

Heteronuclear Intermolecular Resonance-Assisted Hydrogen Bonds. The Structure of Pyrrole-2-Carboxamide (PyCa)

Sławomir J. Grabowski,^{†,‡} Alina T. Dubis,[§] Marcin Palusiak,[†] and Jerzy Leszczynski[‡]

Department of Crystallography and Crystal Chemistry, University of Łódź, ul. Pomorska 149/153, 90-236 Łódź, Poland; Computational Center for Molecular Structure and Interactions, Department of Chemistry, Jackson State University, Jackson, MS 39217; Institute of Chemistry, University of Białystok, Al. J. Piłsudskiego 11/4, 15-443 Białystok, Poland

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The crystal and molecular structure of pyrrole-2-carboxamide (PyCa) determined by single crystal X-ray diffraction is presented. Molecular conformations of PyCa are also analyzed by FT-IR and NMR techniques. Additionally DFT calculations at the B3LYP/6-311++G(d,p) level of approximation are performed for dimers of PyCa and for related species. The existence of two tautomeric forms for the analyzed dimers differing in H-bond motifs, N–H···O or O–H···N, is studied. The geometrical and energetic features of such H-bonds show that these interactions may be classified as intermolecular resonance-assisted hydrogen bonds. Additionally the Bader theory is applied to determine and to analyze bond critical points.

Introduction

It seems that hydrogen bonds as common, strong, and directional interactions are the most important ones influencing the arrangement of molecules in crystals.^{1,2} The possibility to form H-bonds depends on the existence of acidic X–H bonds as well as the Lewis base centers in species constituting crystals.^{3,4} Hence, the question if the hydrogen-bond patterns are predictable is often the subject of investigations.⁵ Etter has indicated the rules of the preferences to form different types of hydrogen bonds in crystals.⁴ The most important general rules state that all good proton donors and acceptors are used in hydrogen bondings, that six-membered-ring intramolecular hydrogen bonds are formed in preference to intermolecular hydrogen bonds, and that the best proton donors and acceptors remaining after intramolecular hydrogen bond formation form intermolecular hydrogen bonds to one another. The additional rules indicated by Etter concern the specific classes of functional groups which usually form hydrogen bonds. It is worth mentioning that the terms “good donors” and “good acceptors” were introduced early on by Donohue.⁶ These terms designate strong proton donors (strong Lewis acids) and strong proton acceptors (strong Lewis bases) in principle.

It is very interesting to note that among these six-membered-rings described by Etter, there are mainly intramolecular resonance-assisted hydrogen bonds (RAHBs) often occurring in crystal structures. RAHBs were described, systematized, and analyzed in detail by Gilli and co-workers in numerous studies.⁷ On the other hand, homonuclear O–H···O bonds were analyzed more often than the other heteronuclear RAHBs. It was also found for O–H···O bonds that, if the H···O distance is shorter, then the interaction is stronger, and the π -electron delocalization and the equalization of bonds within the chelate ring are greater.^{7a,b} In extreme cases of very strong RAHBs there is a very short H···O distance with the H-atom location in the middle

of the O···O distance, or nearly so. In such a case the hydrogen bond may be treated as covalent or at least partly covalent in nature.^{7c,8}

Heteronuclear N–H···O and O–H···N RAHBs were also detected in crystal structures. For example, they were found in crystal structures of ketohydrazones,^{7f} cumarines, and chromones.⁹ It was pointed out that such interactions are usually much weaker than homonuclear H-bonds since there is a difference between the proton affinities of the oxygen and nitrogen centers.^{7g} This may be explained by the principle of the minimum difference between X and Y proton affinities ΔPA within the X–H···Y–H-bond or of the minimum ΔpK_a where ΔpK_a is the difference between the pK_a values of two interacting groups, as measured in a proper polar solvent.^{10–13} The greater the differences, then the weaker are the corresponding H-bonds.

However, for example, for the $-NH_2$ proton donating group of the N–H···O bond, it is possible to decrease the proton affinity of the nitrogen atom by replacing the H-atom not participating in the H-bond formation by a more electronegative one.^{9a} This leads to the strengthening of the N–H···O bond since the difference between the nitrogen and oxygen proton affinities decreases.

Gilli and co-workers have claimed early that intermolecular RAHBs may occur for carboxylic acid dimers, amide dimers, and amide-amidine couplings as well as DNA base pairs.^{7a} The dimers of the Watson–Crick AT and GC base pairs were analyzed in detail, and it was shown that interactions in these base pairs are in essence electrostatic interactions with substantial resonance assistance from the π electrons.¹⁴ The variety of structural motifs of carboxylic acids was analyzed in the 1970s,¹⁵ and it was shown that centrosymmetric dimers of carboxylic acids are formed more often in crystals than the other configurations.

The aim of this study is to analyze the heteronuclear intermolecular resonance-assisted hydrogen bonds in dimers of pyrrole-2-carboxamide (PyCa). Such an investigation is partly connected with the biological importance of pyrrolic compounds. These compounds, containing an amide moiety, often possess

[†] University of Łódź.

[‡] Jackson State University.

[§] University of Białystok.

important biological properties. Some of them are essential constituents of the strong antibacterial agents such as pyrrole tetraamides.¹⁶ This class of compounds is also related to the antitumor agents distamycin A and its derivatives.¹⁷ Furthermore, *N*-benzyl and *N*-propargyl-1*H*-pyrrole-2-carboxamides and some related methyleneamines show monoamine oxidase type A and B inhibitor activity.¹⁸

Conformational isomers and the dimeric forms of the methyl pyrrole-2-carboxylate, pyrrole-2-carboxylic acid, pyrrole-2-carbaldehyde, and their *N*-methyl derivatives have been studied previously by experimental FT-IR and theoretical methods.¹⁹ IR analysis has revealed a higher concentration of the *s*-cis conformer than the *s*-trans conformer in a CCl₄ carbon tetrachloride or cyclohexane solution. Furthermore, ab initio calculations performed at different levels of approximation have shown that IR frequencies of the stretching vibrations of the N-H and C=O groups have lower values for *s*-cis than for *s*-trans conformers.²⁰ Additionally *s*-cis conformers where the carbonyl group is located on the same side as the N-H or N-CH₃ group are more stable than the *s*-trans conformers. In this work the spectroscopic, geometrical and topological parameters of pyrrole-2-carboxamide (PyCa) and its dimer were calculated and compared with experimental data.

In our previous studies we have analyzed the molecular structures and vibrational spectrum of dimers of pyrrole-2-carboxylic acid (PCA) using DFT results (B3LYP/6-311+G(d) level of approximation) as well as applying infrared and Raman spectroscopic studies.²⁰ The PCA dimers were found to be connected through O-H...O centrosymmetric intermolecular RAHBs. The crystal and molecular structure of PCA was also investigated²¹ showing that X-ray crystal structure results are in excellent agreement with the previous theoretical and experimental ones. Additionally in order to obtain the more detailed understanding of the influence of π -electrons on H-bonds, the DFT and higher level ab initio calculations (MP2/6-311+G(d,p) and MP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ) were performed on PCA and its dimers and on model dimers for which similar H-bonded patterns exist.²¹

In this study, DFT calculations were performed on PyCa dimers since N-H...O H-bonds existing for that system are expected to be RAHBs. Additionally the X-ray crystal structure of PyCa is investigated to analyze the intermolecular motifs in crystals. FT-IR spectra are also studied and the "atoms in molecules" (AIM) theory²² is applied to analyze the N-H...O bonds.

Experimental Section: Tools and Theoretical Methods

Synthesis of Pyrrole-2-carboxamide. Synthesis of PyCa proceeding according to the description given earlier by Israel et al.²³ The methyl pyrrole-2-carboxylate (5 g, 0.04 mol) was dissolved in 50 mL of concentrated NH₄OH. The mixture was stirred and heated at 80 °C for 3 h. After cooling the solvent was removed under reduced pressure on a rotary evaporator; toluene (50 mL) was added; and the mixture was evaporated to dryness. The solid product was crystallized from methanol to give 1.5 g (38%) of white crystals, mp 155 °C.

¹H NMR (DMSO) δ ppm: 11.51 (bs, 1H, H-N_{Ar}); 8.06 (bs, 1H, H-N_{amide}); 7.57 i 6.94 (2 x bs, 1H, H-N_{amide}); 6.83 (m, 1H, 5-H); 6.80 i 6.59 (2 x m, 1H, 3-H); 6.06 (m, 1H, 4-H).

¹³C NMR (DMSO) δ ppm: 163.4 i 162.4 (C=O); 126.3 i 126.0 (C2); 121.64 i 121.45 (C5); 113.1 i 110.8 (C3); 108.74 i 108.57 (C4).

IR (KBr pelett, ν cm⁻¹) 3415, 3336, 3180, 1644, 1603, 1552.

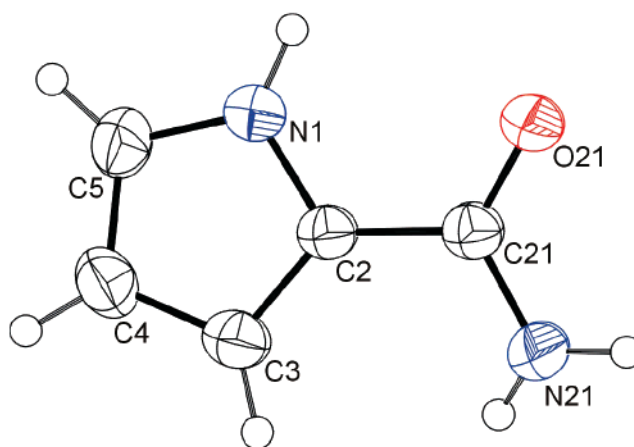


Figure 1. Molecular drawing of pyrrole-2-carboxamide. Displacement ellipsoids are drawn at the 30% probability level.

TABLE 1: Crystallographic Data and Structure Refinement

Formula	C ₅ H ₆ N ₂ O	Formula	C ₅ H ₆ N ₂ O
<i>M</i>	110.12	no. of data collected	4031
crystal system	monoclinic	no. of unique data	1213
Space group	C 2/c	<i>R</i> _{int}	0.0293
<i>a</i> (Å)	14.138(4)	no. of <i>I</i> > 2σ(<i>I</i>) data	683
<i>b</i> (Å)	5.077(2)	no. of parameters	86
<i>c</i> (Å)	14.813(5)	<i>R</i> ₁ (all data)	0.0677
β (deg)	99.545(2)	<i>wR</i> ₂ (all data)	0.0777
<i>V</i> (Å ³)	1048.5(6)	<i>R</i> ₁ [<i>I</i> > 2σ(<i>I</i>)]	0.0277
<i>Z</i>	8	<i>wR</i> ₂ [<i>I</i> > 2σ(<i>I</i>)]	0.0724
<i>D</i> _x (g cm ⁻³)	1.395	$\Delta\rho_{min}$ (e Å ⁻³)	-0.14
μ (mm ⁻¹)	0.101	$\Delta\rho_{max}$ (e Å ⁻³)	0.14
<i>T</i> (K)	293(1)		
λ (Å)	0.71073		
index ranges	-10 ≤ <i>h</i> ≤ 18		
	-6 ≤ <i>k</i> ≤ 6		
	-19 ≤ <i>l</i> ≤ 19		

X-ray Measurement. Block, colorless crystals of the investigated compound (PyCa) suitable for X-ray diffraction were obtained after recrystallization from methanol by slow evaporation of the solvent at room temperature. A single-crystal mounted on a glass fiber was used for measurement at room temperature on a Rigaku AFC5S four circle diffractometer using an MoK α X-ray source. The unit cell dimensions were determined from a least-squares fit to setting angles of 25 reflections. Monitoring of 3 standard reflections measured after each group of 250 reflections showed no significant decays under X-ray irradiation. The structure was solved by direct methods using SHELXS-97²⁴ and refined by the full-matrix least-squares method on *F*² using SHELXL97.²⁵ After refinement with isotropic displacement parameters, the refinement was continued with anisotropic displacement parameters for all non-hydrogen atoms. All hydrogen atoms except H1, H211, and H212 (those attached to nitrogen atoms) were refined using a rigid body model. Positions of the H1, H211, and H212 atoms were found on difference Fourier map and refined with isotropic thermal displacement parameters.

In the final step of refinement, all non-hydrogen atoms were refined with anisotropic thermal parameters. A summary of crystallographic relevant data is given in Table 1. Figure 1 presents the molecular structure of PyCa where the designations of atoms correspond to those applied further in tables and figures.

The molecular geometry was calculated by PARST97²⁶ and PLATON.²⁷ The drawings were made by PLATON.²⁷ Further experimental details, coordinates, and displacement parameters are deposited with CCDC (deposit number 278026).²⁸ Selected

bond distances and angles as well as the other details concerning results of calculations are summarized in the Supporting Information.

Computational Details

The calculations were carried out with Gaussian98²⁹ and Gaussian03³⁰ sets of code using the standard 6-311++G(d,p) basis set³¹ at the hybrid Hartree–Fock density functional (B3LYP).³² These calculations were performed on two conformers. For the *s*-cis conformer, the C=O carbonyl group is at the same side as the N–H bond of the pyrrole ring; for the *s*-trans conformer, the NH₂ group is at the same side as the N–H bond of the pyrrole ring. The geometries of both conformers were fully optimized. Calculations of two dimers of PyCa, corresponding to these two conformers, were also carried out. Optimizations of the dimers were performed with symmetry constraints. Namely, it was assumed that two molecules are linked through equivalent N–H···O hydrogen bonds, and, hence, the dimers are centrosymmetric, i.e., there is an inversion center between the linked moieties. Hence, for each of the dimers, there are pairs of geometrically equivalent molecules. All remaining parameters and H···O intermolecular contacts were optimized. The trends are in line with the experimental results presented here since in crystals there are centrosymmetric dimers of PyCa. Additionally, for the other related systems, calculations and geometry optimizations were performed. Namely the fluoro derivatives of both conformers were considered, where –NFH group is taken into account instead of the –NH₂ one, two related dimers with the same symmetry constraints as for the source systems were analyzed. It should be mentioned that for dimers analyzed here, there are the eight-membered rings, the $R_2^2(8)$ motifs according to the designations introduced by Etter and Bernstein.^{4,33} Such $R_2^2(8)$ motifs often exist in crystal structures of carboxylic acids.¹⁵ In crystal structures of amides (as PyCa crystal structure), the N–H···O H-bonds exist, but the same $R_2^2(8)$ motifs exist as in carboxylic acids. The F-substituent as electronegative decreases the proton affinity of nitrogen and hence may cause the strengthening of N–H···O bonds. Such effects were observed for intramolecular resonance-assisted hydrogen bonds.^{9a}

For centrosymmetric dimers of carboxylic acids the double O–H···O \rightleftharpoons O···H–O proton transfer is often observed.³⁴ The similar double proton transfer is analyzed here for amide structures which is the N–H···O \rightleftharpoons N···H–O process. Hence, the following moieties, monomers with OH donors and dimers with O–H···N H-bonds, are also investigated here including the fluoro derivatives mentioned above. The corresponding calculations were performed. For the O–H···N H-bonded dimers, the symmetry constraints were applied as was done for corresponding tautomeric forms with N–H···O connections. For each pair of tautomers corresponding to minima with N–H···O or O–H···N H-bonds, the transition state was found (for each TS one imaginary frequency was observed). Figure 2 presents the molecular graph of the *s*-cis dimer with N–H···O hydrogen bonds as well as the corresponding dimer configuration obtained after the double proton-transfer process leading to the formation of O–H···N H-bonds.

Binding energies for the analyzed complexes have been computed as the difference between the total energy of the complex and the energies of the isolated monomers and corrected for basis set superposition error (BSSE) via the standard counterpoise method.³⁵ Since there are two equivalent H-bonds for linked moieties, the H-bond energy may be assumed to be half of the binding energy of the dimer.

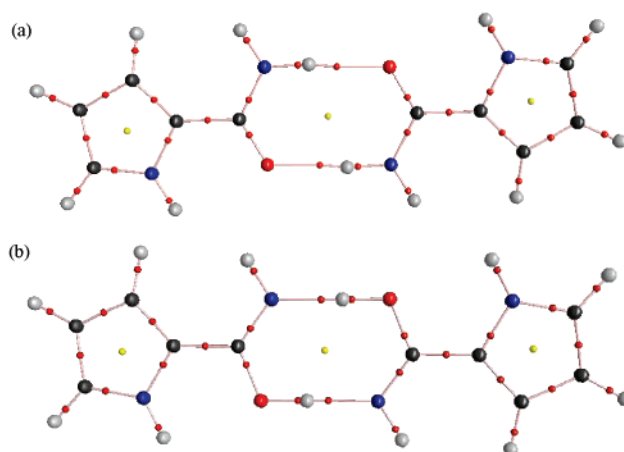


Figure 2. Molecular graphs of the dimers investigated here; big circles correspond to attractors, small ones to the bond critical points (BCPs) and the ring critical points (RCPs). (a) *s*-cis dimer with N–H···O H-bonds (b) the configuration corresponding to *s*-cis dimer with O–H···N hydrogen bonds.

For the analyzed systems the Bader “atoms in molecules” (AIM) theory^{22,36} was applied to find the bond and ring critical points^{37,38} and to analyze them in terms of electron densities and their Laplacians. The AIM calculations were carried out with the use of the AIM2000 program.³⁹

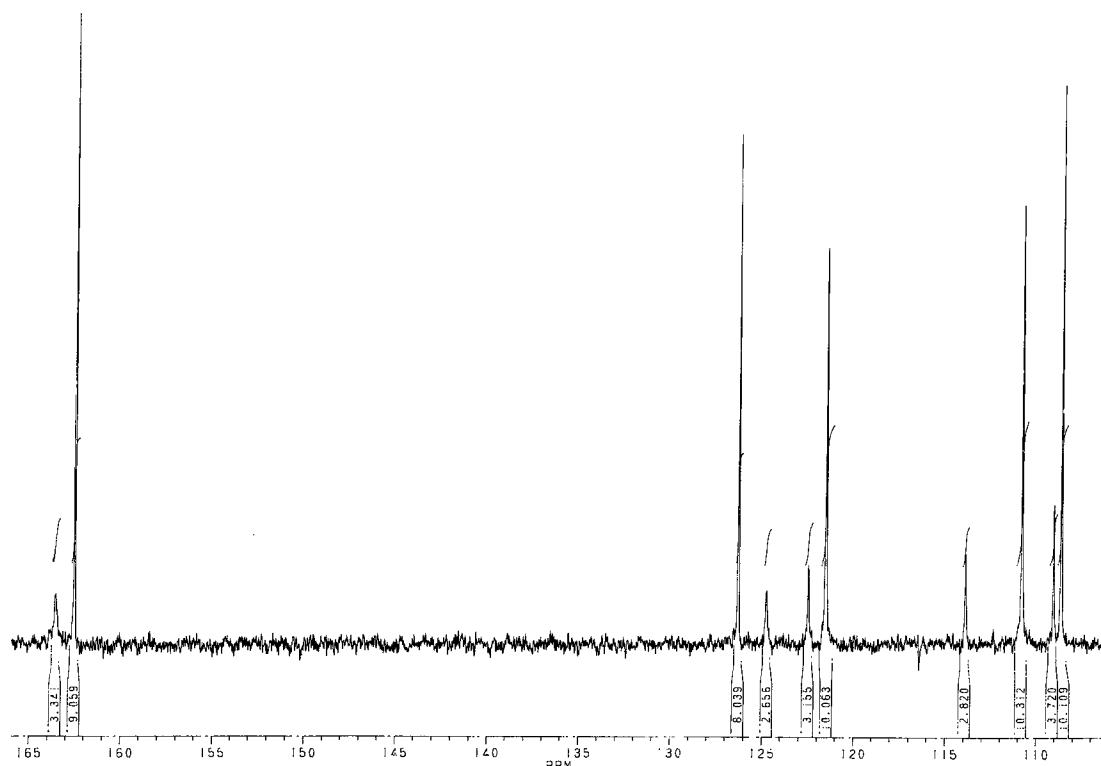
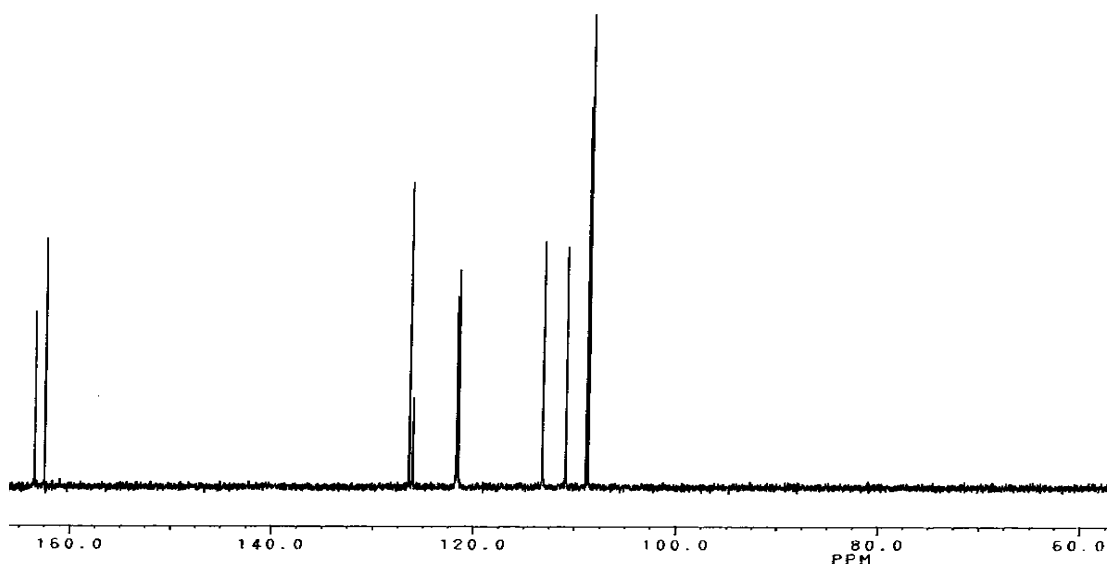
Results and Discussion

Spectroscopic Measurements. Molecular conformations of pyrrole-2-carboxamide have been studied by FT–IR and NMR techniques. The mid-FT–IR spectra were recorded using a Nicolet Magna IR 550 Series II Spectrometer equipped with a KBr beam splitter and a DTGS detector. The sample was measured in DMSO solutions (0.001 M) in a KBr cell of 0.1 mm path length and in a KBr pellet. A spectral resolution of 4 cm^{-1} was used.

The ¹H and ¹³C NMR spectra of pyrrole-2-carboxamide allow two different conformers in DMSO solution (Figures 3 and 4) to be observed. The population of the molecular forms was calculated from the integral intensity of the carbon signals in the ¹³C NMR spectra. The dominant form is *s*-cis pyrrole-2-carboxamide (70%).

Also the IR spectrum of the DMSO solution displays a separated carbonyl doublet (Figure 5). The bands at 1689 and 1667 cm^{-1} of the C=O stretching vibrations appear in the DMSO solution and shift to the 1644 cm^{-1} position in the KBr pellet. This may be attributed to the mixture of conformers *s*-cis and *s*-trans, in which the lower wavenumber band arise from the *s*-cis form. The ¹³C NMR and IR spectroscopy in DMSO solution give evidences of rotational isomerism due to restricted rotation around the C(ring)–C(carbonyl) bond. The *s*-cis/*s*-trans ratio calculated from ¹³C NMR on the basis of the ¹H decoupling without NOE amounts to 3:1.

Crystal and Molecular Structure of PyCa. There are three conventional proton donating bonds for PyCa, two for N–H of the amine group, and one for the N–H bond of the pyrrole ring. There is also the typical carbonyl accepting group (Figure 1). All of them may form hydrogen bonds in the crystal structure. Table 2 presents the shortest intermolecular contacts which may be attributed to the H-bond interactions. One can see that there are three possible kinds of hydrogen bonds. There are two symmetry equivalent N21–H···O21 bonds between the amide groups (see Figure 6). For the crystal structure of PyCa there are the centers of inversion within the eight-member rings

Figure 3. ^{13}C NMR spectrum in DMSO solution.Figure 4. ^{13}C NMR spectrum – ^1H decoupling without NOE in DMSO solution.TABLE 2: Hydrogen Bonding Geometry [\AA , $^\circ$]

D–H \cdots A	D–H	H \cdots A	D \cdots A	D–H \cdots A
N1–H1 \cdots O21 ⁱ	0.891(15)	2.207(16)	2.9867(17)	145.8(14)
N21–H211 \cdots O21 ⁱⁱ	0.832(15)	2.403(15)	3.1564(17)	150.9(13)
N21–H212 \cdots O21 ⁱⁱⁱ	0.892(15)	2.084(16)	2.9716(18)	173.2(14)

^a Symmetry code: i = [7545.00] = 1/2-*x*, -1/2-*y*, -*z*; ii = [1565.00] = *x*, 1+*y*, *z*; iii = [3555.00] = -*x*, -*y*, -*z*.

of the connected amide groups, the $R_2^2(8)$ motif. It is worth mentioning that the same motif exists for compounds containing carboxylic groups. Particularly, the derivatives of benzoic acid often form in crystals similar centro-symmetric dimers connected through the O–H \cdots O H-bonds of carboxylic groups.^{15,40} The N \cdots O distances of NH \cdots O bridges in PyCa are equal to 2.972–(2) \AA (Table 2). Also, take note that the O21 oxygen atom which acts as an acceptor center within the N21–H \cdots O21 H-bridge

is also such a center for the other H-bonds: N21–H \cdots O21 and N1–H \cdots O21 (Table 2). Hence, it is a bifurcated hydrogen bond since there is one accepting center and three donors of protons. Figure 6 shows the same situation in the crystal structure of PyCa and that there are also three H-bond motifs corresponding to three connections of the O21 atom: $R_2^2(8)$ mentioned above, also $R_2^2(10)$ and $R_4^2(8)$. The N–H \cdots O hydrogen bonds as a result of connections through the amide groups seem to be the strongest ones in crystals of PyCa since N \cdots O distances are the shortest ones. However, these and the other heteronuclear N–H \cdots O bonds are rather weak since all N \cdots O distances are close to 3 \AA or even outweigh that value. The O \cdots O distance for stronger H-bonds in centrosymmetric dimers of carboxylic acids in crystals is usually in the range 2.55–2.7 \AA .¹⁵

The C=O and C–N bond lengths of the amide group are equal to 1.249(2) and 1.332 (2) \AA , respectively; thus, there is

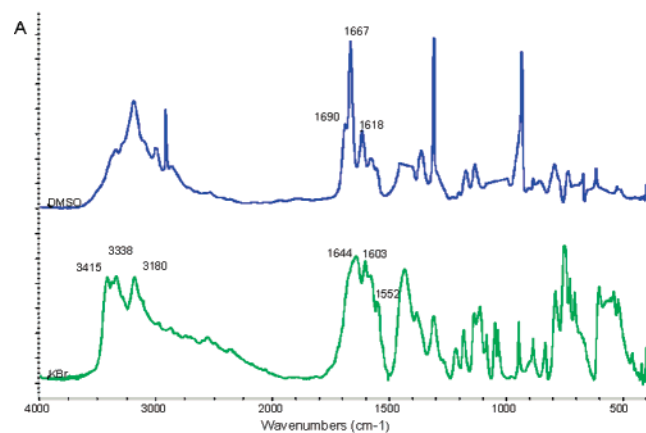


Figure 5. FT-IR spectra of pyrrole-2-carboxamide run as DMSO solution and KBr pellet.

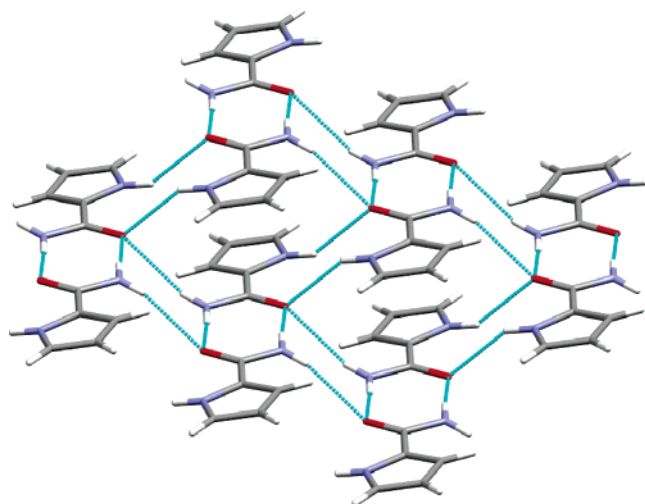


Figure 6. Arrangement of molecules in crystal of PyCa; H-bonds are designated.

only the negligible elongation of the C=O and N–C bonds in comparison to the typical values for amide groups in crystal structures, 1.234 and 1.325 Å, respectively.⁴¹ The elongation of the C=O bond length may be the result of complexation since this bond is sensitive to H-bond interaction.⁴² However, one should know that such an elongation is evident for stronger C=O...H–O homonuclear H-bonds. The second reason for the changes of the N–C and C=O bond lengths may be connected with the π -electron delocalization within the $R_2^2(8)$ -ring. However, again one should remember that these slight changes are connected with the formation of weak H-bonds and, as a consequence, the negligible π -electron delocalization. We observed an effect of the equalization of C–O and C=O bonds within the carboxylic groups in crystal structures of pyrrole-2-carboxylic acid (PCA).²¹ However, for PCA, that effect was more evident due to the existence of stronger O–H...O H-bonds.

DFT Calculations. DFT calculations have been performed here to analyze H-bonds in investigated dimers. The N–H...O and O–H...N bonds in centrosymmetric dimers were taken into account as well as the transition states corresponding to the N–H...O \rightleftharpoons N...H–O double proton transfer reaction. Table 3 presents the binding energies which approximately correspond to two equivalent N(O)–H...O(N) interactions (there are also the less important interactions of the remaining parts of the molecules). The following designations are applied in that table and in the other tables: A, dimers where s-cis moieties are

TABLE 3: Binding Energies for the Systems Analyzed (in kcal/mol)^a

system	E	E _{def}	E'
A(NH...O)	–13.57	1.24	–12.33
A(NH...O,F)	–13.58	1.93	–11.65
A(OH...N)	–29.63	8.97	–20.66
A(OH...N,F)	–20.94	3.28	–17.66
B(NH...O)	–13.93	1.58	–12.35
B(NH...O,F)	–13.85	1.96	–11.89
B(OH...N)	–24.81	6.35	–18.46
B(OH...N,F)	–17.84	2.45	–15.39

^a E corresponds to energies designated according to the supermolecule approach; E' corresponds to energies where the deformations due to complexations are taken into account; E_{Def} designates the Deformation Energy.

connected; B, dimers formed by s-trans conformers, OH...N or NH...O connections are also indicated; and F, if there are –NFH and =NF donating and accepting groups instead of the –NH₂ and =NH ones, respectively. One can see that there is no significant influence of the F-substituent on the H-bond strength for the N–H...O interactions since the binding energies for the A-systems calculated within the supermolecular approach⁴³ amount to 13.57 and 13.58 kcal/mol for the –NH₂ and –NFH donors, respectively. For the same kind of H-bonds for B-systems, the binding energies are equal to 13.93 and 13.85 kcal/mol for the same donating groups as formerly shown. If one takes into account the deformation energy due to the process of complexation, then the binding energies (even for the fluorated systems) are characterized by slightly weaker H-bonds. This is a slightly surprising result since one knows that, for intramolecular RAHBs, such F-substitution of the –NH₂ group causes a decrease in the proton affinity of nitrogen and, hence, the strengthening of the corresponding hydrogen bond.^{9a} However, these astonishing results are also supported by geometrical findings: the calculated C=O and N–C bonds in the molecular structure of dimeric PyCa are equal to 1.243 and 1.348 Å, respectively, while for the fluorated dimer the corresponding values amount to 1.242 and 1.377 Å, respectively. There is no meaningful difference which indicates a lack of the influence of F-substituent on the π -electron delocalization. This may be connected with the additional intramolecular C–H...F hydrogen bonds formed for the fluorine dimer. The situation is quite clear for OH...N H-bond dimers; the F-substitution causes a decrease in the proton affinity of nitrogen and also a decreasing of its proton acceptor properties. Hence, the O–H...N hydrogen bond is stronger than the O–H...N(F) bond for both A and B dimers. Additionally one can observe that O–H...N H-bonds are stronger than the corresponding N–H...O bonds; this is in line with the Leffler–Hammond postulate⁴⁴ since the corresponding hydrogen bonds are stronger for systems closer to the transition state. Such analyses were performed for the intramolecular N–H...O RAHBs, and results in line with that postulate were found.^{7g,h} One can also observe (Table 3) that the deformation energies for the O–H...N systems are greater than for N–H...O systems. This is not surprising since it was mentioned before that the H-bonds for the latter are weaker. The exponential relationship between the binding energy and the deformation energy for the systems analyzed here was found (correlation coefficient is equal to 0.975) showing that for stronger H-bonds the molecular deformations are greater. It is worth mentioning that the deformation is not only connected with the proton donating bonds (NH and OH), but it also concerns the whole amide O=C–NH₂ group and all related groups considered in this study: O=C–NFH, H–O–C=NH, and H–O–C=NF. For the systems analyzed here there is the

TABLE 4: Differences in Energies between the System Indicated and the More Stable Corresponding N–H···O Configuration (in kcal/mol)

system	energy difference
A(OH···N)	20.63
A(TS)	20.97
A(OH···N,F)	4.26
A(TS,F)	10.42
B(OH···N)	18.25
B(TS)	19.49
B(OH···N,F)	1.45
B(TS,F)	10.02

elongation of the C=O or N=C bond and the shortening of the N–C or C–O bond due to complexation. These are slight changes of 0.01–0.03 Å for CN bonds and of 0.02–0.05 Å for CO bonds. Generally the changes are greater for stronger O–H···N bonds than for weaker N–H···O bonds. The changes for TSs are even greater since the C–N and C–O bonds are equal to, for example, 1.302 and 1.307 Å, respectively, for PyCa dimer formed by *s*-cis conformers, showing their equalization. The following tendencies are fulfilled: the greater equalization results in greater π -electron delocalization and stronger H-bonds. This is typical for RAHB systems as dimers of PyCa are connected through N–H···O H-bonds.

There is the NH(H···N) vs H···O(OH) monotonic relationship for all systems analyzed in this study, including also transition states. Such dependence is in line with the classical statements on the properties of hydrogen bonds that for the shorter proton–acceptor distance there is a greater elongation of the proton donating bond.^{1,2}

Table 4 presents differences in total energies of A- and B-type dimers (fluorated and nonfluorated) between the less stable OH···N H-bond or TS species and the more stable NH···O H-bonded ones. One can easily observe that OH···N systems are closer to the corresponding TSs than NH···O H-bond dimers. This nicely confirms the Leffler–Hammond postulate mentioned above. For nonfluorated dimers the differences in energies between OH···N H-bond species and corresponding TSs are even less than 1 kcal/mol. The NH···O H-bond dimers are characterized by much less energies than the corresponding OH···N H-bond dimers. This explains why the former systems are more often observed in crystals than the latter systems. Such findings supported by the results of the Cambridge Structural Database⁴⁵ were presented for intramolecular NH···O and OH···N RAHBs.^{9a} The conclusion might be stated that if NH···O H-bond species exist then the proton-transfer process is not probable. In the case of OH···N systems, which are close to the corresponding transition states, this process is very probable.

AIM Results. The Bader theory was applied here to get more insight into the interactions analyzed. Table 5 presents geometrical as well as topological parameters of atom–atom contacts within the hydrogen bonds investigated. Table 5 concerns the NH/OH bonds and H···N/H···O contacts. For these pairs of atoms involved in bonds or intermolecular interactions, the topological parameters related to them were considered; the electron densities at the corresponding bond critical points (BCPs– ρ_C 's) and their Laplacians ($\nabla^2\rho_C$'s). Additionally the energetic properties of the BCPs were taken into account, such as the electron energy density at BCP (H_C) as well as its components, the potential electron energy density (V_C) and the kinetic electron energy density (G_C). There is the excellent exponential relationships between the H···N (H···O) distance and the electron density at the corresponding BCP; if covalent bonds as well as contacts are taken into account for the sample of species analyzed here thus the correlation coefficient for both

TABLE 5: NH/OH Bond Lengths and the H···N/H···O Distances (in Å) as well as the Electron Density at NH/OH (H···N/H···O) BCP – ρ_{BCP} and Its Laplacian – $\nabla^2\rho_{BCP}$, the Total Electron Energy Density (H_{BCP}), the Electron Potential Energy Density (V_{BCP}), and the Electron Kinetic Energy Density (G_{BCP}) – Topological Parameters in au

system	NH(H···N)	ρ_{BCP}	$\nabla^2\rho_{BCP}$	G_{BCP}	V_{BCP}	H_{BCP}
A(NH···O)	1.026	0.3205	–1.6845	0.0461	–0.5133	–0.4672
A(NH···O,F)	1.034	0.3203	–1.7527	0.0431	–0.5245	–0.4814
A(OH···N)	1.579	0.0719	0.0898	0.0468	–0.0711	–0.0243
A(OH···N,F)	1.709	0.0508	0.1058	0.0363	–0.0461	–0.0098
A(TS)	1.409	0.1115	0.0038	0.0610	–0.1210	–0.0600
A(TS,F)	1.263	0.1624	–0.2695	0.0670	–0.2013	–0.1343
B(NH···O)	1.027	0.3211	–1.6708	0.0466	–0.5109	–0.4643
B(NH···O,F)	1.035	0.3207	–1.7549	0.0430	–0.5248	–0.4818
B(OH···N)	1.634	0.0626	0.0981	0.0421	–0.0597	–0.0176
B(OH···N,F)	1.749	0.0456	0.1053	0.0331	–0.0399	–0.0068
B(TS)	1.370	0.1232	–0.0403	0.0634	–0.1368	–0.0734
B(TS,F)	1.248	0.1690	–0.3188	0.0667	–0.2130	–0.1463
System	OH(H···O)	ρ_{BCP}	$\nabla^2\rho_{BCP}$	G_{BCP}	V_{BCP}	H_{BCP}
A(NH···O)	1.865	0.0303	0.1036	0.0248	–0.0236	0.0012
A(NH···O,F)	1.812	0.0339	0.1139	0.0282	–0.0279	0.0003
A(OH···N)	1.039	0.2798	–1.7363	0.0714	–0.5770	–0.5056
A(OH···N,F)	1.006	0.3114	–2.1255	0.0650	–0.6614	–0.5964
A(TS)	1.113	0.2242	–0.9435	0.0838	–0.4035	–0.3197
A(TS,F)	1.218	0.1653	–0.2404	0.0887	–0.2374	–0.1487
B(NH···O)	1.872	0.0298	0.1024	0.0243	–0.0230	0.0013
B(NH···O,F)	1.811	0.0338	0.1142	0.0282	–0.0278	0.0004
B(OH···N)	1.025	0.2942	–1.9131	0.0688	–0.6158	–0.5470
B(OH···N,F)	1.000	0.3190	–2.2059	0.0642	–0.6798	–0.6156
B(TS)	1.137	0.2096	–0.7352	0.0864	–0.3567	–0.2703
B(TS,F)	1.233	0.1589	–0.1817	0.0884	–0.2221	–0.1337

exponential relations amounts to unity; one relation concerns O and H atomic pairs while the second one N and H pairs.

One can observe that, for all NH and OH bonds, the $\nabla^2\rho_C$ -values are negative (Table 5). This is usual for covalent (share) interactions.²² Additionally, for all N···H and O···H contacts of transition states, the $\nabla^2\rho_C$'s are negative which supports the statement that, for hydrogen bonds of transition states, the interactions of the X···H···Y bridge are at least partially covalent in nature. For share interactions a negative Laplacian value designates a concentration of electron density, while a positive Laplacian value indicates a depletion of electron charge.²² For the sample analyzed here there is only one exception, the transition state of the proton transfer for the dimer formed by *s*-cis conformers of PyCa; in this case for the H···N contact, $\nabla^2\rho_C$ is positive. However, the H_C -value in this case is negative. Rozas et al. have stated that the following classification may be introduced for H-bond interactions: strong H-bonds are characterized by negative values of $\nabla^2\rho_C$ and, as a consequence, H_C ; for medium strength H-bonds, $\nabla^2\rho_C$ is positive, but H_C is negative; and, finally, if both $\nabla^2\rho_C$ and H_C are positive, then there are weak H-bonds.⁴⁶ Sometimes one can also find the statement that $\nabla^2\rho_C$ is negative for covalent interactions, and if $\nabla^2\rho_C$ is positive then H_C is negative; thus, the interactions are partially covalent in nature.⁴⁷ The covalence of H-bond interactions was discussed very recently for dihydrogen bond species where very short (close to 1 Å) H···H intermolecular contacts exist.⁴⁸

It is worth mentioning that H_C values for all H···N interactions are negative since they correspond to covalent bonds, to transition states and to O–H···N tautomers, those which are closer to the transition states than the corresponding N–H···O systems. This was analyzed in the previous section. However, it is very important that all O–H···N H-bonds considered here may be treated as partially covalent in nature since H_C values are negative for all H···N contacts. This is not the rule for N–H···O hydrogen bonds where the H_C values for H···O contacts are positive. Table 5 shows that H_C s of H···O

interactions are negative only for covalent bonds and in the case of transition states.

Summary

The heteronuclear resonance-assisted hydrogen bonds were considered for pyrrole-2-carboxamide (PyCa) dimers and related complexes. The FT-IR and NMR spectra were analyzed, and the DFT calculations were carried out. Additionally the crystal structure of PyCa was investigated since X-ray diffraction measurements were performed. It was found that *s*-cis conformers are preferable in liquids, and only such conformers exist in crystals forming N-H \cdots O bifurcated hydrogen bonds. The DFT calculations and AIM analyses indicate that N-H \cdots O hydrogen bonds are resonance-assisted. The investigation of different tautomeric forms in dimers shows the following: (1) OH \cdots N bonds are stronger than NH \cdots O bonds since the former are closer to the corresponding transition states; (2) the OH \cdots N H-bonds are partially covalent in nature; (3) almost all H \cdots O and H \cdots N contacts within the transition states possess negative values of Laplacian at corresponding BCPs, which may indicate the covalent nature of such interactions; (4) the π -electron delocalization of the amide and related groups is reflected in the changes of bond lengths (the greatest is the change for TSs and the smallest for NH \cdots O systems).

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Supporting Information Available: Selected bond distances and angles as well as the other details concerning results of calculations. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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