

Rotational and Core Level Spectroscopies As Complementary Techniques in Tautomeric/Conformational Studies: The Case of 2-Mercaptopyridine

Sonia Melandri,[†] Luca Evangelisti,[†] Assimo Maris,[†] Walther Caminati,^{*,†} Barbara M. Giuliano,[‡] Vitaliy Feyer,[§] Kevin C. Prince,[§] and Marcello Coreno^{||}

Dipartimento di Chimica "G. Ciamician" dell'Università, Via Selmi 2, I-40126 Bologna, Italy, Departamento de Química da Universidade de Coimbra, 3004-535 Coimbra, Portugal, Sincrotrone Trieste, Area Science Park, I-34012 Basovizza, Trieste, Italy, and CNR-IMIP, Montelibretti, Rome, I-00015, Italy

Received June 3, 2010; E-mail: walther.caminati@unibo.it

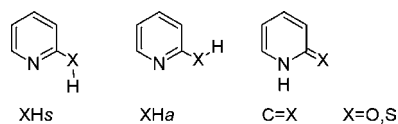
Abstract: Millimeter wave free jet absorption and core level photoemission spectroscopies give complementary and precise information on the conformational/tautomeric equilibrium of 2-mercaptopyridine.

In this communication we report a detailed conformational/tautomeric investigation of 2-mercaptopyridine (2MP), obtained from the combination of two relatively rapid techniques, namely free jet microwave (MW) spectroscopy and core level photoemission spectroscopy. Interestingly, the energies of the corresponding photons lie at opposite extremes: $\sim 2 \times 10^{-4}$ for the MW spectroscopy and $\sim 5 \times 10^2$ eV for the synchrotron radiation, respectively.

Impressive progress has been achieved in the past few years in gas phase investigations of conformational/tautomeric properties of isolated biomolecules, thanks to the developments and applications of several spectroscopic techniques.^{1–14} Among them are rotational spectroscopy, in the form of free jet MW absorption techniques,^{9,10} or Fourier transform microwave (FTMW) spectroscopy.^{11,12} More recently, core level photoemission spectra of some biomolecules have been measured in the gas phase.^{13,14} However to date MW and core level techniques have not been combined to solve a single problem, as we present here.

2-Hydroxypyridine (2HP) and 2MP can each exist in three forms, the two conformers due to the internal rotation of the hydroxyl or mercapto group around the C–O or C–S bond and the tautomeric keto or thione isomer, as shown in Chart 1.

Chart 1. Tautomeric/Conformational Species of 2-Hydroxy (X = O) and 2-Mercapto (X = S) Pyridine^a



^a *s* and *a* stand for *syn* and *anti*.

The prototype molecule 2HP has been investigated with more or less all the techniques mentioned above, and only the forms OHs (more stable by 3.2 kJ/mol¹⁵) and C=O in Chart 1 have been detected, form OHa being estimated to be higher in energy by more

than 2000 cm⁻¹. The final labels "s" or "a" indicate the *syn* or *anti* orientation of the hydroxyl hydrogen with respect to the ring nitrogen. It has been observed that increasing the number of OH groups attached to aromatic, heterocyclic rings and the number of N atoms embedded in the ring shift the tautomeric equilibrium considerably toward the keto forms, as in going, for example, from 2-OH pyridine to 4-OH pyrimidine, or to uracil.¹⁶ However no spectroscopic investigations have been reported of the related molecule 2MP, which also represents a tautomeric problem of biological interest.

Preliminary ab initio calculations¹⁷ suggest the SHa species to be close in energy to SHs, but the C=S form is much higher in energy, ca. 850 cm⁻¹, as shown in Table 1, where the ab initio values of the relative energies and the relevant spectroscopic constants are reported for the three species. The table shows that the energy difference increases even more when taking into account the ZPE corrections, or the thermal contributions.

Since MW spectroscopy gives conformational/tautomeric assignments directly from the experimentally determined moments of inertia, we applied first this technique to the study of 2MP. The rotational spectrum in the 60–78 GHz frequency region was measured at 403 K using a free jet MW absorption spectrometer described elsewhere,¹⁸ with further details given in the Supporting Information.

Table 1. Ab Initio (MP2/6-311++G**) Energies and Spectroscopic Constants of the Three Species of 2MP^a

	SHs	SHa	C=S
A/MHz	5733.5	5741.9	5709.2
B/MHz	1635.5	1632.7	1644.3
C/MHz	1272.9	1271.9	1276.9
μ_a/D	-1.9	1.9	-5.2
μ_b/D	1.0	2.7	-1.4
$\Delta E/kJmol^{-1}$	0 ^b	5.5	10.1
$\Delta E_0/kJmol^{-1}$	0 ^c	7.0	21.3
$\Delta G_{339}/kJmol^{-1}$	0 ^d	7.7	23.0
$\Delta G_{403}/kJmol^{-1}$	0 ^e	8.0	23.7

^a Subscripts to ΔG represents the absolute temperatures (K) of the experiments. ^b Absolute energy: -645.281848 E_h. ^c Absolute energy: -645.195458 E_h. ^d Absolute energy: -645.238876 E_h. ^e Absolute energy: -645.249085 E_h.

We assigned first the strong coalesced transitions (due to near prolate degeneracy, only K_a is given) of the type $J_6 \leftarrow J_5$, (J in the range 5–8). Then many more μ_b and μ_a type transitions were measured. A second set of transitions was observed, with intensity ratios with respect to the first species of approximately 1/10, as well as a third set of very weak lines. These three spectra were tentatively assigned to forms SHs, SHa, and C=S in Chart 1 and Table 1, respectively. However, since the rotational constants of

[†] Dipartimento di Chimica "G. Ciamician" dell'Università.

[‡] Departamento de Química da Universidade de Coimbra.

[§] Sincrotrone Trieste.

^{||} CNR-IMIP.

the three species are very close to each other, we attempted to confirm this assignment by investigating also the monodeuterated species (easily obtainable by direct exchange with D₂O). We assigned the spectra of the SD forms of the mercapto species, but due to only partial exchange, we were not able to observe the spectrum of the ND isotopologue of the less abundant thione species.

Table 2. Experimental Spectroscopic Constants of the Observed Species of 2MP

	SHs	SDs	SHa	SDa	C=S
<i>A</i> /MHz	5758.02(1) ^a	5655.638(2)	5765.76(1)	5660.364(3)	5756.2(6)
<i>B</i> /MHz	1644.832(6)	1616.511(2)	1642.758(9)	1613.087(7)	1641.38(2)
<i>C</i> /MHz	1279.490(7)	1257.380(4)	1278.671(9)	1255.307(4)	1278.94(2)
<i>D_y</i> /kHz	0.056(7)	[0.056] ^b	0.071(9)	[0.071]	0.075(9)
<i>D_{JK}</i> /kHz	0.32(1)	[0.32]	0.33(2)	[0.33]	0.33(2)
<i>D_K</i> /kHz	0.9(1)	[0.9]	0.7(2)	[0.7]	
<i>d₁</i> /kHz	-0.015(3)	[-0.015]	-0.013(4)	[-0.013]	
<i>d₂</i> /kHz	-0.003(1)	[-0.003]			
<i>σ</i> /kHz	44	62	69	51	47
<i>N</i> ^c	53	13	27	10	15

^a The error (in parentheses) is expressed in units of the last digit. ^b In brackets are values fixed to those of normal species, because they were not determined in the fit. ^c Number of transitions in the fit.

All measured rotational transitions are given as Supporting Information. They were fitted with a Watson type Hamiltonian¹⁹ (S-reduction I' representation), yielding the spectroscopic constants reported in Table 2.

We calculated the substitution coordinates²⁰ (shown in Table 3) of the SH hydrogen atom in the principal axes system of the parent species, analyzing the changes of the planar moments of inertia when going to the SD species. One can see that they satisfactorily fit the values expected for the two thiol conformers.

Table 3. Comparison between the Two Experimental and the Three Theoretical Sets of Substitution Coordinates

	SHs		SHa		C=S
	exptl.	calc.	exptl.	calc.	calc.
<i>a</i> /Å ^a	±2.315 (2)	-2.331	±2.373	-2.389	-0.368
<i>b</i> /Å	±1.278(3)	1.253	±1.296	1.260	1.962

^a The coordinate *c* has been set to zero for symmetry reasons.

While observation of the monodeuterated form of the mercapto species proved their conformational assignment, doubts remained in attributing the third weak observed peak to the thione form. The weak feature could have been, for example, due to a partially relaxed vibrational satellite.

Our core level photoemission experiment on 2MP confirmed the observation of the less abundant thione tautomer. The spectra were measured at the gas-phase photoemission beamline (Elettra, Trieste),²¹ with the experimental methods described in detail elsewhere.²² The C 1s, N 1s, and S 2p core photoemission spectra were taken at 382, 495, and 260 eV photon energy, respectively, and the binding energies were calibrated as described in ref 22. The temperature of the sample was 339 K.

The full list of observed peak energies and a complete set of spectra are given as Supporting Information. While the C 1s spectra were quite complicated because the energies of the peaks of the five different carbon atoms are very close, those of the N 1s and S 2p signals were very clear and displayed unequivocal signals due to the two tautomers, as shown in Figure 1 for the S 2p peaks.

As expected, the peaks of the two mercapto conformers could not be distinguished, since they have almost the same electronic structure. Statistical analysis give the relative populations, with the

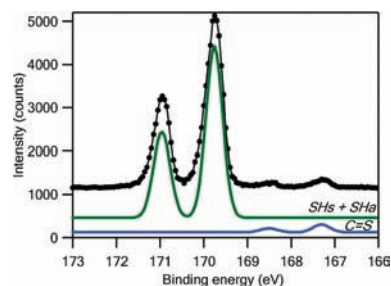


Figure 1. Experimental (line and points) and deconvoluted (green: mercapto, blue: thione forms) S 2p photoemission spectrum of 2MP.

thione form being 4.6(5)%. From this datum we estimated the free energy differences among the various species, $\Delta(\Delta G)$ between the mercapto (SHs+SHa) and the thione forms. In the case of the MW data, we can determine two $\Delta(\Delta G)$ values, but we need to assume that all vibrational states relax to the ground vibrational state upon supersonic expansion. However we assume no conformational or tautomeric interconversion because of the high barriers for these processes.

By comparing the intensities of several pairs of nearby transitions, we obtained the relative abundance of the two adducts, using standard equations.²³ The results are also given in Table 4.

Table 4. Experimental Relative Population and Energy of the Observed Species of 2MP

	SHs	SHa	C=S
Population (%)			
XPS (339 K)	95.4 ± 1		4.6 ± 0.5
MW (403 K)	89 ± 5	8 ± 2	3 ± 1
$\Delta G/\text{kJ}\cdot\text{mol}^{-1}$			
XPS (339 K)		0.0	8.6
MW (403 K)	0.0	8.1	11.4

It is interesting to note how the tautomeric/conformational behavior of 2-OH-pyridine changes dramatically when replacing the oxygen with a sulfur atom. The *anti* conformer, not detectable for 2-OH-pyridine, was easily observed in the case of 2MP. On the contrary, the C=X form (keto, X = O for 2HP, thione, X = S for 2MP) is much less stable in the case of X = S. However, the above-mentioned theoretical calculations give relative energies of this C=S tautomer that are much higher than the value obtained from these experimental measurements. The thione ΔG value in particular is overestimated by these calculations. In conclusion, the combination of the high quantitative accuracy of XPS with the detailed structural information of MW spectroscopy has allowed us to give a detailed description of the structure and energetics of the tautomers of 2MP.

Acknowledgment. The Bologna authors thank the University of Bologna for financial support. B.M.G. thanks FCT for a postdoctoral grant.

Supporting Information Available: Completion of ref 17, experimental details, table of experimental transition frequencies and of the XPS material. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) Dian, B. C.; Longarte, A.; Zwier, T. S. *Science* **2002**, *296*, 2369.
- (2) Pratt, D. W. *Science* **2002**, *296*, 2347.
- (3) Çarçabal, P.; Jockusch, R. A.; Hünig, I.; Snoek, L. C.; Kroemer, R. T.; Davis, B. G.; Gamblin, D. P.; Compagnon, I.; Oomens, J.; Simons, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 11414.
- (4) Chin, W.; Piuze, F.; Dognon, J.-P.; Dimicoli, I.; Tardivel, B.; Mons, M. *J. Am. Chem. Soc.* **2005**, *127*, 11900.
- (5) Bakker, J. M.; Plützer, C.; Hünig, I.; Häber, T.; Compagnon, I.; von Helden, G.; Meijer, G.; Kleinermaans, K. *ChemPhysChem* **2005**, *6*, 120.

- (6) Fago, G.; Filippi, A.; Giardini, A.; Laganà, A.; Paladini, A.; Speranza, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 4051.
- (7) Abo-Riziq, A.; Grace, L.; Nir, E.; Kabelac, M.; Hobza, P.; de Vries, M. S. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 20.
- (8) Dong, F.; Miller, R. E. *Science* **2002**, *298*, 1227.
- (9) For example, see: Brown, R. D.; Godfrey, P. D.; McNaughton, D.; Pierlot, A. P. *J. Am. Chem. Soc.* **1989**, *111*, 2308, and references therein.
- (10) For example, see: Caminati, W.; Maccaferri, G.; Favero, P. G.; Favero, L. B. *Chem. Phys. Lett.* **1996**, *251*, 189, and references therein.
- (11) Blanco, S.; Sanz, M. E.; López, J. C.; LAlonso, J. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 20183.
- (12) Alonso, J. L.; Peña, I.; López, J. C.; Vaquero, V. *Angew. Chem., Int. Ed.* **2009**, *48*, 6141.
- (13) Feyer, V.; Plekan, O.; Richter, R.; Coreno, M.; Vall-Iloera, G.; Prince, K. C.; Trofimov, A. B.; Zaytseva, I. L.; Moskovskaya, T. E.; Gromov, E. V.; Schirmer, J. *J. Phys. Chem. A* **2009**, *113*, 5736.
- (14) Plekan, O.; Feyer, V.; Richter, R.; Coreno, M.; Vall-Iloera, G.; Prince, K. C.; Trofimov, A. B.; Zaytseva, I. L.; Moskovskaya, T. E.; Gromov, E. V.; Schirmer, J. *J. Phys. Chem. A* **2009**, *113*, 9376.
- (15) Hatherley, L. D.; Brown, R. D.; Godfrey, P. D.; Pierlot, A. P.; Caminati, W.; Damiani, D.; Melandri, S.; Favero, L. B. *J. Phys. Chem.* **1993**, *97*, 46.
- (16) Sanchez, R.; Giuliano, B. M.; Melandri, S.; Favero, L. B.; Caminati, W. *J. Am. Chem. Soc.* **2007**, *129*, 6287.
- (17) Frisch, M. J. *Gaussian 03*, revision B.01; Gaussian, Inc.: Pittsburgh, PA, 2003.
- (18) Melandri, S.; Caminati, W.; Favero, L. B.; Millemaggi, A.; Favero, P. G. *J. Mol. Struct.* **1995**, *352/353*, 253.
- (19) Watson, J. K. G. In *Vibrational Spectra and Structure*; Durig, J. R., Ed.; Elsevier: New York/Amsterdam, 1977; Vol. 6, pp 1–89.
- (20) Kraitchman, J. *Am. J. Phys.* **1953**, *21*, 17.
- (21) Prince, K. C.; Blyth, R. R.; Delaunay, R.; Zitnik, M.; Krempasky, J.; Slezak, J.; Camilloni, R.; Avaldi, L.; Coreno, M.; Stefani, G.; Furlani, C.; de Simone, M.; Stranges, S. *J. Synchrotron Radiat.* **1998**, *5*, 565.
- (22) Plekan, O.; Feyer, V.; Richter, R.; Coreno, M.; de Simone, M.; Prince, K. C.; Trofimov, A. B.; Gromov, E. V.; Zaytseva, I. L.; Schirmer, J. *Chem. Phys.* **2008**, *347*, 360.
- (23) Gordy, W.; Cook, L. R. In *Microwave Molecular Spectra*, 3rd ed.; Weissberger, A., Ed.; *Techniques of Chemistry*; John Wiley & Sons Inc.: New York; Vol. XVIII, p 198.

JA104484B