Molecular dynamics of the self-organising strong hydrogen bonded 3,5-dimethylpyrazole

John A. Stride,*[ab] Upali A. Jayasooriya,[c] Jean-Marc Zanotti[d] and Remi Kahn[d]

Received (in Montpellier, France) 11th April 2005, Accepted 12th December 2005
First published as an Advance Article on the web 26th January 2006
DOI: 10.1039/b504987c

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. We have previously reported the use of quasielastic neutron scattering (QENS) to study 3,5-dimethylpyrazole which showed that the hydrogen-bonded amide protons within individual trimer units undergo a short range hopping motion between two equivalent sites straddling the direct N···H hydrogen-bond axis. This work was the first report of such a novel dynamic process in this family of materials. The current work extends the earlier study with additional QENS measurements of other isotopic variants, providing information on the methyl group dynamics, which lead us to the conclusion that the short-range amide motions are decoupled from the methyl torsions. Whilst the methyl groups were found to undergo 3-fold diffusive hopping motions on the QENS timescale ($\sim 10^{11}$–12^{12} s^{-1}), an appreciable non-mobile fraction of methyl groups was also detected at all temperatures studied.

Introduction

The self-organising system 3,5-dimethylpyrazole (3,5-DMP) provides an ideal model for studying the dynamics of H-bonding interactions using the technique of quasi-elastic neutron scattering (QENS). The structure has been accurately determined by X-ray diffraction, which shows that the molecules lie in planar three-fold units within the *ab*-plane and are linked *via* NH···N bonds along the vertices of equilateral triangles.[1] The tautomeric 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, having an associated activation energy of 46 kJ mol^{-1}.[1] Further, the family of methylpyrazoles to which 3,5-DMP belongs displays a propensity to self-organise into such multimember units and differences in the inter-molecular interactions within these compounds are believed to underpin the marked differences in physical properties such as the melting points.[2] In an earlier QENS study of 3,5-DMP, the amide proton was found to undergo a 0.60(5) Å hopping motion between two minima, either side of the direct H···N direction vector.[3] The activation energy for this motion was determined to be 1.7(1) kJ mol^{-1} and a rationale incorporating the coupling between the methyl group torsions and the in-plane whole body rotations was proposed. The present work makes use of the non-substituted $(CH_3)_2C_3HN_2H$ (**1**) and the isotopic variant $(CH_3)_2C_3HN_2D$ (**2**) to probe the motions of both the methyl groups and the whole body motions to complement the previous study of the amide proton motions. The present study therefore provides a rigorous evaluation of the proposed coupling of methyl librations and the whole body dynamics.

Neutron methods are particularly suited to the study of hydrogen-bonded systems such as 3,5-DMP as both spatial and temporal dimensions of molecular motions can be probed simultaneously. In addition, the large difference in the neutron scattering cross-sections between ^1H and ^2D provides the possibility of using isotopic variants to isolate specific motions. In short, deuterium substitution makes the scattering contribution from the deuterated centre effectively disappear. This is demonstrated very clearly in our previous work.[3] Here, we have again made use of the QENS technique, but this time at the cold neutron time-of-flight (TOF) spectrometer, MIBEMOL at the LLB (Saclay, France),[4] to study both the fully protonated (NH/CH), **1**, and the ND/CH, **2**, systems. These measurements extend the range of the previous study by focusing on the methyl torsions and the in-plane molecular re-orientation.

Experimental

The samples were synthesised following established methods and characterised using elemental analysis and IR and Raman spectroscopies.[5]

Quasielastic neutron measurements were performed on the cold time-of-flight spectrometer MIBEMOL at the Laboratoire Léon Brillouin, situated at the Orphée reactor, Saclay, France,[4] at an incident wavelength of 5.0 Å and a resolution (FWHM) of 185 μeV, corresponding to the highest available count rate for this instrument. The samples (**1**: 554 mg; **2**: 679

---

[a] *School of Chemistry, University of New South Wales, Sydney, NSW 2052, Australia. E-mail: j.stride@unsw.edu.au; Fax: +61 (0)2 9385 4672; Tel: +61 (0)2 9385 6141*
[b] *Bragg Institute, Australian Nuclear Science and Technology Organisation, PMB 1, Menai, NSW 2234, Australia*
[c] *School of Chemical Sciences and Pharmacy, University of East Anglia, Norwich, UK NR4 7TJ*
[d] *Laboratoire Léon Brillouin, (CEA-CNRS)CEA Saclay, (CEA-CNRS), 91191 Gif-sur-Yvette Cedex, France*

mg) were loaded into thin-walled Al cans of thickness 0.2 mm, giving a scattering power of ~11% for both samples, when placed at 135° to the incident beam, such that the detected neutrons were measured in transmission through the sample. The high transmission of *ca.* 90% was used to reduce multiple scattering events within the sample. The MIBEMOL spectrometer uses a large array of 432 ^{3}He detectors, covering the angular range of $23.5° < 2\theta < 141.8°$ (where 2θ is the scattering angle); individual spectra were corrected for relative differences in efficiency by using a vanadium sample which scatters isotropically. The spectrum of the empty Al can was then removed from that of the sample to yield 10 spectra at each temperature, with each spectrum covering a distinct range in momentum transfer. The spectrum around 90° was found to be contaminated by Bragg peaks, whilst that at 137.0° was obscured due to self-absorption of the sample. Therefore both were discarded from further data analysis. This resulted in eight incoherent quasielastic spectra, obtained at temperatures in the range of T = 225–350 K, controlled by a closed cycle thermal bath.

The QENS data were iteratively fitted to a scattering model consisting of a Gaussian elastic component, a Lorentzian quasielastic component and a linear background, see below. The data were of sufficient quality to allow for the free fitting of all six parameters (peak heights and FWHM's and the two points to determine the linear background at the spectral extremes).

Inelastic neutron scattering data on **1** were measured in reflection on the thermal neutron TOF spectrometer IN4 at the ILL, Grenoble, France,[6] at an incident wavelength of 1.3 Å and resolution with FWHM at the elastic line of 2.3 meV. The sample (524 mg) was loaded into a thin-walled Al can of thickness 0.2 mm (12% scatterer) and placed at an angle of 45° to the incident beam, with a 0.5 mm Cd plate fixed onto the back-side of the can. This allowed access into approximately half of the 300 ^{3}He detectors of IN4, resulting in a scattering angular range of $45° < 2\theta < 120.3°$, with each detector normalised for relative efficiency with a vanadium sample.

Results and discussion

The principle of QENS is detailed in our previous work[3] and so will not be repeated here. The QENS technique makes use of the broadening of the peak due to neutrons scattered elastically from the sample from a quasi-continuum of states brought about by thermal diffusive motions within the material. By carefully determining the relative contributions, both purely elastic and quasielastic, both spatial and temporal information on the diffusive motion can be extracted from the total scattering $S(Q,\omega)$ within the quasielastic region, eqn (1).

$$S(Q,\omega) = A_0(Q)\delta(\omega) + [1 - A_0(Q)]\mathrm{L}(\omega) \qquad (1)$$

It was found that eqn (1), in which $A_0(Q)$ is the elastic incoherent structure factor (EISF), with $\delta(\omega)$ the purely elastic delta-function, $\delta(\omega \neq 0) = 0$, $\delta(\omega = 0) = 1$, $L(\omega)$ is a Lorentzian function of full half width at half maximum (FWHM) Δ(meV) and of integrated intensity $I^{\exp} = I^{qe} \times \beta\left(\beta = \frac{1}{kT}\ \mathrm{meV}\right)$, was sufficient to fit the experimental data when convoluted with the instrument resolution function (approximated to a Gaussian). No additional contributions due to inelastic scattering or general zero-point motions (Debye–Waller factor) were required as $\omega \ll kT$ at all of the temperatures used. The data can be further reduced to the EISF and Arrhenius plots, from which one can obtain a diffusive jump radius and an activation energy for that motion respectively.[7] The EISF is simply the ratio of the quasielastic intensity to the total scattered intensity, and is shown in Fig. 1 for the two samples, **1** and **2** at T = 300 K. The EISF's are fitted with a model function which incorporates all of the proton motions present: the methyl rotations and the two proton motions (amide and ring) induced by the whole molecule rotation about the normal to the molecular plane.[3] An additional term allowing for only some fraction of the Me's to be mobile, n, is also included resulting in the general expression

$$\mathrm{EISF} = \frac{1}{7+\xi}\left\{\left(\frac{1}{2}+\frac{j_{0(R_\mathrm{r})}}{2}\right)+\xi\left(\frac{1}{2}+\frac{j_{0(R_\mathrm{NH})}}{2}\right)\right.$$
$$\left.+6\left[(1-n)+n\left(\frac{1}{3}+\frac{2j_{0(R_\mathrm{Me})}}{3}\right)\right]\right\} \qquad (2)$$

where $j_0(R_\mathrm{i}) = \frac{\sin\left(2QR_i\sin\left(\frac{\pi}{p}\right)\right)}{2QR_i\sin\left(\frac{\pi}{p}\right)}$, for a p-fold jump and ξ = 0 for **2** and 1 for **1** accounting for the presence of a ring proton in **1**, or not, as in **2**.

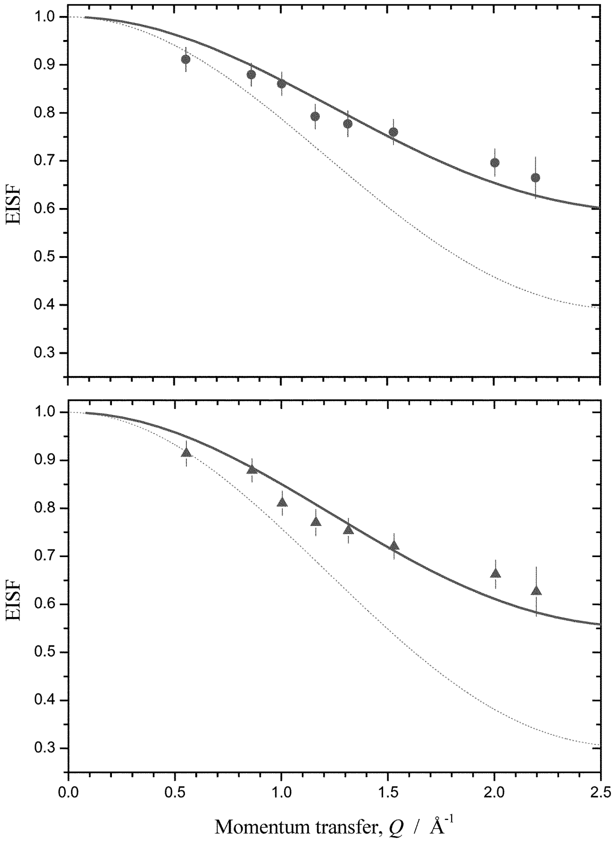

Fig. 1 EISF obtained from QENS data of **1** (*upper panel*) and **2** (*lower panel*) measured on MIBEMOL at T = 300 K and λ_i = 5.0 Å. The dotted line is the response due to an ideal methyl group rotation. The solid line is the fit through the data points for the generalised expression given in the text.

The jump radii for each motion, as designated by R_{Me} for the methyl groups, R_{NH} for the amide and R_{r} for the ring proton hopping motions, respectively, are intrinsically accounted for in this model. However, the effect of the molecular rotation on the methyl groups (Me) is neglected, as the predominant hopping motion of the Me protons is about the Me torsional axis. In order to reduce the number of fit parameters, the jump radii were fixed to standard values, R_{NH} and R_{r} were determined from the motion of the amide motion (see below) and a typical value of 0.99 Å was used for R_{Me}.[8] Given that the two isotopic variants studied herein differ only in the amide hydrogen isotope, the difference in the EISF's should reflect this and so be consistent with the previously reported data on **3**,[3] as is shown in Fig. 2. Clearly, a very good agreement between the two data sets exists, allowing the previously determined value of $R_{\mathrm{NH}} = 0.30(3)$ Å to be refined to 0.291(5) Å, relating to a jump distance of 0.582(10) Å. This value was used directly in eqn (2) as R_{NH} and also allowed for the direct determination of R_{r}. Hence the only fit parameter in eqn (1) was n, the mobile fraction of Me protons, which is found to show some temperature dependence. A plot of the temperature dependence of n across the range studied is shown in Fig. 3 for both **1** and **2** and clearly indicates that below $T \approx 265$ K only 49(1)% of all Me's are undergoing a 3-fold hopping motion. This is probably a result of steric hindrance due to intermolecular interactions within the molecular planes and of course reflects the situation where, on average, one of the two Me's on each molecule undergoes the diffusive motion, with the other sterically locked within the QENS timeframe, *i.e.* slower than $10^{11}\ \mathrm{s}^{-1}$. However, as the temperature increased beyond $T \approx 265$ K, so the mobile fraction was found to increase to 60(2)% indicating that for $>20\%$ of the molecules, the previously locked Me's are freed on the measurement timescale. To the knowledge of the authors, there is no structural or indeed corresponding spectroscopic evidence of this apparent transition; indeed it is probably dynamic in nature and so invisible to temporally-averaged structural methods, falling at different temperatures, corresponding to the dynamic timescale of the spectroscopic probe used.

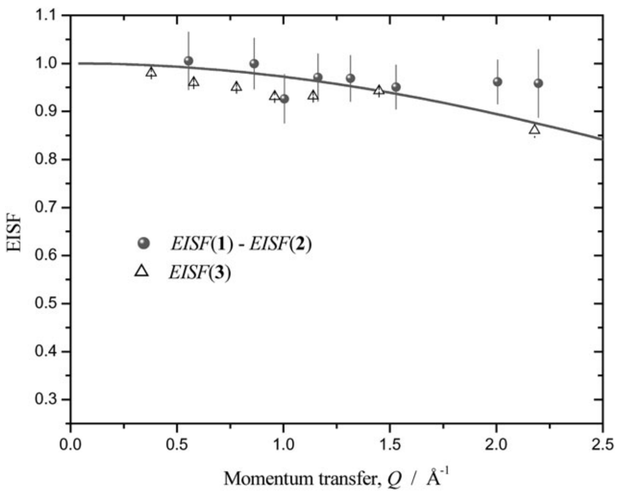

Fig. 2 EISF due purely to the amide hopping across the direct intermolecular hydrogen bond. The circles are the difference in the response from **1** and **2** obtained in this work and the triangles are those points reported previously on the third isotopic variant **3**.

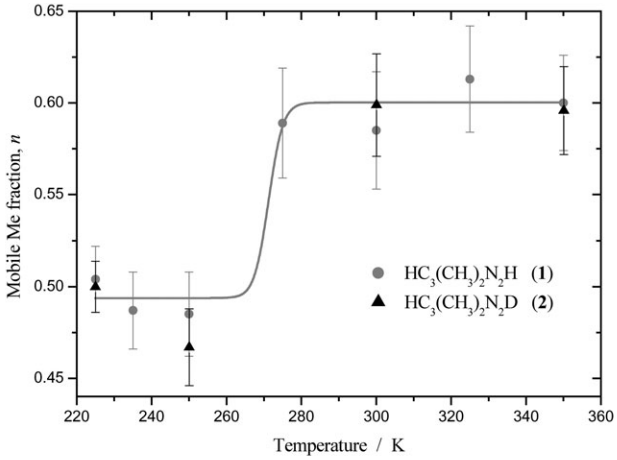

Fig. 3 Temperature dependence of the mobile fraction of methyl groups, n, in the two samples **1** and **2**.

The global activation energy for the dynamic processes observed in QENS can be obtained by using an Arrhenius plot of the correlation times obtained from the widths of the quasielastic components ($\tau_{\mathrm{c}} = 3h/4\pi\Delta$, Δ = FWHM) at each temperature, Fig. 4. A good agreement between **1** and **2** was observed, with the activation energy $E_{\mathrm{a}} = 5.0(4)\ \mathrm{kJ\ mol}^{-1}$ and a pre-exponential factor corresponding to a vibrational mode at 18.7(30) meV.[9] Both are in accord with literature values for Me torsional hopping and the τ_{Me} vibration. Indeed, the low temperature inelastic spectrum of **1** obtained on IN4, Fig. 5, clearly displays two such τ_{Me} modes at 15.6 and 18.8 meV. In addition, the pre-exponential term reported in the study of **3** relates to a vibrational mode at 2.4(1) meV, which corresponds to the broad band of excitations below *ca.* 5 meV observed in the INS spectrum of **1**. This spectral intensity is thought to consist predominantly of the acoustic (translational) phonon modes and the low energy whole body rotations. One difference of INS to other spectroscopic probes of vibrational/librational spectra is the absence of selection rules, the measured spectral density being a direct product of the nuclear neutron cross-section and the amplitude of vibration/libration. Hence Me torsional modes which construe zero dipole moment or polarizability change are usually intense features in INS spectra, along with other optically weak modes which may nevertheless posses a considerable amplitude of motion of nuclei of significant cross-section. The present data are best interpreted with reference to the work of Orza *et al.*[10] covering the infrared and Raman spectra of 3,5-DMP in the solid, liquid, solution and vapour phases (along with isotopic variants), coupled to normal mode calculations of the system. Interestingly, these authors reported the presence of two strong peaks in the Raman spectra at 10.2 and 14.3 meV (1 meV = 8.065 cm^{-1}) being intrinsic to the presence of the trimeric motif and assigned to the deformation and breathing modes of the trimer, respectively. Such modes would be expected to posses a large spectral density in the INS spectrum courtesy of the concerted motion of all of the protons (the

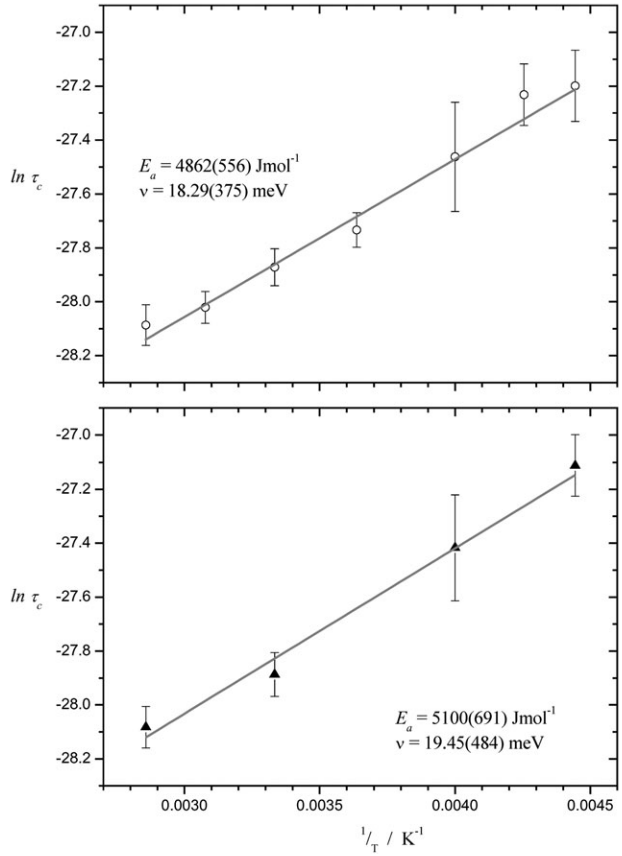

Fig. 4 Arrhenius plots averaged across Q for the dynamic processes observed in **1** (*upper panel*) and **2** (*lower panel*). The methyl group dynamics dominate both scenarios, with a common activation energy of 5 kJ mol^{-1}.

dominant term in the nuclear cross-section due to the large incoherent cross-section of ^{1}H). Under the relaxed resolution of the IN4 spectrometer, these two modes appear as a single, intense and broad feature at the mean value of the two reported Raman modes, 12.2 meV. Note that IR and Raman spectroscopies sample only the modes close to the Brillouin zone (B.Z.) centre while the INS spectra measure these modes summed across the zone. The remaining modes are also in accord with the Raman spectra, namely the out-of-plane Me bending mode at 27 meV (Orza: 26.3 meV), whilst the peaks at 33.1 and 35.4 meV correspond to very weakly Raman active modes visible in the spectrum of **1** at *ca.* 32.7 and 35 meV, (Fig. 7, top, of ref. 10). The most obvious assignment of these bands is to the in-plane Me bending modes, again the presence of two peaks indicating the lowered symmetry of the Me sites with respect to that of the reported crystal structure.[1]

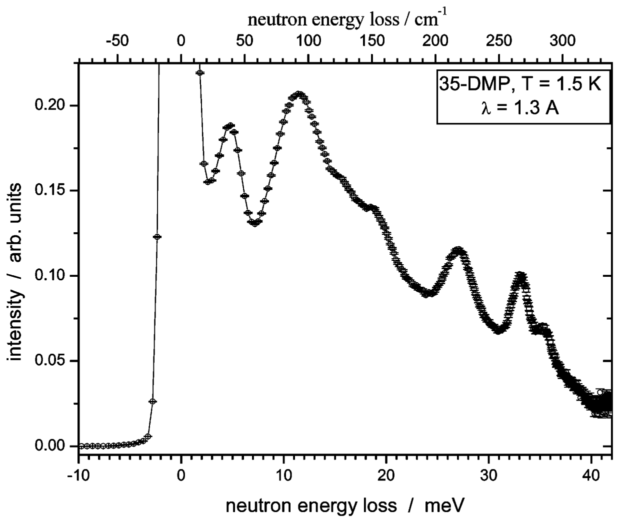

Fig. 5 Inelastic neutron scattering spectrum of **1** obtained on IN4 at λ_i = 1.3 Å and T = 1.5 K.

The observation of discrete energy-scales for the Me- and amide-centered librations, indicate that the Me dynamics are largely decoupled from the whole body rotations of the planar molecular rings. The activation energy for the Me-dominated dynamics is 2.98(10) times that of the purely amide proton hopping induced by the whole body molecular rotations and translations, with the respective modes also well separated in the inelastic spectrum. The presence of two broad features in the τ_{Me} region (15–20 meV) indicates that, in 3,5-DMP, the Me's occupy a range of librational potentials, but which remain unresolved in the present data, an indication of the lower supra-molecular symmetry than that proposed in the room temperature crystal structure. Any dispersion of these modes across the B.Z. is unlikely to be of sufficient magnitude to explain this band broadening; methyl torsions in molecular systems typically have dispersion effects <1 meV from the Γ-point position, and so fall within the instrumental resolution at the wavelength used. No attempt was made to anneal the sample at low temperature and the possibility of low temperature structural phase transitions cannot be neglected. However, the extrapolation of the elevated temperature QENS data to the low temperature INS data is valid in terms of generalised assignments, in the absence of an accurate low temperature structure.

The librational diffusion of the tautomeric amide proton perpendicular to the main hydrogen bond vector and in the molecular plane has not been explored experimentally in reports detailing the proton transfer processes in the supramolecular cyclic pyrazoles.[11–13] QENS provides an experimental probe of this motion which complements those results obtained from NMR in mapping out the potential energy landscape of proton transfer, with verification of simplified computational models which indicate some degree of transverse proton motion and/or molecular rearrangement (heavy atom relaxation).[14] The N–H$\cdots$N bond angle is not constant across the series of cyclic pyrazoles: the similar trimeric system, 4-methylpyrazole, for example, has a bond angle of 167.2(9)°[2] which corresponds to a proton hopping distance of 0.92(6) Å, clearly experimentally discernible from the case of 3,5-DMP examined herein. Whilst the perpendicular amide libration may appear to be of secondary importance to more direct modes such as the trimer breathing mode as a precursor to proton exchange, a complete picture of tautomerism cannot ignore this trajectory along the potential energy surface of the amide protons, a low energy pathway which brings the N–H$\cdots$N units closer at the mid-point of the libration.

Conclusion

The cyclic pyrazoles are an intriguing family of relatively simple organic molecules displaying a complex interaction of attractive dipolar hydrogen-bonding and repulsive intermolecular interactions, leading to a range of structural motifs and unusual physical properties. The observation in 3,5-DMP of a transverse component in the dynamics of the tautomeric proton as a result of whole body rotations in the solid state has opened an additional degree of freedom in models of intermolecular proton transfer, believed up to now to occur only coherently in the trimeric cycles. Whilst the energy scale of this motion is naturally much lower than that of proton transfer, 1.7 *vs.* 46 kJ mol^{-1}, it defines an additional dimension in the potential energy landscape and may be of considerable importance in systems in which the non-linearity of the hydrogen bond is more pronounced.

The Me groups in 3,5-DMP also undergo librational/torsional dynamics for which neutron scattering techniques are ideally suited. The Me's undergo relatively free rotation (E_a = 5 kJ mol^{-1}), although some temperature-dependent fraction appears to remain hindered to the extent of appearing static on the QENS timescale. That different Me's experience small differences in the rotational potentials is somewhat reinforced by the INS measurements, indicating that a range of librational frequencies exist at low temperature. Accurate temperature-dependent crystallographic data on these systems would help to clarify the picture of the dynamics obtained from these spectroscopic measurements.

References

1 J. A. S. Smith, B. Wehrle, F. Aguilar-Parilla, H. H. Limbach, M. Foces-Foces, F. H. Cano, J. Elguero, A. Baldy, M. Pierrot, M. M. T. Khurshid and J. B. Larcombe-McDouall, *J. Am. Chem. Soc.*, 1989, **111**, 7304.
2 R. Goddard, R. M. Claramunt, C. Escolástico and J. Elguero, *New J. Chem.*, 1999, **23**, 237.
3 J. A. Stride, U. A. Jayasooriya, N. Mbogo, R. P. White, B. Nicolaï and G. J. Kearley, *New J. Chem.*, 2001, **25**, 1069.
4 http://www-llb.cea.fr/spectros/pdf/mibemol-llb.pdf.
5 (*a*) R. H. Wiley and P. E. Hexener, *Org. Synth.*, 1963, **Coll. Vol. IV**, 351; (*b*) F. N. Mbogo, PhD Thesis, University of East Anglia, 1992.
6 http://www.ill.fr/YellowBook/IN4/.
7 M. Bee, *Quasielastic Neutron Scattering: Principles and Applications in Solid State Chemistry, Biology and Materials Science*, Adam Hilger Ltd, Bristol, 1988.
8 M. Kolarschik and G. Voll, *Physica B*, 1996, **222**, 1.
9 C. Brot, *Chem. Phys. Lett.*, 1969, **3**, 319.
10 J. M. Orza, M. V. Garcia, I. Alkorta and J. Elguero, *Spectrochim. Acta, Part A*, 2000, **56**, 1469.
11 C. Foces-Foces, F. H. Cano, M. V. Roux, F. Aguilar-Parrilla and H. H. Limbach, *J. Heterocycl. Chem.*, 1995, **32**, 451.
12 F. Aguilar-Parrilla, O. Klein, J. Elguero and H. H. Limbach, *Ber. Bunsen-Ges. Phys. Chem.*, 1997, **101**, 889.
13 O. Klein, F. Aguilar-Parrilla, J. M. Lopez, N. Jagerovic, J. Elguero and H. H. Limbach, *J. Am. Chem. Soc.*, 2004, **126**, 11718.
14 J. L. G. de Paz, J. Elguero, C. Foces-Foces, A. L. Llamas-Saiz, F. Aguilar-Parrilla, O. Klein and H. H. Limbach, *J. Chem. Soc., Perkin Trans. 2*, 1997, 101.