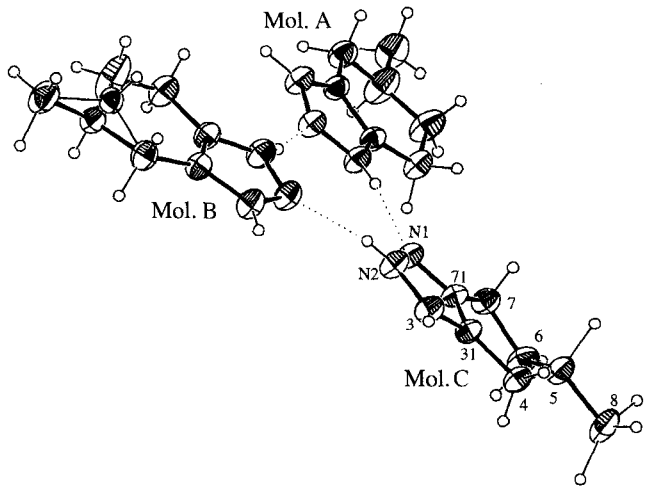


Fig. 2. A perspective view of the trimer showing the numbering system. The displacement ellipsoids are drawn at 30% probability level. The disorder of the chiral C(5) atom in molecule **B** is represented by thin lines. Dotted lines indicate hydrogen bonds; only those hydrogens with the higher population values are retained.

independent molecules do not show significant differences (tested by half normal probability plots).[28] Their geometry closely approximates the mean geometry (Table 2) describing the molecular structure of structurally related compounds: 1*H*- and 2*H*-pyrazole moieties fused to a six-membered aliphatic ring system (CSD refs: BAKTUC, CAVPAQ, YAXYIF and HXBIND, JEZGAW, LABHEB, respectively).[29] The angles at the nitrogen atoms are a sensitive indicator of the position of the hydrogen atom,[30] the protonation being associated with an increase in the N(1) and N(2) angles (1*H* or 2*H* tautomer, respectively). In the present compound these angles, which somewhat resemble those of the corresponding tautomers **1a** and **1b**, range from 107.3(3) to 109.3(2)° in fairly good agreement with the disorder model found for the corresponding hydrogen atoms, that is, two thirds of tautomer **1a** and one third of tautomer **1b**. An interpolation of the N(1) and N(2) values for **A**, **B** and **C** yields a population of 0.60 ± 0.02 for **1a** instead of the result of 2/3 found for the proton disorder.

As far as the aliphatic rings are concerned, the Csp^2–Csp^3 and Csp^3–Csp^3 distances in molecule **C** are in agreement with the reported values.[31] The differences between molecules **A** and **B** could be a result of the presence of both enantiomers within the trimer. Only the C(5) chiral atom, not the C(6) atom, in molecule **B** (Figure 2), was split into two positions (see experimental) which correspond to the *S* and *R* configurations (in one trimer there are 0.33 *R* molecules and 2.67 *S* molecules, or vice versa in the centrosymmetrically related trimer, 0.33 *S* and 2.67 *R*). Although the displacement parameters in **A** are higher

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Table 2. Selected geometrical parameters (Å, °).

				CSD results	
	A	**B**/**B′** [a]	**C**	1*H*	2*H*
N(1)–N(2)	1.352(5)	1.348(4)	1.353(4)	1.355(7)	1.363(6)
N(2)–C(3)	1.324(4)	1.327(5)	1.334(4)	1.335(11)	1.351(8)
C(3)–C(31)	1.392(5)	1.387(5)	1.380(5)	1.407(13)	1.365(6)
C(31)–C(71)	1.390(4)	1.378(4)	1.390(4)	1.371(16)	1.397(6)
N(1)–C(71)	1.345(4)	1.348(5)	1.332(4)	1.349(8)	1.325(7)
C(31)–C(4)	1.468(5)	1.487(6)	1.499(5)		
C(4)–C(5)/C(5′)	1.452(7)	1.559(7)/1.402(13)	1.526(5)		
C(5)/C(5′)–C(6)	1.384(6)	1.369(8)/1.516(14)	1.518(6)		
C(5)/C(5′)–C(8)	1.517(6)	1.557(10)/1.535(14)	1.532(7)		
C(6)–C(7)	1.459(5)	1.477(8)	1.521(5)		
C(7)–C(71)	1.451(6)	1.478(5)	1.496(5)		
N(2)-N(1)-C(71)	109.3(2)	108.6(3)	107.3(3)	112.2(5)	103.6(8)
N(1)-N(2)-C(3)	107.3(3)	107.5(3)	108.9(3)	104.7(11)	112.3(5)
N(2)-C(3)-C(31)	110.7(3)	110.5(3)	109.3(3)	111.2(9)	106.8(2)
C(3)-C(31)-C(71)	104.0(3)	104.1(3)	104.1(3)	104.9(4)	104.7(4)
N(1)-C(71)-C(31)	108.5(3)	109.1(3)	110.2(3)	107.0(6)	112.5(9)
C(31)-C(4)-C(5)/C(5′)-C(6)	−25.3(6)	−35.2(7)/29.1(12)	−47.6(4)		
C(4)-C(5)/C(5′)-C(6)-C(7)	34.5(7)	45.5(9)/−25.6(13)	65.1(4)		
C(5)/C(5′)-C(6)-C(7)-C(71)	−23.5(6)	−29.5(8)/6.8(9)	−45.4(4)		
C(6)-C(7)-C(71)-C(31)	6.4(5)	6.6(6)	14.3(5)		
C(7)-C(71)-C(31)-C(4)	−0.0(5)	−1.6(6)	−0.8(5)		
C(71)-C(31)-C(4)-C(5)/C(5′)	8.6(5)	14.5(5)/−17.4(8)	17.5(4)		
Cremer and Pople parameters					
*q*2 (Å)	0.175(4)	0.235(6)/0.211(9)	0.377(3)		
*q*3 (Å)	−0.146(4)	−0.205(5)/0.109(7)	−0.324(4)		
*θ*2 (°)	129.8(8)	131.1(7)/62.0(11)	130.6(4)		
*ϕ*2 (°)	−34.6(12)	−44.9(12)/102.7(14)	−33.3(6)		
Central ring of the trimer					
N(1A)–N(2A)···N(1B)–N(2B)	12.5(4)	q2(Å)	0.165(3)		
N(2A)···N(1B)–N(2B)···N(2C)	−4.9(3)	q3(Å)	0.006(3)		
N(1B)–N(2B)···N(2C)–N(1C)	−6.3(3)	*θ*2(°)	87.9(9)		
N(2B)···N(2C)–N(1C)···N(1A)	11.3(3)	*ϕ*2(°)	81.2(9)		
N(2C)–N(1C)···N(1A)–N(2A)	−4.2(4)				
N(1C)···N(1A)–N(2A)···N(1B)	−7.7(3)				
Hydrogen interactions	X–H	H···X	X···Y	X–H···Y	
N(1A)–H(1A)···N(1C)	0.85(6)	2.02(6)	2.879(4)	175(7)	
N(1B)–H(1B)···N(2A)	0.93(8)	1.94(8)	2.866(4)	173(7)	
N(2C)–H(2C)···N(2B)	0.83(–)	2.07(–)	2.893(5)	168(–)	
N(2A)–H(2A)···N(1B)	1.14(15)	1.78(14)	2.866(4)	157(11)	
N(2B)–H(2B)···N(2C)	1.09(15)	1.83(15)	2.893(5)	165(11)	
N(1C)–H(1C)···N(1A)	0.82(–)	2.07(–)	2.879(4)	164(–)	

[a] A prime (′) stands for the disordered positions in molecule B.

than those of molecule **C**, a disorder model for **A** could not be established. The six-membered ring in molecules **A** and **C** adopts a slightly distorted half-chair conformation (Table 2) more puckered in **C** [Q_T = 0.228(5) vs. 0.498(4) Å],[32] while the conformations of the disordered molecules, **B** and **B′**, are intermediate between half-chair and envelope conformations, with total puckering amplitudes of 0.313(7) and 0.238(8) Å, respectively. The presence of disorder in **B** and probably to a lesser extent in **A** affects their conformation, increasing their puckering.

The six nitrogen atoms of the independent trimer form a pseudo six-membered ring, neglecting the hydrogen atoms, which adopts a nearly ideal skew conformation (Table 2). The molecules in a trimer are connected by rather strong and linear hydrogen bonds, as compared with those reported for compounds **8** and **14** (Tables 2 and 3). The largest N···N distance exists in compound **11** with methyl groups at C(3) and C(5) and a planar central ring; the weighted average distance is 2.909(1) Å. Only van der Waals interactions are responsible for the packing of the trimers (Figure 3).

Table 3. Geometry of the independent hydrogen interactions in cyclic trimers of N*H* pyrazoles (Å, °). Compounds **9** and **11** present dynamic disorder.

Compound	N···N	N–H···N
8, R^3 = H, R^4 = NO_2, R^5 = Me	2.875(7)	163(8)
	2.872(9)	157(7)
	2.900(7)	162(10)
9, R^3 = R^5 = H, R^4 = NO_2	2.858(4)	168(6)
	2.872(4)	159(8)
	2.880(3)	167(6)
	2.880(3)	177(9)
	2.858(4)	172(9)
	2.872(4)	167(7)
10, R^3 = Ph, R^4 = Br, R^5 = H	2.851(7)	170(9)
	2.869(7)	166(7)
	2.931(8)	162(7)
11, R^3 = R^4 = Me, R^5 = H	2.978(6)	172(–)
12, Campho[*c*]pyrazole	2.911(4)	177(5)
	2.931(3)	171(5)
	2.933(3)	173(5)
	2.936(3)	178(3)
	2.914(3)	170(3)
	2.910(3)	179(5)
14, R^3 = CO_2Me, R^4 = CF_3, R^5 = H	2.874(5)	168(5)
	2.902(6)	168(4)
	2.964(5)	163(4)

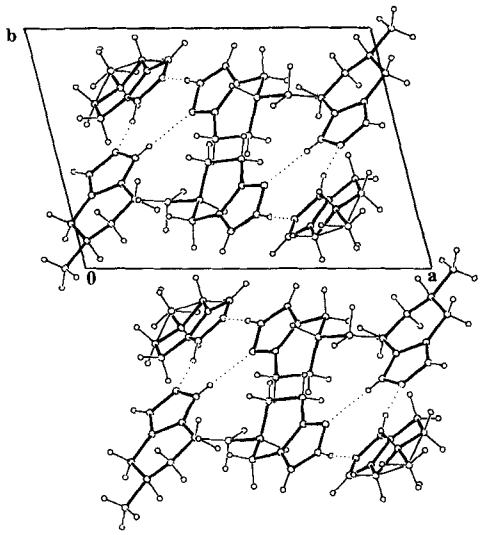

Fig. 3. Packing of the trimers (diagram along the *c* axis).

^{1}H NMR spectroscopy: In order to obtain information about the conformation of the six-membered ring in solution, we recorded the spectrum of pyrazole **1** in $CDCl_3$ at 500 MHz. We also carried out semiempirical AM1 calculations[33] on the compound to obtain the values of the dihedral angles. The system formed by the 11 protons [H(3)–H(4a)–H(4b)–H(5)(CH_3)–H(6a)–H(6b)–H(7a)–H(7b)] is too complex to be analyzed directly, so the analysis[32] was carried out on a series of ^{1}H-decoupled spectra [H(3) decoupled and Me decoupled]; the assignment of the different protons was sustained by ^{1}H–^{1}H two-dimensional spectroscopy. The result of the analysis is reported in Table 4.

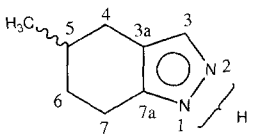

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Table 4. ^{1}H NMR chemical shifts (δ) and coupling constants (Hz) of compound **1** in $CDCl_3$ at 499.88 MHz according to the iterative analysis (rms error 0.01 Hz). Calculated vicinal coupling constants in Hz (H-C-C-H dihedral angles in degrees) for AM1 optimized geometries.

	δ		δ
H(4a)	2.090	H(7a)	2.628
H(4e)	2.637	H(7e)	2.751
H(5)	1.809	Me(5)	1.054
H(6a)	1.440	H(3)	7.265
H(6e)	1.881		
^3J vicinal coupling constants		Me_{eq}	Me_{ax}
^3J[H(4a),H(5)]	10.16	11.55 (166.17)	1.16 (78.78)
^3J[H(4e),H(5)]	5.05	5.28 (48.89)	5.83 (−38.19)
^3J[H(5),H(6a)]	11.04	12.31 (177.05)	2.83 (−61.24)
^3J[H(5),H(6e)]	2.72	2.53 (−65.46)	3.55 (55.83)
^3J[H(6a),H(7a)]	11.15	12.42 (163.39)	1.19 (71.51)
^3J[H(6a),H(7e)]	5.61	5.96 (45.47)	5.80 (−46.39)
^3J[H(6e),H(7a)]	5.94	5.80 (46.06)	5.76 (−45.50)
^3J[H(6e),H(7e)]	3.04	1.19 (−71.86)	12.42 (−163.42)

Other coupling constants

^4J[H(4e),H(6e)](W) = 1.32 Hz; ^5J[H(4a),H(7a)] = 1.55 Hz;
^5J[H(4a),H(7e)] = 0.84 Hz; ^5J[H(4e),H(7a)] = 0.83 Hz;
^5J[H(4e),H(7e)] = 0.00 Hz; ^4J[H(4e),H(3)] = 0.82 Hz;
^3J[Me(5),H(5)] = 6.69 Hz.

Semiempirical calculations with the AM1 Hamiltonian for the two conformations of the 5-methyl group, axial and equatorial, led to two local minima, the equatorial situation being more stable by 1.5 kcal mol^{-1}. The crystallographically observed molecule **C** is very similar to the calculated one (methyl equatorial); for instance the H-C-C-H torsion angles show a linear relationship [AM1 (torsion angles) = 0.98 ± 0.01 mol; **C** (torsion angles) $n = 8$, $r^2 = 0.999$]. The geometries of molecule **A** and particularly molecule **B** differ more from those calculated by AM1, but this could partly be a consequence of the disorder.

If the vicinal H-C-C-H coupling constants of Table 4 are compared with the couplings calculated (by means of a Karplus relationship[35]) for the equatorial and axial conformations (AM1 minimized geometries) it appears that in solution 85% of Me_{eq} and 15% of Me_{ax} is present instead of the 100% of Me_{eq} present in the crystal (note that the disorder in the crystal involves C(5) and not the methyl group).

^{13}C CPMAS NMR spectroscopy: Compound **1** presents the following signals assigned in ^{1}H–^{13}C 2D experiments at 125 MHz in $CDCl_3$ solution: $\delta = 22.02$ [CH_3(5)], 25.06 [CH(5)], 29.44 [CH_2(4)], 30.40 [CH_2(7)], 31.98 [CH_2(6)], 115.66 [C(3a)], 132.26 [broad, C(3)], 143.68 [broad, C(7a)]. The CPMAS NMR spectrum at 100 MHz is represented in Figure 4.

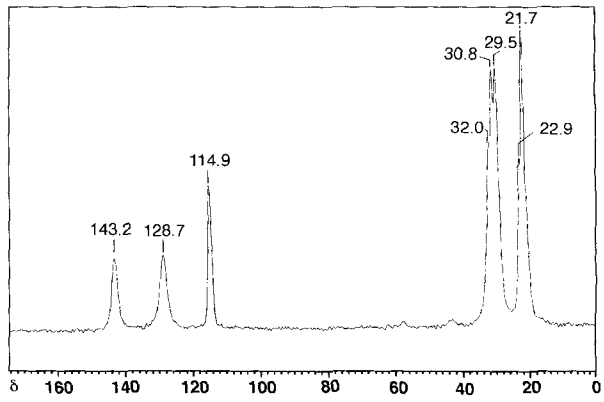

Fig. 4. ^{13}C CPMAS NMR spectrum of compound **1**.

The highfield part originates with sp^3 carbons, 21.7 [CH_3(5)], 22.9 [CH_3(5)], 29.5 and 30.8, CH(5), CH_2(4) and CH_2(7)] and 32.0 [CH_2(6)], and the lowfield part to the three pyrazole sp^2 carbons, 114.9 [C(3a)], 128.7 [C(3)] and 143.2 [C(7a)]. Two points should be noted, the existence of two signals for the 5-methyl group, and the broadening of pyrazole carbons C(3) and C(7a) compared with pyrazole C(4). The splitting of the 5-methyl group is not due to the presence of tautomers **1a** and **2a** (see later on) but to the crystallographic disorder of chiral C(5) in the racemic compound (1/8 ratio).

From related pyrazoles[4] it is possible to estimate the chemical shifts of aromatic carbons in both tautomers: **1a**: 133.3 C(3), 114.9 C(3a) and 139.1 C(7a); **1b**: 123.1 C(3), 114.9 C(3a) and 148.3 C(7a). The signals of C(3a) for both tautomers are identical or very similar, but those of C(3) and C(7a) appear as two broad signals centred at $\delta = 128.7$ and 143.2 instead of four signals. The position corresponds to approximately 50% of **1a** and 50% of **1b** and the broadening (including that of C(3a)) can

0947-6539/97/0301-0124 $ 15.00+.25/0 Chem. Eur. J. 1997, 3, No. 1

be simulated with a bandwidth of 30 Hz and a rate constant $k_{ab} = 1800\ s^{-1}$. For the experimental temperature of 300 K, this rate corresponds to $\Delta G^{\ddagger}_{ab} = 13.1$ kcal mol^{-1}.

Conclusions

Tetrahydroindazole **1** presents a mixture of static and dynamic disorder that only the combined use of crystallography and NMR was able to resolve. The static disorder (narrow lines in NMR) concerns C(5): of the two trimers present in the unit cell one contains 1/9 *S* enantiomer and 8/9 *R* enantiomer, while the other contains 1/9 *R* enantiomer and 8/9 *S* enantiomer. Obviously the splitting of the *C*-methyl signals (Figure 4) is not directly due to the enantiomerism but rather to the presence of the minor enantiomer in a trimer formed by the other predominant enantiomer. The ratio in the ^{13}C CPMAS NMR spectrum seems larger than the crystallographic 1/8 ratio, indicating that may be there is also disorder in another molecule of the trimer (molecule **A**).

The dynamic disorder involves the N*H* protons, and in order to discuss it we have represented the equilibrium of a trimer in Figure 5. In crystallography there are two methods for estimation of the populations of the two trimers: the direct method based on the electron density of the N*H* protons (66% of the left trimer and 34% of the right trimer) and the indirect method based on the interpolation of the internal angles of the N atoms (60% of the left trimer and 40% of the right trimer). Since both methods give roughly the same populations, let us assume there is a 60/40 ratio of trimers in equilibrium. To calculate the percentages of tautomers **1a** and **1b**, it suffices to calculate $0.6(2\times\mathbf{1a}) + 0.4(\mathbf{1a}) = 1.6$ of **1a**, and $0.6(\mathbf{1b}) + 0.4(2\times\mathbf{1b}) = 1.4$, that is 53% **1a** and 47% **1b** ($K_T = 1.14$) (if the 66/34 ratio is used, the results are 56% **1a**, 44% **1b**, $K_T = 1.25$).

In summary, the asymmetric N*H*-pyrazoles crystallize in single tautomeric forms or in 1:1 mixtures of both tautomers, with the exception of compound **1**. This is the only pyrazole which crystallizes as a trimer in which both tautomers are present in amounts that are different but not very different (55:45) owing to a fast proton exchange (on the NMR timescale). The activation energy, 13.1 kcal mol^{-1}, is similar to that measured accurately for 3,5-dimethylpyrazole, 13.47 kcal mol^{-1} at 302 K[13]. More generally, the presence of two tautomers in a single crystal is a very infrequent situation, and when this happens they are present in exactly equal proportions, compound **1** being the only exception to this observation. Of the eight possibilities that compound **1** could present (see introduction) only four are found in the crystal, since all the methyl groups are equatorial: 26% **1a** *R*, 26% **1a** *S*, 22% **1b** *R* and 22% **1b** *S*.

Table 5. Crystal analysis parameters at 200 K.

crystal data formula	$C_8H_{12}N_2$
crystal habit	colourless prism
crystal size (mm)	0.63 × 0.23 × 0.30
symmetry	triclinic, $P\bar{1}$
unit cell determination	least-squares fit from 37 refins ($\theta < 45°$)
a (Å)	13.612(3)
b (Å)	9.618(2)
c (Å)	9.435(2)
α, β, γ (°)	96.31(2), 81.18(1), 104.97(3)
packing: V (Å^3), Z	1176.1(5), 6
ρ_{calcd} (g cm^{-3}), M, $F(000)$	1.154, 136.19, 444
μ (cm^{-1})	5.474
experimental data technique	four-circle diffractometer: Philips PW1100, bisecting geometry. Graphite oriented monochromator: $\omega/2\theta$ scans. Detector apertures 1 × 1°, 0.5 min/refln.
radiation	$Cu_{K\alpha}$
scan width (°)	1.5
θ_{max} (°)	65
no. of independent refins	3995
no. of observed refins	2627 ($2\sigma(I)$ criterion)
standard refins	2 refins every 90 minutes; no variation
solution and refinement	
solution	direct methods: Sir92
refinement	least-squares on F_{obs}, full matrix
parameters:	
number of variables	401 [a]
degrees of freedom	2226
ratio of freedom	6.6
final shift/error	0.036
H atoms	from difference synthesis
weighting scheme	empirical as to give no trends in $\langle\omega\Delta^2F\rangle$ vs. $\langle\lvert F_{obs}\rvert\rangle$ and $\langle\sin\theta/\lambda\rangle$
max. thermal value (Å^2)	U11 (C(6) mol · B) = 0.136(4)
final ΔF peaks (e Å^{-3})	−0.36/0.27
final *R and Rw*	0.062, 0.069

[a] See experimental.

Experimental Section

Equipment: ^{1}H and ^{13}C NMR spectra in solution were acquired on a Varian 500 Unity spectrometer. The ^{13}C CPMAS NMR spectrum was recorded on a Bruker DSX-500 at 125.76 MHz with the facilities of Bruker Analytische Messtechnik (Karlsruhe, Germany).

5-Methyl-4,5,6,7-tetrahydro-1*H*-indazole (1) was prepared as described in ref. [5]. Crystals suitable for X-ray diffraction were obtained by slow evaporation of an ethanol solution. M.p. 75 °C.

X-ray structure determination: The most relevant details of data collection and the refinement procedure are given in Table 5. The crystal used in data collection was enclosed in a Lindemann capillary to prevent sublimation and was cooled to 200 K with an Oxford Cryostream device;

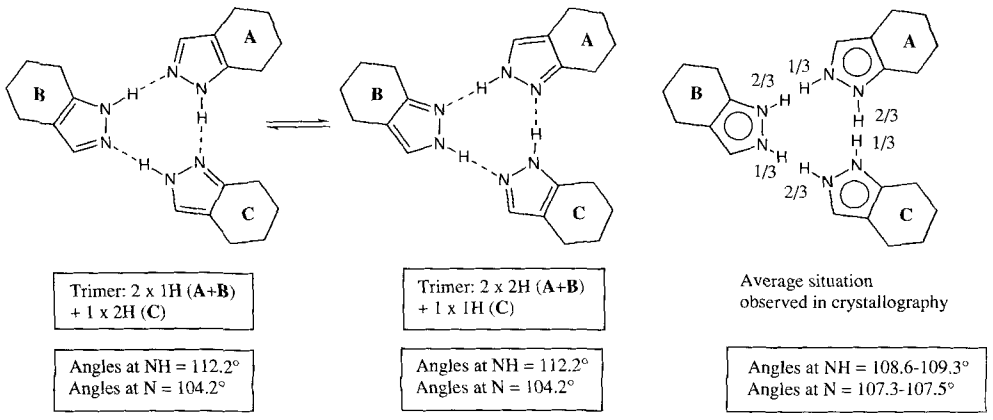

Fig. 5. A schematic representation of the tautomers in tetrahydroindazole **1** (for simplicity the 5-Me group has been omitted).

the stated temperature was measured continuously during data collection. The structure was solved by means of the SIR92 program [36]. The refinement was carried out by full-matrix least-squares procedures on F_{Obs}. The hydrogen atoms, the positions of which were obtained from difference Fourier synthesis, were included in the refinement, although some of them were kept fixed in the last cycles. The six-membered rings in molecule **B** appear to be statistically disordered because of the presence of both *S* and *R* configurations (occupancy factors of 0.66(2) and 0.34(2), respectively). In spite of the high thermal factors displayed by the atoms C(5), C(6) in molecule **A** and mainly by C(6) in molecule **B**, a disorder model for these atoms could not be obtained (Figure 2). Besides, disorder of the protons at N(1) and N(2) is also observed (0.65(4) and 0.35(4) population factors). Most of the calculations were performed by the XTAL3.2-system [37], PESOS [38] and PARST [39] programmes. The atomic scattering factors were taken from ref. [40]. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1220-39. Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (Fax: Int. code +(1223)336-033; e-mail: teched@chemcrys.cam.ac.uk).

Acknowledgments: The authors thank the European Community for financial support, Project No. CHRX-CT94-0582. O. H. gratefully acknowledges a grant from the same project. We are indebted to Dr. Marfisi (Bruker Española) for the ^{13}C CPMAS NMR spectrum.

Received: July 8, 1996 [F412]

[1] J. Elguero, C. Marzin, A. R. Katritzky, P. Linda, *The Tautomerism of Heterocycles*, Academic Press, New York, **1976**, pp. 29, 266 and 412.
[2] J. Catalán, J. L. G. de Paz, J. Elguero, *J. Chem. Soc. Perkin Trans.* **1996**, 257–260.
[3] C. Foces-Foces, O. Hager, S. Trofimenko, N. Jagerovic, J. Elguero, *Acta Crystallogr. Sect. C* **1996**, in press.
[4] A. Martínez, M. L. Jimeno, J. Elguero, A. Fruchier, *New. J. Chem.* **1994**, *18*, 269–277.
[5] J. Elguero, A. Fruchier, R. Jacquier, *Bull. Soc. Chim. Fr.* **1967**, 2619–2630.
[6] J. Jacques, A. Collet, S. H. Willem, *Enantiomers, Racemates, and Resolutions*, Krieger, Malabar, Florida, **1994**.
[7] C. Foces-Foces, A. L. Llamas-Saiz, R. M. Claramunt, C. López, J. Elguero, *J. Chem. Soc. Chem. Commun.* **1994**, 1143–1145.
[8] F. Aguilar-Parrilla, G. Scherer, H. H. Limbach, C. Foces-Foces, F. H. Cano, J. A. S. Smith, C. Toiron, J. Elguero, *J. Am. Chem. Soc.* **1992**, *114*, 9657–9659.
[9] A. L. Llamas-Saiz, C. Foces-Foces, F. H. Cano, P. Jiménez, J. Laynez, W. Meutermans, J. Elguero, H. H. Limbach, F. Aguilar-Parrilla, *Acta Crystallogr. Sect. B* **1994**, *50*, 746–762.
[10] F. Aguilar-Parrilla, H. H. Limbach, C. Foces-Foces, F. H. Cano, N. Jagerovic, J. Elguero, *J. Org. Chem.* **1995**, *60*, 1965–1970.
[11] F. Aguilar-Parrilla, C. Cativiela, M. D. Diaz de Villegas, J. Elguero, C. Foces-Foces, J. I. García, F. H. Cano, H. H. Limbach, J. A. S. Smith, C. Toiron, *J. Chem. Soc. Perkin Trans. 2* **1992**, 1737–1742.
[12] A. Baldy, J. Elguero, R. Faure, M. Pierrot, E. J. Vincent, *J. Am. Chem. Soc.* **1985**, *107*, 5290–5291.
[13] J. A. S. Smith, B. Wehrle, F. Aguilar-Parrilla, H. H. Limbach, C. Foces-Foces, F. H. Cano, J. Elguero, A. Baldy, M. Pierrot, M. M. T. Khursid, J. B. Larcombe-McDouall, *J. Am. Chem. Soc.* **1989**, *111*, 7304–7312.
[14] A. L. Llamas-Saiz, C. Foces-Foces, I. Sobrados, J. Elguero, W. Meutermans, *Acta Crystallogr. Sect. C* **1993**, *49*, 724–729.
[15] C. Foces-Foces, C. Fontenas, J. Elguero, H. H. Limbach, O. Klein, unpublished results.
[16] B. Beagley, K. J. Farnworth, E. T. Moss, R. G. Pritchard, S. Tajammal, A. E. Tipping, *Acta Crystallogr. Sect. C* **1994**, *50*, 1130–1132.
[17] E. N. Maslen, J. R. Cannon, A. H. White, A. C. Willis, *J. Chem. Soc. Perkin Trans. 2* **1974**, 1298–1301.
[18] F. H. Moore, A. H. White, A. C. Willis, *J. Chem. Soc. Perkin Trans. 2* **1975**, 1068–1071.
[19] J. Elguero, N. Jagerovic, C. Foces-Foces, F. H. Cano, M. V. Roux, F. Aguilar-Parrilla, H. H. Limbach, *J. Heterocycl. Chem.* **1995**, *32*, 451–456.
[20] P. Domiano, A. Musatti, *Cryst. Struct. Commun.* **1974**, *3*, 713–715.
[21] J. Berthou, J. Elguero, C. Rérat, *Acta Crystallogr. Sect. B* **1970**, *26*, 1880–1881.
[22] F. K. Larsen, M. S. Lehmann, I. Søtofte, S. E. Rasmussen, *Acta Chem. Scand.* **1970**, *24*, 3248–3258.
[23] T. La Cour and S. E. Rasmussen, *Acta Chem. Scand.* **1973**, *27*, 1845–1854.
[24] C. Foces-Foces, F. H. Cano, J. Elguero, *Gazz. Chim. Ital.* **1993**, *123*, 477–479.
[25] A. L. Llamas-Saiz, C. Foces-Foces, J. Elguero, *J. Mol. Struct.* **1994**, *319*, 231–260.
[26] J. L. M. Abboud, P. Cabildo, T. Cañada, J. Catalán, R. M. Claramunt, J. L. G. de Paz, J. Elguero, H. Homan, R. Notario, C. Toiron, G. I. Yranzo, *J. Org. Chem.* **1992**, *57*, 3938–3946.
[27] A. El Hammadi, M. El Mouhtadi, R. Notario, J. L. M. Abboud, J. Elguero, *J. Chem. Res.* **1995**, 172–173 (M, 1080–1096).
[28] S. Abrahams, E. T. Keve, *Acta Crystallogr.* **1971**, *A27*, 157–165.
[29] F. H. Allen, J. E. Davies, J. J. Galloy, O. Johnson, O. Kennard, C. F. Macrae, E. M. Mitchell, J. F. Mitchell, J. M. Smith, D. G. Watson, *J. Chem. Info. Comput. Sci.* **1991**, *31*, 187–204.
[30] F. Toda, K. Tanaka, C. Foces-Foces, L. Infantes, R. M. Claramunt, C. López, J. Elguero, *J. Phys. Org. Chem.* **1996**, *9*, 611–618.
[31] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc. Perkin Trans. 2* **1987**, S1–S19.
[32] D. Cremer, J. A. Pople, *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
[33] M. J. S. Dewar, E. B. Zoebisch, E. F. Healy, J. J. P. Stewart, *J. Am. Chem. Soc.* **1986**, *108*, 8075–8086.
[34] PANIC86, Bruker Program Library (Germany).
[35] C. Altona, J. H. Ippel, A. J. A. W. Hoekzema, C. Erkelens, M. Groesbeek, L. A. Donders, *Magn. Reson. Chem.* **1989**, *27*, 564, and references cited therein.
[36] A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, G. Polidori, *J. Appl. Crystallogr.* **1994**, 435–435.
[37] S. R. Hall, H. D. Flack, J. M. Stewart, Xtal3.2, Univ. of Western Australia, Perth, **1994**.
[38] M. Martínez-Ripoll, F. H. Cano, **1975**, program not published.
[39] M. Nardelli, *Comput. Chem.* **1983**, *7*, 95–98.
[40] *International Tables for X-Ray Crystallography, Vol. IV*, Kynoch, Birmingham, **1974**.