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HOST–GUEST CHEMISTRY. THE STRUCTURE AND PROTON DISORDER OF THE THREE-COMPONENT CRYSTAL FORMED BY 3(5)-METHYL-4-NITROPYRAZOLE, (*R*,*R*)-(−)-*TRANS*-4,5-BIS(HYDROXYDIPHENYLMETHYL)-2,2-DIMETHYL-1,3-DIOXOLANE AND TOLUENE

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The crystal structure at 200 K of the complex formed by the optically active host (*R*,*R*)-(−)-*trans*-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxolane (2) and 4-nitro-5-methylpyrazole (1b) and toluene as guests was determined by x-ray analysis. Although only the NH protons corresponding to tautomer 1b were found in the structure, some anomalies in the bond angles involving the nitrogen atoms of the pyrazole ring suggested the presence of about 25% of a structure containing the 3-methyl-4-nitropyrazole tautomer (1a). This hypothesis was confirmed by ^{13}C cross polarization magic angle spinning NMR spectroscopy.

INTRODUCTION

Previously, we have reported that pyrazole itself (guest $\mathbf{G_1}$) when included in 1,1-bis(2,4-dimethylphenyl)but-2-yn-1-ol (host $\mathbf{H_1}$) forms a cyclic structure $(\mathbf{H_1G_1})_2$ which shows intermolecular proton transfer in the crystal.[1] In addition, we have determined the structure of 3(5)-methyl-4-nitropyrazole (**1**): this compound presents an unusual phenomenon of desmotropy; depending on the solvent, the 3-methyl (**1a**) or the 5-methyl tautomer (**1b**) crystallizes.[2] In this paper, we report the preparation of the inclusion compound of **1** into Seebach diol **2** as host,[3–5] its solid-phase crystallographic study and cross polarization magic angle spinning (CP/MAS) NMR characterization. Our aim was to study the problems related to proton disorder by crystallography and CP/MAS NMR.

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RESULTS AND DISCUSSION

X-ray crystallography

By slow evaporation of an equimolar mixture of **1** and **2** in toluene, we obtained single crystals the ^1H NMR spectra of which in solution revealed to be a 1:1:1 mixture of **1**, **2** and toluene. The crystal structure determination showed that there are two complexes in the asymmetric unit which include two solvent toluene molecules (a 2:2:2 mixture). The absolute configuration of **2** was not determined since it was known from its synthetic origin (tartaric acid). The molecular structure of the host [Figure 1(a)], as previously reported,[6,7] appears to be rigid owing to the formation of an intramolecular hydrogen bond (Table 1). The dioxolane rings exhibit slightly distorted chair conformations where the C-(12)/C-(13) and C-(22)/C-(23) atoms lie above and below the planes defined by

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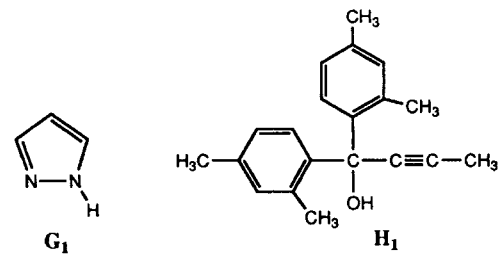
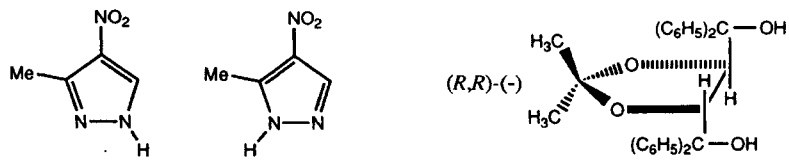


G_1 H_1



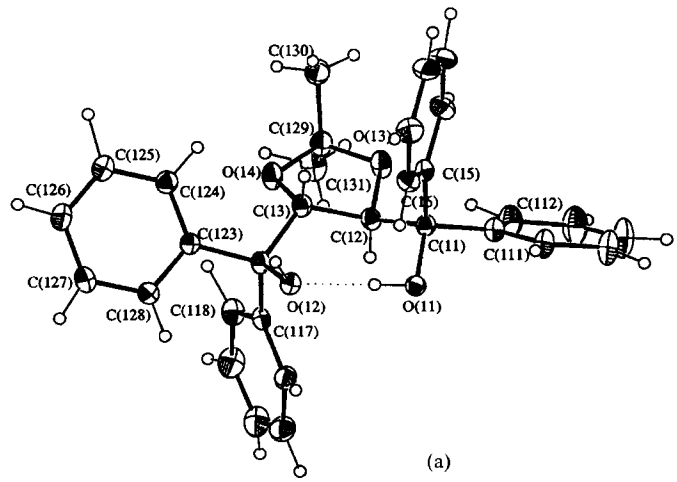
1a **1b** **2**

Table 1. Selected geometrical parameters (bond lengths in Å, angles in degrees)[a]

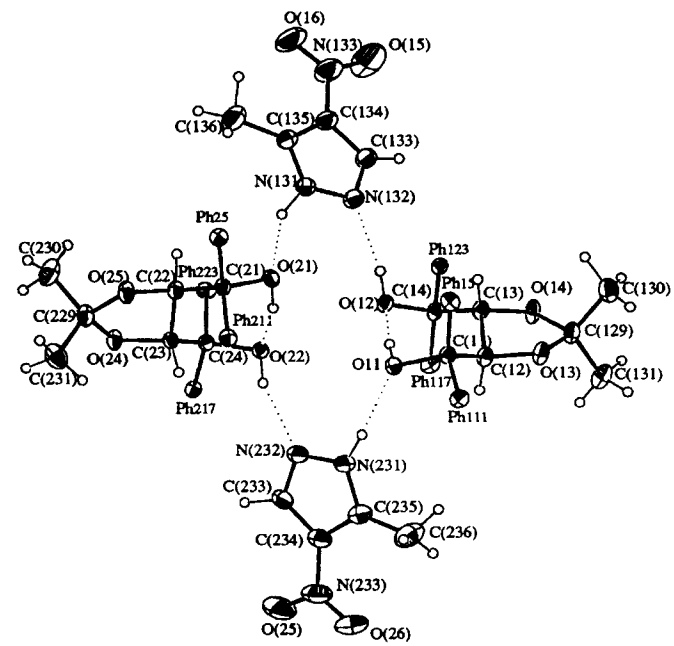
Host	$i=1$	$i=2$	Host	$i=1$	$i=2$
O(i1)—C(i1)	1·439(6)	1·449(4)	C(i1)—C(i2)	1·553(5)	1·540(7)
C(i2)—C(i3)	1·547(7)	1·548(7)	C(i3)—C(i4)	1·548(7)	1·558(5)
O(i2)—C(i4)	1·437(5)	1·438(6)			
O(i1)—C(i1)—C(i2)—C(i3)	72·7(5)	71·6(5)	C(i1)—C(i2)—C(i3)—C(i4)	−83·5(5)	−81·4(5)
C(i2)—C(i3)—C(i4)—O(i2)	70·5(5)	71·5(5)	O(i3)—C(i2)—C(i3)—O(i4)	36·2(4)	37·1(4)
C(i29)—O(i3)—C(i2)—C(i3)	−31·3(5)	−32·2(4)	O(i4)—C(i29)—O(i3)—C(i2)	14·3(5)	14·7(5)
C(i3)—O(i4)—C(i29)—O(i3)	11·1(5)	11·1(5)	C(i2)—C(i3)—O(i4)—C(i29)	−29·3(5)	−29·8(4)
C(i2)—C(i1)—C(i5)—C(i6)	112·0(5)	105·2(5)	C(i2)—C(i1)—C(i11)—C(i12)	8·8(7)	−7·1(6)
C(i3)—C(i4)—C(i17)—C(i18)	−65·9(5)	−48·7(6)	C(i3)—C(i4)—C(i23)—C(i24)	−5·8(6)	−2·2(6)
C(i35)—C(i34)—C(i33)—O(i6)	−1·6(12)	4·8(11)			
Guest: pyrazole	$i=1$	$i=2$	Guest: pyrazole	$i=1$	$i=2$
N(i31)—N(i32)	1·358(6)	1·357(7)	N(i32)—C(i33)	1·316(7)	1·316(8)
C(i33)—C(i34)	1·373(8)	1·384(9)	C(i34)—C(i35)	1·387(7)	1·393(9)
N(i31)—C(i35)	1·342(8)	1·333(8)			
N(i32)—N(i31)—C(i35)	111·6(5)	112·1(5)	N(i31)—N(i32)—C(i33)	106·8(4)	106·8(4)
N(i32)—C(i33)—C(i34)	109·2(5)	108·9(5)	C(i33)—C(i34)—C(i35)	107·9(5)	107·5(5)
N(i31)—C(i35)—C(i34)	104·6(5)	104·6(5)			

Hydrogen interactions	XH	X···Y	H···Y	X—H···Y
O(11)—H(101)···O(12)	0·87(7)	2·630(4)	1·76(7)	174(7)
O(12)—H(102)···N(132)	0·83(7)	2·780(6)	1·97(7)	168(7)
N(131)—H(131)···O(21)	1·09(8)	2·802(5)	1·80(8)	151(7)
O(21)—H(201)···O(22)	1·10(10)	2·621(4)	1·54(10)	166(8)
O(22)—H(202)···N(232)	0·84(9)	2·809(6)	2·01(9)	159(9)
N(231)—H(231)···O(11)	0·94(8)	2·820(6)	1·92(8)	160(6)
C(140)—H(140)···O(16)(1 − x, 1/2 + y, 1 − z)	1·03(19)	3·363(22)	2·60(18)	131(12)
C(226)—H(226)···C(A)(1 − x, −1/2 + y, 1 − z)	0·96(10)	3·597(7)	2·73(10)	150(8)

[a] O(i1)—C(i1), i = 1, 2 means O(11)–C(11) and O(21)–C(21), and so on. C(A) stands for the centroid of the undisordered toluene ring.

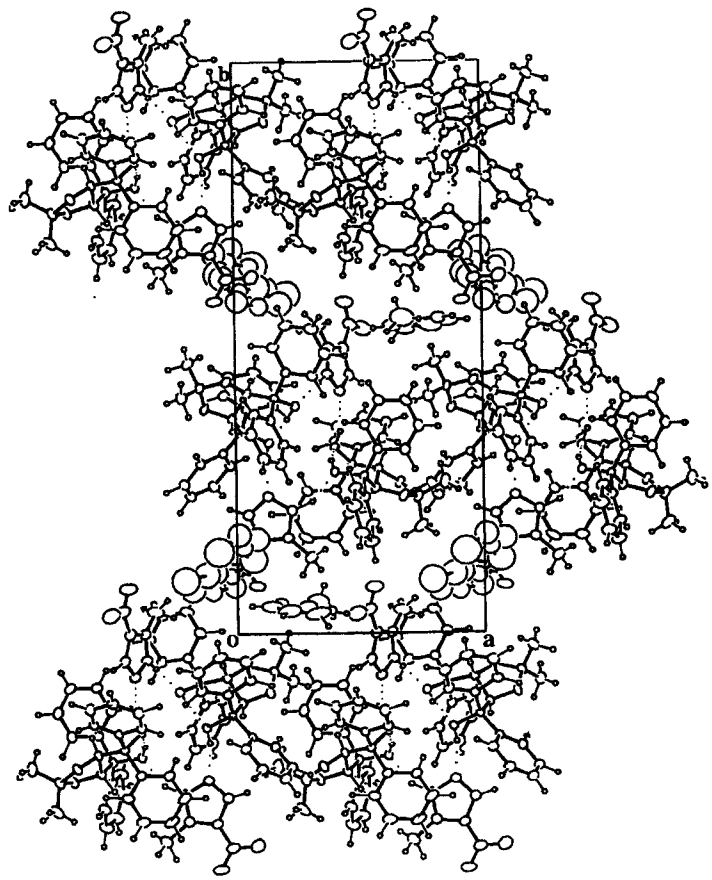


(a)



(b)

Figure 1. (a) An Ortep[12] view of the host (molecule 1) showing the atomic numbering. (b) View of the complex showing the symmetry of the dimer and the hydrogen bonds system (dotted lines). Phenyl rings are omitted for clarity. (c) Crystal packing along the c axis. Ellipsoids are drawn at the 30% probability level

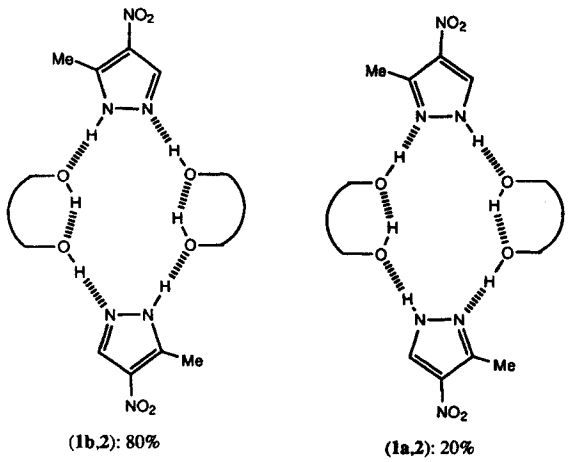


(c)

Figure 1. *Continued*

the other atoms [Cremer and Pople's parameters[8] are $q_2 = 0{\cdot}325(4)$, $0{\cdot}359(4)$ Å and $\Phi_2 = -164{\cdot}2(7)$, $-164{\cdot}5(7)°$ vs $\Phi_2 = -162°$ for an ideal chair conformation]. The differences between host molecules, as tested by half-normal probability plots,[9] are mainly those concerning the different twist of the phenyl rings (Table 1). Apart from that, the host and the guest molecules are almost related by a twofold axis parallel to the z axis.[10] The pyrazole guest molecules are similar, the nitro group being coplanar with the five-membered ring. The bond distances and angles follow a pattern relatively similar to that of the free guest[2] (CSD refcode: HEHVAR)[11] which displays average values (three molecules in the asymmetric unit) for the five N(H)—N, N—C, ... C—N(H) distances of 1·366(5), 1·318(5), 1·391(6), 1·387(6) and 1·339(5) Å and the five N—N(H)—C, C—N—N(H), ... C—C—N(H) angles of 113·7(3), 104·9(3), 110·0(4), 107·5(4) and 103·9(3)°, vs distances of 1·358(4), 1·316(5), 1·379(6), 1·390(4) and 1·338(6) Å and angles of 111·9(4), 106·8(3), 109·1(4), 107·7(4) and 104·6(4)° (average values for the present structure).

The molecular entities form an H-bonded associate containing four molecules: two diols and two pyrazoles. This gives rise to a 14-membered ring of hydrogen bonded species with strong N—H ··· O, O—H ··· O and O—H ··· N interactions [(Figure 1(a) and 1(b)] analogously to the 12-membered ring present in the complex with *n*-propylamine,[6] where two guest molecules are also inserted between two hosts. The packing of these H-bonded associates is governed by weak C—H ··· O interactions in which the pyrazole and the toluene molecules are involved [Figure 1(c)]. There are two voids in the structure of 26·8 Å^3 each, the total packing coefficient being low (0.65).[13]



Scheme 1

Finding the position of residual hydrogen atoms by the use of pyrazole internal angles at the nitrogen atoms

We have shown that the internal angles of the pyrazole pentagon are very different for the two nitrogen atoms: the N—NH—C angle is on average 8·9° larger than the C—N—NH angle (x-ray geometries).[14] This is an intrinsic phenomenon since in the gas phase the difference is 7·8° (microwave) and 8·9° (MP4/6–31G**).[15] Static or dynamic disorder due to tautomerism results in lowering this difference to the point that in the case of a 50 : 50 disorder it becomes zero.

The smaller (−1·8°) and larger (+1·9°) values of angles at the N(H) and N atoms in the complex with respect to the free guest (**1b**, see above) are indicative of proton disorder (about 20% of 3-methyl-4-nitropyrazole tautomer **1a**, see Scheme 1); however, only peaks of low electron density (<0·19 e Å^{-3}) could be observed in the final ΔF map at bond distances of some hydroxyl groups and the other nitrogen atoms (see below for hydrogen bonding system).

Table 2. ^{13}C NMR chemical shifts (solutions in $CDCl_3$)

	Host		Toluene solution	3-Me-4-NO_2pz (**1a**) CP/MAS	4-NO_2-5-Mepz (**1b**) CP/MAS	1 : 1 : 1 Complex CP/MAS
	Solution	CP/MAS				
Me	28·1	27·0	—	—	—	25·0
		28·6	—	—	—	26·4
C-2	109·5	108·7	—	—	—	108·4
C-4	80·8	79·9	—	—	—	80·6
						81·9
C(OH)	78·1	79·9	—	—	—	77·0
						78·3
Ph (*o*, *m*)	127·2	126·8	—	—	—	126·7
	127·6	126·8	—	—	—	126·7
	128·1	126·8	—	—	—	126·7
	128·6	126·8	—	—	—	126·7
Ph (*p*)	127·2	126·8	—	—	—	126·7
	127·5	126·8	—	—	—	126·7
Ph (i)	142·6	142·0	—	—	—	141·9
	145·9	146·5	—	—	—	144·6
Me	—	—	21·3	—	—	21·3
Ph (*o*)	—	—	129·3	—	—	126·7
Ph (*m*)	—	—	128·5	—	—	126·7
Ph (*p*)	—	—	125·8	—	—	126·7
Ph (*i*)	—	—	137·8	—	—	136·2
3-Me (**1a**)	—	—	—	12·9	—	11·6
C-3 (**1a**)	—	—	—	147·2	—	146·6
C-4 (**1a**)	—	—	—	132·1	—	131·4
C-5 (**1a**)	—	—	—	132·1	—	132·7
5-Me (**1b**)	—	—	—	—	11·2	9·6
C-3 (**1b**)	—	—	—	—	137·2	140·0
C-4 (**1b**)	—	—	—	—	132·4	132·7
C-5 (**1b**)	—	—	—	—	142·6	143·1

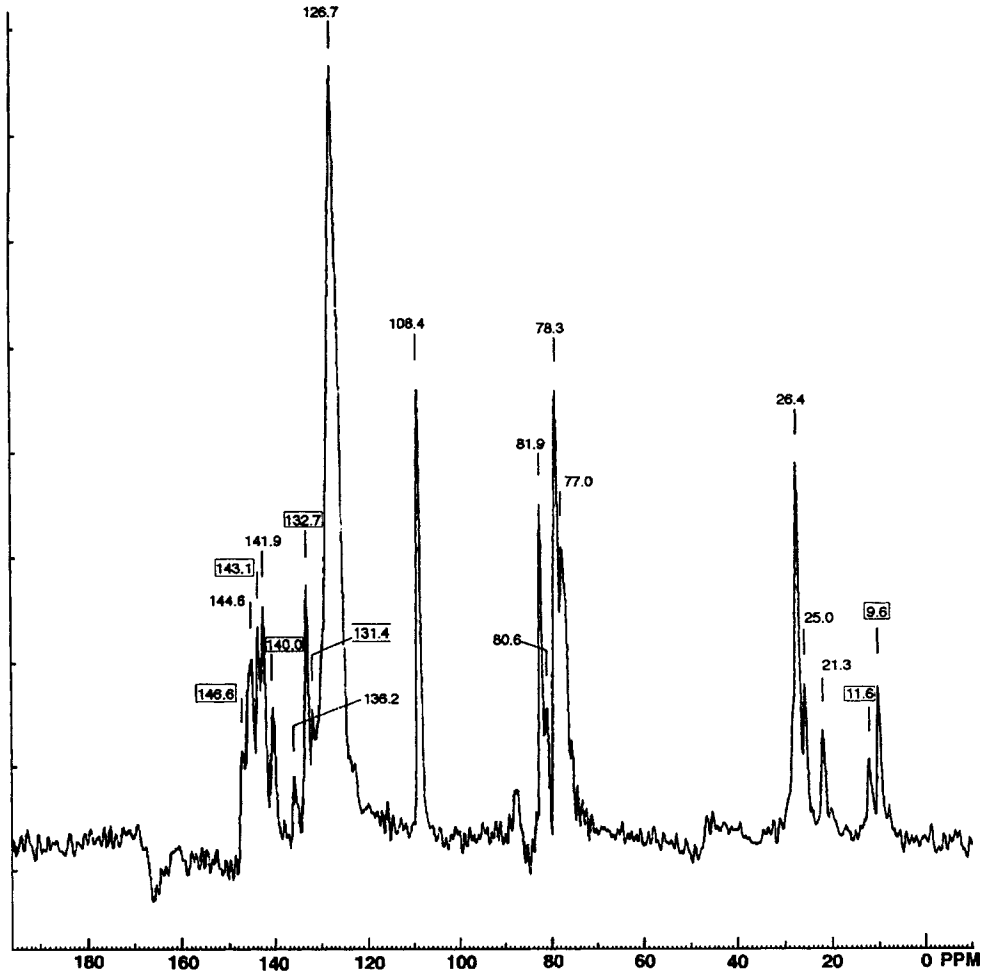


Figure 2. ^{13}C CP/MAS NMR spectrum (100 MHz) of the 2 : 2 : 2 complex

^{13}C NMR spectroscopy

We recorded in $CDCl_3$ solution the ^{13}C NMR spectrum of the free host **2** (assignment based on two-dimensional experiments and on couplings) and that of toluene; that of compound **1** in solution corresponds to an average mixture of tautomers **1a** and **1b** and it is not useful for the present discussion. The results are reported in Table 2; the phenyl rings in the host **2** are diastereotopic, all the signals being split, particularly the *ipso* carbons. The solid-state ^{13}C CP/MAS NMR spectra of **1a** and **1b** were already known;[2] those of the free host **2** have been assigned using the solution data; the *gem*-dimethyl groups at position 2 are split since in the crystal the host loses its C_2 symmetry. The ^{13}C CP/MAS NMR spectrum of the 1 : 1 : 1 complex (actually a 2 : 2 : 2 complex) is shown in Figure 2 (100 MHz) and the assignment is reported in Table 2.

We have framed the signals belonging to pyrazole carbons. It appears that both tautomers are present; assuming that the intensity of signals in ^{13}C CP/MAS NMR is proportional to the abundance, there is 20–30% of tautomer **1a** and 80–70% of tautomer **1b**.

CONCLUSIONS

The present work illustrates the synergy between crystallography and CP/MAS NMR: there are problems where only the combination of both methods may lead to a satisfactory conclusion.[16] Concerning the reason why a 25 : 75 mixture of tautomers **1a** and **1b** is present in the host–guest compound, there are

Table 3. Crystal analysis parameters at 200 K

Crystal data	
Chemical formula	$C_{31}H_{30}O_4 \cdot C_4H_5N_3O_2 \cdot C_7H_8$
Crystal colour and description	Colourless, plates
Crystal size (mm)	0·33 × 0·33 × 0·17
Crystal system	Monoclinic
M_r	1371·64
Space group	$P2_1$
a (Å)	12·6230(4)
b (Å)	28·0226(26)
c (Å)	11·1498(4)
β (°)	109·517(2)
Z	4
D_x (gr cm^3)	1·225
V (Å^3)	3717·4(3)
Radiation	Cu Kα
No. of reflections for lattice parameters	92
θ Range for lattice parameters (°)	3–45
Absorption coefficient (cm^{-1})	6·61
Data collection	
Diffractometer type	Philips PW1100, four circle. Graphite oriented monochromator. 1 min/reflection, detector apertures (°), 1 × 1; collection method, $\omega/2\theta$ scans Scan width (°): 1·5
θ_{max} (°)	65
No. of standard reflections (interval)	2 (90 min). No decay
No. of independent reflections	6493
No. of observed reflections, $I \geq 2\sigma(I)$	5775
Refinement	
Hydrogen atoms	From difference synthesis
Refinement	Least-squares on F_o. Full matrix
Secondary extinction correction (/10^3)	10(2)
No. of parameters refined	1147
Degrees of freedom	4522
Ratio of freedom	5·03
⟨Shift/error⟩	0·05
R	0·056
wR	0·061
$(\Delta\rho)_{max}$ (e Å^{-3})	0·51 near the disordered toluene molecule
Max. thermal value (Å^2)	U11[C140] = 0·26(6)
Weighting scheme:	Empirical so as to give no trends in $\langle \omega\Delta^2 F \rangle$ vs $\langle \lvert F_{obs} \rvert \rangle$ and $\langle \sin\theta/\lambda \rangle$.

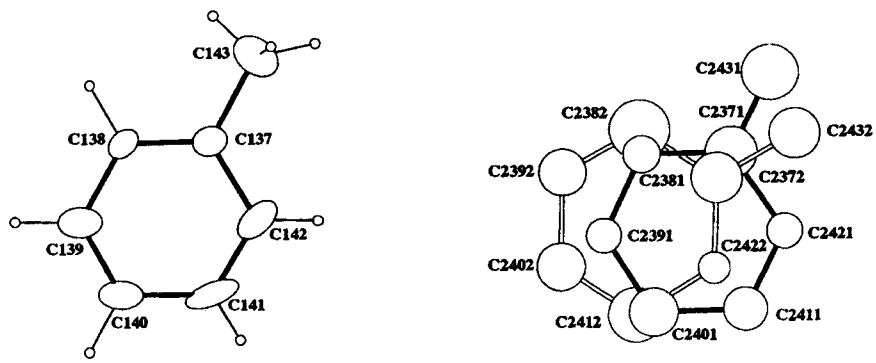


Figure 3. Toluene molecules showing the disorder model and the numbering system. Ellipsoids are drawn at the 10% probability level

two different explanations of increasing complexity: (i) it is an intrinsic property, that is, the 5-methyl tautomer is more stable than the 3-methyl tautomer; (ii) it is a consequence of the hydrogen bonds, O—H···N and N—H···O, present in the H-bonded associate. 3-Methylpyrazole tautomers are slightly less stable than the 5-methyl tautomers but the difference in energy is so small that it results in 45:55 mixtures at equilibrium.[17] Explanation (ii) requires (a) that the O—H···N H-bond is stronger than the N—H···O H-bond, which is reasonable, the NH-pyrazoles being fairly strong bases but very weak acids, and (b) that tautomer **1b** is a stronger base (but a weaker acid) than tautomer **1a**, which is also reasonable.[18] In summary, the predominance of tautomer **1b** is consistent with the thermodynamic properties of pyrazoles.

EXPERIMENTAL

X-ray structure determination. Table 3 gives the crystal analysis parameters; the structure was solved by direct methods.[19] One of the toluene molecules appears to be extensively disordered and two positions twisted by 34° were modelled with occupancy factors of 50% (Figure 3). Most of the calculations were performed on a VAX 6410 computer using the XTAL System.[12] The atomic scattering factors were taken from the *International Tables for X-Ray Crystallography*, Vol. IV.[20]

Supplementary data. Lists of atomic coordinates and anisotropic displacement parameters for the non-hydrogen atoms, hydrogen parameters and structure factors tables have been deposited at the Cambridge Crystallographic Data Centre.

NMR spectroscopy. The ^{13}C NMR spectra were recorded at 50·3 MHz (solution) and 100·6 MHz (CP/MAS) on Bruker AC-200 and MSL-400 instruments. The experimental conditions have been described elsewhere.[21]

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