Adamantylazoles. 5. The Molecular Structure of 1-(1-Adamantyl)pyrazoles

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The crystal structures of 1-(1-adamantyl)-3,5-dimethylpyrazole **1** and 1-(1-adamantyl)-3,4,5-trimethylpyrazole **2** were studied by X-ray analysis. The space groups and cell parameters are: **1**, Cc, 13.4452(4), 14.9407(4), 7.1119(2) Å, 90, 111.944(2), 90°, with Z = 4. **2**, $P2_1/c$, 6.7466(1), 21.2565(7), 10.1462(2) Å, 90, 106.368(2), 90°, with Z = 4. The final disagreement factors were 0.069 and 0.061, for 721 [2σ(I)] and 1950 [2σ(I)] observed reflexions, respectively. Compound **1** presents the adamantyl residue disordered between the two usual conformations. The experimental dipole moments and the carbon-13 chemical shifts (both in hexadeuteriodimethylsulfoxide and in the solid state) were measured and discussed in connection with the structure of these compounds.

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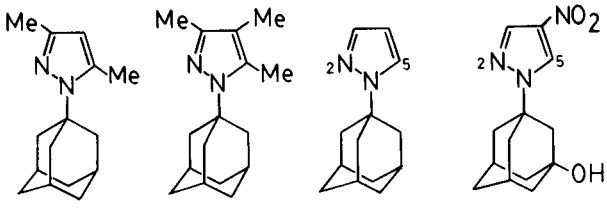
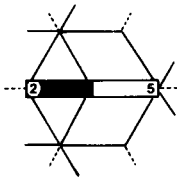
Our continued interest in adamantyl-substituted azoles [1-4] promptes us to report the results obtained from the X-ray study of two adamantyl pyrazoles **1** and **2** comparatively to those previously described **3** and **4**:

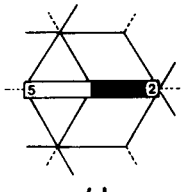


1 2 3 4

The quasi-spherical structure of the adamantyl residue (as clearly apparent from Leybold compact models) leads to two equally probable conformations **a** and **b** separated by a very low activation energy (0.5 kcal/mol, STO-3G calculation) [3].



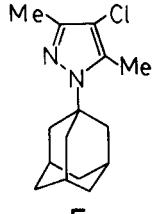
3a



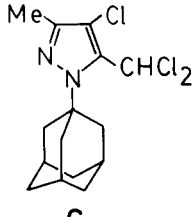
4b

In both cases the substituent in position 5 was an hydrogen atom. The question arises about the effect of a 5-methyl group on the structure: would it be of type **a** or of type **b**?

Crystals of compound **1** were obtained and the structure solved. The results were anomalous in the sense that although the 3,5-dimethylpyrazole ring was normal, the 1-adamantyl residue was fully distorted: the bottom part was shaped as a flatted cyclohexane ring, the carbon-carbon distances C_7-C_8, C_{10}-C_{11} and C_{12}-C_{13} were too high and the thermal ellipsoids indicated and artefact of the refinement. So more careful work was undertaken, not only in the crystallogtaphy of this compound (see experimental) but with parallel studies of dipole moments and of carbon-13 chemical shifts, in order to detect possible molecular deformations (see below). Moreover, with the aim of knowing the influence of the methyl group at position 5,



5



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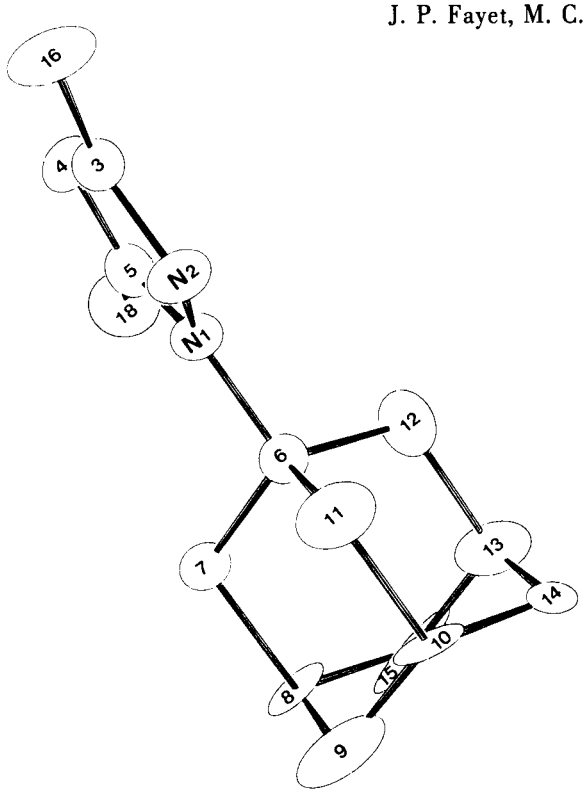


Figure 1a. ORTEP [12] view of the **1** molecule in the **b** conformation of the presented disorder. The atomic numbering is also shown.

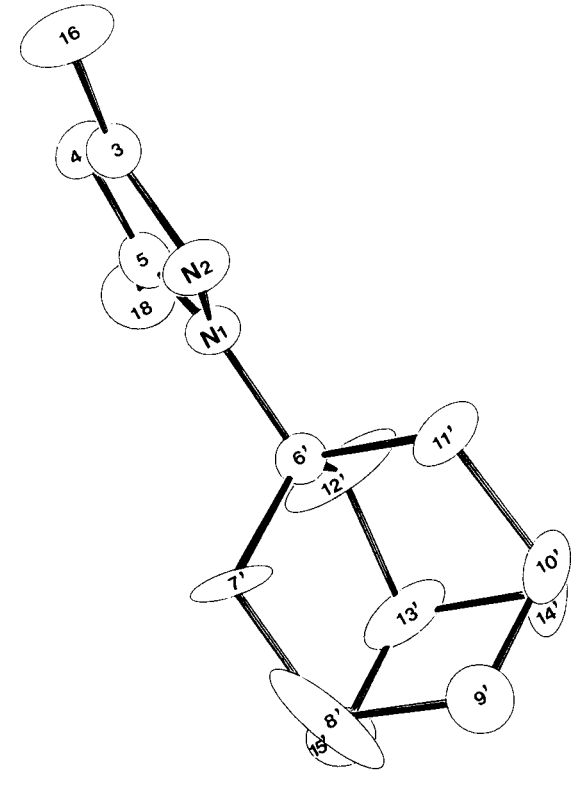


Figure 1b. Same as 1a for the **a** conformation.

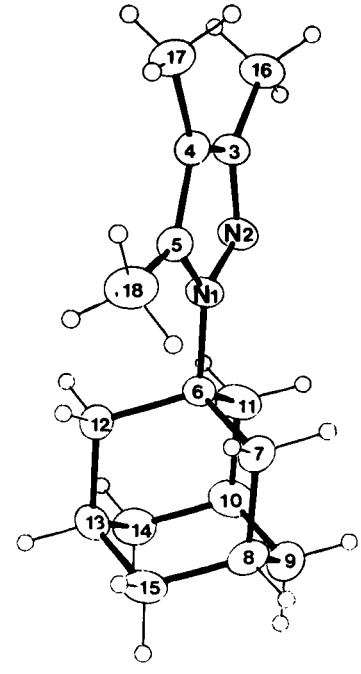


Figure 2. ORTEP [12] view of the **2** molecule showing the atomic numbering.

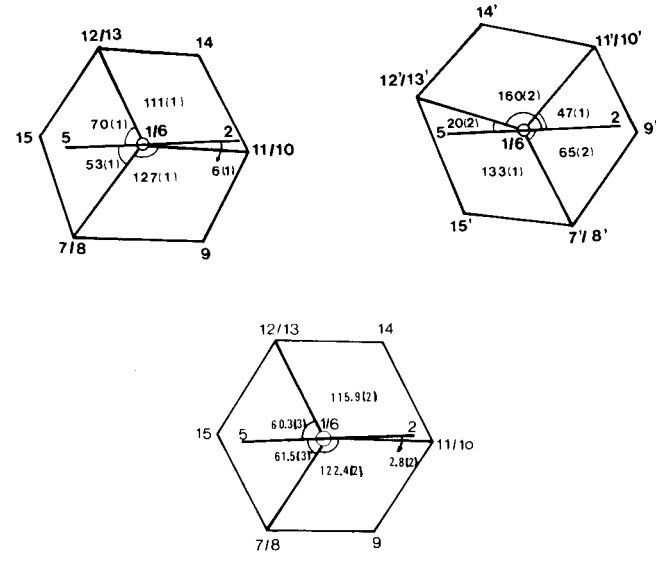


Figure 3. Projections along N_1-C_6 bond showing the relative disposition of the pyrazole ring with respect to the adamantyl residue for the three molecules present in the crystal of the two compounds.

we tried to prepare the 1-(1-adamantyl)-3,5-dimethyl-4-chloropyrazole **5** by chlorination of **1**, but we obtained a trichlorinated compound, identified as **6**. Compound **2** was then synthesized, crystallized and its X-ray structure solved.

Table 1

Selected Bond Lengths (Å) and Angles (°)

Molecules	1	1'	2
N1-N2	1.393(7)		1.364(3)
N2-C3	1.312(13)		1.326(3)
C3-C4	1.399(15)		1.390(4)
C4-C5	1.362(12)		1.380(3)
C5-N1	1.340(10)		1.369(13)
C3-C16	1.483(13)		1.499(5)
C4-C17	–		1.504(4)
C5-C18	1.513(13)		1.488(4)
N1-C6	1.489(9)		1.483(3)
C6-C12	1.518(23)	1.545(31)	1.538(4)
C6-C11	1.550(20)	1.517(26)	1.532(4)
C6-C7	1.545(16)	1.524(41)	1.535(3)
C7-C8	fixed		1.547(4)
C11-C10	"		1.543(4)
C12-C13	"		1.537(4)
C8-C9	"		1.509(5)
C9-C10	"		1.535(5)
C10-C14	"		1.520(5)
C14-C13	"		1.526(4)
C13-C15	"		1.514(4)
C8-C15	"		1.512(5)
C5-N1-N2	110.5(6)		110.9(2)
C5-N1-C6	133.3(4)		130.3(2)
N2-N1-C6	116.2(5)		118.7(2)
N1-N2-C3	105.7(7)		105.4(2)
N2-C3-C4	110.1(8)		111.7(2)
N1-C5-C4	106.8(7)		106.5(2)
C3-C4-C5	106.9(9)		105.5(2)
N2-C3-C16	121.5(10)		120.0(3)
C4-C3-C16	128.4(10)		128.3(2)
C3-C4-C17	–		126.7(3)
C5-C4-C17	–		127.8(3)
C4-C5-C18	126.6(10)		127.2(2)
N1-C5-C18	126.6(8)		126.3(2)
N1-C6-C12	109.1(11)	109.5(18)	109.6(2)
N1-C6-C7	110.9(8)	110.0(12)	111.0(2)
N1-C6-C11	111.6(8)	108.2(11)	109.5(2)
C7-C6-C12	111.2(11)	120.2(20)	110.0(2)
C11-C6-C12	105.5(12)	104.2(19)	108.3(2)
C7-C6-C11	108.4(13)	103.9(20)	108.3(2)

Table 2

Experimental Dipole Moments (in debyes), Solvent: Dioxane

Compound	α	β	R_{MD}	$P_{2\infty}$	μ
1-(1-Adamantyl)-3,5-dimethylpyrazole **1**	3.80	−0.05	59.19	180.40	2.43
1-(1-Adamantyl)-3,4,5-trimethylpyrazole **2**	3.23	−0.045	68.48	184.94	2.38
1-(1-Adamantyl)-pyrazole **3**	2.79	−0.043	73.13	177.70	2.26
1-(1-Adamantyl-3-ol)-4-nitropyrazole **4**	5.31	−0.27	66.90	303.06	3.40
1-(1-Adamantyl)-4-bromopyrazole **7**	12.48	−0.39	66.41	586.10	5.04
1-(1-Adamantyl-3-ol)-3,5-dimethyl-4-nitropyrazole **8**	12.03	−0.45	75.70	621.89	5.17
1-(1-Adamantyl)-3-methyl-5-aminopyrazole **9**	5.44	−0.13	67.25	263.57	3.10
Adamantylhydrazine	4.16	−0.05	49.22	158.13	2.31

Molecular Geometry.

The disordered structure of compound **1** presents the usual pyrazole ring, but the adamantyl residue is in the two conformations **a** and **b** (dashed and undashed, respectively), as seen in Figures 1a and 1b and in Figures 3. The ranges of C-C bond lengths and C-C-C bond angles in this residue are [1.517-1.601]Å, [99.2-120.2]° and [1.446-1.601]Å, [105.6-114.5]° for the dashed and undashed respectively, and with torsion angles in between 51.0 and 78.1° and 59.3 and 62.8°. The significance of these values is poor due to the disorder (see experimental). The structure of compound **2** is quite similar to that of **3** (see Figures 2 and 3). The conformation is of type **b** and all angles and distances are as expected. The ranges of values in the adamantyl residue are: [1.509(5)-1.547(4)]Å, [108.3(2)-110.3(3)]°, [58.0(3)-61.7(3)]°.

The pyrazole ring in both compounds (this part not being disordered in **1**) presents the same type of delocalization of the double bonds (see Table 1) as that already reported [3], with higher values in the C_5-N_1-N_2 and N_2-C_3-C_4 angles and an asymmetry in the substituent on N_1, with C_5-N_1-C_6 higher than N_2-N_1-C_6.

The hydrogen atoms of the methyl group substituted at C_5 are interacting with some hydrogen atoms of the adamantyl moiety: H_{18a}...H_{7b}, 2.261; H_{18b}...H_{12b}, 2.320; H_{18a}...$H_{12'b}$, 1.933; H_{18b}...$H_{12'a}$, 2.006, and H_{18b}...$H_{12'b}$, 2.257 Å in compound **1** and H_{18a}...H_{7a}, 1.957(65); H_{18b}...H_{12b}, 2.134(58) Å in compound **2**, were there is also a contact between H_{18c}...H_{17c} of 2.203(7) Å. This methyl-adamantyl interactions seem not to fix the relative twist as suggested by the disorder presented in compound **1**.

Dipole Moment of 1-(1-Adamantyl)pyrazoles.

The dipole moments of seven adamantylpyrazoles were measured in dioxane (see experimental part). Adamantylhydrazine was also measured but adamantylamine is too insoluble in dioxane ($\omega < 0.00002$) to determine its dipole moment (Table 2). An MNDO calculation gives 3.90 D for this last compound.

1-(1-Adamantyl)pyrazole **3** has a dipole moment of 2.43 D similar to that of 1-methylpyrazole (μ exp = 2.25 D [5], μ calcd. (MNDO) = 2.34 D) and to that of 1-*t*-butylpyrazole (μ calcd. (MNDO) = 2.32 D). The dipole moments of compounds **1** and **2** are similar and do not show any electronic anomaly in compound **2**. The presence of an hydroxy group at position 2 of the adamantane increases considerably the dipole moment.

Carbon-13 NMR Spectra of Adamantylpyrazoles.

The spectra of several adamantylpyrazoles have already been described [2,3]. The only new compounds are **2** and **6**. That of the last one is to be found in the experimental

Table 3

Carbon-13 NMR Study: a) DMSO-d_6; b) Solid State

Compound	C_3	C_4	C_5	C_6	C_7	C_8	C_9	Substituents
	143.6	107.5	137.9	59.6	41.8	29.3	35.7	13.3 (Me_3), 14.3 (Me_5)
a)	^2J = 5.8 (H_4)	^1J = 170.8	^2J = 8.6 (H_4)		^1J = 129.0	^1J = 132.5	^1J = 126.9	^1J = 126.2 ^1J = 128.2
1	^2J = 5.8(Me)	^3J = 3.5 (Me)	^2J = 6.4 (Me)					
		^3J = 3.5 (Me)						
b)	144.7	107.9	136.6	60.1	42.6	29.8	36.5 [a]	13.0 (Me_3), 14.6 (Me_5)
a)	142.2	111.8	134.0	59.2	41.7	29.3	35.7	11.9 (Me_3), 7.9 (Me_4), 12.5 (Me_5)
2					^1J = 130.3	^1J = 131.1	^1J = 123.8	^1J = 126.3, ^1J = 125.9, ^1J = 127.8
b)	141.2	110.9	134.5	58.4	41.0	29.8	35.7 [a]	12.7 (Me_3), 8.9 (Me_4), 14.0 (Me_5)
	137.7	104.3	125.3	57.7	42.4	29.0	35.6	
a)	^1J = 183.4	^1J = 175.0	^1J = 185.9		^1J = 129.4	^1J = 132.3	^1J = 126.3	
3	^2J = 5.8 (H_4)	^2J = 10.7 (H_3)	^2J = 9.5 (H_4)					
	^3J = 8.4 (H_5)	^2J = 8.5 (H_5)	^3J = 4.4 (H_5)					
b)	137.9	103.2	126.3	57.9	42.7	28.9	35.9 [a]	

[a] Broad.

Table 4

Crystal Analysis Parameters at Room Temperature

Crystal Data		
Formula	C15 H22 N2	C16 H24 N2
Crystal habit	Transparent plate	Transparent plate
Crystal size (mm)	0.24 x 0.13 x 0.40	0.30 x 0.13 x 0.07 (Inside capilar)
Symmetry	2/m, Monoclinic, Cc	2/m, Monoclinic, $P2_1/c$
Unit cell determination:	Least-squares fit from 42 reflexions ($\theta < 45°$)	Least-squares fit from 52 reflexions ($\theta < 45$)
Unit cell dimensions	13.4452(4), 14.9407(4), 7.1119(2) 90, 111.944(2), 90	6.7466(1), 21.2565(7), 10.1462(2) Å 90, 106.368(2), 90°
Packing: V(Å^3), Z	1325.1(1), 4	1396.1(1), 4
Dc(g. cm^{-3}), M, F(000)	1.155, 230.35, 504	1.163, 244.38, 536
Experimental data		
Technique	Four circle diffractometer: PW1100 Philips Bisecting geometry Graphite oriented monochromator: CuKα w/2θ scans, scan width: 1.5° Detector apertures 1 x 1°, up θ max. 65° 1 min/reflex.	
Number of reflexions:		
Measured	4519	2440
Independent	1131	2359
Observed	721 (2 σ(I) criterion)	1950 (2 σ(I) criterion)
Value of Rint	0.024	–
	2 reflexiones every 90 minutes Variation: none	2 reflexiones every 90 minutes Variation: 6% overall decay
Solution and refinement		
Solution	Direct methods	
Refinement	L. S. on Fobs with 1 blocks	
Parameters:		
Number of variables	179	259
Degrees of freedom	542	1691
Ratio of freedom	4.0	7.5
H atoms	Calculated + Difference synthesis	Difference synthesis
Final shift/error	0.08	0.16
w-scheme	Empirical as to give no trends in $<w\Delta^2F>$ vs $<\|Fobs\|>$ and $<\sin\theta/\lambda>$	
Max thermal value	U11(C15') = 0.38(7) Å^2	U11(C17) = 0.104 (3) Å^2
Final Δ F peaks	0.21 eÅ^3	0.22 eA^{-3}
Final R and Rw	0.069, 0.087	0.061, 0.069
Computer and programs	VAX 11/750, MULTAN80 [9], X-RAY 76 [10]	
Scattering factors	Int. Tables for X-Ray Crystallography [11]	

Table 5

C 15 H 22 N2. Final Atomic Coordinates and Thermal Parameters as UEQ = (1/3). Sum (UIJ.AI*.AJ*.AI.AJ.COS(AI,AJ)).10**3

ATOM	X/A	Y/B	Z/C	UEQ
N1	0.4189	0.1720(4)	0.4558	49(3)
N2	0.5199(6)	0.1549(5)	0.6025(12)	55(3)
C3	0.5052(8)	0.0930(6)	0.7209(13)	59(4)
C4	0.3971(8)	0.0683(6)	0.6506(14)	61(4)
C5	0.3451(7)	0.1191(5)	0.4835(13)	55(3)
C6	0.4138(6)	0.2421(5)	0.3036(12)	42(3)
C7	0.3585(17)	0.2058(10)	0.0857(21)	87(9)
C7'	0.4755(30)	0.2115(18)	0.1738(42)	112(20)
C8	0.3609(-)	0.2792(-)	-0.0628(-)	118(13)
C8'	0.4724(-)	0.2853(-)	0.0204(-)	176(-)
C9	0.4751(-)	0.3073(-)	-0.0272(-)	128(15)
C9'	0.5250(-)	0.3696(-)	0.1332(-)	66(-)
C10	0.5279(-)	0.3459(-)	0.1849(-)	56(-)
C10'	0.4643(-)	0.4027(-)	0.2621(-)	81(13)
C11	0.5270(13)	0.2760(12)	0.3291(28)	74(7)
C11'	0.4760(27)	0.3231(17)	0.4159(38)	92(14)
C12	0.3551(18)	0.3233(12)	0.3389(31)	81(10)
C12'	0.2973(23)	0.2762(27)	0.2025(70)	133(22)
C13	0.3490(-)	0.3968(-)	0.1738(-)	90(12)
C13'	0.2958(-)	0.3363(-)	0.0150(-)	102(15)
C14	0.4567(-)	0.4273(-)	0.2109(-)	117(16)
C14'	0.3473(-)	0.4211(-)	0.1295(-)	110(22)
C15	0.2969(-)	0.3590(-)	-0.0388(-)	117(12)
C15'	0.3567(-)	0.3042(-)	-0.1141(-)	163(31)
C16	0.5955(9)	0.0585(8)	0.8992(15)	86(4)
C18	0.2269(8)	0.1155(8)	0.3527(18)	89(5)

Table 6

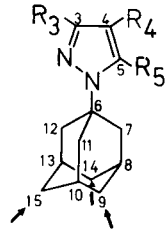
C 16 H 24 N 2. Final Atomic Coordinates and Thermal Parameters as UEQ = (1/3). Sum (UIJ.AI*.AJ*.AI.AJ.COS(AI,AJ)).10**4

ATOM	X/A	Y/B	Z/C	UEQ
N1	0.25260(30)	0.22919(9)	0.58325(21)	412(7)
N2	0.06469(33)	0.20105(10)	0.53308(23)	492(7)
C3	0.10233(44)	0.13973(11)	0.54132(26)	487(9)
C4	0.31189(43)	0.12714(11)	0.59483(25)	467(9)
C5	0.40633(38)	0.18516(11)	0.62141(25)	425(8)
C6	0.26413(34)	0.29886(10)	0.58220(23)	366(7)
C7	0.35994(46)	0.32467(12)	0.72753(27)	484(9)
C8	0.37085(49)	0.39730(13)	0.72188(29)	560(10)
C9	0.15551(56)	0.42376(14)	0.66839(37)	657(13)
C10	0.05706(47)	0.39860(13)	0.52275(36)	606(11)
C11	0.04619(43)	0.32616(13)	0.52739(38)	582(11)
C12	0.39254(43)	0.31998(12)	0.48667(27)	473(9)
C13	0.40289(48)	0.39219(13)	0.48450(30)	552(10)
C14	0.18488(53)	0.41854(14)	0.42822(32)	615(11)
C15	0.50031(49)	0.41629(13)	0.62864(34)	588(11)
C16	-0.07228(63)	0.09384(16)	0.49556(42)	704(14)
C17	0.41200(70)	0.06335(14)	0.61909(40)	678(14)
C18	0.63024(48)	0.19798(16)	0.68310(43)	651(12)

part. The chemical shifts and first-order ^1H-^{13}C coupling constants of compounds **1-3** in DMSO-d_6 are gathered in Table 3.

In this solvent, compound **1** behaves as compounds **2** and **3**. Consistently with the dipolar moment study, compound **1** in solution does not show any particularity being a 'standard' 1-(1-adamantyl)pyrazole.

^{13}C-cross polarization/magic angle spinning (CP/MAS) spectroscopy is a useful tool to study heterocycles, for instance pyrazoles [6,7], in the solid state. The spectra of compounds **1-3** were recorded at 100 MHz: the results are in Table 3. The spectra are extremely well resolved as a consequence of the globular structure of adamantane [8]. The only slightly broad signal belongs to C_9 (C_{14}, C_{15}).



The very close similarity between the chemical shifts in solution and in the solid state, demonstrated that there is no change in the structure due to lattice effects. Once again compound **1** is completely normal.

Conclusion.

1-(1-Adamantyl)-3,5-dimethylpyrazole **1** is normal in its properties (μ and $\delta^{13}C$). Experiments on thermal treatment (sublimation, water reflux) do not produce any change in its ir spectra. The disorder present in its crystal state seems to be due to the low activation energy between the two usual conformations, **a** and **b**. Compound **2** has the usual structure found in these adamantylpyrazoles, with a conformation of type **b**.

EXPERIMENTAL

All compounds discussed here have already been described save **2** and **6** [1-4]. The ^1H and ^{13}C nmr spectra were obtained with Varian EM390 (90 MHz) and Varian XL-300 (75.4 MHz), respectively, in the solvents indicated. Chemical shifts and coupling constants were measured in ppm (δ) and Hz (J) with respect to tetramethylsilane. All melting points are uncorrected.

1-(1-Adamantyl)-3,4,5-trimethylpyrazole (**2**).

A mixture of 3 g (0.0125 mole) of 1-adamantylhydrazine dihydrochloride and 2.28 g (0.02 mole) of 3-methyl-2,4-pentanedione in 25 ml of ethanol was heated under reflux during 3 hours. After cooling the ethanol was removed and the residue obtained was then dissolved in the minimal amount of water and neutralized with potassium carbonate. This aqueous solution was extracted with chloroform and the evaporation under vacuum of the chloroform afforded a crude product (2.2 g) which was recrystallized from ethanol-water yielding 1.8 g of **2** (63% yield), mp 77-79°.

Anal. Calcd. for $C_{16}H_{24}N_2$: C, 78.6; H, 9.9; N, 11.5. Found: C, 78.8; H, 9.9; N, 11.5.

1-(1-Adamantyl)-3-methyl-4-chloro-5-dichloromethylpyrazole (**6**).

1-(1-Adamantyl)-3,5-dimethylpyrazole **1** 2.70 g, (0.012 moles) was dissolved in 50 ml of carbon tetachloride and with external cooling a stream

of dry chlorine was bubbled for 1 hour. A white precipitate was obtained which after recrystallization from ethanol afforded 1.7 g of **6** (43% yield), mp 125-127°; ^{1}H nmr (deuteriochloroform): 1.76 (m, 6H), 2.26 (m, 9H), 2.20 (s, 3-CH_3), 7.30 (s, $CHCl_2$); ^{13}C nmr (deuteriochloroform): 144.3 (C_3), 112.6 (C_4), 135.2 (C_5), 62.4 (C_6), 43.0 (C_7), 29.9 (C_8), 36.0 (C_9), 11.0 (3-CH_3), 60.7 ppm ($CHCl_2$); ^{1}J coupling constants: 128.5 (3-CH_3), 174.8 ($CHCl_2$), 130.6 (C_7), 134.2 (C_8), 126.9 (C_9).

Anal. Calcd. for $C_{15}H_{19}Cl_3N_2$: C, 54.0; H, 5.7; N, 8.4. Found: C, 54.2; H, 6.0; N, 8.2.

X-Ray Analysis.

The final crystal analysis parameters are given in Table 4. In Tables 5 and 6 the fractional atomic coordinates are given according to the numbering scheme shown in Figures 1 and 2. Lists of structure factors, thermal parameters and hydrogen parameters are available from the authors on request. These are the final results of the study of compound **1**. But in this compound five sets of data have been investigated. From the original synthesis of the compound we have examined three sets of data of different crystals, obtained from different solvents, mounted on glass capillaries and in the monoclinic space group Cc. All lead to the same mentioned anomalous results. From a second synthesis of the compound and a new crystallization process, two samples were introduced into Lindeman capillaries, from the mother liquid, and data collected for monoclinic and triclinic asymmetric sets respectively. With the monoclinic data the same results appeared. The triclinic data were reduced to monoclinic, as the disagreement index between those data symmetry related was just 0.024. Once reduced these data were statistically tested for centrosymmetry and the possible extinctions carefully checked. All lead us to confirm the Cc space group. So the next step was to try a disorder model for the 1-adamantyl residue. Using this set of data, the residue was allowed to refine with the two alternative conformations **a** and **b**, initially with 50% populations. Weigths least-squares refinements only converged when the coordinates of the two bottom parts of the disordered adamantyl moiety and the thermal factors of $C_{8'}$, $C_{9'}$ and C_{10} were fixed. The resulting model, with populations of 0.60(4) and 0.40(4) for the **b** (undashed) and **a** (dashed) disordeded moieties, accounts quite well for the observed spectrum (R = 0.069, $\Delta\rho$ = 0.21 e Å^{-3}) with a reasonable geometry. In conclusion, we think this is the most probable explanation for the anomalous results above mentioned.

Dipole Moment Measurements.

The electrical dipole moments were measured in dioxane at 25°C. The debye formula was used as the Halverstadt and Kumler extrapolation method [5] for calculations of total polarization.

^{13}C CP/MAS NMR Spectra.

The spectra in the solid state were obtained at 106.3 MHz on a Bruker MSL-400 spectrometer in Bruker Analytische Messteknik GmbH, Karlsruhe (spinning rate, 4.26 kHz; spectral width, 31.25 kHz). Dixon TOSS technique [13] was used to suppress spinning sidebands.

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