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STRUCTURE OF 1-(1-ADAMANTYL)PYRAZOLES

CRYSTAL GEOMETRY AND CARBON-13 NMR SPECTROSCOPY

P. Cabildo,* R. M. Claramunt and D. Sanz
Química Orgánica, UNED, Ciudad Universitaria, Madrid-3, Spain

M. C. Foces-Foces and F. Hernandez Cano
Departamento de Rayos X, Instituto de Química Física "Rocasolano", Serrano 119, Madrid-6, Spain

J. Catalan
Departamento de Química Física y Química Cuántica, Facultad de Ciencias, C-XIV, Universidad Autónoma de Madrid, Cantoblanco, Madrid-34, Spain

and

J. Elguero
Instituto de Química Médica, C.S.I.C., Juan de la Cierva, 3, Madrid-6, Spain

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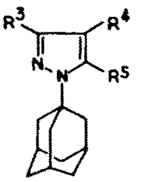
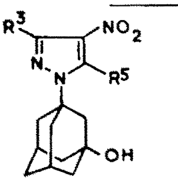
Abstract—Crystal structures of 1-(1-adamantyl)pyrazole, **1a**, and 1-(1-adamantyl-3-ol)-4-nitropyrazole, **2a**, have been solved by X-ray analysis. The space groups and cell parameters are $P2_1$, *a*, 7.4021(3), *b*, 10.7529(5), *c*, 6.9651(2)Å, *β*, 90.206(3)° for **1a** with Z = 2 and P2/n, *a*, 31.1172(14), *b*, 6.8506(1), *c*, 12.0313(3)Å, *β*, 94.873(3)° for **2a** with Z = 8. Refinements were carried out down to R values of 0.043 (R_w = 0.046) and 0.079 (R_w = 0.061) for the 951 (2σ(I)) and 2461 (3σ(I)) observed reflections respectively. The conformation about the bond between the heterocycle and the carbocycle is discussed on theoretical grounds (INDO calculations): the adamantane behaves as a free rotor. The steric interactions of the adamantyl residue with the methyl substituents in 2- and 5-position of pyrazole are apparent in the C-13 chemical shifts.

In a previous paper[1] we have described the still unknown 1-(1-adamantyl)pyrazoles (compound **1e** has been prepared subsequently[2]):



1



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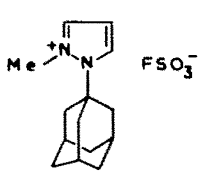


3

a $R^3 = R^4 = R^5 = H$
b $R^3 = R^5 = Me, R^4 = H$
c $R^3 = R^5 = H, R^4 = Br$
d $R^3 = Me, R^4 = H, R^5 = NH_2$
e $R^3 = H, R^4 = CO_2Et, R^5 = NH_2$

a $R^3 = R^5 = H$
b $R^3 = R^5 = Me$

In order to study this new class of derivatives we have undertaken the determination of the crystal structures of **1a** and **2a** and the examined ^{13}C-NMR behaviour of all of them. **2a** has two crystallographically independent molecules (**2a** and **2a′**, see Experimental).

RESULTS AND DISCUSSION

Molecular geometry of 1-(1-*adamantyl*)*pyrazoles* **1a** *and* **2a**

All three molecules map each other quite well. Molecules **2a** and **2a′** are linked through H-bonds, involving the O19 H-atoms. The most favorable one, as measured by the O—H···O angle, being that of **2a** (Table 1).

In the three adamantane moieties all the C—C—C angles are within the range [108.0(4)–110.7(4)°] with weighted mean values of 109.4(1)°, 109.2(2)° and 109.3(1)° respectively for **1a**, **2a** and **2a′**. The whole set of bond distances range from 1.515(7) to 1.546(4)Å (see Table 1), but some differences, just in the limit of significance within precision, can be observed between the group of distances in the bottom rings, with lower values, from the rest of the values somewhat higher, the weighted means being 1.521(1) vs. 1.536(4)Å, 1.524(4) vs. 1.533(3)Å and 1.527(2) vs. 1.531(3)Å respectively. Similar relative differences can be observed in other adamantyl derivatives.[3,4]

All 6-membered rings have chair conformation, with absolute values of the torsion angles between 59.5(5) and 62.0(5)°, except, again, for the bottom rings which seem less puckered mainly in molecules **1a** and **2a** where that range is 57.8(4)–59.8(6)°.

The 5-atom rings show the delocalization of the double bonds in the values of the bond lengths and bond angles (C5—N1—N2 and N2—C3—C4 being higher), all being planar within precision.

Table 1. Bond lengths (Å) and selected bond angles (°)

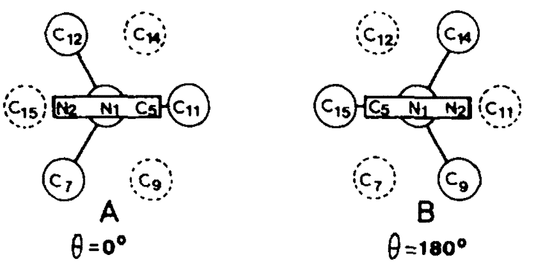
Molecules	**1a**	**2a**	**2a′**
N1—N2	1.349(4)	1.370(6)	1.369(5)
N2—C3	1.333(5)	1.314(7)	1.329(6)
C3—C4	1.373(8)	1.371(8)	1.382(7)
C4—C5	1.375(5)	1.363(6)	1.356(6)
C5—N1	1.343(5)	1.342(6)	1.335(6)
C4—N16	—	1.429(6)	1.428(7)
N16—O17	—	1.226(6)	1.210(6)
N16—O18	—	1.214(7)	1.233(7)
N1—C6	1.484(3)	1.493(6)	1.487(6)
C6—C7	1.526(5)	1.535(7)	1.531(7)
C6—C12	1.532(4)	1.536(8)	1.527(8)
C6—C11	1.522(6)	1.521(7)	1.531(7)
C7—C8	1.540(5)	1.532(7)	1.523(7)
C11—C10	1.541(5)	1.532(6)	1.535(7)
C12—C13	1.546(4)	1.542(7)	1.540(7)
C8—C9	1.518(7)	1.515(7)	1.522(7)
C9—C10	1.517(6)	1.536(9)	1.531(8)
C10—C14	1.519(5)	1.519(10)	1.524(9)
C14—C13	1.521(7)	1.519(9)	1.525(9)
C13—C15	1.527(6)	1.535(8)	1.535(8)
C8—C15	1.525(6)	1.523(8)	1.525(7)
C8—O19	—	1.447(6)	1.435(6)
O19—H19	—	0.95(11)	0.80(9)
H19···O19*	—	1.88(9)	1.99(9)
O19···O19*	—	2.822(5)	2.786(5)
C5—N1—N2	112.0(2)	112.3(4)	111.7(4)
C5—N1—C6	128.5(2)	128.4(4)	128.5(4)
N2—N1—C6	119.5(2)	119.3(4)	119.6(4)
N1—N2—C3	104.3(3)	103.7(4)	104.7(4)
N2—C3—C4	112.0(4)	111.6(5)	110.3(4)
N1—C5—C4	106.6(4)	105.6(4)	106.4(4)
C3—C4—C5	105.1(4)	106.7(4)	106.9(4)
C3—C4—N16	—	127.9(5)	125.9(4)
C5—C4—N16	—	125.4(5)	127.2(5)
C4—N16—O17	—	118.1(5)	119.6(5)
C4—N16—O18	—	118.3(4)	116.9(4)
O17—N16—O18	—	123.5(5)	123.5(5)
N1—C6—C7	109.5(2)	109.0(4)	108.7(4)
N1—C6—C11	109.8(2)	109.5(4)	109.3(3)
N1—C6—C12	108.5(2)	108.2(4)	109.2(4)
C7—C6—C11	109.4(3)	110.4(4)	110.2(4)
C7—C6—C12	109.9(3)	110.0(4)	109.6(4)
C11—C6—C12	109.8(3)	109.8(4)	109.9(4)
C7—C8—O19	—	107.4(4)	108.9(4)
C9—C8—O19	—	109.9(4)	108.5(4)
C15—C8—O19	—	109.4(4)	110.1(4)
O19—H19···O19*	—	168(10)	174(9)

* The symmetry operations are 1/2 − X, 1 + Y, 1/2 − Z and X, 1 + Y, Z for **2a** and **2a′** respectively.

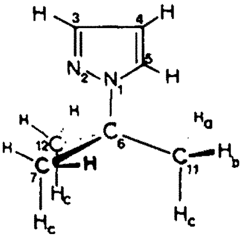
Some asymmetry at the N1 substitution can be observed, in the three molecules, as C5—N1—C6 > N2—N1—C6.[3,4] On the other hand between the **2a** and **2a′** molecules the NO_2 groups present a relative twist of almost 10° (Fig. 1).

Structurally, the main difference between both compounds is related to the conformation about the $N_1(sp^2)$—$C_6(sp^3)$ bond (Fig. 1). Compound **1a** exists in the solid state with a type A conformation (bonds N_1C_5 and C_6C_{11} eclipsed) whereas the two independent molecules in the crystal lattice of **2a** one is the type A and the other of type B conformation (bonds N_1N_2 and C_6C_{11} eclipsed).

Obviously neither the OH on C_8 nor the NO_2 on C_4 can account for this different behaviour. The only reasonable hypothesis is that both conformations are of comparable energy and the choice is due to slight differences in the crystal packing. To test this hypothesis we have carried out INDO calculations.[5]



1-t-Butylpyrazole was chosen, considering that the bottom part of the adamantane is irrelevant when only variations in energy are at stake. The pyrazole ring has been taken coplanar with the plane defined by carbons $C_6C_{11}C_{10}C_{15}$. The t-Bu residue has been built from the corresponding adamantane fragment in **1a**, but taking mean values for carbons C_7 and C_{12}. The third H-atom has been situated along the CC bond at 1.0248 Å. For our purpose it is enough to rotate the pyrazole from $\theta = 0°$ (conformation A) to $\theta = 60°$ (≡ 180°, conformation B).



$\theta = C_5N_1C_6C_{11}$ dihedral angle

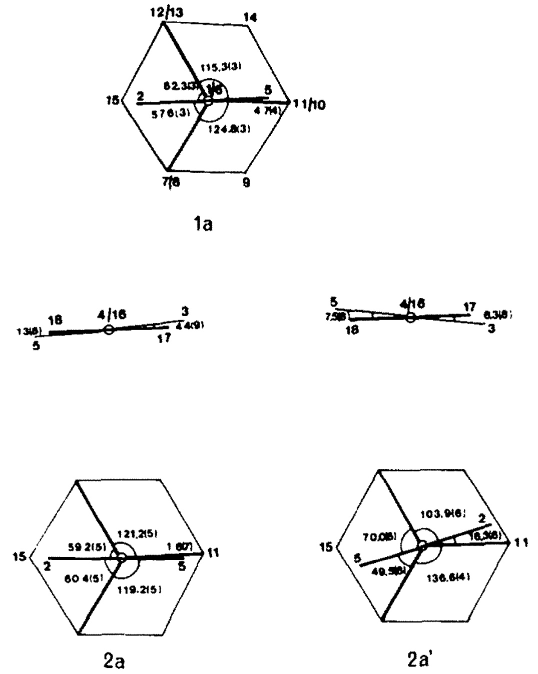
$C_6C_{11} = 1.5221 Å$
$C_6C_7 = C_6C_{12} = 1.5289 Å$
$C_{11}H_a = C_{11}H_b = 1.06 Å$
$C_{12}H_a = C_{12}H_b = C_7H_a = C_7H_b = 1.026 Å$
$C_{11}H_c = C_7H_c = C_{12}H_c = 1.0248 Å$

The calculated energies are collected in Table 2. The calculated dipole moment is 2.54D.

Both conformations, A and B, have the same energy confirming our hypothesis. There is almost no rotational barrier, thus 5-unsubstituted (**1** or **2**, $R^5 = H$) 1-(1-adamantyl)pyrazoles can adopt any conformation about the N_1C_6 bond. *Ab initio* STO-3G calculations for $\theta = 0°$ ($E_T = -376.268132$ au, $\mu = 2.64D$) and for $\theta = 30°$ ($E_T = -376.267360$ au, $\mu = 2.59D$) were carried out in order to have an

Table 2. Relative energies in kcal/mol of 1-tertbutylpyrazole

θ	ΔE
0°, conformation A	0
10°	0.05
20°	0.14
30°	0.17
40°	0.12
50°	0.04
60°, conformation B	0.01



1a

2a 2a'

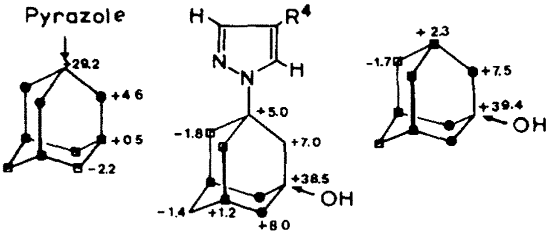
Fig. 1. Stereographic projections showing the relative disposition of the five-membered ring with respect to the adamantyl moiety for the three molecules and the Newman projections to show the disposition of the NO_2 groups in molecules **2a** and **2a**'. The numbering in the adamantyl moiety has been omitted in the bottom figures.

independent estimation of the barrier. The value of $\Delta E = 0.000772$ au = 0.48 kcal/mol is consistent with the INDO value of Table 2 (0.17 kcal/mol).

^{13}C-NMR *study of* 1-(1-*adamantyl*)*pyrazoles* **1a**–**3**

The chemical shifts and some coupling constants of the eight compounds are given in Table 3.

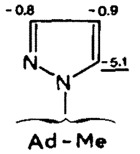
The assignment of pyrazolic carbons was straightforward.[6,7] The adamantyl carbons were assigned from literature values of adamantane[8] and adamantanol.[9] The following SCS (substituent chemical shifts) show the consistence of Table 3 values:



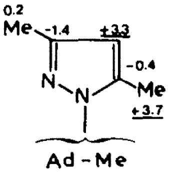
Pyrazole SCS on adamantane carbons (compound **1a** minus adamantane values[8])	Hydroxyl SCS on adamantane carbons (compound **2a** minus compound **1a**)	Hydroxyl SCS on adamantane carbons (adamantanol[9] minus adamantane[8])

The larger effect on C_6(+5.0 ppm) may contain some contribution from the 4-nitro group present in **2a** ($R^4 = NO_2$).

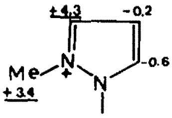
Concerning the pyrazole counterpart, the coupling constants measured for **1a** and **3** are almost identical with those of 1-methylpyrazole.[10] The replacement of an N-Me group by an N-adamantyl group, modifies the pyrazolic C chemical shifts. Three compounds summarize the most important effects (for the corresponding N-methylpyrazoles in the same solvent, see [6,7]):



1a



1b



3

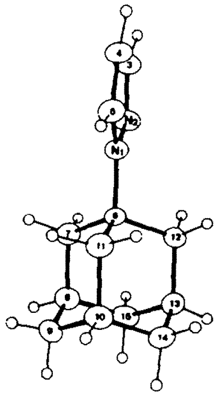
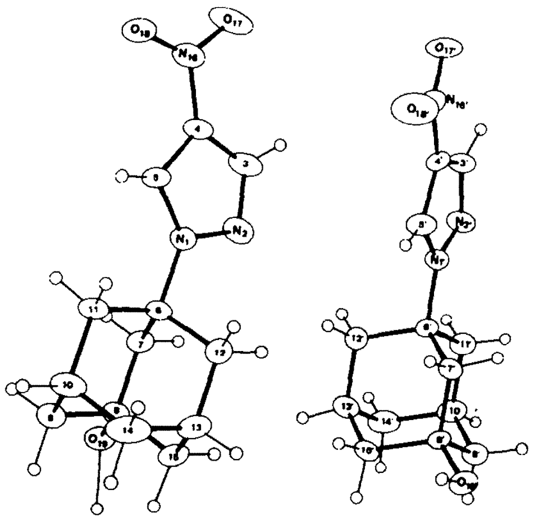


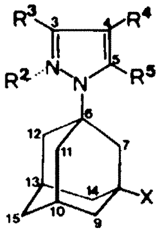
Fig. 2a. An ORTEP view of the **1a** molecule with the atomic numbering.



2a **2a**'

Fig. 2b. Same as Fig. 2a for the **2a** and **2a**' molecules.

Table 3. Carbon-13 chemical shifts (in ppm) and ^1H—^{13}C coupling constants (in Hz) of 1-(1-adamantyl)pyrazoles (solvent : DMSO—d_6)



Compound	R^2	R^3	R^4	R^5	X	C_3	C_4	C_5	C_6	C_7	C_{11}	C_{12}	C_8	C_{10}	C_{13}	C_9	C_{14}	C_{15}	Substituents
1a	—	H	H	H	H	137.7 $^1J = 183.6$ $^3J = 8.3$ $^2J = 6.4$	104.3 $^1J = 174.8$ $^2J = 9.2$ $^2J = 10.9$	125.3 $^1J = 186.3$ $^2J = 9.2$ $^3J = 4.6$	57.7		42.4			29.0			35.6		
1b	—	Me	H	Me	H	143.6	107.5	137.9	59.6		41.8			29.3			35.7		13.3 (Me_3); 14.3 (Me_5)
1c	—	H	Br	H	H	138.2	91.2	126.3	59.0		42.0			29.0			35.5		
1d	—	Me	H	NH_2	H	143.1	91.6	146.7	57.9		40.8			29.2			35.7		13.8 (Me_3)
1e	—	H	CO_2Et	NH_2	H	136.2 $^1J = 187.4$	94.8	149.1 $^3J = 3.8$	58.9		39.5			28.7			34.9		163.7 (CO); 58.2 (CH_2); 14.0 (CH_3)
2a	—	H	NO_2	H	OH	135.0	134.9	127.0	62.7	49.4		40.6	67.5		30.2	43.6		34.2	
2b	—	Me	NO_2	Me	OH	143.0	131.6	140.0	65.1	49.2		40.2	67.8		30.5	43.6		34.2	14.0 (Me_3); 13.5 (Me_5)
3	Me^+	H	H	H	H	141.9 $^1J \sim 199$*	106.7 $^1J = 189.2$ $^2J = 6.4$ $^2J = 6.4$	137.0 $^1J = 199.3$ $^2J = 6.7$ $^3J = 6.7$	67.2		40.3			29.3			34.5		42.0 (Me_2)

* Broad signal, coupling with Me_2 protons.

Table 4. Crystal analysis parameters at room temperature

Crystal data		
Formula	C13 H18 N2	C13 H17 N3 O3
Crystal habit	Colourless, prismatic	Colourless, prismatic
Crystal size (mm)	0.07 × 0.23 × 0.47 (inside capillar)	0.03 × 0.13 × 0.30
Symmetry	2/m. Monoclinic. $P2_1$	2/m. Monoclinic. P2/n
Unit cell determination: least-squares fit to θ (Cu) < 45 deg.	55 reflections	52 reflections
Unit cell dimensions (Å)	7.4021(3), 10.7529(5), 6.9651(2) β = 90.206(3)°	31.1172(14), 6.8506(1), 12.0313(3) β = 94.873(3)°
Packins: V(Å^3), Z	554.38(3), 2	2555.4(1), 8
D (g cm^{-3}), M, F(000)	1.212, 202.301, 220	1.368, 263.297, 1120
Experimental data		
Radiation and technique	Cu—K_α. PW1100 Philips Diffractometer Bisecting geometry	
Monochromator	Graphite oriented	
Collection mode	w/2θ, 1 × 1 deg. det. apertures, θ < 65°, 1 min/refl, scan width of 1.5 deg.	w/2θ, 1 × 1 deg. det. apertures, θ < 60°, 1 min/refl, scan width of 1.3 deg.
Total independent data	990	3814
Observed data	951 I > 2σ(I)	2464 I > 3σ(I)
Stability	Two reflections every 90 min no variation	
Solution and refinement		
Solution mode	Multan 80,[12] X-Ray 76 System[13] Vax 11/750	
Refinement mode	Least-squares on F's, observed reflections only 1 blocks in the final cycles	only 2 blocks in the final cycles
Final shift/error	0.12	0.07
Parameters:		
no. of variables	207	480
degrees of freedom	744	1984
ratio of freedom	4.6	5.1
Weighting scheme	Empirical as to give no trends in ⟨wΔ^2⟩ vs. ⟨Fo⟩ or ⟨sin θ/λ⟩	
Max. thermal values (Å^2)	U22 (C14) = 0.104(4)	U22 (O8) = 0.173(6)
Final F-peaks	0.14 eÅ-3	0.34 eÅ-3
Final R, Rw	0.043, 0.046	0.079, 0.061
Atomic factors	International Tables for X-Ray Crystallography[14]	

The steric interactions between the adamantyl group and the methyls in positions 5 (**1b**) and 2 (**3**) is clearly apparent. The γ-effect on C_5 (-5.1 ppm) is also normal and similar to the value found in the couple toluene/t-butylbenzene (-3.9 ppm).[11] In **1b**, carbon C_4, and in **3**, carbon C_3, are shifted downfield; this abnormal behaviour is probably related to the steric compression between the adamantane and the Me on C_5 and N_2, respectively.

CONCLUSION

In agreement with semiempirical calculations, the crystallographic study of two 1-(1-adamantyl)-

Table 5. C13 H18 N2: final atomic coordinates and thermal parameters as UEQ*

Atom	X/A	Y/B	Z/C	UEQ
N1	−0.0659(3)	0.2500(0)	0.3746(3)	413(7)
N2	−0.1515(4)	0.1439(4)	0.4231(5)	566(9)
C3	−0.2749(5)	0.1796(5)	0.5506(5)	600(13)
C4	−0.2678(5)	0.3053(5)	0.5850(5)	594(12)
C5	−0.1318(5)	0.3489(4)	0.4691(5)	525(10)
C6	0.0780(4)	0.2466(4)	0.2268(4)	360(7)
C7	0.2254(4)	0.1558(5)	0.2888(5)	524(10)
C8	0.3733(5)	0.1518(5)	0.1341(5)	586(11)
C9	0.4531(5)	0.2808(5)	0.1088(6)	653(15)
C10	0.3058(5)	0.3705(4)	0.0468(5)	579(11)
C11	0.1591(5)	0.3758(4)	0.2029(5)	507(10)
C12	−0.0059(4)	0.2038(4)	0.0365(4)	460(9)
C13	0.1430(4)	0.1986(4)	−0.1184(5)	529(10)
C14	0.2224(5)	0.3281(5)	−0.1417(5)	589(12)
C15	0.2890(5)	0.1072(5)	−0.0538(6)	631(13)

* ⅓Σ(UIJ.AI*.AJ*.AI.AJ.COS(AI, AJ)). 10**4

Table 6. C13 H17 N3 O3. Final atomic coordinates and thermal parameters as UEQ*

Atom	X/A	Y/B	Z/C	UEQ
N1	0.0702(1)	−0.2182(7)	0.4209(3)	41(2)
N2	0.0588(1)	−0.1672(8)	0.3123(3)	60(2)
C3	0.0161(2)	−0.1649(10)	0.3058(5)	63(3)
C4	0.0007(1)	−0.2124(8)	0.4058(4)	41(2)
C5	0.0358(1)	−0.2475(8)	0.4788(4)	40(2)
C6	0.1169(1)	−0.2355(8)	0.4602(4)	38(2)
C7	0.1375(1)	−0.3931(8)	0.3914(4)	39(2)
C8	0.1854(1)	−0.4058(7)	0.4319(4)	37(2)
C9	0.1903(2)	−0.4608(10)	0.5543(5)	50(2)
C10	0.1695(2)	−0.3020(10)	0.6220(4)	54(2)
C11	0.1214(1)	−0.2890(9)	0.5833(4)	45(2)
C12	0.1384(2)	−0.0373(8)	0.4431(5)	47(2)
C13	0.1868(2)	−0.0525(9)	0.4819(5)	52(2)
C14	0.1914(2)	−0.1075(11)	0.6047(5)	67(3)
C15	0.2073(2)	−0.2110(8)	0.4132(4)	48(2)
N16	−0.0433(1)	−0.2285(8)	0.4307(5)	56(2)
O17	−0.0715(1)	−0.1853(8)	0.3575(4)	86(2)
O18	−0.0506(1)	−0.2808(7)	0.5236(4)	75(2)
O19	0.2044(1)	−0.5553(5)	0.3666(3)	52(1)
N1′	0.0593(1)	0.2394(6)	0.0401(3)	38(1)
N2′	0.0297(1)	0.2243(7)	−0.0503(3)	46(2)
C3′	−0.0081(1)	0.2531(8)	−0.0094(5)	45(2)
C4′	−0.0025(1)	0.2845(8)	0.1043(4)	39(2)
C5′	0.0405(2)	0.2718(9)	0.1339(4)	48(2)
C6′	0.1057(1)	0.2030(8)	0.0264(4)	34(2)
C7′	0.1326(1)	0.3600(8)	0.0905(4)	36(2)
C8′	0.1802(1)	0.3241(7)	0.0772(4)	36(2)
C9′	0.1882(2)	0.3343(9)	−0.0457(4)	49(2)
C10′	0.1613(2)	0.1772(9)	−0.1097(4)	50(2)
C11′	0.1131(2)	0.2111(9)	−0.0977(4)	47(2)
C12′	0.1181(2)	0.0019(8)	0.0735(4)	44(2)
C13′	0.1663(2)	−0.0335(8)	0.0600(5)	53(2)
C14′	0.1743(2)	−0.0232(10)	−0.0632(5)	61(2)
C15′	0.1930(2)	0.1241(8)	0.1248(4)	44(2)
N16′	−0.0358(1)	0.3236(7)	0.1757(4)	52(2)
O17′	−0.0732(1)	0.3148(7)	0.1388(3)	67(2)
O18′	−0.0244(1)	0.3692(9)	0.2729(4)	97(2)
O19′	0.2052(1)	0.4737(5)	0.1358(3)	50(1)

* $\frac{1}{3}$Σ(UIJ.AI*.AJ*.AI.AJ.COS(AI, AJ)). 10**3

pyrazoles shows that there are two eclipsed conformations about the N(sp^2)—C(sp^3) bond equally probable. Steric interactions appear in ^{13}C-NMR only when a Me group substitutes one "*ortho*" pyrazolic position (N_2 or C_5).

EXPERIMENTAL

Crystal structure parameters are given in Table 4. Compound **2a** has two independent molecules, **2a** and **2a**′. In Tables 5 and 6 the final atomic coordinates are presented following the number schemes given in Figs 2a and 2b. A list of structure factors, thermal parameters and hydrogen coordinates are available on request. (Departamento de Rayos X, Instituto de Química Fisica "Rocasolano".)

^{13}C-NMR spectra were recorded by Mrs. M. D. Casado and M. Plaza on a Bruker WP80SY (20 MHz). Chemical shifts are given in ppm from internal TMS and coupling constants in Hz.

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