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# Microwave spectra, molecular geometries, and internal rotation of CH<sub>3</sub> in *N*-methylimidazole· ·H<sub>2</sub>O and 2-methylimidazole· ·H<sub>2</sub>O Complexes†

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Broadband microwave spectra have been recorded between 7.0 and 18.5 GHz for *N*-methylimidazole· ·H<sub>2</sub>O and 2-methylimidazole· ·H<sub>2</sub>O complexes. Each complex was generated by co-expansion of low concentrations of methylimidazole and H<sub>2</sub>O in argon buffer gas. The rotational spectra of five isotopologues of each complex have been assigned and analysed to determine rotational constants ( $A_0$ ,  $B_0$ ,  $C_0$ ), centrifugal distortion constants ( $D_J$ ,  $D_{JK}$ ) and parameters that describe the internal rotation of the CH<sub>3</sub> group. The results allow the determination of parameters in the ( $r_0$ ) molecular geometry of each complex. H<sub>2</sub>O is the hydrogen bond donor and the pyridinic nitrogen of imidazole is the hydrogen bond acceptor in each case. The  $\angle(\text{O}-\text{H}_b \cdots \text{N}_3)$  angles are 177(5)° and 166.3(28)° for *N*-methylimidazole· ·H<sub>2</sub>O and 2-methylimidazole· ·H<sub>2</sub>O respectively. These results are consistent with the presence of a weak electrostatic interaction between the oxygen atom of H<sub>2</sub>O and the hydrogen atom (or CH<sub>3</sub> group) attached to the C2 carbon atom of imidazole, and with the results of density functional theory calculations. The ( $V_3$ ) barrier to internal rotation of the CH<sub>3</sub> group within *N*-methylimidazole· ·H<sub>2</sub>O is essentially unchanged from the value of this parameter for the *N*-methylimidazole monomer. The same parameter is significantly higher for the 2-methylimidazole· ·H<sub>2</sub>O complex than for the 2-methylimidazole monomer as a consequence of the weak electrostatic interaction between the O atom and the CH<sub>3</sub> group of 2-methylimidazole.

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## 1. Introduction

Imidazole rings are found within the anti-fungal drug clotrimazole,<sup>1</sup> the antibiotic and antiprotozoal drug metronidazole<sup>2</sup> and various antivirals inhibiting replication of hepatitis viruses (HAV, HBV, HCV *etc.*).<sup>3</sup> In biological environments, these molecules primarily interact with others through hydrogen bonds. Gas phase spectroscopic experiments provide microscopic and selective insight into individual hydrogen bonding interactions. It is thereby possible to distinguish the microscopic properties of individual hydrogen bonds from properties that result from synergistic (cooperative or competitive) effects that operate at the level of an entire network.

A recent work by our group described the geometries of two isomers of a complex formed between imidazole and H<sub>2</sub>O.<sup>4</sup> One of these isomers (denoted as imid· ·H<sub>2</sub>O) contains a hydrogen bond between H<sub>2</sub>O and the pyridinic nitrogen, N3, of the imidazole ring (atom numbering of imidazole is shown in Fig. 1). This work and recent results from theoretical calculations<sup>5</sup> confirm similarities between the structure of imid· ·H<sub>2</sub>O and those of other complexes formed of water and a heteroaromatic molecule such as thiazole,<sup>6</sup> isoxazole<sup>7</sup> or pyrimidine.<sup>8</sup> Specifically, structures of these complexes usually feature H<sub>2</sub>O acting as a proton donor, a heteroatom of the ring acting as a proton acceptor and a secondary interaction where the oxygen atom of water binds to a hydrogen atom of a C–H group on the ring. The present work will show that the geometry of a complex formed of 2-methylimidazole (2-MI) and water is determined by interactions which are very similar to those described above. However, in this case, the secondary interaction is between the oxygen atom of H<sub>2</sub>O and the CH<sub>3</sub> group attached to C2 of the imidazole ring.

An aim of the present work is to perform the first experimental determination of the change in a ( $V_3$ ) barrier to internal rotation of CH<sub>3</sub> which is caused by formation of an electrostatic

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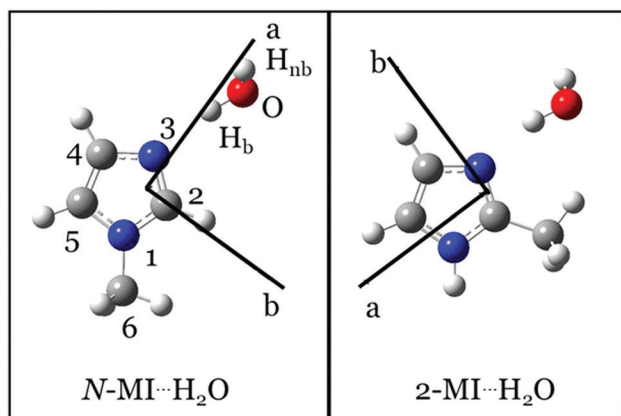


Fig. 1 Equilibrium ( $r_e$ ) geometries of  $N$ -MI··H<sub>2</sub>O (left) and 2-MI··H<sub>2</sub>O (right) calculated at the  $\omega$ B97XD/aug-cc-pVQZ level.

interaction between H<sub>2</sub>O and a CH<sub>3</sub> group. It thus begins experimental investigation of how electrostatic interactions of CH<sub>3</sub> with one or more H<sub>2</sub>O molecules influence barriers to internal rotation. Alongside works that have explored the geometrical preferences of water-containing molecular complexes, the present work contributes to knowledge of the effects of solvation on conformational flexibility. It will be shown that  $V_3$  of the CH<sub>3</sub> group of 2-MI increases significantly on formation of a complex between H<sub>2</sub>O and 2-MI. In contrast,  $V_3$  of CH<sub>3</sub> in  $N$ -MI··H<sub>2</sub>O (where  $N$ -MI is  $N$ -methylimidazole) is very similar to the value of this parameter in the isolated  $N$ -MI monomer.<sup>9</sup> It will be shown that these observations are consistent with the geometries of the complexes. An electrostatic (through-space) interaction between the H<sub>2</sub>O molecule and CH<sub>3</sub> group is present in the geometry of 2-MI··H<sub>2</sub>O but not in  $N$ -MI··H<sub>2</sub>O. Experimentally-determined structural parameters that define the position and orientation of the water molecule will also be reported for both the complexes examined by this work.

## 2. Experimental and theoretical methods

The microwave spectrum of each complex was recorded while probing a gaseous sample containing low concentrations of methylimidazole and water in argon. Experiments to study  $N$ -MI··H<sub>2</sub>O vaporised  $N$ -methylimidazole (Sigma Aldrich, 99%) from a reservoir, heated to a temperature of 90 °C, into a flow of argon (BOC, 99.998%) containing water vapour. Supersonic expansion ensued after injection of the gas sample into an evacuated chamber from a pulsed nozzle (Parker, Series 9) using a backing pressure of 5 bar. Separate experiments to generate and study 2-MI··H<sub>2</sub>O used a focussed laser pulse to vaporise the substance from a cylindrical target rod into the argon/H<sub>2</sub>O flow. The backing pressure of argon used for the experiments to study 2-MI··H<sub>2</sub>O was 7 bar. The target rod was prepared to contain 2-methylimidazole (Sigma Aldrich, 98%) and copper in a 1:1 ratio by mass. This rod composition was found to maximise signal intensities for transitions in the

spectrum of 2-MI··H<sub>2</sub>O. The fundamental (1064 nm, 43 mJ pulse<sup>-1</sup>) of a Nd:YAG (Minilite II) was used for the laser vaporisation. Supersonic expansion of each gas sample led to an effective rotational temperature of approximately 3 K (estimated from the relative intensities of observed transitions). The heated reservoir, laser vaporisation source and the CP-FTMW spectrometer used by the present experiments have been described in detail elsewhere.<sup>10–12</sup> Immediately prior to experiments that used either D<sub>2</sub>O (Sigma-Aldrich, 99.9% D atom) or H<sub>2</sub><sup>18</sup>O (Sigma Aldrich, 97% <sup>18</sup>O atom), a syringe was used to introduce a small amount of the isotopically-enriched sample into the gas line immediately before the pulsed nozzle. Typically, the introduction of 0.1 mL of isotopically-enriched sample allowed for an experiment to continue for 6 hours or longer. It was occasionally necessary to pause operation and add an additional dose of 0.1 mL in order to extend the period over which the spectrum was acquired.

The rotational spectra of  $N$ -MI··H<sub>2</sub>O and 2-MI··H<sub>2</sub>O were recorded between 7.0 and 18.5 GHz. The CP-FTMW spectrometer mixes a microwave pulse that linearly sweeps from 12.0 to 0.5 GHz over a duration of 1  $\mu$ s against the 19 GHz reference signal of a Phase-locked Dielectric Resonant Oscillator (PDRO). Chirped pulses are generated from a 20 GS s<sup>-1</sup> arbitrary waveform generator (AWG) (Tektronix AWG 7102). A low pass filter selects the 7.0–18.5 GHz sideband which is amplified by a 300 W Traveling-Wave Tube Amplifier (TWT) prior to its introduction from a horn antenna into the vacuum chamber perpendicular to the direction of the expanding gas jet. Subsequent to the molecular polarisation, the free induction decay (which has duration of 20  $\mu$ s) of the molecular emission is detected by a second horn antenna and digitally recorded by a 100 GS s<sup>-1</sup> oscilloscope (Tektronix DPO72304XS). Successive free induction decays are co-added in the time domain. The polarisation pulse and free induction decay are each sufficiently short that eight distinct measurements of the broadband microwave spectrum are routinely performed following each gas introduction pulse while taking advantage of the “fast frame” mode of the oscilloscope. A high resolution window function was used by the Fourier transform employed herein such that linewidths of transitions in the frequency domain spectrum are approximately 100 kHz for a well-isolated line at full-width half-maximum. This linewidth correlates with an estimated accuracy of 10 kHz in the measurement of line centre frequencies. Phase coherence in the time domain and accuracy in transition frequencies were provided by an Rb-clock (SRS FS725) to which the AWG, the PDRO and the oscilloscope were phase-locked.

Optimisations of the geometries of  $N$ -MI··H<sub>2</sub>O and 2-MI··H<sub>2</sub>O were performed using the Gaussian09 package.<sup>13</sup> The harmonic hybrid functional<sup>14–16</sup> of Becke, Lee, Yang, Parr, B3LYP, in conjunction with Grimme's dispersion correction effects<sup>17</sup> and damping function,<sup>18</sup> D3BJ, was initially used alongside Dunning's<sup>19,20</sup> augmented triple- $\zeta$  aug-cc-pVTZ basis set. Geometry optimisations were subsequently performed with the long range corrected hybrid functional,<sup>21</sup>  $\omega$ B97X-D, of Chai and Gordon and Dunning's augmented quadrupole- $\zeta$  basis set



with tight convergence criteria. The same level of theory was used during a previous study of  $\text{imid} \cdot \cdot \text{H}_2\text{O}$ .<sup>4</sup> Structural parameters that describe the interaction between  $\text{H}_2\text{O}$  and imidazole were assumed equal to those calculated for  $\text{imid} \cdot \cdot \text{H}_2\text{O}$  in the starting point of the geometry optimisation for each of  $N\text{-MI} \cdot \cdot \text{H}_2\text{O}$  and  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$ . In each case, it was assumed that the molecule is oriented such that  $\angle(\text{O-H}_b \cdot \cdot \text{N3-C2}) = 0^\circ$ . The  $V_3$  barrier to internal rotation was calculated by scanning the  $\angle(\text{H-C6-N1-C2})$  or  $\angle(\text{H-C6-C2-N3})$  dihedral angle as appropriate to each complex. The results of the geometry optimisation for each complex are shown in Table S1 (ESI<sup>†</sup>) and Fig. 1 while the calculated rotational constants ( $A_e$ ,  $B_e$ ,  $C_e$ ), nuclear quadrupole coupling constants, dipole moment components ( $|\mu_a|$ ,  $|\mu_b|$  and  $|\mu_c|$ ) and ( $V_3$ ) barriers to internal rotation are summarized in Table S2 (ESI<sup>†</sup>) which also shows the differences between calculated and experimentally-determined parameters. Calculations of anharmonic force fields employed the B3LYP functional with the D3BJ correction and the jun-cc-pVDZ basis set.

### 3. Results and discussion

#### 3.1. Observations and spectral assignment

The most intense transitions of each methylimidazole monomer were typically observed with a S/N of at least 5 : 1 after fewer than 120 averages and were the most intense signals recorded during the described experiments. The water dimer transition at 12321 MHz was another useful reference point during initial optimisation of the spectrometer and gas expansion conditions. The DFT-calculated geometries of each of  $N\text{-MI} \cdot \cdot \text{H}_2\text{O}$  and  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$  have a dipole moment that is nearly aligned with

the  $a$  inertial axis (Fig. 1). The most intense transitions in the spectrum of each of  $N\text{-MI} \cdot \cdot \text{H}_2\text{O}$  and  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$  are  $a$ -type transitions which were readily identified and assigned to the spectrum of a near-prolate symmetric rotor. Initial assignments of the molecular carriers of the observed spectra were made on basis of the agreement between the experimentally-determined and theoretically-calculated rotational constants.

A previous experimental study observed two isomers of a 1 : 1 complex formed between water and imidazole.<sup>4</sup> Water was the hydrogen bond donor in the first of these isomers (denoted as  $\text{imid} \cdot \cdot \text{H}_2\text{O}$ ) and the hydrogen bond acceptor in the second (denoted as  $\text{H}_2\text{O} \cdot \cdot \text{imid}$ ). The bifunctional nature of the imidazole ring implies that the method employed herein might allow the generation of  $\text{H}_2\text{O} \cdot \cdot 2\text{-MI}$  as well as  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$ . Ultimately, conclusive proof that the observed spectrum should be assigned to  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$  was obtained by measuring the shifts in rotational constants on isotopic substitution. Spectra were measured for  $2\text{-MI} \cdot \cdot \text{H}_2^{16}\text{O}$ ,  $2\text{-MI} \cdot \cdot \text{H}_2^{18}\text{O}$ ,  $2\text{-MI} \cdot \cdot \text{DOH}$ ,  $2\text{-MI} \cdot \cdot \text{HOD}$  and  $2\text{-MI} \cdot \cdot \text{D}_2\text{O}$  isotopologues of  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$ . All measured isotopic shifts were highly consistent with assignment of  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$  as the carrier of the observed spectrum. The experiments did not reveal evidence for the formation of  $\text{H}_2\text{O} \cdot \cdot 2\text{-MI}$ . Beyond the spectra identified and discussed above, a number of transitions observed during the present work assign to products generated by the fragmentation of imidazole. The same range of fragmentation products was observed during previous studies<sup>4,22</sup> of  $(\text{imid})_2$  and  $\text{imid} \cdot \cdot \text{H}_2\text{O}$  which were performed by the same method.

Partially resolved hyperfine structure (Fig. 2, bottom panels) was observed as consistent with the presence of two nitrogen nuclei ( $I = 1$  for  $^{14}\text{N}$ ) in each complex. Initially,  $A$ -species

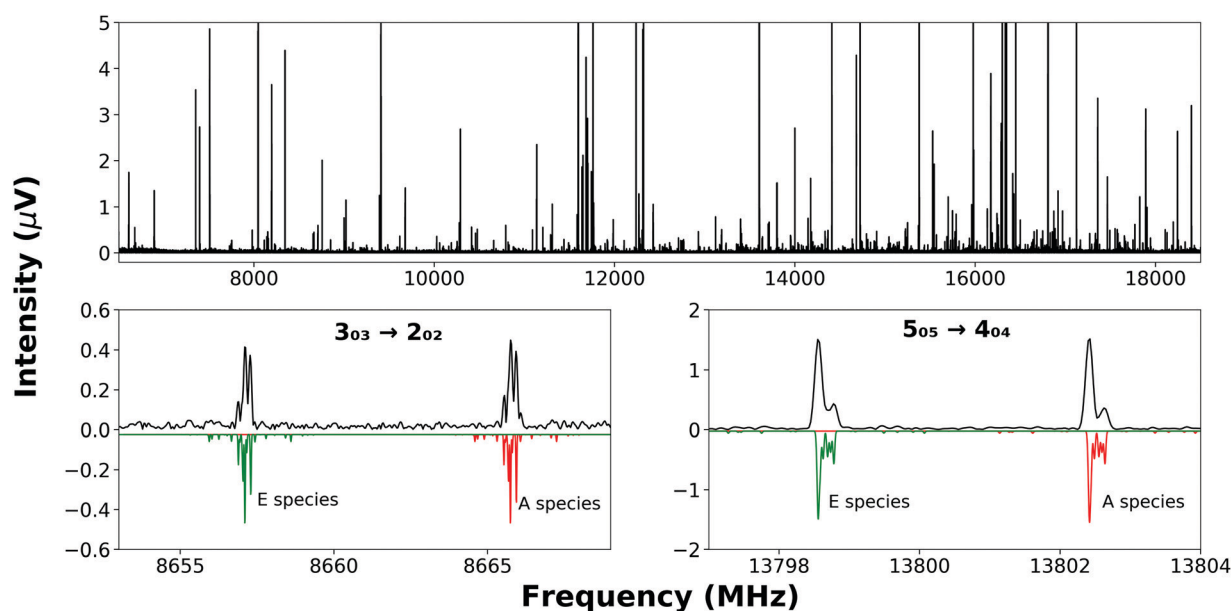


Fig. 2 (top panel) The broadband rotational spectrum recorded while probing a sample containing  $2\text{-MI}$ ,  $\text{H}_2^{16}\text{O}$  and argon averaged over  $5.1 \times 10^5$  FID's. Some peaks are off-scale to allow the display of weaker features. (bottom panels) Experimentally-observed  $A$ - and  $E$ -species transitions of  $2\text{-MI} \cdot \cdot \text{H}_2\text{O}$  are displayed (black) above a simulation (green and red) that uses the fitted values of parameters. Blending of hyperfine transitions is apparent in the experimental spectrum.



transition frequencies were fit with Watson's S-reduced Hamiltonian,<sup>23</sup> implemented in PGOPHER,<sup>24</sup>

$$H = H_R - \frac{1}{6}\mathbf{Q}(\text{N1})\cdot\nabla\mathbf{E}(\text{N1}) - \frac{1}{6}\mathbf{Q}(\text{N3})\cdot\nabla\mathbf{E}(\text{N3}) \quad (1)$$

where  $H_R$  is the energy operator for a semi-rigid asymmetric rotor and the remaining terms represent interactions between the nuclear electric quadrupole moment and the electric field gradient at each nitrogen atom.  $H_R$  includes the "effective" rotational constants,  $A'_0$ ,  $B'_0$  and  $C'_0$  and the centrifugal distortion terms,  $D_J$  and  $D_{JK}$ , for both  $N\text{-MI}\cdot\cdot\text{H}_2\text{O}$  and  $2\text{-MI}\cdot\cdot\text{H}_2\text{O}$ . The Hamiltonian used for  $N\text{-MI}\cdot\cdot\text{H}_2\text{O}$  required inclusion of an additional centrifugal distortion term,  $d_1$ . The values of rotational constants and centrifugal distortion constants determined during the initial fits of spectroscopic parameters to  $A$ -species ( $m = 0$ ) transition frequencies for five isotopologues of each complex are presented in Tables S3 and S4 (ESI<sup>†</sup>). The rotational constants,  $A_0$ ,  $B_0$  and  $C_0$  will be determined through a combined analysis of  $A$ - and  $E$ -species transitions to be presented in Section 3.2.

The nuclear quadrupole moment dyadic is represented by  $\mathbf{Q}$  and the dyadic of the electric field gradient is  $\Delta\mathbf{E}$ . Matrix elements were constructed in the coupled asymmetric rotor basis,  $J + I_{\text{N1}} = F_1$ ,  $F + I_{\text{N3}} = F_2$ , and diagonalised in blocks of the quantum number,  $F$ . Components of the nuclear quadrupole coupling tensor of each quadrupolar nitrogen nucleus are denoted by  $\chi_{aa}$  and  $(\chi_{bb} - \chi_{cc})$  with nitrogen atoms numbered according to the convention when labelling heteroaromatic molecules with N1 and N3 denoting the pyrrolic and pyridinic nitrogen atoms respectively. Hyperfine structure was observed to be extensively blended but values of  $\chi_{aa}(\text{N1})$  and  $\chi_{aa}(\text{N3})$  were fitted for every isotopologue of each complex. Values of  $[\chi_{bb}(\text{N1}) - \chi_{cc}(\text{N1})]$  for  $N\text{-MI}\cdot\cdot\text{DOH}$ ,  $N\text{-MI}\cdot\cdot\text{HOD}$  and  $N\text{-MI}\cdot\cdot\text{D}_2\text{O}$  were fixed equal to the experimental result for  $N\text{-MI}\cdot\cdot\text{H}_2^{16}\text{O}$ . Values of  $[\chi_{bb}(\text{N3}) - \chi_{cc}(\text{N3})]$  were held fixed for most isotopologues of each complex. The procedure yielded satisfactory agreement between simulated and experimentally-observed line shapes (Fig. 2, lower panel), and between the experimentally-determined and DFT-calculated results. The electron distribution at each nitrogen atom is confirmed to be very similar to that for the corresponding atom of the imidazole monomer (Table S5, ESI<sup>†</sup>). The final cycle of each spectroscopic fit is provided within the supplementary data. The standard deviations of all fits of  $A$ -species transitions (Tables S3 and S4, ESI<sup>†</sup>) are between 15 and 35 kHz. Spectroscopic parameters are thus determined with high precision in spite of the line blending and assumed values of hyperfine parameters. This is consistent with previous work which found that good agreement was achieved between DFT-calculated and experimental results for  $\chi_{aa}$  and  $(\chi_{bb} - \chi_{cc})$  for nitrogen atoms within N-heterocyclic rings.

### 3.2 Analysis of internal rotation of methyl group

It is known that there is a negligible barrier to the internal rotation of  $\text{CH}_3$  in toluene<sup>25</sup> while the addition of substituents to the benzene ring introduces an asymmetry into molecular orbitals that leads to an increased barrier.<sup>26–29</sup> The ( $V_3$ ) barrier to internal rotation of  $\text{CH}_3$  has been determined for different

structural isomers of methylthiazole,<sup>30–32</sup> methyloxazole<sup>33</sup> and methylimidazole.<sup>9</sup> The magnitude of the parameter depends on the asymmetry of the molecular orbitals with which the  $\text{CH}_3$  group interacts. For example, the  $V_3$  barrier to internal rotation of  $\text{CH}_3$  in 2-methylimidazole is smaller than that in 4- or 5-methylimidazole by a factor of three. In all of the forementioned cases, the changes in  $V_3$  result from electronic rather than steric effects. An important aim of the present work is to investigate whether the attachment of  $\text{H}_2\text{O}$  to  $N\text{-MI}$  or  $2\text{-MI}$  changes the magnitude of  $V_3$  in either isomer.

Subsequent to the identification and assignment of  $E$ -species transitions, combined fits of spectroscopic parameters to the frequencies of both  $A$ - and  $E$ -species transitions were performed by two different methods. Previous papers have noted that the determined value of  $V_3$  can vary depending on the Hamiltonian model employed. Fits performed in XIAM<sup>34</sup> employ a Hamiltonian that is constructed in the principal axis system. XIAM treats each torsional state separately without accounting for interactions between different torsional states. The BELGI-C<sub>s</sub> program<sup>35</sup> employs the alternative reference framework of the rho axis method and allows the inclusion of higher-order terms. Parameters were fitted using each of XIAM and BELGI-C<sub>s</sub> to explore dependencies of the results on the models employed. The experiments probed complexes in their vibrational ground states preventing the independent determination of  $F_0$  and  $V_3$ . The former was therefore fixed at the value for the corresponding methylimidazole monomer in the fits performed for each of  $N\text{-MI}\cdot\cdot\text{H}_2\text{O}$  and  $2\text{-MI}\cdot\cdot\text{H}_2\text{O}$ . It was also assumed that the axis of the  $\text{CH}_3$  rotor lies in the  $ab$  plane. Nuclear quadrupole coupling of multiple quadrupolar nuclei is not currently implemented by either XIAM or BELGI-C<sub>s</sub> so a bespoke procedure was used to establish line centre frequencies for  $A$ - and  $E$ -species transitions. First, the rotational and centrifugal distortion constants determined by fitting  $A$  species transitions (those in Tables S3 and S4, ESI<sup>†</sup>) were used to determine the unsplit line centres of  $A$ -species rotational transitions. Next, the shift of each  $E$ -species transition was measured relative to its  $A$ -species counterpart while assisted by PGOPHER<sup>24</sup> visualisation tools that aid spectral assignment. Specifically, these tools allow (i) hyperfine structure to be toggled on or off in the displayed simulation, (ii) display of a simulated spectrum which correctly mirrors the instrument resolution and (iii) simulated and experimental spectra to be overlaid and/or offset in order to match simulated features with observations. The precisely-measured interval between each  $A$ -species transition and its  $E$ -species counterpart was thus used to determine the unsplit line centre frequency for each  $E$ -species transition. Fits performed using XIAM determined rotational constants and centrifugal distortion constants in the principal axis system, those performed using BELGI-C<sub>s</sub> determined constants in the rho axis system. The linelist used by each BELGI-C<sub>s</sub> fit was the same as that used by the XIAM fit for the corresponding isotopologue. A summary of results for one isotopologue of each complex is provided in Table 1 with full details for all isotopologues provided in Tables S6–S9 (ESI<sup>†</sup>).



**Table 1** Results of XIAM and BELGI-C<sub>s</sub> fits of spectroscopic parameters to the frequencies of *A*- and *E*-species transitions. The values of  $F_0$  are fixed to the results for the methylimidazole monomers available in ref. 9.  $N_A$  and  $N_E$  denote the number of *A*-species and *E* species transitions respectively included in the fit

	<i>N</i> -MI ··· H <sub>2</sub> <sup>16</sup> O		2-MI ··· H <sub>2</sub> <sup>16</sup> O	
	XIAM	BELGI-C <sub>s</sub>	XIAM	BELGI-C <sub>s</sub>
$A_0$ (MHz)	5010.78(21)	5011(10) <sup>a</sup>	4233.93(21)	4233.2(50) <sup>a</sup>
$B_0$ (MHz)	1409.5628(67)	1409.5(15) <sup>a</sup>	1732.5621(61)	1731.00(95) <sup>a</sup>
$C_0$ (MHz)	1107.2884(60)	1107.3099(43) <sup>a</sup>	1240.3104(66)	1238.69(18) <sup>a</sup>
$D_J$ (kHz)	2.392(33)	3.111(49) <sup>b</sup>	0.233(81)	[0.233] <sup>bc</sup>
$D_{JK}$ (kHz)	-18.57(40)	-20.6(5) <sup>b</sup>	7.28(78)	4.33(71) <sup>b</sup>
$d_1$ (kHz)	0.820(42)	[0.959] <sup>bd</sup>	—	—
$F_0$ (GHz)	[157.929]	[157.929]	[157.690]	[157.690]
$V_3$ (cm <sup>-1</sup> )	182.23(10)	173.6(16)	154.99(8)	150.68(90)
$D_{\pi 2J}$ (kHz)	—	—	-114(7)	—
$F_V$ (MHz)	—	—	—	5.49(60)
$\angle(i, b)$ (°)	47.16(10)	46.3(3)	36.55(6)	36.56(5)
$\sigma_{\text{RMS}}$ (kHz)	50	55	64	79
$N_A/N_E$	26/19	26/19	19/14	19/14

<sup>a</sup> Rotational constants in the principal axis system after transformation of the rho axis system inertia tensor determined by BELGI-C<sub>s</sub>. <sup>b</sup> Values in the rho axis system. Centrifugal distortion constants determined by BELGI-C<sub>s</sub> cannot be directly compared with those determined by XIAM because of the different models employed. <sup>c</sup> Could not be determined by fitting and therefore fixed to the result determined by XIAM. <sup>d</sup> Fixed to the result obtained for the *N*-MI ··· D<sub>2</sub>O isotopologue (Table S7, ESI).

The internal rotation parameters included in XIAM fits were the barrier to internal rotation of the CH<sub>3</sub> group,  $V_3$ , and the angle between the axis of the CH<sub>3</sub> rotor and the *b* inertial axis which is denoted by  $\angle(i, b)$ . A term which couples the methyl rotation with the overall molecular rotation and centrifugal distortion,  $D_{\pi 2J}$ , was included when fitting the data for 2-MI ··· H<sub>2</sub>O. The BELGI-C<sub>s</sub> fits determined the off-diagonal component of the inertia tensor in the rho axis system,  $D_{AB}$ , and the internal rotation parameters,  $V_3$  and  $\rho$  for each isotopologue of each complex. A term that describes the  $J(J+1)$  dependence of the  $V_3$  barrier,  $F_V$ , was also fitted for isotopologues of 2-MI ··· H<sub>2</sub>O. The  $\sigma_{\text{RMS}}$  of the XIAM and BELGI-C<sub>s</sub> fits were higher than those obtained when fitting the *A*-species transitions in PGOPHER and higher than would typically be expected given the experimental linewidth of 100 kHz because of blending of different hyperfine components in the observed spectra and the need to estimate rotational line centre frequencies for the XIAM and BELGI-C<sub>s</sub> fits.

The rotational constants and distortion constants output by BELGI-C<sub>s</sub> fits are in the rho axis system so the inertia tensor is not diagonalised and rotational constants cannot be directly compared with those determined in the principal axis system. The inertia tensor determined by the BELGI-C<sub>s</sub> fits was transformed into the principal axis system for the purposes of the comparison shown in rows 1–3 of Table 1. The value of  $V_3$  for the CH<sub>3</sub> group of *N*-MI ··· H<sub>2</sub><sup>16</sup>O is determined to be 182.23(10) cm<sup>-1</sup> by XIAM with other isotopologues having  $V_3$  ranging from 182.08(8) cm<sup>-1</sup> to 182.41(7) cm<sup>-1</sup>. These results are very similar to the value of this parameter for the *N*-MI monomer<sup>9</sup> which was determined to be 185.104(11) cm<sup>-1</sup> through fitting in XIAM. The same parameter for *N*-MI ··· H<sub>2</sub><sup>16</sup>O

is 173.6(16) cm<sup>-1</sup> when fitted using BELGI-C<sub>s</sub> with other isotopologues having  $V_3$  ranging from 173.2(2) cm<sup>-1</sup> to 177.2(7) cm<sup>-1</sup>. The XIAM fits yielded a result for  $V_3$  of 154.99(8) cm<sup>-1</sup> for 2-MI ··· H<sub>2</sub><sup>16</sup>O with results spanning from 152.65(4) cm<sup>-1</sup> to 156.02(12) cm<sup>-1</sup> for other isotopologues. The fits performed using BELGI-C<sub>s</sub> determined the parameter to be 150.68(90) cm<sup>-1</sup> for 2-MI ··· H<sub>2</sub><sup>16</sup>O with values determined for other isotopologues ranging from 152.58(11) cm<sup>-1</sup> to 155.5(24) cm<sup>-1</sup>. The results determined for  $V_3$  of the CH<sub>3</sub> group in 2-MI ··· H<sub>2</sub><sup>16</sup>O are all significantly higher than the value of the parameter for the 2-MI monomer which was reported to be 122.7529(38) cm<sup>-1</sup>.<sup>9</sup> The reasons for this difference will be explored further in Section 4.

Values of  $\angle(i, b)$  fitted using XIAM and BELGI-C<sub>s</sub> are in excellent agreement for all isotopologues. This parameter ranges from 46.06(3) to 47.54(7)° in the fits of internal rotor parameters for *N*-MI ··· H<sub>2</sub>O whereas the value implied by the  $r_0$  fit of the molecular geometry (to be described in Section 3.3) is 46.1°. The values of  $\angle(i, b)$  determined in the fits of internal rotor parameters for isotopologues of 2-MI ··· H<sub>2</sub>O range from 34.86(3) to 36.56(5)° while the  $r_0$  fit of the molecular geometry implies a result of 35.3° for this parameter. This high level of agreement provides confidence in the results of the internal rotor fits while also justifying assumptions that will be made to determine the  $r_0$  geometries of *N*-MI ··· H<sub>2</sub>O and 2-MI ··· H<sub>2</sub>O.

### 3.3 Characterisation of molecular geometries

In the discussion that follows, H<sub>b</sub> denotes a hydrogen atom of water that forms a hydrogen bond to the pyridinic nitrogen of imidazole. The free hydrogen of the water sub-unit will be labelled as H<sub>nb</sub>. Inertial defects calculated from the rotational constants provide the first insight into the molecular geometry and are determined as follows,

$$\Delta_0 = I_{cc} - I_{aa} - I_{bb} \quad (2)$$

where  $I_{aa}$ ,  $I_{bb}$  and  $I_{cc}$  are respectively the moments of inertia about the *a*, *b* and *c* inertial axes. The inertial defects,  $\Delta_0$ , of *N*-MI and 2-MI were previously shown to be  $-3.2070(1)$  u<sup>2</sup> and  $-3.1497(7)$  u<sup>2</sup> respectively, consistent with expectations for geometries where only the hydrogen atoms of the CH<sub>3</sub> group lie outside the *ab* plane. The  $\Delta_0$  for *N*-MI ··· H<sub>2</sub><sup>16</sup>O and 2-MI ··· H<sub>2</sub><sup>16</sup>O are herein determined to be  $-2.983(6)$  u<sup>2</sup> and  $-3.60(4)$  u<sup>2</sup> respectively. These results (and those which follow in Section 3.3) were determined from the values of  $A_0$ ,  $B_0$  and  $C_0$  yielded by the XIAM fits which have lower uncertainties than those obtained while using BELGI-C<sub>s</sub>.

The small changes in  $\Delta_0$  when H<sub>2</sub>O attaches to either *N*-MI or 2-MI thus confirm that each complex forms in a geometry where all heavy atoms lie within the *ab* plane. In general, contributions of in-plane vibrations to  $\Delta_0$  are negative whereas out-of-plane vibrations make positive contributions. The magnitudes of changes in  $\Delta_0$  on addition of H<sub>2</sub>O to each of imidazole,<sup>4</sup> thiazole<sup>6</sup> and isoxazole<sup>7</sup> are  $-0.02$ ,  $-0.05$  and  $+0.2$  u<sup>2</sup> respectively which are broadly consistent with the observations of the present work. In striking contrast, the change in  $\Delta_0$  when attaching H<sub>2</sub>O to pyridine<sup>36</sup> has been observed to be greater than 8 u<sup>2</sup>. There are significant



**Table 2** Comparison of DFT-calculated ( $r_e$ ) and experimentally-determined ( $r_s$ ) coordinates

Method	$a/\text{\AA}$	$b/\text{\AA}$	$c/\text{\AA}$
<i>N</i> -MI ···H <sub>2</sub> O			
H <sub>b</sub>	$r_e$ (calc.) <sup>a</sup>	2.6691	-0.1954
	$r_s$ (exp.)	2.7785(8) <sup>b</sup>	[0] <sup>c</sup>
O	$r_e$ (calc.)	3.5881	-0.5061
	$r_s$ (exp.)	3.4036(5)	-0.650(3)
H <sub>nb</sub>	$r_e$ (calc.)	3.9972	0.7223
	$r_s$ (exp.)	3.9163(7)	-0.728(4)
2-MI ···H <sub>2</sub> O			
H <sub>b</sub>	$r_e$ (calc.)	2.1105	-0.7120
	$r_s$ (exp.)	2.064(1)	-0.784(3)
O	$r_e$ (calc.)	3.0707	-0.5535
	$r_s$ (exp.)	3.0709(6)	-0.538(3)
H <sub>nb</sub>	$r_e$ (calc.)	3.4265	-1.0444
	$r_s$ (exp.)	3.5032(6)	-1.181(2)

<sup>a</sup>  $r_e$  geometries are calculated at the  $\omega$ B97XD/aug-cc-pVQZ level. <sup>b</sup> Numbers in parentheses are Costain errors.<sup>38</sup> <sup>c</sup> Imaginary values were obtained by the  $r_s$  method for coordinates indicated in square brackets which are assumed equal to zero.

changes in  $\Delta_0$  upon isotopic substitution at H<sub>nb</sub> which are presented in Tables S6 and S8 (ESI†) and discussed further below.

Determination of the rotational constants for five isotopologues of each complex allows the calculation of substitution ( $r_s$ ) coordinates for the hydrogen and oxygen atoms of the water molecule using Kisiel's program "KRA" available from the PROSPE website.<sup>37</sup> The rotational constants obtained from the XIAM fits of *A*- and *E*-species transitions were used to calculate  $r_s$  coordinates for H<sub>b</sub>, H<sub>nb</sub> and O which are shown alongside Costain errors<sup>38</sup> in Table 2. The Kraitchman method determines the magnitudes of atomic coordinates while the signs are those inferred from the results of the DFT calculations. The results unambiguously confirm that the oxygen atom lies in the *ab* plane in each complex and that the molecular geometry of each of *N*-MI ···H<sub>2</sub>O and 2-MI ···H<sub>2</sub>O contains a hydrogen bond between water (acting as a proton donor) and the pyridinic nitrogen.

The  $r_0$  method<sup>39</sup> (as implemented within Kisiel's STRFIT program<sup>37</sup>), which allows a determination of structural parameters from zero-point rotational constants, was used to determine the orientation of the water molecule relative to the imidazole ring. The geometrical parameters that are internal to the *N*-MI and 2-MI monomers<sup>9</sup> must first be assumed equal to their values in the DFT-calculated ( $r_e$ ) geometries of *N*-MI ···H<sub>2</sub>O and 2-MI ···H<sub>2</sub>O respectively. The experimentally-determined rotational constants ( $A_0$ ,  $B_0$  and  $C_0$ ) determined by XIAM now allow fitting of the length of the intermolecular hydrogen bond,  $r(\text{H}_b \cdots \text{N}3)$ , and two angles which define the position and orientation of the water molecule,  $\angle(\text{H}_b \cdots \text{N}3\text{-C}2)$  and  $\angle(\text{O-H}_b \cdots \text{N}3)$ , for each of *N*-MI ···H<sub>2</sub>O and 2-MI ···H<sub>2</sub>O. Results were determined while assuming  $\angle(\text{H}_{\text{nb}}\text{-O-H}_b \cdots \text{N}3) = 180^\circ$  and  $\angle(\text{O-H}_b \cdots \text{N}3\text{-C}2) = 0^\circ$  for each complex. These dihedral angles lead to sets of structural parameters (shown in Table 3) that are highly consistent with the results of the DFT calculations. An alternative assumption that  $\angle(\text{O-H}_b \cdots \text{N}3\text{-C}2) = 180^\circ$  for 2-MI ···H<sub>2</sub>O would yield  $r(\text{H}_b \cdots \text{N}3) = 1.957(23) \text{ \AA}$ ,

**Table 3** Comparison of DFT-calculated ( $r_e$ ) and experimentally-determined ( $r_0$ ) coordinates

Molecule	Parameter	Method	Value
<i>N</i> -MI ···H <sub>2</sub> O			
	$r(\text{H}_b \cdots \text{N}3)/\text{\AA}$	$r_e$ (calc.) <sup>a</sup>	1.897
		$r_0$ (exp.)	1.922(4) <sup>b</sup>
	$\angle(\text{H}_b \cdots \text{N}3\text{-C}2)/^\circ$	$r_e$ (calc.)	115.7
		$r_0$ (exp.)	101.0(16)
	$\angle(\text{O-H}_b \cdots \text{N}3)/^\circ$	$r_e$ (calc.)	170.1
		$r_0$ (exp.)	177(5)
2-MI ···H <sub>2</sub> O			
	$r(\text{H}_b \cdots \text{N}3)/\text{\AA}$	$r_e$ (calc.)	1.8807
		$r_0$ (exp.)	1.923(5)
	$\angle(\text{H}_b \cdots \text{N}3\text{-C}2)/^\circ$	$r_e$ (calc.)	114.3
		$r_0$ (exp.)	116.9(9)
	$\angle(\text{O-H}_b \cdots \text{N}3)/^\circ$	$r_e$ (calc.)	165.4
		$r_0$ (exp.)	166.3(28)

<sup>a</sup>  $r_e$  geometries are calculated at the  $\omega$ B97XD/aug-cc-pVQZ level. <sup>b</sup> Numbers in parentheses are one standard deviation in units of the final significant figure.

$\angle(\text{H}_b \cdots \text{N}3\text{-C}2) = 107.3(18)^\circ$  and  $\angle(\text{O-H}_b \cdots \text{N}3) = 154.4(60)^\circ$  which are somewhat different from the DFT-calculated results. The assumption that  $\angle(\text{O-H}_b \cdots \text{N}3\text{-C}2) = 180^\circ$  for *N*-MI ···H<sub>2</sub>O would yield  $\angle(\text{O-H}_b \cdots \text{N}3) = 127(6)^\circ$  which is certainly not consistent with the DFT calculated results. Fits performed while assuming that  $\angle(\text{H}_{\text{nb}}\text{-O-H}_b \cdots \text{N}3) = 0^\circ$  do not converge for either complex.

The DFT calculations of the present work identify that H<sub>nb</sub> lies outside the plane of the imidazole ring in each of *N*-MI ···H<sub>2</sub>O and 2-MI ···H<sub>2</sub>O in the equilibrium ( $r_e$ ) geometry. Previous works<sup>4,6</sup> have found that similar "free" hydrogen atoms in related complexes undergo rapid zero-point vibrational motions such that they cannot be precisely located by  $r_0$  or  $r_s$  methods. Comparing the results obtained by the  $r_s$  and  $r_e$  methods, the *a* and *b* coordinates of H<sub>b</sub> and O are highly consistent. The Kraitchman method is less precise when used to calculate the position of an atom that is close to an inertial axis. *N*-MI ···H<sub>2</sub>O represents a particularly challenging case because both hydrogen atoms are very near to the *a* inertial axis. Changes in zero-point vibrational motions on isotopic substitution also introduce inaccuracies and these are particularly severe when the  $r_s$  coordinates of a hydrogen atom are determined. These sources of inaccuracy explain small variations in the results for the *b*-coordinate of H<sub>b</sub> obtained by the  $r_e$  and  $r_s$  methods for each complex. Significant variation in the  $|b|$  and  $|c|$  coordinates of H<sub>nb</sub> as determined by the  $r_0$ ,  $r_s$  and  $r_e$  methods results from the rapid, zero-point vibrational motions mentioned earlier. Variation in the inertial defects measured for different isotopologues is informative here (Tables S6 and S8, ESI†). For each of *N*-MI ···H<sub>2</sub>O and 2-MI ···H<sub>2</sub>O, the  $\Delta_0$  of isotopologues that contain H<sub>2</sub><sup>16</sup>O, DOH or H<sub>2</sub><sup>18</sup>O are very similar (within 0.02 u  $\text{\AA}^2$  of each other) supporting the conclusion that H<sub>b</sub> and O are localised within the plane of the imidazole ring in the zero-point state. However, isotopologues that are deuterated in the H<sub>nb</sub> position have  $|\Delta_0|$  which are between 0.2 and 0.4 u  $\text{\AA}^2$  higher than those of isotopologues which are not deuterated at H<sub>nb</sub>. Evidently, out-of-plane contributions to zero-point vibrational motions mean that H<sub>nb</sub> is not localised to the *ab* plane on the timescale of the



molecular rotation. To facilitate broader comparisons, Tables S10 and S11 (ESI†) provide atomic coordinates calculated by the  $r_0$  method.

The analysis thus far has used the experimentally-determined rotational constants for the zero-point vibrational state of each complex to determine  $r_0$  and  $r_s$  geometrical parameters. These  $r_0$  and  $r_s$  parameters cannot necessarily be expected to agree with  $r_e$  (equilibrium) parameters with very high precision because the former are influenced by zero-point vibrational motions. However, it is possible to calculate semi-experimental equilibrium rotational constants<sup>5,40</sup> ( $B_e^i$ ) from experimentally-determined rotational constants ( $B_0^i$ ), where  $i$  indicates permutation over the  $a, b, c$  inertial axes, using

$$B_e^i = B_0^i - \Delta B_{\text{vib}}^i = B_0^i + \frac{1}{2} \sum_r \alpha_r^i \quad (3)$$

where the  $\alpha_r^i$  are vibration-rotation interaction constants determined by summing over all  $r$  vibrational modes. First, the anharmonic force field (and thus  $\Delta B_{\text{vib}}^i$ ) of the complex is computed using density functional theory. Next, the calculated value of  $\Delta B_{\text{vib}}^i$  is subtracted from the experimentally-determined value of  $B_0^i$  to yield  $B_e^i$  (this step is performed for each isotopologue of the complex). Finally, geometrical parameters (denoted as semi-experimental equilibrium, or  $r_e^{\text{SE}}$ , parameters) are fitted to the  $B_e^i$  determined for the various isotopologues. Provided that the anharmonic force field has been accurately computed, the resulting  $r_e^{\text{SE}}$  parameters can then be directly compared with the results of theoretical calculations that yield  $r_e$  parameters.

During the present work, calculations of anharmonic force fields to yield values of  $\alpha_r^i$  for each of  $N\text{-MI}\cdots\text{H}_2\text{O}$  and  $2\text{-MI}\cdots\text{H}_2\text{O}$  were performed using the B3LYP functional, the partially-augmented double- $\zeta$  jun-cc-pVDZ basis set and Grimme's DFT-D3 scheme with the Becke-Johnson (BJ) damping function for the treatment of dispersion effects. Prior to calculation of the anharmonic force field, the geometry of the complex was re-optimised at this level of theory. This scheme for calculation of the anharmonic force field was previously used by Melli *et al.* during their recent study of  $\text{imid}\cdots\text{H}_2\text{O}$ . Values of  $\alpha_r^i$  and hence the semi-experimental equilibrium rotational constants,  $B_e^i$ , were calculated for isotopologues of each complex as shown in Tables S12 and S13 (ESI†). A least squares fit of the values of  $r(\text{H}_b\cdots\text{N3})$ ,  $\angle(\text{H}_b\cdots\text{N3-C2})$  and  $\angle(\text{O-H}_b\cdots\text{N3})$  to the semi-experimental equilibrium rotational constants ( $B_e^i$ ) determined for the various isotopologues of  $2\text{-MI}\cdots\text{H}_2\text{O}$  yielded values of 1.912(10) Å, 116.6(12)° and 160.8(38)° respectively for these parameters. A determination of  $r_e^{\text{SE}}$  parameters for  $N\text{-MI}\cdots\text{H}_2\text{O}$  by the same method yielded  $r(\text{H}_b\cdots\text{N3}) = 1.904(20)$  Å,  $\angle(\text{H}_b\cdots\text{N3-C2}) = 104.0(42)$ ° and  $\angle(\text{O-H}_b\cdots\text{N3}) = 168(13)$ °. For each complex, the  $r_e^{\text{SE}}$  value of  $r(\text{H}_b\cdots\text{N3})$  is in better agreement with the DFT-calculated  $r_e$  result than is the  $r_0$  parameter. However, particularly for  $N\text{-MI}\cdots\text{H}_2\text{O}$ , the determined  $r_e^{\text{SE}}$  angles are associated with high uncertainties. The discussion of Section 4 will therefore compare values of  $r_0$  parameters determined with high precision for  $\text{imid}\cdots\text{H}_2\text{O}$ ,  $N\text{-MI}\cdots\text{H}_2\text{O}$  and  $2\text{-MI}\cdots\text{H}_2\text{O}$ . Differing

zero-point vibrational motions within each complex mean that precise agreement should not necessarily be expected in comparisons of  $r_0$  parameters determined for different complexes.

## 4. Discussion

Both the DFT calculations and the experimental measurements confirm that a hydrogen bond forms between  $\text{H}_b$  and the pyridinic nitrogen of imidazole in both  $N\text{-MI}\cdots\text{H}_2\text{O}$  and  $2\text{-MI}\cdots\text{H}_2\text{O}$ . The length of this hydrogen bond when determined by the  $r_0$  method is 1.922(4) Å in  $N\text{-MI}\cdots\text{H}_2\text{O}$ , 1.923(5) Å in  $2\text{-MI}\cdots\text{H}_2\text{O}$  and was found to be 1.927(27) Å in the earlier study of  $\text{imid}\cdots\text{H}_2\text{O}$ . The results for these bond lengths are effectively identical given the approximations involved. The results for the determined bond angles and barriers to internal rotation provide insight into a weak electrostatic interaction between  $\text{H}_2\text{O}$  and the neighbouring hydrogen atom or methyl group that is attached to C2 of imidazole in  $N\text{-MI}\cdots\text{H}_2\text{O}$  and  $2\text{-MI}\cdots\text{H}_2\text{O}$  respectively.

Melandri *et al.*, McGlone *et al.*, Caminati *et al.*, McKenzie *et al.* and Li *et al.* identified non-linear hydrogen bonds in pyrimidine $\cdots\text{H}_2\text{O}$ ,<sup>8</sup> isoxazole $\cdots\text{H}_2\text{O}$ ,<sup>7</sup> pyridazine $\cdots\text{H}_2\text{O}$ ,<sup>41</sup> pyrazine $\cdots\text{H}_2\text{O}$ ,<sup>42</sup> pyridine $\cdots\text{H}_2\text{O}$ <sup>36</sup> and thiazole $\cdots\text{H}_2\text{O}$ <sup>6</sup> respectively. Our group recently reported that  $\text{imid}\cdots\text{H}_2\text{O}$ <sup>4</sup> contains a non-linear hydrogen bond where  $\angle(\text{O-H}_b\cdots\text{N3}) = 172.1(26)$ ° in the  $r_0$  geometry. In each of the studies listed above, the non-linearity of the hydrogen bond results from a weak electrostatic interaction between the oxygen of  $\text{H}_2\text{O}$  and a hydrogen on the C2 position of the aromatic ring. The local environments at the pyridinic nitrogen atoms of imidazole and  $N$ -methylimidazole are very similar. Unsurprisingly, therefore, the  $r_0$  results of  $\angle(\text{H}_b\cdots\text{N3-C2}) = 101.1(16)$ ° and  $\angle(\text{O-H}_b\cdots\text{N3}) = 177(5)$ ° reported herein for  $N\text{-MI}\cdots\text{H}_2\text{O}$  are similar to the results reported for  $\text{imid}\cdots\text{H}_2\text{O}$ . The oxygen atom is a distance of 3.081(6) Å from the hydrogen attached to C2 in the  $r_0$  geometry of  $N\text{-MI}\cdots\text{H}_2\text{O}$  while the separation between these two atoms in  $\text{imid}\cdots\text{H}_2\text{O}$  is 3.13(8) Å. The separation between oxygen and the hydrogen atoms of the  $\text{CH}_3$  in  $2\text{-MI}\cdots\text{H}_2\text{O}$  depends on the value of the dihedral angle,  $\angle(\text{N3-C2-C6-H})$ , which is scanned by the  $\text{CH}_3$  internal rotation. When  $\angle(\text{N3-C2-C6-H}) = 0$ °, the separation between oxygen and the nearest hydrogen is 2.566(3) Å while the assumption that  $\angle(\text{N3-C2-C6-H}) = 60$ ° places two hydrogen atoms only 3.175(3) Å from the oxygen atom. Evidently, oxygen interacts with its neighbouring hydrogen atoms over shorter distances (on average) within  $2\text{-MI}\cdots\text{H}_2\text{O}$  than within  $\text{imid}\cdots\text{H}_2\text{O}$  or  $N\text{-MI}\cdots\text{H}_2\text{O}$ . These shorter interaction distances lead to  $\angle(\text{O-H}_b\cdots\text{N3}) = 166.3(28)$ ° and hence enhanced non-linearity of the primary hydrogen bond in  $2\text{-MI}\cdots\text{H}_2\text{O}$  relative to either  $\text{imid}\cdots\text{H}_2\text{O}$  or  $N\text{-MI}\cdots\text{H}_2\text{O}$ . The hydrogen bond<sup>7</sup> in isoxazole $\cdots\text{H}_2\text{O}$  was reported to be significantly longer, and less linear, than those identified in  $\text{imid}\cdots\text{H}_2\text{O}$ ,  $N\text{-MI}\cdots\text{H}_2\text{O}$  and  $2\text{-MI}\cdots\text{H}_2\text{O}$  (Table 4).

Barriers to internal rotation have been extensively explored for  $\text{CH}_3$  substituents of aromatic rings. Where there is two-fold symmetry about the axis of a  $\text{CH}_3$  rotor, electronic overlap



**Table 4** Comparison of experimentally-determined ( $r_0$ ) structural parameters for complexes<sup>4,7</sup> formed between 5-membered N-heterocyclic rings and H<sub>2</sub>O

	$r(\text{H}_b \cdots \text{N3})/\text{\AA}$	$\angle(\text{O}-\text{H}_b \cdots \text{N3})/^\circ$
Imidazole $\cdots$ H <sub>2</sub> O	1.927(27) <sup>a</sup>	174.7(24)
N-Methylimidazole $\cdots$ H <sub>2</sub> O	1.922(4)	177(5)
2-Methylimidazole $\cdots$ H <sub>2</sub> O	1.923(5)	166.3(28)
Isoxazole $\cdots$ H <sub>2</sub> O	2.1467	141.12

<sup>a</sup> Uncertainties in parentheses are those quoted in the primary source.

between a  $\pi$ -like orbital on the CH<sub>3</sub> and  $\pi$ -orbitals on the ring leads to a very low barrier to internal rotation.<sup>43</sup> The magnitude of the barrier increases with the asymmetry of participating molecular orbitals such that it is significantly higher for 4- or 5-methylimidazole than for 2-methylimidazole.<sup>9</sup> The same trend is apparent in published results for the 2-, 4- and 5- isomers of methylthiazole<sup>30–32</sup> and methyloxazole.<sup>33</sup> The value for  $V_3$  of the *N*-methylimidazole monomer<sup>9</sup> (determined using XIAM) is 185.104(11) cm<sup>-1</sup> which is very similar to the results of 182.21(12) cm<sup>-1</sup> and 173.6(16) cm<sup>-1</sup> for *N*-MI  $\cdots$  H<sub>2</sub><sup>16</sup>O determined through fits performed using XIAM and BELGI-C<sub>s</sub> respectively. The water molecule is on the opposite side of the molecule so does not interact through space with the CH<sub>3</sub> group within *N*-MI  $\cdots$  H<sub>2</sub>O. The evidence of the experiments reported herein is that the attachment of H<sub>2</sub>O to *N*-MI does not significantly change the electronic environment at the CH<sub>3</sub> group either. The results for *N*-MI  $\cdots$  H<sub>2</sub>O are thus consistent with previous studies where ( $V_3$ ) barriers to internal rotation of CH<sub>3</sub> groups were not observed to change in response to the attachment of H<sub>2</sub>O to a remote site of the molecule.

The  $V_3$  barrier determined for 2-MI  $\cdots$  H<sub>2</sub><sup>16</sup>O (determined to be 154.99(8) cm<sup>-1</sup> by XIAM and 150.68(90) cm<sup>-1</sup> by BELGI-C<sub>s</sub>) is significantly greater than the value determined for the 2-MI monomer<sup>9</sup> by XIAM (122.7529(38) cm<sup>-1</sup>). An important question is whether this difference arises primarily because of electronic or steric effects. Does the attachment of H<sub>2</sub>O induce changes in the symmetry of molecular orbitals on the imidazole ring? Alternatively, is the presence of a weak electrostatic interaction between the oxygen atom and the CH<sub>3</sub> group of 2-MI sufficient to explain the change in  $V_3$  that follows the attachment of H<sub>2</sub>O? It is impossible to exclude a contribution for electronic effects but these did not lead to a significant change in  $V_3$  on attachment of H<sub>2</sub>O to *N*-MI. It is therefore more likely that the weak electrostatic interaction between the oxygen atom and the CH<sub>3</sub> group is the predominant cause of the difference between the  $V_3$  determined for 2-MI and 2-MI  $\cdots$  H<sub>2</sub>O. It is noted that an earlier analysis<sup>44</sup> of the microwave spectrum of the toluene  $\cdots$  SO<sub>2</sub> complex also observed a large increase (from 4.9 cm<sup>-1</sup> in free toluene to 87.3 cm<sup>-1</sup> in toluene  $\cdots$  SO<sub>2</sub>) in the barrier to internal rotation of the CH<sub>3</sub> group on formation of that complex. The authors of that study modelled electrostatic interactions between SO<sub>2</sub> and the CH<sub>3</sub> group and found these to be sufficient to explain the observed change in the barrier. The authors did not exclude the possibility that electronic effects also contribute.

## Conclusions

Each of *N*-MI  $\cdots$  H<sub>2</sub>O and 2-MI  $\cdots$  H<sub>2</sub>O contains a primary hydrogen bond between the hydrogen of H<sub>2</sub>O and the pyridinic nitrogen of the imidazole ring. The length of the primary hydrogen bond is very similar in *N*-MI  $\cdots$  H<sub>2</sub>O, 2-MI  $\cdots$  H<sub>2</sub>O and imid  $\cdots$  H<sub>2</sub>O. A weak electrostatic interaction between the oxygen atom of H<sub>2</sub>O and hydrogens (or the CH<sub>3</sub> group) attached to the C2 position of the imidazole ring leads to a non-linear hydrogen bond being present in each of *N*-MI  $\cdots$  H<sub>2</sub>O and 2-MI  $\cdots$  H<sub>2</sub>O. The ( $V_3$ ) barrier to internal rotation of the CH<sub>3</sub> group of *N*-MI  $\cdots$  H<sub>2</sub>O is essentially unchanged from that observed for the *N*-MI monomer. In contrast, the ( $V_3$ ) barrier to internal rotation of the CH<sub>3</sub> group within the 2-MI  $\cdots$  H<sub>2</sub>O complex is significantly higher than that of the CH<sub>3</sub> group within the 2-MI monomer because of the weak interaction between the oxygen atom of water and the CH<sub>3</sub> group.

## Author contributions

Medcraft and Heitkämper contributed to investigation. Gougoula, Cummings contributed to conceptualisation, formal analysis, investigation, validation and writing. Walker contributed to supervision, funding acquisition and writing.

## Conflicts of interest

There are no conflicts to declare.

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## References

- H. Takahashi, M. Abe, T. Sugawara, K. Tanaka, Y. Saito, S. Fujimura, M. Shibuya and Y. Sato, *Jpn. J. Cancer Res.*, 1998, **89**, 445–451.
- Beena, N. Kumar, R. K. Rohilla, N. Roy and D. S. Rawat, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 1396–1398.
- S.-C. Tsay, S.-Y. Lin, W.-C. Huang, M.-H. Hsu, K. C. Hwang, C.-C. Lin, J.-C. Horng, I. C. Chen, J. R. Hwu, F.-K. Shieh, P. Leyssen and J. Neyts, *Molecules*, 2016, **21**, 228.
- E. Gougoula, D. J. Cole and N. R. Walker, *J. Phys. Chem. A*, 2020, **124**, 2649–2659.
- A. Melli, V. Barone and C. Puzzarini, *J. Phys. Chem. A*, 2021, **125**, 2989–2998.





- 6 W. Li, J. Chen, Y. Xu, T. Lu, Q. Gou and G. Feng, *Spectrochim. Acta, Part A*, 2020, **242**, 118720.
- 7 S. McGlone, P. Moreschini, T. K. Ha and A. Bauder, *Mol. Phys.*, 2001, **99**, 1353–1364.
- 8 S. Melandri, M. E. Sanz, W. Caminati, P. G. Favero and Z. Kisiel, *J. Am. Chem. Soc.*, 1998, **120**, 11504–11509.
- 9 E. Gougoula, C. Medcraft, J. Heitkämper and N. R. Walker, *J. Chem. Phys.*, 2019, **151**, 144301.
- 10 D. Loru, M. A. Bermúdez and M. E. Sanz, *J. Chem. Phys.*, 2016, **145**, 074311.
- 11 S. L. Stephens, W. Mizukami, D. P. Tew, N. R. Walker and A. C. Legon, *J. Chem. Phys.*, 2012, **136**, 064306.
- 12 D. P. Zaleski, S. L. Stephens and N. R. Walker, *Phys. Chem. Chem. Phys.*, 2014, **16**, 25221–25228.
- 13 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox, *Gaussian 09*, Gaussian, Inc., Wallingford CT, 2016.
- 14 B. Miehlich, A. Savin, H. Stoll and H. Preuss, *Chem. Phys. Lett.*, 1989, **157**, 200–206.
- 15 S. H. Vosko, L. Wilk and M. Nusair, *Can. J. Phys.*, 1980, **58**, 1200–1211.
- 16 A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648–5652.
- 17 S. Grimme and M. Steinmetz, *Phys. Chem. Chem. Phys.*, 2013, **15**, 16031–16042.
- 18 S. Grimme, S. Ehrlich and L. Goerigk, *J. Comput. Chem.*, 2011, **32**, 1456–1465.
- 19 T. H. Dunning, *J. Chem. Phys.*, 1989, **90**, 1007–1023.
- 20 R. A. Kendall, T. H. Dunning and R. J. Harrison, *J. Chem. Phys.*, 1992, **96**, 6796–6806.
- 21 J.-D. Chai and M. Head-Gordon, *Phys. Chem. Chem. Phys.*, 2008, **10**, 6615–6620.
- 22 J. C. Mullaney, D. P. Zaleski, D. P. Tew, N. R. Walker and A. C. Legon, *ChemPhysChem*, 2016, **17**, 1154–1158.
- 23 J. K.-G. Watson, *J. Chem. Phys.*, 1968, **48**, 4517–4524.
- 24 C. M. Western, *J. Quantum Spectrosc. Radiat. Transfer*, 2017, **186**, 221–242.
- 25 V. Amir-Ebrahimi, A. Choplin, J. Demaison and G. Roussy, *J. Mol. Spectrosc.*, 1981, **89**, 42–52.
- 26 V. Alvin Shubert, D. Schmitz and M. Schnell, *Mol. Phys.*, 2013, **111**, 2189–2197.
- 27 J. Susskind, *J. Chem. Phys.*, 1970, **53**, 2492–2501.
- 28 K. P. Rajappan Nair, M. K. Jahn, A. Lesarri, V. V. Ilyushin and J.-U. Grabow, *Phys. Chem. Chem. Phys.*, 2015, **17**, 26463–26470.
- 29 H. D. Rudolph and A. Trinka, *Z. Naturforsch. A*, 1968, **23**, 68–76.
- 30 J. U. Grabow, H. Hartwig, N. Heineking, W. Jäger, H. Mäder, H. W. Nicolaisen and W. Stahl, *J. Mol. Struct.*, 2002, **612**, 349–356.
- 31 W. Jäger and H. Mäder, *Z. Naturforsch. A*, 1987, **42**, 1405–1409.
- 32 W. Jäger and H. Mäder, *J. Mol. Struct.*, 1988, **190**, 295–305.
- 33 E. Fliege, H. Dreizler, M. Meyer, K. Iqbal and J. Sheridan, *Z. Naturforsch. A*, 1986, **41**, 623–636.
- 34 H. Hartwig and H. Dreizler, *Z. Naturforsch. A*, 1996, **51**, 923–932.
- 35 J. T. Hougen, I. Kleiner and M. Godefroid, *J. Mol. Spectrosc.*, 1994, **163**, 559–586.
- 36 R. B. Mackenzie, C. T. Dewberry, R. D. Cornelius, C. J. Smith and K. R. Leopold, *J. Phys. Chem. A*, 2017, **121**, 855–860.
- 37 Z. Kisiel, PROSPE – Programs for ROTational SPEctroscopy, <https://info.ifpan.edu.pl/~kisiel/prospe.htm> (accessed 29/11/2021, 2021).
- 38 C. C. Costain, *Trans. Am. Crystallogr. Assoc.*, 1966, **2**, 157–164.
- 39 Z. Kisiel, *J. Mol. Spectrosc.*, 2003, **218**, 58–67.
- 40 J. Chen, Y. Zheng, A. Melli, L. Spada, T. Lu, G. Feng, Q. Gou, V. Barone and C. Puzzarini, *Phys. Chem. Chem. Phys.*, 2020, **22**, 5024–5032.
- 41 W. Caminati, P. Moreschini and P. G. Favero, *J. Phys. Chem. A*, 1998, **102**, 8097–8100.
- 42 W. Caminati, L. B. Favero, P. G. Favero, A. Maris and S. Melandri, *Angew. Chem., Int. Ed.*, 1998, **37**, 792–795.
- 43 L. H. Spangler, *Annu. Rev. Phys. Chem.*, 1997, **48**, 481–510.
- 44 A. Taleb-Bendiab, K. W. Hillig and R. L. Kuczkowski, *J. Chem. Phys.*, 1993, **98**, 3627–3636.

