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SCF MO Calculations of Uracil, Lumazine, and Alloxazine, and Their Tautomeric Isomers*[1]

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The electronic structures of uracil, lumazine, and alloxazine, and all their possible tautomeric isomers have been calculated by the LCAO MO SCF method based on variable beta approximation. The calculated singlet transition energies for diketo forms agree quite well with the experimental results. The present theory suggests that some tautomeric forms of lumazine and alloxazine will behave as both electron donors and electron acceptors. In biological systems, uracil, lumazine, alloxazine, and isoalloxazine will act as both oxidizers and reducers through hydrogen bonds with some molecules, such as protein and DNA.

In order to correlate the biological activities with the electronic structure of molecules, many quantum mechanical calculations have been made.[1] However, the calculations have always included some ambiguities in the estimation of basic parameters, particularly in the core integral, $\beta_{\mu\nu}$. It has been shown[2] that the Pariser-Parr-Pople method based on variable β modification with NM gamma[3] can very nicely calculate various molecular properties, such as electronic spectra, charge distributions, and bond orders, associated with the π-electronic structure of conjugated systems.

In a variable β approximation, β_{CO} associated with an enol-type bond is given by the same expression as that associated with a keto-type bond. Similarly, the β_{CN} concerned with an amino-type bond is given by the same formula as for the β_{CN} of an aromatic C–N bond. Therefore, we can remove some uncertainties from the theory.

Uracil, lumazine, and isoalloxazine show important biological activities and have many tautomeric isomers, so they will be very interesting molecules for our theoretical consideration. In this paper, the π-electronic structures of these molecules will be calculated by the SCF MO method based on variable β modification with NM gamma.

Calculations

The detail of the method used in this paper have been described in previous papers.[2] In the variable β procedure, precise geometry is not required, and all bond lengths have been chosen as 1.40 Å. Bond angles of 120°C have been assumed throughout.

The transition energies have been calculated by including configuration interactions between all singly-excited configurations within 3.5 eV of the lowest-excited singlet state. The parameters used are summarized in Table 1. For convenience, molecules are marked by code numbers, shown in Fig. 1. A-*j* has the same heteroatom arrangement as the corresponding L-*j*.

TABLE 1. PARAMETERS

Core	I_μ (eV)	A_μ (eV)	$\gamma_{\mu\mu}$ (eV)	a_μ (A)
C^+	11.16	0.03	11.13	1.294
N^+	14.12	1.78	12.34	1.167
N^{2+}	26.70	9.26	17.44	0.826
O^+	17.70	2.47	15.23	0.945
O^{2+}	32.90	11.37	21.53	0.669

$\beta_{\mu\nu}$

Uracil and the tautomers

$$\beta_{\mathrm{CC}} = -0.51p - 2.04$$
$$\beta_{\mathrm{CN}} = -0.53p - 2.24$$
$$\beta_{\mathrm{CO}} = -0.56p - 2.44$$

Lumazine and the tautomers

$$\beta_{\mathrm{CC}} = -0.51p - 1.90$$
$$\beta_{\mathrm{CN}} = -0.53p - 2.09$$
$$\beta_{\mathrm{CO}} = -0.56p - 2.27$$

Alloxazine and the tautomers

$$\beta_{\mathrm{CC}} = -0.51p - 1.84$$
$$\beta_{\mathrm{CN}} = -0.53p - 2.02$$
$$\beta_{\mathrm{CO}} = -0.56p - 2.20$$

[*1] Presented at the 19th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1966.

1) For example; a) A. Pullman and B. Pullman, *Bull. soc. chim. France,* **1958**, 766; **1959**, 549; b) J. Ladik and T. A. Hoffmann, *Biopolymers,* Symposia No. 1, 117 (1964); c) A. Veillard and B. Pullman, *J. Theoret. Biol.,* **4**, 37 (1963); d) C. Nagata, A. Imamura, Y. Tagashira and M. Kodama, This Bulletin, **38**, 1638 (1965).

2) K. Nishimoto and L. S. Forster, *Theoret. chim. Acta,* **3**, 407 (1965); **4**, 155 (1966).

3) K. Nishimoto and N. Mataga, *Z. Physik. Chem.* [*Frankfurt*], **12**, 335 (1957).

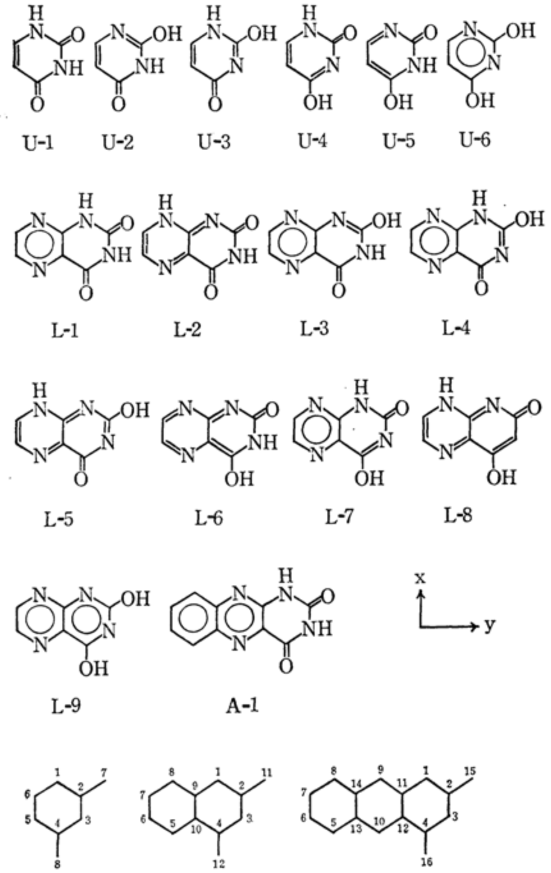
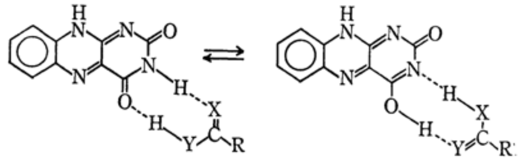


Fig. 1.

Results and Discussion

Electron Affinities and Ionization Potentials. The electron affinity, A, and the ionization potential, I, of a given molecule are very important in the study of oxidation-reduction reaction and charge transfer complex formation. According to Koopman's theorem,4) I and A are given by the negative of the highest occupied orbital energy, ε_1, and the lowest vacant orbital energy, $\varepsilon_{1'}$, respectively. The calculated orbital energies are summarized in Table 2. As has been shown in previous papers,2) the experimental ionization potentials might be smaller by about 1.1 eV than the calculated values. From this table, the electron affinities of diketo forms may be expected to be quite large. Therefore, they will be good electron acceptors and oxidizers in some reactions. The present calculations suggest that L-6, L-8 and A-6 will be both electron donors and electron acceptors, for their ionization potentials are small and they have large electron affinities. It may, therefore, be expected that they will form charge transfer complexes by themselves.

Rearrangement through Hydrogen Bonds. In the present molecules, there is a possibility of rearrangement through the hydrogen bond. For example, in isoalloxazine (A-2), which is the parent nucleus of Vitamine B$_2$, the following type of hydrogen bond will be formed with biological systems:



A-2 A-8

where X and Y represent electronegative atoms, oxygen or nitrogen. When we name A-8 as a conjugate isomer of A-2 and A-2 as the mother molecule, the following isomer groups are obtained:

Mother molecule	The conjugate isomer
U-1	U-2, U-3, U-4
L-1	L-3, L-4, L-7
L-2	L-5, L-8
A-1	A-3, A-4, A-7
A-2	A-5, A-8

Table 2. Highest occupied (ε_1) and lowest vacant ($\varepsilon_{1'}$) orbital energies of uracil, lumazine, alloxazine, and their isomers (in eV)

Molecule	$-\varepsilon_1$	$-\varepsilon_{1'}$
U-1	10.13	2.11
U-2	9.23	1.50
U-3	9.29	1.26
U-4	9.43	1.92
U-5	9.29	1.92
U-6	9.50	0.85
L-1	10.02	2.70
L-2	9.53	3.56
L-3	9.29	2.32
L-4	9.46	2.41
L-5	9.08	3.30
L-6	8.91	3.35
L-7	9.58	2.96
L-8	9.04	3.65
L-9	9.31	2.49
A-1	9.81	3.37
A-2	9.60	3.88
A-3	9.15	2.96
A-4	9.44	3.04
A-5	9.18	3.58
A-6	8.70	3.90
A-7	9.55	3.51
A-8	9.17	3.90
A-9	9.05	3.14

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4) T. Koopman, *Physica*, **1**, 104 (1933).

From Table 2, mother molecules may be expected to be good electron acceptors or oxidizers, whereas the conjugate isomers should be good electron donors or reducers. In other words, uracil (U-1), lumazines (L-1, L-2), alloxazine (A-1), and isoalloxazine will behave as both electron donors and acceptors in oxidation-reduction reactions in biological systems, through hydrogen bonds with protein or DNA. In order to discuss this type of tautomerization quantitatively, we need to make total energy calculations.

Electronic Spectra. Calculated lower singlet transition energies and the oscillator strengths are given in Table 3. It should be noted that the electronic spectra of some mother forms are expected to be very similar to those of their conjugate isomers. For example, the spectra of L-2 and L-5 or A-2 and A-5 are very similar. Therefore, an electronic spectral investigation of the tautomeric equilibrium will be rather difficult in some cases.

It will be interesting to discuss the solvent effect on electronic absorption spectra from the electrostatic point of view, that is, on the basis of change in dipole moments on excitation. According to McRae,[5] the frequency shift in a transition from the ground state to the i-th excited state of an isotropic molecule is given approximately by:

$$\Delta\nu - \Delta\nu_{\mathrm{ref}} = \frac{1}{hc}(\mu_0 - \mu_i)\,R + \frac{3}{2hc}(\alpha_0 - \alpha_i)R^2 \qquad (1)$$

where $\Delta\nu_{\mathrm{ref}}$ represents the frequency shift induced by a non-polar reference solvent. μ and α are the dipole moment and the polarizability of the solute molecule respectively. The suffixes 0 and i refer the ground and ith excited states respectively. The reaction field, R, is given by:

$$R = \frac{2\mu_0}{a^3}\left[\frac{D-1}{D+2} - \frac{n^2{}_0 - 1}{n^2{}_0 + 2}\right]$$

where

D: static dielectric constant
n_0: solvent refractive index
a; cavity radius

The first term of Eq. (1) gives a shift due to the change in dipole moment associated with the electronic transition. The second term measures a shift due to the change in dispersion force, which always contributes to a red shift, because $\alpha_i > \alpha_0$. Therefore, the first term determines the direction of the shift.

The calculated π-moments of the ground state and the lower excited states are given in Table 4. The solvent arrangement is favorable for the ground-state dipole of the solute molecule and remains unchanged upon excitation, agreeing with the Franck-Condon principle. When the solvent arrangement is unfavorable for an excited-state dipole, dipole-dipole interaction should contribute to a blue shift. Unfortunately, there is no reliable method for the calculation of a sigma-moment. However, Table 4 suggests that some transitions (for example, the second lowest transition of L-2) are shifted in the blue direction in a polar solvent by dipole-dipole interaction.

Table 3. Lower singlet transition energies (eV) and oscillator strengths (f) of uracil, lumazine, alloxazine, and their isomers

Molecule	1st transition	2nd transition	3rd transition	
U-1	4.81 (0.357)	5.56 (0.147)	5.91 (0.352)	
U-2	4.46 (0.315)	5.37 (0.398)	6.76 (0.326)	
U-3	4.54 (0.036)	5.25 (0.505)	6.09 (0.204)	
U-4	4.20 (0.146)	5.64 (0.106)	6.30 (1.479)	
U-5	3.99 (0.263)	5.70 (0.415)	6.33 (0.328)	
U-6	4.79 (0.147)	6.00 (0.233)	6.81 (0.955)	
L-1	4.08 (0.348)	4.84 (0.213)	5.50 (0.337)	
L-2	3.18 (0.425)	4.11 (0.058)	4.48 (0.765)	
L-3	3.95 (0.471)	4.43 (0.311)	5.74 (0.356)	
L-4	3.98 (0.376)	4.56 (0.004)	5.40 (0.358)	
L-5	2.94 (0.324)	4.06 (0.016)	4.22 (0.560)	
L-6	2.80 (0.270)	4.37 (0.119)	5.13 (0.728)	
L-7	3.66 (0.452)	4.59 (0.070)	5.15 (0.309)	
L-8	2.77 (0.396)	3.72 (0.030)	4.40 (0.733)	
L-9	3.79 (0.373)	4.51 (0.027)	5.47 (1.221)	
A-1	3.42 (0.296)	3.75 (0.127)	4.70 (0.961)	
A-2	2.99 (0.579)	3.73 (0.150)	4.42 (0.774)	
A-3	3.35 (0.437)	3.77 (0.067)	4.37 (0.750)	
A-4	3.44 (0.395)	3.83 (0.097)	4.94 (0.553)	
A-5	2.82 (0.418)	3.81 (0.174)	4.31 (0.402)	
A-6	2.29 (0.284)	3.34 (0.093)	4.70 (1.234)	
A-7	3.21 (0.500)	3.65 (0.217)	5.18 (1.115)	
A-8	2.74 (0.566)	3.52 (0.210)	4.27 (0.417)	
A-9	3.22 (0.443)	3.67 (0.211)	5.04 (1.843)	
		Experimental data		Ref.
U-1	4.81 (0.22)	5.40 (—)	6.11 (0.33)	6
L-1	3.77 (—)	4.96 (—)	5.34 (—)	7
L-2	3.05 (—)	4.51 (—)	4.84 (—)	8
A-1	3.24 (—)	3.77 (—)	4.77 (—)	9
A-2	2.82 (—)	3.60 (—)	4.57 (—)	9

The π-electron densities calculated for various electronic states are given in Table 5. This table shows that the charge distributions in the present molecules deviate greatly from the uniformity. In this case, a short-range interaction, such as a hydrogen bond formation, will be superior to a long range dipole-dipole interaction. The hydrogen bond-forming power of μth electronegative atom will, to a first approximation, be estimated

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TABLE 4. CALCULATED π-MOMENTS (D_π) FOR VARIOUS ELECTRONIC STATES OF DIKETO FORMS (IN UNIT OF D)

Molecule	Ground state D_π	Ground state θ_x	1st excited state D_π	1st excited state θ_x	2nd excited state D_π	2nd excited state θ_x	3rd excited state D_π	3rd excited state θ_x
U-1	4.57	129°	4.20	108°	2.42	78°	3.63	147°
L-1	3.92	−40°	5.03	99°	2.84	115°	10.45	12°
L-2	8.36	−15°	7.35	112°	3.65	19°	4.28	121°
A-1	3.66	−34°	8.26	−35°	9.03	−23°	8.83	−23°
A-2	8.07	−11°	7.88	123°	8.38	−16°	6.17	−23°

θ_x gives an angle between the transition moment vector and x-axis of the molecule.

TABLE 5. CALCULATED NET CHRAGES IN VARIOUS ELECTRONIC STATES OF DIKETO FORMS (IN UNIT OF e)

Molecule	Atom	Ground state	First excited state	Second excited state	Third excited state
U-1	1	0.335	0.473	0.363	0.418
	2	0.169	0.129	0.000	−0.096
	3	0.338	0.308	0.495	0.420
	4	0.195	0.029	0.051	0.062
	5	−0.074	0.063	−0.085	0.016
	6	0.029	−0.211	−0.165	−0.047
	7	−0.520	−0.402	−0.330	−0.438
	8	−0.473	−0.390	−0.329	−0.335
L-1	1	0.306	0.479	0.458	0.318
	2	0.199	0.172	0.141	0.176
	3	0.320	0.316	0.309	0.616
	4	0.226	0.117	0.183	0.122
	5	−0.141	−0.339	−0.178	−0.350
	6	0.085	0.215	0.046	0.061
	7	0.130	0.055	0.168	−0.045
	8	−0.231	−0.329	−0.262	−0.371
	9	0.075	0.153	−0.132	0.065
	10	0.014	0.086	0.120	−0.090
	11	−0.525	−0.455	−0.454	−0.223
L-2	1	−0.384	−0.082	−0.351	−0.200
	2	0.245	0.228	0.239	0.206
	3	0.333	0.331	0.604	0.373
	4	0.226	0.174	0.180	0.202
	5	−0.124	−0.347	−0.321	−0.174
	6	0.034	0.163	0.025	−0.047
	7	0.028	−0.093	−0.136	−0.025
	8	0.412	0.386	0.330	0.461
	9	0.116	0.076	0.033	−0.134
	10	0.079	−0.002	−0.057	0.081
	11	−0.503	−0.330	−0.273	−0.330
	12	−0.463	−0.505	−0.274	−0.410
A-1	1	0.301	0.398	0.339	0.385
	2	0.187	0.160	0.161	0.127
	3	0.315	0.309	0.309	0.300
	4	0.217	0.141	0.144	0.125
	5	0.018	0.057	0.084	0.090
	6	0.009	0.119	0.009	0.076
	7	0.026	−0.001	0.128	0.039
	8	−0.005	0.076	0.084	0.073
	9	−0.245	−0.301	−0.346	−0.231
	10	−0.136	−0.305	−0.321	−0.172
	11	0.084	0.107	0.067	−0.021
	12	0.034	−0.015	0.062	0.015
	13	0.055	0.097	0.170	0.054
	14	0.087	0.125	0.077	0.091
	15	−0.508	−0.480	−0.503	−0.491
	16	−0.438	−0.485	−0.463	−0.459
A-2	1	−0.370	−0.140	−0.372	−0.380
	2	0.238	0.217	0.224	0.228
	3	0.328	0.335	0.425	0.477
	4	0.217	0.168	0.169	0.169
	5	0.036	−0.035	0.113	0.085
	6	0.006	0.063	0.033	0.051
	7	0.038	0.014	0.035	0.015
	8	−0.038	−0.049	0.082	0.060
	9	0.366	0.398	0.340	0.330
	10	−0.125	−0.344	−0.313	−0.336
	11	0.135	0.070	0.057	0.069
	12	0.090	−0.005	−0.018	−0.042
	13	0.011	0.106	0.048	0.038
	14	−0.004	0.026	−0.041	−0.026
	15	−0.486	−0.331	−0.396	−0.361
	16	−0.445	−0.493	−0.387	−0.376

by the net charge. We may classify the changes in charge distributions on excitation as:

A) An increase in the negative net charge at an aromatic nitrogen. In this case, the proton-accepting power of a nitrogen lone pair increases on excitation, so that a red shift may be expected in a proton-donating polar solvent.

B) An increase in the positive net charge at an amino-type nitrogen. In this case, the proton-donating power of an N–H bond increases on excitation. Therefore, a red shift may be anticipated in a proton-accepting polar solvent.

The remarkable changes in charge distributions are summarized in Table 6, which shows us that L-2 and A-2 have a possibility of a blue shift in a proton-donating polar solvent through hydrogen

TABLE 6. REMARKABLE CHANGES IN CHARGE DISTRIBUTIONS ON EXCITATIONS

Molecule	Position	1st lowest singlet transition	2nd lowest singlet transition	3rd lowest singlet transition	Molecule	Posision	1st lowest singlet transition	2nd lowest singlet transition	3rd lowest singlet transition
U-1	1	B		B		5	A	A	
	3		B		A-1	1	B		
L-1	1	B	B			9	A	A	
	3			B		10	A	A	
	5	A		A	A-2	1	C		
	8	A		A		3		B	B
L-2	1	C				10	A	A	A
	3		B						

A means an increase in negative net charge at an aromatic nitrogen, which should contributes a red shift by a hydrogen bond formation.

B means an increase in positive net charge at an amino type nitrogen, which contributes to a red shift.

C means a decrease in negative net charge at an aromatic nitrogen contributing to a blue shift.

bond formation. At any rate, Tables 4 and 6 will be useful for a theoretical examination of the spectral behavior of diketo forms in polar solvents.

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