NIR-laser-induced selective rotamerization of hydroxy conformers of cytosine †

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The relative populations of two amino-hydroxy conformers of cytosine, differing in rotation of the OH group by ~180°, were selectively and repeatedly manipulated with narrowband, near-infrared laser light. For cytosine monomers isolated in a low-temperature Ar matrix, laser irradiations at 7013 cm⁻¹ and at 7034 cm⁻¹ were found to induce effective transformations of the two conformers into each other.

Near-IR irradiation can induce conformational changes in small molecules isolated in cryogenic matrices.¹ However, these phenomena have not been reported for larger heterocyclic molecules, such as cytosine. In polyatomic molecules containing more than 10 atoms, the higher density of vibrational states may affect the pathways of vibrational energy redistribution and hence the efficiency of rotational isomerization stimulated by excitation of the overtones of stretching vibrations.

The amino-hydroxy (AH) form of cytosine (see Scheme 1) is the most stable tautomer of the monomeric compound. This tautomer was theoretically predicted to be more stable (by 4.9–6.3 kJ mol⁻¹) than the amino-oxo (AO) form² and was experimentally found, using microwave³ and photoelectron⁴ techniques, to be a dominating species in the gas phase. The AH tautomer is also the most populated form in low-temperature matrices⁵ and helium nanodroplets,⁶ as revealed by IR spectroscopy.

Two conformers of the amino-hydroxy form of cytosine are possible (Scheme 1). They differ in rotation of the hydroxyl group by ca. 180°. According to theoretical calculations,² the energy difference between the two conformers is 2.9–3.1 kJ mol⁻¹ (in favor of AH₁); hence the AH₁:AH₂ ratio in the gas phase (at 495 K) should be ~2.1:1. Both amino-hydroxy conformers were recently identified for cytosine monomers trapped in helium nanodroplets at 0.37 K.⁶ This result shows that no rapid conformational cooling occurs for cytosine, differing in rotation of the OH group by 180°.

To prepare a low-temperature Ar matrix containing cytosine monomers, a sample of the solid compound (Sigma-Aldrich) was heated in a miniature glass oven to ca. 495 K. The vapors of cytosine were deposited together with a large excess of argon on a CsI window mounted at the cold (12 K) tip of a helium-cooled cryostat. Mid-IR absorption spectra were recorded using a Thermo Nicolet 670 FTIR spectrometer equipped with a KBr beam splitter and a DTGS detector. Near-IR spectra were recorded using the same spectrometer but equipped with a CaF₂ beam splitter and an InGaAs detector. Monomers of cytosine isolated in an Ar matrix were irradiated using a narrowband, tunable near-IR light emitted by a Quanta-Ray MOPO-SL pulsed optical parametric oscillator (FWHM ~0.2 cm⁻¹, repetition rate 10 Hz, pulse energy ~3 mJ) pumped with a pulsed Spectra-Physics Quanta-Ray PRO-230-10 Nd: YAG laser.

A fragment of the near-IR spectrum of cytosine monomers isolated in an Ar matrix is presented in Fig. 1. Absorption bands observed in the 7100–6700 cm⁻¹ range are due to overtones of the stretching vibrations of the OH and NH groups. Narrowband, near-IR irradiations at different wavelengths, corresponding to the overtone absorptions (shown in Fig. 1), were carried out. The changes induced on the populations of AH₁ and AH₂ forms were monitored by observation of the mid-IR spectra of the matrix-isolated cytosine monomers. The irradiations at 7034 and 7013 cm⁻¹ were found to be particularly effective. Upon irradiation at 7013 cm⁻¹, the initially most-populated AH₁ conformer converted into AH₂, whereas upon irradiation at 7034 cm⁻¹ a transformation of AH₂ into AH₁ was observed. The full mid-IR absorption spectrum collected before any irradiation as well as the spectra recorded after irradiations at 7034 and 7013 cm⁻¹ are shown in Fig. S1 (in the ESI†). Fragments of the mid-IR spectra recorded after each of these irradiations are presented in Fig. 2. By performing successive cycles of near-IR (7034, 7013 cm⁻¹) irradiation, we have experimentally proven that the population of the amino-hydroxy tautomer can be transferred many times between AH₁ and AH₂ without any loss of the total amount (Scheme 2).

The assignment of the experimentally observed IR bands to AH₁ and AH₂ forms of cytosine is confirmed by comparison (see Fig. 2) with the band positions theoretically predicted at the

![Scheme 1](image-url)
DFT(B3LYP)/6-31++G(d,p) level using the GAUSSIAN 03 program. The two bands observed at 3601 and 3591 cm\(^{-1}\) are due to the stretching vibrations of the hydroxyl group \(\nu(OH)\) in AH2 and AH1 conformers, respectively. In both conformers, the hydrogen atom of the OH group interacts with a nitrogen atom placed in a \(\alpha\) position in the pyrimidine ring. Therefore, the closest vicinity of the OH group is very similar in both conformers. Only the presence of the amino group in the \(\beta\) position is the reason for different frequencies of the \(\nu(OH)\) bands and different energies of AH1 and AH2. Whereas in AH2 the OH group competes with NH2 for the density of the N3 lone electron pair, in AH1 the OH group can interact with the density of the N1 lone electron pair without any competitor. As a consequence, the OH group in AH1 is involved in a stronger intramolecular interaction. This makes the energy of AH1 and the frequency of the \(\nu(OH)\) vibration in this form lower than the respective parameters of AH2. The current assignment of the bands at 3601 and 3591 cm\(^{-1}\) to AH2 and AH1, respectively, is in agreement with the results of the studies of cytosine monomers in helium nanodroplets, where the corresponding absorptions were observed at 3618 and 3610 cm\(^{-1}\).

The observed frequency difference of the \(\nu(OH)\) bands in AH2 and AH1 (10 cm\(^{-1}\) in Ar matrix and 8 cm\(^{-1}\) in He nanodroplets) is in agreement with the theoretically calculated value of 6 cm\(^{-1}\). A larger difference (12 cm\(^{-1}\)) is predicted for normal modes in AH1 and AH2 with frequencies of ca. 1430 cm\(^{-1}\). These modes have significant contribution of the stretching vibration of the C–O bond. In the experimental spectrum of cytosine isolated in an Ar matrix, the corresponding bands, found at 1439 cm\(^{-1}\) and 1428 cm\(^{-1}\), are separated by 11 cm\(^{-1}\) (see Fig. 2).

The region below 3000 cm\(^{-1}\) was not observed in the investigation of cytosine in He nanodroplets. Because of the structural similarity of forms AH1 and AH2, many other mid-IR bands due to these two forms are experimentally found and theoretically predicted at frequencies differing only by 2–3 cm\(^{-1}\) or less. This is the case for the bands observed at 1623 and 1620 cm\(^{-1}\) (theoretical frequency difference 3 cm\(^{-1}\)) and for the bands found at 807.4 and 806.0 cm\(^{-1}\) (theoretical frequency difference 2 cm\(^{-1}\)), see Fig. 2. The general agreement between the experimentally observed and theoretically predicted frequency differences strongly supports the assignment of the two sets of bands to the two AH1 and AH2 rotamers of the amino-hydroxy tautomer of cytosine.

Alongside the two sets of bands assigned to AH1 and AH2, which were identified on the basis of large-scale intensity changes induced by irradiations at 7013 and 7034 cm\(^{-1}\) (see Fig. 2 and 3), a third group of mid-IR bands was also observed in the spectrum of matrix-isolated cytosine. The bands belonging to this group (marked with asterisks in Fig. 3 and 4) did not change their intensities upon any near-IR irradiations. These bands are due to the amino-oxo (AO) or imino-oxo (IO) tautomers of cytosine, which are also populated (though in smaller amounts) in the matrix-isolated sample.

In the frequency range 3650–3400 cm\(^{-1}\) (Fig. 4), the only absorptions due to AH2 and AH1 forms, which neither overlap significantly with each other nor with the bands attributed to other tautomers, are the bands corresponding to \(\nu(OH)\) vibrations, found at 3601 and 3591 cm\(^{-1}\) (bands 1 and 2). The band observed at 3445 cm\(^{-1}\) (band 7) is a nearly perfect overlap of the absorptions resulting from the symmetric NH2 stretching vibrations \(\nu_s(NH_2)\) in both amino-hydroxy conformers. The antisymmetric NH2 stretching vibrations

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**Scheme 2** The effects of near-IR irradiations.
and $AH_2$ have somewhat more distinct frequencies 3565 and 3563 cm$^{-1}$ (bands 3 and 4 in Fig. 4). Other bands observed in the 3650–3400 cm$^{-1}$ region do not change their intensities and shapes upon near-IR irradiation. Two of these bands are the spectral signatures of the amino-oxo ($AO$) tautomeric form and can be assigned to the $\nu_a(NH_2)$ (3471 cm$^{-1}$, band 6) and symmetric $\nu_s(NH_2)$ (3440 cm$^{-1}$, band 8) vibrations, whereas the low-intensity band at 3497 cm$^{-1}$ (band 5 in Fig. 4) is the sole spectral manifestation of the minor imino-oxo ($IO$) form observed in this spectral range.

In conclusion, two amino-hydroxy conformers of cytosine were shown to undergo mutual conversions selectively induced by narrowband near-IR laser light. It was also demonstrated that other forms of cytosine (amino-oxo and imino-oxo) are not affected by near-IR irradiation. We believe that a variety of conformational isomerizations in heterocyclic molecules can be controlled using an analogous approach.

References


