Tautomerism of 1-(2′,4′-dinitrophenyl)-3-methyl-2-pyrazolin-5-one: theoretical calculations, solid and solution NMR studies and X-ray crystallography‡

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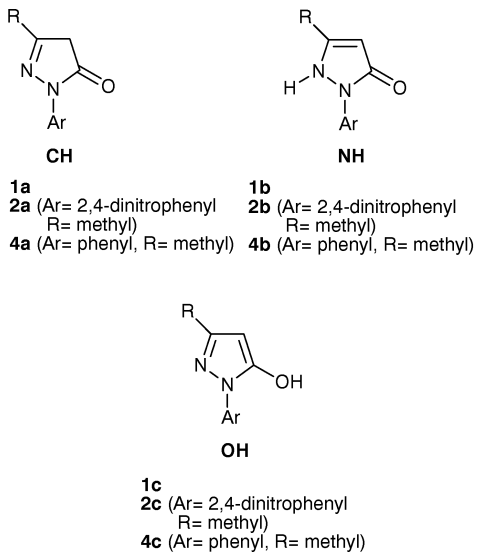
To gain a better understanding of the tautomerism of 1-(2′,4′-dinitrophenyl)-3-methyl-2-pyrazolin-5-one, **2**, different studies were performed. In order to simulate the gas phase, several MO calculations at the semiempirical (AM1 and PM3) and *ab initio* (HF/6-31G* and B3LYP/6-31G*) levels were carried out on the different tautomers of this compound and on those of the corresponding 1-phenyl derivative **4**. The ^{1}H and ^{13}C NMR spectra were recorded in solution for compound **2**. Finally, to investigate the solid state, ^{13}C CPMAS NMR studies and the crystal structure analysis of this pyrazolinone and that of its isomer [1-(2′,4′-dinitrophenyl)-3-hydroxy-5-methylpyrazole, **3**, whose chemical structure was incorrectly reported in the literature] were performed. In solution, the most abundant tautomer for both pyrazolinones, **2** and **4**, depends on the solvent used. For compound **2** it was found that the CH tautomer was the most stable in the gas and solid states as opposed to its 1-phenyl analogue, which appears as the CH form in the gas phase and as NH and OH tautomers in the crystal.

Heterocyclic tautomerism is a challenging field of study because of its importance in biological systems, chemical reactivity and molecular recognition. For this reason, it has been extensively studied over the past decades.[1] In particular, the problem of tautomerism in pyrazolinones has been the objective of a large number of studies.[1,2] In the specific case of 1-aryl-substituted pyrazolin-5-ones (**1**), several structural studies by solution and solid NMR and by X-ray analysis concluded that the three possible tautomers exist (CH: **1a**, NH: **1b** and OH: **1c**, see Scheme 1). NMR studies in solution proved that these three tautomers coexist and that the relative proportions depend mainly on the solvent used and on the nature of the R group and the aryl substituent.[3] The effect of solvent on pyrazolinone tautomerism is predictable in qualitative terms; thus, experimental results show that the NH form of the unsubstituted pyrazolin-5-one is the most stable in water.[4] In the solid state (determined by X-ray spectroscopy or CPMAS NMR), only the 'aromatic' tautomers (**1b** and **1c**) have been detected in the case of the 1-phenyl-3-methyl, 1-*p*-bromophenyl-3-methyl and 1-(2′-pyridyl)-3-methyl derivatives.[5] This behaviour seemed to be general for 1-aryl-substituted pyrazolin-5-ones. However, in 1966, to interpret IR results ($\nu_{C=O}$ at 1730 cm^{-1} in Nujol), it was proposed that the 1-(2′,4′-dinitrophenyl)-3-methyl-2-pyrazolin-5-one (**2**, see Scheme 1) exists in the solid state as the nonaromatic tautomer (**2a**), as an exception to this 'rule'.[1a,6]

In a theoretical approach, several high-level MO (molecular orbital) studies have been performed on the unsubstituted pyrazolin-5-one ring in the gas phase, and taking into account the effects of a solvent.[7–9] The tautomers considered in these studies included forms that are not possible for *N*-substituted pyrazolin-5-ones, and their results are not consistent. Whereas Hillier and coworkers[7] concluded that the most stable form in the gas phase is the CH tautomer, Cao *et al.*[8] and Luque *et al.*[9] considered the OH tautomer as the most stable one. When they included solvent effects and depending on the method used to simulate solution, they found that tautomers NH or CH[7–9] were the most stable ones. Recently, some radical reactions in which 1,3-dimethyl-2-pyrazolin-5-one is involved have been studied at the DFT level; these find that the CH tautomer has the lowest ground state energy among the three possible tautomers of the 1-substituted pyrazolin-5-ones.[10] Recent *ab initio* studies on the tautomerism of 1-



Scheme 1 Different possible tautomeric forms for 1-aryl-2-pyrazolin-5-ones

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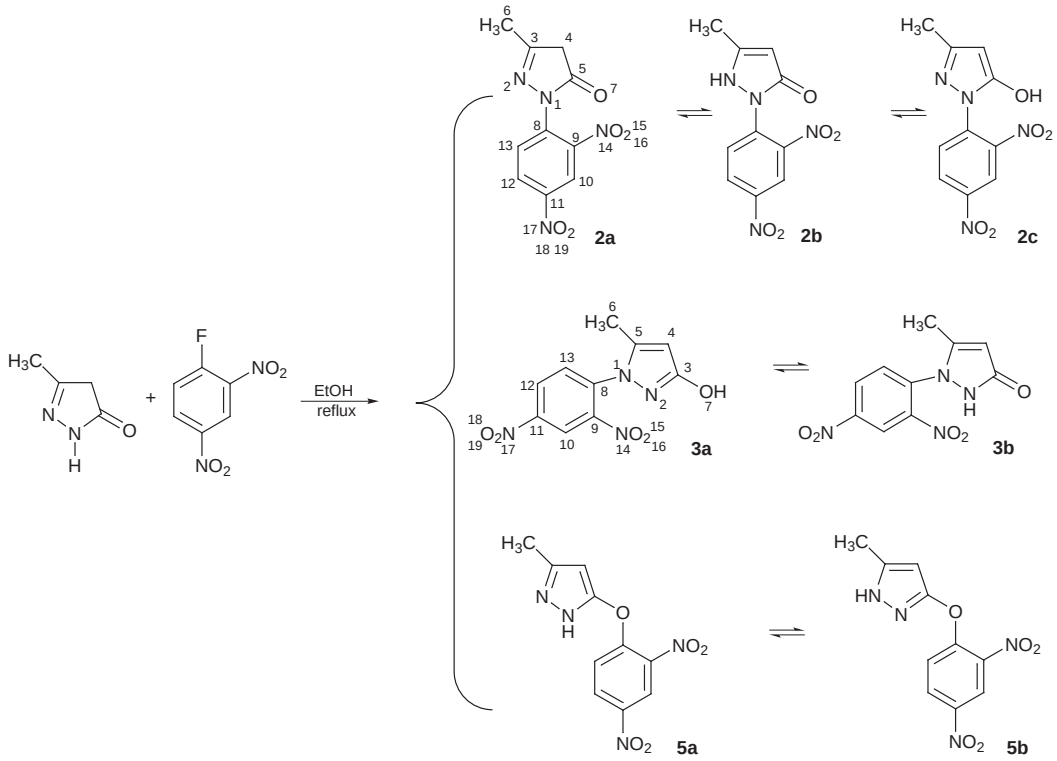
‡ Non-SI units employed: 1 kcal ≈ 4.18 kJ; 1 au ≈ 2.63 × 10^{6} J mol^{-1}; 1 Debye ≈ 3.33 × 10^{-30} C m.



Scheme 2

methyl-2-pyrazolin-5-one have been carried out at the HF/6-31G* level[11] and find that the order of stability is: CH > NH > OH.

In the present paper, we propose to clarify the situation for 1-(2′,4′-dinitrophenyl)-3-methyl-2-pyrazolin-5-one (**2**). Thus, after the preparation of this compound following the method previously described by some of us,[6] the nature of the tautomer present in the solid state (by CPMAS NMR and X-ray analysis), in solution (by ^{1}H and ^{13}C NMR) and in the gas phase (by means of MO semiempirical and *ab initio* calculations) will be reported.

Experimental

General methods

Melting points were determined with a Reichert–Jung Thermovar and are uncorrected. The high-resolution solid state ^{13}C CPMAS NMR spectra were obtained at room temperature on a Bruker MSL 400 spectrometer operated at 100.61 MHz under cross polarization (CP) and magic angle spinning (MAS) conditions, using a high speed probehead that achieves rotational frequencies of about 12 kHz. Samples (approximately 200 mg of material) were carefully packed in ZrO_2 rotors. The standard CPMAS pulse sequence was applied with a 6.5 μs ^{1}H-90° pulse width, 3 ms contact pulses and 5 s repetition time, the spectral width being 100 000 Hz. All chemical shifts (δ) are given with respect to the TMS signal. ^{13}C NMR decoupling spectra in solution were recorded on a Bruker AM-200 at 50 MHz and on a Varian XL-500 unit at 125 MHz. ^{1}H NMR spectra in solution (coupling constants in Hz) were recorded on a Varian Gemini-200 spectrometer at 200 MHz using $CDCl_3$ as external reference. Infrared spectra were recorded on a Perkin Elmer 983 spectrophotometer as KBr pellets.

Syntheses

The compounds were prepared as previously described[6] by heating, under reflux, a solution of equimolar quantities of 3-methyl-2-pyrazolin-5-one and 1-fluoro-2,4-dinitrobenzene (51 mmol) in 250 mL of dry ethanol for 30 min. The solution was allowed to cool to room temperature and then concentrated to dryness. Crystallization of the products from the crude residue with ethanol, as described, was not successful. Finally, two compounds (**2** and **3**) were isolated by fractional crystallization with a mixture of ethyl acetate–toluene (10 : 6). The numbering used for both compounds is that shown in Scheme 2.

1-(2′,4′-Dinitrophenyl)-3-methyl-2-pyrazolin-5-one (2). Yellow crystals; mp 130–131 °C; IR (KBr) ν_{max} 3425br, 3123, 1742, 1735, 1605, 1543, 1530, 1490, 1350, 1305 cm^{-1}; ^{1}H NMR ($CDCl_3$) 8.7 (1H, $J_m = 2.5$), 8.47 (1H, dd, $J_p = 1.1$, $J_m = 2.54$, $J_o = 9.02$), 7.95 (1H, dd, $J_p = 0.8$, $J_o = 9.02$), 3.48 (2H, s), 2.23 (3H, s); ^{13}C NMR ($CDCl_3$) 170.3 (C5), 159.3 (C3), 144.27 (C11), 141.54 (C8), 134.17 (C9), 127.4 (C12), 124.7 (C13), 121 (C10), 41.56 (C4), 16.9 (C6); MS (EI, *m*/*z*) 264 (100%) $[M]^{+\cdot}$, 218, 191, 172, 145, 117.

1-(2′,4′-Dinitrophenyl)-3-hydroxy-5-methylpyrazole (3). Yellow crystals; mp 222–225 °C; IR (KBr) ν_{max} 3450br, 3100, 3010, 1610, 1590, 1540, 1530, 1510, 1350, 1345 cm^{-1}; ^{1}H NMR ($CDCl_3$–DMSO-d_6) 9.99 (1H, br, OH), 8.6 (1H, d, J_m = 2.3), 8.4 (1H, dd, $J_m = 2.5$, $J_o = 8.8$), 7.57 (1H, d, $J_o = 8.8$), 5.65 (1H, d, $^4J = 0.8$), 2.2 (3H, d, $^4J = 0.8$); ^{13}C NMR ($CDCl_3$–DMSO-d_6) 162.6 (C3), 143.95 (C5 or C11), 143.91 (C11 or C5), 140.38 (C8), 136.39 (C9), 127.27 (C12), 126.31 (C13), 119.83 (C10), 95.61 (C4), 11.08 (C6); MS (ES$^+$, *m*/*z*) 265 $[MH]^+$, 219, 202, 173, 156, 145, 98.

The ^{13}C CPMAS NMR results for both compounds are gathered in Table 1.

Computational methods

The three tautomers considered for compound **2** (**a**, **b** and **c**: see Scheme 1) have been studied at both the semiempirical and *ab initio* levels, optimizing all the geometrical parameters and taking into account the rotation between rings. At the semiempirical level the PM3 and AM1 Hamiltonians were

Table 1 ^{13}C CPMAS NMR chemical shifts for the synthesized pyrazolinone derivatives

	C3	C4	C5	C6	C8	C9	C10	C11	C12	C13
2a	161.4	42.9	170.7	17.1	140.3	133.2	124.0	143.8	128.0	126.3
3a	164.1	96.4	145.4* 143.5	11.6	137.3	134.0	120.4	145.4 143.5*	129.7	129.7

* These signals can be inverted.

used, increasing the precision by a factor of 100 and optimizing until a gradient of 0.01 was reached.[12] *Ab initio* calculations were carried out using the Gaussian 94 package[13] with both the HF and hybrid HF/DFT B3LYP[14] methods and using the 6-31G* basis set. B3LYP calculations were performed since the importance of including electron correlation effects to describe these tautomers properly was already pointed out.[9] At the semiempirical, as well as at the *ab initio*, levels the nature of the stationary structures was determined by frequency calculations; all were positive and increasing.

For each tautomer two different rotamers were considered, that with the *o*-NO_2 oriented towards the CO(H) group of the pyrazole ring (denoted as [NO_2 > CO]) and that with the *o*-NO_2 oriented towards the N(H) group of the pyrazole ring (denoted as [NO_2 > N]), both series were local minima. One of the transition structures to the rotation between the dinitrophenyl and the pyrazole ring was found, characterized and its energy computed using the AM1 Hamiltonian. The three tautomers for 1-phenyl-3-methyl-2-pyrazolin-5-one (**4a**–**c**) were also computed at the AM1, PM3, HF/6-31G* and B3LYP/6-31G* levels for comparison.

X-Ray crystal structure determination

A summary of the data collection and refinement process is given in Table 2. The structures were solved by direct methods (SIR92)[15] and refined by least-squares full-matrix procedures on F_{obs}. All hydrogen atoms were obtained from difference Fourier synthesis and were included and refined isotropically in the last cycles of the refinement. The scattering factors were taken from ref. 16. The calculations were carried out with the XTAL,[17] PESOS[18] and PARST[19] sets of programs. CCDC reference number 440/074.

Results

MO calculations

The energy results obtained for all the structures at the semiempirical and *ab initio* levels are gathered in Table 3 and the *ab initio* optimized systems are represented in Fig. 1. The keto species are, in general, more stable than the hydroxy ones, and contiguous N atoms of the same hybridization type are strongly destabilizing due to lone pair repulsion between contiguous sp^2 N atoms or dipolar repulsion between contiguous N—(H,R) groups.[2a] Thus, as expected, tautomer **2a** is the most stable at all levels of theory used here (see Table 3). However, the differences in energy are dependent on the method used. Therefore, considering both sets of *ab initio* results as a reference we can say that the AM1 method overestimates the energy differences. It is known that with the AM1 approach nitro compounds are systematically too positive in energy.[20]

At the semiempirical level, some of the N atoms of the pyrazole rings are pyramidal. This is expected for the PM3 method where almost all trigonal N atoms are predicted to be pyramidal.[20] At the *ab initio* and DFT levels, all tautomers are predicted to have planar pyrazole rings apart from tautomer **2b**, which, although usually considered 'aromatic', shows

Table 2 Crystal analysis parameters at room temperature[a]

	2a	**3a**
Formula	$C_{10}H_8N_4O_5$	$C_{10}H_8N_4O_5$
Crystal habit	Yellow, plate	Yellow, plate
Crystal size/mm	0.50 × 0.50 × 0.17	0.43 × 0.50 × 0.10
Symmetry	Monoclinic, $P2_1/c$	Triclinic, $P\bar{1}$
a/Å	9.4248(4)	6.5974(3)
b/Å	15.9759(10)	7.3075(4)
c/Å	7.6589(3)	13.0001(9)
α/°	90	83.638(6)
β/°	93.809(3)	88.966(5)
γ/°	90	115.7417(4)
U/Å^3, *Z*	1150.7(1), 4	559.5(1), 2
D_c/g cm^{-3}, *M*, *F*(000)	1.525, 264.2, 544	1.568, 264.2, 272.0
μ/cm^{-1}	10.83	11.14
Scan width/°	1.6	1.5
No. indep. refl.	1945	1909
No. obsd. refl. [2σ(*I*) criterion]	1679	1703
Secondary extinction/10^4	2.13(6)	0.56(2)
Number of variables	204	204
Degrees of freedom	1475	1705
Ratio of freedom	8.23	9.36
Final shift/error	0.01	0..003
Max. thermal value/Å^2	U33[O16] = 0.158(2)	U11[O19] = 0.111(2)
Final Δ*F* peaks/eÅ^{-3}	0.20	0.37
Final *R* and *wR*	0.047, 0.054	0.045, 0.053

[a] Philips PW1100 four-circle diffractometer, bisecting geometry. CuKα radiation (1.5418 Å), graphite-oriented monochromator. Detector apertures 1 × 1°. ω/θ scans, θ_{max} = 65°. **2a**: 80 s per reflection, **3a**: 60 s per reflection. Two standard reflections were taken every 90 min, no variation was seen. The unit cell was determined from a least-squares fit to 77 (for **2a**) or 70 (for **3a**) reflections (θ < 45°). Weighting scheme: empirical as to give no trends in $\langle \omega \Delta^2 F \rangle$ *vs.* $\langle |F_{obs}| \rangle$ and $\langle \sin \theta/\lambda \rangle$.

Table 3 Dihedral angles of rotation between the phenyl and pyrazolinone rings and between the *o*-NO_2 group and the phenyl ring, torsional angle around N1 and N2 of the pyrazolinone ring, semiempirical heats of formation, *ab initio* total energies, relative energies and dipole moments of the tautomers of compound **2**

	ω/° [C5—N1—C8—C9], [C8—C9—N14—O15]	ω/° [H—N2—N1—C8]	H_f/kcal mol^{-1} or E_T/au	ΔH_f/kcal mol^{-1} or ΔE_T/au	μ/Debye
AM1					
2a [NO_2 > CO]	−41.4, −25.2	—	59.74	2.24	8.25
2a [NO_2 > N]	146.2, −52.8	—	57.50	0.0	7.71
2b [NO_2 > CO]	−71.0, −41.8	89.0	72.26	14.76	9.25
2b [NO_2 > N]	142.8, −71.2	81.3	69.77	12.27	6.92
2c [NO_2 > CO]	−54.4, −6.6	—	73.17	15.67	5.41
2c [NO_2 > N]	152.4, −53.5	—	72.76	15.26	7.02
PM3					
2a [NO_2 > CO]	−40.7, −33.6	—	10.45	1.91	7.23
2a [NO_2 > N]	125.2, −56.6	—	8.54	0.0	8.54
2b [NO_2 > CO]	−137.0, −59.8	86.0	12.36	3.82	12.36
2b [NO_2 > N]	106.5, −70.9	88.2	14.11	5.57	6.33
2c [NO_2 > CO]	−60.0, −46.5	—	18.49	9.94	5.75
2c [NO_2 > N]	148.2, −61.0	—	16.88	8.34	7.60
HF/6-31G*					
2a [NO_2 > CO]	−44.7, −35.2	—	−975.1812119	0.03	9.00
2a [NO_2 > N]	138.9, −42.2	—	−975.1812602	0.0	7.24
2b [NO_2 > CO]	−50.3, −29.4	81.5	−975.1623479	11.87	8.65
2b [NO_2 > N]	168.2, −32.0	80.0	−975.1678842	8.39	6.33
2c [NO_2 > CO]	−43.5, −36.9	—	−975.1629374	11.50	6.34
2c [NO_2 > N]	79.3, −39.2	—	−975.1613633	12.49	3.63
B3LYP/6-31G*					
2a [NO_2 > CO]	−40.9, −32.0	—	−980.7886222	0.0	8.48
2a [NO_2 > N]	147.4, −39.6	—	−980.7883058	0.20	7.01
2b [NO_2 > CO]	−34.3, −35.9	57.6	−980.7692818	12.14	9.26
2b [NO_2 > N]	176.3, −30.0	65.0	−980.7815208	4.46	6.09
2c [NO_2 > CO]	−40.8, −34.0	—	−980.7736219	9.41	6.04
2c [NO_2 > N]	67.6, −28.4	—	−980.7748824	8.62	3.49

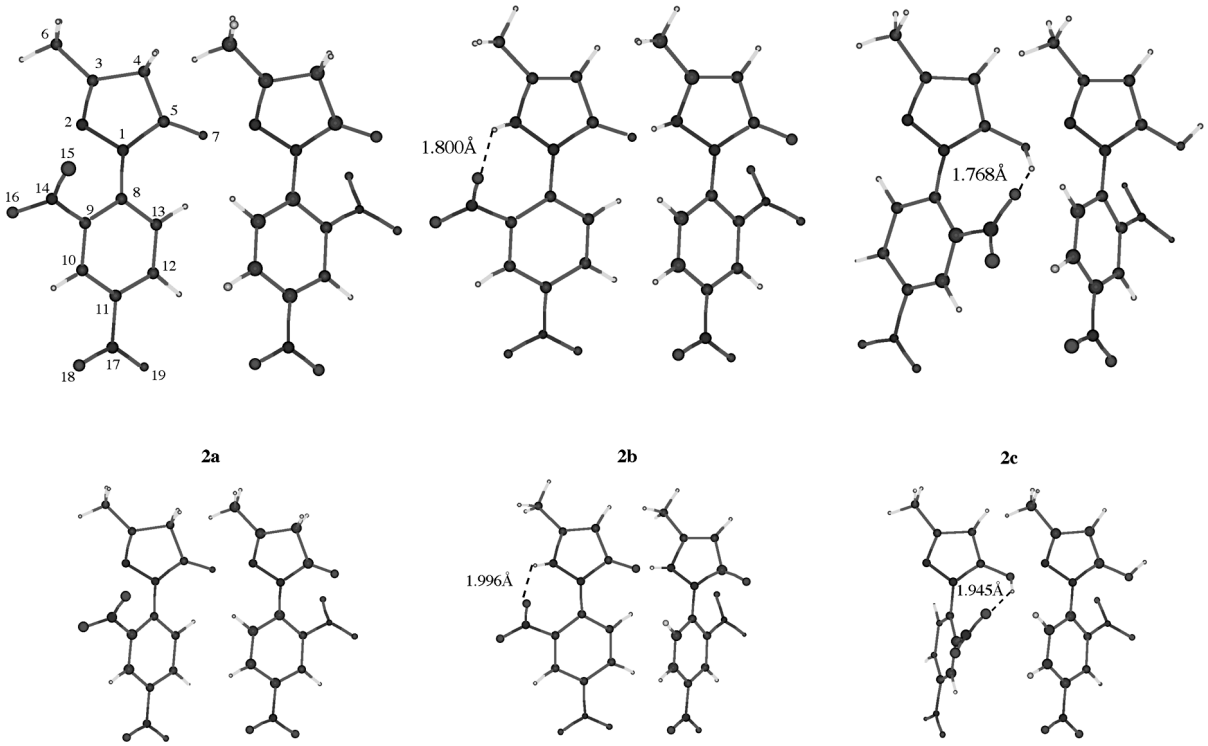


Fig. 1 Optimized structures at both HF/6-31G* (lower part) and B3LYP/6-31G* (upper part) levels obtained for each rotamer of tautomers **2a**, **2b** and **2c**

H—N—N—C torsional angles ranging from 57.6 to 81.5°, depending on the method used (see Table 3), a result already reported by other authors.[7,8]

With all the computational methods utilized here, we conclude that the most stable tautomers in the gas phase are the CH species, in agreement with the results obtained by Hillier and colleagues[7] or by Ono *et al.*[10] for pyrazolin-5-ones.

Synthesis

The synthesis described in the experimental section yielded two derivatives with NMR and IR data in agreement with the results previously reported[6a] (see Scheme 2). However, even though it was proposed that the two compounds isolated were **2** and **5**, the X-ray results here obtained show that they really were compounds **2** and **3**. The origin of the mistake could be that compounds **5** and **3** can exist as 3-hydroxy tautomers (see Scheme 2, tautomers **3a** and **5b**) which would provide similar NMR signals for the 3-CH_3 (which are different from those observed for the CH_3 of pyrazolin-5-ones). In addition, because compound **3** exists as its OH tautomer (see X-ray results) no C=O signal was observed in the IR spectra, which led to the erroneous conclusion of an *O*-alkylation.

^{1}H and ^{13}C NMR spectroscopy in solution

All important results are summarized in the experimental section and they suggest that compound **2** exists in $CDCl_3$ as tautomer **a** (CH) because in the ^{1}H NMR spectra there is a singlet corresponding to two H atoms at 3.48 ppm and the ^{13}C NMR signal for C4 appears at 41.56 ppm. Moreover, the ^{13}C NMR signal for C5 appears at 170.31 ppm (in agreement for a carbonyl pyrazolinone carbon) and that for the CH_3 appears at 16.95 ppm (indicating a pyrazolin-5-one). The ^{13}C NMR chemical shifts obtained for the CH_3, C3, C4 and C5 of the pyrazole ring of the other compound could correspond to structures **3a** or **5** (see Scheme 2) since they agree with an aromatic 3- or 5-hydroxypyrazole ring.

^{13}C CPMAS NMR spectroscopy

All important results are summarized in Table 1. All the chemical shifts obtained for compound **2** agree with tautomer **a** (CH) and they coincide with those obtained in solution. However, the spectrum registered for the other isomer obtained in the synthesis corresponds to an aromatic pyrazole ring of the 3- or 5-hydroxy type. The signal corresponding to the CH_3 appears at 11.6 ppm in agreement with any of these hydroxypyrazoles. The signals corresponding to C3, C4 and C5 could also be assigned either to compounds **3** or **5** (see structures **3a** and **5** in Scheme 2).

X-Ray crystallographic study

The molecular structure of compounds **2a** and **3a** are represented in Fig. 2. In compound **2a**, the N2—C3 distance [1.277(3) Å] is analogous to that tabulated[21] for C_{sp^2}=N (1.279 Å) and the C5=O7 one is close to that observed in carbonyl groups not involved in hydrogen bonding [1.215(15) Å].[22] With the exception of bonds around N1 (Table 4), the bond distances and angles are analogous to those reported for 1-phenyl-3-amino-pyrazolin-5-one (CSD[23] refcode: CIBJIG[24]) although the agreement is worse with the other 4,4-disubstituted pyrazol-3-one (YUCROD[25]) for which delocalization of the N2=C3 double bond is found. In **3a**, the pyrazole geometry is comparable to that observed in the two independent molecules of 1-phenyl-5-methyl-3-hydroxypyrazole (PMPYZL[26]) and to that of the OH tautomer of 1-phenyl-3-methyl-pyrazolin-5-one (PMPZOL[5a]).

In both compounds, the endocyclic angles in the benzene rings show distortions due to the substituents. The values agree with the calculated ones, taking into account the nitro substituents[27] and assuming the influence of the pyrazolinone and pyrazole rings is similar to that of an amino group.[28] The exocyclic angular distortions at C8 and C9 (Table 4) caused by the *ortho* substitution have been analysed by means of the nonadditivity parameter proposed by Krygowsky[29] [NAP = $\sum |\Phi_{i,exp} - \Phi_{i,cal}|$, $\Phi_{i,exp}$ and $\Phi_{i,cal}$ are the experimental and calculated endocyclic angles after applying the corrections due to substituents].[27] The NAP values of 7.2(9)° and 7.4(9)° for **2a** and **3a** suggest a repulsive interaction between the pyrazole ring and the nitro group at C9 because of steric effects, in spite of the twist of these nitro groups as well as the five-membered rings with respect to the benzene ring (Table 4).

The five-membered and dinitrophenyl rings are twisted differently around the N_{sp^2}—C_{sp^2} bond joining them [N2—N1—C8—C9 = −154.0(2)° and −55.8(3)° for **2a** and **3a**, respectively]. The disposition of the *ortho* nitro group in **3a** is analogous to the values of 27.1°, 21.5° and 21.7° for 1-(2′,4′-dinitrophenyl)-4-H-, -4-bromo- and -4-chloropyrazoles, respectively (KAYVAH,[30] NPBRPY,[31] NPCPAZ[32]) while in the two independent molecules of 1-(2′,4′-dinitrophenyl)-3,5-dimethylpyrazole (ZUHXEF[33]) the methyl groups produce an increase of this torsion angle [115.1(4)° and −114.3(4)°]. The greater twist shown by **3a** could be assigned to steric effects due to the formation of the dimer (Fig. 2).

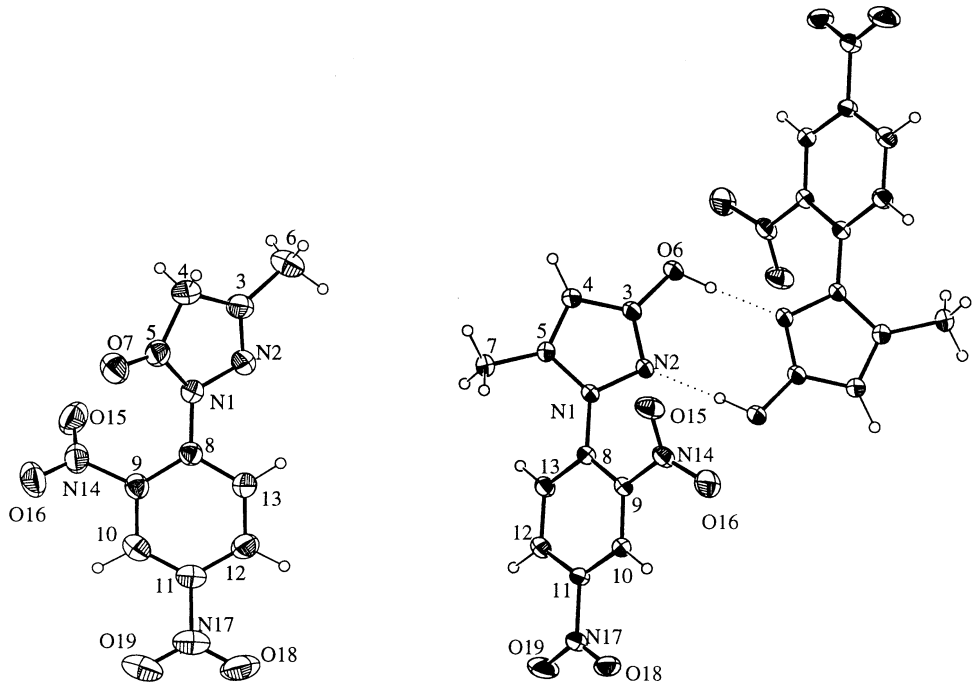
The pyrazolinone ring in **2a** is not planar and adopts a flattened twist conformation as measured by the Cremer and Pople parameters[19] [q_2 = 0.055(2) Å and Φ_2 = 122(2)° *versus* 126° for the ideal twist conformation], with the C4 and C5 atoms out of the plane defined by the other three.

In compound **2a**, the crystal packing is built of sheets parallel to the **bc** plane formed by weak C—H···O interactions that join molecules in chains along the **c** and then along the **b** directions; these sheets are interconnected through van der Waals contacts[34] stabilizing the crystal packing (Fig. 3). Compound **3a** presents the same type of dimers (strong O—H···N hydrogen bonds, Table 4) as in 1-phenyl-5-methyl-3-hydroxypyrazole (PMPYZL[26]). These dimers are then interconnected by weak C—H···O interactions along the **b** direction (Fig. 3 and Table 4). There is a partial pyrazole overlapping with distances between their planes of 3.672(1) Å and a centroid···centroid distance of 3.789(1) Å. The strength of the C—H···O=N interaction in both compounds is similar except that the C10—H10···O18 one in **2a** exhibits a C···O distance shorter than the sum of van der Waals radii. (ref. 34) of 3.22 Å. The geometry of these interactions shows values situated in the lower end of the distance range reported for nitrobenzene derivatives,[35] although only one of them occurs in the lone-pair direction of the acceptor (φ and θ values of 141° and 19° *vs.* observed values[35] of 137(29)° and 29(17)° or values of 120° and 0° for the ideal lone-pair direction). The remaining contacts belong to the scarce number of contacts that take place above the nitro plane (φ and θ ranges: 123–154° and 62–69° as reported in a previous work on the environments of nitro and carbonyl groups).[36] There are no voids in the crystals and their total packing coefficients are 0.71 and 0.69, respectively,[37] for **2a** and **3a**, respectively.

Discussion

By using different techniques, it has been verified that, in contrast to other 1-arylpyrazolin-5-ones, 1-(2′,4′-dinitrophenyl)-3-methyl-2-pyrazolin-5-one, **2**, exists as the CH tautomer (**2a**) in the solid state (confirming the previous IR results[6]), in solution ($CDCl_3$) and in the gas phase (at the MO level). This result can be generalized to other 1-(2′,4′-dinitrophenyl)-2-pyrazolin-5-ones.[6]

Only by X-ray analysis has it been possible to determine



2 **3**

Fig. 2 Molecular structures of **2a** and the dimer of **3a**, showing the atom labelling. Ellipsoids are drawn at the 30% probability level

Table 4 Selected geometrical parameters (Å, °) from the X-ray structures of **2a** and **3a**

	2a	**3a**		**2a**	**3a**
N1—N2	1.412(2)	1.386(2)	N1—C8	1.394(2)	1.407(2)
N1—C5	1.381(3)	1.358(3)	C9—N14	1.465(3)	1.471(3)
N2—C3	1.277(3)	1.319(3)	N14—O15	1.216(3)	1.212(3)
C3—C4	1.485(3)	1.398(3)	N14—O16	1.224(3)	1.215(3)
C4—C5	1.499(3)	1.367(3)	C11—N17	1.473(3)	1.470(3)
C3—C6/O6	1.493(3)	1.345(2)	N17—O18	1.228(3)	1.212(2)
C5—O7/C7	1.207(3)	1.490(3)	N17—O19	1.223(3)	1.207(3)
N2—N1—C5	112.4(2)	111.8(2)	C10—C9—N14	115.9(2)	115.9(2)
N1—N2—C3	107.5(2)	103.5(1)	C8—C9—C10	121.4(2)	121.7(2)
N2—C3—C4	112.8(2)	112.8(2)	C9—C10—C11	118.2(2)	117.6(2)
C3—C4—C5	102.5(2)	105.3(2)	C10—C11—N17	118.6(2)	117.6(2)
N1—C5—C4	104.4(2)	106.6(2)	C12—C11—N17	119.1(2)	119.7(2)
N2—C3—C6/O6	120.1(2)	122.3(2)	C10—C11—C12	122.3(2)	122.7(2)
C4—C3—C6/O6	127.1(2)	125.0(2)	C11—C12—C13	118.9(2)	118.6(2)
C4—C5—O7/C7	130.3(2)	129.9(2)	C12—C13—C8	121.1(2)	121.1(2)
N1—C5—O7/C7	125.2(2)	123.4(2)	C9—N14—O15	117.8(2)	118.2(2)
N2—N1—C8	117.7(1)	119.2(1)	C9—N14—O16	117.0(2)	117.5(2)
C5—N1—C8	128.0(2)	129.0(2)	O15—N14—O16	125.1(2)	124.3(2)
N1—C8—C13	119.3(2)	118.8(2)	C11—N17—O19	117.9(2)	118.0(2)
N1—C8—C9	122.8(2)	122.9(2)	C11—N17—O18	117.4(2)	118.6(2)
C9—C8—C13	118.0(2)	118.3(2)	O18—N17—O19	124.6(3)	123.4(2)
C8—C9—N14	122.4(2)	122.4(2)			
N1—N2—C3—C4	1.6(2)	−0.3(2)	C5—N1—C8—C9	43.3(3)	127.4(2)
N2—C3—C4—C5	2.1(3)	0.1(2)	N2—N1—C8—C9	−154.0(2)	−55.8(3)
C3—C4—C5—N1	−4.9(2)	0.2(2)	C8—C9—N14—O15	38.9(3)	−27.4(3)
N2—N1—C5—C4	6.3(2)	−0.4(2)	C10—C11—N17—O18	−2.9(3)	−5.4(3)
C5—N1—N2—C3	−5.2(2)	0.4(2)			

Intermolecular interactions (Å, °)	D—H	H···A	D···A	D—H···A
2a				
C10—H10···O18 (x, $-\frac{1}{2}-y$, $-\frac{1}{2}+z$)	0.97(3)	2.44(3)	3.113(3)	126(2)
C6—H62···O16 ($-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$)	0.97(5)	2.42(5)	3.261(4)	144(4)
C12—H12···O19 ($1-x$, $-y$, $2-z$)	0.97(3)	2.46(3)	3.256(3)	139(2)
3a				
O6—H6···N2 ($-x$, $-y$, $1-z$)	0.92(3)	1.81(3)	2.722(2)	177(4)
C12—H12···O15 (x, $1+y$, z)	0.95(3)	2.86(3)	3.269(3)	107(2)

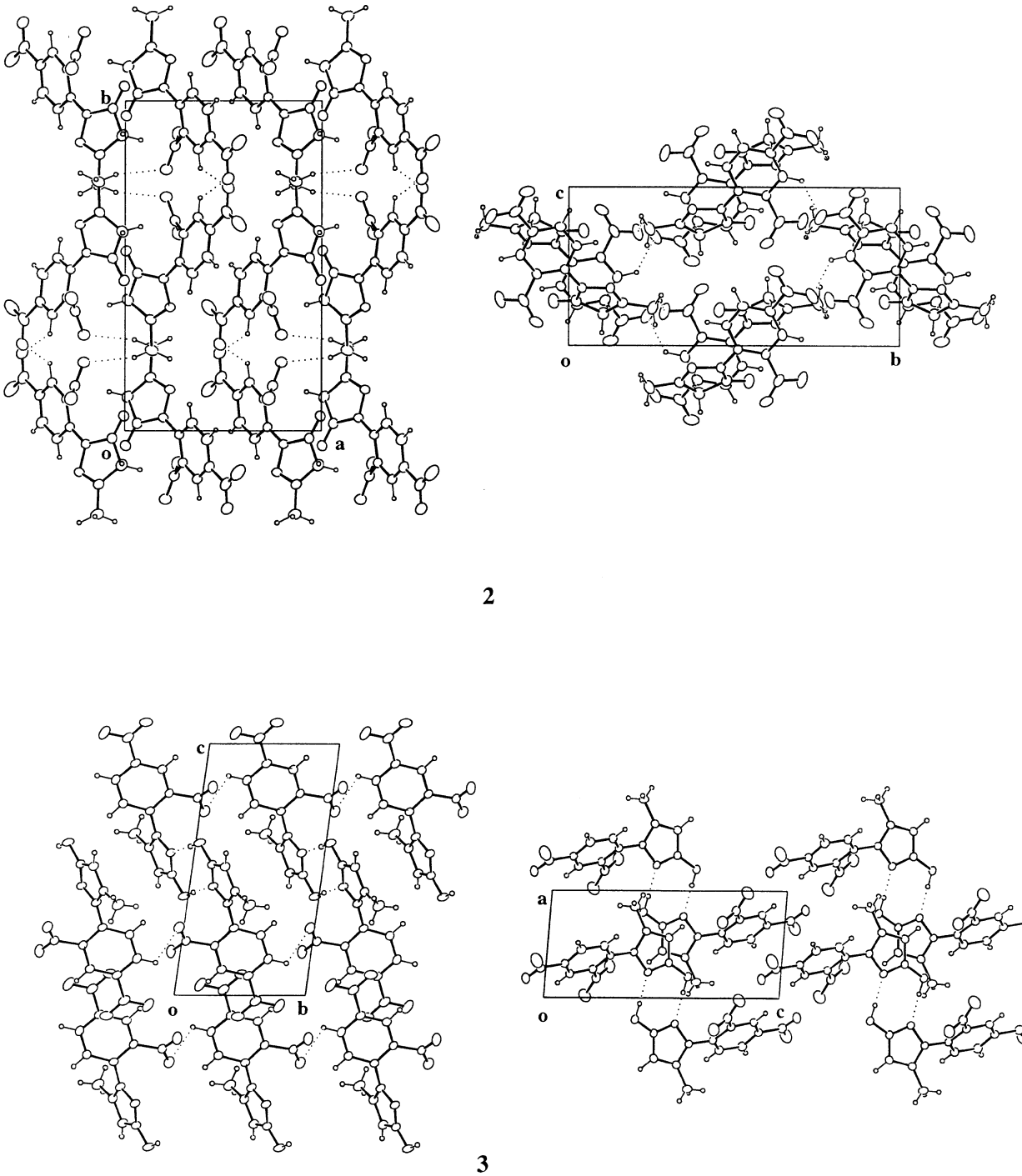


Fig. 3 Crystal structure for compound **2a** projected down the **c** and **a** axes and for compound **3a** down **a** and **b** axes

that the isomer obtained in the synthesis along with **2** and previously described as 3(5)-methyl-5(3)-(2′,4′-dinitrophenyl)-oxypyrazole (**5**)[6a] was actually 1-(2′,4′-dinitrophenyl)-3-hydroxy-5-methylpyrazole (**3**, see Scheme 2).

For tautomer **2a** a first question arises: why does the X-ray diffraction structure obtained for this compound show the *o*-NO_2 group oriented towards the C=O group of the pyrazolinone ring ([NO_2 > CO], see Fig. 2) whereas in MO calculations the most stable conformation for this tautomer has the *o*-NO_2 group pointing towards the N2 of the pyrazolinone ring ([NO_2 > N], see Fig. 1 and Table 3)? To explain this point the potential curve for the rotation between the two rings in tautomer **2a** was evaluated at the AM1 level (by rotating the rigid phenyl ring around the connecting bond in steps of 10 deg). The transition structure between the X-ray structural minimum {ω[C5(O)—N1—C8—C9(NO_2)]: 41.3°; ΔH_f(AM1): 59.74 kcal mol^{-1}} and the total MO minimum {ω[C5(O)—N1—C8—C9(NO_2)]: 146.2°; ΔH_f(AM1): 57.50 kcal mol^{-1}} was located and characterized at the same level of theory. This transition structure {ω[C5(O)—N1—C8—C9(NO_2)]: 120.8°; ΔH_f(AM1): 63.02 kcal mol^{-1}} supposes a barrier of 5.5 kcal mol^{-1} from one rotamer to the other. This small energy barrier could explain the crystal structure of compound **2** since the forces within the crystal could be enough to pass from the [NO_2 > N] rotamer to the [NO_2 > CO] one. Besides, as can be observed in Table 3 the difference in energy, at the *ab initio* level, between the two rotamers of tautomer **2a** is very small ($\Delta\Delta H_f$ = 0.03 or 0.20 kcal mol^{-1} at the HF/ or B3LYP/6-31G* levels); thus their populations should be similar.

All the results obtained here confirm that the tautomerism of 1-arylpyrazolin-5-ones depends on the physical state of the

Table 5 Dihedral angle of rotation between the phenyl and pyrazolinone rings, torsional angle around N1 and N2 of the pyrazolinone ring, semiempirical heats of formation, *ab initio* total energies, relative energies and dipole moments of the tautomers of the phenyl derivative **4**

	ω/° [C(O)—N1—C8—C9]	ω/° [H—N2—N1—C8]	H_f/kcal mol^{-1} or E_T/au	ΔH_f/kcal mol^{-1} or ΔE_T/au	μ/Debye
AM1					
4a	155.6	—	44.75	0.0	2.68
4b	−130.9	88.9	57.06	12.31	3.99
4c	−142.6	—	57.38	12.62	2.06
PM3					
4a	124.3	—	20.04	0.0	2.46
4b	−98.3	86.7	24.48	4.44	3.73
4c	−130.7	—	28.19	8.16	2.53
HF/6-31G*					
4a	166.9	—	−568.2555757	0.0	3.64
4b	−134.9	73.0	−568.2418486	8.61	5.25
4c	−132.0	—	−568.2357656	12.43	2.31
B3LYP/6-31G*					
4a	177.7	—	−571.8026091	0.0	3.31
4b	−149.5	63.0	−571.7901250	7.83	5.03
4c	−140.6	—	−571.7858683	10.51	2.09

corresponding experimental study.[1] Thus, to be able to make a comparison we carried out semiempirical (AM1 and PM3) and *ab initio* (HF/ and B3LYP/6-31G*) calculations over the three tautomers of 1-phenyl-3-methyl-2-pyrazolin-5-one (**4a–c**) and found that the most stable was the CH tautomer **4a** (see Table 5). Therefore, in the gas phase and by MO calculations both compounds **2** and **4** show the same order of stability for the three tautomers: CH (**a**) > NH (**b**) ⩾ OH (**c**). In solution, the NMR studies demonstrate that the stability of each tautomer depends on the solvent. Thus, when the NMR spectrum is recorded in $CDCl_3$ only the CH (**a**) form appears (100%) for both compounds **2** and **4**. When the spectrum is recorded in DMSO-d_6 the situation changes but in an identical way for the two aryl derivatives, the CH (**a**) form appears as the minor tautomer, in a 12% proportion for both compounds, **2a** and **4a** (this work, same molar concentration). However, the situation changes dramatically in the solid state where compound **4** crystallizes as a chain formed by an alternation of the NH (**b**) and OH (**c**) tautomers connected by O—H···:O=C and N—H···:N hydrogen bonds (HBs), whereas compound **2** crystallizes as the CH (**a**) tautomer.

Why does the dinitro derivative crystallize as the CH tautomer (**2a**) whereas the X-ray structure of the phenyl derivative is a chain of the NH (**4b**) and OH (**4c**) tautomers (all other 1-arylpyrazolin-5-ones crystallize as hydrogen-bonded chains of either NH or OH tautomers[38])? From the data gathered in Tables 3 and 5 we can conclude that the introduction of nitro groups in the *ortho* and *para* positions modifies neither the stability nor the dipole moment of the tautomers enough to explain the differences in the crystal. Thus, the stability of the isolated monomers does not account for the different crystal structures of compounds **2** and **4**. Then, only the ability in the solid state to form HBs between the different tautomers could account for these differences. The NH and OH tautomers of the phenyl derivative **4** can act as acceptors (by the C=O: and =N: groups) and donors (by the N—H and O—H groups) of HBs. By forming these strong HBs, the complex will gain in stability with respect to the CH monomer.

The fact that the crystal structure of the dinitro derivatives corresponds to the CH form **a** should be due to either a steric effect of the *o*-nitro group, an electronic effect or, more likely, a combination of both. Two arguments can be used. On one hand, both tautomers **2b** and **2c** can exhibit intramolecular HBs between one O of the *o*-nitro group and the N—H or O—H of the pyrazolinone ring, respectively (see Fig. 1). In both cases, and according to the B3LYP results, the *o*-NO_2 groups have rotated enough to yield O···H distances around 1.8 Å and (N)(O)—H···O angles of 137.9° and 147.8°, respec-

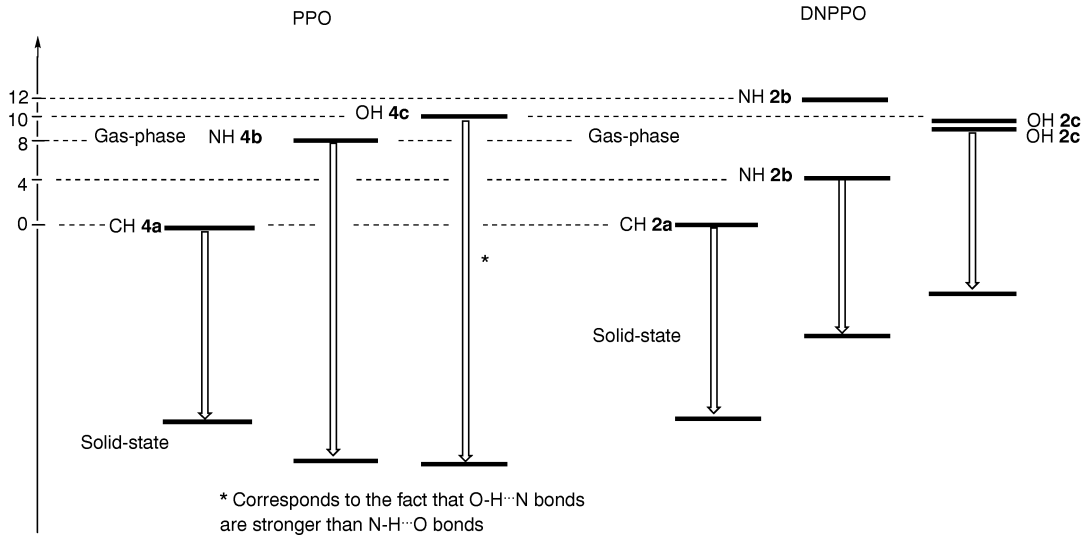


Fig. 4 Simplified energy diagram for PPO and DNPPO in the gas phase and in the solid state (energy differences from B3LYP results are in kcal mol^{-1})

tively. Taking into account these HB distances, both interactions should be very strong and therefore, very stabilizing. Thus, if compound **2** would crystallize in any of these **b** or **c** forms, the intramolecular HBs formed with the *o*-NO_2 group would prevent the stabilization by intermolecular HBs (as those present in the crystal of compound **4**). Thus, we have both effects present: the steric effect of the bulky *o*-NO_2 group obstructing the formation of HB chains and the electronic one by the formation of intramolecular HBs.

On the other hand, it is now accepted that the C—H···O HBs are important in the solid state, especially for crystal packing.[39] Thus, we should remember the presence, in the crystal structure of compound **2a**, of three intermolecular C—H···O bonds (see Table 4 and Fig. 3). These HBs have H···O distances shorter than the sum of the van der Waals radii (2.75 Å)[32] although only one of them is oriented towards the lone-pair direction.

The stabilization provided by these C—H···O bonds and the fact that the HB existing between the CH_3 and the *o*-NO_2 group would only be formed in the case of the **2a** (which cannot form intermolecular HBs) could explain the crystal structure of compound **2**. To go further in the understanding of the structure of pyrazolinones in the solid state would require computational studies far beyond our present capability.

Conclusions

The experimental and theoretical results allow us to propose an explanation for the existence of dinitrophenylpyrazolinones (DNPPOs, **2**) as CH tautomers in the solid state. The stability is not related to an intrinsic property, because the three tautomers of DNPPO and of phenylpyrazolinone (PPO, **4**) have similar relative stabilities in the gas phase (see Fig. 4). Therefore, the explanation must be related to some other property and we propose that this property is the formation of hydrogen bonds (HBs) and the fact that intermolecular HBs can only exist in the condensed phases while intramolecular HBs (IMHBs) can be present for isolated molecules in the gas phase.

Consider first the case of PPO (left side of Fig. 4). The intermolecular HBs existing in the crystal stabilize the NH and OH tautomers to the point that they become more stable (same relative stability) than the CH one. Consider now the case of DNPPO (right side of Fig. 4). Its NH and OH tautomers show IMHBs with the *o*-nitro group in the gas phase and one can assume that, in the absence of these IMHBs, the difference in stability with the CH tautomer would be much larger. Since these IMHBs would prevent the formation of intermolecular HBs in the solid state, the differences in energy would be maintained in the solid state and this will result in the observation of the CH tautomer for DNPPOs.

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