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PII: S0022-2860(18)30562-3

DOI: 10.1016/j.molstruc.2018.05.006

Reference: MOLSTR 25178

To appear in: Journal of Molecular Structure

Received Date: 13 December 2017

Revised Date: 2 May 2018

Accepted Date: 3 May 2018

Please cite this article as: L.E. Fernández, G.E. Delgado, L.V. Maturano, R.M. Tótaro, E.L. Varetti, Experimental and theoretical vibrational study of *N*-carbamoyl-L-proline, *Journal of Molecular Structure* (2018), doi: 10.1016/j.molstruc.2018.05.006.

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# Experimental and theoretical vibrational study of N-carbamoyl-L-proline

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### Abstract

The infrared and Raman spectra of *N*-carbamoyl-L-proline,  $C_6H_{10}N_2O_3$  [(2*S*)-1carbamoylpyrrolidine-2-carboxylic acid] were obtained and interpreted with the help of DFT calculations. Six relatively stable molecular conformers were predicted by theory, being one of these similar to the conformer present in the crystal whose X-ray study was already known. The vibrational study was based in that conformer. The experimental vibrational data and assignments were used as basis for the definition of the Scaled Quantum Mechanics (SQM) force field for the molecule. The Potential Energy Distribution (P.E.D.), which revealed the complex nature of many molecular vibrations, and a set of internal force constants were calculated from this SQM force field.

*Keywords:* N-carbamoyl-L-proline; molecular structure; vibrational spectra; force field; DFT calculation

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#### 1. Introduction

The *N*-carbamoyl derivates have interesting biotechnological applications as, for example, the production of optically pure amino acids by the enzymatic kinetic resolution technique [1-3]. They are also used in the preparation of *N*-carboxyanhydride precursors in peptide synthesis [4]. These compounds are also of great importance in the pharmaceutical industry; for instance, *N*-carbamoyl-L-glutamic acid is used in the treatment of patients with *N*-acetylglutamate synthase deficiency, a urea cycle disorder [5,6,7]. The *N*-carbamoyl amino acids are used as precursors in the synthesis of hydantoins, which possess clinically useful activities; in fact, hydantoins can be used as anticonvulsants, antiepileptic, antiarrhythmics, antimicrobial, and potential anticancer agents. They also have other biological properties as herbicides and fungicides [8-13].

The crystal structure of *N*-carbamoyl-L-proline was determined by X-ray diffraction [14], as part of the structural study of synthesized derivatives [14-18]. However, no information is known about the vibrational properties of the title compound. Therefore, this substance has been synthesized and the FTIR and Raman spectra have been measured and analysed with the aid of the theoretical calculations. A complete assignment of the observed bands is proposed in the present work.

#### 2. Experimental details

The *N*-carbamoyl-L-proline was prepared by the reaction of L-proline and potassium cyanate in acid medium at 60  $^{\circ}$ C. The same sample was used in the crystallographic study [14] and in the present work.

The IR spectra of the substance in KBr pellets were run on a Perkin-Elmer GX FTIR instrument at room temperature in the range 4000-400 cm<sup>-1</sup>, with a resolution of  $2 \text{ cm}^{-1}$ .

The Raman spectra were obtained with the Bruker FRA 106 accessory mounted in a Bruker IFS66 FTIR instrument, using 1064 nm light from a Nd-YAG laser for sample excitation, with a resolution of  $2 \text{ cm}^{-1}$ .

The used spectroscopic techniques, IR and Raman, should give the same frequencies for each mode of vibration of the *N*-carbamoyl-L-proline molecule, which have no symmetry elements (point group  $C_1$ ). However, both techniques are complementary regarding the

relative intensity of bands: weak bands in IR could appear strong in Raman and vice versa, facilitating the measurement of frequencies.

#### 3. Computational details

A theoretical structural study was performed on the isolated molecule using B3LYP/6-31G(d,p) approximations, in order to obtain information about the different conformers. All calculations were made using the Gaussian 03 set of programs [19].

Optimized geometries and vibrational properties of the conformer present in the crystal lattice were calculated using the B3LYP/6-311++G(d,p) combination. That combination turned out to be the one that best adjusts to the experimental values, after analyzing the results obtained from some exploratory calculations using the B3LYP and B3PW91 functional with different basis sets.

The Cartesian force constants obtained by the calculation were transformed to the natural (local symmetry) coordinates as defined by Fogarasi *et al.* [20] using the corresponding B matrix [21] calculated with a standard program. Then, this force field was scaled following the formalism of Pulay *et al.* [22], according to which the diagonal force constants are multiplied by scale factors  $f_i$ ,  $f_j$ ,... and the corresponding interaction constants are multiplied by ( $f_i.f_j$ )<sup>1/2</sup>, adjusting these factors in order to reproduce as well as possible the experimental frequencies. This procedure generates a SQM (Scaled Quantum Mechanics) force field. No anharmonicity corrections of the frequencies were made because of the lack of necessary experimental data.

The SQM force field was obtained with the FCARTP program developed by Collier [23], whereas the atomic displacement vectors corresponding to each molecular vibration were visualized by means of the Moldraw program [24]. The resulting SQM force field was used to calculate the Potential Energy Distribution (P.E.D.) of the molecule, which represents the contribution of each main force constant to the different vibrational modes.

The relative Raman intensities included in **Table 4** are calculated from the Raman activities given by the Gaussian program using the following expression, as reported in the literature [25]:

 $I_i = f(v_{exc} - v_i)^4 S_i / v_i [1 - exp(-h c v_i / k T)]$ 

where  $v_{exc}$  is the Raman excitation frequency (in cm<sup>-1</sup>),  $v_i$  is the *i*th. vibrational mode,  $S_i$  is the corresponding Raman scattering activity, *h*, *c* and *k* are fundamental constants, T is the absolute temperature and *f* is an arbitrary constant defined to give the 100 value to the largest Raman intensity. The calculations were made with  $v_{exc} = 9398.5 \text{ cm}^{-1}$  (1064 nm) and T = 293 K.

### 4. Results and discussion

#### 4.1 Molecular geometry

The *N*-carbamoyl-L-proline molecule can exist in a variety of conformations on the potential energy surface, with a number of local minima defined by the relative position of the carboxyl and ureide groups, which can rotate with respect to the pentagonal ring.

The existence of possible stable conformers was investigated by varying the dihedral angles that define the positions of the mentioned functional groups, using the B3LYP/6-31G(d,p) approximation for the calculations. The results of these calculations showed the existence of six conformers. The corresponding optimized structures without geometry constraints are depicted in **Fig. 1**. The frequencies calculated for the six cases were all real (positive) confirming that they correspond to minima in the potential energy surface.

The most stable structure predicted for the molecule (conformer I, Fig. 1) does not correspond to the conformer present in the crystal lattice (conformer V, Fig. 1). In fact, the three relatively more stable structures investigated (conformers I, II and III) include the formation of different intramolecular hydrogen-bonds, which are detailed in **Table 1**. The molecule existing in the crystal, however, has an structure stabilized by three *intermolecular* hydrogen-bonds which have donor-acceptor distances something smaller than those which appear in the isolated conformers, as can be seen in **Table 1**.

A set of the selected optimized structural parameters recalculated at the B3LYP/6-311++G(d, p) level for the conformer V are summarized in **Table 2** together with the crystallographic measured values [14]. As can be seen, there is an acceptable agreement between the theoretical and experimental values. However, a rather large difference (0.086 Å) appears between the experimental and calculated  $C_3$ - $C_4$  distance, a discrepancy which we cannot explain at this time. Other differences in **Table 2** can be justified taking into account that the calculation was performed on the isolated molecule while the experimental data correspond to molecules that interact in the crystalline structure.

### 4.2 Vibrational analysis

The infrared and Raman spectra obtained for *N*-carbamoyl-L-proline are shown in **Figs. 2** and 3, along with the corresponding calculated spectra with the B3LYP/6-311++G(d,p) combination. The frequencies used to plot the theoretical spectra were calculated using the SQM force field, which corresponds to the conformer V existing in the crystal, as discussed before.

*N*-carbamoyl-L-proline was studied in its crystalline form, a fact which can in principle modify the number and activity of the bands expected for the molecular vibrations. However, there is no clear evidence that this effect appears in the vibrational spectra obtained and therefore the interpretation of the experimental data was based on the isolated molecule.

The *N*-carbamoyl-L-proline molecule has  $C_1$  symmetry and their 57 normal modes of vibration are all active in the infrared and Raman spectra. The frequencies of the bands observed in the infrared and Raman spectra are collected in **Table 3**.

The assignment of the experimental bands was performed by comparison with the calculated frequencies and the visualization of the atomic displacement vectors corresponding to each vibrational mode. In some cases, an observed band was assigned to two normal modes of vibration very close in frequency, according to the obtained values in the theoretical calculation.

Some comments can be made regarding the assignment of bands appearing in the spectra to the different modes of vibration, as follows:

OH and NH<sub>2</sub> stretching modes.

The OH stretching mode and  $NH_2$  stretching modes are strongly affected by the anharmonicity, so the calculated (harmonic) and experimental (anharmonic) values differ by approximately 300 cm<sup>-1</sup>. After applying the scaled force field method, the obtained frequencies are closer to the experimental values, with differences smaller than 20 cm<sup>-1</sup>, as shown in **Table 4**.

The region of the infrared spectrum of *N*-carbamoyl-L-proline between  $3500-2800 \text{ cm}^{-1}$  is complicated due to the broad bands originated by the hydrogen-bonds in the crystal. In

addition, the formation of hydrogen-bonds causes displacement of the bands of the functional groups involved to lower frequencies, as expected. Hence, the band in the IR spectrum located at 3420 cm<sup>-1</sup> is assigned to the OH stretching mode, whereas the bands at 3349 and 3235 cm<sup>-1</sup> are assigned to the antisymmetric and symmetric NH<sub>2</sub> stretching modes, respectively. *CH stretching and deformation modes*.

Four bands in the range 2994 to 2885 are assigned to the antisymmetric and symmetric stretching modes of the three  $CH_2$  groups, as detailed in **Table 4**. Besides, the Raman band at 2968 cm<sup>-1</sup> is assigned to the C-H stretching mode.

The three  $CH_2$  deformation modes generate the band with an intense component at 1457 cm<sup>-1</sup> in infrared and 1446 cm<sup>-1</sup> in Raman.

# C=O stretching and rocking modes.

The intense bands in the IR spectrum at 1687 and 1657 cm<sup>-1</sup> are assigned to the C=O stretching modes of the carboxyl and ureide groups, respectively, according to the calculated frequencies and the corresponding atomic displacements associated with each vibration. The same arguments locate the in-plane and out-of-plane C=O rocking vibrations in the 771-567 cm<sup>-1</sup> range.

#### Ring modes.

Nine vibrational modes are associated to the five-member ring which appears in the molecule: five stretchings, two ring bendings and two ring torsions. The atomic displacements associated with each vibration and the calculated frequencies allowed the assignment of these modes to the corresponding bands, as detailed in **Table 4**, but the potential energy distribution shows that these ring modes are in some cases strongly mixed with the carbamoyl and carboxyl groups vibrations.

The rest of the bands observed in the vibrational spectra were assigned according to the frequencies predicted by calculation and the visualization of the normal modes of vibration, as already mentioned. However, for many vibrational modes a simple description is not possible, as shown by the Potential Energy Distribution (**Table 4**). In fact, in some complex vibrations several coordinates are involved.

The proposed assignment of the bands observed in the vibrational spectra was used as basis for the calculation of the SQM force field (see Computational details). The Cartesian force constants given by the Gaussian calculation were transformed to the set of natural internal coordinates defined in **Table S1** (Supplementary material). The resulting force field was then scaled with the Pulay *et al.* methodology [22] in order to reproduce the experimental frequencies as best as possible. The scale factors obtained in such procedure are listed in **Table S2** (Supplementary material).

The experimental, theoretical and SQM frequencies and the corresponding RMSD (Root Mean Square Deviation) values are shown in **Table 4**. As can be seen, the RMSD value resulting from the comparison between experimental and calculated frequencies, which was initially 93 cm<sup>-1</sup>, decreases to 11 cm<sup>-1</sup> after the force field scaling procedure.

The SQM force field was used to calculate the Potential Energy Distribution (P.E.D.) of the *N*-carbamoyl-L-proline molecule, which represents the contribution of each main force constant (associated with a given natural internal coordinate), to the different normal modes of vibration. **Table 4** shows the P.E.D values considering contributions  $\geq 10\%$ .

The SQM force field was used to calculate a set of internal force constants for the *N*-carbamoyl-L-proline molecule. A selection of these force constants are collected in **Table S3** (Supplementary material).

#### 5. Conclusions

N-carbamoyl-L-proline,  $C_6H_{10}N_2O_3$ , (2*S*)-1-carbamoylpyrrolidine-2-carboxylic acid, was synthetized and its FTIR and Raman spectra were obtained.

A series of DFT calculations allowed the determination of six possible molecular conformers for *N*-carbamoyl-L-proline, most of which are more stable than the (ideally isolated) conformer which appears in the crystal. However, the conformer located in the crystal lattice is clearly stabilized by the formation of three intermolecular hydrogen-bonds.

The frequencies corresponding to the normal modes of vibration and the molecular force field were also calculated. The theoretical results and the experimental vibrational data were used to define a Scaled Quantum Mechanics (SQM) force field for the molecule. The Potential Energy Distribution calculated with the SQM force field revealed the complex nature of many molecular vibrations. A set of internal force constants for *N*-carbamoyl-L-proline was also calculated from the SQM force field.

#### Acknowledgements

Research grants from the following institutions from Argentina are gratefully acknowledged: CONICET (Consejo Nacional de Investigaciones Científicas y Técnicas), UNLP (Universidad Nacional de La Plata) and CIUNT (Consejo de Investigaciones de la Universidad Nacional de Tucumán). From Venezuela: FONACIT (Fondo Nacional de Ciencia, Tecnología e Innovación) and CDCHT-ULA (Consejo de Desarrollo Científico y Humanístico).

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D-HA	D-H	НА	DA	<b>D-HA</b>
Conformer I				
O <sub>15</sub> -H <sub>16</sub> O <sub>18</sub>	0.997	1.673	2.644	163.1
Conformer II				
N <sub>19</sub> -H <sub>20</sub> O <sub>14</sub>	1.015	2.078	2.997	149.4
Conformer III				Y
N <sub>19</sub> -H <sub>20</sub> O <sub>15</sub>	1.012	2.126	3.014	145.3
Crystal <sup>a</sup>				
Crystat				
O <sub>15</sub> -H <sub>16</sub> O	0.82	1.73	2.536(3)	167
N <sub>19</sub> -H <sub>21</sub> O	0.86	2.08	2.914(4)	165
N <sub>19</sub> -H <sub>20</sub> O	0.86	2.13	2.901(3)	149

**Table 1.-** Intramolecular hydrogen-bonds geometry for conformers I, II and III; intermolecular hydrogen-bonds geometry in the crystal (Å, degrees).

<sup>a</sup> Data from ref. 14.

1

Bond length (Å)	Exp. <sup>a</sup>	Calc. <sup>b</sup>	Bond angles (°)	Exp. <sup>a</sup>	Calc. <sup>b</sup>
C <sub>13</sub> =O <sub>14</sub>	1.215(3)	1.204	O <sub>14</sub> =C <sub>13</sub> -O <sub>15</sub>	124.0(3)	123.1
C <sub>13</sub> -O <sub>15</sub>	1.300(3)	1.353	O <sub>14</sub> =C <sub>13</sub> -C <sub>2</sub>	121.0(3)	123.5
O <sub>15</sub> -H <sub>16</sub>	0.82 <sup>c</sup>	0.969	$C_{13}$ - $O_{15}$ - $H_{16}$	-	107.0
C <sub>13</sub> -C <sub>2</sub>	1.513(4)	1.530	$C_{13}$ - $C_2$ - $C_3$	112.5(3)	111.3
C <sub>17</sub> =O <sub>18</sub>	1.265(3)	1.224	$C_{13}$ - $C_2$ - $N_{12}$	113.2(2)	114.8
C <sub>17</sub> -N <sub>19</sub>	1.327(4)	1.387	N <sub>12</sub> -C <sub>17</sub> =O <sub>18</sub>	119.4(3)	122.2
$C_{17}$ - $N_{12}$	1.337(4)	1.373	N <sub>12</sub> -C <sub>17</sub> -N <sub>19</sub>	119.3(3)	115.5
N <sub>19</sub> -H <sub>20,21</sub>	0.86 <sup>c</sup>	1.008	O <sub>18</sub> =C <sub>17</sub> -N <sub>19</sub>	121.4(3)	122.3
C <sub>2</sub> -C <sub>3</sub>	1.542(5)	1.546	C <sub>17</sub> -N <sub>19</sub> -H <sub>20</sub>	-	119.8
C <sub>3</sub> -C <sub>4</sub>	1.452(6)	1.538	$C_{17}$ - $N_{19}$ - $H_{21}$	-	113.2
$C_4$ - $C_1$	1.503(5)	1.538	C <sub>2</sub> -C <sub>3</sub> -C <sub>4</sub>	105.9(3)	103.6
$C_1 - N_{12}$	1.462(4)	1.469	C <sub>2</sub> -N <sub>12</sub> -C <sub>1</sub>	113.9(3)	113.5
N <sub>12</sub> -C <sub>2</sub>	1.455(4)	1.456	C <sub>1</sub> -C <sub>4</sub> -C <sub>3</sub>	108.0(3)	103.8
			$C_3 - C_2 - N_{12}$	102.3(3)	102.7
			$C_{17}$ - $N_{12}$ - $C_2$	119.6(2)	119.6
			$C_{17}$ - $N_{12}$ - $C_1$	126.4(3)	126.4
			$N_{12}$ - $C_1$ - $C_4$	102.6(3)	103.7
			O <sub>15</sub> -C <sub>13</sub> -C <sub>2</sub>	115.0(2)	113.3

**Table 2**.-Selected experimental and optimized geometric parameters for *N*-carbamoyl-L-proline (For atom numbering see Figure 1 (conformer V).

<sup>a</sup> Ref. [14]; <sup>b</sup> B3LYP/6-311++G(d,p) approximation; <sup>c</sup> Fixed in the cristallographic study (14).

IR <sup>a</sup>	Raman <sup>b</sup>	
3420 s		
3349 s	3338 (11)	
3235 s	3231 (11)	
2994 w	2991 (63)	
	2968 (63)	
2954 w	2954 (62)	
2941 w	2941 (76)	
2885 w	2885 (66) 🖌	
2720 w <sup>d</sup>		
2498 w <sup>e</sup>		
1944 w <sup>c</sup>		
1687 vs	1691 (50)	
1657 vs	1642 (51)	
1542 vs	1544 (50)	
1465 s	1472 (73)	
1457 s	1457 sh	
1448 s	1446 (83)	
1357 m	1361 (53)	
1314 s	1325 (59)	
1302 s	1307 (51)	
1274 m	1276 (67)	
1244 m	1247 (60)	
1201 m	1206 (53)	
1164 m	1168 (42)	
1147 m	1148 (48)	
1093 sh	1095 (49)	
1079 m	1074 (56)	
1048 m	1041 (50)	

**Table 3.**-Observed bands in the infrared and Raman spectra of *N*-carbamoyl-L-proline (units are  $\text{cm}^{-1}$ ).

983 (47)
926 (62)
921 (62)
875 (93)
824 (53)
806 (53)
757 (48)
690 (57)
663 (48)
618 (42)
565 (43)
524 (39)
444 (100)
413 (48)
350 (42)
319 (41)
285 (58)
241 (50)
160 (57)
120 (120)
75 (633)

<sup>a</sup> v, very; s, strong; m, medium; w, weak; sh, shoulder.

<sup>b</sup> Relative Raman intensities appear in parentheses.

<sup>c</sup> Unassigned bands.

<sup>d</sup> Tentatively assigned as 1357 cm<sup>-1</sup> x 2 = 2714 cm<sup>-1</sup>.

<sup>e</sup> Tentatively assigned as 1244 cm<sup>-1</sup> x 2 = 2488 cm<sup>-1</sup>.

Mode	Exp. <sup>a</sup>	Calc. <sup>b</sup>	Calc. SQM <sup>c</sup>	IR int. <sup>d</sup>	Raman int. <sup>e</sup>	P.E.D. (contributions $\geq$ 10 %) <sup>f</sup>	Main coordinate
$\nu_1$	3420	3758	3400	0.177	41.7	100 S <sub>1</sub>	O-H str.
$v_2$	3349	3696	3343	0.088	17.5	100 S <sub>2</sub>	NH <sub>2</sub> antisym. str.
ν <sub>3</sub>	3235	3582	3242	0.065	58.2	100 S <sub>3</sub>	NH <sub>2</sub> sym. str.
$\nu_4$	2994	3114	3004	0.050	43.6	$71 S_4 + 21 S_5$	CH <sub>2</sub> antisym. str.
<b>v</b> <sub>5</sub>	2994	3102	2992	0.053	77.5	73 S <sub>5</sub> + 14 S <sub>4</sub>	CH <sub>2</sub> antisym. str.
$\nu_6$	2968*	3101	2968	0.016	54.4	96 S <sub>6</sub>	C-H str.
$\nu_7$	2954	3064	2955	0.084	86.1	$62 S_7 + 25 S_8 + 11 S_{10}$	CH <sub>2</sub> sym. str.
$\nu_8$	2941	3054	2945	0.004	38.0	$35  S_8 + 27  S_7 + 18  S_9 + 16  S_{10}$	CH <sub>2</sub> antisym. str.
ν <sub>9</sub>	2941	3051	2942	0.053	78.1	$62 S_9 + 14 S_4$	CH <sub>2</sub> sym. str.
$\nu_{10}$	2885	2981	2876	0.144	100.0	$70 S_{10} + 32 S_8$	CH <sub>2</sub> sym. str.
$\nu_{11}$	1687	1813	1683	0.862	26.5	85 S <sub>11</sub>	C=O str. (carboxyl)
$v_{12}$	1657	1739	1647	1.000	33.8	$66 \ S_{12} + 17 \ S_{15} + 14 \ S_{48}$	C=O str. (ureide)
v <sub>13</sub>	1542	1625	1553	0.400	11.0	$48 \ S_{13} + 28 \ S_{46} + 11 \ S_{15}$	NH <sub>2</sub> bend.

Table 4.- Experimental and calculated frequencies, infrared and Raman intensities and potential energy distribution for N-carbamoyl-L-proline.

$v_{14}$	1472*	1530	1478	0.005	14.8	76 S <sub>14</sub>	CH <sub>2</sub> bend.
<b>v</b> <sub>15</sub>	1465	1502	1468	0.011	18.6	$33 \ S_{15} + 19 \ S_{31} + 13 \ S_{42} + 11 \ S_{14}$	$C_{17}$ -N <sub>12</sub> str.
$\nu_{16}$	1457	1493	1449	0.015	30.6	$47 \ S_{16} + 38 \ S_{17} + 13 \ S_{14}$	CH <sub>2</sub> bend.
$v_{17}$	1448	1435	1440	0.594	6.8	54 S <sub>17</sub> + 46 S <sub>16</sub>	CH <sub>2</sub> bend.
$\nu_{18}$	1361*	1386	1371	0.009	9.6	$56 \; S_{18} + 24 \; S_{20} + 15 \; S_{50} + 11 \; S_{25}$	CH <sub>2</sub> wag.
<b>v</b> <sub>19</sub>	1357	1364	1362	0.029	3.9	$\begin{array}{c} 22\ S_{19} + 18\ S_{50} + 17\ S_{38} + 16\ S_{27} + 15\ S_{44} \\ + \ 15\ S_{20} \end{array}$	C-OH str.
$v_{20}$	1325*	1362	1337	0.050	5.1	$64 \ S_{20} + 36 \ S_{21} + 32 \ S_{50} + 10 \ S_{29}$	C-H def. in-plane
$v_{21}$	1325*	1351	1336	0.014	4.4	$70 \ S_{20} + 26 \ S_{50} + 21 \ S_{21}$	CH <sub>2</sub> wag.
$v_{22}$	1314	1328	1314	0.006	6.6	$52 \; S_{22} + 16 \; S_{26} + 12 \; S_{18} + 10 \; S_{33}$	CH <sub>2</sub> wag.
V <sub>23</sub>	1302	1300	1295	0.026	17.0	$26 \ S_{23} + 14 \ S_{36} + 11 \ S_{20} + 14 \ S_{21}$	C-H def. out-of-plane
$v_{24}$	1274	1267	1252	0.009	32.9	$38 \; S_{24} + 17 \; S_{29} + 12 \; S_{20}$	CH <sub>2</sub> twist.
V <sub>25</sub>	1244	1230	1234	0.081	21.4	$\begin{array}{l} 27 \; S_{25} + 18 \; S_{36} + 16 \; S_{23} + 12 \; S_{18} + 13 \; S_{24} \\ + \; 10 \; S_{45} \end{array}$	$C_2$ - $N_{12}$ str. (ring)
$\nu_{26}$	1244	1216	1227	0.008	10.4	$18 \ S_{26} + 15 \ S_{34} + 14 \ S_{47} + 12 \ S_{29} + 12 \ S_{28}$	CH <sub>2</sub> twist.
V <sub>27</sub>	1201	1195	1186	0.099	9.8	$28 \ S_{27} + 19 \ S_{24} + 13 \ S_{26}$	COH def.
V <sub>28</sub>	1164	1169	1166	0.217	13.1	$21  {\rm S}_{28} + 16  {\rm S}_{23} + 12  {\rm S}_{26}$	$NH_2$ rock.
V <sub>29</sub>	1147	1144	1144	0.091	17.3	$18 S_{29} + 16 S_{27} + 15 S_{24} + 14 S_{19} + 13 S_{35}$	CH <sub>2</sub> twist.
V <sub>30</sub>	1093	1104	1104	0.104	9.4	$23  \text{S}_{28} + 15  \text{S}31 + 6  \text{S}_{30}$	CH <sub>2</sub> rock.

v <sub>31</sub>	1079	1079	1074	0.049	22.4	$13  S_{31} + 13  S_{35} + 11  S_{30} + 11  S_{37}$	$N_{19}$ - $C_{17}$ str.
<b>v</b> <sub>32</sub>	1048	1035	1047	0.015	30.6	$24 S_{32} + 15 S_{33} + 15 S_{34}$	$C_1$ - $C_4$ str. (ring)
V <sub>33</sub>	983	985	994	0.020	19.1	$27 S_{33} + 22 S_{32}$	$C_2$ - $C_3$ str. (ring)
<b>v</b> <sub>34</sub>	924	922	934	0.009	9.5	50 S <sub>34</sub> + 15 S <sub>32</sub>	$C_3$ - $C_4$ str. (ring)
V <sub>35</sub>	917	919	922	0.017	43.8	$18 \ S_{35} + 13 \ S_{36} + 11 \ S_{29}$	CH <sub>2</sub> rock.
$v_{36}$	874	879	886	0.008	27.3	$13 \ S_{26} + 13 \ S_{50} + 12 \ S_{35} + 12 \ S_{47} + 9 \ S_{36}$	$C_1$ - $N_{12}$ str. (ring)
$v_{37}$	874	874	877	0.025	35.4	$26 S_{37} + 25 S_{45}$	CH <sub>2</sub> rock.
V <sub>38</sub>	824	813	817	0.008	27.1	$20  {\rm S}_{38} + 17  {\rm S}_{30} + 11  {\rm S}_{19}$	$C_2$ - $C_{13}$ str.
V39	771	770	780	0.075	6.6	96 S <sub>39</sub>	C=O rock. out-of-plane (ureide)
$v_{40}$	757*	747	761	0.056	60.3	$38 \ S_{40} + 13 \ S_{33} + 11 \ S_{43}$	C=O rock. out-of-plane (carboxyl)
$v_{41}$	687	665	679	0.060	65.4	$23 \; S_{42} + 13 \; S_{43} + 6 \; S_{41}$	COOH bend.
$v_{42}$	666	643	652	0.077	4.9	$24 \; S_{42} + 11 \; S_{45} + 12 \; S_{47} + 12 \; S_{37}$	C=O rock. in-plane (ureide)
<b>v</b> <sub>43</sub>	608	593	607	0.123	24.8	$45  S_{43} + 16  S_{48}$	OH def. out-of-plane
$v_{44}$	567	580	590	0.062	4.3	$28 \; S_{44} + 18 \; S_{45} + 10 \; S_{41} + 12 \; S_{30}$	C=O rock. in-plane (carboxyl)
$v_{45}$	567	547	556	0.083	38.7	$22 \; S_{45} + 16 \; S_{43} + 10 \; S_{48} + 10 \; S_{36}$	Bend.' (ring)
$v_{46}$	536	515	499	0.297	10.1	$48  {s_{46}} + 30  {s_{13}} + 15  {s_{49}} + 11  {s_{31}}$	NH <sub>2</sub> wag.
$v_{47}$	446	415	425	0.035	78.8	$27 \ S_{47} + 21 \ S_{42}$	Bend. (ring)
V <sub>48</sub>	413*	399	408	0.035	73.7	$29  S_{48} + \overline{14  S_{44} + 11  S_{25}}$	$\text{CONH}_2$ bend.

<b>v</b> <sub>49</sub>	350*	392	370	0.145	25.2	93 S <sub>49</sub> + 37 S <sub>46</sub> + 18 S <sub>13</sub>	NH <sub>2</sub> twist.
V <sub>50</sub>	319*	302	310	0.009	18.8	$42 \ S_{50} + 40 \ S_{41} + 19 \ S_{55} + 16 \ S_{56}$	$C_{13}$ - $C_2$ rock.
V <sub>51</sub>	285*	268	275	0.009	22.8	$40 \ S_{51} + 26 \ S_{53} + 14 \ S_{40}$	$C_{13}$ - $C_2$ rock.
V <sub>52</sub>	241*	212	217	0.009	13.3	$47 \ S_{52} + 36 \ S_{53} + 14 \ S_{48} + 11 \ S_{55}$	C <sub>17</sub> -N <sub>12</sub> rock. in-plane
V <sub>53</sub>	160*	154	158	0.004	11.5	$40 \ S_{53} + 23 \ S_{51} + 17 \ S_{55} + 16 \ S_{50}$	Torsion (ring)
V <sub>54</sub>	120*	118	119	0.008	36.7	$85 \ S_{54} + 49 \ S_{55} + 40 \ S_{56}$	Torsion around N <sub>12</sub> -C <sub>17</sub>
V <sub>55</sub>	-	82	83	0.012	355.8	$86  S_{55} + 63  S_{56} + 12  S_{54}$	Torsion' (ring)
V <sub>56</sub>	75*	72	72	0.008	724.6	42 S <sub>56</sub> + 26 S <sub>57</sub>	C <sub>17</sub> -N <sub>12</sub> rock. out-of-plane
V <sub>57</sub>	-	46	46	0.002	844.6	$145 \ S_{57} + 57 \ S_{55} + 23 \ S_{56} + 19 \ S_{54}$	Torsion around C <sub>2</sub> -C <sub>13</sub>
RMS	$D(cm^{-1})$	93	11				

<sup>a</sup> From the infrared spectrum except those marked: \*From the Raman spectrum.
<sup>b</sup> From B3LYP/6-311++G(d.p) approximation.
<sup>c</sup> From Scaled Quantum Mechanics force field (see text).
<sup>d</sup> Relative absorption intensities normalized with the highest band absorbance equal to 1.0.
<sup>e</sup> Raman intensities calculated and normalized with the highest value (for frequencies larger than 100 cm<sup>-1</sup>) equal to 100 (see text).
<sup>f</sup> Potential Energy Distribution values. Coordinate numbers correspond to Table S1 (Supplementary material).



**Fig. 1.** The most stable conformers of *N*-carbamoyl-L-proline. The relative energies calculated at the B3LYP/6-31G(d,p) approximation (in kJ mol<sup>-1</sup>) are given in parentheses.



Fig. 2. The experimental and calculated infrared spectra of *N*-carbamoyl-L-proline.



Fig. 3. The experimental and calculated Raman spectra of N-carbamoyl-L-proline.

AHPro – Highlights.

- The infrared and Raman spectra of *N*-carbamoyl-L-proline were obtained and interpreted with the help of DFT calculations.
- The molecule have six relatively stable conformers in the potential energy surface.
- The most stable conformer for the isolated molecule does not correspond to the conformer present in the crystal lattice, which is stabilized by intermolecular hydrogen-bonds.
- An assignment of the infrared and Raman bands was made after the theoretical calculation of the corresponding vibrational frequencies.
- A Scaled Quantum Mechanics force field was calculated, which allowed the definition of a Potential Energy Distribution and a set of internal force constants.