

Site-Selective Processes: The Role of Environment in the Control of Proton Transfer Processes in Crystalline Systems of 2-(2,4-Dinitrobenzyl)-3-methylpyridine

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Induced proton-transfer (PT) reactions play an important role in many biological systems such as the vision unit¹ and the photosynthetic reaction center² as well as in various devices having potential commercial applications. However, even rather “simple” PT reactions are not fully understood due to the complex interrelation between intra- and intermolecular effects. These processes are often interpreted within schemes of isolated or small molecular fragments, underestimating supramolecular effects. In this context, PT processes taking place in well-defined crystalline environments are of particular interest since both the PT energetics and the molecular and supramolecular structures can be fully resolved and thus correlated.

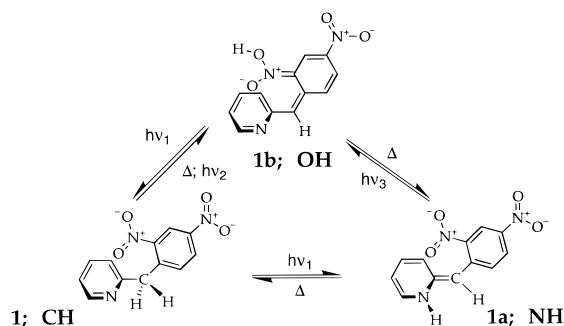
One of the most interesting PT processes that take place in the crystalline state is the tautomerization process of 2-(2,4-dinitrobenzyl)pyridine (α -DNBP, **1**), illustrated in Scheme 1.^{3,4} Recently, these tautomerization processes were shown to exhibit a primary isotope effect, indicating that the transfer of a proton is indeed the rate-determining step in these reactions.

In this paper, we describe an investigation of the effect of the molecular environment on a thermally activated PT process in crystals of 2-(2,4-dinitrobenzyl)-3-methylpyridine (**2**).

Upon near-UV irradiation, crystals of 2-(2,4-dinitrobenzyl)-3-methylpyridine (**2**) develop a blue-green color ($\lambda_{\max} = 611 \pm 2$ nm), indicating the formation of the NH phototautomer. This blue-green band decays homogeneously in time without any significant variation in the band shape. However, in contrast to all other 2-(2,4-dinitrobenzyl)pyridine derivatives in which the thermally activated NH \rightarrow CH back PT reaction follows a monoexponential decay, the back PT process in **2** follows a biexponential decay. This unusual behavior was previously attributed to the formation of two slightly different NH conformers having different thermal stability but similar optical properties.⁴ A biexponential analysis of the decay curves at different temperatures yielded activation energies of 27.2 and 18.9 kcal mol⁻¹, corresponding to the highest and lowest activation energies ever reported for such systems.^{3,4} It was surprising that extremely small conformational differences account for such a large difference in the activation energies.

Recently, we have found that the ratio between the initial populations of the two NH species is temperature dependent, as can be seen in Figure 1. At the lower temperature regime

Scheme 1



($T < \sim 315$ K), the initial population of the NH states is dominated by the long-lived species, whereas at higher temperatures ($T > \sim 315$ K) the short-lived species becomes dominant. However, the two NH species coexist at varying ratios over a relatively wide range of temperatures. Cooling the crystal to the lower temperature regime does not significantly change the relative populations observed in the high-temperature regime (see points *a* and *a'* in the insert in Figure 1).

The variation in the initial population of the two NH species can be partially rationalized by a differential scanning calorimetry experiment which shows an endothermic, first-order⁵ crystal to crystal phase transition in crystals of **2** ($\Delta H = 26 \pm 2$ J g⁻¹) at a temperature of 318 ± 0.4 K. X-ray crystal structural analysis performed on the crystals at 343 and 293 K⁶ reveals that the phase transition is expressed by the elongation of the *a*-axis of the unit cell by ca. 2%, while the other crystallographic parameters remain practically unaltered. The intermolecular arrangement of the molecules of **2** in the high-temperature phase is presented in Figure 2 and is compared with the previously reported low-temperature phase.⁴

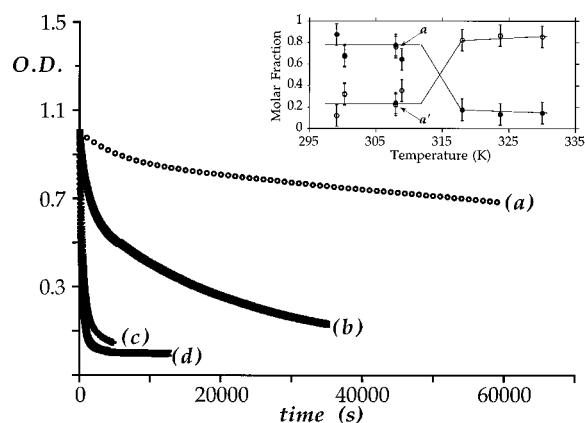


Figure 1. The absorption of an irradiated crystal of **2** at 611 nm as a function of time at different temperatures. The experimental data was normalized for reasons of clarity: (a) 299 K, (b) 309 K, (c) 318 K, (d) 324 K. Insert: The relative initial populations of the two NH species as a function of the temperature.

(5) Confirmed by a temperature-dependent X-ray determination of the unit cell parameters. A solid state NMR investigation reveals that the two conformers coexist in the crystals at the temperature range that is relevant to the optical measurement.

(6) Crystal data for **2** at a temperature of 343 K: $C_{13}H_{11}N_3O_4$, $M_r = 273.25$, monoclinic, space group $P2_1/c$, $a = 11.617(3)$, $b = 15.355(5)$, and $c = 7.641(3)$ Å, $\beta = 105.97(3)^\circ$, $V = 1310.4(7)$ Å³, $Z = 4$, $\lambda(\text{Mo K}\alpha) = 0.71070$ Å, $\mu = 0.105$ cm⁻¹. Crystallographic data were collected on a PHILIPS PW1100 diffractometer, $2.25^\circ < \theta < 21.99^\circ$ ($\omega/2\theta$ scans); 1600 independent reflections, 1044 with $I > 2\sigma(I)$ were observed and used for structure refinement. The structure was solved by direct methods and refined on F_o^2 to $R = 0.0773$. Further details of the crystal structure investigation are available on request from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB2 1EZ (UK) on quoting the full journal citation.

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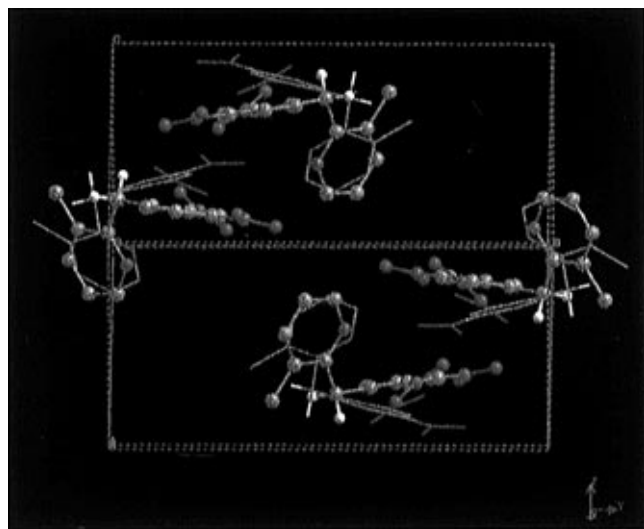


Figure 2. The intermolecular arrangements of the molecules of **2** in the high- (balls and sticks) and low- (sticks) temperature phases.

Table 1. Selected Intramolecular and Intermolecular Dimensions (Å, deg)

phase	293 K	343 K
Intramolecular Parameters		
pyridine-phenyl (deg)	55.85	68.31
<i>o</i> -nitro-phenyl (deg)	41.64	33.38
<i>p</i> -nitro-phenyl (deg)	14.23	8.23
N1-H1 (Å)	3.07(3)	3.13(8)
N1-H2 (Å)	3.12(3)	2.95(7)
O1-H1 (Å)	2.43(4)	2.37(8)
N1-O1 (Å)	3.136(4)	3.278(8)
Intermolecular Distances		
O1-O1 (Å)	3.481(4)	>4.0
N1-O3 (Å)	3.703(4)	3.560(8)
H _{Me} -O2 (Å)	2.53(4)	2.54(9)
O3-H2 (Å)	2.62(4)	2.93(7)
O1-H1 (Å)	2.84(4)	>4.0
O1-H2 (Å)	>4.0	2.79(7)

Clearly, the two phases consist of roughly the same conformer of **2**, differing only by minor variations in the intramolecular coordinates (Table 1). The difference of 12.4° in the tilt angle between the phenyl and the pyridine rings is compensated by the change in the deviation of the *o*-nitro plane from the plane of the phenyl ring ($33.38 \pm 0.40^\circ$ at 343 K and $41.64 \pm 0.37^\circ$ at 293 K) so that the distance between the oxygen atom O1 of the *o*-nitro group and the benzylic hydrogen atom H1 is almost unaltered: $d_{O1 \cdots H1} = 2.43(4)$ and $2.37(8)$ Å for the low- and high-temperature phases. Similarly, the distances between the nitrogen N1 of the pyridine ring and the benzylic protons are only slightly influenced by the phase transition, $d_{N1 \cdots H1} = 3.13(8)$ at 343 K and $3.07(3)$ Å at 293 K; $d_{N1 \cdots H2} = 2.95(7)$ Å at 343 K and $3.12(3)$ Å at 293 K. These differences between the two phases of **2** are small when compared to similar differences in homologous series of (2,4-dinitrobenzyl)pyridine systems and, therefore, seem to be insufficient to explain the significant difference in their PT kinetics.

In spite of the similarities in the intramolecular parameters, the two polymorphs are notably different in the nature of the site accommodating the molecule. Some significant differences

in the way the active protons of the different tautomers (i.e., the acidic proton in the CH, NH, and OH forms) interact with basic groups belonging to neighboring molecules are expected to influence the kinetics and thermodynamics of the tautomerization process. For example, the distance between two oxygen atoms of neighboring molecules related by the $-x, -y, 1-z$ symmetry operation changes from 3.481(4) Å at the low-temperature phase to >4 Å at the high-temperature phase. The intramolecular distances between the nitrogen atom N1 of the pyridine ring and the oxygen atom O1 of the *o*-nitro group changes from 3.136(4) Å at 293 K to 3.278(8) Å at 343 K, while the distance between the same nitrogen atom and the oxygen atom O3 of the *p*-nitro group of a neighboring molecule related by the $+x, 1/2-y, 1/2+z$ symmetry operation changes from 3.703(4) Å at 293 K to 3.560(8) Å at 343 K. These changes in the relative position of the basic atoms and acidic hydrogens correspond to different interactions of the phototautomerized molecule with its environment and thus to different relative stability of the NH tautomer in the two phases.

Preliminary semiempirical electronic structure calculations (MOPAC PM3⁷) suggest that the enthalpy change in the NH \rightarrow CH thermally activated reaction is hardly altered by the phase transition when only an isolated molecule⁸ is considered ($\Delta H = 13.43$ and 12.96 kcal mol⁻¹ for the high- and low-temperature phases, respectively). However, when the neighboring molecule having the shortest N1 \cdots O3 distance is added to the calculation, the NH form is stabilized by an intermolecular hydrogen bond (-N1-H \cdots O3-). As a result, the reaction enthalpies change to $\Delta H = 14.64$ and 11.56 kcal mol⁻¹ at the high- and low-temperature phases, respectively. According to this calculation, the NH tautomer is more stable in the low-temperature phase than in the high-temperature phase by 1.49 kcal mol⁻¹ (for comparison, for the isolated molecule, the NH form is 0.03 kcal mol⁻¹ more stable at the high-temperature phase).

In both phases, the reacting molecule is surrounded by 16 different molecules, forming its first "solvation" shell (up to 4 Å distance from the reacting molecule). It is expected that the relative stability of the different tautomers and the activation energies for the different thermal reactions will be significantly influenced by the differences in the relative orientation and interactions of the molecules in their solvation shell.

The present results indicate that small changes in the supramolecular structure of the reacting molecule and its "solvation" shell correlate with a large variation of the activation energies of an intramolecular PT process in crystals of **2**. Surprisingly, the effect of such changes in the supramolecular interactions are more pronounced than the effect of chemical derivatizations of the molecule.^{3,4} It is clear that a deeper understanding of such effects requires the investigation of the molecule together with its solvation shell as an integrated "unit" and that descriptions limited to the molecular level are insufficient.

The fact that even small differences in the supramolecular structure can be well characterized in crystalline systems allows a more detailed experimental as well as theoretical investigation of the solvation effects on the kinetics and thermodynamics of the systems. These investigations are currently in progress.

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(8) As the PT seems to be the rate-determining step in the thermally activated NH \rightarrow CH process, only a minor skeletal reorganizations are expected to occur during this process. Therefore, as a first approximation, the calculation was performed assuming no change in the inter-ring interplanar angle (two atoms at each ring were fixed during the calculation). All other molecular parameters were left free for minimization.