Protonated pyrimidine nucleosides probed by IRMPD spectroscopy

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\textbf{Abstract}

The ESI-formed protonated 2'-deoxycytidine, cytidine, cytarabine, and gemcitabine have been probed using infrared multiphoton dissociation (IRMPD) spectroscopy performed in the 900–2000 cm\textsuperscript{-1} region at CLIO, the Orsay Free Electron Laser facility, and in the 2800–3800 cm\textsuperscript{-1} region using a YAG-laser coupled to a tabletop optical parametric oscillator/amplifier (OPO/OPA). The IRMPD spectra are compared of the protonated nucleosides with the IR spectra of their B3LYP/6-311++G(d,p)-optimized isomeric forms. The stability at room temperature of some conformers has been investigated by means of \textit{ab initio} molecular dynamics simulations. The IRMPD spectra are consistent with the formation in the ESI source of both the N3- and the O2-protonated nucleosides. The most favoured members of both families are characterized by the pyrimidine base oriented anti to the furanose moiety. Concerning the O2-protonated nucleosides, IRMPD spectra and thermochemical considerations support the predominant formation of the structures with the proton oriented \textit{up} relative to the furanose moiety.

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\textbf{1. Introduction}

Nucleosides are fundamental DNA/RNA components [1] which exhibit a variety of specialized functions including long-range electron transport over the RNA and DNA molecules and repair mechanisms after their radiation damage [2,3]. Their structure consists in a free nucleobase linked to a furanose-type ring (sugar) by the N-glycosidic bond. Besides the RNA nucleosides adenosine, guanosine, cytidine, thymidine, and uridine, numerous naturally occurring and chemically synthesized or modified nucleosides (nucleoside analogues) do exist which are used in medicinal and pharmaceutical sciences as prodrugs [4–6]. Compounds with a wide variety of modifications of the furanose ring have been synthesized and tested for activities. Nucleoside analogues are cytotoxic and have found expanding therapeutic use as antiviral and antitumor agents and most antimetabolites of nucleoside analogues possess the skeletal chemical structure of cytidine, such as cytarabine and gemcitabine (Fig. 1) [1,7].

Assessment of the dynamical structure and conformation of nucleosides and of their physicochemical properties is a fundamental requirement for unravelling their intimate mechanism of functioning in living matter. Cleavage of the N-glycosidic bond is a repair mechanism for damaged RNA and DNA molecules [8–13] which has been found to be sensitive to the conformation of the furanose ring [14] as well as to environmental and chemical agents, such as pH, metal cations, and alkylating compounds [15–19]. The nucleobase is available at prototropic equilibria which may favour on point mutations during the replication of the nucleic acid [20,21]. Protonated nucleobases are known to be involved in RNA catalysis [22]. The location of the protonation site of the nucleobases plays a role in the stabilization of triplex structures as well [23].

In this frame, gas-phase studies on protonated nucleosides can appear of some interest, since they may provide precious information on the intrinsic properties of the selected species by eliminating the influence from solvent and counter-ions and any conformational ensemble averaging effects. Besides, gas-phase studies allow for a simpler direct comparison between experimental results and quantum mechanical calculations.

Mass spectrometry (MS), coupled to high-level theoretical calculations, is the method of choice to characterize charged species in the dilute gas state and to investigate their behaviour towards specific reactants. The gas-phase thermodynamics of fundamental DNA/RNA components has been the matter of intense investigation by MS. Despite several MS approaches have been employed to measure the gas-phase basicity and proton affinity of nucleobases [24–28] and nucleosides [28–34], positive information on the actual structure of their protonated forms remains...
elusive. For instance, comparison of the proton affinity of cytosine (228 ± 3 kcal mol⁻¹; gas-phase basicity = 220 ± 3 kcal mol⁻¹) with the B3LYP/6-31+G*—calculated values points to the presence of a mixture of the canonical tautomer, two enol tautomers, and possibly an imine tautomer under the used experimental conditions [25,27]. A similar picture applies to basic nucleosides with the furanosyl in the B3LYP/6-31+G*-calculated values points to the presence of a (228 ± 3 kcal mol⁻¹)

Indeed, the three-dimensional (3D) shape of the nucleosides (as well as of their protonated forms) is determined by [35,36]:

(a) the torsional angle \( \chi = O'4'-C'1'-N1-C2 \) of the N-glycosidic bond which determines the orientation of the nucleobase ring to the sugar ring (Fig. 2). If \( \chi = 180 \pm 90^\circ \), the nucleobase/sugar orientation is anti, if \( \chi = 0 \pm 90^\circ \), the nucleobase/sugar orientation is syn;

(b) the conformation of the furanose ring is described by the pseudorotational angle \( P \) defined as [35,36]:

\[
P = \arctan \left[ \frac{(v_4 + v_1) - (v_3 + v_0)}{2v_2 (\sin 36^\circ + \sin 72^\circ)} \right]
\]

where \( v_i \) s are the five endocyclic torsion angles: \( C'4'-O'4'-C'1'-C2' \) (\( v_0 \)), \( O'4'-C'1'-C2'-C3' \) (\( v_1 \)), \( C1'-C2'-C3'-C4' \) (\( v_2 \)), \( C2'-C3'-C4'-O'4' \) (\( v_3 \)), \( C3'-C4'-O'4'-C1' \) (\( v_4 \)). For any phase angle \( P, v_0 + v_1 + v_2 + v_3 + v_4 = 0 \). The sugar puckering of natural ribo- and deoxyribonucleosides are known to exist preferentially in the North (\( P = 0^\circ \); sugar puckering: \( 2'-\text{exo}/3'-\text{endo} \)) and the South (\( P = 180^\circ \); sugar puckering: \( 2'-\text{endo}/3'-\text{exo} \)) conformations (Fig. 2; see also Fig. S1 in the Supplementary Data (SD) Section);

(c) the torsional angle \( \gamma = C3'-C4'-C5'-O5' \) (Fig. 2), which defines the orientation of the O5'-endo atom with respect to the sugar ring as \( \gamma = 60^\circ \) (trans-gauche (tg)), 180° (gauche-trans (gt)), and 300° (gauche-gauche (gg)); and, for the O2-protonated nucleosides:

(d) the dihedral angle \( \omega = N1-C2 = O2^-H \) (Fig. 2), which describes the orientation of the proton in the O2-protonated nucleobase with \( \omega = 0 \pm 90^\circ \) (down) or \( \omega = 180 \pm 90^\circ \) (up).

This complex conformational landscape stimulated us to undertake a comprehensive study on protonated nucleosides through the use of the infra-red multi-photon dissociation (IRMPD) spectroscopy. In recent years, this methodology has been successfully applied to determine the protonation site(s) of simple nucleobases, like uracil [37,38], thiouracil [38], thymine [37], and cytosine [37] and to exclude their tendency to undergo water-catalyzed prototropic rearrangements [39,40].

In this work, the same approach has been used to investigate the structure and the conformation of the protonated forms (henceforth generically denoted as \( \text{Nu}^+ \)) of some RNA/DNA pyrimidine nucleosides, namely 2’-deoxycytidine and cytidine, as well as of their analogues cytarabine, an epimer of cytidine, and gemcitabine, the gem-difuoro derivative of 2’-deoxycytidine (Fig. 1) [41]. Considering the narrow structural differences of the selected nucleosides, the assessment of the structural and conformational landscapes of their protonated forms necessarily requires a detailed IRMPD study over the extended wavenumber range from 900 to 3800 cm⁻¹.

2. Experimental and computational details

The \( \text{Nu}^+ \) ions have been generated by ESI of 10⁻⁵ M methanolic solutions of the corresponding nucleoside and selected in a modified Bruker Esquire 6000 quadrupole ion trap. Multistage mass spectrometry was carried out using the standard Bruker Esquire Control (v6.2) software. ESI conditions used were as follows: syringe pump rate: 180 µl h⁻¹, spray voltage: 3500 V; capillary temperature: 250 °C. Mass-selected ions were irradiated using the MS2 step, where the excitation amplitude was set to zero to avoid any collision-induced dissociation (CID) process. Mass spectra were recorded after five accumulations, using the standard mass range.
(m/z 50–3000) and normal scan mode resolution (13,000 m/z s⁻¹), the accumulation time being in the range of 200–500 ms in the FEL region and 1–2 s in the OPO/OPA one, depending on the fragmentation efficiency of the process. The IR beam has been focused in the modified quadrupole Paul ion trap through a conical hole in the ring electrode. IR spectroscopy in the 900–2000 cm⁻¹ wavenumber range was performed using the CLIO FEL. The light is produced in 8 μs long pulse trains, the macropulses, of IR laser pulses a few picoseconds in duration, the micropulses. The macropulses repetition rate is 25 Hz while that of the micropulses is 62.5 MHz. Typical energies reached within one macropulse can be 40–60 mJ; the macropulse energy in the present experiments is ca. 20 mJ [42]. The 2800–3800 cm⁻¹ wavenumber range was explored using an IR optical parametric oscillator/amplifier (OPO/OPA) system of LaserVision, pumped by 10 Hz Nd:YAG laser (Excel Technology Europe GmbH Surelite-II, 650 mJ per pulse, 8 ns pulse duration). The output energy, measured between 3400 and 3600 cm⁻¹, is ca. 23 mJ per pulse with a spectral bandwidth of ca. 5 cm⁻¹. The loss of energy in the other spectral regions is not more than 14%.

If the IR photons are in resonance with a IR-activable vibrational mode of Nu⁺, energy can be transferred by sequential absorption of several IR photons (>2 at 3400 cm⁻¹) and the ions can undergo fragmentation by formal loss of the corresponding [uranosyl-H]CN fragment ([C5H6O3R1R2]). By recording the number of the parent Nu⁺ ions (R₁/R₂ = m/z 228 (H/H); m/z 244 (H/OH; OH/H); m/z 264 (F/F)) and that of the protonated cytosine residue (m/z 112) while varying the wavelength of the IR photons, an IRMPD spectrum is obtained. The IR-FEL photon energy was increased at a rate of ca. 2.5 cm⁻¹ s⁻¹, while that from the OPO/OPA systems at a rate of ca. 0.1 cm⁻¹ s⁻¹. The IRMPD fragmentation efficiency is defined as: \( R = -\log I_p/[I_p + I_f] \), where \( I_p \) is the intensity of the parent Nu⁺ ion and \( I_f \) of the protonated cytosine fragment [43].

The IRMPD spectra of Nu⁺ have been interpreted with the aid of the corresponding absorption spectra calculated using density functional theory (DFT) [44]. The relative proton affinities (ΔPA’s) of the n-centres of each given nucleoside have been calculated using the B3LYP exchange-correlation functional [45,46] and the 6-31G(d) basis set as implemented in the Gaussian03 set of programme suites [47]. At this level of theory, the N3 and the O2 atoms of the dc, c, ct, and gc nucleosides are by far the most basic centres (Table S1 in the SD Section), the former being always more basic than the latter.

The zero-order stationary points on the potential energy hypersurfaces of N3-protonated dc, c, ct, and gc (henceforth denoted as dcN⁺, cN⁺, ctN⁺, and gcN⁺, respectively) and of their O2-protonated isomers (henceforth denoted as dcO⁺, cO⁺, ctO⁺, and gcO⁺, respectively) have been investigated at the B3LYP/6-311++G(d,p) level of theory (geometry optimization and frequency calculation on the optimized structures) as a function of the torsional angles \( \gamma, \rho \), and \( \omega \), as well as by the pseudorotational angle \( P \) (see Section 1). Eight input structures for dcN⁺, cN⁺, ctN⁺, and gcN⁺ (nine for ctO⁺) and sixteen for dcO⁺, cO⁺, ctO⁺, and gcO⁺ were employed. This means a total of twenty-four structures for dc⁺, c⁺, ct⁺, and gc⁺ (twenty-five for ct⁺) optimized without using any constraint. The calculations indicate that the proton affinities gap (ΔPA’s) between the N3 and the O2 centres of the nucleosides is sensitive to sugar puckering and orientation relative to aglycone so that ΔPA > 0.2 for (c, 1.4 for dc, 1.5 for GC, and 1.7 kcal mol⁻¹ for (ct) (Tables S2–S5 in the SD Section).

Harmonic vibrational frequencies were determined at this level to characterize the stationary points as local minima and to estimate their zero-point vibrational energy (ZPE) corrections as well as the relevant 298 K enthalpies [48]. As far as the positions of the IR bands are concerned, a scaling factor of 0.961 [49] was applied to the calculated frequencies in the 2800–3800 cm⁻¹ range on the basis of their good agreement with the experimental frequencies for a large set of molecules [50] (Tables S6–S9).

To investigate the conformational stability of selected conformers, ab initio molecular dynamics simulations at room temperature using the gaussian and plane wave formalism [51] as implemented in the cp2k package [52] were employed. We used the PBE functional [53,54] together with corrections for the dispersion interactions using the Grimme [55] formalism. The effect of core electrons has been taken into account by Goedecker–Teter–Hutter pseudopotentials [56]. Double zeta short range basis sets [57] have been employed. The electronic density was described using an energy cutoff for the plane waves expansion of 280 Ry. For each considered system, Born–Oppenheimer molecular dynamics were carried using a 0.25 fs time step for 10 ps at constant energy, after an equilibration time of 2 ps at constant temperature. Infrared spectra from the ab initio molecular dynamics has been calculated by Fourier transform of the dipole autocorrelation function [58,59].

### 3. Results

#### 3.1. IRMPD spectra

Figs. 3–6 shows the IRMPD spectra of the ESI-formed protonated dc, c, ct, and gc, respectively, in the 1400–2000 and 2800–3800 cm⁻¹ spectral ranges. The complete 500–2000 and 2800–3800 cm⁻¹ spectra are reported in the SD Section (Fig. S6). For the sake of comparison, Figs. 3–6 report also the IR spectra of the corresponding most stable N3- and O2-protonated conformers calculated at the B3LYP/6-311+G(d,p) level of theory (Tables S2–S5).

It is evident that all the four Nu⁺ exhibit similar spectral features. Four relatively narrow IR bands are observed in the 3400–3700 cm⁻¹ range whose maxima fall within 3444–3449, 3552–3562, 3583–3588, and 3653–3680 cm⁻¹. The strong bands at 3444–3449 cm⁻¹ are always accompanied by a distinct shoulder on the red side, which is attributed to a fifth resonance at 3420–3425 cm⁻¹. The frequencies of these IR bands fall in the spectral range typical of the NH and OH stretchings. In the 2900–3300 cm⁻¹ spectral region of dc⁺ and c⁺, several weak peaks can be discerned which are accompanied by a more intense signal at 2957 cm⁻¹ in c⁺. Similar peaks are absent or barely observable in ct⁺ and gc⁺.

In the 900–2000 cm⁻¹ range (Figs. 3–6 and Fig. S6), all the spectra are characterized by at least seven broad bands with maxima at ca. 1760–80, 1620–40, 1533–50, 1466–80, 1261–85, 1220–25, and 1074–1107 cm⁻¹. The intense band at 1760–80 cm⁻¹ is typical of the C=O stretch.

#### 3.2. Optimized structures and energies of protonated nucleosides

Aim of the present work is to assess the protonation site(s) of the selected nucleosides and to discern the most probable conformations of their protonated forms by comparing experimental IRMPD with ab initio calculated vibrational spectra.

On the theory side, the harmonic B3LYP/6-311++G(d,p) calculations are critical to guarantee the necessary accuracy for our work. B3LYP/6-311++G(d,p)-optimization of the twenty-four input geometries for dc⁺, c⁺, and gc⁺ (twenty-five for ct⁺) led to the same number of optimized structures, denoted in order of increasing relative enthalpy with the numerical order from 1 to 8, for each of dcN⁺, cN⁺, and GCN⁺ (1–9 for ctN⁺), and from 9 to 24, for each of dcO⁺, cO⁺, and GCO⁺ (10–25 for ctO⁺).
Fig. 3. IRMPD spectrum of ESI-formed protonated dC recorded in the 1400–2000 and 2800–3800 cm$^{-1}$ ranges (c). B3LYP/6-311++G(d,p)-calculated spectra of the most stable conformer of dCN$^+$ (a) and dCO$^+$ (b), i.e., 1 and 9 of Table S2. The calculated plots were constructed using Molden 4.7. (G. Schaftenaar, J. H. Noordik, J. Comput.-Aided Mol. Des. 2000, 14, 123–134) programme, by selecting “10” as the width parameter.

The complete lists of the B3LYP/6-311++G(d,p)-optimized geometrical parameters of the protonated nucleosides are reported in Tables S2–S5, together with the 298 K enthalpy and free energy gaps relative to the corresponding global minima, i.e., isomer 1. Sugar puckering mode and maximum extent in the optimized nucleoside structures, respectively, expressed by the corresponding pseudorotation angle $P$ and the pucker amplitude $V_{pm}$ are graphically reproduced in the pseudorotational cycles of Figs. S2–S5 of SD. Their inspection indicates that, in general, the $P$ values cluster around 35° (N) and 152° (S). The ratio between the N and S states is always below 0.5 and increases in the order: C' < GC' < dC' < CT'. The fact that the $P$ values never fall around 90° or 270° indicates the presence of two pseudorotational barriers involved in the sugar 2'-exo/3'-endo$\leftrightarrow$2'-endo/3'-exo interconversion (repuckering) [36].

Inspection of Tables S2–S5 reveals that, in the most stable N3- and O2-protonated structures, the nucleobase is oriented anti to the sugar ring. Besides, in the most stable O2-protonated conformers, the O2-H$^+$ proton is oriented up relative to the furanose moiety.

Some of the most important structural features of the protonated nucleosides are reported again in Tables S6–S9, together with the most intense B3LYP/6-311++G(d,p)-calculated vibrational

Fig. 4. IRMPD spectrum of ESI-formed protonated C recorded in the 1400-2000 and 2800–3800 cm$^{-1}$ ranges (c). B3LYP/6-311++G(d,p)-calculated spectra of the most stable conformer of C$^+$ (a) and C$^+$ (b), i.e., 1 and 9 of Table S3. The calculated plots were constructed using Molden 4.7. (G. Schaftenaar, J. H. Noordik, J. Comput.-Aided Mol. Des. 2000, 14, 123–134) programme, by selecting “10” as the width parameter.
frequencies. Their inspection reveals that the asymmetric and the symmetric N4H2 stretching frequencies are rather insensitive to the nature and the conformation of the sugar moiety of the nucleoside as well as to the protonation site, whether on the N3 or the O2 centre of the pyrimidine moiety. The same can be said as regards to the furanose O-H frequencies. Also the N3+H and the C2-O2 stretching frequencies are rather insensitive to the specific conformation of N3-protonated nucleosides. Contrariwise, the O2+H stretching in O2-protonated nucleosides is strongly influenced by the value of the dihedral angle $\omega$, which defines the down or up orientation of the O2+H proton, as well as by that of the torsional angle $\chi$, which determines the syn or anti nucleobase/sugar orientation.

3.3. Ab initio molecular dynamics of selected protonated nucleosides

The influence of room temperature on the stability and properties of several conformers of protonated cytidine (1, 9, and 11 in Tables S3 and S7) and cytarabine (1, 4, 5, 15, and 23 in Tables S4 and
S8) has been investigated by ab initio molecular dynamics simulations. The lowest energy structures considered (conformer 1 of CTN and conformer 1 of CTG) maintained their overall conformation along the 10 ps of simulated time. At opposite, two higher energy structures, although being local energy minima, were not stable conformers at finite temperatures as they performed spontaneous geometrical rearrangement towards more stable conformers. Conformer 5 of CTN rapidly evolved towards structure 1 and conformer 23 of CTG exhibits a \( 180^\circ \) torsion of the angle \( \gamma \) of the N-glycosidic bond to acquire the same structure of conformer 15. However, other conformers such as 4 of CTN and 15 of CTG were observed to be stable along dynamic. Neither spontaneous change of the protonation site nor sugar repuckering were observed during any of the simulated systems.

3.4. Comparison of experimental and theoretical IR spectra of Nu

An ion structure can be detected in IRMPD experiments only if it can absorb enough photon energy to allow unimolecular dissociation of the ion into the products. If ion dissociation involves the breaking of a covalent bond, e.g., the N-glycosidic one in Nu\(^+\) (B3LYP/6-311++G(d,p)-calculated bond dissociation energy: ca. 22 kcal mol\(^{-1}\); Scheme S1 in SD), calculations indicate that the ion must absorb several IR photons, depending on their energy (more than 2 photon at 3400 cm\(^{-1}\)). The absorption of each photon is followed by intramolecular vibrational energy redistribution (IVR) throughout the ion frame. By this mechanism, the intensity of the experimental IRMPD signal is determined by the probability of depositing enough energy into the specific bond(s) involved in the ion fragmentation which, in turn, depends not only on the efficiency of resonant photon absorption, but also on the efficiency of the IVR process, as well as on the magnitude of the ion dissociation energy barrier [60]. Thus, it may happen that the resonant multiphoton absorption by a given IR-active vibrational mode may produce a barely detectable signal, although calculations predict an intense absorption (see, for instance, Figs. 3–6).

The B3LYP/6-311++G(d,p)-calculated vibrational frequencies for all stable Nu\(^+\) conformers are compared in Tables S6–S9 with the experimental IRMPD frequencies taken in the 1700–3800 cm\(^{-1}\) range (boldface in the last row of the Tables). Below 1700 cm\(^{-1}\), the comparison gets less informative since the calculated spectra as asymmetric and symmetric N\(_4\)H\(_2\) stretchings (3544–3567 cm\(^{-1}\)) and CN\(^{-}\) stretching frequencies and, therefore, no spectroscopic discrimination is allowed. The situation is somewhat different for the conformers of the O2-protonated nucleosides. Although they are characterized by very similar nucleobase N4H\(_2\) and furanose OH stretching frequencies, nevertheless some structural distinction can be made on the grounds of the specific O2\(^-\)H stretching frequencies. As shown in Tables S6–S9 and Figs. 3c–6c, the 3583–3588 cm\(^{-1}\) signals can be most likely assigned to the stretching of the syn-up and anti-up O2\(^-\)H bond in the corresponding conformers.

Discrimination among the conformers displaying syn-up and anti-up O2\(^-\)H bonds appears beyond the sensitivity of the experimental and computational approaches employed. However, taking into account that: (1) all O2-protonated conformers with the anti-up O2\(^-\)H bonds are generally more stable than those with the syn-up O2\(^-\)H bonds by several kilocalories per mole (Tables S2–S5 in SD), and; (2) the relative facile \( \approx 180^\circ \) torsion of the angle \( \chi \) in some CTG\(^+\) conformers resulting from ab initio molecular dynamics simulations, one can safely assume that the favoured ESI-formed conformers of dC\(^{\text{O}}\)\(^+\) and G\(^{\text{O}}\)\(^+\) are 9, 10, 13, and 14, of C\(^{\text{O}}\)\(^+\) are 9, 10, 17, and 18, and of CTO\(^+\) are 10, 11, 13, and 15. As shown in Tables S6–S9, some of them are characterized by relatively stable C2-exo/C3-exo sugar puckering (N), others by the opposite C2-endo/C3-endo one (S). Indeed, although partial, the results of the ab initio molecular dynamics simulations support the view that the C2-exo/C3-endo \( \leftrightarrow \) C2-endo/C3-exo interconversion in these conformers involves a sizable activation barrier.

4. Conclusions

The IRMPD spectra of ESI-protonated 2'-deoxyctydine, cytidine, cytarabine, and gemcitabine in the 900–2000 and 2800–3800 cm\(^{-1}\) regions have been measured. Comparison of the measured IRMPD spectra with the IR spectra calculated at the B3LYP/6-311++G(d,p) level of theory allows the structures most accessed under the employed experimental conditions to be identified. Ab initio molecular dynamics simulations were performed for a few systems, supporting the tendency of some of the higher energy conformers to relax at room temperature to thermodynamically more stable structures.

The IRMPD spectra are consistent with the co-existence of two non-interconverting Nu\(^+\) families, one protonated at the N3 centre of their pyrimidine moiety and the other protonated at the O2 one. Because of the almost identical vibrational spectra of N3-protonated nucleosides, nothing can be said as regards to their most favoured conformers under the ESI conditions. In contrast, some differences in the IRMPD spectra of the ESI-formed O2-protonated nucleosides allow to conclude that their predominant conformers show a strong tendency to orient the O2-H+ proton of the pyrimidine moiety anti-up to the furanose ring. Their furanose rings may adopt either the 2'-endo/3'-exo (S) or/and the 2'-exo/3'-endo (N) conformation without any sign of efficient repuckering in the gas phase.
Supporting Information. Complete reference [47]; calculated proton affinity gaps of the functional groups of the pyrimidine nucleobase in the selected nucleosides; calculated bond dissociation energies of the most stable conformers 1 and 9 of 2-deoxycytidine; pseudorotational distribution of the isomeric structures of protonated nucleosides; IRMPD experimental and calculated vibrational spectra of the conformers of protonated nucleosides.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jims.2013.05.016.

References


As pointed out by Ghomi et al. (J. Phys. Chem. B 2000, 104, 4560-4568), DFT and other electronic levels of theory give similar results for the geometrical and vibrational features of nucleosides. Furthermore, if an appropriate scaling factor is used, hybrid DFT methods, such as B3LYP, may outperform other DFT methods as well as traditional ab initio methods (described in the previous works of Halls, M.D.; Velkovski, J.; Schlegel, H.B. Theor. Chem. Acc. 2001, 105, 413-421) and the relative intensities (Halls, M.D.; Schlegel, H.B. J. Chem. Phys. 1998, 109, 10587-10593) of IR bands.

The NIST Computational Chemistry Comparison and Benchmark Databases can be found at http://srdata.nist.gov/ccdbd.


