PACKING MODES IN EIGHT 3-ETHOXYCARBONYLPYRAZOLE DERIVATIVES. INFLUENCE OF THE SUBSTITUENTS ON THE CRYSTAL STRUCTURE AND ANNULAR TAUTOMERISM

Lourdes Infantes,[1] Concepción Foces-Foces,[1,*] Rosa M. Claramunt,[2,*] Concepción López,[2] Nadine Jagerovic,[3] and José Elguero[3,*]

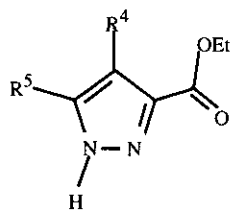
[1]Departamento de Cristalografía, Instituto de Química-Física 'Rocasolano', CSIC, Serrano, 119, E-28006 Madrid, Spain

[2]Departamento de Química Orgánica y Biología, Facultad de Ciencias, UNED, Senda del Rey, s/n, E-28040 Madrid, Spain

[3]Instituto de Química Médica, CSIC, Juan de la Cierva, 3, E-28006 Madrid, Spain

Abstract- The crystal and molecular structures of eight *N*-unsubstituted ethoxycarbonylpyrazole derivatives have been determined by X-Ray analysis. The molecules are linked by bifurcated N-H···N/O bonds giving rise to two hydrogen-bonding motifs: catemers and tetramers that are further joined by weak interactions. Different packing modes are observed depending on the substituent at C5. The 3-ethoxycarbonyl-4-bromo-5-phenylpyrazole presents temperature dependent solid-solid phase transition. Having determined that all these compounds are 3-ethoxycarbonyl tautomers in the solid state, their annular tautomerism was studied by ^{13}C NMR spectroscopy.

Pyrazoles show intermolecular NH proton transfer behavior in the solid state closely related with annular tautomerism and with their secondary crystal structure.[1,2] In the crystalline state, the pyrazole derivatives with a single NH donor and one or several hydrogen acceptors (hydrates, salts and inclusion complexes excluded) can form only one hydrogen bond per molecule where both nitrogens of the pyrazole are involved in the interaction. However, they exhibit a wide diversity of hydrogen-bonding patterns: dimers, trimers, tetramers and catemers as summarized in Table 1. The most common is the dimeric and the trimeric associations, the other, in order of diminishing prevalence are catemers and tetramers. All the pyrazoles studied so far (by X-Ray crystallography and CPMAS NMR spectroscopy), where a dynamical phenomenon is observed, build up hydrogen-bonding cyclic motifs. In the light of the these results and due to the scarce literature on *N*-unsubstituted alkoxycarbonyl pyrazoles (Cambridge Structural Database, CSD hereinafter)[3], the present paper deals with the NMR properties, the molecular structures, and the packing modes of the following compounds:



1: R^4=R^5=H
2: R^4=H, R^5=Me
3: R^4=Me, R^5=H
4: R^4=H, R^5=Ph
5: R^4=Ph, R^5=H
6: R^4=Br, R^5=H
7: R^4=Br, R^5=Me
8: R^4=Br, R^5=Ph

The influence of the methyl, bromine (isosteric with methyl but with different electronic properties) and phenyl substituents on the molecular and crystal structure has been analyzed. The endocyclic angular deformations induced by these substituents in the gas-phase have been also estimated by *ab initio* calculations.

Table 1. Hydrogen-bonding patterns of *N*-unsubstituted pyrazoles in the solid state.

	CSD[3] code	Substituents: $R^3 \neq R^5$	CSD code	Substituents: $R^3 = R^5$
Cyclic dimers:	HEHTUJ	R^3=Me, R^4=NO_2, R^5=H	LADBEX	R^3=R^5=Ph, R^4=Br
	TEHQAY	R^3=H, R^4=H,	RIVBAZ	R^3=R^5=Bu^t, R^4=NO
		R^5=2,5-dimethoxyphenyl	WILBAU	R^3=R^5=Bu^t, R^4=NO_2
	VEHCOA	R^3=H, R^4=NO_2, R^5=$SiMe_3$	WILBEY	R^3=R^5=Ph, R^4=NO_2
			YULNUO	R^3=R^5=Bu^t, R^4=H
Cyclic trimers:	HEHVAR	R^3=H, R^4=NO_2, R^5=Me	DASXEA	R^3=R^5=Me, R^4=H
	LETCES	R^3=COOMe, R^4=CF_3, R^5=H	WIKZUL	R^3=R^5=H, R^4=NO_2
	PAMTAY	R^3=Ph, R^4=Br, R^5=H	reference 5	R^3=R^5=H, R^4=Br
	RIKNOO	R^3=NO_2, R^4=H, R^5=H		
	reference 4	R^3=H, R^4=Me, R^5=Me		
Cyclic tetramers:	GIRNEA	R^3=COOEt, R^4=C≡C–$SiMe_3$, R^5=$SiMe_3$	LADBIB	R^3=R^5=Ph, R^4=H
	MEPHPY	R^3=Ph(Me), R^4=H, R^5=Me(Ph)		
Catemers:	PAZDPY	R^3=N_3, R^4=Ph, R^5=H	LETNAZ	R^3=R^5=Me, R^4=NO_2
	reference 6	R^3=Ad(H), R^4=H, R^5=H(Ad)	PYRZOL	R^3=R^5=H, R^4=H
			reference 7	R^3=R^5=H, R^4=Ad
			reference 4	R^3=R^5=Me, R^4=Me
			reference 5	R^3=R^5=Me, R^4=Br

RESULTS AND DISCUSSION

Crystal and molecular structures

According to Table 2, which shows the relevant features of the molecular structures, the determination of the parent structure was carried out using two different samples (**1** and **1'**) since the first structure solved, **1'**, contained the 6.7% of 3-carboxy-4-bromopyrazole compound as an impurity (see experimental). After purification, both structures turned out to be isomorphous (Table 3) sharing all atoms except those of the CH_2-CH_3 chain and the H or Br ones bonded to C4 as shown in Figure 1 where both models were superimposed. Labels **8** and **8'** (Table 2) refer to the structure of 3-ethoxycarbonyl-4-bromo-5-phenylpyrazole before (**8** = room temperature) and after (**8'** = low temperature) the solid-solid phase transition.

There are two independent molecules in **4** and **8'** and the significant differences[8] between each pair are due the conformation of the ethoxycarbonyl chain as depicted by the torsion angles around the C3-C6, C6-O8 and O8-C9 bonds. In compounds (**2**), (**8**), (**8'**) and in the molecule 1 of **4**, the carbonyl groups are in an *anti* (or *E*) conformation with regard to the nitrogen lone pair of the pyrazole rings (Figure 1 and Table 2). This conformation, as previously reported,[9] is lower in energy by approximately 1.0 kcal mol^{-1} (*ab initio* calculations at HF/6-31G** and B3LYP/6-31G** level[10]) than the *syn* (or *Z*) conformation presumably as a result of the smaller steric repulsion between the lone pairs of the N and O atoms. In the solid state, the steric effect (*syn* conformation) could be compensated by the presence of the N-H···O=C hydrogen bonds (Table 3). In **2**, the shortest N···O distance (N1···O8 because of the *anti* conformation) is

Table 2. Selected geometrical parameters (Å, °). The disordered atoms in **4**, **8** and **8'** are represented with dash.

	1	**1'**	**2**	**3**	**4**		**5**	**6**	**7**	**8**	**8'**	
					mol. 1	mol. 2					mol. 1	mol. 2
N1-N2	1.338(3)	1.331(5)	1.340(4)	1.334(2)	1.342(2)	1.338(3)	1.336(3)	1.337(10)	1.346(5)	1.341(7)	1.341(10)	1.336(10)
N2-C3	1.333(2)	1.335(4)	1.341(4)	1.340(2)	1.338(3)	1.338(3)	1.342(3)	1.343(10)	1.341(4)	1.322(8)	1.326(13)	1.341(13)
C3-C4	1.397(3)	1.397(6)	1.398(4)	1.409(3)	1.397(3)	1.400(3)	1.415(4)	1.410(12)	1.404(5)	1.403(9)	1.413(13)	1.418(13)
C4-C5	1.360(3)	1.360(6)	1.366(5)	1.377(3)	1.382(3)	1.376(3)	1.381(4)	1.359(12)	1.369(5)	1.377(8)	1.379(12)	1.369(11)
C5-N1	1.335(3)	1.341(5)	1.354(4)	1.345(2)	1.358(3)	1.358(3)	1.344(4)	1.320(12)	1.346(5)	1.331(9)	1.360(13)	1.347(13)
C3-C6	1.463(3)	1.462(6)	1.481(5)	1.470(3)	1.467(3)	1.466(4)	1.469(4)	1.471(12)	1.477(5)	1.475(9)	1.490(13)	1.473(11)
C4-R4	-	1.797(9)	-	1.499(3)	-	-	1.487(4)	1.864(8)	1.865(3)	1.866(7)	1.867(10)	1.872(9)
C5-R5	-	-	1.489(5)	-	1.464(3)	1.464(3)	-	-	1.484(7)	1.476(8)	1.453(12)	1.451(11)
C5-N1-N2	113.0(2)	112.9(3)	113.1(3)	113.2(2)	113.1(2)	113.2(2)	113.2(2)	114.0(8)	114.1(3)	114.2(5)	114.1(7)	114.6(7)
N1-N2-C3	104.2(2)	104.6(3)	104.1(3)	103.9(1)	104.6(2)	104.7(2)	104.3(2)	103.7(7)	104.1(3)	104.5(5)	105.2(7)	104.8(7)
N2-C3-C4	111.1(2)	110.8(3)	111.3(3)	112.3(2)	111.2(2)	110.9(2)	111.7(2)	110.5(7)	110.3(3)	110.4(6)	109.8(9)	109.0(9)
C3-C4-C5	104.9(2)	105.1(3)	105.3(3)	103.3(2)	105.5(2)	105.7(2)	103.6(2)	104.9(8)	106.5(3)	105.9(5)	107.0(7)	107.1(7)
C4-C5-N1	106.8(2)	106.6(4)	106.2(3)	107.4(2)	105.6(2)	105.5(2)	107.3(2)	107.0(7)	105.0(3)	105.0(5)	103.9(8)	104.4(8)
N2-C3-C6	118.1(2)	118.6(3)	120.2(3)	117.0(2)	121.4(2)	117.9(2)	115.5(2)	117.5(7)	116.1(3)	119.2(5)	118.9(8)	120.8(8)
C4-C3-C6	130.7(2)	130.6(3)	128.5(3)	130.8(2)	127.4(2)	131.2(2)	132.6(2)	132.0(8)	133.6(3)	130.3(5)	131.2(8)	130.2(7)
C3-C4-R4	-	126.3(4)	-	129.3(2)	-	-	131.2(2)	129.2(6)	130.2(3)	126.2(5)	125.3(7)	124.7(7)
C5-C4-R4	-	128.6(4)	-	127.4(2)	-	-	124.9(2)	126.0(6)	123.3(3)	127.8(5)	127.6(7)	128.2(7)
N1-C5-R5	-	-	120.9(3)	-	123.0(2)	122.7(2)	-	-	122.6(4)	121.6(5)	121.2(8)	121.3(8)
C4-C5-R5	-	-	132.9(3)	-	131.4(2)	131.8(2)	-	-	132.3(4)	133.4(5)	134.9(8)	134.3(7)
N1-N2-C3-C6	179.6(2)	-179.8(3)	179.4(3)	180.0(2)	-179.7(2)	-178.6(2)	177.1(2)	-178.9(7)	178.7(3)	179.0(6)	178.2(8)	- 179.8(8)
N2-C3-C4-R4	-	180.0(4)	-	-178.9(2)	-	-	173.2(3)	-178.5(6)	-178.4(3)	-179.1(4)	-177.0(6)	178.9(6)
N2-N1-C5-R5	-	-	179.1(3)	-	179.2(2)	178.6(2)	-	-	179.3(4)	-178.6(5)	-177.9(8)	179.2(8)
N2-C3-C6-O7	-0.4(3)	-0.9(6)	-176.2(3)	0.3(3)	179.0(2)	2.7(4)/	-12.6(4)	7.5(12)	3.2(6)	166.6(7)	164.3(10)	-167.4(11)
N2-C3-C6-O7'	-	-	-	-	-	-8.0(7)	-	-	-	-	-	-
C3-C6-O8-C9	178.5(2)	178.2(3)	179.9(3)	-177.9(2)	178.0(2)	-177.8(3)	179.2(3)	179.6(7)	179.7(3)	171.3(10)	167.8(13)	172.3(11)
C3-C6-O8'-C9'	-	-	-	-	-	-177.7(5)	-	-	-	-169.8(10)	-154.2(14)	-178.2(12)
C6-O8-C9-C10	-179.9(2)	-179.2(4)	-175.1(3)	177.3(2)	-148.2(3)	-91.7(5)	-175.8(3)	173.6(7)	-165.9(4)	-175.2(15)	-176.2(19)	-172.7(15)
C6-O8'-C9'-C10'	-	-	-	-	-	160.7(7)	-	-	-	168.5(16)	-122.8(21)	176.5(18)
N/C-C-(C-C)(ph)	-	-	-	-	3.8(3)	-1.6(3)	55.4(5)	-	-	-30.6(9)	-29.1(13)	27.2(13)

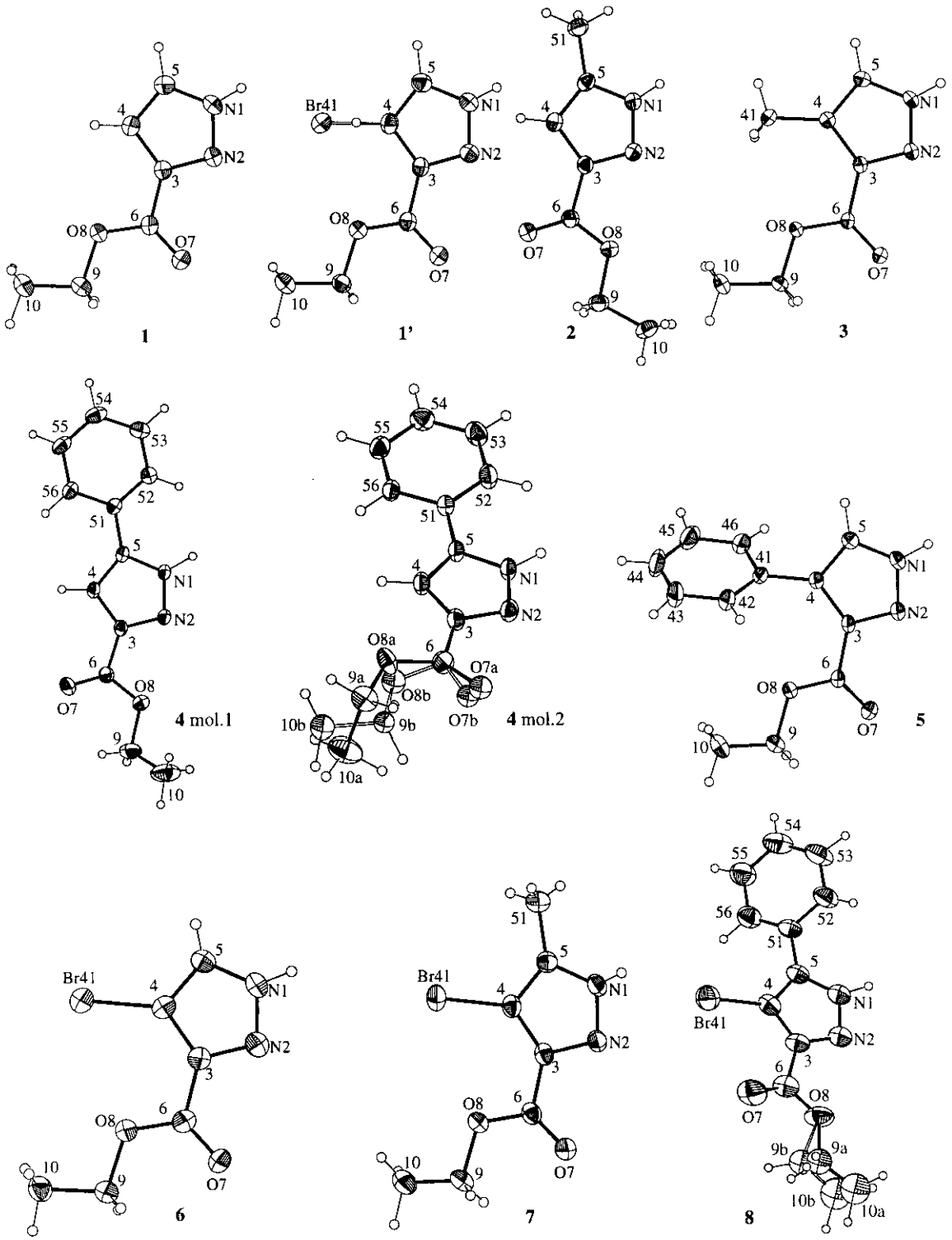


Figure 1. - Molecular structures showing the atomic numbering. Displacement ellipsoids are scaled to enclose 30% probability. The disorder of the ethoxycarbonyl group, in **4** and **8**, is shown with open lines.

analogous to the van der Waals radii of 3.1 Å[11] while in **4** and **8, 8'** both (N1···O7 and N1···O8) are too distant to allow for hydrogen interactions. The inclusion of a methyl group attached to either C5 or C4 (compounds (**2**) and (**3**) respectively) does not affect the stability of the *anti* vs. the *syn* conformation, the differences in energy between both conformers being 1.0 and 1.7 kcal mol^{-1} respectively.

Most of the bond lengths in the pyrazole ring have normal values. However, the elongation of the C3-C4, C4-C5 or C5-N1 bonds is presumably caused by the combination of the electronic properties of substituents at C4 and C5, that might be further enhanced by the steric effects due to the coplanarity of the pyrazole ring and the substituents that also produces significant external angular distortions at the atom to which they are attached (i.e. C3-C4-R4 vs. C5-C4-R4 in **6**, Table 2). This effect is much more pronounced in the structures of **4, 5** and **8**. The comparison of the internal angles of the five-membered ring in the parent compound (**1**), with those of **2-8** reveals the electron withdrawing or donating nature of the Br (isosteric with the methyl group) vs. Me, Ph substituents respectively. The ranges of the C3-C4-C5 and C4-C5-N1 angles, where the substitution take places, are 103.3(2)-107.1(7)° and 103.9(8)-107.4(2) respectively (Table 2). These findings were supported by *ab initio* calculations at HF/6-31G** and B3LYP/6-31G** level. Methyl and phenyl groups contract the *ipso* angle (0.7-0.9° depending on the method and if the substituent is attached to C4 or C5) and expand the adjacent angles (0.4-0.7°) whereas the bromine atom opens the *ipso* angle (1.2-1.2°) and closes the contiguous ones (0.8-1.0°). The magnitudes at these deformations match those observed in **2-8** except in **6** where the bromine effect is much less pronounced.

The solid-solid phase transition in 3-ethoxycarbonyl-4-bromo-5-phenylpyrazole when lowering the temperature (**8 –> 8'**) can be described as a movement, in part of the molecules, of the $-CH_2-CH_3$ end of the ethoxycarbonyl chain that implies a loss of symmetry (see Experimental). These chains did not display a fully *trans*-planar conformation as it happens in almost all the compounds but they show a *gauche* conformation around the O8'-C9' bond. A similar conformation is observed in molecule 2 of **4** where the ethoxycarbonyl chain is also disordered (Table 2).

Two out of four possible hydrogen-bonding motifs are displayed by title compounds: catemers (**1, 2, 3, 5, 6** and **7**) and tetramers (**4** and **8**). In all the structures, except in **4** and **8** (**8'**), the molecules are involved in asymmetric N-H···(N,O) bifurcated hydrogen interactions that assemble the molecules into chains. Molecules in **4** and **8** (**8'**) form tetramers *via* N-H···N bonds. If the ethoxycarbonyl group is in a *syn* conformation (N2-C3-C6=O7 ~ 0°), the major interaction corresponds to the N-H···O=C bond and the minor to the N-H···N one and *vice versa* for the *anti* conformation (N2-C3-C6=O7 ~ 180°), Table 3. In these 3-ethoxycarbonylpyrazole derivatives, the secondary structure seems to be induced by the size of the substituent at C5 hence chains are observed when R^5 = H or Me and tetramers when R^5 = Ph.

Two packing modes can be differentiated in the first motif: (I) the chains packing in layers with all the pyrazole rings within the layer coplanar one to each other and (II) chains packing in a herringbone fashion. These modes, again, can be associated with the size of the substituent at C5 (R^5 in scheme) in such a way that mode I is observed when R^5 = H, compounds (**1**), (**1'**), (**3**), (**5**), (**6**), and mode II when R^5 = Me, compounds (**2**), (**7**) (Examples of these two modes are shown in Figures 2a-d). The bulky substituent at C4 in **5** (Figure 1) induces a distortion of the planarity of the sheets and the angle formed by the adjacent

pyrazole rings is 24.7(2)°. The tertiary structure of the crystal is constructed by stacking the layers at van der Waals separations. In mode II, the pyrazole rings form angles of 71(1) and 48(1)° for **2** and **7** respectively. In both modes, the topological differences refer to (a) the relative orientation of the molecules within the chain since glide planes connect them in **1**, **1'** and two-fold screw axis in the remaining ones and to (b) to the relationship between the chains forming the sheets, symmetry centers in **5** and translation in the rest. The distance between the chains (~ 12.95, 14.10, 14.50 and 16.92 Å for **1**, **3**, **6** and **5** respectively) depends on the size of the substituent at C4 (H, Me, Br and Ph).

Table 3. Selected intermolecular parameters (Å,°). See Figure 1 for the atom labelling scheme. (-) Means the hydrogen atoms were not refined.

Compound:	D-H...A	D-H	H...A	D...A	D-H...A
1	N1-H1...N2(x,3/2-y,z-1/2)	0.86(3)	2.45(3)	3.104(3)	134(3)
	N1-H1...O7(x,3/2-y,z-1/2)	0.86(3)	2.15(3)	2.938(2)	152(3)
	C5-H5...O7(x,y,z-1)	0.99(3)	2.38(4)	3.351(3)	164(2)
1'	N1-H1...N2(x,3/2-y,z-1/2)	0.84(6)	2.50(6)	3.105(5)	130(5)
	N1-H1...O7(x,3/2-y,z-1/2)	0.84(6)	2.14(6)	2.925(4)	156(5)
	C5-H5...O7(x,y,z-1)	1.00(5)	2.39(6)	3.346(6)	161(3)
2	N1-H1...N2(1/2-x,y+1/2,3/2-z)	0.87(6)	2.16(6)	2.995(4)	160(5)
	N1-H1...O8(1/2-x,y+1/2,3/2-z)	0.87(6)	2.51(6)	3.123(4)	129(5)
	C9-H92...O7(1-x,-y,1-z)	1.06(5)	3.05(5)	3.338(5)	96(3)
3	N1-H1...N2(-x,y-1/2,1/2-z)	0.87(3)	2.53(3)	3.178(2)	132(2)
	N1-H1...O7(-x,y-1/2,1/2-z)	0.87(3)	2.07(3)	2.884(2)	154(2)
	C5-H5...O7(x,y-1,z)	0.95(3)	2.51(3)	3.460(2)	180(2)
4	N1-H1(mol.2)...N2(mol.1)	0.92(4)	1.98(4)	2.814(3)	149(3)
	N1-H1(mol.1)...N2(mol.2)(1/2-x,y,1-z)	0.97(3)	1.98(3)	2.924(2)	163(3)
	Cpz(mol.1)...Cpz(mol.1)(1/2-x,y,1-z)			3.659(1)	
	Cpz(mol.2)...Cpz(mol.2)(1/2-x,y,1-z)			3.531(1)	
	C55-H55(mol.2)...O7(mol.1)(x,y+1,z)	0.99(3)	2.62(4)	3.248(3)	122(3)
	C56-H56(mol.2)...O7(mol.1)(x,y+1,z)	1.01(3)	2.69(3)	3.296(3)	119(2)
	C55-H55(mol.1)...O7a(mol.2)(x+1/2,-y,z)	0.94(4)	2.63(4)	3.294(5)	128(3)
	C55-H55(mol.1)...O7b(mol.2)(x+1/2,-y,z)	0.94(4)	2.55(4)	3.291(8)	136(3)
5	N1-H1...N2(1/2-x,y+1/2,3/2-z)	0.91(5)	2.47(5)	3.161(3)	134(4)
	N1-H1...O7(1/2-x,y+1/2,3/2-z)	0.91(5)	2.05(5)	2.872(3)	151(4)
	C5-H5...O7(x,y+1,z)	1.00(4)	2.51(4)	3.382(4)	146(3)
6	N1-H1...N2(1-x,y-1/2,1/2-z)	0.85(-)	2.62(-)	3.153(10)	122(-)
	N1-H1...O7(1-x,y-1/2,1/2-z)	0.85(-)	2.03(-)	2.867(10)	166(-)
	C5-H5...O7(x,y-1,z)	0.87(16)	2.62(16)	3.486(12)	176(11)
7	N1-H1...N2(1/2-x,1/2+y,3/2-z)	0.84(-)	2.71(-)	3.280(5)	126(-)
	N1-H1...O7(1/2-x,1/2+y,3/2-z)	0.84(-)	2.04(-)	2.859(4)	164(-)
8	N1-H1...N2(1/4+y,3/4-x,7/4-z)	0.97(9)	1.95(9)	2.860(8)	156(7)
	Cpz...Cpz(1-x,1/2-y,z)			3.521(3)	
	C52-H52...O7(3/4-y,x-3/4,1/4+z)	0.82(8)	2.57(8)	3.210(11)	136(7)
8'	N1-H1(mol.1)...N2(mol.1)(1/2+y,1/2-x,3/2-z)	0.95(-)	2.15(-)	2.834(12)	128(-)
	N1-H1(mol.2)...N2(mol.2)(y,-x,-z-1)	0.83(-)	2.06(-)	2.862(12)	161(-)
	Cpz(mol.1)...Cpz(mol.1)(1-x,-y,z)			3.490(5)	
	Cpz(mol.2)...Cpz(mol.2)(-x,-y,z)			3.465(5)	
	C52-H52(mol.1)...O7(mol.2)(1/2+y,-x-1/2,1/2-z)	1.07(-)	2.45(-)	3.167(15)	123(-)
	C52-H52(mol.2)...O7(mol.1)(y,1-x,-z)	1.04(-)	2.48(-)	3.192(15)	125(-)

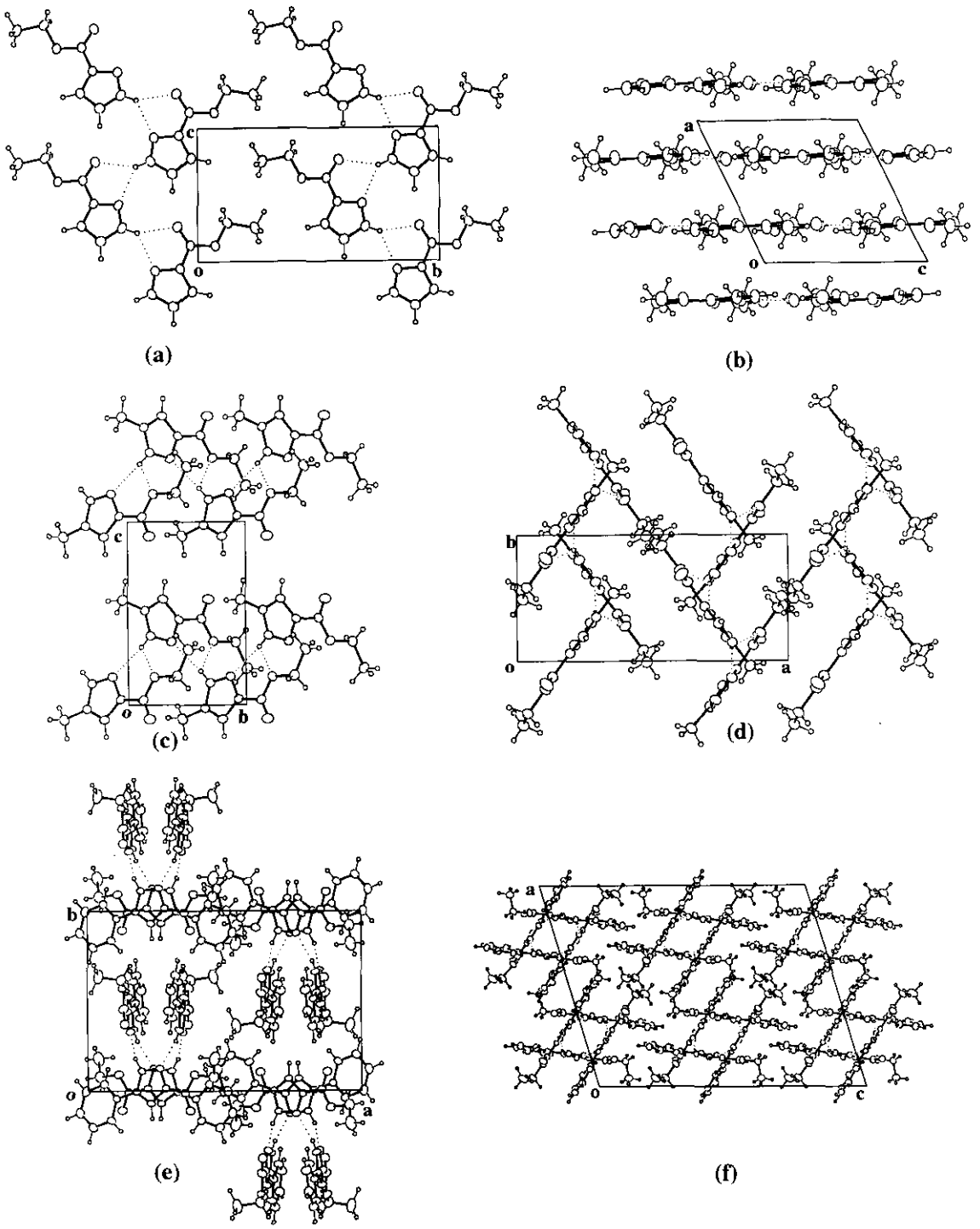


Figure 2. - Crystal structures of compounds (**1**) (a,b), (**2**) (c,d) and (**4**) (e,f) showing, on the left side, the hydrogen-bond motifs in chains and tetramers and the two different packing modes in **1** and **2**. For clarity purposes, in **4**, only one disorder model has been retained. Dotted lines indicate hydrogen bonds.

The tetramers in **4** are formed by two pairs of independent molecules through a two-fold axis while in **8**, **8'** they are generated by four-fold inversion axis, so that, the two different tetramers in **8'** are related by a pseudocenter of symmetry. The tertiary structures of **4**, **8** and **8'** are topologically similar. Weak C-H···O=C interactions assemble tetramers in sheets parallel to the ab plane allowing overlapping of the pyrazole rings (Table 3 and Figures 2e,f).

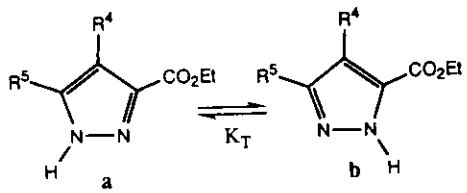
In order to confirm the influence of the substituent attached to C5 on the secondary structure, *N*-unsubstituted 3-alkoxycarbonylpyrazoles derivatives were analyzed in the light of the present results. Only two structures were retrieved from the CSD[3] without other functional donor group in the molecule. The first one (GIRNEA) with an *anti* conformation (N-C-C=O ~ 180°) and R^5 = $SiMe_3$ forms tetramers whereas the remaining one (LETCES) in a *syn* conformation (N-C-C=O ~ 0°) and R^5 = H forms trimers.

These results prompted us to suggest a rule for the prediction of the secondary structure depending on a combination of the substituents at C3 and at C5. In the pyrazoles studied so far, Table 1, the substituents that can be classified in five groups: (1) R^3/R^5 = H, (2) R^3/R^5 = Me, (3) R^3/R^5 = COOR, NO_2, N_3, (4) R^3/R^5 = Ph or Ad (Adamantyl) and (5) R^3/R^5 = Bu^t, $SiMe_3$ or 2,5-dimethoxyphenyl. As a rule of thumb, dimers and tetramers can be observed when the sum of the numbers of the groups are greater than 5, that is, R^3 or R^5 should belong to group 5 and R^5 or R^3 to any of the others simultaneously, i.e. R^3 = H (group 1), R^5 = $SiMe_3$ (group 5), or belonging to group 2 and 4. Trimers and catemers are observed when the sum adds 5 or less, for instance R^3 = R^5 = Me. The exception to this rule, presented by the tautomers HEHTUJ and HEHVAR (dimers and trimers respectively), is an indication that this proposed rule is only a simple interpretation of the results.

A crystal packing analysis using the contact radii of Vainshtein et al.[11] shows that there are no voids in the structures and total packing coefficients in the 0.648-0.701 range, corresponding both ends to structures **8** and **6** respectively.

^{13}C NMR spectroscopy and annular tautomerism

The precedent crystallographic study has demonstrated that the eight ethoxycarbonylpyrazoles have the CO_2Et group at position 3 (tautomer **a**). We decided then to study the annular tautomerism (**a** ⇌ **b** equilibrium) in solution.[12] For this purpose we have recorded the ^{13}C NMR spectra in the solid state (CP-MAS) and in DMSO-d_6 solution of these compounds. Two model compounds (**9**) and (**10**) (see Table 4) have also been studied



In DMSO-d_6 solution, the annular tautomerism is in several cases slow enough to observe the signals of each tautomer (these signals, broad in general, are printed in bold in Table 4), fact also observed for *N*-unsubstituted 3(5)-aminopyrazoles.[13] In three cases (**2**, **3** and **6**), the ^1H NMR spectra show the signals corresponding to C(het)-H and N-H protons (Table 4); in these cases, the proportions of both tautomers (80% **2a**-20% **2b**; 55% **3a**-45% **3b**; 70% **6a**-30% **6b**) were determined by simple integration of these signals.

In most cases, only average signals were obseved, which were often so broad that a very small amount of trifluoroacetic acid has to be added to observe them; the acid increases the rate of the **a**/**b** interconversion without modifying K_T. It is important that the quantity of trifluoroacetic acid added is very small, otherwise the average signals are shifted due to some extent of protonation. These average experimental values are reported in Table 4 in the last row of each compound.

To determine K_T ([**a**]/[**b**]) it is necessary to have an estimation of the ^{13}C NMR chemical shifts of each tautomer. As we have commented, in some cases, these values have been determined (bold values). This gives the opportunity to calculate K_T by integration of the ^{13}C NMR signals, but these signals are broad and, moreover, even the use of the integrals of similar signals is a delicate task in ^{13}C NMR. Anyhow, the interpolation and the integration yield very similar percentages of **a** and **b** tautomers: the values reported in Table 4 have an uncertainty of less than 5%. For the other compounds, we have estimated the chemical shifts of each tautomer using three criteria:

i) For tautomers **a** we have used the ^{13}C chemical shifts determined in the solid state by CPMAS NMR spectroscopy. This only gives a rough estimation; we have reported in Table 4 under $\Delta\delta$, the differences between the chemical shifts in the solid state and in solution (note that in certain cases both are measured chemical shifts). The differences (up to 3.0 ppm) reflect the different environment of ethoxycarbonylpyrazoles in the solid state and in DMSO, especially the hydrogen bonds.

ii) For both tautomers we have used the effect of substituents 5-methyl (**2a**), 4-methyl (**3a**, **3b**), 5-phenyl (**4a**), 4-phenyl (**5a**, **5b**), 4-bromo (**6a**, **6b**, **7a**, **7b**, **8a**, **8b**), 3-methyl (**2b**) and 3-phenyl (**4b**). These SCS (substituent chemical shifts) have been determined statistically for a large collection of *N*-methylpyrazoles.[14] The estimated values agree reasonably well with the reported SCS taking into account that the substituent on the nitrogen atom is different.

iii) When individual signals are observed (bold values) and the populations of both tautomers are different, the assignment of Table 4 always respects the rule that the broader signal corresponds to the less abundant tautomer (a simple consequence of the difference in activation energies).

Table 4 values deserve some comments. The first one concerns the chemical shifts of the CH_3 group of the ester substituent. The value in solution is almost constant (~ 14.2 ppm) while the value measured by CPMAS NMR for **a** tautomers varies between 11.9 (**5a**) and 14.3 ppm (**1a**). There is no obvious relationship between the *E*/*Z* conformation of the CO_2Et group or the secondary structure (catemers and tetramers) and the methyl chemical shifts; it is only possible to note that compound (**4**) which presents two independent molecules (labelled mol. 1 and mol. 2) is the only one which shows two signals (13.2 and 15.9 ppm) in ^{13}C CPMAS NMR (see footnote *b* in Table 4). In the solid state, the signal belonging to C4 when there is a bromine substituent in this position (**6a**, **7a**, **8a**) appears as a rather complex multiplet difficult to observe due to dipolar interactions with both bromine isotopes;[15,16] for this reason, the values reported in Table 4 for the CPMAS spectra are only approximate. Compound (**9**) provides values of $\Delta\delta$ in a case where there is no tautomerism so that all values have been experimentally determined; its values together with those of compound (**10**) confirm the relative chemical shifts of the C=O and CH_2 of the ester groups at 3- and 5-positions.

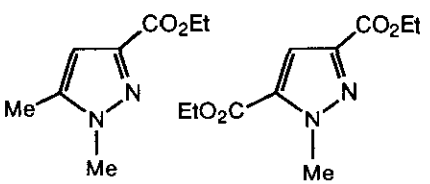
The last comment concerns the tautomeric equilibrium constants [2.3 (**1**), 4.0 (**2**), 1.2 (**3**), 0.8 (**4**), 0.5 (**5**), 2.3 (**6**), 4.0 (**7**), 1.2 (**8**)]. Instead of discussing each case, it is more convenient to assume an additive

Table 4. ^{13}C chemical shifts of ethoxycarbonylpyrazoles in DMSO-d_6 solution (values in bold correspond to observed signals of individual tautomers) and in the solid state (CPMAS). $\Delta\delta = \delta$ (CPMAS) - δ (DMSO-d_6) for tautomer **a**. The last row corresponds to the average values. For the phenyl substituents only the chemical shift of the *ipso* carbon is reported.

Compd	Conditions	C-CO_2Et	C4	C-R	CO	OCH_2	CH_3	R (on C4)	R (on C5)	**a/b** (%)
1	CPMAS (**1a**)	143.7	106.6	131.9	165.0	61.9	14.3	-----	-----	
	DMSO-d_6 (**1a**)	140.8	107.0	**132.0**	162.4	59.6	14.2	-----	-----	
	$\Delta\delta$ (**1a**)	2.9	-0.4	-0.1	2.6	2.3	0.1	-----	-----	
	DMSO-d_6 (**1b**)	131.9	109.0	**141.0**	160.1	60.9	14.2	-----	-----	
	DMSO-d_6 (**1**)	138.1	107.6	134.7	161.7	60.0	14.2	-----	-----	70/30
2[a]	CPMAS (**2a**)	144.7	106.2	141.6	162.3	62.7	12.9	-----	Me: 10.9	
	DMSO-d_6 (**2a**)	142.0	106.1	141.5	162.8	59.7	14.2	-----	Me: 10.0	
	$\Delta\delta$ (**2a**)	2.7	0.1	0.1	-0.5	3.0	-1.3	-----	Me: 0.9	
	DMSO-d_6 (**2b**)	131.2	107.2	149.9	159.7	60.4	14.2	-----	Me: 11.0	
	DMSO-d_6 (**2**)	139.8	106.3	143.2	162.2	59.8	14.2	-----	Me: 10.2	80/20
3[b]	CPMAS (**3a**)	141.2	119.1	131.5	165.6	61.8	12.2	Me: 10.5	-----	
	DMSO-d_6 (**3a**)	138.5	**118.2**	**129.0**	164.0	59.0	14.2	Me: 9.4	-----	
	$\Delta\delta$ (**3a**)	2.7	0.9	2.5	1.6	2.8	-2.0	Me: 1.1	-----	
	DMSO-d_6 (**3b**)	128.6	**120.1**	**140.3**	161.5	61.0	14.2	Me: 9.4	-----	
	DMSO-d_6 (**3**)	134.0	119.0	134.1	162.9	59.9	14.2	Me: 9.4	-----	55/45
4	CPMAS (**4a**)	144.2	102.5	144.2	160.5	59.8	13.2[c]	-----	Ph: 129.1	
	DMSO-d_6 (**4a**)	**143.3**	104.1	**144.0**	**162.0**	59.2	14.2	-----	Ph: 131.8	
	$\Delta\delta$ (**4a**)	0.9	-1.6	0.2	-1.5	0.6	-1.0	-----	Ph: -2.7	
	DMSO-d_6 (**4b**)	**134.7**	105.8	**152.0**	**158.7**	61.2	14.2	-----	Ph: 130.1	
	DMSO-d_6 (**4**)	138.6	105.0	148.4	160.2	60.3	14.2	-----	Ph: 130.9	45/55
5	CPMAS (**5a**)	139.9	122.1	132.3	165.3	62.5	11.9	Ph: 132.3	-----	
	DMSO-d_6 (**5a**)	138.8	124.0	130.7	**162.3**	59.5	13.9	Ph: **132.1**	-----	
	$\Delta\delta$ (**5a**)	1.1	-1.9	1.6	3.0	0.2	-2.0	Ph: 0.2	-----	
	DMSO-d_6 (**5b**)	130.2	124.6	138.0	**161.4**	60.6	13.9	Ph: **131.9**	-----	
	DMSO-d_6 (**5**)	133.6	124.4	135.1	161.8	60.2	13.9	Ph: 132.0	-----	40/60

6[d]	CPMAS (**6a**)	140.0	~ 92	130.0	163.9	62.6	13.5	-----	-----	
	DMSO-d_6 (**6a**)	**139.6**	**94.6**	**131.9**	**160.9**	**60.3**	14.1	-----	-----	
	Δδ (**6a**)	0.4	-2.6	-1.9	3.9	2.3	-0.6	-----	-----	
	DMSO-d_6 (**6b**)	**131.9**	**97.1**	**141.6**	**157.9**	**61.0**	14.1	-----	-----	
	DMSO-d_6 (**6**)	137.7	95.4	134.8	160.0	60.5	14.1	-----	-----	70/30
7	CPMAS (**7a**)	140.3	~ 95	140.3	163.5	61.8	11.9	-----	Me: 11.9	
	DMSO-d_6 (**7a**)	**139.7**	93.5	**139.7**	160.5	60.3	14.2	-----	Me: 9.9	
	Δδ (**7a**)	0.6	~ 1.5	0.6	2.0	1.5	-2.3	-----	Me: 2.0	
	DMSO-d_6 (**7b**)	**132.0**	97.1	**148.0**	157.9	61.0	14.2	-----	Me: 8.3	
	DMSO-d_6 (**7**)	138.2	94.2	141.4	160.0	60.5	14.2	-----	Me: 9.6	80/20
8	CPMAS (**8a**)	141.0	~ 95	140.1	159.6	60.2	12.8	-----	Ph: 129.0	
	DMSO-d_6 (**8a**)	141.4	92.9	141.0	161.5	59.5	14.1	-----	Ph: 130.0	
	Δδ (**8a**)	-0.4	~ 2	-0.9	-1.9	0.7	-1.3	-----	Ph: -1.2	
	DMSO-d_6 (**8b**)	132.7	94.9	149.2	157.9	62.2	14.1	-----	Ph 128.2	
	DMSO-d_6 (**8**)	137.5	93.8	144.7	159.9	60.7	14.1	-----	Ph: 129.2	55/45
9	CPMAS	141.6	109.7	140.5	163.0	61.5	14.1	-----	Me: 9.2	
	DMSO-d_6	140.7	107.6	140.2	161.8	59.8	14.2	-----	10.5	
	Δδ (**9**)	0.9	2.1	0.3	1.2	1.7	-0.1	-----	-1.3	
10	CPMAS	141.2	111.5	132.4	159.7[e]	60.0[e]	14.7[e]	-----	-----	
					158.2[f]	61.6[f]	14.2[f]			
	$CDCl_3$[g]	142.1	113.8	134.0	161.5[e]	61.1[e]	14.2[e]	-----	-----	
					159.2[f]	61.4[f]	14.3[f]			

[a] The ^{1}H NMR spectrum of this compound in DMSO-d_6 at 400 MHz presents two NH signals, major tautomer (**2a**): 13.10, minor tautomer (**2b**): 13.5 ppm. [b] The ^{1}H NMR spectrum of this compound in DMSO-d_6 at 200 MHz presents different signals for the two tautomers: major tautomer (**3a**): 7.59 (H5) and 13.15 ppm (NH), minor tautomer (**3b**): 7.48 (H3) and 13.6 (NH). [c] Another CH_3 signal at 15.9 ppm. [d] The ^{1}H NMR spectrum of this compound in DMSO-d_6 at 200 MHz presents different signals for the two tautomers: major tautomer (**6a**): 8.12 (H5) and 13.80 ppm (NH), minor tautomer (**6b**): 7.74 (H3) and 14.2 (NH). [e] CO_2Et at position 3. [f] CO_2Et at position 5. [g] From reference 14.



9 **10**

model and to determine the contributions of the substituents by multiple regression (n = 8, r^2 = 0.996, RMS residual = 0.1). The unsubstituted ethoxycarbonylpyrazole (**1**) shows for the CO_2Et group a preference to occupy position 3 (70%). The five substituents examined modify K_T by -1.0 (4-methyl), -1.7 (4-phenyl), 0.0 (4-bromo), 1.7 [3(5)-methyl] and -1.3 [3(5)-phenyl]. The effect of the 3(5)-substituents (the methyl group favours the 5 position while the phenyl group favours the 3 position) agrees with previous findings.[17,18] For obvious reasons, the 4-substituents have no effect on K_T in the absence of other substituents; in the present case, they have a clear influence through interactions (attractive or repulsive) with the ethoxycarbonyl group.

CONCLUSIONS

The *N*-unsubstituted pyrazoles in the solid state, when no other functional donor groups are present in the molecule are known to exist in four hydrogen bonding motifs: catemers, dimers, trimers and tetramers. The motif adopted by *N*-unsubstituted alkoxycarbonylpyrazoles depends, in part, on the steric bulk of the susbtituent group at C5 (R^5 in the scheme). The progression in substitution from H to Ph results in different packing modes but in spite of the small number of structure solved, we can conclude that tetramers are formed when phenyl rings are attached to C5. For all the *N*-unsubstituted pyrazoles studied, the rule seems to be a combination of the substituents at C3 and at C5 and, up to now, only a first distinction between two groups can be established (trimers and catemers vs. dimers and tetramers). It may be important to take this relationship into consideration for further investigation on proton transfer when cyclic secondary structures are necessary. Concerning tautomerism, 3(5)-ethoxycarbonylpyrazole (**1**)-(**8**) represent a case where the tautomerism in solution and in the solid state are not congruent. In solution both tautomers are of similar energy ($-0.6 < \ln K_T < 1.4$) while in the solid state all of them are **a** tautomers. The reason of this difference is to be found in the hydrogen bond network which stabilizes preferably this tautomer.

EXPERIMENTAL

The melting point was determined with a hot-stage microscope and is uncorrected. All solution NMR spectra were on two spectrometers to better observe some broad signals, a Bruker AC 200 (^1H at 200 MHz and ^{13}C at 50 MHz) and a Bruker DRX 400 (^1H at 400 MHz and ^{13}C at 100 MHz) (chemical shifts in ppm from TMS). The solid state ^{13}C CPMAS NMR spectra were recorded on a Bruker AC 200 spectrometer using the conditions described in previous publications.[13] Compounds (**1**)-(**7**) and (**9**)-(**10**) have already been described.[14,19]

3(5)-Ethoxycarbonyl-4-bromo-5(3)-phenylpyrazole (**8**). This compound has been prepared by bromination of compound (**4**). 3(5)-Ethoxycarbonyl-5(3)-phenylpyrazole (**4**) was partly disolved in 120 mL of warm glacial acetic acid, then 0.8 mL of bromine was added dropwise in 10 min. The resulting solution was stirred and refluxed for 3 h. White fumes of HBr are liberated and the colour of the solution changes from red-orange to orange-yellow. After cooling the solution was evaporated to dryness and the residue dissolved in chloroform and the solution neutralized with 10% sodium carbonate water solution. The organic layer was dried over sodium sulfate and the solvent was evaporated. The oily residue was stirred with ether and petroleum ether to give a white solid which was filtered off and dried in a vacuum oven.

mp 123-125 °C (methanol). Anal. Calcd for $C_{12}H_{11}N_2O_2Br$: C, 48.84; H, 3.76; N,9.49. Found: C, 48.97; H, 4.01; N, 9.55.

Crystals were obtained by slow evaporation of different kind of solvents: methanol, ethanol, toluene, dichloromethane, trichloromethane, ethylacetate, ether and hexane. The solvent, that afforded the best crystal for the X-Ray analysis, together with the experimental details are given in Table 5. The first sample of compound (**1**), labelled as **1'** in the Tables, contains the 6.7 per cent of 4-bromo-3-carboxypyrazole as an impurity. The formula was obtained by refinement of the occupancy factors of the Br, C9 and C10 atoms, by the agreement this model gave between the observed and the calculated structure factors and by the values of the residual peaks in the difference syntheses together with the values of the displacement parameters. The presence and amount of this impurity was also established by NMR. Data of compounds (**1'**), (**2**), (**3**), (**4**) and (**8**) were collected twice, at room and at low temperature[20] because of the displacement parameters were globally high. Only the last data set was retained except in **8** where a solid-solid phase transition was observed. The phase transition was detected once the data were collected and it was based on the systematic absences and the successful solution and refinement of the structure in the I-4 space group. The two independent molecules in this group were related by a center of symmetry in the room temperature phase, space group $I4_1/a$.

For the bromine derivatives, semi-empirical Ψ scan[21] and empirical absorption corrections[22] were applied. The one which gave better results in the refinement and lower peaks in the final difference synthesis was retained. The structures were solved by Patterson (**6** and **7**) and by direct methods[23] and refined by least-squares procedures on Fo. In one of the two independent molecules in **4** (Figure 1), the ethoxycarbonyl group was disordered and its atoms were allowed to refine over two positions with site-occupancy factors of 0.68(1) and 0.32(1). Only atoms with the major occupancy factors were refined with an anisotropic model. In **8** and **8'**, only a disorder model for C9 and C10 could be modelled in spite of the values of the displacement parameters of the O7 and O8 atoms. The scattering factors were taken from the International Tables for X-Ray Crystallography[24] and most of the calculations were carried out with the XTAL[25], PESOS[26], and PARST[8] programs running on an AXP 600 computer.

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Table 5a. Crystal analysis parameters.

	1	1'	2	3	4
Solvent	AcOEt	EtOH	Toluene	EtOH	MeOH
Crystal data					
Formula	$C_6H_8N_2O_2$	$(C_6H_8N_2O_2)_{0.93(1)}$· $.(C_4H_3N_2O_2Br)_{0.07(1)}$	$C_7H_{10}N_2O_2$	$C_7H_{10}N_2O_2$	$C_{12}H_{12}N_2O_2$
Crystal habit	Colourless, plate	Colourless, plate	Colourless, prism	Colourless, prism	Colourless, prism
Crystal size (mm)	0.70 x 0.33 x 0.13	0.63x0.27x0.13	0.60 x 0.40 x 0.30	0.67 x 0.27 x 0.13	0.50 x 0.27 x 0.17
Symmetry	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, I2/a
Unit cell determination:					
Least-squares fit from					
reflexions (θ<45°):	62	47	67	53	81
Unit cell dimensions (Å,°)	*a*=7.6018(4)	*a*=7.5756(7)	*a*=13.6792(12)	*a*=7.2304(9)	*a*=17.8474(8)
	b=12.9489(10)	*b*=12.9508(13)	*b*=6.1175(3)	*b*=7.9804(9)	*b*=11.2655(4)
	c=7.8167(4)	*c*=7.8234(6)	*c*=9.7777(6)	*c*=13.7393(24)	*c*=22.9882(14)
	90.0, 115.549(4), 90.0	90.0, 115.316(7), 90.0	90.0, 103.338(7), 90.0	90.0, 102.275(11), 90.0	90.0, 106.429(4), 90.0
Packing: V(Å³), Z	694.20(5), 4	693.84(9), 4	796.16(7), 4	774.66(13), 4	4433.3(3), 16
Dc(g/cm³), M, F(000)	1.341, 140.1, 296	1.373, 143.7, 301	1.286, 154.2, 328	1.322, 154.2, 328	1.296, 216.2, 1824
$\mu(cm^{-1})$	8.64	13.33	7.99	8.21	7.37
Experimental data					
Technique	Four circle diffractometer: Bisecting geometry. Graphite oriented monochromator. ω/2θ scans. θ_{max}= 65°. Detector apertures 1 x 1°. CuKα.				
	Philips PW1100, 295K	Philips PW1100, 200K	Philips PW1100, 200K	Philips PW1100, 200K	Philips PW1100, 200K
Scan width; time/reflex	1.5°; 1 min/reflex	1.5°; 1 min/reflex	1.5°; 36 sec/reflex	1.6°; 1 min/reflex	1.6°; 1 min/reflex
2 Standard reflex./90 min.	No variation	2%decay	26%decay	No variation	No variation
Number of reflexions:					
Independent	973	926	1118	1069	3247
Observed (2σ(I) criterion)	1181	1181	1357	1324	3768
Solution:	Direct methods: Sir92				
Refinement-Least-Squares on Fo	Full matrix				
Secondary extinction ($x10^4$)	0.177(5)	0.011(1)	0.264(17)	0.035(1)	0.206(7)
Parameters:					
Number of variables	123	132	140	140	376
Degrees/Ratio of freedom	850/7.9	794/7.0	978/8.0	929/7.6	2871/8.6
max/average final shift/error	0.003/0.000	0.004/0.000	0.032/0.003	0.013/0.006	0.001/0.000
H atoms	From difference synthesis				
Weighting-scheme	Empirical as to give no trends in $<\omega\Delta^2F>$ vs. $<|Fobs|>$ and $<\sin\theta/\lambda>$				
Max. thermal value (Å²):	U11[O7]=0.116(1)	U11[Br41]=0.074(4)	U11[O7]=0.074(2)	U11[C41]=0.068(2)	U22[C10(mol.1)]=0.135(4)
Final Δρ peaks ($eÅ^{-3}$)	-0.26/0.22	-0.33/0.28	-0.31/0.40	-0.25/0.22	-0.48/0.41
Final R and Rw	0.041, 0.049	0.066, 0.073	0.070, 0.084	0.039, 0.045	0.058, 0.067

Table 5b. Crystal analysis parameters.

	5	6	7	8	8'
Solvent	$CHCl_3$+Hexane	MeOH+CH_2Cl_2	Hexane+ether	MeOH	MeOH
Crystal data					
Formula	$C_{12}H_{12}N_2O_2$	$C_6H_7N_2O_2Br$	$C_7H_9N_2O_2Br$	$C_{12}H_{11}N_2O_2Br$	$C_{12}H_{11}N_2O_2Br$
Crystal habit	Colourless, prism	Colourless, prism	Colourless, prism	Colourless, prism	Colourless, prism
Crystal size (mm)	0.33 x 0.17 x 0.13	0.57 x 0.27 x 0.23	0.27 x 0.23 x 0.23	0.57 x 0.33 x 0.20	0.50 x 0.20 x 0.10
Symmetry	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$	Tetragonal, $I4_1/a$	Tetragonal, I-4
Unit cell determination:					
Least-squares fit from reflexions (θ<45°):	47	67	72	71 (θ<35°)	66
Unit cell dimensions (Å,°)	*a*=12.7044(11)	*a*=10.0610(9)	*a*=12.0582(10)	*a*=19.467(1)	*a*=19.1987(14)
	b=7.7894(6)	*b*=7.9972(6)	*b*=7.8190(4)	*b*=19.467(1)	*b*=19.1987(14)
	c=12.4164(9)	*c*=9.8319(7)	*c*=10.2954(7)	*c*=13.384(2)	*c*=13.3912(10)
	90.0, 115.256(5), 90.0	90.0, 93.575(7), 90.0	90.0, 109.467(6), 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Packing: V(Å³), Z	1111.3(1), 4	789.54(8), 4	915.20(8), 4	5072.4(7), 16	4935.8(6), 16
Dc(g/cm³), M, F(000)	1.293, 216.2, 456	1.843, 219.0, 432	1.692, 233.1, 464	1.546, 295.1, 2368	1.589, 295.1, 2368
μ(cm^{-1})	7.35	67.37	58.52	43.66	44.86
Experimental data					
Technique:	*Four circle diffractometer:* Bisecting geometry. Graphite oriented monochromator. $\omega/2\theta$ scans. θ_{max}= 65°. Detector apertures 1 x 1°. CuKα.				
	Philips PW1100, 295K	Philips PW1100, 295K	Philips PW1100, 295K	Seifert, 295K	Philips PW1100, 200K
Scan width; time/reflex	1.6°; 1 min/reflex	1.6°; 1 min/reflex	1.5°; 1 min/reflex	1.5°; 1 min/reflex	1.6°; 1 min/reflex
2 Standard reflex./90 min.	No variation	No variation	2% decay	No variation	No variation
Number of reflexions:					
Independent	1392	1210	1395	1313	1970
Observed (2σ(I) criterion)	1889	1341	1552	2071	2201
Solution:	Direct methods: Sir92	Patterson	Patterson	Direct methods: Sir92	Direct methods: Sir92
Refinement-Least-Squares on Fo			Full matrix		
Secondary extinction (x10^4)	0.190(8)	no correction	0.081(4)	no correction	no correction
Parameters:					
Number of variables	193	125	142	176	323
Degrees/Ratio of freedom	1199/7.2	1085/9.7	1253/9.8	1137/7.5	1647/6.1
max/average final shift/error	0.013/0.001	0.090/0.005	0.047/0.002	0.049/0.004	0.056/0.003
H atoms	From difference synthesis				
Weighting-scheme	Empirical as to give no trends in <$\omega\Delta^2F$> vs. <|Fobs|> and<$\sin\theta/\lambda$>				
Max. thermal value (Å²):	U11[O(7)]=0.131(2)	U11[O(7)]=0.069(4)	U11[Br(41)]=0.0981(4)	U33[C54(mol.1)]=0.140(8)	U33[O7(mol.2)]=0.108(7)
Final $\Delta\rho$ peaks ($eÅ^{-3}$)	-0.41/0.22	-1.57/1.35	-0.67/0.41	-0.77/0.37	-0.62/0.47
Final R and Rw	0.053, 0.067	0.084, 0.107	0.042, 0.047	0.053, 0.063	0.048, 0.061

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