Theoret. chim. Acta (Berl.) 11, 31—37 (1968)

Some Effects of Protonation on the Electronic Structure of Pyridine and Cytosine*

ARMELLE DENIS and MARCEL GILBERT
Institut de Biologie Physico-Chimique
Laboratoire de Biochimie Théorique associé au C.N.R.S., 13, rue Pierre Curie, Paris 5e

Received January 25, 1968

The effects of protonation on the charge distributions of pyridine and cytosine are investigated with the help of the Iterative Extended Hückel technique. The polarization of the σ-electrons is then included explicitly in a Pariser-Parr-Pople computation of the π-π^* transition energies of the pyridinium and cytosinium ions.

Mit Hilfe der IEH-Methode wird die Auswirkung der Protonierung auf die Ladungsverteilung bei Pyridin und Cytosin untersucht. Die Polarisierung der σ-Elektronen wird dann in eine PPP-Rechnung der π-π^*-Übergangsenergie beim Pyridinium- und Cytosiniumion übernommen.

On étudie, à l'aide de la méthode de Hückel étendue iterative, les effets de la protonation sur la répartition des électrons dans les molécules de pyridine et de cytosine. On introduit ensuite explicitement la polarisation des électrons σ dans le calcul des énergies de transition π-π^* des ions pyridinium et cytosinium par la méthode de Pariser, Parr et Pople.

Introduction

The knowledge of the charge distributions (σ and π-charges) in nitrogen protonated molecules would greatly facilitate the discussion of many problems, some of which having a definite biological interest (the protonation of the nucleotide bases of DNA, the interaction of cationic dyes with the nucleic acids and the determination of the basicities of nitrogen heterocycles).

Until now, the studies devoted to the problem of the electronic structure of protonated molecules were limited to the π-electrons and they all made the common assumption that the π-electrons could be treated without taking explicitly into account the σ-system. Mataga and Tsuno [1] obtained good agreement with the first two π-π^* bands of protonated pyridine by assuming that the effect of protonation on the π-electrons could be reduced to the effect of a bare proton located near the nitrogen atom. This oversimplified model is unfortunately difficult to reconcile with the usual covalent description of the N^+–H bond in pyridinium. Besides, it precludes the calculation of the σ-charge distribution since it does not allow electrons to flow from the ring to the proton. Schor [2] has used, with equal success, a modification of Mataga and Tsuno's model, in order to allow such a σ-flow towards the proton, but the way in which the σ-electrons redistribute themselves over the molecular framework remains undetermined. Using their VESCF (variable electronegativity self consistent field) method, Brown and

---

* This work was supported by grant n⁰ GM-12229 of the U.S. Public Health Service (National Institute of General Medical Sciences).

Hefferman [3] obtained reasonably good transition energies for pyridinium, in a π-electron calculation, with the assumption that the whole proton charge is transfered to the nitrogen atom. This also is a rather unrealistic assumption concerning the σ-charge distribution of the protonated molecule.

Despite the relative success of the foregoing procedures, we feel that the π-electron computations of protonated molecules should be based on less arbitrary descriptions of their σ-system. As a preliminary step in the investigation of this problem, we have adopted the following procedure:

1. We first apply the Iterative Extended Hückel (IEH) method to the molecule and to its protonated derivative. By comparing the gross populations obtained for the unprotonated molecule to the corresponding populations for its derivative one can answer the following questions:

i) How much electronic charge is transfered from the neutral molecule to the proton?

ii) What is the contribution of each atom to this flow of electrons towards the proton?

iii) How do the π-electrons react to this transfer of σ-electrons?

2. The σ-charge densities computed by the IEH method are used in the evaluation of the diagonal core parameters U_α^p's for a Pariser-Parr-Pople (PPP) computation of the π-π^* transition energies. This leads to a preliminary answer to a last question:

iv) Is the effect of protonation on the U.V. spectra of nitrogen heterocycles adequately accounted for by the partial inclusion of the polarization of the σ-electrons in the PPP method?

We report here the results obtained for pyridine, cytosine and their respective protonated derivatives.

Method

1. The Iterative Extended Hückel Procedure

We follow a procedure which is essentially the same as the one used by Carroll *et al.* [4] and by Rein *et al.* [5]. We seek the eigenvectors φ_j and the eigenvalues ε_j of an effective hamiltonian H_{eff} of the system of valence electrons. As usual, each molecular orbital φ_j is expressed as a linear combination of atomic orbitals χ_α^p (α designates an atom and p an orbital of atom α):

$$\varphi_j = \sum_\alpha \sum_p \chi_\alpha^p c_{\alpha j}^p .$$

The atomic bases orbitals are Slater $2s$ and $2p$ (N, C, O) or $1s$ (H) orbitals. Clementi and Raimondi's [6] "best" Slater exponents are used[1]. The absolute value of a diagonal matrix element $H_{\alpha\alpha}^{pp}$ is approximated as the valence orbital ionization potential $VOIP_\alpha^p$ and Cusachs' modification of the Wolfsberg-Helmholz relation is used to approximate the "resonance integrals" $H_{\alpha\alpha}^{pq}$ [7]:

$$H_{\alpha\alpha}^{pp} = -VOIP_\alpha^p ,$$

$$H_{\alpha\beta}^{pq} = (2 - |S_{\alpha\beta}^{pq}|)\frac{S_{\alpha\beta}^{pq}}{2}(H_{\alpha\alpha}^{pp} + H_{\beta\beta}^{qq}) .$$

---

[1] The Slater exponent for the $1s$ orbitals is taken as 1.

The charge iteration process is based on the dependence of the valence orbital ionization potential on the atomic charge q_α, as determined by Cusachs and Reynolds [8]:

$$VOIP_\alpha^p = A_\alpha^p + B_\alpha q_\alpha .$$

The constants A and B are given by Cusachs and Reynolds [8]. The dependence of the corresponding diagonal matrix element $H_{\alpha\alpha}^{pp}$ on the atomic charge is screened by a parameter $\lambda = 0.1$, as proposed by Carroll *et al.* [4]. The matrix element ${}^{(n)}H_{\alpha\alpha}^{pp}$, at the n^{th} iteration is given by:

$${}^{(n)}H_{\alpha\alpha}^{pp} = {}^{(n-1)}H_{\alpha\alpha}^{pp}(1-\lambda) + \lambda({}^{(0)}H_{\alpha\alpha}^{pp} - B_\alpha {}^{(n-1)}q_\alpha) .$$

The process is repeated until:

$${}^{(n-1)}q_\alpha - {}^{(n)}q_\alpha \leqq 0.01 \qquad \text{for all atoms.}$$

2. *The Pariser-Parr-Pople Method*

The main features of the PPP method are well known. We have used, in the present work, this SCF procedure supplemented by configuration mixing with the singly excited configurations on the basis of the approximations described by Berthod *et al.* [9, 10]. The various integrals and parameters used here are listed in Table 1. The essential modification introduced concerns the evaluation of the diagonal core matrix elements: $\langle \chi_\alpha^p | H^{\text{core}} | \chi_\alpha^p \rangle$. We start from the following expression for this integral:

$$I_{\alpha\alpha} = -VOIP_\alpha^p + \sum_{\beta \neq \alpha} \langle \chi_\alpha^p | U_\beta | \chi_\alpha^p \rangle ,$$

Table 1. *The values of the diagonal core parameters U_α^p*

	Pyridine	Pyridinium		Cytosine	Cytosinium
N_1	−12.8	−24.6	N_1	−11.8	−18.0
C_2	−10.6	−19.6	C_2	− 9.4	−18.5
C_3	−11.2	−17.2	N_3	−14.7	−26.5
C_4	−11.0	−16.3	C_4	− 9.7	−18.6
			C_5	−13.1	−19.3
			C_6	−10.6	−16.0
			O_7	−17.6	−24.3
			N_8	−13.1	−19.7

The Kon constants are as follows: $-C{=}N-$: 15.700; $-C{=}C-$: 17.538; $C-\dot{N}{<}_H$: 15.195; $O{=}C$: 8.200; ${}^{H}_{H}{>}\ddot{N}-C{\lessgtr}$: 11.200.

The one-center coulombic integrals are as in Ref. [9].

where p stands for the AO of atom α contributing one (or two) electron to the π-system and U_β is the contribution of atom β to the core potential. The core attraction integral $\langle \chi_\alpha^p | U_\beta | \chi_\alpha^p \rangle$ can be written as follows:

$$\langle \chi_\alpha^p | U_\beta | \chi_\alpha^p \rangle = [U_\beta^0 | \chi_\alpha^p \chi_\alpha^p] - n_\beta^p \langle \chi_\alpha^p \chi_\alpha^p | \chi_\beta^p \chi_\beta^p \rangle + \sum_g q_\beta^g \langle \chi_\alpha^p \chi_\alpha^p | \chi_\beta^g \chi_\beta^g \rangle ,$$

where the summation extends over the σ-orbitals of atom β, $[U_\beta^0 | \chi_\alpha^p \chi_\alpha^p]$ is the penetration integral and q_β^g is the gross charge of orbital g on atom β. We approximate the summation by:

$$\sum_g q_\beta^g \langle \chi_\alpha^p \chi_\alpha^p | \chi_\beta^g \chi_\beta^g \rangle = q_\beta^\sigma / R_{\alpha\beta} ,$$

where q_β^σ is the gross σ-charge on atom β and $E_{\alpha\beta}$ the distance between atoms α and β. If the differential effects of penetration are neglected the proper relationships between the diagonal core matric elements should be obtained by using

$$I_{\alpha\alpha} = -VOIP_\alpha^p - n_\beta^p \langle \chi_\alpha^p \chi_\alpha^p | \chi_\beta^p \chi_\beta^p \rangle + \sum_{\beta \neq \alpha} q_\beta^\sigma / R_{\alpha\beta} .$$

The core parameter U_α^p can therefore be approximated as:

$$U_\alpha^p = -A_\alpha^p - B_\alpha q_\alpha^\sigma + \sum_{\beta \neq \alpha} q_\beta^\sigma / R_{\alpha\beta} .$$

At the onset of the π-computation we take: $q_\alpha = q_\alpha^\sigma$.

Results and Discussion

The geometry of the pyridine molecule corresponds to the values given by Sutton [11]. The same geometry is assumed for pyridinium[2]. For the cytosinium ion the geometry determined by Sundaralingan and Jensen is used [12][3].

The gross orbital and atomic populations and the gross atomic charges of pyridine, cytosine and of their protonated derivatives, computed from their IEH wavefunctions are listed in Table 2. These values will be analysed from the limited point of view of the effect of protonation on the electronic structure of the unprotonated molecule. The first two questions mentioned in the introduction are answered by comparing the gross σ-populations of pyridine and cytosine to the corresponding populations of their cation. This comparison is illustrated in Fig. 1. The pyridine molecule loses 0.79 electrons to the proton and the cytosine molecule, 0.83 electrons. The protonated nitrogen atom contributes 0.48 electrons (60%) to this transfer, in the case of pyridine, and 0.505 electrons (61%), in the case of cytosine. The two neighboring carbon atoms lose 0.12 electrons (15%) in pyridine and 0.15 electrons (18%) in cytosine. In both cases, the remaining electronic charge transfered to the proton comes from all other atoms except the para carbon atom. We can conclude that approximately 80% of the proton charge is delocalized over the protonated molecule but that nearly 80% of the delocalized charge is retained by the protonated nitrogen atom and its two neighboring carbon atoms.

The reaction of the π-electrons to this transfer of σ-electrons is illustrated in Fig. 2. For the two molecules considered here, the π-electrons rearrange themselves in such a way as to compensate the loss of electron of the atom contributing most to the neutralization of the bound proton. As a result of these various electron transfers, the unit positive charge of the pyridinium and cytosinium ions is widely distributed over the molecular framework (Table 2).

The transition energies and oscillator strengths obtained in the modified PPP method are reported in Table 3 and compared to the corresponding experimental values. The first π-π^* band of pyridine is shifted towards longer wavelengths and its intensity is increased (4.9 (0.04) – 4.8 (0.1)) by protonation. These effects of protonation are theoretically predicted (4.9 (0.04) 4.8 (0.10)) when the polarization of the σ-electrons is included in the PPP method. The second π-π^* band of pyridine is very strongly shifted towards longer wavelengths wile its intensity remains relatively constant. This also is correctly accounted for by the theory. Like the first band of pyridine, the first band of cytosine is shifted towards

---

[2] The N$^+$–H bond length in pyridinium is 1.03 Å.

[3] The geometry of cytosine is that of Barker and Marsh [13].

Table 2. *Population analysis*

Atom	1*s* or 2*s*	$2p_x$	$2p_y$	$2p_z$	Gross atomic charge
Pyridine					
N_1	1.400	1.745	1.080	1.012	−0.237
C_2	1.182	0.913	0.871	1.039	−0.005
C_3	1.144	0.955	0.945	0.984	−0.028
C_4	1.156	0.973	0.959	0.939	−0.027
H_7	0.930				+0.070
H_8	0.930				+0.070
H_9	0.943				+0.057
Pyridinium					
N_1	1.398	1.147	1.202	1.291	−0.038
C_2	1.156	0.926	0.824	0.994	+0.100
C_3	1.120	0.936	0.966	0.940	+0.038
C_4	1.151	0.993	0.967	0.841	+0.048
H_7	0.791				+0.209
H_8	0.892				+0.208
H_9	0.903				+0.097
H_{10}	0.904				+0.096
Cytosine					
N_1	1.409	1.161	1.140	1.360	−0.071
C_2	1.134	0.828	0.799	1.252	+0.053
N_3	1.344	1.193	1.546	1.214	−0.297
C_4	1.110	0.764	0.895	1.170	+0.061
C_5	1.095	0.965	0.938	1.051	−0.051
C_6	1.125	0.939	0.830	1.084	+0.022
O_7	1.670	1.817	1.598	1.433	−0.517
N_8	1.466	1.070	1.160	1.437	−0.134
H_9	0.773				+0.227
H_{10}	0.768				+0.232
H_{11}	0.891				+0.109
H_{12}	0.906				+0.094
H_{13}	0.730				+0.270
Cytosinium					
N_1	1.392	1.139	1.160	1.330	−0.021
C_2	1.092	0.771	0.739	1.218	+0.180
N_3	1.341	1.115	1.123	1.541	−0.120
C_4	1.085	0.912	0.711	1.146	+0.146
C_5	1.074	0.906	0.981	1.049	−0.010
C_6	1.115	0.974	0.817	1.030	+0.064
O_7	1.636	1.800	1.613	1.358	−0.407
N_8	1.448	1.159	1.125	1.328	−0.060
H_9	0.727				+0.273
H_{10}	0.734				+0.266
H_{11}	0.870				+0.130
H_{12}	0.887				+0.113
H_{13}	0.723				+0.277
H_{14}	0.829				+0.171

longer wavelengths and its intensity is increased when a proton is bound to its "pyridine like nitrogen atom." The corresponding theoretical values agree very well this observation. The strong shift of the second band of cytosine towards shorter wavelengths (5.50—5.90 eV) is only indicated as a trend by the computed transition energies (6.02—6.04 eV). As can be seen in Table 3 the relative failure to reproduce this protonation effect completely is due to the bad location of the second transition of cytosine itself. One may be tempted to infer from this disagreement that the approximations made (replacement of the coulombic integrals by a "$1/r$ law" and neglect of the effect of the σ-polarization on the off-diagonal core parameters) while sufficient when there is a strong charge effect, are too crude to account for the σ-polarization of a complex uncharged molecules. It must also be kept in mind that the IEH method may give a σ-charge distribution which is not completely correct.

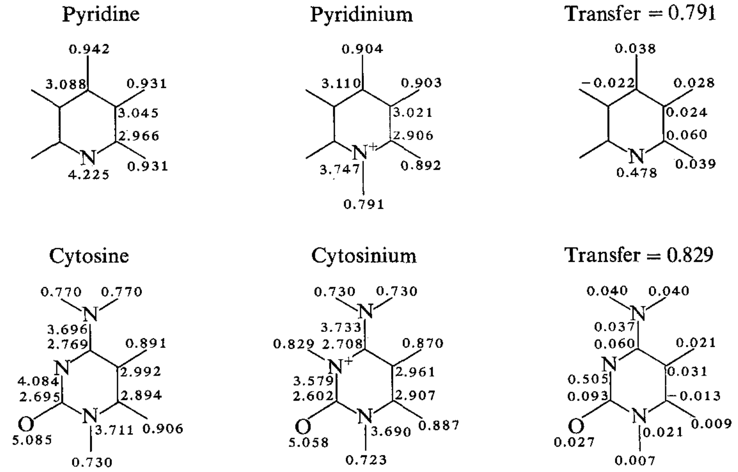

Fig. 1. The effect of protonation on the distribution of the σ-electrons in pyridine and cytosine

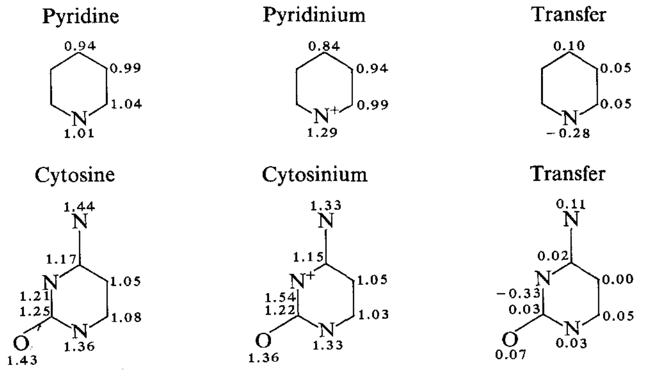

Fig. 2. The effect of protonation on the π-orbital populations of pyridine and cytosine

Acknowledgement. We wish to express our gratitude to Dr. A. Pullman for encouraging this research and for her helpful discussions.

Table 3. *The effect of protonation on the U.V. spectra of pyridine and cytosine*

Experimental		Theoretical		Experimental		Theoretical	
ΔE [14, 15, 16]	f	ΔE	f	ΔE [17]	f	ΔE	f
Pyridine				Cytosine			
4.9	0.04	4.9	0.04	4.66 (4.5)	(0.2)	4.69	0.04
6.4	0.10	6.2	0.12	5.58 (5.2)	(0.2)	6.02	0.09
7.1	1.30	6.9	1.05	6.20 (6.1)	(0.6)	6.54	0.96
		7.0	0.97			6.79	0.02
Pyridinium				Cytosinium			
4.8	[a]	4.8	0.10	4.50	[b]	4.56	0.25
5.5		5.6	0.08	5.90		6.04	0.20
		6.7	0.80			6.46	0.58
		6.8	1.00			7.16	0.24

[a] The intensity of the first π-π^* band of pyridinium is not known with certainty. It is nevertheless near the intensity of the second π-π^* band of pyridine (0.10).

[b] The intensity of the first π-π^* band of cytosinium is known to be much larger than that of the corresponding band in cytosine [17]. The transition energies and intensities given in parenthesis for cytosine are from Ref. [18]. These results are more recent than those of Ref. [17] but unfortunately the corresponding results for the cytosinium ion are not available.

References

1. Mataga, S., and S. Tsuno: Naturwiss. **45**, 333 (1958).
2. Schor, R.: Personal communication.
3. Brown, R. D., and M. L. Heffernan: Austral. J. Chem. **12**, 554 (1959).
4. Carroll, D. G., A. T. Armstrong, and S. P. McGlynn: J. chem. Physics **44**, 5 (1966).
5. Rein, R., N. Fukuda, H. Win, and G. A. Clarke: J. chem. Physics **45**, 4743 (1966).
6. Clementi, E., and R. L. Raimondi: J. chem. Physics **38**, 2686 (1963).
7. Cusachs, L. C.: J. chem. Physics **43**, 157—159 (1965).
8. —, and J. M. Reynolds: J. chem. Physics **43**, 160—164 (1965).
9. Berthod, H., C. Giessner-Prettre, and A. Pullman: Theoret. chim. Acta (Berl.) **5**, 53 (1966).
10. — — — Internat. J. Quantum Chem. **1**, 123 (1967).
11. Sutton, L. E.: Tables of interatomic distances, Supplément 1956—1959. London: The Chemical Society 1965.
12. Sundaralingan, M., and L. H. Jensen: J. molecular Biol. **13**, 930 (1965).
13. Barker, L., and R. E. Marsh: Acta Cryst. **17**, 1581 (1964).
14. Pickett, L. W., M. E. Corming, G. M. Wieder, D. A. Semonow, and J. M. Buckley: J. Amer. chem. Soc. **75**, 1618 (1953).
15. Klevens, H. B., and J. R. Platt: Techn. Rep. Univ. of Chicago, Part I, 145 (1953—1954).
16. Zanker, V.: Z. physik. Chem. N.F. **2**, 52 (1954).
17. Shugar, D., and J. J. Fox: Biochemica Biophysica Acta **9**, 199 (1952).
18. Clark, L. B., and I. Tinoco jr.: J. Amer. Chem. Soc. **87**, 11 (1965).

Dr. A. Denis
Institut de Biologie Physico-Chimique
Laboratoire de Biochimie Théorique
13, Rue Pierre Curie
Paris V^e/France