Hydrogen-bonding in the self-organising system 3,5-dimethylpyrazole

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The family of pyrazoles containing only H and CH_3 substituents displays a wide variation in physical properties which can be directly related to the manner in which the molecules self-organise in the solid state. Hydrogen-bonded multimeric motifs of the substituted pyrazoles are a recurring feature of this family. The quasielastic neutron scattering data for 3,5-dimethylpyrazole presented here indicate that the hydrogen-bonded amide protons within trimer units undergo a short-range hopping motion between two equivalent sites, straddling the direct N···H hydrogen-bond axis. This motion is in addition to the larger tautomeric hop previously observed using NMR. The activation energy of the short-range motion has been determined herein as 1.7(1) kJ mol^{-1}, *ca.* 1/30th of that of the tautomeric proton hopping motion.

Introduction

The processes in which relatively simple molecular motifs interact when crystallising to form molecular solids are of great importance in the desire to control the architecture (and hence physical properties) of such materials. The prediction of the crystal structure from that of the molecular unit is not intuitive and is further complicated by the phenomenon of polymorphism—the tendency of molecules to adopt more than a single structure. One of the major types of interaction between molecules is hydrogen bonding. Whilst structural studies often allude to such interactions by virtue of *apparent proximities*, there is still relatively little work performed on the dynamic nature of these bonds—a problem for which neutron scattering is ideally suited. The self-organising system 3,5-dimethylpyrazole (3,5-DMP) provides an ideal model for studying the dynamics of H-bonding; the structure has been accurately determined by X-ray diffraction in which the molecules are seen to lie in planar three-fold units in the *ab*-plane, linked *via* NH···N bonds along the vertices of equilateral triangles. The dynamic nature of the H-bonds is evidenced by partial occupation numbers of 0.5 in the crystal structure in addition to NMR measurements showing that the rate of the tautomeric proton hop along the H-bonds is *ca.* 10^3 s^{-1} at $T = 300$ K, with an activation energy of 46 kJ mol^{-1}.[1] Furthermore, the family of methylpyrazoles to which 3,5-DMP belongs displays a propensity to self-organise into such multimember units (although it is not isomorphic) and differences in the inter-molecular interactions within these compounds are believed to underpin the marked differences in physical properties, such as phase behaviour.[2]

The presence of mobile protons in both the H-bonded system and in the methyl groups, in which there is the additional three-fold rotational freedom, makes 3,5-DMP a particularly interesting system for study with neutron scattering techniques. Isotopic substitutions can then be used to decouple the various motions by virtue of the large difference in the masses. The large difference in the neutron scattering cross-sections between ^1H and ^2D makes selective observations of the different mobile centres possible *via* neutron scattering. In short, deuterium substitution makes the contribution from that centre almost disappear from the spectrum. We have performed such studies, making use of the quasielastic neutron scattering technique (QENS) at IN6, ILL (Grenoble, France), on the fully protonated system, and the NH/CD system on the NEAT spectrometer at BENSC (Berlin, Germany). We detail here a novel motion of the hydrogen-bonded protons that clearly accounts for the neutron scattering data of the fully protonated (IN6) and partially deuterated (NEAT) samples. There have been several recent reports of neutron scattering studies of proton dynamics in H-bonded and partially disordered systems. The studies of systems similar to 3,5-DMP, such as 2,6-dimethylpyrazine[3] and durene,[4] are of particular interest in that low temperature methyl tunnelling frequencies have been observed which were then related to the dynamics by computer modelling, whilst a QENS study of hydrogen dynamics in hexaaquo metal perchlorates has also been reported.[5]

Experimental

The samples were synthesised following established methods and characterised using elemental analysis and IR and Raman spectroscopies.[6]

The NEAT spectra were run with an incident wavelength of 5.1 Å and a resolution of *ca.* 90 μeV at three temperatures, $T = 250$, 275 and 300 K using a 1.24 g sample of the compound $C_5D_7HN_2$, (sample transmission 93.2%). Quasielastic broadening of the elastic line was observed at all of these temperatures and was modelled to a single Lorentzian together with a Gaussian elastic contribution, both were then convoluted with the instrument resolution function (Fig. 1). The resolution function was determined using a low temperature spectrum ($T = 2$ K) of the same sample.

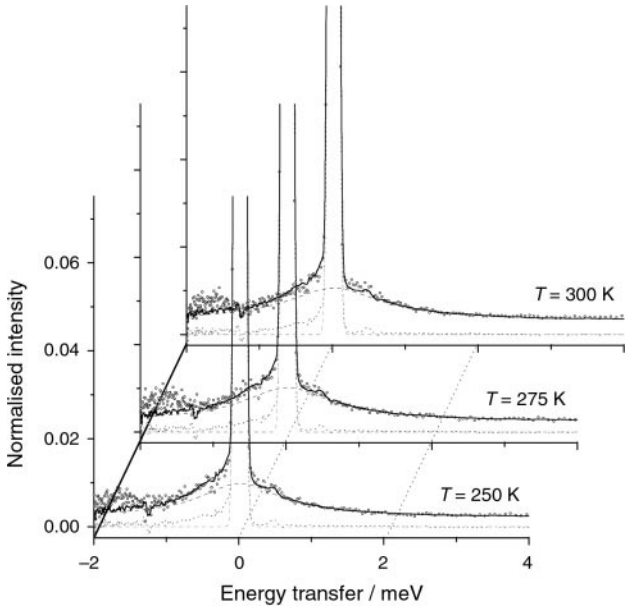

Fig. 1 QENS spectra of 3,5-DMP measured on NEAT over three temperatures as indicated. $\lambda = 5.1$ Å, $2\theta = 124.6°$, $Q_{elas} = 2.18$ Å^{-1}. The dotted line is the $T = 2$ K background measurement used as the resolution function. The dashed lines are the fitted model functions of $S_{el}(Q)\delta(\omega)$ and $S_{qel}(Q,\omega)$. The solid line is the convoluted model fitted to the data (open circles).

The IN6 data were obtained at only one temperature $T = 300$ K on a 0.34 g sample of $C_5H_8N_2$ (sample transmission 90.0%), also at an incident wavelength of 5.1 Å. Again, quasielastic scattering was observed and was modelled to elastic and quasielastic components in the above manner.

Results and discussion

A strength of QENS is that, *via* the incoherent structure factor $S_{inc}(Q,\omega)$, it can yield information relating to both the rate of a diffusive motion and its respective locality in space. This is because $S_{inc}(Q,\omega)$ is readily separable into an elastic component, $S_{el}(Q)\delta(\omega)$, and an inelastic component, $S_{qel}(Q,\omega)$, for motions that are located about a single point in space.[7] One outcome of this is that for liquid and gaseous samples, no $S_{el}(Q)\delta(\omega)$ is observed, due to recoil-type scattering events.[8] The ratio of the elastic component of scattering to the total scattering is the elastic incoherent structure factor (EISF), eqn. (1), and it provides model-dependent information on the nature of the motion leading to the quasielastic scattering,[9]

$$\mathrm{EISF}(Q) = \frac{I^{el}(Q)}{I^{el}(Q) + I^{qel}(Q)} \quad (1)$$

where $I^{el}(Q)$ represents the elastic contribution to the observed intensity and $I^{qel}(Q)$, the quasielastic component. The EISF for a N-jump process has been shown to have the form of a linear combination of Bessel functions incorporating the local hop radius, R (where R = half the hopping distance), eqn. (2).[10]

$$\mathrm{EISF}(Q) = \frac{1}{N}\sum_{P=1}^{N} \frac{\sin\left(2QR\sin\left(\frac{p\pi}{N}\right)\right)}{2QR\sin\left(\frac{p\pi}{N}\right)} \quad (2)$$

The EISF therefore typically falls away from unity (at $Q = 0$ Å^{-1}, $I^{qel} = 0$ and so the $\mathrm{EISF}_{(Q=0)} = 1$) and at a rate dependent upon the localised hopping motion. Two contributions to the observed $S_{inc}(Q,\omega)$ were initially envisioned for 3,5-DMP, due to (i) the three-fold methyl rotational motion, and (ii) the two-fold tautomeric hop of the amide proton. However, with an activation energy of $E_a = 46$ kJ mol^{-1} and a rate of only 10^3 s^{-1} (at $T = 300$ K), the tautomeric hopping motion was found to be beyond the range of QENS (which has a characteristic timescale of *ca.* 10^{12} s^{-1}) at the experimental temperatures. The complete data set obtained to date is shown in Fig. 2 in terms of the EISF at $T = 300$ K, where the lines represent different models for the measured data. The first point to be acknowledged from Fig. 2 is that for the fully protonated sample, neither of the EISF's relating to unique proton motions, the methyl rotor motion nor the tautomeric hops, is sufficient to describe the observed $S_{inc}(Q,\omega)$. The second point of interest is that the $S_{inc}(Q,\omega)$ behaviour is accurately reproduced in both the $C_5H_8N_2$ and $C_5D_7HN_2$ samples by a model that assumes that both the methyl tumbling and a *small* proton hop occur simultaneously, the latter probably driven by the axial rotation of the whole molecule by the torque induced by the methyl motions (Fig. 3). The non-fixed axis of rotation in CH_3 groups in which the centre of mass of the methyl unit moves sinusoidally, has been discussed in the literature.[11] This sinusoidal motion will induce a net torque on the 3,5-DMP molecule as a whole, thus giving rise to a whole body rotation, opposed by the hydrogen-bonding interactions to the other molecules within the trimer.

The simplification of $S_{inc}(Q,\omega)$ obtained upon deuteration of the methyl groups, provided direct access to the residual proton motions within the solid. With only the amide sites protonated, the resultant EISF was successfully fitted to a two-fold jump model,[9,10] with a jump distance of 0.60(5) Å (deviations from the model at $Q \leqslant 1$ Å^{-1} are due to the small quasielastic scattering intensity in this region of $<4\%$ of the total scattering). This contribution to $S_{inc}(Q,\omega)$ was subsequently verified by the inclusion of this hopping distance in the modelling of the fully protonated material, as detailed below. The most apparent rationalisation of the directly determined NH jump distance of 0.60(5) Å is as being due to a cross-H-bond motion, in which the proton hops between two sites on a single nitrogen atom. Assuming a rigid structural molecular body, this motion can be related to the whole body molecular rotation. The molecular angular displacement responsible for a hop of 0.60(5) Å at the amide site, was found to be 16.7°. Making use of this whole body motion results in a realistic EISF for the more complex case of the fully protonated sample, constructed with appropriate weightings for the various contributions of the non-equivalent protons (Fig. 2). This function accurately models the response observed in this

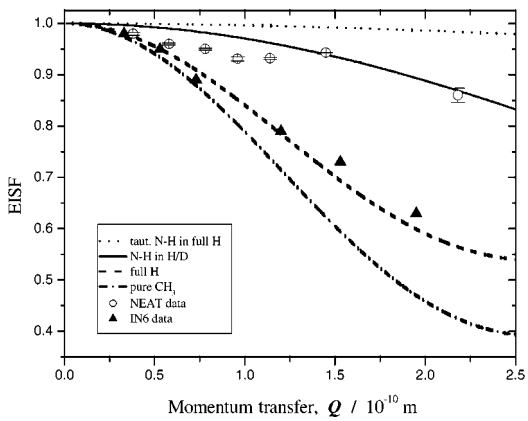

Fig. 2 Measured EISF for 3,5-DMP at $T = 300$ K. The data for the fully protonated sample (▲) are plotted along with that for the partially protonated material (○). The lines represent the response for various idealised jump models fitted to the experimental data. The dotted line is that for amide protons undergoing the tautomeric hop, whilst the dash-dotted line is that due to only the rotor motion of the methyl groups. The lines best representing the data, result from the model detailed in the text in which a small proton hop is coupled to the methyl rotation.

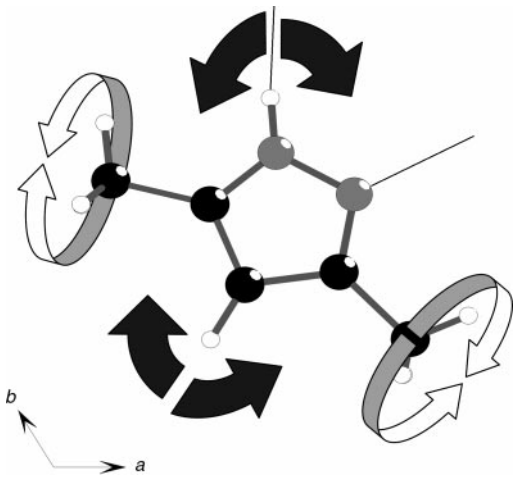

Fig. 3 Schematic diagram of the proposed molecular motion in 3,5-DMP as detailed in the text. Only a single molecule is shown, with the direction vectors to the nearest neighbours indicated by thin lines. Whole molecular rotary motion is indicated only at the H/D positions by solid arrows.

material and is clearly differentiated from models due to pure single-moded hopping motions (also shown in Fig. 2). A closer inspection of the crystal structure, indicates that the NH···N interactions are not perfectly linear, with a bond angle of 172°.[1] Therefore, two equivalent proton positions exist either side of the H-bond axis, with a divergent angle between them of 16°. We therefore propose that the QENS observed during this study on the two isotopically distinct samples of 3,5-DMP are due to the motion of the protons undergoing this two-fold hop in combination with the three-fold rotational motion of the CH_3/CD_3 groups. The presence of the amide proton sites perpendicular to the main H-bond axis has not previously been determined either by spectroscopic or diffraction methods, and it is as a result of the inherent sensitivity of the QENS technique that they have been located in this work. The scant crystallographic evidence for this motion is a result of the existing structure being determined with X-rays, for which an accurate hydrogen site determination is not possible. It is hoped that subsequent neutron diffraction data may clarify this issue with accurate proton site determinations.

It is of interest at this point to consider the relative moments of inertia of the molecular fragments in order to justify the above model for the proton motions observed in this material. Bond distances reported in the X-ray crystal structure were used with appropriate corrections for the CH distances.[1] Using the law of conservation of momentum, the moment of inertia, I_a, acting upon the molecule due to the motion of the centre of mass of the rotating methyl groups will be balanced by the moment of inertia due to the rotation of the whole molecule, I_p. The respective moments are $I_a = 3.647 \times 10^{-45}$ kg m^2 and $I_p = 1.545 \times 10^{-45}$ kg m^2 (where the radius of gyration of the methyl group centre of mass, from the molecular centre of mass, upon the whole body reorientation was assumed to be $R^{Me}_{com.} = 2.69$ Å). Given that the methyl groups may not be coupled and so act upon the molecule incoherently, the root mean square moment $\langle I_a \rangle = 1.824 \times 10^{-45}$ kg m^2 is more relevant for the *net* methyl-induced moment (calculated on the basis that I_a is the peak inertial moment for all $I = 0 < I_a$). The result that $\langle I_a \rangle > I_p$ indicates that the action of the methyl groups at a remote distance from the centre of molecular rotation, is sufficient to induce the whole body rotation, as assumed in the above model. Furthermore, it also indicates that the methyl motions need not act coherently to fulfil this criterion. The nature of the coupling between the methyl groups and/or the amide proton motion is still to be resolved.

In order to further test the validity of the model motion arrived at by considering only the experimental data, a full molecular dynamics (MD) simulation of the system was performed using the Cerius2 software package.[12] The standard force fields Dreiding2.21[13] and UFF[14] with periodic boundary conditions were used and the non-bonding interactions were calculated using the Ewald summation method.[15] In the UFF and Dreiding models, the van der Waal's components are obtained from the Lennard-Jones (6-12) potential, although this has been shown to systematically overestimate the repulsive components.[16] Therefore, we utilised a more reasonable repulsive potential with 6 as the exponential power in place of 12. In addition, the Coulomb interactions were obtained with the charge equilibrium method,[17] which considers both the molecular geometry and conformation and the atomic electronegativities. The Dreiding2.21 method was found to agree most closely with the experimentally determined crystal structure and so was used throughout the simulation. This force field was then used in a full MD simulation of the unit cell over 200 ps and 0.001 ps steps for a canonical ensemble at $T = 300$ K. The dominant motions observed in the simulation were of the methyl-free reorientation and an anisotropic motion of the whole molecule, the centre of mass moving sinusoidally with an amplitude of *ca.* 1.0 Å within the molecular plane and only *ca.* 0.3 Å perpendicular to it. The dominant whole molecule motion derived from the full MD simulation therefore corresponds well to the proposed model based upon the experimental data. The periodicity of the motion within the molecular plane was approximately 3.2 ps, consistent with an excitation of the order of 10's of cm^{-1} and a moment of inertia of $I_{calc} = 1.06 \times 10^{-45}$ kg m^2 (assuming motion about the molecular centre of mass). These values are reasonable, with I_{calc} being in very close agreement to the moment $\langle I_a \rangle$ estimated above. The MD data was then used to obtain an EISF of the MD motions using the program nMOLDYN for the fully protonated material.[18] The resulting function was found to closely resemble the experimentally determined EISF at values of $\boldsymbol{Q} < 1.5$ Å^{-1}, but to tail off to low values at higher $\boldsymbol{Q}$, indicating a non-localised motion in the MD results. This can be attributed as being due to limitations of the applied force field and basis set. By using the well-known Fourier transform relationship between the scattering function and a time-dependent pair correlation function $G(\boldsymbol{r},t)$,[19]

$$G(\boldsymbol{r},t) = \frac{\hbar}{(2\pi)^3} \int S(\boldsymbol{Q},\omega) \exp\{-i(\boldsymbol{Q}\cdot\boldsymbol{r} - \omega t)\} \mathrm{d}\boldsymbol{Q}\, \mathrm{d}\omega \qquad (3)$$

it can be seen that values of $S(\boldsymbol{Q},\omega)$ at large $\boldsymbol{Q}$ are related to $G(\boldsymbol{r},t)$ values at short t and at small values of $\boldsymbol{r}$. In brief, this relates to the correlations in the distribution function of molecular states at $t = 0$ about some point $\boldsymbol{r}$. For well localised motions, this is sharply peaked in t about $t = 0$, but for motions in which the centre of mass of the molecule undergoes what is essentially a random walk, then the elastic contribution to the EISF goes to zero at low t, resulting in an underestimation of the EISF at higher $\boldsymbol{Q}$. This problem is not so apparent at longer times, as the molecular reorientation itself is fast on the timescale of the random walk; the molecule gradually moving away form the initial zero point centre of mass position over several discrete reorientations. This feature highlights one limitation in applying a general force field to molecular systems, however, the fact that the dominant feature of the molecular reorientation lies within the molecular plane clearly supports the assumptions arrived at from the fitting of the experimental data to the two-fold jump model. In these respects, the MD simulations are in full accord with the experimental data given the constraints imposed by the generalised force field approach.

Finally, the width of the Lorentzian function fitted to $S_{qel}(\boldsymbol{Q},\omega)$ was found to vary with temperature in the NEAT experiment. An Arrhenius plot of the correlation times

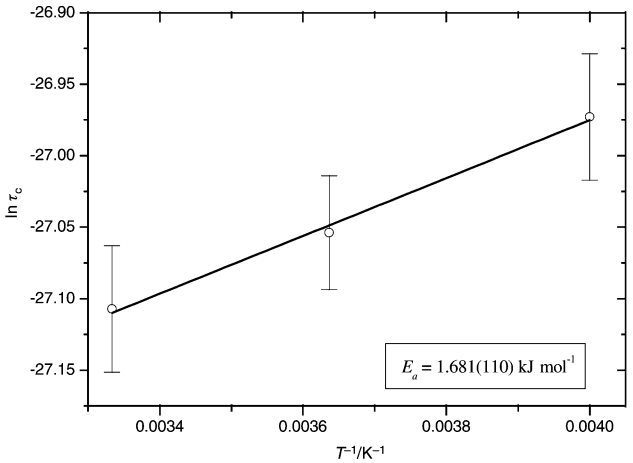

Fig. 4 Arrhenius plot for the proton jump across the hydrogen bond in 3,5-DMP, as measured in the $C_5D_7HN_2$ sample on NEAT. The data relate to the spectra shown in Fig. 1.

obtained from these widths, Fig. 4, gave an activation energy for the cross-H-bond motion of $E_a = 1.7(1)$ kJ mol^{-1}, a reasonable value for such a dynamic process and *ca.* 30 times less than that of the tautomeric hopping motion along the H-bond reported using NMR.[1] The pre-exponential factor (A) in the Arrhenius expression has been related by Brot to twice the frequency, ν, of the normal vibrational mode leading to the n-fold hopping observed in the QENS spectra,[20] in this case $A = 1.17(6) \times 10^{12}$ s^{-1} or $\nu = 20$ cm^{-1}. The accuracy of this correlation has been found to be accurate to a first approximation in other studies,[21] and is comparable to the results of both the molecular simulation performed herein and recently published restricted Hartree–Fock calculations, for which several collective trimer-based modes were found below 100 cm^{-1}.[22]

Conclusion

The use of isotopic variants and QENS has shown that the hydrogen-bonded system 3,5-DMP undergoes small two-fold hopping motions, consistent with a uniaxial rotation of the whole molecular unit, as a result of the non-linearity of the hydrogen bond. The driving force for this hopping motion appears to incorporate the CH_3 rotor groups, although the coupling of these two motions has not been directly proven. We plan further experiments on the system using additional isotopic substitutions to confirm the presence of this coupling and hope also to obtain better quality data for the NH/CD sample, such that the anomalies presented by the small scattering intensity at low $\boldsymbol{Q}$ can be eliminated (at present the low $\boldsymbol{Q}$ data for the $C_5D_7HN_2$ sample displays a large scatter due to the experimental problems discussed in the text). However, as the EISF, by definition, passes through the value of 1 for zero momentum transfer, $\boldsymbol{Q} = 0$ Å^{-1}, the case for these points being statistical outliers is strengthened. Additionally, with accurate neutron diffraction data, we hope to directly demonstrate the presence of the two-fold amide proton sites across the H-bond, as well as the axial whole body molecular rotation.

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