Pergamon

Tetrahedron, Vol. 52, No. 33, pp. 11075-11094, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00625-4

Aromatic Propellenes. Synthesis, X-Ray Structures and Conformational Study of Polypyrazolylpyridines

Pilar Cornago, Consuelo Escolástico, María Dolores Santa María and Rosa María Claramunt*

Departamento de Química Orgánica y Biología, Facultad de Ciencias, UNED, E-28040 Madrid, Spain

Cristina Fernández-Castaño and Concepción Foces-Foces*

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

Jean-Pierre Fayet

Laboratoire de Chimie des Materiaux Inorganiques, Université Paul Sabatier, 118, route de Narbonne,
F-31062 Toulouse, France

José Elguero

Instituto de Química Médica, Centro de Química Orgánica 'Manuel Lora Tamayo',
CSIC, Juan de la Cierva, 3, E-28006 Madrid, Spain

Abstract.— The crystal and molecular structures of three pentapyrazolylpyridines pz_5py, $dmpz_5py$ and $pz_4dmpzpy$ (pz = pyrazol-1'-yl, dmpz = 3,5-dimethylpyrazol-1'-yl) have been determined by X-Ray crystallography. The two pyrazole rings close to the pyridine nitrogen tend to be as coplanar as possible with the pyridine plane. Two different conformations with the nitrogen lone pairs of pyrazole N2 directed towards or opposite to the N1 nitrogen of pyridine, are present in the crystals. Semiempirical AMI calculations have been performed to evaluate the stability of these conformations which appear to be present also in solution (^1H and ^{13}C NMR and dipole moments). Copyright © 1996 Elsevier Science Ltd

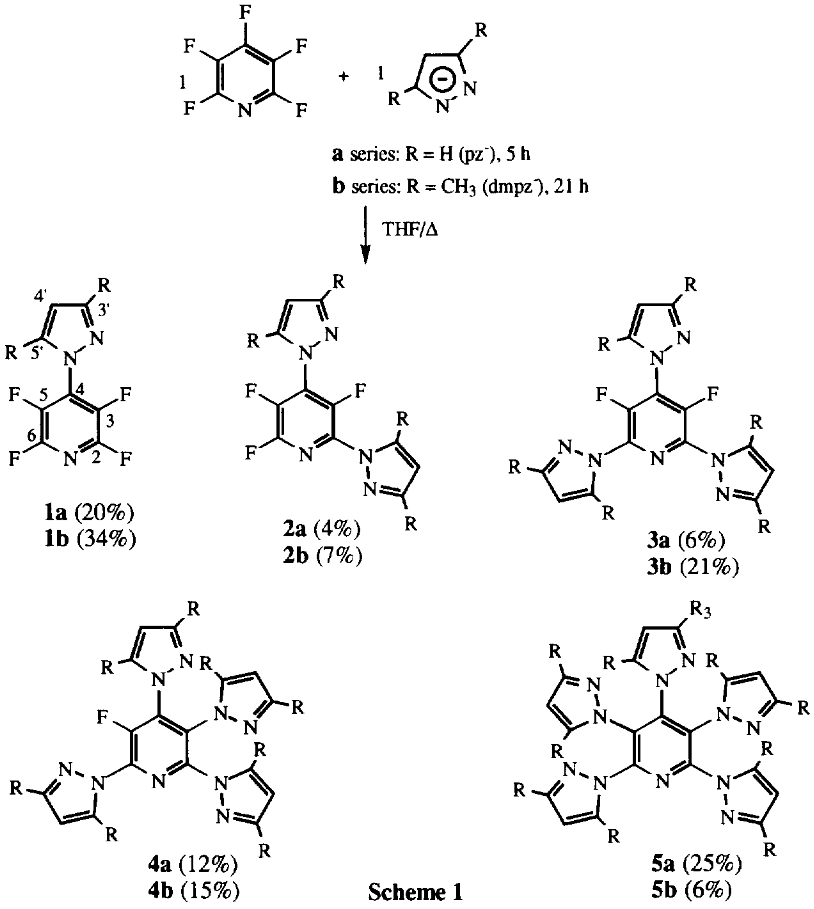
INTRODUCTION

The reaction of polyfluorobenzenes with pyrazole anions afforded with good yields a new family of benzene derivatives partly or fully substituted by pyrazol-1-yl groups, the 'aromatic propellenes' whose properties we have recently reported.[1-4] Compounds having both pyrazole and pyridine rings like 2,6-bis(pyrazol-1-yl)pyridine have been prepared as new tridentate ligands.[5]

For these reasons we decided to study the reaction of pentafluoropyridine with pyrazolate and 3,5-dimethylpyrazolate anions. In Schemes 1-3 are gathered the different products obtained depending on the experimental conditions. Amongst these compounds we have paid a particular attention to the pentapyrazolylpyridines **5a**, **5b**, **6** and **7**.

RESULTS AND DISCUSSION

Chemistry.- When the molar ratio pyrazole/pentafluoropyridine was 1:1, five compounds were formed: the mono-, bis-, tris-, tetrakis- and pentakis-pyrazolyl substituted pyridines **1**-**5**. The **a** and **b** series correspond respectively to R = pyrazol-1'-yl and 3,5-dimethylpyrazol-1'-yl (Scheme 1). By using a molar ratio pyrazole/penta-fluoropyridine 5:1 only the 2,3,4,5,6-pentakis(pyrazol-1'-yl)pyridine (**5a**) and 2,3,4,5,6-pentakis(3',5'-dimethylpyrazol-1'-yl)pyridine (**5b**) were isolated (Scheme 2). Starting from 4-(pyrazol-1'-yl)-2,3,5,6-tetrafluoropyridine (**1a**) and from 4-(3',5'-dimethylpyrazol-1'-yl)-2,3,5,6-tetrafluoropyridine (**1b**) the mixed derivatives 2,3,5,6-tetrakis(3',5'-dimethylpyrazol-1'-yl)-4-(pyrazol-1'-yl)pyridine (**6**) and 2,3,5,6-tetrakis(pyrazol-1'-yl)-4-(3',5'-dimethylpyrazol-1'-yl)pyridine (**7**) were obtained.



1a (20%)
1b (34%)

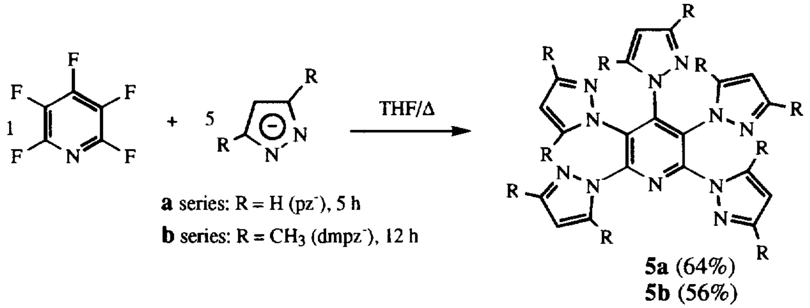
2a (4%)
2b (7%)

3a (6%)
3b (21%)

4a (12%)
4b (15%)

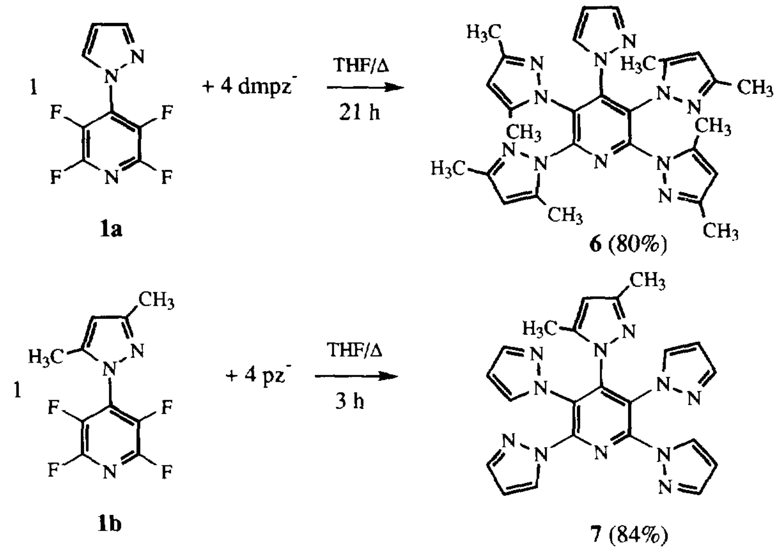
5a (25%)
5b (6%)

Scheme 1



5a (64%)
5b (56%)

Scheme 2



Scheme 3

Considering the structure of the products of partial substitution (Scheme 1), the reactivity of the fluorine atoms in pentafluoropyridine follows the order 4-F > 2-F/6-F > 3-F/5-F. This is the order reported for other nucleophiles although tetrasubstituted derivatives like **4** were not isolated.[6,7]

X-Ray Crystallography .- Two perspective views of the molecular structure of compounds **5a** (pz_5py), **5b** ($dmpz_5py$) and **7** ($pz_4dmpzpy$) showing the conformation of the molecules together with the numbering system are depicted in Fig. 1. The most relevant geometrical parameters are given in Table 1. The pattern of bond distances and angles in the pyridine moiety agree quite well with that of pentachloropyridine[8] (Table 1) with the lengthening of the C-C distances, the opening of the angles at N1 and C4 and the narrowing of those at C3 and C5 with respect to the parent pyridine.[9] When comparing the average geometries (Table 1) of the pyrazole and 3,5-dimethylpyrazole units (pz and dmpz hereinafter) with that of pyrazole itself[10] a greater degree of delocalization has been observed. The C-methyl groups modify the geometry of the pyrazole ring,[1] the main differences being those concerning the lengthening of the Nx1-Nx2 and Cx3-Cx4 distances in the dmpz rings with regard to the pz ones and the fact that the angles at Cx4 and Cx5 interchange their values.

The pyridine rings, mainly in **5a** and **5b**, are not planar in terms of the achieved precision (χ^2 = 89.04, 74.4, 10.94 vs. the tabulated value of 7.81). Moreover, the Nx1 atoms deviate significantly from their planes (Fig. 1) up to 0.096(3), 0.205(3) and 0.174(4)° in **5a**, **5b** and **7** respectively. Distortions from planarity have also been observed in other bulky pentasubstituted pyridines retrieved from the Cambridge Structural Database (October 1995 release),[11] the greatest deviations being presented by 2,3,4-tris-(*t*-butyl)-5-*t*-butoxycarbonyl-6-ethoxycarbonylpyridine.[12]

The pz or dmpz rings, in the less crowded region, appear to be more coplanar with the pyridine ring showing torsion angles as low as 18.9(7)° (Table 2). If the nitrogen lone pairs of the pyrazoles are considered as to be placed *up* (*u*) or *down* (*d*) with respect to the pyridine plane, the conformation of the molecules can be

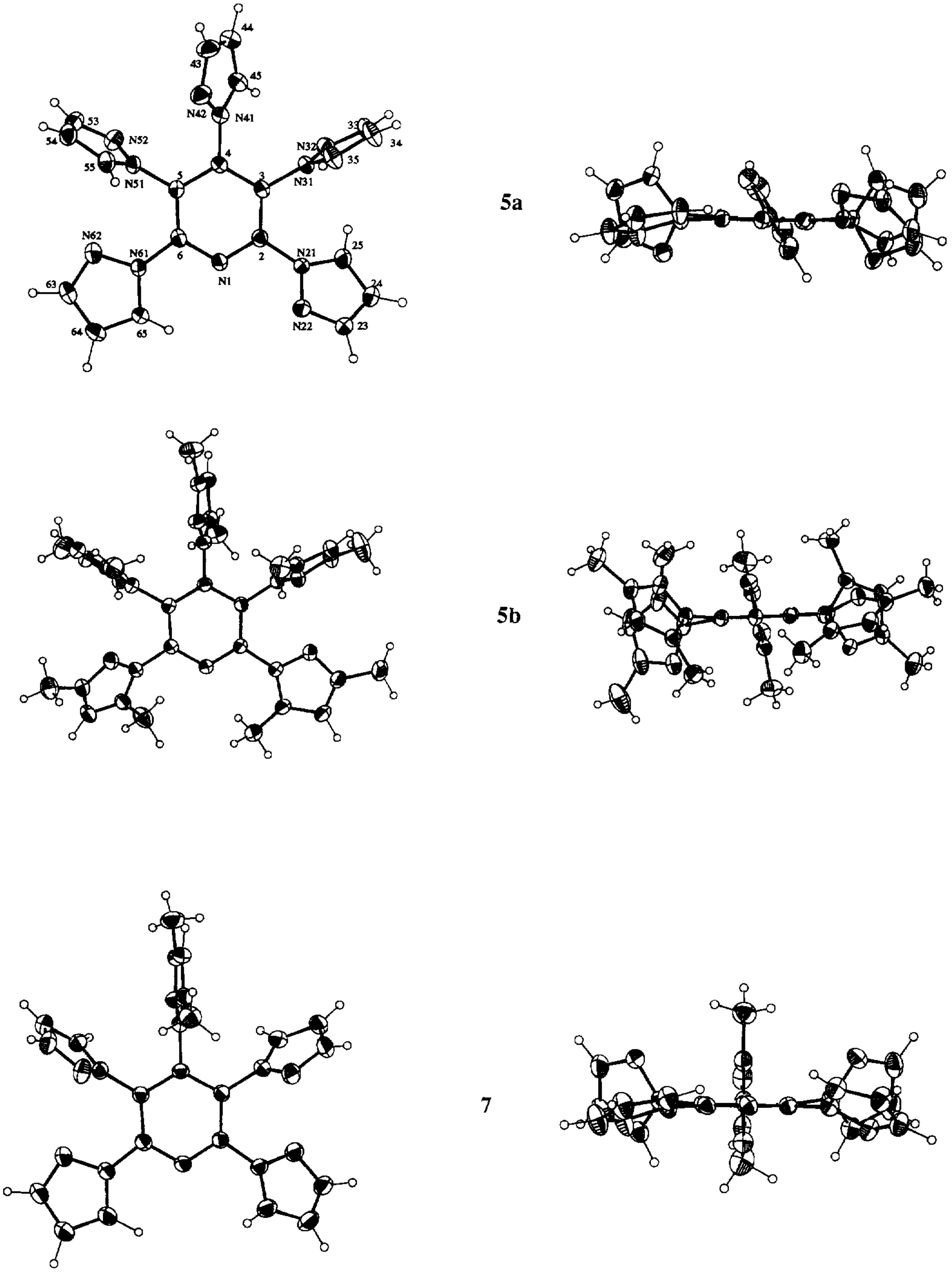


Fig.1 .-Two perpective views of the molecular structure of compounds **5a**,**5b** and **7** as projected onto the piridine plane and perpendicular to it. Displacement parameters are drawn at the 30% level.

Table 1. Selected geometrical parameters (Å,°) according to the numbering system given in Fig. 1; x=4 and Nx1-Nx2 means N41-N42, py stands for the average geometry of the anhydrous and hydrated pyridine and Cl_5py for that of pentachloropyridine

Compound:	**5a**	**5b**	**7**	**py**	**Cl_5py**
N1-C2	1.320(5)	1.335(3)	1.323(5)	1.337	1.323
C2-C3	1.391(4)	1.397(4)	1.388(7)	1.378	1.411
C3-C4	1.392(5)	1.394(4)	1.391(6)	1.376	1.410
C4-C5	1.391(6)	1.387(4)	1.382(5)	1.376	1.410
C5-C6	1.388(4)	1.379(4)	1.406(7)	1.378	1.411
C6-N1	1.335(5)	1.335(4)	1.337(6)	1.337	1.323
N1-C2-C3	123.4(3)	122.4(2)	123.6(4)	123.8	123.9
C2-C3-C4	117.4(3)	117.5(2)	116.6(4)	118.6	116.8
C3-C4-C5	120.0(4)	120.3(2)	121.3(4)	118.8	119.8
C4-C5-C6	117.3(3)	117.5(3)	117.2(4)	118.6	116.8
N1-C6-C5	123.3(3)	123.5(2)	121.9(4)	123.8	123.9
C2-N1-C6	118.5(3)	118.8(2)	119.4(4)	116.5	118.8
C2-N21	1.418(5)	1.413(4)	1.410(6)		
C3-N31	1.421(5)	1.417(3)	1.420(5)		
C4-N41	1.417(4)	1.423(3)	1.417(7)		
C5-N51	1.416(5)	1.420(4)	1.419(6)		
C6-N61	1.410(5)	1.414(3)	1.398(5)		

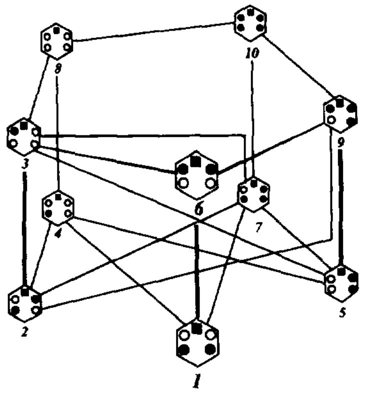
Compound:	**5a**		**5b**		**7**	
	x=2	x=6	x=2	x=6	x=2	x=6
Nx1-Nx2	1.365(4)	1.362(6)	1.379(3)	1.383(3)	1.365(4)	1.360(5)
Nx2-Cx3	1.323(5)	1.338(6)	1.320(4)	1.321(4)	1.312(7)	1.315(7)
Cx3-Cx4	1.395(6)	1.380(7)	1.396(5)	1.385(5)	1.379(8)	1.389(9)
Cx4-Cx5	1.357(6)	1.350(7)	1.369(5)	1.367(5)	1.365(7)	1.366(6)
Cx5-Nx1	1.364(5)	1.362(4)	1.377(4)	1.354(4)	1.350(7)	1.358(7)
Cx3-Cx6	-	-	1.489(6)	1.505(5)	-	-
Cx5-Cx7	-	-	1.470(5)	1.490(5)	-	-
Nx1-Nx2-Cx3	103.8(3)	104.1(4)	104.7(2)	103.6(2)	103.5(3)	104.0(4)
Nx2-Cx3-Cx4	112.4(4)	111.8(4)	111.2(3)	112.1(3)	113.0(5)	113.1(6)
Cx3-Cx4-Cx5	105.3(4)	105.9(5)	107.4(3)	106.5(3)	105.2(5)	104.5(5)
Nx1-Cx5-Cx4	106.6(4)	107.1(3)	104.7(3)	105.6(3)	106.3(4)	107.0(5)
Nx2-Nx1-Cx5	111.8(3)	111.2(3)	112.0(2)	112.2(2)	112.0(4)	111.5(4)
Nx2-Cx3-Cx6	-	-	119.2(3)	119.6(3)	-	-
Cx4-Cx3-Cx6	-	-	129.6(3)	128.3(3)	-	-
Cx4-Cx5-Cx7	-	-	129.1(3)	130.9(3)	-	-
Nx1-Cx5-Cx7	-	-	126.1(3)	123.4(3)	-	-
	x=3	x=5	x=3	x=5	x=3	x=5
Nx1-Nx2	1.358(4)	1.359(5)	1.367(3)	1.364(4)	1.361(5)	1.355(6)
Nx2-Cx3	1.318(7)	1.330(5)	1.323(4)	1.340(5)	1.334(6)	1.327(7)
Cx3-Cx4	1.372(8)	1.376(6)	1.390(5)	1.392(7)	1.369(9)	1.367(9)
Cx4-Cx5	1.364(8)	1.362(6)	1.364(4)	1.359(7)	1.358(6)	1.350(8)
Cx5-Nx1	1.337(6)	1.350(4)	1.356(4)	1.365(4)	1.347(6)	1.345(6)
Cx3-Cx6	-	-	1.502(7)	1.488(9)	-	-
Cx5-Cx7	-	-	1.493(5)	1.484(7)	-	-
Nx1-Nx2-Cx3	103.7(3)	103.2(3)	103.5(2)	103.6(3)	102.6(4)	102.8(4)
Nx2-Cx3-Cx4	112.1(4)	112.7(4)	112.1(3)	111.0(3)	113.3(6)	113.1(5)
Cx3-Cx4-Cx5	105.7(5)	105.4(4)	106.0(3)	107.3(5)	105.0(5)	105.1(5)
Nx1-Cx5-Cx4	106.0(4)	106.3(4)	105.6(3)	104.9(3)	106.9(5)	106.9(4)
Cx2-Nx1-Cx5	112.4(3)	112.5(3)	112.7(2)	113.2(3)	112.3(4)	112.1(4)
Cx2-Cx3-Cx6	-	-	119.8(3)	119.7(5)	-	-
Cx4-Cx3-Cx6	-	-	128.1(4)	129.3(5)	-	-
Cx4-Cx5-Cx7	-	-	132.4(3)	132.5(5)	-	-
Nx1-Cx5-Cx7	-	-	121.9(3)	122.6(3)	-	-

Table 1 cont. **pyrazole** represents the geometry of the parent compound and **pz** and **dmpz** the averaged geometries of the pyrazole and 3,5-dimethylpyrazole moities in the present work.

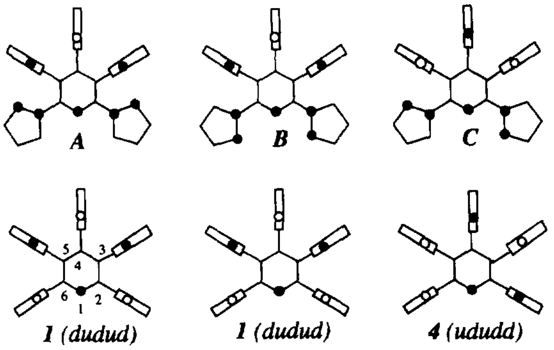
Compound:	**5a**	**5b**	**7**	**pyrazole**	**pz**	**dmpz**
	x=4	x=4	x=4			
Nx1-Nx2	1.362(4)	1.369(3)	1.376(5)	1.341(6)	1.357(2)	1.373(2)
Nx2-Cx3	1.334(5)	1.318(4)	1.329(8)	1.329(10)	1.327(2)	1.323(2)
Cx3-Cx4	1.386(7)	1.400(5)	1.400(8)	1.382(10)	1.375(2)	1.393(2)
Cx4-Cx5	1.358(5)	1.367(4)	1.352(8)	1.376(10)	1.359(2)	1.365(2)
Nx1-Cx5	1.363(5)	1.350(4)	1.366(7)	1.333(10)	1.354(2)	1.361(2)
Cx3-Cx6	-	1.507(6)	1.489(8)			
Cx5-Cx7	-	1.478(5)	1.487(8)			
Nx1-Nx2-Cx3	103.2(3)	104.0(2)	103.5(4)	104.9(6)	103.5(1)	103.9(1)
Nx2-Cx3-Cx4	112.7(4)	111.5(3)	111.1(5)	111.6(6)	112.6(1)	111.5(1)
Cx3-Cx4-Cx5	105.4(4)	106.1(3)	107.6(5)	104.4(7)	105.3(2)	106.6(1)
Nx1-Cx5-Cx4	106.4(4)	105.6(3)	104.8(5)	107.3(6)	106.6(1)	105.2(1)
Nx2-Nx1-Cx5	112.3(3)	112.8(2)	113.0(4)	111.8(6)	112.0(1)	112.5(1)
Nx2-Cx3-Cx6	-	120.3(3)	120.8(5)			
Cx4-Cx3-Cx6	-	128.2(3)	128.2(5)			
Cx4-Cx5-Cx7	-	132.1(3)	133.8(5)			
Nx1-Cx5-Cx7	-	122.3(3)	121.4(5)			
N1-C2-N21-N22	-34.3(4)	-153.6(2)	147.8(4)			
C2-C3-N31-N32	97.1(4)	76.2(3)	-59.4(6)			
C3-C4-N41-N42	-121.1(4)	-100.6(3)	91.3(5)			
C4-C5-N51-N52	74.5(4)	87.5(3)	-105.6(5)			
C5-C6-N61-N62	19.1(5)	-55.4(4)	18.9(7)			

Hydrogen interactions

Compound: **5a**	X-H	H...Y	X...Y	X-H..Y
C65-H65...N1	0.90(6)	2.41(5)	2.705(6)	100(4)
C25-H25...N32	0.99(4)	2.40(4)	3.205(4)	135(3)
C45-H45...N32	1.05(4)	2.54(5)	3.129(5)	114(3)
C35-H35...N22(−x,1−y,−z)	0.95(4)	2.58(5)	3.414(5)	147(4)
C23-H23...N42(−x,1−y,−z)	1.03(4)	2.51(4)	3.455(5)	153(3)
C25-H25...N52(−x,−y,−z)	0.99(4)	2.60(4)	3.289(5)	126(3)
C33-H33...N62(−x,−y,−z)	0.99(5)	2.80(4)	3.643(6)	144(4)
C64-H64...N22(−x,1−y,1−z)	1.01(5)	2.58(6)	3.474(5)	147(4)
Compound: **5b**				
C27-H271...N1	0.97(4)	2.74(4)	2.961(5)	94(2)
C27-H272...N1	1.00(5)	2.78(5)	2.961(5)	90(3)
C37-H373...N42	0.96(8)	2.64(8)	3.461(5)	144(6)
C47-H472...N32	0.96(6)	2.65(5)	3.357(5)	132(4)
C57-H571...N62	1.01(8)	2.53(8)	3.235(5)	126(6)
C57-H573...N42	0.99(7)	2.65(7)	3.348(5)	128(5)
C26-H262...N62(−x,−y,1−z)	0.96(7)	2.79(6)	3.631(6)	146(5)
Compound: **7**				
C25-H25...N1	0.88(4)	2.68(5)	2.826(6)	90(3)
C65-H65...N1	1.04(5)	2.50(5)	2.761(5)	94(3)
C35-H35...N42	0.95(4)	2.77(5)	3.276(5)	114(3)
C55-H55...N42	0.97(5)	2.80(4)	3.222(5)	107(3)
C25-H25...N52(−x,1/2−y,1/2+z)	0.88(4)	2.57(5)	3.425(6)	166(4)
C55-H55...N22(1−x,−y,−z)	0.97(5)	2.64(4)	3.320(6)	128(3)
C64-H64...N32(x−1,1/2−y,−1/2+z)	1.01(6)	2.58(6)	3.539(7)	157(4)



Scheme 4



Scheme 5

Table 2. Theoretical (AM1) and experimental conformations (°), heats of formation (kcal mol^{-1}) and dipole moments (Debyes)

Angle	Conf. A	Theoretical Conf. B	Conf. C	Experimental
pz_5py				Compound **5a**
N1-C2-N21-N22	-142.2	–68.7	-66.9	-34.3(4)
C2-C3-N31-N31	71.2	78.2	79.3	97.1(4)
C3-C4-N41-N42	–64.0	–123.4	–121.7	–121.1(4)
C4-C5-N51-N52	115.7	58.9	58.8	74.5(4)
C5-C6-N61-N62	–39.6	–120.6	35.1	19.1(5)
Heat of formation	468.7	472.4	470.7	–
Dipole moment	0.91	3.01	1.46	–
$dmpz_5py$				Compound **5b**
N1-C2-N21-N22	–134.0	a*	a*	–153.6(2)
C2-C3-N31-N31	83.3	–	–	76.2(3)
C3-C4-N41-N42	–90.9	–	–	–100.6(3)
C4-C5-N51-N52	94.3	–	–	87.5(3)
C5-C6-N61-N62	–56.4	–	–	–55.4(4)
Heat of formation	395.5	–	–	–
Dipole moment	1.26	–	–	–
pz_4dmpy				Compound **7**
N1-C2-N21-N22	–140.1	–76.4	–73.8	147.8(4)
C2-C3-N31-N31	61.8	63.1	64.2	–59.4(6)
C3-C4-N41-N42	–92.0	–99.0	–97.7	91.3(5)
C4-C5-N51-N52	115.1	63.3	60.9	–105.6(5)
C5-C6-N61-N62	-39.4	–120.9	35.3	18.9(7)
Heat of formation	435.4	457.8	455.9	–
Dipole moment	1.26	3.86	0.91	–

*These conformations are not minima

represented as shown in Schemes 4 and 5 in a similar way to that described for hexa(dmpz or pz)benzene derivatives.[1,2] All possible conformations are represented in Scheme 4 together with the interconversion paths between them; a black circle stands for a pz *up*, a white one for pz *down* and a black square for a dmpz *up* and a white square for a dmpz ring *down* when the mixed compounds, like **6** and **7**, are considered. All conformations are obtained when only one pyrazole is twisted by 180° and assuming all torsion angles, in absolute value, equal to 90°. Two conformations labelled as ***1**:dudud* and ***4**:ududd* are observed in the solid state for compounds **5a** on one hand and for compounds **5b** and **7** on the other. If the torsion angles differ from 90°, three additional situations ***A**-**C***, placing the N22 and N62 outwards or inwards with regard to the nitrogen of the pyridine, should be considered, see Scheme 5 and Table 2. The stability of these last conformations has been evaluated using the AM1 Hamiltonian and eigenvector follow (EF) at the highest precision level.[13] The computed minimum energy for conformer ***1**:**A*** is 2.0 kcal mol^{-1} more stable than ***1**:**C*** presented by **5a**. In all cases there is a good agreement between the observed and the calculated torsion angles although in the theoretical calculations the pyrazole rings are found more perpendicular to the pyridine ring. In summary, the three X-ray structures correspond respectively to: **5a** → ***1**:**C***, **5b** and **7** → ***4**:**A***.

The crystal packing is due to C-H···N contact (Table 1). There are no voids in the structures and the total packing coefficients are 0.69, 0.63 and 0.67 for compound **5a**, **5b** and **7** respectively.[14]

^{1}H and ^{13}C NMR Studies.- The ^{1}H NMR results are reported in Table 3 (pz derivatives, **1a**-**5a**), Table 4 (dmpz derivatives, **1b**-**5b**), Table 5 (compound **6**) and Table 6 (compound **7**) while the ^{13}C NMR results are reported in Table 7 (pz derivatives, **1a**-**5a**, pyridine carbons), Table 8 (dmpz derivatives, **1b**-**5b**, pyridine carbons), Table 9 (pz derivatives, **1a**-**5a**, pyrazole carbons), Table 10 (dmpz derivatives, **1b**-**5b**, pyrazole carbons) and Tables 11 and 12 (compounds **6** and **7**). The assignments are based on the extensive use of 2D-NMR spectroscopy (^{1}H-^{1}H and ^{1}H-^{13}C).

The main use of these Tables is to establish without ambiguity the structure of the different compounds independently of the X-ray determinations. We have checked the additivity of the substituents effects (SCS) both in ^{1}H and in ^{13}C NMR. Two kinds of experiments deserve a longer comment. First, in ^{1}H NMR some compounds appear as mixtures of isomers and not others, fact related to the *u* → *d* rotational barriers.[1-3] Thus, pz derivatives, like **5a** and **7**, have low rotational barriers and only average spectra are observed in solution while dmpz derivatives, like **5b** and **6**, have high rotational barriers and two isomers are observed in a 80:20 ratio for **5b** and 50:50 ratio for **6**. We assign these isomers to conformations ***1*** and ***4*** of Scheme 4. We have checked that these relative proportions are time independent by recording the ^{1}H NMR spectra with very few scans (very short time) and after a week in $CDCl_3$ solution.

The other experiment which deserves to be commented is the series of ^{13}C CPMAS NMR spectra. Compounds **5a** and **5b** show solid state spectra consistent with the X-ray structures (***1**:**C*** and ***4**:**A*** respectively). Compound **7** (Table 12) presents the signals of only one isomer which according to the X-ray structure has the conformation ***4**:**A***, only the pyridine carbon C-3(6) is split owing to a loss of symmetry in the solid state. The case of compound **6** is more complex. After many attempts (different solvents, different conditions) we failed to obtain crystals of **6**, the apparently most beautiful crystals were always twins. The ^{13}C CPMAS NMR spectrum (Table 11) proves without doubt that this compound in the solid state is a mixture of isomers ***1*** and ***4***, the ***A**-**C*** conformation cannot be ascertained.

In summary, i) when there is only one isomer in solution (**5a** and **7**) there is only one isomer in the solid

Table 3 ^{1}H NMR data (chemical shifts, δ in ppm, and coupling constants, *J* in Hz) in deuteriochloroform

	Position 2			Position 3			Position 4			Position 5			Position 6		
	H-3′	H-4′	H-5′	H-3′	H-4′	H-5′	H-3′	H-4′	H-5′	H-3′	H-4′	H-5′	H-3′	H-4′	H-5′
1a	-	-	-	-	-	-	7.93 $J_{H\text{-}4'}=1.5$	6.63 $J_{H\text{-}5'}=2.2$	7.94	-	-	-	-	-	-
2a	7.85 $J_{H\text{-}4'}=1.8$	6.55 $J_{H\text{-}5'}=2.4$	8.26	-	-	-	7.92 $J_{H\text{-}4'}=1.9$	6.62 $J_{H\text{-}5'}=2.5$	7.96	-	-	-	-	-	-
3a	7.86 $J_{H\text{-}4'}=1.8$	6.55 $J_{H\text{-}5'}=2.6$	8.33	-	-	-	7.92 $J_{H\text{-}4'}=1.9$	6.62 $J_{H\text{-}5'}=2.5$	7.96	-	-	-	7.86 $J_{H\text{-}4'}=1.8$	6.55 $J_{H\text{-}5'}=2.6$	8.33
4a	7.58 $J_{H\text{-}4'}=1.9$	6.31 $J_{H\text{-}5'}=2.4$	7.40	7.91 $J_{H\text{-}4'}=1.8$	6.58 $J_{H\text{-}5'}=2.6$	8.47 $J_F=0.8$	7.68 $J_{H\text{-}4'}=1.8$	6.37 $J_{H\text{-}5'}=2.7$	7.49 $J_F=1.7$	-	-	-	7.58 $J_{H\text{-}4'}=1.9$	6.35 $J_{H\text{-}5'}=2.8$	7.84
5a	7.58 $J_{H\text{-}4'}=1.9$	6.29 $J_{H\text{-}5'}=2.4$	7.38	7.60 $J_{H\text{-}4'}=1.8$	6.40 $J_{H\text{-}5'}=2.6$	8.02	7.43 $J_{H\text{-}4'}=1.8$	6.12 $J_{H\text{-}5'}=2.5$	7.21	7.60 $J_{H\text{-}4'}=1.8$	6.40 $J_{H\text{-}5'}=2.6$	8.02	7.58 $J_{H\text{-}4'}=1.9$	6.29 $J_{H\text{-}5'}=2.4$	7.38

Table 4 ^{1}H NMR data (chemical shifts, δ in ppm) in deuteriochloroform

	Position 2			Position 3			Position 4			Position 5			Position 6		
	H-4′	Me3′	Me5′	H-4′	Me3′	Me5′	H-4′	Me3′	Me5′	H-4′	Me3′	Me5′	H-4′	Me3′	Me5′
1b	-	-	-	-	-	-	6.11	2.30	2.24	-	-	-	-	-	-
2b	6.05	2.28[a]	2.34	-	-	-	6.11	2.31[a]	2.25	-	-	-	-	-	-
3b	6.02	2.28	2.33	-	-	-	6.08	2.29	2.27	-	-	-	6.02	2.28	2.33
4b	5.67	2.00	1.92	5.81	2.05	2.22	5.86	2.11	2.14	-	-	-	6.05	2.30	2.40
5b[b]	5.63	2.00	1.97	5.84	2.04	2.35	5.58	1.94	2.07	5.84	2.04	2.35	5.63	2.00	1.97
5b[c]	5.63	1.99	1.97	5.81	2.04	2.39	5.67	1.84	2.21	5.81	2.04	2.39	5.63	2.01	1.97

[a] These signals can be reversed; [b] Major isomer (80%); [c] Minor isomer (20%).

Table 5 ^{1}H NMR data (chemical shifts, δ in ppm, and coupling constants, *J* in Hz) in deuteriochloroform for compound **6**

Position 2			Position 3			Position 4		
H-4'	Me3'	Me5'	H-4'	Me3'	Me5'	H-3'	H-4'	H-5'
5.70	2.10	1.93	5.85	2.06	2.40	7.47 $J_{H\text{-}4'}$=1.8	6.15 $J_{H\text{-}5'}$=2.6	7.05
5.68	2.00	1.82	5.84	2.03	2.31	7.35 $J_{H\text{-}4'}$=1.8	6.10 $J_{H\text{-}5'}$=2.5	7.19

Table 6 ^{1}H NMR data (chemical shifts, δ in ppm, and coupling constants, *J* in Hz) in deuteriochloroform for compound **7**

Position 2			Position 3			Position 4		
H-3'	H-4'	H-5'	H-3'	H-4'	H-5'	H-4'	Me3'	Me5'
7.53 $J_{H\text{-}4'}$=1.8	6.26 $J_{H\text{-}5'}$=2.5	7.40 $J_{H\text{-}3'}$=0.5	7.57 $J_{H\text{-}4'}$=1.8	6.40 $J_{H\text{-}5'}$=2.8	8.03 $J_{H\text{-}3'}$=0.5	5.61	2.09	1.88

Table 7 ^{13}C NMR data for the pyridine carbon atoms (chemical shifts, δ in ppm, and coupling constants, J in Hz) in deuteriochloroform

	C-2	C-3	C-4	C-5	C-6		C-2	C-3	C-4	C-5	C-6
1a	144.2 ^1J=244.4 ^2J=15.4 ^3J=15.4 ^4J=2.9	135.5 ^1J=265.3	130.2	135.5 ^1J=265.3	144.2 ^1J=244.4 ^2J=15.4 ^3J=15.4 ^4J=2.9	**4a**	142.8	122.7 ^3J=2.4	138.9 ^2J=8.5	142.1 ^1J=274.4	138.6 ^2J=10.7
2a	131.9	139.6 ^1J=269.2 ^3J=2.5 ^4J=5.5	130.0 ^2J=13.8 ^2J=8.8 ^3J=5.1	136.2 ^1J=269.7 ^2J=31.3	146.0 ^1J=240.6 ^2J=14.7 ^3J=3.0	**5a**	147.0	123.0	148.6	123.0	147.0
3a	134.7 ^2J=8.2 ^4J=4.9	141.2 ^1J=274.0 ^3J=1.6	130.0	141.2 ^1J=274.0 ^3J=1.6	134.7 ^2J=8.2 ^4J=4.9	**5a**[a]	147.9	123.2	150.0	123.2	147.9

[a] CPMAS

Table 8 ^{13}C NMR data for the pyridine carbon atoms (chemical shifts, δ in ppm, and coupling constants, J in Hz) in deuteriochloroform

	C-2	C-3	C-4	C-5	C-6		C-2	C-3	C-4	C-5	C-6
1b	143.7 ^1J=245.9 ^2J=15.2 ^3J=15.2 ^4J=3.0	137.7 ^1J=265.7	130.3	137.7 ^1J=265.7	143.7 ^1J=245.9 ^2J=15.2 ^3J=15.2 ^4J=3.0	**4b**	143.8 ^4J=4.8	128.9 ^3J=1.5	137.7 ^2J=11.7	146.7 ^1J=272.9	139.2 ^2J=10.7
1b[a]	144.6	141.0	130.8	141.0	144.6	**5b**[b]	148.3	128.6	148.8	128.6	148.3
2b	132.1 ^2J=13.5 ^3J=13.5 ^4J=5.3	145.3 ^1J=269.1 ^3J=2.5 ^4J=6.1	129.0 ^2J=14.9 ^2J=11.3 ^3J=5.0	139.8 ^1J=271.7 ^2J=30.8	145.6 ^1J=242.5 ^2J=14.2 ^3J=3.5	**5b**[c]	148.2	128.3	148.7	128.2	148.2
3b	135.2 ^2J=9.7 ^4J=6.2	146.9 ^1J=274.5	128.2 ^2J=13.8 ^2J=13.8	146.9 ^1J=274.5	135.2 ^2J=9.7 ^4J=6.2	**5b**[a]	149.4	124.9 128.9	149.4	124.9 128.9	149.4

[a] CPMAS, [b] Major isomer; [c] Minor isomer;

Table 9 ^{13}C NMR data for the pyrazolyl carbons atoms (chemical shifts, δ in ppm, and coupling constants, *J* in Hz) in deuteriochloroform

	Position 2			Position 3			Position 4			Position 5		Position 6		
	C-3'	C-4'	C-5'	C-3'	C-4'	C-5'	C-3'	C-4'	C-5'	C-3' and C-5'	C-4'	C-3'	C-4'	C-5'
1a	-	-	-	-	-	-	143.5 $^{1}J=188.8$ $^{2}J_{H-4'}=6.2$ $^{3}J_{H-5'}=8.0$	109.0 $^{1}J=180.4$ $^{2}J_{H-3'}=9.6$ $^{2}J_{H-5'}=9.6$	132.0 $^{1}J=193.2$ $^{2}J_{H-4'}=9.2$ $^{3}J_{H-3'}=4.4$ $^{4}J_{F}=4.4$	-	-	-	-	-
2a	143.2 $^{1}J=188.3$ $^{2}J_{H-4'}=5.8$ $^{3}J_{H-5'}=8.5$	108.2 $^{1}J=179.3$ $^{2}J_{H-3'}=10.2$ $^{2}J_{H-5'}=10.2$	129.7 $^{1}J=193.0$ $^{2}J_{H-4'}=9.2$ $^{3}J_{H-3'}=4.4$ $^{5}J_{F}=3.5$	-	-	-	143.2 $^{1}J=188.3$ $^{2}J_{H-4'}=5.8$ $^{3}J_{H-5'}=8.5$	108.7 $^{1}J=181.1$ $^{2}J_{H-3'}=9.3$ $^{2}J_{H-5'}=9.3$	132.1 $^{1}J=193.6$ $^{2}J_{H-4'}=9.2$ $^{4}J_{F}=5.5$ $^{4}J_{F}=2.4$	-	-	-	-	-
3a	143.2 $^{1}J=188.2$ $^{2}J_{H-4'}=5.9$ $^{3}J_{H-5'}=8.3$	108.2 $^{1}J=179.0$ $^{2}J_{H-3'}=9.3$ $^{2}J_{H-5'}=9.3$	129.8 $^{1}J=193.2$	-	-	-	143.1 $^{1}J=188.2$	108.5 $^{1}J=179.7$ $^{2}J_{H-3'}=9.4$ $^{2}J_{H-5'}=9.4$	132.3 $^{1}J=192.4$ $^{4}J_{F}=3.3$	-	-	143.2 $^{1}J=188.2$ $^{2}J_{H-4'}=5.9$ $^{3}J_{H-5'}=8.3$	108.2 $^{1}J=179.0$ $^{2}J_{H-3'}=9.3$ $^{2}J_{H-5'}=9.3$	129.8 $^{1}J=193.2$
4a	141.6 $^{1}J=186.9$ $^{2}J_{H-4'}=5.9$ $^{3}J_{H-5'}=8.4$	107.5 $^{1}J=178.6$ $^{2}J_{H-3'}=9.5$ $^{2}J_{H-5'}=9.5$	133.3 $^{1}J=191.0$ $^{2}J_{H-4'}=9.2$ $^{3}J_{H-3'}=4.6$	144.0 $^{1}J=188.0$ $^{2}J_{H-4'}=5.5$ $^{3}J_{H-5'}=8.8$ $^{6}J_{F}=3.3$	108.6 $^{1}J=179.2$ $^{2}J_{H-3'}=9.5$ $^{2}J_{H-5'}=9.5$ $^{6}J_{F}=1.5$	130.0 $^{1}J=192.3$ $^{2}J_{H-4'}=9.3$ $^{3}J_{H-3'}=4.5$ $^{5}J_{F}=3.3$	142.5* $^{1}J=187.7$ $^{2}J_{H-4'}=7.7$ $^{3}J_{H-5'}=6.0$	108.0 $^{1}J=179.3$ $^{2}J_{H-3'}=9.4$ $^{2}J_{H-5'}=9.4$	131.9 $^{1}J=192.4$ $^{2}J_{H-4'}=9.5$ $^{3}J_{H-3'}=4.5$ $^{4}J_{F}=2.0$	-	-	142.7* $^{1}J=187.7$ $^{2}J_{H-4'}=7.7$ $^{3}J_{H-5'}=6.0$	107.9 $^{1}J=178.7$ $^{2}J_{H-3'}=9.5$ $^{2}J_{H-5'}=9.5$	130.1 $^{1}J=192.3$ $^{2}J_{H-4'}=9.3$ $^{3}J_{H-3'}=4.5$
5a	141.4 $^{1}J=186.7$ $^{2}J_{H-4'}=5.6$ $^{3}J_{H-5'}=8.5$	107.4 $^{1}J=179.1$ $^{2}J_{H-3'}=10.5$ $^{2}J_{H-5'}=8.4$	133.0 $^{1}J=190.6$ $^{2}J_{H-4'}=9.3$ $^{3}J_{H-3'}=4.7$	143.6 $^{1}J=187.9$ $^{2}J_{H-4'}=5.8$ $^{3}J_{H-5'}=8.8$	108.4 $^{1}J=179.1$ $^{2}J_{H-3'}=10.7$ $^{2}J_{H-5'}=8.4$	130.2 $^{1}J=193.1$ $^{2}J_{H-4'}=9.6$ $^{3}J_{H-3'}=4.3$	141.8 $^{1}J=187.4$ $^{2}J_{H-4'}=5.9$ $^{3}J_{H-5'}=8.5$	107.4 $^{1}J=179.1$ $^{2}J_{H-3'}=10.5$ $^{2}J_{H-5'}=8.5$	131.8 $^{1}J=192.4$ $^{2}J_{H-4'}=9.4$ $^{3}J_{H-3'}=4.6$	C-3' 143.6 $^{1}J=187.9$ $^{2}J_{H-4'}=5.8$ $^{3}J_{H-5'}=8.8$	108.4 $^{1}J=179.1$ $^{2}J_{H-3'}=10.7$ $^{2}J_{H-5'}=8.4$	141.4 $^{1}J=186.7$ $^{2}J_{H-4'}=5.6$ $^{3}J_{H-5'}=8.5$	107.4 $^{1}J=179.1$ $^{2}J_{H-3'}=10.5$ $^{2}J_{H-5'}=8.4$	133.0 $^{1}J=190.6$ $^{2}J_{H-4'}=9.3$ $^{3}J_{H-3'}=4.7$
5a										C-5' 130.2 $^{1}J=193.1$ $^{2}J_{H-4'}=9.6$ $^{3}J_{H-3'}=4.3$				
5a[a]	143.0	106.8	134.2	144.3	110.1	132.1	142.4	108.8	134.2	C-3': 144.3 C-5': 132.1	110.1	143.0	106.8	134.2

[a] CPMAS

Table 10 ^{13}C NMR data (chemical shifts, δ in ppm, and coupling constants, J in Hz) in deuteriochloroform

	Position 2					Positions 3(5)					Position 4					Position 6				
	C-3'	C-4'	C-5'	Me$_{3'}$	Me$_{5'}$	C-3'	C-4'	C-5'	Me$_{3'}$	Me$_{5'}$	C-3'	C-4'	C-5'	Me$_{3'}$	Me$_{5'}$	C-3'	C-4'	C-5'	Me$_{3'}$	Me$_{5'}$
1b	-	-	-	-	-	-	-	-	-	-	152.8	108.0 ^{1}J=175.2 ^{3}J=3.4	142.1	13.2 ^{1}J=127.8	10.5 ^{1}J=129.4 $^{5}J_{F}$=2.7	-	-	-	-	-
1b[a]	-	-	-	-	-	-	-	-	-	-	152.7	108.1	144.6	12.1	12.1	-	-	-	-	-
2b	151.4	108.0 ^{1}J=175.0 ^{3}J=3.4	141.9	13.2 ^{1}J=127.9	11.4 ^{1}J=129.6 $^{5}J_{F}$=1.9	-	-	-	-	-	152.6	107.7 ^{1}J=175.5 ^{3}J=3.4	142.4	13.2 ^{1}J=127.9	10.6 ^{1}J=132.6 ^{5}J$_{F}$=2.2	-	-	-	-	-
3b	151.0	107.7 ^{1}J=174.2 ^{3}J=3.3	141.5	13.4 ^{1}J=127.6	11.7 ^{1}J=129.3	-	-	-	-	-	152.1	107.4 ^{1}J=174.9 ^{3}J=3.3	142.1	13.4 ^{1}J=127.6	10.8 ^{1}J=131.8 $^{5}J_{F}$=2.0	151.0	107.7 ^{1}J=174.2 ^{3}J=3.3	141.5	13.4 ^{1}J=127.6	11.7 ^{1}J=129.3
4b	150.0[b]	105.3 ^{1}J=173.3 ^{3}J=3.3	143.6[c]	13.0[d] ^{1}J=127.2	10.6 ^{1}J=129.3	149.9[b]	106.7 ^{1}J=173.5 ^{3}J=3.2	141.9	13.1[d] ^{1}J=127.4	11.7 ^{1}J=129.2	151.1[e]	106.3 ^{1}J=174.4 ^{3}J=3.3	142.6[c]	13.1 ^{1}J=127.3	10.8 ^{1}J=132.7 $^{5}J_{F}$=2.1	151.2[e]	108.3 ^{1}J=174.2 ^{3}J=3.3	141.4	13.4 ^{1}J=127.6	12.1 ^{1}J=129.5 $^{5}J_{F}$=1.6
5b[g]	150.0	104.9 ^{1}J=173.2 ^{3}J=3.3	143.5	13.2[f] ^{1}J=127.1	10.9 ^{1}J=128.8	149.5	107.2 ^{1}J=173.6 ^{3}J=3.4	141.7	13.3[f] ^{1}J=127.3	12.3 ^{1}J=129.4	149.9	105.0	143.9	13.0[f] ^{1}J=127.1	11.1 ^{1}J=129.2	150.0	104.9 ^{1}J=173.2 ^{3}J=3.3	143.5	13.2[f] ^{1}J=127.3	10.9 ^{1}J=128.8
5b[h]	150.2	105.3	142.0	13.3[e] ^{1}J=127.3	10.6	149.7	106.9	141.3	13.3[e] ^{1}J=127.3	12.4	149.9	105.8	144.4	13.0[f] ^{1}J=127.1	10.8	150.2	105.3	141.8	13.3[e] ^{1}J=127.3	10.6
5b[a]	150.5	105.8	142.2	14.1	11.4	150.5	107.8 109.1	141.7	14.7	12.6	147.7	105.8	142.2	12.6	12.2	150.5	105.8	142.2	14.1	11.4

[a] CPMAS; Pairs of signals marked b, c, d, e, f can be reversed; [g] Major isomer; [h] Minor isomer.

Table 11 ^{13}C NMR data (chemical shifts, δ in ppm, and coupling constants, *J* in Hz) in deuteriochloroform for compound **6**

Pyridine Carbons			Position 2				Position 3				Position 4		
C-2(6)	C-3(5)	C-4	C-3'	C-4'	C-5'	Me$_{3'}$ Me$_{5'}$	C-3'	C-4'	C-5'	Me$_{3'}$ Me$_{5'}$	C-3'	C-4'	C-5'
149.4	126.4	146.9	150.0	105.3 ^1J=173.3 ^3J=3.2	143.5	13.4 ^1J=127.5 10.8	150.2	107.2 ^1J=173.4 ^3J=3.5	141.9	13.2 ^1J=127.3 12.3 ^1J=129.5	141.7 ^1J=186.6 ^3J=8.5 ^2J=5.9	107.4	130.6 ^1J=192.1 ^2J=9.6 ^3J=4.4
149.0	125.3	148.4	150.1	105.3 ^1J=173.3 ^3J=3.2	143.7	13.3 ^1J=127.3 10.6 ^1J=129.2	150.3	107.2 ^1J=173.4 ^3J=3.5	142.0	13.3 ^1J=127.3 12.1 ^1J=129.4	141.7 ^1J=186.6 ^3J=8.5 ^2J=5.9	107.0	131.8 ^1J=193.0 ^2J=9.5 ^3J=4.6
149.0[a]	127.5 127.8	148.4	150.6 151.5	105.1 104.8	143.5	13.6 11.0 9.5 9.1	150.1	110.0 108.6	142.5 142.9	13.6 12.1 10.4	141.5	107.5 107.1 106.7	131.2

[a] This row corresponds to the CPMAS spectrum.

Table 12 ^{13}C NMR data (chemical shifts, δ in ppm, and coupling constants, *J* in Hz) in deuteriochloroform for compound **7**

Pyridine Carbons			Position 2			Position 3			Position 4			
C-2(6)	C-3(6)	C-4	C-3'	C-4'	C-5'	C-3'	C-4'	C-5'	C-3'	C-4'	C-5'	Me$_{3'}$ Me$_5$
146.4	125.1	147.5	141.3 ^1J=186.6 $^3J_{H\text{-}5'}$=8.4 $^2J_{H\text{-}4'}$=5.9	107.1 ^1J=178.3 $^2J_{H\text{-}3'}$=10.4 $^2J_{H\text{-}5'}$=8.7	132.1 ^1J=191.0 $^2J_{H\text{-}4'}$=9.3 $^3J_{H\text{-}3'}$=4.5	143.4 ^1J=187.6 $^3J_{H\text{-}5'}$=8.9 $^2J_{H\text{-}4'}$=5.9	108.3 ^1J=179.1 $^2J_{H\text{-}3'}$=10.4 $^2J_{H\text{-}5'}$=8.7	130.1 ^1J=192.9 $^2J_{H\text{-}4'}$=9.5 $^3J_{H\text{-}3'}$=4.2	150.9	105.8 ^1J=174.3 $^3J_{Me_{3'}}$=3.3 $^3J_{Me_{5'}}$=3.3	142.7	13.3 ^1J=127.5 10.6 ^1J=129.4
145.6[a]	124.3 125.3	145.6	138.8	107.3	132.1	143.0	110.2	130.9	150.3	106.0	143.0	12.6 11.4

[a] This row corresponds to the CPMAS spectrum.

state; ii) when there are two isomers in solution but one is largely predominant (**5b**) only the most stable is found in the solid state, and iii) when there are two isomers of the same stability in solution (**6**), both are present in the solid state.

Dipole Moments.- The dipole moments of Table 15 (see Experimental Part) contain indications about the conformation of molecules **1a**-**7**. We will discuss only the case of compounds containing only pz residues, the case of compounds containing dmpz residues, **1b**-**5b**, **6** and **7**, is similar since the corresponding dipole moments are generally 0.2 D lower. According to the AM1 calculations (see Scheme 5) conformation ***B*** (pyrazole N2 lone pair towards the pyridine N1 lone pair, i.e. ZZ) is much less stable than conformations ***A*** (EE) and ***C*** (EZ), thus we have only consider conformations *A* and *C*. We have calculated vectorially (from pyrazole and fluorine group contributions) the dipole moments and interpolated the experimental value between the calculated values (remember that only the square of the dipole moment is an additive property). Regarding the E/Z conformation of pyrazole rings at positions 2 and 6 of the pyridine ring the results are: compound **2a** 80% E-20% Z, **3a** 45% EZ-55% ZZ, **4a** 70% EZ-30% ZZ and **5a** 85% EZ-15% ZZ. These results are only indicative in which concerns the proportions of different conformers but it is certain that these compounds exist in solution as mixtures of conformers *A* and *C*. Thus finally, crystallography, NMR and dipole moments provided a consistent picture of polypyrazolylpyridines.

EXPERIMENTAL

General.- Melting points were determined in a microscope hot stage apparatus and are uncorrected. Column chromatography was performed on silica gel Merck 60 (70-230 mesh) using the appropriate eluent. The R_f were measured in tlc aluminium sheets of silica gel 60 F_{254} (layer thickness 0.2 mm) with the solvent indicated in each case. ^1H and ^{13}C NMR spectra in solution were recorded on a Bruker AC200 instrument working respectively at 200.14 and 50.32 MHz. Chemical shifts (δ) are given from external tetramethylsilane with an accuracy of 0.01 (for ^1H NMR) and 0.1 (for ^{13}C NMR) ppm. Coupling constants (J) are accurate to ± 0.2 and ± 0.6 Hz, respectively. Mass spectra were performed on a Shimadzu QP-5000 spectrometer at 60 eV using the electron impact mode. The starting compounds, pyrazole, 3,5-dimethylpyrazole and pentafluoropyridine, are commercial products.

Synthetic procedures.

Method A (Molar ratio pyrazole/pentafluoropyridine 1:1). 0.5 g (7.3 mmoles) of pyrazole or 0.5 g (5.2 mmoles) of 3,5-dimethylpyrazole in 5 mL of anhydrous THF were placed in a three-necked round bottomed flask provided with a reflux refrigerant, argon atmosphere and magnetic stirring. To the foregoing solution an equimolar amount of NaH (60% oil dispersion) was added in small portions and the reaction mixture was heated to 65°C for 1 h. After cooling down, addition of the equimolar amount of pentafluoropyridine was achieved and the mixture heated under reflux for 6 h in the case of the pyrazolate anion or 21 h for the reaction with 3,5-dimethyl-pyrazolate. The solvent was evaporated off under vacuum and the separation of products **1**, **2**, **3**, **4** and **5** belonging to the **a** and **b** series was achieved by column chromatography using hexane/ethyl acetate 6:4 as eluent.

4-(Pyrazol -1'-yl)-2,3,5,6-tetrafluoropyridine (**1a**): (Yield 20%). R_f 0.85 (hexane/ethyl acetate 6:4); mp. 48-50 °C ($CHCl_3$/hexane); Anal. $C_8H_3F_4N_3$; Calc. (%): C 44.25; H 1.39; N 19.35. Found (%): C 44.38; H 1.79; N 19.15; MS, m/z (%): 218 (M+1, 9.8), 216 (M, 100).

2,4-Bis(pyrazol -1'-yl)-3,5,6-trifluoropyridine (**2a**): (Yield 4%). R$_f$. 0.65 (hexane/ethyl acetate 6:4); mp. 86-88 °C ($CHCl_3$/hexane); Anal. $C_{11}H_6F_3N_5$; Calc. (%): C 49.82; H 2.28; N 26.41. Found (%): C 49.80; H 2.46; N 26.03; MS, m/z (%): 266 (M+1, 14.2), 265 (M, 100).

2,4,6-Tris(pyrazol -1'-yl)-5,6-difluoropyridine (**3a**): (Yield 6%). R$_f$. 0.25 (hexane/ethyl acetate 6:4); mp. 186-187 °C ($CHCl_3$/hexane); Anal. $C_{14}H_9F_2N_7$; Calc. (%): C 53.68; H 2.90; N 31.30. Found (%): C 53.72; H 3.0; N 30.92; MS, m/z (%): 314 (M+1, 18.1), 313 (M, 100).

2,3,4,6-Tetrakis(pyrazol -1'-yl)-5-fluoropyridine (**4a**): (Yield 12%). R$_f$. 0.11 (hexane/ethyl acetate 6:4); mp. 143-148 °C ($CHCl_3$/hexane); Anal. $C_{17}H_{12}FN_9$; Calc. (%): C 56.51; H 3.35; N 34.89. Found (%): C 56.40; H 3.41; N 34.51; MS, m/z (%): 362 (M+1, 20.1), 361 (M, 100), 360 (M-1, 55.4).

2,3,4,5,6-Pentakis(pyrazol -1'-yl)pyridine (**5a**): (Yield 25%). R$_f$. 0.04 (hexane/ethyl acetate 6:4); mp. 235-239 °C (Ethanol) [DSC, mp. 238.7 °C]; Anal. $C_{20}H_{15}N_{11}$; Calc.(%): C 58.67; H 3.69; N 37.63. Found (%): C 58.68; H 3.74; N 37.36; MS, m/z (%): 410 (M+1, 25.8), 409 (M, 100), 408 (M-1, 50.2).

4-(3,5-Dimethylpyrazol -1'-yl)-2,3,5,6-tetrafluoropyridine (**1b**): (Yield 34%). R$_f$. 0.85 (hexane/ethyl acetate 6:4); mp. 46-48 °C (hexane); Anal. $C_{10}H_7F_4N_3$; Calc. (%): C 48.99; H 2.88; N 17.14. Found (%): C 48.90; H 2.94; N 17.00; MS, m/z (%): 246 (M+1, 11.8), 245 (M, 100), 244 (M-1, 45.9).

2,4-Bis(3,5-dimethylpyrazol-1'-yl)-3,5,6-trifluoropyridine (**2b**): (Yield 7%). R$_f$. 0.68 (hexane/ethyl acetate 6:4); oil; MS, m/z (%): 322.15 (M+1, 22.0), 321.05 (M, 100).

2,4,6-Tris(3,5-dimethylpyrazol-1'-yl)-5,6-difluoropyridine (**3b**): (Yield 21%). R$_f$. 0.35 (hexane/ethyl acetate 6:4); mp. 156-159 °C (hexane/$CHCl_3$); Anal. $C_{20}H_{21}F_2N_7$ Calc. (%): C 60.44; H 5.33; N 24.67. Found (%): C 60.40; H 5.31; N 24.54; MS, m/z (%): 398 (M+1, 13.4), 397 (M, 100).

2,3,4,6-Tetrakis(3,5-dimethylpyrazol -1'-yl)-5-fluoropyridine (**4b**): (Yield 15%). R$_f$. 0.20 (hexane/ethyl acetate 6:4); oil; MS, m/z (%): 474.30(M+1, 29.7), 473.15 (M, 100).

2,3,4,5,6-Pentakis(3,5-dimethylpyrazol -1'-yl)pyridine (**5b**): (Yield 6%). R$_f$. 0.10 (hexane/ethyl acetate 6:4); mp. 150-153 °C (hexane) [DSC, mp. 152.9 °C]; Anal. $C_{30}H_{35}N_{11}$; Calc. (%): C 65.55; H 6.42; N 28.03. Found (%): C 65.72; H 6.45; N 28.11; MS, m/z (%): 550.5 (M+1, 26.0), 549.35 (M, 71.7).

Method B. (Molar ratio pyrazole/pentafluoropyridine 5:1). The experimental procedure was similar to that described in method A, but using the molar ratio pyrazole/pentafluoropyridine 5:1.

With 1 g (14.6 mmoles) of pyrazole, the refluxing reaction time was 5 h and the *2,3,4,5,6-Pentakis(pyrazol-1'-yl)pyridine* (**5a**) precipitated from the reaction mixture. **5a** was filtered, washed with water and recrystallized from ethanol (Yield 64%).

With 1 g (10.4 mmoles) of 3,5-dimethylpyrazole the reflux time was 12 h; in this case because *2,3,4,5,6-pentakis(3,5-dimethylpyrazol -1'-yl)pyridine* (**5b**) was soluble in THF, the solvent was evaporated off under vacuum and the purification achieved by column chromatography using $CHCl_3$/ethanol 96:4 as eluent, R$_f$. 0.65 (Yield 56%).

Method C. 2,3,5,6-Tetrakis(3,5-dimethylpyrazol -1'-yl)-4-(pyrazol -1'-yl)pyridine (**6**). 0.354 g (3.69 mmoles) of 3,5-dimethylpyrazole in 5 mL of anhydrous THF were placed in a three-necked round bottomed flask provided with a reflux refrigerant, argon atmosphere and magnetic stirring. To the foregoing solution 0.148 g (3.69 mmoles) of NaH (60% oil dispersion) were added and the reaction mixture was heated to 65°C for 1 h. After cooling down at room temperature, 0.2 g (0.92 mmoles) of 4-(pyrazol-1'-yl)-2,3,5,6-tetrafluoropyridine (**1a**) were added and the mixture heated under reflux for 21 hours. The solvent was evaporated off under vacuum and compound **6** was purified by column chromatography using $CHCl_3$/ethanol 92:8. R$_f$. 0.71. (Yield 80%), mp. 170-175°C ($CHCl_3$/hexane) [DSC, mp. 177.5 °C]; Anal. $C_{28}H_{31}N_{11}$; Calc.(%): C 64.47; H 5.99; N 29.54. Found (%): C 64.29; H 5.97; N 29.52; MS, m/z (%): 522 (M+1, 25.0), 521 (M, 42.2), 520 (M-1, 10.2), 42 (100).

Method D. 2,3,5,6-Tetrakis(pyrazol-1'-yl)-4-(3,5-dimethylpyrazol-1'-yl)pyridine (**7**). 0.34 g (4.9 mmoles) of pyrazole in 5 mL of anhydrous THF were placed in a three-necked round bottomed flask provided with a reflux refrigerant, argon atmosphere and magnetic stirring. Then, 0.196 g (3.69 mmoles) of NaH (60% oil dispersion) were added and the reaction mixture was heated to 65°C for 1 h. After cooling down at room temperature, 0.3 g (1.22 mmoles) of 4-(3',5'-dimethylpyrazol-1'-yl)-2,3,5,6-tetrafluoropyridine (**1b**) were added and the mixture heated under reflux for 3 h. Compound **7** precipitated from the reaction mixture, filtered, washed with water and recrystallized from $CHCl_3$/hexane. R_f. 0.58 ($CHCl_3$/etanol 92:8). (Yield 84%), mp. 271-3°C ($CHCl_3$/hexane) [DSC, mp. 273 °C]; Anal. $C_{22}H_{19}N_{11}.1/2\ H_2O$; Calc.(%): C 59.18; H 4.52; N 34.51 Found (%): C 59.40; H 4.36; N 34.40; MS, m/z (%): 438 (M+1, 16.7), 437 (M, 61.9), 436 (M-1, 17.2), 369 (100).

X-ray Analysis.- The most relevant parameters of data collection and refinement process are given in Table 13. The structures were solved by direct methods (SIR92)[15] and refined by least-squares procedures on Fobs. All hydrogen atoms were obtained from difference Fourier synthesis and included and refined isotropically in the last cycles. The scattering factors were taken from the *International Tables for X-Ray Crystallography*.[16] Table 14 list the final atomic coordinates and equivalent thermal factors for non-hydrogen atoms. The calculations were carried out with the XTAL,[17] PESOS[18] and PARST[19] set of programs running on a VAX 6410 computer.

Semiempirical calculations.- A geometrical optimization of several conformations has been carried out using the AMl Hamiltonian as implemented in the MOPAC6.0 package.[13] The only restriction imposed was the planarity of the pyrazole units and the pyridine ring. The calculations were performed using an ALPHA3000-300X DEC station.

Dipole moments.- Dipole moments were measured in benzene at 25°C. The Debye formula was used as the Halverstadt and Kumler[20] extrapolation method for calculation of total polarization, with $\alpha = (d\varepsilon/d\omega_2).\omega_2 \rightarrow 0$; $\beta = (dv/d\omega_2)\omega_2 \rightarrow 0$, and $0.0001 < \omega_2 < 0.0500$. ε is the dielectric constant, ω_2 the massic fraction of the sample and v the massic volume. Electronic polarization can be replaced by molecular refraction R_{MD}. The experimental data are collected in Table 15.

Table 15. Experimental data for dipole moment measurements (solvent: benzene; temperature: 25°C)

Comp.	α	β	R_{MD}	$P_{2\infty}$	μ (D)
1a	4.32	~0	34.59	250.47	**3.25**
2a	8.13	~0	49.60	418.17	**4.24**
3a	3.10	~0	61.52	289.49	**3.33**
4a	2.26	~0	79.61	276.81	**3.11**
5a	1.61	~0	94.61	263.59	**2.87**
1b	5.06	~0	43.88	316.96	**3.65**
2b	2.35	~0	68.19	251.59	**2.99**
3b	2.04	~0	89.40	288.02	**3.12**
4b	1.18	~0	123.98	264.88	**2.69**
5b	1.00	~0	141.08	290.92	**2.71**
6	1.28	~0	131.79	303.45	**2.90**
7	0.96	~0	103.91	228.16	**2.46**

Table 13. Crystal analysis parameters at room temperature.

	5a	**5b**	**7**
Crystal data			
Formula	$C_{20}H_{15}N_{11}$	$C_{30}H_{35}N_{11}$	$C_{22}H_{19}N_{11}$
Crystal habit	Yellow prism	Colourless prism	Colourless plate
Crystal size (mm)	0.33 x 0.10 x 0.10	0.37x 0.20 x 0.20	0.23 x 0.20 x 0.03
Symmetry	Triclinic, P-1	Monoclinic, $P2_1/n$	Monoclinic, $P2_1/c$
Unit cell determination:	Least-squares fit from 41 reflexions ($\theta < 45°$)	Least-squares fit from 61 reflexions ($\theta < 45°$)	Least-squares fit from 49 reflexions ($\theta < 45°$)
Unit cell dimensions (Å,°)	a=11.7056(6)	a=9.3448(5)	a=11.0949(6)
	b=9.3228(8)	b=25.3711(33)	b=20.2529(16)
	c=10.0245(13)	c=12.9310(7)	c=10.9354(5)
	101.07(1), 115.45(1), 78.87(1)	90, 92.368(4), 90	90, 119.425(4), 90
Packing: V(Å^3), Z	961.9(2), 2	3063.2(5), 4	2140.2(2), 4
Dc(g/cm^3), M, F(000)	1.414, 409.41, 424	1.192, 549.68, 1168	1.357, 437.47, 912
μ(cm^{-1})	7.72	6.04	7.28
Experimental data			
Technique	Four circle diffractometer: Philips PW1100, Bisecting geometry Graphite monochromator :CuKα, $\omega/2\theta$ scans Detector apertures 1 x 1°. Scan width = 1.5°. Scan speed =1 min./reflex.		
$\theta_{max.}$	60°	65°	65°
Number of reflexions:			
Independent	2864	5224	3644
Observed	1961 (2σ(I) criterion)	3520 (2σ(I) criterion)	2077 (2σ(I) criterion)
Standard reflexions:	2 reflexions every 90 minutes. No variation		
Solution and refinement			
Solution	Direct Methods: SIR92		
Refinement:	Least-Squares on Fo, full matrix		
Secondary extinction (10^4)	0.056(8)	0.300(40)	0.152(20)
Parameters:			
Number of variables	341	351	375
Degrees of freedom	1620	3169	3269
Ratio of freedom	5.8	10.0	5.5
H atoms	From difference synthesis		
Weighting-scheme	Empirical as to give no trends in <$\omega\Delta^2F$> vs. <|Fobs|> and <sinθ/λ>		
Max. thermal value (Å^2)	U11(C34)=0.095(4)	U22(C36)=0.164(6)	U22(C63)=0.106(5)
Final $\Delta\rho$ peaks (eÅ^{-3})	±0.25	±0.29	±0.30
Final R and Rw	0.049, 0.052	0.054, 0.062	0.058, 0.060

Table 14. Final atomic coordinates and $U_{eq}=(1/3)\Sigma[U_{ij}\cdot a_i^*\cdot a_j^*\cdot a_i\cdot a_j\cdot \cos(a_i,a_j)]$

Atom	x	y	z	Ueq
Compound **5a**				
N1	-0.0416(3)	0.3331(3)	0.1534(3)	0.041(1)
C2	0.0117(3)	0.2837(4)	0.0582(4)	0.039(1)
C3	-0.0506(3)	0.2081(3)	-0.0817(4)	0.039(1)
C4	-0.1776(3)	0.1911(3)	-0.1244(3)	0.038(1)
C5	-0.2364(3)	0.2455(4)	-0.0270(4)	0.039(1)
C6	-0.1627(3)	0.3132(4)	0.1121(4)	0.039(1)
N21	0.1382(2)	0.3153(3)	0.1074(3)	0.039(1)
N22	0.1706(3)	0.4453(3)	0.1946(3)	0.049(1)
C23	0.2929(4)	0.4402(4)	0.2248(4)	0.052(2)
C24	0.3404(4)	0.3094(4)	0.1610(4)	0.054(2)
C25	0.2398(3)	0.2313(4)	0.0868(4)	0.052(2)
N31	0.0076(2)	0.1645(3)	-0.1842(3)	0.040(1)
N32	0.0678(3)	0.0258(3)	-0.1966(4)	0.054(1)
C33	0.1120(4)	0.0276(5)	-0.2970(5)	0.063(2)
C34	0.0811(5)	0.1620(6)	-0.3486(5)	0.076(3)
C35	0.0143(4)	0.2490(5)	-0.2736(5)	0.059(2)
N41	-0.2474(3)	0.1245(3)	-0.2701(3)	0.044(1)
N42	-0.3550(3)	0.2008(4)	-0.3624(3)	0.057(1)
C43	-0.3944(4)	0.1064(6)	-0.4865(5)	0.067(2)
C44	-0.3156(4)	-0.0264(5)	-0.4749(5)	0.065(2)
C45	-0.2219(4)	-0.0130(4)	-0.3353(4)	0.057(2)
N51	-0.3665(2)	0.2315(3)	-0.0720(3)	0.040(1)
N52	-0.4015(3)	0.0984(3)	-0.0798(4)	0.053(1)
C53	-0.5273(4)	0.1270(5)	-0.1232(5)	0.058(2)
C54	-0.5720(4)	0.2723(5)	-0.1438(4)	0.057(2)
C55	-0.4670(3)	0.3380(4)	-0.1102(4)	0.051(2)
N61	-0.2062(3)	0.3675(3)	0.2256(3)	0.042(1)
N62	-0.3095(3)	0.3267(4)	0.2312(4)	0.071(2)
C63	-0.3091(4)	0.3953(5)	0.3615(5)	0.067(2)
C64	-0.2098(4)	0.4793(5)	0.4362(4)	0.062(2)
C65	-0.1452(4)	0.4602(5)	0.3490(4)	0.057(2)
Compound **5b**				
N1	0.2702(3)	0.0320(1)	0.3700(2)	0.047(1)
C2	0.2365(3)	0.0635(1)	0.4481(2)	0.042(1)
C3	0.2545(3)	0.1181(1)	0.4444(2)	0.042(1)
C4	0.3139(3)	0.1392(1)	0.3564(2)	0.043(1)
C5	0.3513(3)	0.1066(1)	0.2759(2)	0.045(1)
C6	0.3246(3)	0.0534(1)	0.2859(2)	0.045(1)
N21	0.1781(3)	0.0378(1)	0.5337(2)	0.047(1)
N22	0.0890(3)	0.0666(1)	0.5946(2)	0.053(1)
C23	0.0573(3)	0.0342(1)	0.6702(2)	0.056(1)
C24	0.1238(4)	-0.0147(1)	0.6590(2)	0.061(1)
C25	0.2017(3)	-0.0122(1)	0.5718(2)	0.053(1)
C26	-0.0358(5)	0.0531(2)	0.7532(3)	0.073(1)
C27	0.2954(5)	-0.0523(1)	0.5281(3)	0.072(1)
N31	0.2206(2)	0.1530(1)	0.5254(2)	0.043(1)
N32	0.3107(3)	0.1563(1)	0.6112(2)	0.053(1)
C33	0.2423(4)	0.1883(1)	0.6732(2)	0.063(1)
C34	0.1109(4)	0.2044(1)	0.6299(3)	0.060(1)
C35	0.0983(3)	0.1810(1)	0.5351(2)	0.050(1)
C36	0.3094(8)	0.2029(4)	0.7769(4)	0.112(3)
C37	-0.0194(4)	0.1803(2)	0.4534(4)	0.077(2)
N41	0.3399(3)	0.1944(1)	0.3507(2)	0.046(1)
N42	0.2440(3)	0.2250(1)	0.2947(2)	0.054(1)
C43	0.2952(4)	0.2731(1)	0.3055(3)	0.056(1)
C44	0.4210(4)	0.2739(1)	0.3681(3)	0.058(1)
C45	0.4478(3)	0.2227(1)	0.3955(2)	0.049(1)
C46	0.2203(6)	0.3188(2)	0.2518(5)	0.085(2)
C47	0.5671(4)	0.1978(2)	0.4560(3)	0.070(1)
N51	0.4292(3)	0.1274(1)	0.1932(2)	0.053(1)
N52	0.5748(3)	0.1275(1)	0.2061(2)	0.063(1)
C53	0.6182(5)	0.1518(1)	0.1209(3)	0.078(1)
C54	0.5019(6)	0.1665(1)	0.0566(3)	0.083(2)
C55	0.3814(5)	0.1510(1)	0.1035(2)	0.066(1)
C56	0.7740(8)	0.1590(3)	0.1058(8)	0.123(3)
C57	0.2269(6)	0.1560(2)	0.0737(4)	0.090(2)
N61	0.3481(3)	0.0189(1)	0.2025(2)	0.049(1)
N62	0.2780(3)	0.0311(1)	0.1092(2)	0.059(1)
C63	0.3105(4)	-0.0087(1)	0.0486(2)	0.060(1)
C64	0.3961(4)	-0.0457(1)	0.0999(3)	0.062(1)
C65	0.4184(3)	-0.0277(1)	0.1988(2)	0.053(1)
C66	0.2508(7)	-0.0102(2)	-0.0613(3)	0.088(2)
C67	0.5070(5)	-0.0493(2)	0.2874(3)	0.075(1)
Compound **7**				
N1	0.4669(3)	0.1631(2)	0.0658(3)	0.045(2)
C2	0.5884(4)	0.1382(2)	0.1577(4)	0.043(2)
C3	0.6691(4)	0.0999(2)	0.1205(4)	0.044(2)
C4	0.6143(4)	0.0864(2)	-0.0218(4)	0.042(2)
C5	0.4867(4)	0.1107(2)	-0.1203(4)	0.042(2)
C6	0.4148(4)	0.1496(2)	-0.0707(4)	0.045(2)
N21	0.6302(3)	0.1545(2)	0.2983(3)	0.044(2)
N22	0.7084(4)	0.1118(2)	0.4047(4)	0.057(2)
C23	0.7232(5)	0.1423(3)	0.5171(5)	0.063(2)
C24	0.6578(6)	0.2028(3)	0.4876(5)	0.071(3)
C25	0.5979(5)	0.2096(3)	0.3454(5)	0.060(3)
N31	0.8072(3)	0.0811(2)	0.2167(3)	0.046(2)
N32	0.9036(4)	0.1289(2)	0.2836(4)	0.060(2)
C33	1.0168(5)	0.0941(3)	0.3669(5)	0.069(3)
C34	0.9958(5)	0.0273(3)	0.3531(5)	0.066(3)
C35	0.8597(5)	0.0199(3)	0.2574(5)	0.056(2)
N41	0.6944(3)	0.0501(2)	-0.0670(3)	0.045(2)
N42	0.6814(4)	-0.0175(2)	-0.0766(4)	0.052(2)
C43	0.7694(5)	-0.0356(2)	-0.1200(4)	0.053(2)
C44	0.8369(5)	0.0193(3)	-0.1363(5)	0.060(2)
C45	0.7885(4)	0.0736(2)	-0.1025(4)	0.053(2)
C46	0.7887(9)	-0.1066(3)	-0.1417(7)	0.079(4)
C47	0.8191(7)	0.1453(3)	-0.0972(7)	0.072(3)
N51	0.4415(3)	0.1000(2)	-0.2647(3)	0.045(2)
N52	0.4430(4)	0.1510(2)	-0.3443(4)	0.064(2)
C53	0.4062(5)	0.1223(3)	-0.4669(5)	0.069(3)
C54	0.3818(5)	0.0561(3)	-0.4671(5)	0.065(3)
C55	0.4055(5)	0.0428(2)	-0.3362(5)	0.053(2)
N61	0.2839(3)	0.1768(2)	-0.1562(4)	0.053(2)
N62	0.1983(4)	0.1535(2)	-0.2877(4)	0.080(2)
C63	0.0841(6)	0.1881(3)	-0.3304(6)	0.086(3)
C64	0.0921(5)	0.2332(3)	-0.2312(6)	0.074(3)
C65	0.2211(5)	0.2240(2)	-0.1189(5)	0.062(2)

Acknowledgements

Financial support was provided by the Spanish DGICYT (Projects nos. PB93-0125, PB93-0197-C02 and PB93-0289-C02-01). C. F.-C. and C. E. thank the 'Comunidad de Madrid' for fellowships (Acción Especial AE00067/95).

References

1. Foces-Foces, C.; Llamas-Saiz, A. L.; Claramunt, R. M.; Jagerovic, N.; Jimeno, M. L.; Elguero, J. *J. Chem. Soc. Perkin Trans.2* **1995**, 1359.
2. Foces-Foces, C.; Llamas-Saiz, A. L.; Escolástico, C.; Claramunt, R. M.; Elguero, J. *J. Phys. Org. Chem.* **1996**, *9*, 137.
3. Fernández-Castaño, C.; Foces-Foces, C.; Cano, F. H.; Claramunt, R. M.; Escolástico, C.; Fruchier, A.; Elguero, J. *New J. Chem.* submitted for publication.
4. Foces-Foces, C.; Fernández-Castaño, C.; Claramunt, R. M.; Escolástico, C.; Elguero, J.*J. Phys. Org. Chem.* (?) submitted for publication.
5. (a) Downard, A. J.; Honey, G. E.; Steel, P. J. *Inorg. Chem.* **1991**, *30*, 3733. (b) García, M. A. M.; Gelling, A.; Noble, D. R.; Orrell, K. G.; Osborne, A. G.; Sik, V. *Polyhedron* **1996**, *15*, 371.
6. Chambers, R.D.; Sargent, C. R. *Adv. Heterocycl. Chem.* **1981**, *28*, 1.
7. Silvester, M. J. *Adv. Heterocycl. Chem.* **1994**, *59*, 1.
8. Rossell, H. J.; Scott, H. G. J. Cryst. Mol. Struct. **1973**, *3*, 259
9. Mootz, D.; Wussow, H.-G. *J. Chem. Phys.* **1981**, *75*,1517
10. Larsen, F. K.; Lehmann, M. S.; Sotofte, I.; Rasmusen, S. E. *Acta Chem. Scand.* **1970**, *24*, 3248
11. Allen, F. H.; Davies, J. E.; Galloy, J. J.; Johnson, O.; Kennard, O.; Macrae, C. F.; Mitchell, E. M.; Mitchell, J. F.; Smith J. M.; Watson, D. G. *J. Chem. Info. Comput. Sci.*, **1991**, *31*, 187.
12. Maas, G.; Fink, J.; Wingert, H.; Blatter, K.; Regitz, R. *Chem.Ber.* **1987**, *120*, 819.
13. Stewart, J. J. P. J. Comput.-Aided Mol. Des. **1990**, *4*, 1.
14. Cano, F. H.; Martinez-Ripoll, M. *J. Mol. Struct.* **1992**, *258*, 139.
15. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Polidori, G. SIR92, *J. Appl. Cryst.* **1994**, *27*, 435.
16. *International Tables for X-Ray Crystallography*, 1974, Birmingham, Kynoch Press, England.
17. Hall, S. R.; Flack, H. D.; Stewart, J. M. 'Xtal3.2', Ed. Univ. of Western Australia. Lamb, Perth, **1994**.
18. Martinez-Ripoll, J. M.; Cano, F. H. "PESOS" Unpublished Program.
19. Nardelli, M. *Comput. Chem.*, **1983**, *7*, 95.
20. Halverstadt, I. F.; Kumler, W. D. *J. Am. Chem. Soc.* **1942**, *64*, 2988.

(*Received in UK* 11 *June* 1996; *revised* 2 *July* 1996; *accepted* 4 *July* 1996)