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The Electronic Spectrum and Spacial Configuration of Phenothiazine

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The electronic spectrum and ionization potential of phenothiazine were calculated parametrizing the angle of fold between the two lateral benzene planes on the basis of the Pariser-Parr-Pople SCF-MO-CI method, and the calculated results at the dihedral angles in a range of the values determined by other methods were found to be in good agreement with the observed spectral data. Also, the all valence-electronic structure, especially the hybridization state of the valence-atomic orbitals of the heteroatoms, was calculated using the extended Hückel method in order to compare the electronic structures of the two possible spacial configurations with respect to the position of the proton attached to the nitrogen atom.

Introduction

The electronic properties of the phenothiazine molecule have undergone a number of theoretical investigations in the course of primary steps for understanding the excellent electron-donating properties and pharmacological actions of its drugs; First, Pullman and Pullman[2] indicated from the Hückel-type calculation that phenothiazine is characterized by a high energy level, *i.e.* an antibonding HMO energy level of the highest occupied molecular orbital (h.o.m.o), and by Karreman, *et al.*[3] an analogous trend was also extended to the chlorpromazine drug. On the contrary, Orloff and Fitts[4] predicted that phenothiazine itself should not have such an extreme electron-donating property because the h.o.m.o. is lowered to a bonding state by the Hückel-type calculation taking account of the sulfur *d*-orbitals. More recently, Malrieu and Pullman,[5] and Tyutyulkov, *et al.*[6] performed the modified Hückel-type calculations in order to predict the relative electronic stability of the two most probable configuration of the phenothiazine molecule which are folded about the axis joining the two central heteroatoms. Moreover, the Pariser-Parr-Pople (P-P-P) method was also utilized by Pullman,[7] and Bloor, *et al.*[8] for the calculation of ionization potential and electron distribution. The main aims of these calculations, however, appears to lie in explaining the chemical and biological reactivities, and hence little attentions have been paid to the precise calculation of the π-π^* electronic transition and vertical ionization potential which are regarded to be sensitive functions of the angle of fold between the two lateral benzene planes.

As a part of the molecular orbital studies on the electronic structures of the heteroaromatic compounds of biological interest,[9-12] this paper reports the semiempirical SCF-MO-CI calculations on the electronic spectrum and ionization potential of phenothiazine which

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have been performed systematically as a function of the dihedral angle, and, in addition, the extended Hückel calculation on the all valence-electronic structures for the two possible spacial configurations.

Method of Calculation

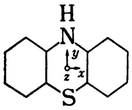
In the semiempirical SCF-MO method (P-P-P approximation)[13,14] the valence-state ionization potential (I) and electron affinity (A) of the π-orbitals are taken as follows with reference to the paper of Hinze and Jaffe;[15a]

I (=C-) 11.16 eV; I (-$\overset{|}{\mathrm{N}}$-) 26.70 eV;
I (-S-) 23.59 eV
A (=C-) 0.03 eV; A (-$\overset{|}{\mathrm{N}}$-) 9.26 eV;
A (-S-) 10.54 eV

The sulfur *d*-orbitals are not explicitly included because it has been pointed out by Johnstone and Ward[16] that the observed π-π^* transitions of sulfur heterocycles are generally reproduced by a small variation in

Table I. Calculated and Observed Data on π-π^* Transition

Coordinate Axes of Phenothiazine



a) Calculated Data

Dihedral angle														
180°			170°		160°		150°		140°		130°		120°	
ΔE_s[1]	f[2]		ΔE_s	f	ΔE_s	f	ΔE_s	f	ΔE_s	f	ΔE_s	f	ΔE_s	f
3.208	0.042	(x)[3]	3.213	0.042	3.232	0.042	3.262	0.042	3.303	0.042	3.354	0.043	3.413	0.043
3.587	0.219	(x)	3.591	0.219	3.602	0.211	3.621	0.198	3.646	0.180	3.679	0.159	3.717	0.136
3.913	0.008	(y)	3.915	0.008	3.918	0.010	3.925	0.013	3.934	0.016	3.946	0.019	3.962	0.023
4.808	0.165	(y)	4.808	0.165	4.808	0.163	4.807	0.159	4.804	0.154	4.800	0.146	4.791	0.138
4.880	1.264	(x)	4.879	1.264	4.877	1.217	4.874	1.142	4.870	1.042	4.863	0.922	4.854	0.789
5.389	0.008	(y)	5.387	0.008	5.381	0.015	5.371	0.027	5.356	0.041	5.336	0.057	5.311	0.072
5.615	0.037	(x)	5.615	0.037	5.615	0.037	5.614	0.037	5.611	0.037	5.607	0.038	5.599	0.039
ΔE_T[4]			ΔE_T		ΔE_T		ΔE_T		ΔE_T		ΔE_T		ΔE_T	
1.633			1.637		1.646		1.662		1.684		1.710		1.741	
1.923			1.923		1.923		1.922		1.922		1.922		1.922	
2.724			2.730		2.746		2.773		2.810		2.856		2.910	
2.828			2.832		2.844		2.863		2.890		2.925		2.966	

b) Observed Data[5]

ΔE_s	$\log \varepsilon_{max}$	f
3.87	3.64	0.13
4.89	4.65	0.79

1) singlet π-π^* transition energy in eV
2) oscillator strength
3) polarization direction
4) triplet π-π^* excitation energy in eV
5) in 95% ethanol solution. Taken from R.J. Warren, I.B. Eisdorfer, W.E. Thompson, and J.E. Zarembo, *J. Pharm. Sci.*, 55, 144 (1966).

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the core integrals. The two-center repulsion integral (δ_{rs}) is obtained using the Mataga–Nishimoto formula.[17] The core-resonance integral (β_{rs}) is evaluated for neighbouring atomic pairs by the variable β procedure,[18] where the parametrizations are taken as follows;

$$\beta_{C\text{-}C} = -0.51P_{C\text{-}C} - 1.84, \text{ (eV)}$$
$$\beta_{C\text{-}N} = -0.53P_{C\text{-}N} - 2.02,$$
$$\beta_{C\text{-}S} = -0.33P_{C\text{-}S} - 1.80.$$

$P_{C\text{-}C}$, $P_{C\text{-}N}$, and $P_{C\text{-}S}$ correspond to the usual π-bond-order of the C-C, C-N, and C-S bonds, respectively. Here, in allowing for non-planarity the $\beta_{C\text{-}X}$ (X = central heteroatom) is corrected by the equation of $\beta_{C\text{-}X}(\alpha) = \beta_{C\text{-}X}(O)\cos\alpha$, where the $\beta_{C\text{-}X}(O)$ is the value for the planar structure, and the α is the distortion angle from planarity.

In the CI method all singly excited configurations are allowed to interact, and the calculations of the interconfigurational matrix elements are performed with the zero-differential-overlap approximation.

In the calculation of the extended Hückel theory (EHT) developed by Hoffmann[19] the exchange integral (H_{rs}) is evaluated using the equation of $H_{rs} = K/2\ S_{rs}(H_{rr} + H_{ss})$ where $K = 1.75$. All overlap integrals are retained, and calculated from the Mulliken's method.[20] The Coulomb integral (H_{rr}) is taken as follows from the spectroscopic data by Pritchard and Skinner;[15b]

H (1S): 13.6 eV, C (2S): 21.43 eV, C (2P): 11.42 eV,
N (2S): 27.5 eV, N (2P): 14.49 eV, S (3S): 20.08 eV,
S (3P): 13.32 eV.

All the bond lengths in the phenothiazine ring are assumed as 1.395 Å, and the C-H and N-H bond lenghts are taken as 1.08 Å and 1.012 Å, respectively. The cooridnate axes of the phenothiazine molecule are denoted in Table I.

Result and Discussion

The P-P-P calculations of the π-π^* electronic transitions of phenothiazine were performed varying the dihedral angle between 180° and 120°. The calculated results of the singlet π-π^* transition energy, oscillator strength, polarization direction and triplet excitation energy are listed in Table I together with the experimental spectral data. The calculated values of the transition energy appear to be rather sensitive functions of the dihedral angle; As the molecule is folded, the values for the lowest three singlet π-π^* transitions that are comparatively less lowered by the CI mixing are raised moderately, but those for the higher transitions tend to be lowered slightly. On such structural variation the oscillator strengths of the weak π-π^* transitions tend to be raised, and those of the most intense second and fifth π-π^* transitions are lowered. In a wide range of the dihedral angle the calculated second singlet π—π^* transition is situated close to the observed 3.87 eV transition which corresponds to the maximum absorption of the longest wavelength band, and the calculated first and third π-π^* transitions with much less oscillator strengths are also situated around this observed transition. This suggests that the broad longest wavelength band seems to consist of the three transitions. In fact, the polarized excitcation spectrum of phenothiazine by Mantsch and Dehler[21] indicates that this broad band is composed of the weak and intense transitions with perpendicular directions.

The second observed transition at 4.89 eV also appears to be correlated with both of the fourth (y-polarized) and fifth (x-polarized) theoretical transitions. This is consistent with the previously quoted polatization data[21] which indicate that the second observed band is composed of the two transitions with perpendicular polarization directions.

It may be said that the posirions of the two absorption maxima in the ultraviolet (UV) spectrum of phenothiazine are successfully predicted by the present P-P-P calculations assuming the folded structures, and comparison of the observed and calculated values of the rela-

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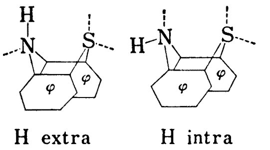
tive intensity of the two π-π^* transitions also serves to support the folded structure to some extent; On a decrease of the dihedral angle in going from 180° to 120°, the theoretical ratio of the oscillator strength of the fifth transition to that of the second transition goes on increasing, though slightly, towards the value of ~6.0 which can be estimated from the observed spectrum using the equation of $f = 4.32 \times 10^{-9} \varepsilon_{max} \Delta\nu$, where $\Delta\nu$ is the half-width of an absorption band. This fact is certainly in line with the experimental data on dipole moment[22] and X-ray analysis[23] which indicate that phenothiazine has considerably (by 140—150°) folded spacial configurations.

With respect to the triplet excited state of phenothiazine, it is known from recent studies by Lhoste, *et al.*[24,25] that the lowest triplet excitation energy (E_{T_1}) is 2.4 eV and the zero-field splitting parameters of this state are characterized by the values for $^3(\pi,\pi^*)$ state of aromatic molecules. The calculated excitation energy of the lowest $^3(\pi,\pi^*)$ state is lower by ~0.8 eV than the E_{T_1} value, whereas the orbital symmetry of the lowest triplet state which was assigned from the observed spin distribution to the B_2 representation in the C_{2v} symmetry point group[25] is in agreement with the predicted orbital symmetry of the lowest $^3(\pi,\pi^*)$ state.

The two different types of the most probable spacial conformation of phenothiazine are classified by the position of the imino-proton because the proton can be pushed out either to an external or to an internal position with respect to the side benzene rings. Hereafter they will be referred as "H extra" and "H intra," respectively, according to the notation by Malrieu and Pullman.[5] The all valence-electronic structures of both conformation

TABLE II. Atomic Orbital Populations and Atom Populations of the N and S Atoms



Configuration	Atomic orbital population								Atom population	
	N (2S)	N (2Px)	N (2Py)	N (2Pz)	S (3S)	S (3Px)	S(3Py)	S (3Pz)	N	S
H intra	1.470	1.272	1.317	1.789	1.267	1.130	1.743	1.482	5.848	5.622
H extra	1.468	1.272	1.779	1.395	1.266	1.130	1.742	1.480	5.914	5.618

TABLE III. Calculated Values of Ionization Potential (Ip)

a) Calcd. with the P-P-P Method

Dihedral angle	180°	170°	160°	150°	140°	130°	120°
Ip (eV)	8.077	8.082	8.099	8.126	8.164	8.214	8.273

b) Calcd. with the EHT Method

Configuration	Ip (eV)
H intra	10.142
H extra	10.253

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Table IV. Atomic Orbital Coefficients of the N and S Atoms in the h.o.m.o.

	N (2S)	N ($2P_x$)	N ($2P_y$)	N ($2P_z$)	S (3S)	S ($3P_x$)	S ($3P_y$)	S ($3P_z$)
H intra	−0.053	0.000	−0.080	−0.168	0.063	0.000	0.492	−0.299
H extra	0.013	0.000	−0.249	−0.123	0.078	0.000	0.513	−0.236

have been calculated with the EHT method. Table II shows the calculated results of the atomic and atomic orbital populations of the heteroatoms. The all valence-electronic energy of "H intra" is −1189.404 eV and is lower by ~0.2 eV than the value for "H extra," *i.e.* −1189.193 eV. This ordering of the relative stability is in agreement with that obtained from the simple Hückel-type calculation in the preceding literature.5) The atomic orbital populations of the imino-nitrogen atom are much affected by the proton position; The *p*-orbital that is most capable of contributing to the lone pair orbital formation, *i. e.* P_z-orbital in "H intra" and P_y-orbital in "H extra," takes the largest value of the atomic orbital population. On the other hand, the atomic orbital population of the sulfur atom is scarcely affected by the structural change. The atomic population of the nitrogen atom is most sensitive to the structural change, and the decrease of this value on the structural change in going from "H extra" to "H intra" seems to take place against the loss of the localization of the electrons in the nitrogen lone pair orbital; The sum of the atomic orbital populations of the 2S- and 2P-orbitals which are most capable of contributing to the lone pair formation increases on this structural change, just alike the atomic population value.

The vertical ionization potentials calculated by Koopmans' theorem26) are shown in Table III. The data calculated with the EHT method are too high to be compared with the experimental value of 4—8 eV. Here, it is known from Table IV that the h.o.m.o. is mainly composed of the P_y- and P_z-orbitals of the heteroatoms, and this appears to suggest that the electron-donating property of phenothiazine is largely due to the lone pair hybridization of the heteroatoms, just as indicated by Kuboyama27) from the analysis of the charge-transfer spectrum of the analogous compounds. The structural change in going from "H extra" to "H intra" lowers the ionization potential slightly. Considering the above mentioned suggestion and taking account of the more localization of the lone pairs in "H intra," it is not so unreasonable to admit an indication by Bloor, *et al.*8) that the lone pairs of the nitrogen and not the sulfur atom is largely responsible for the electron-donating property. The ionization potentials calculated by the P-P-P method are also given in Table III, and these values go on increasing along with the increase of the dihedral angle which makes the central heteroatoms retract π-electrons. The value of 8.164 eV predicted with an appropriate dihedral angle value of 140° falls in good agreement with the experimental value of 8.17 eV obtained from the contact charge-transfer spectrum.28)

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