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Picolinic and Isonicotinic Acids: A Fourier Transform Microwave Spectroscopy Study

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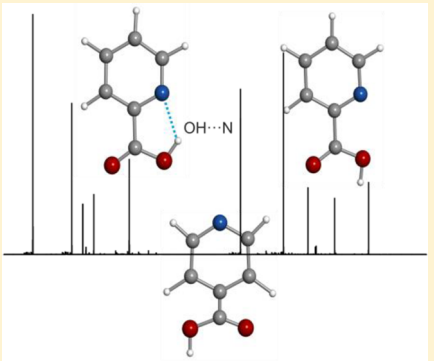
Supporting Information

ABSTRACT: The rotational spectra of laser ablated picolinic and isonicotinic acids have been studied using broadband chirped pulse (CP-FTMW) and narrowband molecular beam (MB-FTMW) Fourier transform microwave spectroscopies. Two conformers of picolinic acid, s-*cis*-I and s-*cis*-II, and one conformer of isonicotinic acid have been identified through the analysis of their rotational spectra. The values of the inertial defect and the quadrupole coupling constants obtained for the most stable s-*cis*-I conformer of picolinic acid, evidence the formation of an O−H···N hydrogen bond between the acid group and the endocyclic N atom. The stabilization provided by this hydrogen bond compensates the destabilization energy due to the adoption of a −COOH trans configuration in this conformer. Its r_s structure has been derived from the rotational spectra of several ^{13}C, ^{15}N, and ^{18}O species observed in their natural abundances. Mesomeric effects have been revealed by comparing the experimental values of the ^{14}N nuclear quadrupole coupling constants in the isomeric series of picolinic, isonicotinic, and nicotinic acids.



INTRODUCTION

The two isomeric molecules picolinic (pyridine-2-carboxylic acid) and isonicotinic (pyridine-4-carboxylic acid) acids ($C_6H_5NO_2$) are pyridine derivatives, which have a great interest due to their chemical and biological properties. The isonicotinic acid is a main metabolite of isonicotinic acid hydrazide, which is used as a therapeutic drug for tuberculosis.[1] The picolinic acid is an endogenous metabolite of L-tryptophan, which has been detected in several biological mediums as blood serum, cerebrospinal fluid, human milk, pancreatic juice, and intestinal homogenates.[2−5] Picolinic acid is also known as a metal chelating agent in the human body. They have been investigated in condensed phases using IR, Raman, and X-ray techniques,[6−13] but none of them provide a detailed conformational picture about these isomeric species. Hence, the experimental and theoretical vibrational spectra have been interpreted in terms of the wavenumbers and intensities of selected experimental bands,[11] which have been compared and discussed on the basis of the position of the nitrogen atom in the aromatic ring. All results indicate that the structural propensities observed in condensed phases are strongly biased by interactions with the solvent or the crystal packing forces.[12,13]

The unambiguous characterization of the intrinsic conformational preferences can be achieved through the analysis of the rotational spectra. Molecules placed in an isolated environment such as that provided by the gas phase, free of the interactions with the solvent, exhibit their intrinsic molecular properties. In the present work we have investigated the rotational spectra of the biological active molecules, picolinic and isonicotic acids, to obtain precise information on their conformation and structure. The combination of narrowband molecular beam Fourier transform microwave (MB-FTMW) spectroscopy and broadband chirped pulse Fourier transform (CP-FTMW) with laser ablation (LA) vaporization provides a powerful experimental tool,[14,15] which allows the investigation of the rotational spectra of solid biomolecules such as natural amino acids,[16] dipeptides,[17] nucleic acid bases,[18] and monosaccharides[19] in the gas phase. We present here the first experimental rotational studies of picolinic and isonicotinic acids using a combination of the aforementioned techniques. The results have been compared with those previously reported for nicotinic acid (pyridine-3-carboxylic acid), in which two conformers, s-*cis* and s-*trans*, have been recently unveiled.[14]

EXPERIMENTAL SECTION

Details of the Chirped-pulse Fourier transform microwave (CP-FTMW) spectrometer coupled with a laser ablation source are given elsewhere.[14] Cylindrical rods of picolinic acid (m.p.: 138 °C) and isonicotinic acid (m.p.: 310 °C) samples were obtained by pressing a mixture formed by fine powder of the substances with a few drops of a commercial binder, in a hydraulic bench press. They were vaporized in the ablation nozzle of the spectrometer[14] using the third harmonic (355 nm) of a ps Nd:YAG laser (Ekspla, 20 ps 15 mJ/pulse). The vaporized molecules seeded in the carrier gas Ne (stagnation pressure of

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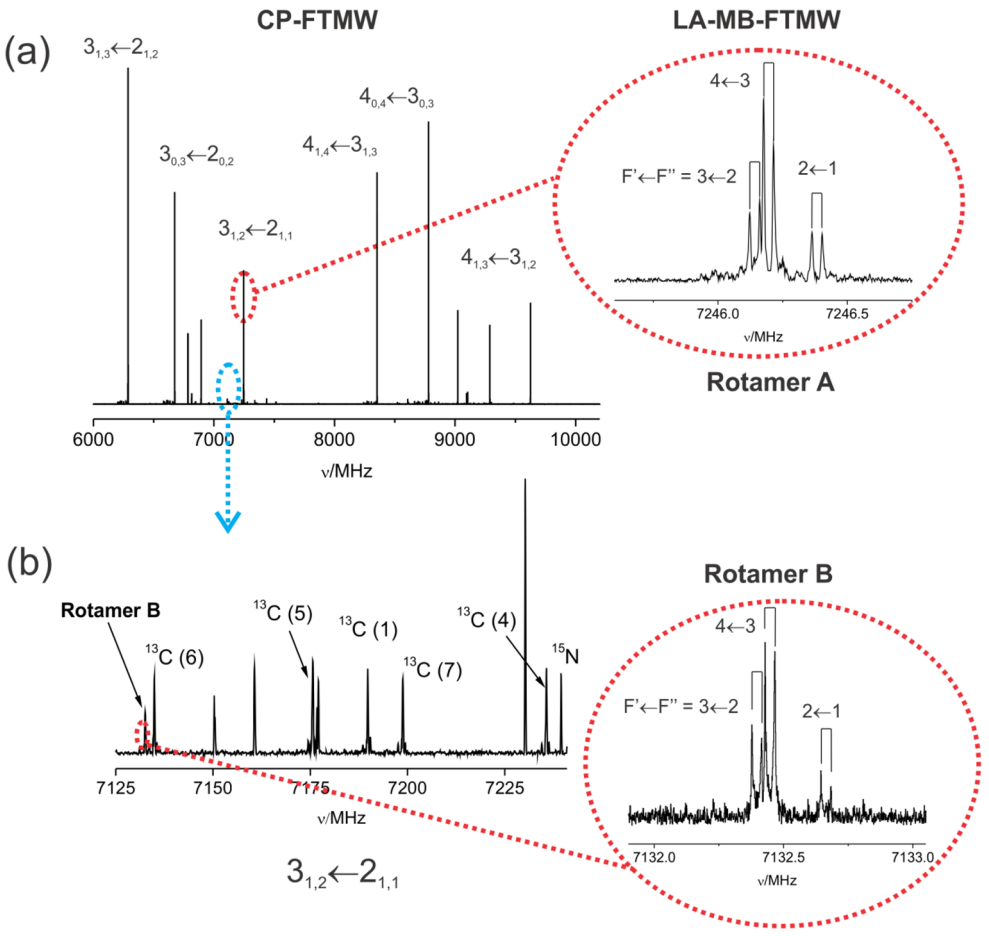

Figure 1. (a) CP-FTMW spectrum of laser ablated picolinic acid showing the groups of μ_a R-branch transitions for rotamer A. The inlet shows the quadrupole hyperfine structure for the $3_{1,2} \leftarrow 2_{1,1}$ transition measured with the LA-MB-FTMW spectrometer. (b) The $3_{1,2} \leftarrow 2_{1,1}$ rotational transition for the different isotopic species of rotamer A observed in their natural abundances. The same rotational transition is observed for rotamer B. The resolved quadrupole hyperfine structure by LA-MB-FTMW spectroscopy is also shown in the inlet.

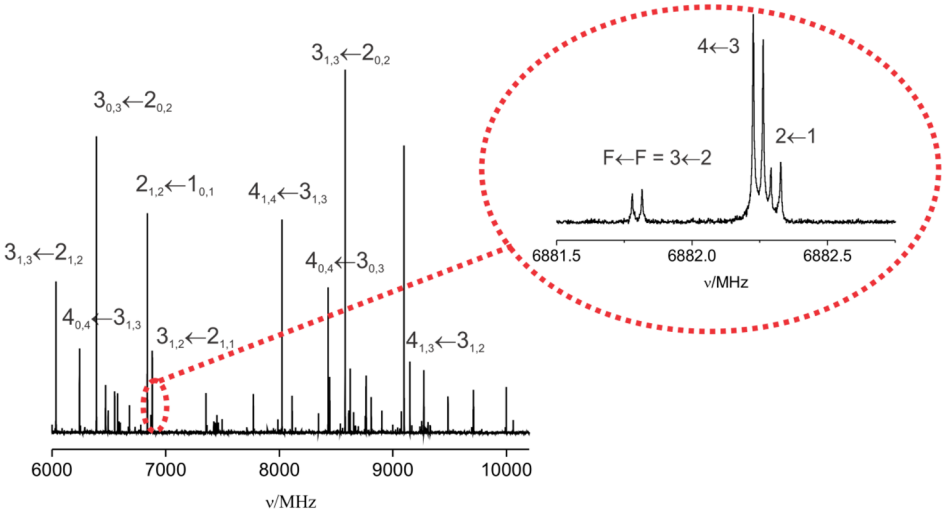

Figure 2. CP-FTMW spectrum of laser ablated isonicotinic acid and the quadrupole hyperfine structure for the $3_{12}-2_{11}$ rotational transition obtained by LA-MB-FTMW spectroscopy.

10 bar) were expanded supersonically into the vacuum chamber and probed by a microwave chirped pulse. Up to 60 000 individual free induction decays (4 FIDs on each valve cycle) for picolinic and isonicotinic acids were averaged in the time domain and Fourier transformed to obtain the frequency domain rotational spectra from 6 to 10.2 GHz shown in Figures 1 and 2. A Kaiser−Bessel window was applied to increase the baseline resolution.

Additional measurements were done using the higher resolution of our LA-MB-FTMW spectrometer[15] to resolve

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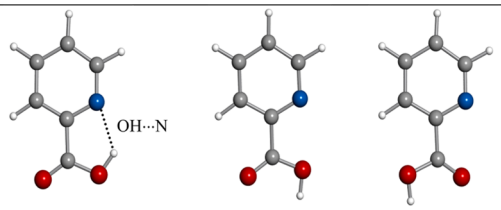
the ^{14}N nuclear quadrupole coupling hyperfine structure. This spectrometer, which works in the 4−12 GHz frequency region, uses a laser ablation system with a ps-laser (Quantel, 35 ps 12 mJ/pulse). The vaporized molecules were seeded in Ne at 15 bar of pressure and introduced into a Fabry−Pérot resonator to form a supersonic jet. A short microwave radiation pulse (0.3 μs) was then applied to macroscopically polarize the molecules in the beam. The subsequent molecular emission signal was collected and Fourier transformed to obtain the spectrum in the frequency domain. In our setup, the microwave radiation travels parallel to the axis of the resonator, and consequently, all transitions appear as doublets because of the Doppler effect (see inlets of Figure 1). The line width in this experiment is ca. 5 kHz, and the accuracy of the frequency measurements is better than 3 kHz.

RESULTS AND DISCUSSION

Rotational Spectra Analysis. According to simple considerations based on the expected coplanarity of the acid and pyridine moieties, two possible arrangements s-*cis* or s-*trans* of the −COOH group relative to the N atom can be anticipated for picolinic acid. In the s-*cis* configuration, in which the −OH group and the N atom are at the same side, two conformers s-*cis*-I and s-*cis*-II have to be considered. Conformer s-*cis*-I presents an O−H···N intramolecular hydrogen bond with a destabilizing −COOH trans configuration, while conformer s-*cis*-II shows a −COOH cis configuration. Geometry optimizations for the three plausible conformers were carried out at the MP2/6-311++G(d,p)[20] level of theory with the Gaussian suite of programs,[21] and the predicted rotational spectroscopic constants are summarized in Table 1.

Table 1. Plausible Conformers of Picolinic Acid Together with the Calculated[a] Spectroscopic Parameters and Energies



	s-cis-I	s-cis-II	s-trans
A/ B/C[b]	3880/ 1286/ 966	3931/ 1262/ 960	3922/ 1255/ 960
$\lvert\mu_a\rvert/\lvert\mu_b\rvert/\lvert\mu_c\rvert$	5.8/ 0.4 /0.0	2.4/ 0.6/ 0.3	2.3/ 3.1/ 0.0
$\chi_{aa}/\chi_{bb}/\chi_{cc}$	-0.43/ -2.49/ 2.92	-0.40/ -2.89/ 3.30	-0.21/ -3.08/ 3.29
ΔE_{MP2}[c]	0	1175	1486
ΔG_{MP2}[d]	0	1107	1497

[a]Ab initio calculations performed at the MP2/6-311++G(d,p) level of theory. [b]A, B, and C are the rotational constants (in MHz); χ_{aa}, χ_{bb}, and χ_{cc} are the diagonal elements of the ^{14}N nuclear quadrupole coupling tensor (in MHz); $\lvert\mu_a\rvert$, $\lvert\mu_b\rvert$, and $\lvert\mu_c\rvert$ are the electric dipole moment components (in D). [c]Relative electronic energies calculated at MP2/6-311++G(d,p) electronic energies (in cm^{-1}). [d]Gibbs energies calculated at 298 K (in cm^{-1}).

The conformers of picolinic acid are near prolate asymmetric tops with recognizable rotational spectrum patterns of μ_a-type R-branch transitions separated by frequency intervals of approximately B + C values of rotational constants. Initial inspection of the broadband CP-FTMW rotational spectrum shown in Figure 1a soon revealed two sets of intense R-branch μ_a-type rotational transitions (with $J' \leftarrow J''$= 3 ← 2 and 4 ← 3) belonging to a first rotamer A. Rotational transitions exhibit the typical hyperfine structure arising from the interaction between the electric quadrupole moment of the ^{14}N nucleus (I = 1) and the electric field gradient created by all the molecular charges at the site of this nucleus. Nevertheless, this hyperfine structure is not well resolved by the CP-FTMW technique so only the central frequencies were used in a rigid rotor analysis to obtain a preliminary set of rotational constants employed in the initial stage of the assignment procedure. μ_b- and μ_c-type transitions were also predicted but not observed. All the assigned rotational transitions were subsequently submitted to the high resolution of our LA-MB-FTMW spectrometer to resolve their hyperfine structure (see inlet of Figure 1a). Hence, a total of 30 hyperfine components belonging to nine μ_a-type R-branch transitions were collected and fitted[22] to a Hamiltonian $H = H_R + H_Q$, where H_R is the rigid rotor Hamiltonian term and H_Q is the nuclear quadrupole coupling interaction term.[23] The Hamiltonian was set up in the coupled basis set $I + J = F$, so the energy levels involved in each transition are labeled with the quantum numbers J, K_{-1}, K_{+1}, and F. The derived spectroscopic parameters for rotamer A are listed in Table 2. Only the

Table 2. Spectroscopic Parameters Determined for Rotamers of A and B of Picolinic Acid

	rotamer A (s-*cis*-I)	rotamer B (s-*cis*-II)
A[a] (MHz)	3903.906 (16)[d]	3958.969 (17)
B (MHz)	1290.82296 (17)	1268.13439 (16)
C (MHz)	970.41622 (15)	961.33930 (15)
Δ_c (μÅ^2)	−0.18579(66)	−0.47279 (68)
χ_{aa} (MHz)	−0.5601 (22)	−0.5637 (38)
χ_{bb} (MHz)	−2.5718 (39)	−3.030 (16)
χ_{cc} (MHz)	3.1218 (39)	3.594 (16)
N[b]	30	24
σ[c] (kHz)	1.9	1.7

[a]A, B, and C represent the rotational constants; $\Delta_c = (I_c - I_a - I_b) = -2\Sigma_i m_i c_i^2$ is the inertial defect; χ_{aa}, χ_{bb}, and χ_{cc} are elements of the ^{14}N nuclear quadrupole coupling tensor. [b]Number of fitted hyperfine components. [c]rms deviation of the fit. [d]Standard error in parentheses in units of the last digit.

diagonal elements (χ_{aa}, χ_{bb}, and χ_{cc}) of the quadrupole coupling tensor χ were determined in the fit of the observed transitions within the estimated accuracy of the frequency measurements. The anisotropic quadrupole coupling tensor χ is related to the electric field gradient tensor q at the quadrupolar nucleus through the nuclear quadrupole moment eQ by $\chi = eQq$.

The high sensitivity reached in our experiment allowed us to extend the spectral measurements to five monosubstituted ^{13}C, ^{15}N, and one ^{18}O species observed in their natural abundances (approximately 1%, 0.4%, and 0.2%) for the A rotamer (see Figure 1b).The analysis of the ^{13}C spectra was performed with the same Hamiltonian used for the parent species. For the ^{15}N species no quadrupole coupling interaction takes place so its spectrum does not show hyperfine structure. The ^{18}O species was only observed using the CP-FTMW spectrometer and thus its quadrupole coupling hyperfine structure was not resolved. The derived spectroscopic parameters for the isotopic species are collected in Table 3.

Once the analysis of the parent and isotopic species of rotamer A was completed and the lines discarded from the rotational spectra, very weak μ_a-type R-branch transitions, belonging to a second rotamer B, were identified. The intensities of the transitions are similar to those observed for

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Table 3. Experimental Spectroscopic Parameters for the Observed Isotopic Species of Rotamer A of Picolinic Acid

	C_1	C_4	C_5	C_6	C_7	^{15}N	^{18}O
A[a] (MHz)	3860.328 (16)	3856.905 (10)	3863.912 (12)	3903.771 (16)	3903.719 (19)	3865.356 (17)	3832.35 (41)
B (MHz)	1281.01642 (17)	1289.77504 (10)	1278.27790 (12)	1269.79114 (17)	1281.84845 (19)	1290.33767 (18)	1257.0929 (64)
C (MHz)	962.17613 (17)	966.89405 (10)	960.85157 (12)	958.47311 (16)	965.32392 (18)	967.74067 (18)	946.9194 (43)
Δ_c (μÅ^2)	−0.1843 (7)	−0.1843 (4)	−0.1840 (5)	−0.1858 (7)	−0.1858 (8)	−0.184 (16)	−0.185 (19)
χ_{aa} (MHz)	−0.5366 (27)	−0.5744 (25)	−0.6259 (29)	−0.568 (15)	−0.5557 (29)		
χ_{bb} (MHz)	−2.6033 (65)	−2.540 (10)	−2.516 (12)	−2.583 (22)	−2.5784 (60)		
χ_{cc} (MHz)	3.1399 (65)	3.115 (10)	3.1418 (12)	3.151 (22)	3.1340 (60)		
N[b]	26	24	23	19	27	9	5
σ[c] (kHz)	1.9	1.1	1.3	1.7	2.1	1.2	24.9

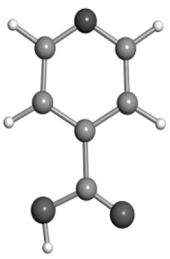
[a]A, B, and C represent the rotational constants; Δ_c is the inertial defect; χ_{aa}, χ_{bb}, and χ_{cc} are elements of the ^{14}N nuclear quadrupole coupling tensor. [b]Number of fitted hyperfine components. [c]rms deviation of the fit. [d]Standard error in parentheses in units of the last digit.

^{13}C species of rotamer A, as can be seen in Figure 1b for the $3_{12}-2_{11}$ transition. No μ_b- and μ_c-type transitions were observed. A total of 24 hyperfine components corresponding to the detected nine μ_a-type R-branch transitions were measured using LA-MB-FTMW spectroscopy and analyzed with the same Hamiltonian mentioned above. The final set of rotational and nuclear quadrupole coupling constants are listed in the second column of Table 2.

The spectrum of isonicotinic acid has been investigated following a similar procedure to that described for picolinic acid. Differently from picolinic acid (*ortho*-COOH substituted), in isonicotinic acid (*para*-COOH substituted), only the conformer in Table 4 can be expected. Hence, the broadband

Table 4. Calculated[a] and Experimental Spectroscopic Parameters for the Observed Rotamer of Isonicotinic Acid

	Isonicotinic acid	
	Theor.	Exp.
A[b]/MHz	4006	4027.83775 (63)[e]
B/MHz	1213	1219.95126 (12)
C/MHz	933	937.018821 (90)
Δ_c/uÅ^2	-1.3	-0.38541 (11)
$\lvert\mu_a\rvert$/D	1.4	Obs.[f]
$\lvert\mu_b\rvert$/D	1.2	Obs.
$\lvert\mu_c\rvert$/D	0.1	
χ_{aa} /MHz	-4.94	-5.0395 (46)
χ_{bb} /MHz	1.50	1.3574 (44)
χ_{cc} /MHz	3.44	3.6822 (44)
N[c]		38
σ[d]/kHz		1.6



[a]Ab initio calculations performed at the MP2/6-311++G(d,p) level of theory. [b]A, B, and C are the rotational constants; $\Delta_c = (I_c - I_a - I_b) = -2\Sigma_i m_i c_i^2$ is the inertial defect; $\lvert\mu_a\rvert$, $\lvert\mu_b\rvert$, and $\lvert\mu_c\rvert$ are the electric dipole moment components; χ_{aa}, χ_{bb}, and χ_{cc} are the diagonal elements of the ^{14}N nuclear quadrupole coupling tensor. [c]Number of fitted hyperfine components. [d]rms deviation of the fit. [e]Standard error in parentheses in units of the last digit. [f]Observation of a- and b-type spectra.

CP-FTMW rotational spectrum of Figure 2 only shows sets of intense R-branch μ_a- and μ_b-type rotational transitions attributable to one rotamer of isonicotinic acid. A total of 25 ^{14}N hyperfine components from nine μ_a-type R-branch transitions and 13 corresponding to five μ_b-type R-branch transitions were resolved and measured using LA-MB-FTMW spectroscopy (see inlet of Figure 2). All hyperfine components were fitted using the same Hamiltonian as described for picolinic acid. The determined spectroscopic parameters are also shown in Table 4. All frequency measurements for picolinic and isonicotinic acids are provided as Supporting Information (Table S1−S10).

Conformational Identification and Structure. Conformational identification is commonly achieved by comparing the experimentally determined molecular properties with those predicted ab initio.[24] In particular, the rotational constants (A, B, C), the ^{14}N nuclear quadrupole coupling constants (χ_{aa}, χ_{bb}, χ_{cc}), and the values of the electric dipole moment components along the principal inertial axis (μ_a, μ_b, μ_c) should all be consistent with ab initio values, even if only one of these tools is acting as the discriminating element.

The values of the rotational constants depend on the mass distribution around the principal inertial axes, so they are commonly used as conclusive tool in the identification of the observed species. In picolinic acid, the experimental values for A and B rotamers in Table 2 are similar to those predicted for s-*cis*-I, s-*cis*-II, and s-*trans* conformers in Table 1, thus making their assignment difficult. The same works for the ^{14}N nuclear quadrupole coupling constants. This is reflected in nearly identical quadrupole hyperfine patterns for both A and B rotamers, as can be seen in the inlets of Figure 1 for the same $3_{12}-2_{11}$ rotational transition. On this basis, the two observed rotamers can be ascribed to the lowest energy conformers, but an unambiguous identification to specific conformers cannot be achieved using rotational and quadrupole coupling constants as conformational tools.

The nonobservation of μ_b-type spectra for rotamers A and B and the predicted low values of the μ_b electric dipole moment component for conformers s-*cis*-I and s-*cis*-II points to the presence of these conformers in the supersonic expansion. On the same basis, conformer s-*trans* should be discarded due to the predicted high value of the μ_b dipole moment component. Conformer s-*cis*-I is predicted to be, by far, the most stable conformer of picolinic acid in accordance with the intense observed rotational spectrum for rotamer A. Additionally, the predicted changes in the rotational constants going from s-*cis*-I to s-*cis*-II are $\Delta A \approx 50.9\ (55.1)$ MHz, $\Delta B \approx -23.62\ (-22.7)$ MHz, and $\Delta C \approx -6.0\ (-9.1)$ MHz, which match nicely with those experimentally observed (in parentheses) in going from rotamer A to rotamer B. This allows the identification of rotamers A and B as conformers s-*cis*-I and s-*cis*-II, respectively. For isonicotinic acid, the predicted values of the rotational and quadrupole coupling constants for the most stable species (see Table 4) are in excellent agreement with those experimentally observed.

The inertial defect values Δ_c in Table 2 obtained for the observed conformers give a measure of the mass extension out of the *ab* plane. While for planar rigid molecules Δ_c should be strictly zero, the ground state vibrational motions give rise to inertial defect values, which are negative and close to zero.[25−27]

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Hence, the planarity of all conformers is confirmed by the experimental values of the inertial defect Δ_c (see Table 2). The differences in the experimental inertial defect values for picolinic acid conformers s-*cis*-I ands-*cis*-II and isonicotinic acid can be rationalized if we compare them with those observed for related planar pyridine,[28] benzoic acid,[29] or nicotinic acid.[14] Hence, while in pyridine Δ_c is very small and positive (Δ_c = 0.039 μÅ^2), the negative values observed for the rest of them collected in Table 6 indicates that out-of-plane vibrations related to the presence of −COOH group have dominant contributions.

A close look to the values in Table 6 shows that the inertial defect for conformer s-*cis*-I (Δ_c = −0.186μÅ^2) is roughly half the value of benzoic (Δ_c = −0.366 μÅ^2), nicotinic (Δ_c = −0.352μÅ^2 and Δ_c = −0.374μÅ^2 for conformers s-*cis* and s-*trans*, respectively) and isonicotinic acids (Δ_c = −0.38541μÅ^2), which is, in turn, smaller than the inertial defect for conformer s-*cis*-II (Δ_c = −0.473 μÅ^2). In other words we can affirm that the out of plane vibrational contributions of −COOH in s-*cis*-I are smaller than in the rest of species. This is in accordance with the observation of an intramolecular O−H···N hydrogen bond in the s-*cis*-I conformer, which limits in some extent the amplitude of the out-of-plane −COOH vibration in this conformer. The fact that the Δ_c value observed for conformer s-*cis*-II is slightly higher than those of benzoic acid, nicotinic acid, or isonicotinic acid may be explained in terms of the N···O repulsions, which would contribute to increase the amplitude of the out-of-plane −COOH vibrations in this conformer. These N···O repulsions are not present in the meta and para positions of the −COOH groups in nicotinic and isonicotinic acids.

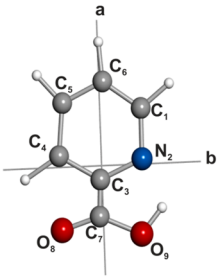
Finally, it should be noted that the value of the inertial defect is practically invariant in all the isotopic species (Table 3), which constitutes an additional test for the planarity of the s-*cis*-I conformer. This isotopic information was used to determine the coordinates of the substituted atoms in the principal axis system using Kraitchmann's substitution method[30−32] and to determine the bond distances and angles of the heavy atom skeleton listed in Table 5.

Quadrupole Coupling Constants: Intramolecular Hydrogen Bonding and Mesomeric Effect. An inspection of the experimental values of the nuclear quadrupole coupling constants could reveal interesting information on the different nature of the observed conformers. The ^{14}N nucleus present in all the conformers possess a nonzero quadrupole moment (I = 1) owing to a nonspherical distribution of the nuclear charge, which interacts with the electric field gradient created by the rest of the molecule at the site of the nucleus. The associated experimentally determinable molecular properties are the diagonal elements (χ_{aa}, χ_{bb}, χ_{cc}) of the nuclear quadrupole coupling tensor that are directly related to the electronic environment around the nitrogen nucleus referred to the principal inertial axes. For planar molecules, like those of isomeric picolinic, nicotinic,[14] and isonicotinic acids, the χ_{cc} element of the quadrupole coupling tensor is coincident with one of the elements of the principal quadrupole coupling tensor and provides information on the electric field gradient along the direction of an axis perpendicular to the aromatic ring. For pyrrolic nitrogens (−N<) χ_{cc} is negative.[33−35] In contrast, pyridinic nitrogens (−N=) have positive values of χ_{cc}.[34−36] Conformerss-*cis*-I and s-*cis*-II of picolinic acid have positive values for χ_{cc} indicating their pyridinic nature. However, while conformer s-*cis*-II presents a value for χ_{cc} of 3.594 MHz very close to that of pyridine (see Table 6), a markedly lower value of 3.122 MHz is found for the s-*cis*-I conformer. This difference cannot be attributed to possible changes in the orientation of the principal inertial axes; both conformers differ only in the orientation of the hydroxyl group. It must be ascribed to the formation of an intramolecular hydrogen bond O−H···N in the s-*cis*-I conformer, which increase slightly the pyrrolic character of the nitrogen nucleus by diminishing the χ_{cc} value.

A more detailed analysis of the nuclear quadrupole coupling constants shows small discrepancies in the χ_{cc} values in passing from *ortho*- and *para*-COOH substituted species to the *meta*-COOH ones. Hence, in the case of s-*cis*-II picolinic (*ortho*-COOH substituted) and isonicotinic (*para*-COOH substituted) acids, one observes a small increase of the χ_{cc} with respect to the values of nicotinic s-*cis* or s-*trans*[14] (*meta*-COOH substituted), which adopt practically the same value as for pyridine (see Table 6). Here an effect based on the exchange interaction of the lone electron pairs of the −COOH substituent with the π electrons of the pyridine ring[36] can be considered. This type of electron shift is termed mesomeric effect[37,38] and is signified by −M or +M, depending on whether the electron shift takes place from the aromatic ring to the substituent (−M) or in the reverse direction (+M). In the case of the isomeric series of picolinic, nicotinic, and isonicotinic acids, the electron distribution shift is in favor of the carboxylic group (−M), extracting electrons from the π-ring system in ortho and para positions (see Figure 3), which is reported by a small but noticeable increase in the χ_{cc} values of about 0.2 MHz. For the s-*cis*-I conformer, the decrease in the value of χ_{cc} with respect to s-*cis*-II conformer might be due to a negative polarization at the N atom arising from the formation of a −COOH···N hydrogen bond.

Table 5. Substitution Coordinates and r_s Structure for Conformer s-*cis*-I of Picolinic Acid

atom	|a|	|b|	|c|[a]
C_1	1.73073 (69)[b]	1.21898 (98)	0
N_2	0.3847 (31)	1.1396 (11)	0
C_3	-[c]	-	-
C_4	0.5643 (21)	1.26006 (95)	0
C_5	1.96007 (61)	1.1692 (10)	0
C_6	2.55258 (47)	0.068 (18)	0
C_7	1.65955 (72)	0.079 (15)	0
O_8	2.29744 (52)	1.1289 (11)	0
$r(C_1–N_2)$	1.35 (39)[d]	**$\angle C_4–C_5–C_6$**	119.32 (47)
$r(C_6–C_1)$	1.41 (16)	**$\angle C_5–C_6–C_1$**	118.88 (22)
$r(C_5–C_6)$	1.37 (17)	**$\angle C_6–C_1–N_2$**	122.15 (57)
$r(C_4–C_5)$	1.40 (29)		
$r(C_7–O_8)$	1.23 (14)		



[a]Planar structure has been assumed. [b]Principal inertial axis coordinates in Å; derived errors in parentheses in units of the last digit; These were calculated according to Constains formula: $\sigma(x) = K/|x|$; $\sigma(x)$ is the error in the x coordinate and K = 0.0012 Å^2. [c]The rotational transitions of the ^{13}C species of the C_3 carbon atom are so close to those of the parent species that become undetectable. [d]Distances in Å and angles in degrees.

CONCLUSIONS

In this work, two of the three plausible conformers of picolinic acid and the only plausible conformer for isonicotinic acid have been observed. For the most stable conformer of picolinic acid s-*cis*-I the heavy atom skeleton structure has been determined from the observation of ^{13}C, ^{18}O, and ^{15}N isotopologues in natural abundance using the CP-FTMW spectrometer. The formation of an intramolecular O−H···N hydrogen bond in the most stable conformer of picolinic acid has been also revealed by its signatures in the quadrupole coupling constants and the

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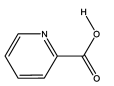
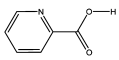
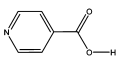
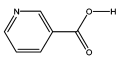
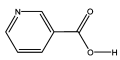
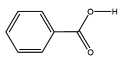
Table 6. Experimental Inertial Defects (in μÅ^2) and ^{14}N Quadrupole Coupling Constants (in MHz) of Picolinic and Isonicotinic Acids Compared to Those of Nicotinic Acid, Benzoic Acid, and Pyridine

	Picolinic acids-cis-I	Picolinic acid s-cis-II	Isonicotinic acid	Nicotinic acid s-cis	Nicotinic acid s-trans	Benzoic acid	Pyridine
							
Δ_c	-0.186[a]	-0.473[a]	-0.385[a]	-0.352[b]	-0.374[b]	-0.366[c]	0.039[d]
χ_{cc}	3.122[a]	3.594[a]	3.682[a]	3.422[b]	3.453[b]	-	3.474[e]

[a]Present work. [b]From ref 14. [c]From ref 29. [d]From ref 28. [e]From ref 36.

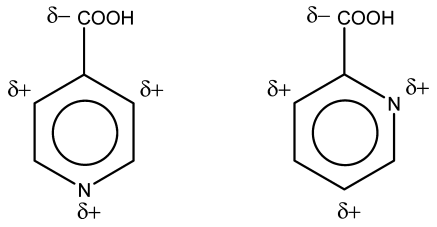


Figure 3. Resonance withdrawing effect in picolinic (left) and isonicotinic (right) acids.

vibrational contributions to the inertial defect values. The formation of this hydrogen bond forces the −COOH group to adopt a trans configuration, considerably less stable than its usual *cis* configuration. The stabilization energy provided by this hydrogen bond interaction thus compensates the destabilization due to the adoption of a −COOH trans configuration.

The role of the quadrupole coupling constants has been also found to be essential to detect the subtle effects of exchange interactions in aromatic systems. Hence, mesomeric effect from −COOH group in ortho and para positions has been unveiled in picolinic and isonicotinic acids by comparing the χ_{cc} values of the quadrupole coupling constants to those found for nicotinic acid and pyridine molecules.

It has been shown that the combination of laser ablation with the chirped-pulse Fourier transform microwave spectroscopy (CP-FTMW) provides an efficient tool in the analysis of the rotational spectra of biomolecules with high melting points. This technique is complementary to LA-MB-FTMW spectroscopy with superior resolution to resolve the hyperfine structure. Both techniques constitute sensitive tools for the structure determination of biomolecules.

■ ASSOCIATED CONTENT

Supporting Information

Complete ref 21, list of measured transitions for the observed conformers of picolinic and isonicotinic acids, and ab initio coordinates and structural parameters for conformer s-*cis*-I of picolinic acid. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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