

# A Computational NQR Study on the Hydrogen-Bonded Lattice of Cytosine-5-Acetic Acid

MAHMOUD MIRZAEI, NASSER L. HADIPOUR

Department of Chemistry, Tarbiat Modares University, P.O. Box 14115-175, Tehran, Iran

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**Abstract:** A computational study at the level of density functional theory (DFT) employing 6-311++G\*\* standard basis set was carried out to evaluate nuclear quadrupole resonance (NQR) spectroscopy parameters in cytosine-5-acetic acid (C5AA). Since the electric field gradient (EFG) tensors are very sensitive to the electrostatic environment at the sites of quadrupole nuclei, the most possible interacting molecules with the target one were considered in a five-molecule model system of C5AA using X-ray coordinates transforming. The hydrogen atoms positions were optimized and two model systems of original and H-optimized C5AA were considered in NQR calculations. The calculated EFG tensors at the sites of  $^{17}\text{O}$ ,  $^{14}\text{N}$ , and  $^2\text{H}$  nuclei were converted to their experimentally measurable parameters, quadrupole coupling constants and asymmetry parameters. The evaluated NQR parameters reveal that the nuclei in original and H-optimized systems contribute to different hydrogen bonding (HB) interaction. The comparison of calculated parameters between optimized isolated gas-phase and crystalline monomer also shows the relationship between the structural deformation and NQR parameters in C5AA. The basis set superposition error (BSSE) calculations yielded no significant errors for employed basis set in the evaluation of NQR parameters. All the calculations were performed by Gaussian 98 package of program.

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**Key words:** NQR; hydrogen bond; cytosine-5-acetic acid; DFT; oxygen; nitrogen; hydrogen

## Introduction

Nuclear quadrupole resonance (NQR) spectroscopy is among the most versatile and important techniques to study the physical properties of matters in solid-phase.<sup>1,2</sup> This technique deals with quadrupole nuclei with nuclear spin angular momentum greater than one-half, e.g.,  $^{17}\text{O}$ ,  $^{14}\text{N}$ , and  $^2\text{H}$ . Experimentally, the interaction energy between the nuclear electric quadrupole moment ( $eQ$ ) and the electric field gradient (EFG) tensors arisen at the sites of quadrupole nuclei is measured by NQR as quadrupole coupling constant ( $C_Q$ ). Another important measurable parameter which refers to the EFG tensors deviation from the cylindrical symmetry at the sites of quadrupole nuclei is asymmetry parameter ( $\eta_Q$ ). High-level quantum chemical calculations can also reproduce reliable NQR parameters which these results can either predict or interpret the experimental measurements.<sup>3–5</sup> However, since the EFG tensors are very sensitive to the electrostatic environment at the sites of quadrupole nuclei considering a proper model system in calculations, especially including hydrogen-bonding (HB) interactions, is a crucial step to evaluate reliable NQR parameters.<sup>6,7</sup>

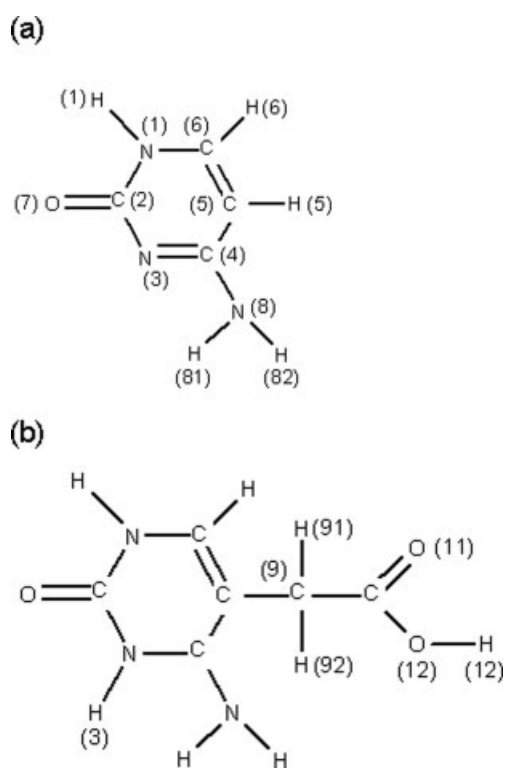
Very soon after the pioneering work of Watson and Crick<sup>8</sup> who indicated the key role of HB interactions in the nucleobase pairing stabilization in living cells, numerous studies employing

various techniques, and also NQR, were performed to investigate these interactions in the nucleobases and the related compounds.<sup>9–12</sup> Among them, study of pyrimidines 5-derivatives is an interesting subject because of its significant pharmacological activities as antitumor and antibacterial drugs.<sup>13–15</sup> Cytosine-5-acetic acid (C5AA) is a cytosine 5-derivative compound where the hydrogen of C5 is replaced by acetic acid (see Fig. 1). The single crystal X-ray diffraction study<sup>16</sup> exhibits the contribution of C5AA to HB interactions in solid-phase (see Fig. 2); however, to our knowledge, to this point, no systematic NQR study was reported to the literature for this interesting biological compound. Comparing the structures of cytosine and C5AA in Figure 1 reveals that since N3 is protonated in C5AA, it seems that C4 may play as a radical in this structure whereas the structure of cytosine is neutral.

This work evaluates NQR parameters ( $C_Q$  and  $\eta_Q$ ) by density functional theory (DFT) calculations of EFG tensors at the sites of  $^{17}\text{O}$ ,  $^{14}\text{N}$ , and  $^2\text{H}$  nuclei in the real hydrogen-bonded lattice of C5AA. To this aim, a five-molecule model system of C5AA

**Correspondence to:** M. Mirzaei; e-mail: mirzaei\_md@yahoo.com or N.L. Hadipour; hadipour.n@gmail.com

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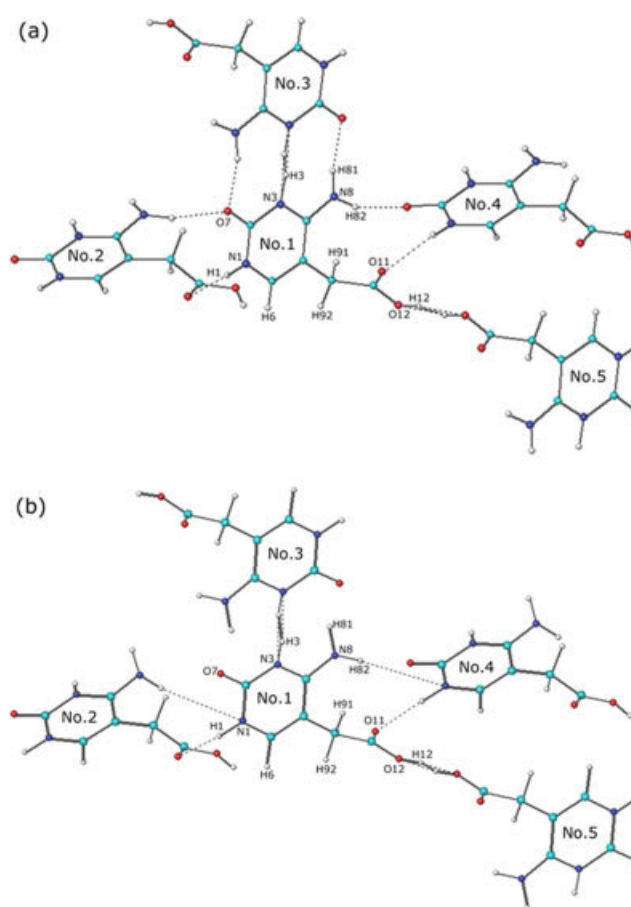


**Figure 1.** (a) Cytosine and (b) monomer form of C5AA.

was created using the reported crystalline coordinates by earlier X-ray study<sup>16</sup> (see Fig. 2). Since X-ray does not locate the accurate positions of hydrogen atoms, only these positions were optimized in the reported structure. Furthermore, to show the importance of this optimization for HB interactions properties in C5AA, NQR calculations were performed for 2 five-molecule model systems, the original model created by the original reported coordinates and the hydrogen-optimized model based on the optimized hydrogen positions (see Fig. 2 and Table 1 for details). To systematically investigate the influence of HB interactions on NQR parameters, the calculations were also performed for either crystalline monomer or optimized isolated gas-phase C5AA. The evaluated NQR parameters are exhibited in Tables 2–5.

### Computational Details

The quantum chemical calculations were performed at the level of density functional theory (DFT) using Gaussian 98<sup>19</sup> package of program. B3LYP<sup>20,21</sup> method and 6-311++G\*\* standard basis set were employed to evaluate NQR parameters. In this work to kinds of optimization were performed. One, an isolated gas-phase C5AA was fully optimized at the level of B3LYP/6-311G\*\* to show the structural deformation due to HB interactions in the lattice. Two, as mentioned earlier, since the accurate positions of hydrogen atoms are not located by X-ray, only the hydrogen atoms positions of C5AA were optimized at the level of B3LYP/6-311G\*\* whereas the other atoms positions were



**Figure 2.** (a) Five-molecule lattice before H-optimization. (b) Five-molecule lattice after H-optimization. The dash lines show HB interactions.

**Table 1.** Geometrical Parameters of Intermolecular Interactions<sup>a</sup>.

	Model-A	Model-B
$r_{N1-H1...O11}$	2.12 Å	1.93 Å
$r_{N...O11}$	2.89 Å	2.89 Å
$r_{N3-H3...N3}$	1.77 Å	1.84 Å
$r_{N3-N3}$	2.82 Å	2.82 Å
$r_{N8-H81...O7}$	1.88 Å	1.99 Å
$r_{N8...O7}$ (No.3)	2.79 Å	2.79 Å
$r_{N8-H82...O7}$	1.93 Å	2.23 Å
$r_{N8...O7}$ (No.4)	2.82 Å	2.82 Å
$r_{O12-H12...O12}$	1.65 Å	1.65 Å
$r_{O12...O12}$	2.51 Å	2.51 Å
$\angle_{N1-H1...O11}$	157°	159°
$\angle_{N3-H3...N3}$	174°	163°
$\angle_{N8-H81...O7}$	167°	134°
$\angle_{N8-H82...O7}$	157°	115°
$\angle_{O12-H12...O12}$	153°	169°

<sup>a</sup>Model-A is the five-molecule lattice before H-optimization and Model-B is the five-molecule lattice after H-optimization.

Table 2. The Calculated  $^{17}\text{O}$  NQR Parameters<sup>a</sup>.

Nuclei	$C_Q$ (MHz)						$\eta_Q$					
	Model 1	Model 2	Model 3	Model 4	Model 5	Expt. <sup>b</sup>	Model 1	Model 2	Model 3	Model 4	Model 5	Expt. <sup>b</sup>
O7	8.42	9.15	9.15	8.01	8.72	7.20	0.38	0.50	0.49	0.83	0.60	0.70
O11	9.08	9.91	9.94	9.84	9.75	–	0.06	0.04	0.01	0.04	0.09	–
O12	9.11	7.53	9.08	7.65	9.52	–	0.50	0.70	0.41	0.72	0.47	–

<sup>a</sup>Model 1 is the optimized isolated gas-phase, Model 2 is the crystalline monomer before H-optimization, Model 3 is the crystalline monomer after H-optimization, Model 4 is the target molecule in five-molecule lattice before H-optimization, and Model 5 is the target molecule in five-molecule lattice after H-optimization.

<sup>b</sup>Available experimental values of cytosine from Ref. 17.

remained frozen during the optimization. The five-molecule model system of C5AA created by X-ray coordinates transforming<sup>16</sup> (see Fig. 2) was considered in NQR calculations. However, to show the importance of hydrogen positions optimization, NQR calculations were performed on 2 five-molecule model systems where the hydrogen positions before and after optimization are considered in the original and H-optimized model systems, respectively.

Quantum chemical calculations yield the EFG tensors at the sites of quadrupole nuclei in the principal axis system (PAS). Therefore, to directly relate the calculated EFG tensors to the experimentally measurable NQR parameters, quadrupole coupling constant ( $C_Q$ ) and asymmetry parameter ( $\eta_Q$ ), eqs. (1)–(2) are used.  $C_Q$  defines the interaction energy of the nuclear electric quadrupole moment ( $eQ$ ) with the EFG tensors while  $\eta_Q$  defines the deviation of EFG tensors from the cylindrical symmetry at the sites of quadrupole nuclei. The standard  $Q$  values reported by Pyykkö<sup>22</sup> are employed in Eq. (1) to evaluate  $C_Q$  values,  $Q(^{17}\text{O}) = 25.58$  mb,  $Q(^{14}\text{N}) = 20.44$  mb, and  $Q(^2\text{H}) = 2.86$  mb. The evaluated NQR parameters for an optimized isolated gas-phase, crystalline monomers, and the target molecules in five-molecule model systems of C5AA are exhibited in Tables 2–4. The basis set super position error (BSSE) was also examined for the employed basis set based on counterpoise<sup>23</sup> method and the results are presented in Table 5.

$$C_Q \text{ (MHz)} = e^2 Q q_{zz} h^{-1} \quad (1)$$

$$\eta_Q = |(q_{xx} - q_{yy})/q_{zz}| \quad (0 < \eta_Q < 1; |q_{xx}| < |q_{yy}| < |q_{zz}|) \quad (2)$$

## Results and Discussion

The  $^{17}\text{O}$ ,  $^{14}\text{N}$ , and  $^2\text{H}$  NQR parameters in the real H-bonded lattice of C5AA are evaluated in present computational study. To this aim, a five-molecule model system of C5AA created by X-ray coordinates transforming was considered in the calculations (see Fig. 2 and Table 1 for details). However, to systematically investigate HB interactions properties in C5AA lattice, NQR calculations were performed for five model systems of C5AA. Model 1 is an optimized isolated gas-phase C5AA. Models 2 and 3 are the crystalline monomers of C5AA before and after H-optimization, respectively. Models 4 and 5 are the five-mole-

cule model systems of C5AA before and after H-optimization, respectively. The calculated EFG tensors at the sites of  $^{17}\text{O}$ ,  $^{14}\text{N}$ , and  $^2\text{H}$  nuclei are converted to the experimentally measurable NQR parameters ( $C_Q$  and  $\eta_Q$ ) using eqs. (1)–(2) and the results are presented in Tables 2–4. Since to our knowledge, to this point, no experimental NQR data have been reported for C5AA, the available experimental NQR data for cytosine<sup>17,18</sup> are added to the Tables 2–4 that the calculated results of backbone cytosine of C5AA and the available experimental data of cytosine are may compared by the reader. The BSSE for the employed basis set of 6-311++G\*\* was examined in the representative H-optimized model system and the results are presented in Table 5. The following text will discuss more on the results of this study.

### Five-Molecule Model System

As mentioned earlier, the EFG tensors are very sensitive to the electrostatic environment at the sites of quadrupole nuclei. Since the characteristic nature of HB interactions is electrostatic, EFG tensors are very sensitive elements to the influence of various HB types in the considered systems, therefore, NQR is a proper technique to investigate the properties of these interactions. Hence, to have reliable calculated results, the considered model system in the calculations must be selected as much closer to the experiment including HB interactions as possible. As a result, the calculated parameters are proper to either predict or interpret the experimental measurements.

Within this study, the most possible interacting molecules with the target one (molecule No. 1 in Fig. 2) were considered in a five-molecule model system. However, because of the X-ray deficiency in locating accurate positions of hydrogen atoms, an optimization at the level of B3LYP/6-311G\*\* was performed to optimize only the hydrogen positions while the other atoms positions remained frozen during this process. As shown in Figures 2a and 2b, the HB interactions properties are changed at the sites of some nuclei after hydrogen optimization. Previously, it was shown that the hydrogen atoms of  $-\text{NH}_2$  group are not in molecular plane of cytosine<sup>24</sup>; however, X-ray detected their positions in the plane and caused the HB interactions in Figure 2a while after hydrogen optimization, the two hydrogen atoms relaxed to out of plane, therefore, different HB interactions are resulted in Figure 2b. The significant difference in HB interactions properties is easily seen at the sites of O7 and N8 where

both nuclei contribute to two N—H...O HB in Figure 2a but N8 contributes to one N—H...N HB and O7 contributes to almost no major HB in Figure 2b. Additionally, the calculated energies of these 2 five-molecule model systems reveal that the total energy of H-optimized model is less than that of original one.

#### Optimized Isolated Gas-Phase and Crystalline Monomers

To investigate the influence of HB interactions on the EFG tensors at the sites of various nuclei from non-H-bonded system to H-bonded one, NQR calculations were also performed for monomer form of C5AA (see Fig. 1b). Furthermore, to show the relationship between the structural deformation and NQR parameters, an isolated gas-phase C5AA was fully optimized at the level of B3LYP/6-311G\*\* as a reference model. It is noted that since the calculations of this work are based on the reported crystalline coordinates by earlier X-ray study,<sup>16</sup> the final reported coordinates of the crystalline monomer were optimized to indicate the structural deformation in two monomer forms of optimized and crystalline, therefore, the number of atoms and overall view of the two monomers are the same (see Fig. 1). The evaluated NQR parameters for three monomer systems show that after H-optimization, since O12 is an O—H group, its NQR parameters differ in two crystalline monomers, however, for O7 and O11, this difference is not seen. Comparison of the optimized isolated gas-phase and crystalline monomers reveals the structural deformation effects on <sup>17</sup>O NQR parameters which it is more significant for O7. Since X-ray detects the  $d_{N-H}$  less than reality, <sup>14</sup>N NQR parameters are remarkably different in two original and H-optimized crystalline monomers. Furthermore, the structural deformation of being in H-bonded system causes different <sup>14</sup>N NQR parameters in optimized isolated gas-phase and crystalline monomers C5AA. Because of X-ray deficiency in accurately locating of hydrogen positions, <sup>2</sup>H NQR parameters significantly change after H-optimization. In addition, they are also influenced by structural deformation of C5AA in H-bonded system. It is noted that N3 is not protonated in neutral cytosine; however, it is protonated in C5AA by partial transferring of proton from carboxylic group to N3. This trend is reported as an outstanding feature of crystal structure of C5AA by X-ray study and its relation with the calculated NQR parameters of the transferred hydrogen will be discussed later in <sup>2</sup>H NQR Parameters section of this article.

#### <sup>17</sup>O NQR Parameters

Table 2 presents the evaluated NQR parameters from the calculated EFG tensors at the sites of three <sup>17</sup>O nuclei in C5AA. A quick look at the results reveals that HB interactions influence on the <sup>17</sup>O NQR parameters in C5AA; however, this influence is not equivalent for various oxygen nuclei. As mentioned earlier, HB interactions properties are changed after H-optimization which is easily seen by the calculated NQR parameters for O7. In the original five-molecule model, O7 contributes to two major N—H...O HB with molecules number 2 and 3 and  $C_Q(^{17}O7)$  reduces 1.14 MHz and  $\eta_Q(^{17}O7)$  increases 0.33 from crystalline monomer to the target molecule in five-molecule model system, see Models 2 and 4 in Table 2. However, in the H-optimized

model system, since the hydrogen atoms of —NH<sub>2</sub> are not in the molecular plane, from the crystalline monomer to the target molecule in five-molecule model system,  $C_Q(^{17}O7)$  reduces 0.43 MHz and  $\eta_Q(^{17}O7)$  increases 0.11 (see Models 3 and 5 in Table 2). This trend reveals that after H-optimization, O7 contributes to two N—H...O HB weaker than those of original model system with molecules numbers 2 and 3.

O11 is one of the carboxylic oxygen that contributes to N—H...O HB with N1—H1 of molecule number 4. Since X-ray usually determines the N—H bond lengths shorter than the reality, the N1—H1 length in the original C5AA is 0.18 Å shorter than that of H-optimized system,  $d_{N1-H1}$  is 0.82 Å and 1.00 Å for the two mentioned systems, respectively. Therefore,  $r_{N1-H1...O11}$  is 2.12 Å in the original model system whereas it is 1.93 Å in the H-optimized one. The different geometrical parameters of N—H...O for O11 causes different HB strengths in the two systems. From crystalline monomer to the target molecule in five-molecule model system,  $C_Q(^{17}O11)$  reduces 0.07 MHz and 0.19 MHz in the original and H-optimized model systems, respectively. This trend reveals more strength of HB interactions for O11 in the H-optimized system rather than the original one. O12 is the other carboxylic oxygen of C5AA which exists as O—H group in C5AA and contributes to O—H...O HB with molecule number 5 in the five-molecule model system. Different geometrical parameters of H12 yielded different NQR parameters for O12 in C5AA model systems where  $C_Q(^{17}O12)$  shifted to down-field in the original system rather than the H-optimized system,  $\angle C-O12-H12 = 96^\circ$  and  $d_{O12-H12} = 0.93$  Å in the original model system and  $\angle C-O12-H12 = 107^\circ$  and  $d_{O12-H12} = 0.97$  Å in the H-optimized system. From crystalline monomer to the target molecule in five-molecule model system,  $C_Q(^{17}O12)$  of the original systems increases 0.12 MHz whereas that of the H-optimized system increase 0.44 MHz. This trend reveals the major influence of O—H...O HB on the <sup>17</sup>O12 EFG tensors of the H-optimized system rather than that of the original system.

#### <sup>14</sup>N NQR Parameters

The evaluated  $C_Q$  and  $\eta_Q$  parameters of C5AA at the sites of three <sup>14</sup>N nuclei are presented in Table 3. As illustrated in Figure 2, the nitrogen nuclei contribute to two N—H...N and N—H...O HB types in the five-molecule model system; however, their strengths are not equivalent in the original and H-optimized model systems. N1 contributes to N—H...O HB with O11 of molecule number 2 in the original five-molecule model system,  $\angle N1-H1...O11 = 157^\circ$  and  $r_{N1-H1...O11} = 2.12$  Å, where  $C_Q(^{14}N1)$  reduces 0.56 MHz and  $\eta_Q$  increases 0.23 from crystalline monomer to the target molecule, see Models 2 and 4 in Table 3. On the other hand, in the H-optimized five-molecule model system, N1 contributes to two N—H...O and N—H...N HB types with molecule number 2,  $\angle N1-H1...O11 = 159^\circ$ ,  $r_{N1-H1...O11} = 1.93$  Å,  $\angle N8-H82...N1 = 161^\circ$ , and  $r_{N8-H82...N1} = 3.09$  Å, where  $C_Q(^{14}N1)$  reduces 0.58 MHz and  $\eta_Q$  increases 0.19 from monomer to the target molecule, see Models 3 and 5 in Table 3. This trend reveals that although N1 contributes to two HB interactions but N1—H1...O11 plays the major role in both model systems of original and H-optimized and also the

Table 3. The Calculated  $^{14}\text{N}$  NQR Parameters<sup>a</sup>.

Nuclei	$C_Q$ (MHz)						$\eta_Q$					
	Model 1	Model 2	Model 3	Model 4	Model 5	Expt. <sup>b</sup>	Model 1	Model 2	Model 3	Model 4	Model 5	Expt. <sup>b</sup>
N1	4.42	3.93	4.23	3.37	3.65	2.16	0.10	0.44	0.08	0.67	0.27	0.76
N3	4.69	4.88	4.29	4.94	4.20	3.41	0.07	0.11	0.07	0.18	0.13	0.20
N8	5.02	4.94	5.32	3.70	5.08	2.93	0.25	0.08	0.07	0.42	0.11	0.39

<sup>a</sup>Model 1 is the optimized isolated gas-phase, Model 2 is the crystalline monomer before H-optimization, Model 3 is the crystalline monomer after H-optimization, Model 4 is the target molecule in five-molecule lattice before H-optimization, and Model 5 is the target molecule in five-molecule lattice after H-optimization.

<sup>b</sup>Available experimental values of cytosine form Ref. 18.

influence of HB interactions on the  $^{14}\text{N1}$  EFG tensors is equivalent in these model systems.

N3 contributes to N—H...N HB type with molecule number 3 in the five-molecule model system,  $\angle\text{N3—H3...N3} = 174^\circ$  and  $r_{\text{N3—H3...N3}} = 1.77 \text{ \AA}$  in the original system and  $\angle\text{N3—H3...N3} = 163^\circ$  and  $r_{\text{N3—H3...N3}} = 1.84 \text{ \AA}$  in the H-optimized system.  $C_Q(^{14}\text{N3})$  increases 0.06 MHz and reduces 0.09 MHz from the crystalline monomers to the target molecule in the two model systems, respectively. Since —NH<sub>2</sub> group plays the major role in nucleic acids and the related compounds, N8 is the most important nitrogen of C5AA. As mentioned earlier, this group is not in the same molecular plane and it is out of this plane. However, in X-ray study, the positions of hydrogen atoms, H81 and H82, were reported in the planar status whereas these atoms were allowed to relax to out of molecular plane during H-optimization. Therefore, this process caused different HB interactions in the two model systems. In the original system, N8 contributes to two N—H...O HB with O7 of molecules number 3 and 4,  $\angle\text{N8—H81...O7-3} = 167^\circ$ ,  $r_{\text{N8—H81...O7-3}} = 1.88 \text{ \AA}$ ,  $\angle\text{N8—H82...O7-4} = 157^\circ$ , and  $r_{\text{N8—H82...O7-4}} = 1.93 \text{ \AA}$ , where  $C_Q(^{14}\text{N8})$  reduces 1.24 MHz and  $\eta_Q(^{14}\text{N8})$  increases 0.34 from crystalline monomer to the target molecule meaning the significant influence of HB interactions on the EFG tensors at the site of  $^{14}\text{N8}$  nucleus. In the H-optimized system,  $C_Q(^{14}\text{N8})$  reduces 0.24 MHz and  $\eta_Q(^{14}\text{N8})$  increases 0.04 from crystalline mono-

mer to the target molecule which means less influence of HB interactions on the  $^{14}\text{N8}$  EFG tensors in this system rather than the original system.

### $^2\text{H}$ NQR Parameters

Table 4 exhibits the evaluated NQR parameters at the sites of  $^2\text{H}$  nuclei in C5AA. As mentioned earlier, since the hydrogen atoms positions are not located accurately by X-ray, their positions were allowed to relax by performing H-optimization. However, to show the importance of this process, two model systems are considered in NQR calculations, original, and H-optimized systems (see Fig. 2 and Table 4 for details). The results reveal that HB interactions influence on the  $C_Q(^2\text{H})$  at the sites of those hydrogen nuclei contribute to the interaction while the other  $C_Q(^2\text{H})$  are remained almost unchanged. H6, H91, and H92 are those hydrogen nuclei which do not contribute to HB interactions in the five-molecule model system, therefore, their calculated NQR parameters from crystalline monomers to the target molecules do not change in two model systems; however, it is noted that their calculated parameters are not the same in the two original and H-optimized systems. H1 is chemically bonded to N1 and interacts with O11 of molecule number 2 which from crystalline monomer to the target molecule,  $C_Q(^2\text{H1})$  reduces 18

Table 4. The Calculated  $^2\text{H}$  NQR Parameters<sup>a</sup>.

Nuclei	$C_Q$ (kHz)						$\eta_Q$					
	Model 1	Model 2	Model 3	Model 4	Model 5	Expt. <sup>b</sup>	Model 1	Model 2	Model 3	Model 4	Model 5	Expt. <sup>b</sup>
H1	276	886	283	868	259	162	0.18	0.10	0.17	0.09	0.18	0.23
H3	273	201	269	479	325	—	0.19	0.25	0.18	0.15	0.03	—
H6	222	434	217	434	218	—	0.16	0.12	0.16	0.12	0.16	—
H81	278	466	269	434	252	230	0.18	0.18	0.19	0.18	0.20	0.19
H82	256	425	267	401	267	236	0.18	0.17	0.18	0.15	0.19	0.18
H91	195	298	203	295	200	—	0.03	0.01	0.04	0.01	0.05	—
H92	202	355	204	355	204	—	0.04	0.03	0.05	0.03	0.05	—
H12	295	393	292	405	798	—	0.10	0.10	0.09	0.36	0.10	—

<sup>a</sup>Model 1 is the optimized isolated gas-phase, Model 2 is the crystalline monomer before H-optimization, Model 3 is the crystalline monomer after H-optimization, Model 4 is the target molecule in five-molecule lattice before H-optimization, and Model 5 is the target molecule in five-molecule lattice after H-optimization.

<sup>b</sup>Available experimental values of cytosine form Ref. 18.



**Table 5.** The BSSE for the Calculated NQR Parameters<sup>a</sup>.

Nuclei	$C_Q$ (MHz)	$\eta_z$
O7	0.02	0.00
O11	0.01	0.00
O12	0.02	0.00
N1	0.00	0.00
N3	0.00	0.00
N8	0.01	0.00
H1	0	0.00
H3	0	0.00
H6	0	0.00
H81	0	0.00
H82	0	0.01
H91	0	0.00
H92	0	0.00
H12	0	0.00

<sup>a</sup>The five-molecule lattice after H-optimization is considered as the representative system. The  $C_Q$  values for hydrogen are in kHz.

kHz and 24 kHz in the original and H-optimized systems, respectively.

As mentioned earlier about the reported outstanding feature of the crystal structure of C5AA by earlier X-ray study,<sup>16</sup> the relation between the half proton transferring from O12 of carboxylic group to N3 and the calculated NQR parameters at the sites of <sup>2</sup>H3 and <sup>2</sup>H12 nuclei are discussed here. However, it is noted that exact interpretation of the results of X-ray study is not the aim of this work. In normal cases, when a hydrogen atom is contributed to HB interactions, the EFG tensors at the sites of <sup>2</sup>H nuclei are influenced and the magnitude of  $C_Q(^2\text{H})$  reduces from monomer to the target molecule which it is clearly seen for the hydrogen nuclei of C5AA other than H3 and H12. Regarding to X-ray trend about the half proton transferring, when these protons are placed toward each other in the hydrogen bonded system (H3 of target molecule toward H3 of molecule No. 3 and H12 of target molecule toward H12 of molecule No. 5) the  $C_Q(^2\text{H})$  increases from monomer to the target molecule. In this case,  $C_Q(^2\text{H3})$  increases 278 kHz and 56 kHz and  $C_Q(^2\text{H12})$  increases 12 kHz and 506 kHz from crystalline monomer to the target molecule in the original and H-optimized model systems, respectively. H3 contributes to N—H...N and H12 contributes to O—H...O types of HB interactions and the calculated NQR results reveals that  $C_Q(^2\text{H3})$  of the target molecule and molecule No. 3 has the same magnitude of 479 kHz in original and 325 kHz in H-optimized model system and  $C_Q(^2\text{H12})$  of the target molecule and molecule No. 5 also has the same magnitude of 405 kHz in original and 798 kHz in H-optimized model system. It is noted that the different calculated NQR parameters of <sup>2</sup>H3 and <sup>2</sup>H12 in comparison with other H nuclei, reveal the outstanding feature of these two nuclei reported by earlier X-ray study.<sup>16</sup>

#### Basis Set Superposition Error

The basis set superposition error (BSSE) of employed basis set within this study was examined based on counterpoise method<sup>23</sup>

and the results are summarized in Table 5. The H-optimized five-molecule model system was considered as representative system in the BSSE calculations. The standard basis set of 6-311++G\*\* is employed to calculate NQR parameters which the calculated BSSE for the results at the sites of various nuclei is almost negligible and show the validity of calculated parameters.

#### Conclusion

This computational work evaluated <sup>17</sup>O, <sup>14</sup>N, and <sup>2</sup>H NQR parameters in the H-bonded lattice of C5AA using B3LYP DFT method and 6-311++G\*\* standard basis set. From the calculated NQR parameters, some trends are concluded. First, the calculated NQR parameters of the original and H-optimized systems remarkably reveal the importance of hydrogen positions optimization in the X-ray structures. This trend shows the major role of computational methods in refinement of experimental measurements. Second, the comparison of NQR parameters between optimized isolated gas-phase and crystalline monomer C5AA shows the relationship between NQR parameters and the structural deformation. Third, from crystalline monomer to the target molecule in five-molecule model system, the influence of HB interactions on the calculated NQR parameters are observed. Fourth, in agreement with the X-ray study trend about half transferring of proton from O12 to N3, the NQR parameters of <sup>2</sup>H3 and <sup>2</sup>H12 show discrepancy among other H nuclei. Fifth, performing BSSE calculations yielded almost no significant errors for employed basis sets, therefore, the evaluated NQR parameters are valid in magnitude.

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