

A MULTINUCLEAR NMR STUDY (^1H , ^{13}C , ^{15}N) OF 1-MONOSUBSTITUTED PYRAZOLES[#]

Rosa María Claramunt,^{1,*} Dionisia Sanz,¹ María Dolores Santa María,¹ José Antonio Jiménez,¹ María Luisa Jimeno,² and José Elguero^{2,*}

¹ Departamento de Química Orgánica y Biología, Facultad de Ciencias, UNED, Senda del Rey, s/n, E-28040 Madrid, Spain

² Instituto de Química Médica, CSIC., Juan de la Cierva 3, E-28006 Madrid, Spain

Abstract- The chemical shifts and coupling constants of twenty-three pyrazoles bearing different substituents at position 1 have been studied by ^1H , ^{13}C and ^{15}N NMR spectroscopy in solution. Three new pyrazoles (*N*-pyrazolyl-*P,P,P*-triphenylphospha- λ^5 -azene, sodium 1-hydroxypyrazolate and 1-trifluoromethanesulfonylpyrazole) have been prepared; moreover, to assign the signals of some compounds, two other pyrazoles have been synthesized labelled in both nitrogen atoms with ^{15}N (1-benzyl and 1-hydroxypyrazole). The tautomerism of 1-hydroxypyrazole has been reexamined.

A reliable database of 1-substituted pyrazoles is necessary for studies on two related questions: i) how substituent effects are transmitted through the nitrogen and ii) how the aromaticity of pyrazole ring is affected by *N*-substituents.¹ Concerning the first point, knowledge about the transmission of substituent effects is restricted to *C*-substituents (benzene and other aromatic rings including *C*-substituted heterocycles).²⁻⁴ Regarding the second point, the only available information concerns pyrazole itself ($\text{X} = \text{H}$).⁵⁻¹⁰

We have selected fourteen NMR properties: **1-6**) the ^1H chemical shifts of the three ring protons H3, H4, H5 and the three corresponding ^1H - ^1H coupling constants, J_{34} , J_{45} , J_{35} determined by ^1H -NMR; **7-12**) the ^{13}C NMR chemical shifts of the three ring carbons C3, C4, C5 and the three $^1\text{J}(^1\text{H}-^{13}\text{C})$ coupling constants, both measured in ^{13}C -NMR; **13,14**) the ^{15}N chemical shifts of N1 and N2 determined by ^{15}N -NMR spectroscopy either in natural abundance or using ^{15}N labelled compounds.

Taking into account the synthetic feasibility, we have selected twenty-two 1-substituted pyrazoles (the NH derivative, $\text{X} = \text{H}$, was excluded due to annular prototropy between N1 and N2 atoms): boron derivatives: $\text{X} = [\text{HBPz}_2]^-$ (trispyrazolylborate anion) (**1**); carbon derivatives: methyl (**2**), ethyl (**3**); 1-adamantyl (**4**); benzyl (**5**); trityl (**6**); phenyl (**7**); acetyl (**8**); carbamoyl (CONH_2) (**9**); nitrogen derivatives: amino (**10**);

[#]Dedicated to Professor Koji Nakanishi on the occasion of his 75th anniversary

methylamino (**11**); formylamino (NHCHO) (E and Z) (**12,13**); acetylamino (NHCOCH₃) (Z) (**14**); the Schiff base (N=CHC₆H₅) (**15**); *P,P,P*-triphenylphospha- λ^5 -azanyl [N=P(C₆H₅)₃] (**16**); nitro (**17**); oxygen derivatives: benzyloxy (OCH₂C₆H₅) (**18**); *N*-oxide anion (O⁻ Na⁺) (**19**); silyl derivatives: trimethylsilyl [Si(CH₃)₃] (**20**); phosphorus derivatives: bis(dimethylamino)phosphine {P[N(CH₃)₂]₂} (**21**); sulfur derivatives: triflyl (SO₂CF₃) (**22**).

The case of *N*-hydroxypyrazole **23** (X = OH) will be discussed but not used in the analyses since it also has a problem of prototropy.¹¹ The fourteen NMR parameters as well as the ³J(H4H5)/³J(H3H4) ratios are collected in Table 1.

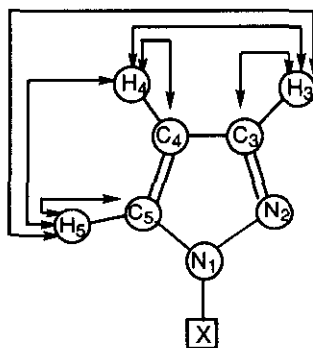


Table 1. NMR parameters of 1-substituted pyrazoles (chemical shifts in ppm and coupling constants in Hz)

No	1-Substituent	1 δ H3	2 δ H4	3 δ H5	4 ³ J(H3H4)	5 ³ J(H4H5)	6 ³ J(H3H5)	Ratio J ₄₅ /J ₃₄
1	[HBPz ₂] ⁻	7.36	6.05	7.24	1.6	2.1	0.65	1.31a
2	CH ₃	7.49	6.22	7.35	2.0	2.3	0.7	1.15b
3	C ₂ H ₅	7.49	6.23	7.38	1.87	2.27	0.69	1.21b
4	1-adamantyl	7.54	6.23	7.52	1.81	2.37	0.71	1.31b
5	CH ₂ C ₆ H ₅	7.56	6.28	7.38	1.88	2.30	0.69	1.22b
6	C(C ₆ H ₅) ₃	7.67	6.24	7.37	1.79	2.49	0.68	1.39b
7	C ₆ H ₅	7.72	6.46	7.87	1.9	2.5	0.7	1.32b
8	COCH ₃	7.70	6.43	8.25	1.49	2.85	0.68	1.91b
9	CONH ₂	7.63	6.42	8.23	1.6	2.8	0.7	1.75b
10	NH ₂	7.36	6.14	7.39	2.1	2.3	0.9	1.10b
11	NHCH ₃	7.38	6.09	7.34	2.1	2.3	0.9	1.10b
12	NHCHO (E)	7.53	6.39	7.90	1.8	2.3	0.7	1.28a
13	NHCHO (Z)	7.49	6.34	7.72	1.7	2.4	0.7	1.41a
14	NHCOCH ₃ (Z)	7.47	6.31	7.44	2.2	2.5	0.8	1.14b
15	N=CHC ₆ H ₅	7.64	6.49	8.04	2.0	2.4	0.9	1.20a
15	N=CHC ₆ H ₅	7.56	6.38	7.71	2.1	2.4	0.7	1.14b
16	N=P(C ₆ H ₅) ₃	7.07	5.97	7.17	2.2	2.1	1.1	0.95b
17	NO ₂	7.77	6.66	8.65	1.7	3.1	0.9	1.82c
18	OCH ₂ C ₆ H ₅	7.25	6.15	7.53	2.3	2.4	1.0	1.04a
19	O ⁻ Na ⁺	6.62	5.74	6.80	2.5	1.7	1.2	0.68a
20	Si(CH ₃) ₃	7.79	6.33	7.60	1.6	2.3	---	1.44b
21	P[N(CH ₃) ₂] ₂	7.70	6.30	7.53	1.9	2.2	---	1.16b
22	SO ₂ CF ₃	7.99	6.66	8.08	1.6	3.0	0.6	1.88b

No	1-Substituent	7 $\delta C3$	8 $\delta C4$	9 $\delta C5$	10 $^1J(C3H3)$	11 $^1J(C4H4)$	12 $^1J(C5H5)$	13 $\delta N1$	14 $\delta N2$
1	[HBPz ₂] ⁻	141.9d	106.0d	135.7d	182.6d	175.8d	186.1d	-141.9a	-68.8a
2	CH ₃	139.0b	105.3b	129.6b	184.7b	176.4b	186.3b	-180.8a	-73.7a
3	C ₂ H ₅	138.5b	104.8b	127.7b	184.4b	176.2b	184.9b	-166.3b	-80.0b
4	1-adamantyl	137.7a	104.3a	125.3a	183.4a	175.0a	185.9a	-145.7b	-82.8b
5	CH ₂ C ₆ H ₅	138.9a	105.4a	130.1a	184.1a	175.9a	187.7a	-167.3a	-72.9a
6	C(C ₆ H ₅) ₃	139.6b	104.3b	132.2b	185.2b	176.5b	188.0b	-155.9b	-71.1b
7	C ₆ H ₅	140.9a	107.8a	127.6a	185.8a	177.5a	189.9a	-159.9a	-77.3a
8	COCH ₃	143.6b	109.3b	127.8b	187.1b	178.7b	190.3b	-139.9b	-77.0b
9	CONH ₂	142.3a	108.6a	128.8a	186.8a	178.7a	192.9a	-153.4a	-81.4a
10	NH ₂	136.6b	103.9b	129.0b	186.1b	177.5b	190.0b	-162.1a	-72.4a
11	NHCH ₃	137.2b	103.7b	127.8b	185.9b	177.2b	187.9b	-151.8b	-82.4b
12	NHCHO (E)	138.4a	106.2a	131.3a	187.3a	178.5a	193.4a	-173.4a	-70.1a
13	NHCHO (Z)	137.6a	105.4a	130.8a	187.0a	178.2a	193.0a	-176.4a	-71.9a
14	NHCOCH ₃ (Z)	137.3a	105.1a	130.9a	186.6a	177.8a	192.5a	-172.6a	-71.9a
15	N=CHC ₆ H ₅	137.9a	106.7a	129.3a	187.6a	178.8a	192.9a	-136.5a	-69.3a
15	N=CHC ₆ H ₅	137.4b	105.9b	128.7b	187.0b	178.3b	191.0b	-----	-----
16	N=P(C ₆ H ₅) ₃	132.9b	102.1b	125.8b	183.5b	175.2b	187.9b	-167.2b	-78.1b
17	NO ₂	141.6a	109.8a	126.8a	193.4a	183.1a	203.2a	-107.8c	-82.9c
18	OCH ₂ C ₆ H ₅	133.1b	102.9b	122.3b	188.4b	178.4b	192.8b	-132.9b	-90.8b
19	O ⁻ Na ⁺	126.1a	99.3a	117.3a	181.3a	172.1a	186.0a	-101.9a	-91.8a
20	Si(CH ₃) ₃	143.1b	106.0b	133.7b	182.9b	175.6b	183.2b	-161.1b	-71.4b
21	P[N(CH ₃) ₂] ₂	142.2b	106.2b	132.2b	183.1b	174.8b	183.1b	-147.3b	-66.0b
22	SO ₂ CF ₃	148.1b	111.6b	133.8b	191.3b	182.7b	199.3b	-162.0b	-72.3b

a DMSO-d₆, b CDCl₃, c Acetone-d₆, d D₂O.

The ¹H NMR chemical shifts of pyrazole H3, H4 and, mainly, H5 are very sensitive to the nature of the solvent,^{12,13} and since different solvents have to be used for solubility reasons, columns **1** to **3** are not very useful to carry out comparisons. The same happens to the ¹H-¹H coupling constants (columns **4** to **6**); J₃₅ is rather insensitive to the X substituent and in some cases difficult to measure with precision; instead of using J₃₄ and J₄₅ is better to use the ratio J₄₅/J₃₄ (J₄₅ is, in general, larger than J₃₄) which reflects the localization of the π -system of pyrazoles.¹⁴ The extreme values of Table 1 are concentrated in a few compounds: the sodium *N*-hydroxylate (**19**) [J₄₅/J₃₄, $\delta C3$, $\delta C4$, $\delta C5$, ¹J(C3H3), ¹J(C4H4), $\delta N1$ and $\delta N2$], the 1-nitro (**17**) [¹J(C3H3), ¹J(C4H4) and ¹J(C5H5)] and 1-trifluoromethanesulphonyl (triflyl) (**22**) derivatives [J₄₅/J₃₄, $\delta C3$ and $\delta C4$].

The correlation matrix corresponding to the columns Ratio (J₄₅/J₃₄) and **7-14** shows that these nine NMR parameters form four clusters: i) J₄₅/J₃₄, $\delta C3$ and $\delta C4$ (correlation coefficients between 0.836 and 0.900); ii) ¹J(C3H3), ¹J(C4H4) and ¹J(C5H5) (correlation coefficients between 0.945 and 0.974); iii) $\delta C5$ and $\delta N2$ (correlation coefficient 0.875), and iv) $\delta N1$. It is worth noticing that the chemical shift of N1 is not related to any other NMR property. It is as if the effect of the substituent X was wave-like propagating through the pyrazole ring: first N1, then N2 and C5, and finally towards the hydrogen periphery. This is clearly apparent in the unrotated loadings plot (Figure 1) corresponding to a factorial analysis (the variables have been coded):

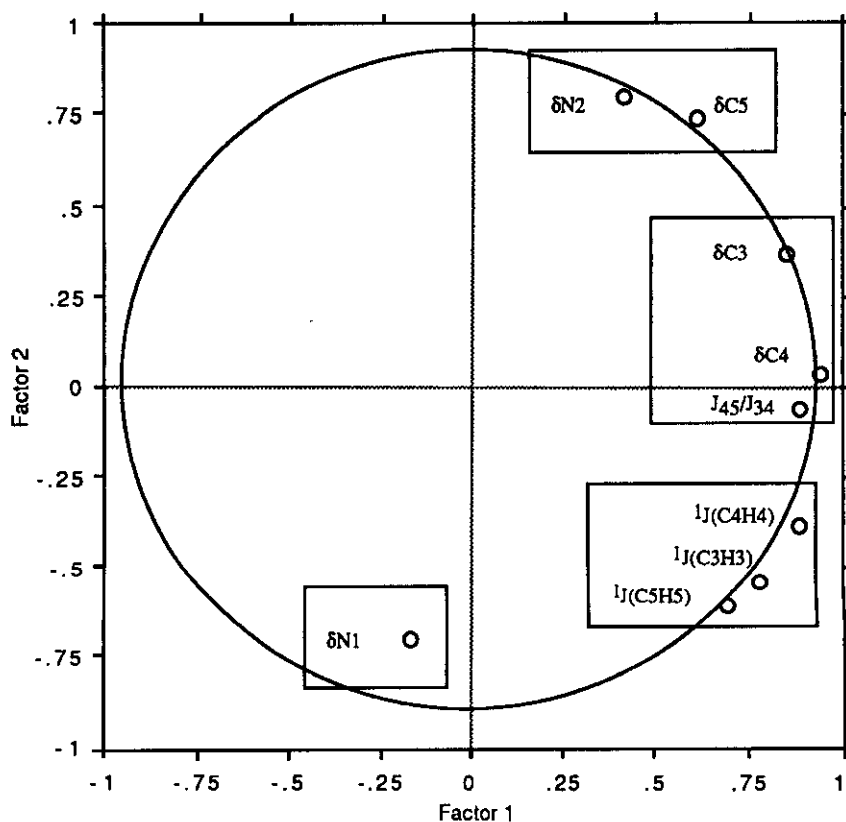
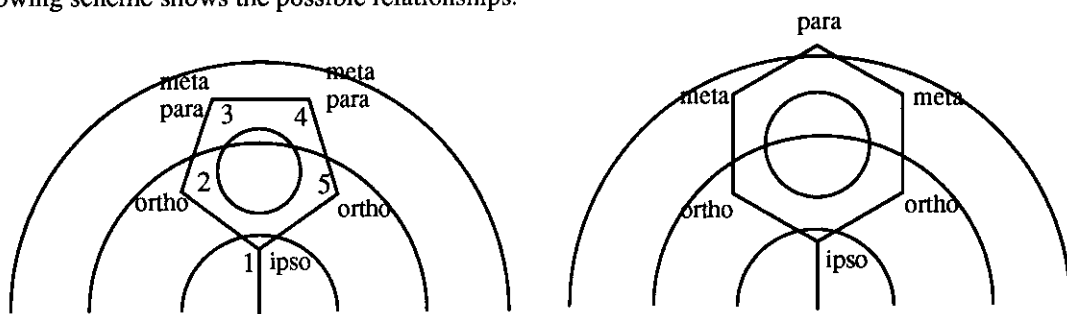


Figure 1

Although the comparisons between aromatic five and six-membered rings present some problems, the following scheme shows the possible relationships.



If that formal analogy holds, then pyrazole N1 should correspond to an *ipso* benzene position and N2 and C5 to *ortho* positions. Regarding pyrazole C3 and C4 they can be considered either *meta* or *para* positions, but it is known that in benzenes the ^{13}C chemical shifts of the carbon atom in the *meta* position are very insensitive to substituent effects (SCS). We have found the SCS for twenty benzenes (Table 2, assuming that OBn can be replaced by OMe)¹⁵

Table 2. ^{13}C SCS of monosubstituted benzenes in ppm

No	1-Substituent	<i>Cipso</i>	<i>Cortho</i>	<i>Cmeta</i>	<i>Cpara</i>
1	[HBPz ₂] ⁻	----	----	----	----
2	CH ₃	9.2	0.7	-0.1	-3.0
3	C ₂ H ₅	15.6	-0.5	0.0	-2.6
4	1-adamantyl	23.3	-3.2	0.1	-2.5
5	CH ₂ C ₆ H ₅	12.3	-0.3	0.2	-2.7
6	C(C ₆ H ₅) ₃	18.3	2.8	-1.1	-2.6
7	C ₆ H ₅	13.1	-1.1	0.4	-1.1
8	COCH ₃	8.9	0.1	-0.1	4.4
9	CONH ₂	5.0	-1.2	0.1	3.4
10	NH ₂	18.2	-13.4	0.8	-10.0
11	NHCH ₃	21.4	-16.2	0.8	-11.6
12 ^a	NHCHO (E)	9.9	-10.8	0.9	-4.7
13 ^a	NHCHO (Z)	9.8	-9.1	0.4	-4.8
14	NHCOCH ₃ (Z)	9.7	-8.1	0.2	-4.4
15	N=CHC ₆ H ₅	24.7	-6.5	1.3	-1.5
16	N=P(C ₆ H ₅) ₃	22.6	-5.1	0.0	-11.2
17	NO ₂	19.9	-4.9	0.9	6.1
18	OR	30.2	-15.5	0.0	-8.9
19	O ⁻ Na ⁺	39.6	-8.2	1.9	-13.6
20	Si(CH ₃) ₃	11.6	4.9	-0.7	0.4
21	P[N(CH ₃) ₂] ₂	----	----	----	----
22	SO ₂ CF ₃	2.8	2.6	2.2	9.1

^a This work (see experimental part).

Equations (1)-(4) represent the results obtained when pyrazoles and benzenes are compared:

$$\delta\text{C3} = 140.6 \pm 0.5 + 0.68 \pm 0.08 \text{ SCS}(\text{para}), n = 20, r^2 = 0.79 \quad (1)$$

$$\delta\text{C4} = 107.0 \pm 0.3 + 0.45 \pm 0.04 \text{ SCS}(\text{para}), n = 20, r^2 = 0.87 \quad (2)$$

$$\delta\text{C5} = 134 \pm 1.1 - 0.35 \pm 0.06 \text{ SCS}(\text{ipso}), n = 20, r^2 = 0.67 \quad (3)$$

$$\delta\text{N1} = -180 \pm 7 + 1.6 \pm 0.4 \text{ SCS}(\text{ipso}), n = 20, r^2 = 0.47 \quad (4)$$

δN2 is not correlated to any benzene SCS and $\text{SCS}(\text{ortho})$ is not correlated with any chemical shift of the five pyrazole ring atoms. In the case of equations (1) and (2), the worst point is **19** (O⁻ Na⁺); if this point is removed ($n = 19$), the r^2 values increase up to 0.80 and 0.93.

The most interesting of these equations is number (4) which, although of very bad quality, shows that N1 behaves like a C(*ipso*) for 20 substituents [largest deviations NO₂ and N=P(C₆H₅)₃]. An examination of the plot (Figure 2) shows two lines: a first line formed by four points (COMe, CONH₂, NO₂, SO₂CF₃) [Eq. (5)] and another line formed by the sixteen remaining substituents [Eq. (6), largest deviation N=P(C₆H₅)₃]. If this last point is removed, Eq. (7) is obtained [in the Figure are represented the regression lines corresponding to Eqs. (5) and (7)]

$$\delta\text{N1} = -169.5 \pm 1.4 + 3.1 \pm 0.1 \text{ SCS}(\text{ipso}), n = 4, r^2 = 0.997 \quad (5)$$

$$\delta\text{N1} = -196 \pm 4 + 2.2 \pm 0.2 \text{ SCS}(\text{ipso}), n = 16, r^2 = 0.88 \quad (6)$$

$$\delta\text{N1} = -196 \pm 3 + 2.3 \pm 0.1 \text{ SCS}(\text{ipso}), n = 15, r^2 = 0.95 \quad (7)$$

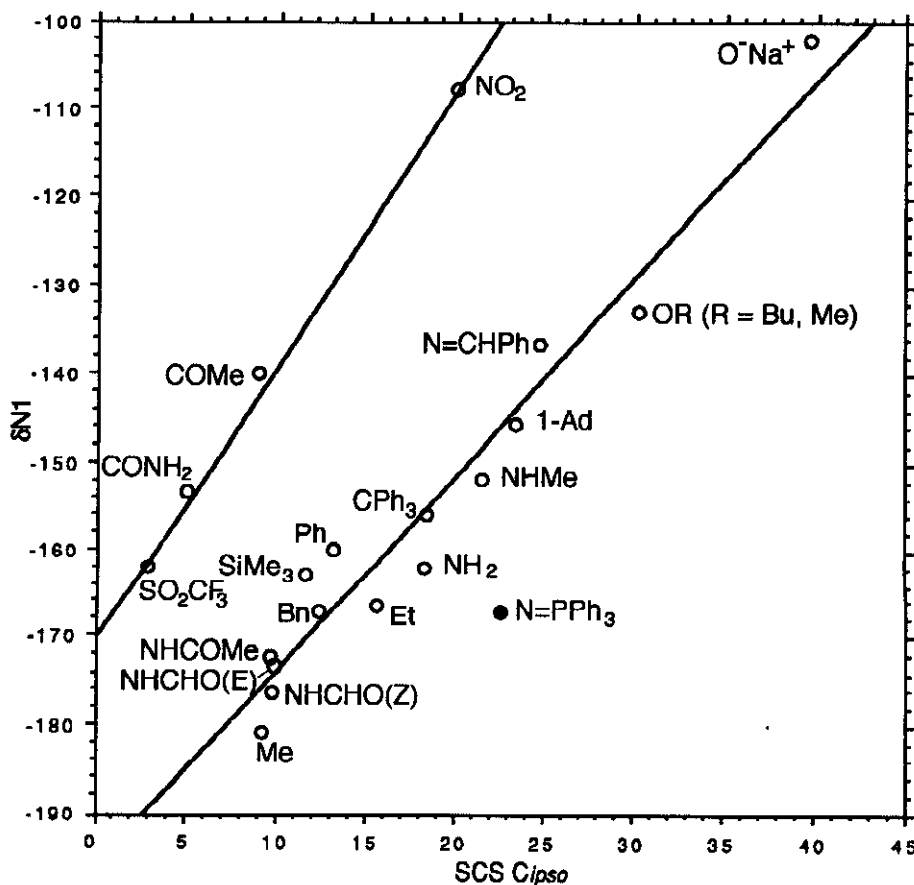
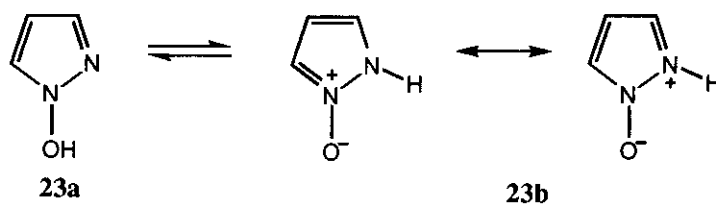


Figure 2

Although we have no explanation, we wish to point out that a plot of $^3J_{35}$ vs the ratio J_{45}/J_{34} also shows two sets of *N*-substituents, one formed by NO_2 , COMe , CONH_2 and SO_2CF_3 , and the other formed by the remaining compounds.

The case of pyrazole *N*-oxide **23**.

We haven't used the data of pyrazole *N*-oxide **23** in the correlation analysis since Begtrup and Vedsø found that this compound exists in solution as a mixture of two tautomers, the *N*-hydroxide (**23a**) and the *N*-oxide (**23b**).¹¹ According to theoretical calculations (MP2-6-31G**), in the case of the isolated molecule (formally corresponding to the gas phase), the 1-hydroxy tautomer (**23a**) ($E = -300.511$ Hartrees) is more stable than the *N*-oxide (**23b**) ($E = -300.495$ Hartrees) by 10 kcal mol⁻¹ (1 Hartree = 627.51 kcal mol⁻¹).¹⁶



According to Begtrup and Vedsø, who use ^1H - ^{13}C coupling constants as the most reliable NMR parameter for interpolation, the percentage of *N*-OH form (**23a**) is 79% in benzene- d_6 , 82% in CDCl_3 , 98% in acetone- d_6 .¹¹ The presence of significant amounts of *N*-oxide (**23b**) in solution must be due to the large difference in dipole moments (**23a**, $\mu = 0.08$ D, **23b**, $\mu = 3.82$ D).¹⁶

Since the ^1H and ^{13}C NMR spectroscopic data have already been discussed,¹¹ we will only comment the two ^{15}N signals which have been obtained in CDCl_3 . Assuming that the *N*-benzyloxy derivative (**18**) is a good model for the OH tautomer (this corresponds to neglecting the effects of the benzyl group on the ^{15}N chemical shifts through two and three bonds), then to the 18% of tautomer (**23b**) present in this solvent¹¹ should correspond $\delta\text{N1 (N-O)} = -194.6$ ppm and $\delta\text{N2 (N-H)} = -184.1$ ppm. The similarity of chemical shifts may reflect the delocalization of the positive charge between both nitrogen atoms.

CONCLUSIONS

i) How substituent effects are transmitted through the nitrogen? We have previously shown that angular deformations which affect the endocyclic angles in pyrazoles (N1) and in benzenes (C_{ipso}) are linearly related, excepting the OH substituent, for different X groups from BH_2 to NO_2 (13 substituents).¹⁶ Figure 2 shows a similar representation but using chemical shifts instead of bond angles. The OH substituent (**23a**) is not present for the reasons discussed above, but the OR behaves normally. The powerful electron-withdrawing substituents behave differently in benzenes and in 1-substituted pyrazoles with regard to other substituents. It is difficult to establish which is the "normal" equation, but since the intercepts of Equations (5) and (7) are -169.5 ± 1.4 and -196 ± 3 (which corresponds to SCS $C_{ipso} = 0$, that is $\text{X} = \text{H}$) and the δN1 for pyrazole itself (in THF at low temperature to slow down the prototropy) is -168.2 ppm,¹⁷ it appears that substituents SO_2CF_3 , CONH_2 , COCH_3 and NO_2 behave "normally" while the remaining ones produce on N1 smaller effects than in C_{ipso} (the *P,P,P*-triphenylphosphazene- λ^5 -azanyl derivative (**16**) having this anomaly exalted). Not taking into account the difference in slope, i.e. assuming that both lines of Figure 2 are parallel, the gap between both series of compounds is 36 ppm (slope 2.35). As pointed out by Bird, ^{15}N chemical shifts are useless as aromaticity criteria.⁹

ii) How the aromaticity of pyrazole ring is affected by *N*-substituents? In the already mentioned paper dealing with geometric changes in pyrazoles,¹⁶ we have proposed an aromaticity criterion based on bond distances: the more aromatic a pyrazole, the more alike should be the pairs of CC (C3C4 and C4C5) and CN (N2C3 and C5N1) bond lengths. According to this definition, the aromaticity of a *N*-X pyrazole increases in the order (the peculiar nature of X is due to simplifications required by the high-level calculations): $\text{BH}_2 < \text{CHO} < \text{AlH}_2 < \text{NO}_2 < \text{SO}_2\text{H} < \text{CF}_3 < \text{SiH}_3 < \text{PH}_2 < \text{H} < \text{CH}_3 < \text{NH}_2 < \text{BH}_3^- < \text{OH}$.

Amongst the criteria of aromaticity, Sternhell *et al.* proposed to use *ortho* benzylic coupling constants as a measure of relative "degree of aromaticity".¹⁴ If instead of these $^4\text{J}(\text{H}^1\text{H})$ couplings, we use the $^3\text{J}_{45}/^3\text{J}_{34}$ ratio of Table 1 and if we assume that the largest is the value, the less aromatic the pyrazole should be, then, the order of increasing aromaticity is: $\text{COCH}_3 < \text{SO}_2\text{CF}_3 < \text{NO}_2 < \text{CONH}_2 < \text{Si}(\text{CH}_3)_3 = \text{PPh}_3 < \text{NHCHO(Z)} < \text{Ph} < \text{Ad} = [\text{HBPz}_2]^- < \text{NHCHO(E)} < \text{Bn} < \text{N=CHPh} < \text{P}[\text{N}(\text{CH}_3)_2]_2 < \text{C}_2\text{H}_5 = \text{CH}_3 < \text{NHCOCH}_3 < \text{NHCH}_3 < \text{NH}_2 < \text{OCH}_2\text{Ph} < \text{N=PPh}_3 < \text{O}^- \text{Na}^+$. Note that the four less aromatic deriva-

tives (COCH_3 , SO_2CF_3 , NO_2 , CONH_2) are those that appear as different in Figure 2. It is difficult to compare both classifications owing to some differences but if we consider that BH_3^- is quite different from $[\text{HBPz}_2]^-$, then there is a good agreement: CHO (COCH_3) $\approx$ NO_2 $<$ SiH_3 [$\text{Si}(\text{CH}_3)_3$] $<$ PH_2 [$\text{P}(\text{N}(\text{CH}_3)_2)_2$] $<$ CH_3 $<$ NH_2 $<$ OH (OCH_2Ph). This gives confidence as to propose a combination of both classifications as an answer to question ii: with regard to pyrazole itself ($\text{X} = \text{H}$) the pyrazolate *N*-oxide (19) is more aromatic while the trifluoromethanesulfonyl derivative (22) has a large dienic character.

iii) Since these LFER-CAOC (Linear Free Energy Relationships-Correlation Analysis in Chemistry)² are not entirely satisfactory we intend to carry out *ab initio* calculations of the chemical shifts (columns 1-3, 7-9 and 13,14) to approach the above problems with a different perspective.

EXPERIMENTAL

Melting points were determined with a hot-stage microscope and are uncorrected.

N-Pyrazolyl-*P,P,P*-triphenylphospha- λ^5 -azene (16). To a solution of 1.66 g (0.020 mol) of 1-aminopyrazole in 60 mL of dry acetonitrile, 5.56 g (0.024 mol) of triphenylphosphine, 4.04 g (0.040 mol) of triethylamine and 4.74 g (0.020 mol) of hexachloroethane were added. The reaction mixture was stirred at rt under nitrogen for 24 h. The solvent was removed under reduced pressure. The reaction crude was washed first with cold water to eliminate the triethylamine hydrochloride and then with cold hexane (2 x 15 mL). The residue is dried and recrystallized (benzene/hexane, both anhydrous). Yield: 5.84 g (85%), mp 113-115 °C.

Sodium 1-hydroxypyrazolate (19). To a solution of 1 g (0.012 mol) of 1-hydroxypyrazole¹⁸ in 20 mL of anhydrous THF, 0.48 g (0.012 mol) of NaH (60% oil dispersion) were added in little portions. The reaction mixture was heated to 65 °C for 1 h under nitrogen. The product is filtered and collected as a white solid. Yield: 1.25 g (98%), mp $>$ 300 °C.

1-Trifluoromethanesulfonylpyrazole (22). To a cold solution of 2.04 g (0.030 mol) of pyrazole in 30 mL of anhydrous dichloromethane, a solution of 2.90 g (0.010 mol) of trifluoromethanesulfonic anhydride in 5 mL of dry ether was added, with external cooling, in little portions. The reaction mixture was stirred for 18 h at -16 °C. The crude is filtered at rt and then the solvents removed under vacuum. Distillation at 60 °C (0.5 mm) yields 1-trifluoromethanesulfonylpyrazole as a colorless compound. Yield: 2.0 g (50%), mp 17 °C.

[¹⁵N₂] *1-Benzylpyrazole* (5). To a solution of 0.107 g (1.57 mmol) of [¹⁵N₂]pyrazole¹⁹ in 2 mL of CH₃CN and 0.5 mL of 20% NaOH in H₂O were added 0.271 g (1.58 mmol) of benzyl bromide. The reaction mixture was stirred for 24 h at rt. The mixture was extracted with chloroform (3 x 5 mL) and evaporated to dryness. The resulting solid residue (0.353 g) was purified by column chromatography (silica gel, eluent: CHCl₃) yielding 0.20 g (80%) of the compound (5).

[¹⁵N₂] *1-Hydroxypyrazole* (23). The compound was prepared according to Begtrup and Vedsø¹⁸ starting from a solution of 0.50 g (0.007 mol) of [¹⁵N₂]pyrazole¹⁹ in 30 mL of ethyl acetate and 1.73 g (0.007

mol) of *m*-chloroperbenzoic acid (70%). Then following the reported procedure, unchanged [$^{15}\text{N}_2$]-pyrazole was recovered (0.18 g, 36%) and the desired compound (**23**, 0.308 g) was obtained in 50% yield. Crystallization from heptane-ethyl acetate provides a white solid, mp 70 °C (lit.,¹⁸ mp 72 °C). The corresponding [$^{15}\text{N}_2$]-(**19**) sodium salt was prepared like the unlabelled compound (see above).

NMR Spectroscopy

The ^1H , ^{13}C and ^{15}N NMR spectra were recorded at 200.13, 50.32 and 20.3 MHz on a Bruker AC-200 instrument. Most assignments have been established through 2D (^1H - ^{13}C) experiments. The study of compound (**5**) was carried out using a Varian Unity 500 (^1H at 499.88 MHz, ^{15}N at 50.67 MHz). The experimental conditions have been described elsewhere.²⁰

For the ^{15}N NMR spectra the samples were dissolved in DMSO- d_6 or CDCl_3 (see Table 1); the concentration was 10-25 (w/v) and the internal diameter of the tube 10 mm. Nitromethane was used as external standard, no corrections for bulk differences were applied. Typical conditions were as follows: 90° pulse angle; spectral width 15.5 kHz; data points 32 K; pulse repetition time 60 s for compounds (**14**) and (**15**) and 30 s for (**22**). The sequence used was INVGATE for the NOE suppression. The chemical shifts of compounds (**3**, **8**, **9**, **14**, **16**, **18**, **20** and **22**) were determined with the aid of the polarization-transfer pulse sequence INEPT.²¹ The width of a nitrogen 90° pulse was 19 μs and the width of a proton 90° pulse was 14 μs . The delay time between the pulses was 0.021-0.042 ms which corresponds to a J value of 12-6 Hz (0.25/JNH).²² The values given in Table 1 will not be reported (all coupling constants are in Hz).

1. Tris(pyrazol-1-yl) borate. ^1H NMR.²³

2. 1-Methylpyrazole. ^1H NMR.¹³

3. 1-Ethylpyrazole. ^{13}C NMR (CDCl_3), (C3, $^3J = 8.3$, $^2J = 5.7$), (C4, $^2J = 10.5$, $^2J = 8.6$), (C5, $^2J = 11.3$, $^3J = 4.8$, $^3J(\text{CH}_2) = 2.4$), 15.1 (CH_3 , $^1J = 127.8$, $^2J = 3.4$), 46.3 (CH_2 , $^1J = 139.2$, $^2J = 4.4$).

4. 1-(1-Adamantyl)pyrazole. ^1H NMR (CDCl_3), 1.77 and 2.19 (adamantyl).

5. 1-Benzylpyrazole. Iterative analysis of the complete ^1H - ^{15}N spin system of [$^{15}\text{N}_2$]-1-benzylpyrazole (**5**) *N*- CH_2 decoupled. To get a set of accurate values of the ^1H - ^1H and ^1H - ^{15}N coupling constants, the ^1H and ^{15}N NMR five-spins spectra of compound (**5**) in acetone- d_6 was analyzed after decoupling the CH_2 protons. The values obtained (RMS error = 0.061 Hz) are reported in Table 3 together with the first-order analysis (Table 4 and reference 17), and with the recent determined coupling constant (absolute sign) of [$^{15}\text{N}_2$]₃-labelled tris(pyrazol-1-yl)methane (**24**).²⁴ It appears that first order coupling constants are a reasonable approximation and that coupling constants in compounds (**5**) and (**24**) are quite similar.

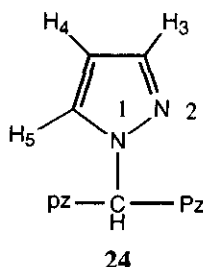
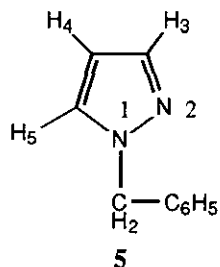


Table 3. ^1H and ^{15}N NMR parameters of $^{15}\text{N}_2$ -1-benzylpyrazole (**5**) and tris(pyrazol-1-yl)methane (**24**) (chemical shifts in ppm and coupling constants in Hz)

	First-order analysis in CDCl_3 (see Table 4)	Iterative analysis in acetone- d_6	Data for (24) in CDCl_3 ^a
δN1	-169.9	-167.83	-169.5
δN2	-76.9	-70.86	-76.8
δH3	7.56	7.648	7.65
δH4	6.28	6.239	6.35
δH5	7.38	7.427	7.55
δCH_2	5.32	-----	8.45 ^a
$1\text{J}(\text{N1-N2})$	12.7	12.95	-13.0
$3\text{J}(\text{N1H3})$	8.29	8.37	8.8
$3\text{J}(\text{N1H4})$	5.77	5.70	6.2
$2\text{J}(\text{N1H5})$	4.66	4.59	4.5
$2\text{J}(\text{N1CH}_2)$	1.67	-----	-1.2 ^a
$2\text{J}(\text{N2H3})$	12.59	12.71	13.0
$2\text{J}(\text{N2H4})$	1.13	1.07	1.2
$3\text{J}(\text{N2H5})$	0.00	0.00	-0.1 ^a
$3\text{J}(\text{N2CH}_2)$	1.67	-----	1.4 ^a
$3\text{J}(\text{H3H4})$	1.88	1.82	1.6
$3\text{J}(\text{H4H5})$	2.30	2.29	2.5
$4\text{J}(\text{H3H5})$	0.69	0.70	-----
$4\text{J}(\text{H5CH}_2)$	<1.0	-----	-----

^a Corresponds to a CH group.Table 4. NMR parameters for $^{15}\text{N}_2$ -1-benzylpyrazole (**5**) in four solvents (chemical shifts in ppm and coupling constants in Hz)

Solvent:	C_6D_6	CDCl_3	Acetone- d_6	DMSO- d_6
^1H NMR				
H3	7.59 $3\text{J}(\text{H3H4})=1.86$ $4\text{J}(\text{H3H5})=0.70$ $3\text{J}(\text{H3N1})=8.44$ $2\text{J}(\text{H3N2})=12.69$	7.56 $3\text{J}(\text{H3H4})=1.88$ $4\text{J}(\text{H3H5})=0.69$ $3\text{J}(\text{H3N1})=8.29$ $2\text{J}(\text{H3N2})=12.59$	7.44 $3\text{J}(\text{H3H4})=1.84$ $4\text{J}(\text{H3H5})=0.71$ $3\text{J}(\text{H3N1})=8.39$ $2\text{J}(\text{H3N2})=12.74$	7.46 $3\text{J}(\text{H3H4})=1.84$ $4\text{J}(\text{H3H5})=0.74$ $3\text{J}(\text{H3N1})=8.36$ $2\text{J}(\text{H3N2})=12.72$
H4	6.06 $3\text{J}(\text{H4H5})=2.29$ $3\text{J}(\text{H4N1})=5.77$ $3\text{J}(\text{H4N2})=1.13$	6.28 $3\text{J}(\text{H4H5})=2.30$ $3\text{J}(\text{H4N1})=5.77$ $3\text{J}(\text{H4N2})=1.13$	6.25 $3\text{J}(\text{H4H5})=2.29$ $3\text{J}(\text{H4N1})=5.82$ $3\text{J}(\text{H4N2})=1.05$	6.26 $3\text{J}(\text{H4H5})=2.26$ $3\text{J}(\text{H4N1})=5.84$ $3\text{J}(\text{H4N2})=1.08$
H5	6.83 $2\text{J}(\text{H5N1})=4.60$	7.38 $2\text{J}(\text{H5N1})=4.66$	7.66 $2\text{J}(\text{H5N1})=4.64$	7.81 $2\text{J}(\text{H5N1})=4.65$
CH_2	4.85 $2\text{J}(\text{CH}_2\text{N1})=1.95$ $3\text{J}(\text{CH}_2\text{N2})=1.95$	5.32 $2\text{J}(\text{CH}_2\text{N1})=1.67$ $3\text{J}(\text{CH}_2\text{N2})=1.67$	5.35 $2\text{J}(\text{CH}_2\text{N1})=2.0$ $3\text{J}(\text{CH}_2\text{N2})=2.0$	5.33 $2\text{J}(\text{CH}_2\text{N1})=2.0$ $3\text{J}(\text{CH}_2\text{N2})=2.0$

^{13}C NMR

C3	139.5 $^1\text{J}(\text{C3H3})=184.3$ $^2\text{J}(\text{C3H4})=5.6$ $^3\text{J}(\text{C3H5})=8.3$	139.4 $^1\text{J}(\text{C3H3})=184.8$ $^2\text{J}(\text{C3H4})=5.7$ $^3\text{J}(\text{C3H5})=8.3$	139.6 $^1\text{J}(\text{C3H3})=184.1$ $^2\text{J}(\text{C3H4})=5.8$ $^3\text{J}(\text{C3H5})=8.3$	138.9 $^1\text{J}(\text{C3H3})=184.1$ $^2\text{J}(\text{C3H4})=5.9$ $^3\text{J}(\text{C3H5})=8.3$
C4	106.0 $^2\text{J}(\text{N2C4})=1.9$ $^2\text{J}(\text{N1C4})=5.6$ $^1\text{J}(\text{C4H4})=175.5$ $^2\text{J}(\text{C4H3})=10.6$ $^2\text{J}(\text{C4H5})=8.7$	105.8 $^2\text{J}(\text{N2C4})=1.9$ $^2\text{J}(\text{N1C4})=5.5$ $^1\text{J}(\text{C4H4})=176.5$ $^2\text{J}(\text{C4H3})=10.4$ $^2\text{J}(\text{C4H5})=8.6$	106.2 $^2\text{J}(\text{N2C4})=2.0$ $^2\text{J}(\text{N1C4})=5.6$ $^1\text{J}(\text{C4H4})=175.8$ $^2\text{J}(\text{C4H3})=10.5$ $^2\text{J}(\text{C4H5})=8.9$	105.4 $^2\text{J}(\text{N2C4})=2.0$ $^2\text{J}(\text{N1C4})=5.5$ $^1\text{J}(\text{C4H4})=175.9$ $^2\text{J}(\text{C4H3})=10.3$ $^2\text{J}(\text{C4H5})=9.2$
C5	-----	129.1 $^1\text{J}(\text{C5N1})=12.8$ $^1\text{J}(\text{C5H5})=185.8$ $^2\text{J}(\text{C5H4})=8.8$ $^3\text{J}(\text{C5H3})=4.6$ $^3\text{J}(\text{C5CH}_2)=2.8$	130.1 $^1\text{J}(\text{C5N1})=12.3$ $^1\text{J}(\text{C5H5})=186.5$ $^2\text{J}(\text{C5H4})=8.9$ $^3\text{J}(\text{C5H3})=4.6$ $^3\text{J}(\text{C5CH}_2)=2.8$	130.1 $^1\text{J}(\text{C5N1})=12.2$ $^1\text{J}(\text{C5H5})=187.7$ $^2\text{J}(\text{C5H4})=8.9$ $^3\text{J}(\text{C5H3})=4.6$ $^3\text{J}(\text{C5CH}_2)=2.8$
CH ₂	55.7 $^1\text{J}(\text{CH}_2\text{N1})=13.5$ $^2\text{J}(\text{CH}_2\text{N2})=6.0$ $^1\text{J}(\text{CH})=139.2$ $^3\text{J}(\text{CH}_{\text{ortho}})=4.1$	55.8 $^1\text{J}(\text{CH}_2\text{N1})=13.3$ $^2\text{J}(\text{CH}_2\text{N2})=5.8$ $^1\text{J}(\text{CH})=139.5$ $^3\text{J}(\text{CH}_{\text{ortho}})=4.2$	55.9 $^1\text{J}(\text{CH}_2\text{N1})=13.4$ $^2\text{J}(\text{CH}_2\text{N2})=5.7$ $^1\text{J}(\text{CH})=139.6$ $^3\text{J}(\text{CH}_{\text{ortho}})=4.0$	54.6 $^1\text{J}(\text{CH}_2\text{N1})=13.0$ $^2\text{J}(\text{CH}_2\text{N2})=5.6$ $^1\text{J}(\text{CH})=139.8$ $^3\text{J}(\text{CH}_{\text{ortho}})=4.2$
C _{ipso}	137.6	136.6	138.7	137.7
C _{ortho}	-----	127.5 $^1\text{J}=158.5$	128.3 $^1\text{J}=161.7$	127.4 $^1\text{J}=160.7$
C _{meta}	-----	128.7 $^1\text{J}=161.2$	129.3 $^1\text{J}=160.6$	128.4 $^1\text{J}=160.6$
C _{para}	-----	127.9 $^1\text{J}=160.6$	128.3 $^1\text{J}=161.7$	127.5 $^1\text{J}=160.7$

 ^{15}N NMR

N1	-169.7 $^1\text{J}(\text{N1N2})=12.8$	-169.9 $^1\text{J}(\text{N1N2})=12.7$	-167.8 $^1\text{J}(\text{N1N2})=13.0$	-167.3 $^1\text{J}(\text{N1N2})=12.9$
N2	-70.7	-76.9	-71.1	-72.9

A study of solvent effects on NMR parameters has been carried out on this compound (first order analyses). The results, reported on Table 4 illustrates the sensitivity of δH5 to solvent effects.

6. 1-Tritylpyrazole. ^1H NMR (this work and ref. 25).

7. 1-Phenylpyrazole. ^1H NMR.¹³

8. 1-Acetylpyrazole. ^1H NMR (this work).

9. Pyrazole-1-carboxamide. ^1H NMR (CDCl_3), 5.5 and 7.1 (NH_2); ^1H NMR ($\text{DMSO}-d_6$), 7.73 (H3), 6.48 (H4), 8.25 (H5), 7.80 and 7.85 (NH_2), $J_{45} = 2.7$, $J_{34} = 1.6$, $J_{35} = 0.7$. ^{15}N NMR ($\text{DMSO}-d_6$) -295.8 (NH_2 , $^1\text{J} = 91.0$).

10. 1-Aminopyrazole. ^1H NMR (CDCl_3), 5.37 (NH_2); ^1H NMR ($\text{DMSO}-d_6$), 7.25 (H3), 6.10 (H4), 7.46 (H5), 6.37 (NH_2), $J_{45} = 2.2$, $J_{34} = 2.1$, $J_{35} = 1.0$. ^{13}C NMR (CDCl_3), (C3, $^3J = 8.7$, $^2J = 5.0$), (C4, $^2J = 9.0$, $^2J = 9.0$), (C5, $^2J = 8.6$, $^3J = 3.9$).
11. 1-Methylaminopyrazole. ^1H NMR.²⁶
12. 1-Formylaminopyrazole (E). ^1H NMR.²⁶
13. 1-Formylaminopyrazole (Z). ^1H NMR.²⁶
14. 1-Acetylaminopyrazole (Z). ^1H NMR (CDCl_3), 2.06 (CH_3), 10.61 (NH). There is 27% of E isomer: 7.52 (H3), 6.31 (H4), 7.52 (H5), 1.77 (CH_3), 9.4 (NH); ($\text{DMSO}-d_6$), 7.43 (H3), 6.29 (H4), 7.66 (H5), 1.98 (CH_3), 11.56 (NH), $J_{45} = 2.4$, $J_{34} = 2.1$, $J_{35} = 0.8$. There is 11% of isomer E: 7.53 (H3), 6.37 (H4), 7.87 (H5), 1.58 (CH_3), 11.0 (NH). ^{13}C NMR ($\text{DMSO}-d_6$), Z isomer, (C3, $^3J = 8.8$, $^2J = 5.3$), (C4, $^2J = 9.1$, $^2J = 9.1$), (C5, $^2J = 9.1$, $^3J = 3.9$), 169.1 (CO), 20.6 (CH_3 , $^1J = 128.7$). ^{13}C NMR ($\text{DMSO}-d_6$), E isomer, 138.6 (C3, $^1J = 187.5$), 106.0 (C4, $^1J = 178.2$), 131.3 (C5, $^1J = 193.4$), 173.6 (CO), 18.9 (CH_3 , $^1J = 128.9$). ^{15}N NMR ($\text{DMSO}-d_6$), Z isomer -232.9 (NH). ^{15}N NMR ($\text{DMSO}-d_6$), E isomer, -170.8 (N1), -70.4 (N2), -230.3 (NH).
15. 1-Benzylideneaminopyrazole. ^1H NMR (CDCl_3).²⁶ ^1H NMR ($\text{DMSO}-d_6$), 9.21 (CH), 7.87-7.93 (H_0), 7.48-7.55 (H_m , H_p), $^6J_{\text{H}_3\text{CH}} = 0.6$. ^{13}C NMR ($\text{DMSO}-d_6$), (C3, $^3J = 9.0$, $^2J = 5.4$), (C4, $^2J = 9.6$, $^2J = 8.7$), (C5, $^2J = 9.1$, $^3J = 3.8$), 150.0 (CH, $^1J = 167.9$, $^3J = 4.7$), 132.8 (C_{ipso}), 129.0 (C_{ortho}), 128.2 (C_{meta}), 131.3 (C_{para}). ^{15}N NMR ($\text{DMSO}-d_6$) -95.0 (-N=).
16. *N*-Pyrazolyl-*P,P,P*-triphenylphospha- λ^5 -azene. ^1H NMR (CDCl_3), 7.40-7.80 (m, C_6H_5), $J_{\text{H}_5\text{P}} = 1.1$, $J_{\text{H}_3\text{P}} = 1.1$, $J_{\text{H}_4\text{P}} = 0.5$. ^{13}C NMR (CDCl_3), (C3, $^3J = 9.1$, $^2J = 4.9$), (C4, $^2J = 9.2$, $^2J = 9.2$), (C5, $^2J = 8.7$, $^3J = 4.1$, $^3J_{\text{P}} = 8.7$), 128.0 (C_{ipso} , $^1J_{\text{P}} = 96.6$), 132.7 (C_{ortho} , $^2J_{\text{P}} = 9.2$), 128.2 (C_{meta} , $^3J_{\text{P}} = 11.9$), 131.9 (C_{para} , $^4J_{\text{P}} = 2.7$). ^{15}N NMR (CDCl_3) -147.1 (-N=P).
17. 1-Nitropyrzazole. ^1H NMR.¹³
18. 1-Benzoyloxypyrzazole. ^1H NMR (CDCl_3), 7.28 (H3), 6.04 (H4), 6.98 (H5), 5.28 (CH_2), 7.29-7.38 (m, C_6H_5), $J_{45} = 2.35$, $J_{34} = 2.25$, $J_{35} = 1.02$; ^1H NMR ($\text{DMSO}-d_6$), 5.26 (CH_2), 7.37 (s, C_6H_5). ^{13}C NMR (CDCl_3), (C3, $^3J = 9.0$, $^2J = 4.5$), (C4, $^2J = 9.4$, $^2J = 8.0$), (C5, $^2J = 9.1$, $^3J = 3.7$), 80.2 (CH_2 , $^1J = 148.2$), 133.7 (C_{ipso}), 129.4 (C_{ortho}), 128.4 (C_{meta}), 128.9 (C_{para}).
19. Sodium 1-hydroxypyrzolate. ^{13}C NMR ($\text{DMSO}-d_6$), 126.1 (C3, $^1J = 181.3$ Hz, $^3J = 8.6$ Hz, $^2J = 4.5$ Hz), 99.3 (C4, $^1J = 172.1$ Hz, $^2J = 9.3$ Hz, $^2J = 9.3$ Hz), 117.2 (C5, $^1J = 186.0$ Hz, $^2J = 8.8$ Hz, $^3J = 3.6$ Hz). ^{15}N NMR ($\text{DMSO}-d_6$), -101.9 (N1), -91.8 (N2). Sodium [$^{15}\text{N}_2$] 1-hydroxypyrzolate. ^1H NMR ($\text{DMSO}-d_6$), 6.58 (H3), 5.70 (H4), 6.74 (H5), $J_{45} = 1.69$, $J_{34} = 2.49$, $J_{35} = 1.21$, $J_{\text{H}_3\text{N}_1} = 8.0$, $J_{\text{H}_3\text{N}_2} = 11.9$, $J_{\text{H}_4\text{N}_1} = 6.2$, $J_{\text{H}_4\text{N}_2} = 0.7$, $\Sigma(J_{\text{H}_5\text{N}_1} + J_{\text{H}_5\text{N}_2}) = 2.4$. ^{13}C NMR ($\text{DMSO}-d_6$), 125.7 (C3), 99.0 (C4, $^2J_{\text{C}_4\text{N}_1} = 6.5$), 116.8 (C5, $^1J_{\text{C}_5\text{N}_1} = 16.9$). ^{15}N NMR ($\text{DMSO}-d_6$), -100.4 (N1), -89.8 (N2, $^1J_{\text{N}_1\text{N}_2} = 12.5$).
20. 1-Trimethylsilylpyrazole. ^1H NMR (CDCl_3), 0.46 (CH_3). ^{13}C NMR (CDCl_3), (C3, $^3J = 7.2$, $^2J = 7.2$), (C4, $^2J = 11.4$, $^2J = 9.3$), (C5, $^2J = 8.9$, $^3J = 5.2$), -1.1 (CH_3 , $^1J = 120.2$, $^3J = 1.3$).
21. 1-Bis(dimethylamino)phosphinylpyrazole. ^1H NMR.¹³
22. 1-Trifluoromethanesulfonylpyrazole. ^{13}C NMR (CDCl_3), (C3, $^3J = 9.1$, $^2J = 5.9$), (C4, $^2J = 10.7$, $^2J = 8.4$), (C5, $^2J = 9.9$, $^3J = 4.3$), 118.8 (CF_3 , $^1J_{\text{CF}} = 322.9$).

23.1-Hydroxypyrazole. ^1H NMR (CDCl_3), 7.15 (H3), 6.17 (H4), 7.35 (H5), $J_{45} = 2.3$, $J_{34} = 2.5$, $J_{35} = 1.1$ ($J_{45}/J_{34} = 0.92$); ^1H NMR ($\text{DMSO}-d_6$), 7.13 (H3), 6.16 (H4), 7.55 (H5), 12.23 (OH), $J_{45} = 2.2$, $J_{34} = 2.3$, $J_{35} = 1.1$. ^{13}C NMR (CDCl_3), 131.5 (C3, $1J = 189.2$, $3J = 8.6$, $2J = 4.8$), 103.3 (C4, $1J = 179.7$, $2J = 8.2$, $2J = 8.2$), 122.8 (C5, $1J = 193.2$, $2J = 8.7$, $3J = 4.1$). ^{13}C NMR ($\text{DMSO}-d_6$), 131.9 (C3, $1J = 187.2$, $3J = 9.0$, $2J = 4.6$), 103.3 (C4, $1J = 177.2$, $2J = 8.8$, $2J = 8.8$), 122.6 (C5, $1J = 192.5$, $2J = 9.2$, $3J = 3.8$). ^{15}N NMR (CDCl_3), -144.0 (N1), -107.6 (N2). [$^{15}\text{N}_2$] 1-Hydroxypyrazole. ^1H NMR (CDCl_3), 7.15 (H3), 6.17 (H4), 7.34 (H5), 10.55 (OH), $J_{45} = 2.32$, $J_{34} = 2.55$, $J_{35} = 1.06$ ($J_{45}/J_{34} = 0.91$), $J_{\text{H3N1}} = 9.1$, $J_{\text{H3N2}} = 11.7$, $J_{\text{H4N1}} = 7.4$, $J_{\text{H4N2}} = 1.3$, $J_{\text{H5N1}} = 2.35$; ^1H NMR ($\text{DMSO}-d_6$), 7.13 (H3), 6.16 (H4), 7.54 (H5), 12.23 (OH), $J_{45} = 2.35$, $J_{34} = 2.30$, $J_{35} = 1.07$, $J_{\text{H3N1}} = 10.0$, $J_{\text{H3N2}} = 12.9$, $J_{\text{H4N1}} = 7.5$, $J_{\text{H4N2}} = 0.8$, $J_{\text{H5N1}} = 2.35$. ^{13}C NMR (CDCl_3), 131.6 (C3, $1J_{\text{N2}} = 3.8$, $2J_{\text{N1}} = 1.1$), 103.3 (C4, $2J_{\text{N1}} = 7.1$, $2J_{\text{N2}} = 1.3$), 122.6 (C5, $1J_{\text{N1}} = 17.6$).

Formanilide. E Isomer (minor): ^{13}C NMR ($\text{DMSO}-d_6$), 162.6 (CHO, $1J = 193.6$, $2J = 1.7$), 138.4 (C_{ipso}), 117.7 (C_{ortho} , $1J = 164.9$), 129.4 (C_{meta} , $1J = 160.9$, $3J = 7.8$), 123.8 (C_{para} , $1J = 162.4$, $3J = 3J = 7.3$); Z isomer (major): ^{13}C NMR ($\text{DMSO}-d_6$), 159.7 (CHO, $1J = 195.9$, $2J = 2.4$), 138.4 (C_{ipso}), 119.4 (C_{ortho} , $1J = 164.9$), 128.9 (C_{meta} , $1J = 161.5$, $3J = 8.2$), 123.7 (C_{para} , $1J = 161.8$, $3J = 3J = 7.6$).

ACKNOWLEDGMENTS

This work was supported by the DGICYT of Spain (Project numbers PB93-0125 and PB93-0197-C01/C02). Professor Mikael Begtrup (Department of Medicinal Chemistry, Royal Danish School of Pharmacy, DK-2100 Copenhagen, Denmark) generous gift of 1-benzyloxypyrazole **18** is greatly acknowledged. One of us (J.A.J.) is greatly indebted to the Ministry of Education of Spain for an FPI grant.

REFERENCES AND NOTES

1. A preliminary communication of this work has appeared: J. Elguero, R. M. Claramunt, C. López, and D. Sanz, *Afinidad*, 1993, **50**, 383.
2. L. P. Hammett, "Physical Organic Chemistry", McGraw-Hill, New York, 1940; N. B. Chapman and J. Shorter, "Advances in Linear Free Energy Relationships", Plenum Press, London, 1972; N. B. Chapman and J. Shorter, "Correlation Analysis in Chemistry", Plenum Press, New York, 1978; C. Hansch, A. Leo, and R. W. Taft, *Chem. Rev.*, 1991, **91**, 165; C. Hansch, A. Leo, and D. Hoekman, "Exploring QSAR, Hydrophobic, Electronic and Steric Constants", ACS Professional Reference Book, American Chemical Society, Washington DC, 1995.
3. M. Decouzon, O. Exner, J.-F. Gal, and P.-C. Maria, *J. Phys. Org. Chem.*, 1994, **7**, 615.
4. J. Elguero, M. Gil, N. Iza, C. Pardo, and M. Ramos, *Appl. Spectrosc.*, 1995, **49**, 1111.
5. P. Friedman and K. F. Ferris, *Int. J. Quantum Chem.*, 1990, **24**, 843.
6. A. R. Katritzky, P. Barczynski, G. Musumarra, D. Pisano, and M. Szafran, *J. Am. Chem. Soc.*, 1989, **111**, 7.

7. A. R. Katritzky, V. Feygelman, G. Musumarra, P. Barczynski, and M. Szafran, *J. Prakt. Chem.*, 1990, **332**, 870.
8. L. Caruso, G. Musumarra, and A. R. Katritzky, *Quant. Struct.-Act. Relat.*, 1993, **12**, 146.
9. C. W. Bird, *Tetrahedron*, 1985, **41**, 1409; C. W. Bird, *Tetrahedron*, 1992, **48**, 335; C. W. Bird, *Tetrahedron*, 1996, **52**, 9945; C. W. Bird, *Tetrahedron*, 1997, **53**, 3319.
10. S. Clementi, G. Cruciani, P. Fifi, D. Riganelli, R. Valigi, and G. Musumarra, *Quant. Struct.-Act. Relat.*, 1996, **15**, 108.
11. M. Begtrup and P. Vedsø, *Acta Chem. Scand.*, submitted (personal communication).
12. J. Elguero, J.-L. Imbach, and R. Jacquier, *J. Chim. Phys.*, 1965, **62**, 643; J. Elguero, R. Jacquier, and H. C. N. Tien Duc, *Bull. Soc. Chim. Fr.*, 1966, 3727; J. Elguero and R. Jacquier, *J. Chim. Phys.*, 1966, **63**, 1242;
13. J. Elguero, 'Pyrazoles and their Benzo Derivatives' in *Comprehensive Heterocyclic Chemistry*, ed. by A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, Vol. 5, pp. 167-303.
14. J. E. Gready, P. M. Hatton, and S. Sternhell, *J. Heterocycl. Chem.*, 1992, **29**, 935.
15. D. F. Ewing, *Org. Magn. Res.*, 1979, **12**, 499; S. Chalais, A. Cornélis, A. Gersttmans, W. Kolodziejewski, P. Laszlo, A. Mathy, and P. Métra, *Helv. Chim. Acta*, 1985, **68**, 1196; J. Elguero, R. M. Claramunt, R. Garcerán, S. Julià, L. Avila, and J. M. del Mazo, *Magn. Res. Chem.*, 1987, **25**, 260; H. Fritz and C. D. Weis *J. Org. Chem.*, 1978, **43**, 4900; V. Bzhezovskii, L. M. Yagupol'skii, S. V. Iksanova, N. V. Kondratenko, A. Aliev, A. A. Kudryavtsev, and R. Garla'uskaite, *Ukr. Khim. Zh.*, 1991, **57**, 1310.
16. O. M6, M. Yáñez, A. L. Llamas-Saiz, C. Foces-Foces, and J. Elguero, *Tetrahedron*, 1995, **51**, 7045.
17. R. M. Claramunt, D. Sanz, C. López, J. A. Jiménez, M. L. Jimeno, J. Elguero, and A. Fruchier, *Magn. Reson. Chem.*, 1997, **35**, 35.
18. M. Begtrup and P. Vedsø, *J. Chem. Soc., Perkin Trans. 1*, 1995, 243.
19. A. Fruchier, V. Pellegrin, R. M. Claramunt, and J. Elguero, *Org. Magn. Reson.*, 1984, **22**, 473.
20. P. Molina, M. Alajarín, P. Sánchez-Andrada, J. Server, M. M. Ripoll, J. E. Anderson, M. L. Jimeno, and J. Elguero, *J. Org. Chem.*, 1996, **61**, 4289.
21. G. A. Morris and R. J. Freeman, *J. Am. Chem. Soc.*, 1979, **101**, 760.
22. G. L. Martin, M. L. Martin, and J. P. Gouesnard, "15N NMR Spectroscopy" in "NMR Basic Principles and Progress", ed. by P. Diehl, E. Fluck, and R. Kosfeld, Springer, Berlin, 1981.
23. C. López, R. M. Claramunt, D. Sanz, C. Foces-Foces, F. H. Cano, R. Faure, E. Cayón, and J. Elguero, *Inorg. Chim. Acta*, 1990, **176**, 195.
24. G. Otting, B. A. Messerle, and L. P. Soler, *J. Am. Chem. Soc.*, 1996, **118**, 5095.
25. R. M. Claramunt, J. Elguero, and R. Garcerán, *Heterocycles*, 1985, **23**, 2895.
26. L. Salazar, M. Espada, C. Avendaño, R. M. Claramunt, D. Sanz, and J. Elguero, *J. Org. Chem.*, 1992, **57**, 1563.