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Electronic Properties of the Tautomers of Hydroxy-substituted Purines and Pyrimidines

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The purines and pyrimidines bearing potential amino- or hydroxyl-groups have been the subjects of a number of spectroscopic studies, since they present several interesting problems concerning tautomerism in solution. One of the most useful methods for approaching this problem has been a comparison of the UV spectrum of a given compound with those of the reference compounds, such as the *N*-methyl derivatives. In recent years, the SCF-MO calculation has also been used in the inspection of the correlation between the electronic spectrum and the tautomeric structure of biological purines and pyrimidines.[1-4] These works led to the finding that the P-P-P method, when properly modified, can afford to support fairly well the observations of the predominant tautomers on the basis of the π-electronic transitions and energies. In this work, a more general consideration of the keto-enol tautomerism of purines and pyrimidines was made using the P-P-P method coupled with the variable-β procedure.[5]

The calculations were performed including all singly excited configurations. The variable-β procedure was adopted in order to take account of the remarkable π-bond localization at the keto-tautomers. The parametrizations adopted are analogous to that used previously.[6] The observed transition energies of pyrimidine can be explained well by the present calculation, provided that the second weak band is reduced to $n\rightarrow\pi^*$ in accord with the assignment by Clark and Tinoco.[7] It has been indicated that the 2-, 4-, and 2,4-hydroxypyrimidines take keto-forms in an aqueous solution.[8-10] In this respect, the present calculation of the electronic spectrum shows that the predominant forms of the 2- and 4-isomers are certainly keto-forms, but that of the dihydroxypyrimidine is not necessarily restricted to the diketo-form. In view of the π-electronic energy, the predominance of the diketo-form is supported.

The calculations of purines were performed on the basis of the N(9)H form of purine, since the majority of biological purines exist essentially as derivatives of this form; the calculated data of the electronic spectrum of this form are in good accord with the observed data. The UV spectra of monohydroxypurines in an aqueous solution suggested that the 2- and 8-isomers exist largely in a keto-form type of –CO–NH–, but the 6-isomer is likely to take the enol-form which might contain an intramolecular hydrogen-bond.[11] The above suggestions for the 2- and 8-isomers are well

Table 1. Experimental UV data of purines and pyrimidines

Pyrimidine derivatives	$\Delta E^{a)}$ ($\varepsilon_{\max}\times 10^{-3}$)
None[f]	5.12 (2.0), 5.90 (1.0), 6.53 (6.0)
2-Hydroxy[c]	4.14 (4.6), 5.77 (10.0)
4-Hydroxy[d]	4.77 (3.7), 5.59 (7.4)
2,6-Dihydroxy[b]	4.77 (9.0)
Purine derivatives	
None[f]	4.68 (6.9), 5.17 (3.0), 6.20 (18.1), 6.59 (21.1)
2-Hydroxy[e]	3.94 (4.9), 5.21 (2.9),
6-Hydroxy[e]	4.98 (10.5)
8-Hydroxy[e]	4.47 (11.2), 5.28 (3.2)
2,6-Dihydroxy[e]	4.64 (7.9)
2,8-Dihydroxy[e]	4.00 (5.0), 5.39 (7.9)
6,8-Dihydroxy[e]	4.43 (5.7), 4.82 (12.0)

a) ΔE is transition energy in eV obtained from spectra in neutral solution.
b) L. F. Cavalieri *et al.*, *J. Amer. Chem. Soc.*, **72**, 2587 (1950).
c) M. P. V. Boarland *et al.*, *J. Chem. Soc.*, **1952**, 3716.
d) D. J. Brown *et al. J. Chem. Soc.*, **1953**, 331.
e) S. F. Mason, *J. Chem. Soc.*, **1954**, 2071.
f) L. B. Clark *et al.*, *J. Amer. Chem. Soc.*, **87**, 11 (1965).

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1) C. Giessner-Prette and A. Pullman, *Theore. Chim. Acta*, **9**, 279 (1968).

2) B. Pullman, "Quantum Aspects of Chemical and Biochemical Heterocycles," *Proc. Int. Symp.*, 2nd, 292 (1969).

3) A. Julg and P. Carles, *Theore. Chim. Acta*, **17**, 301 (1970).

4) B. Pullman and H. Berthod, *Tetrahedron*, **26**, 1483 (1970).

5) K. Nishimoto and L. S. Forster, *Theore. Chim. Acta*, **4**, 155 (1966).

6) M. Kamiya and Y. Akahori, *Nippon Kagaku Zasshi*, **92**, 118 (1971).

7) L. B. Clark and I. Tinoco, Jr., *J. Amer. Chem. Soc.*, **87**, 11 (1965).

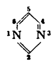
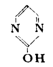
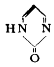
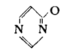
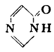
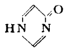
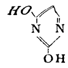
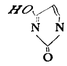
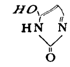
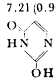
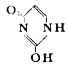
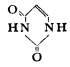
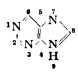
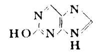
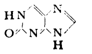
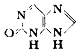
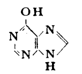
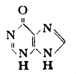
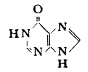
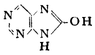
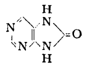
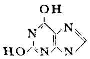
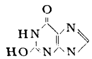
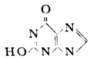
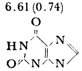
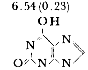
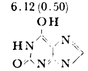
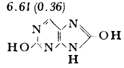
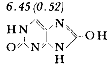
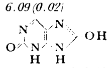
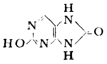
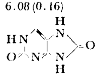
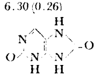
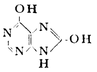
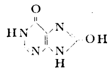
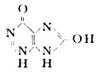
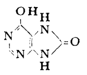
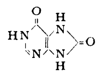
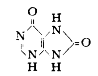
8) M. P. V. Boarland and J. F. W. McOmie, *J. Chem. Soc.*, **1952**, 3716.

9) D. J. Brown and L. N. Short, *ibid.*, **1953**, 331.

10) J. R. Marshall and J. Walker, *ibid.*, **1951**, 1004.

11) S. F. Mason, *ibid.*, **1954**, 2071.

TABLE 2. THEORETICAL DATA OF THE UV SPECTRUM AND π-ELECTRONIC ENERGY

Pyrimidine derivatives			
None  -151.20	*ΔE* (f) 5.16 (0.07) 6.49 (0.09) 7.44 (1.09) 7.49 (1.11)		
2-Hydroxy	 -248.99 4.95 (0.13) 6.31 (0.26) 7.36 (1.05) 7.51 (0.96)	 -248.08 4.08 (0.22) 5.77 (0.18) 6.76 (0.70) 7.18 (0.52)	
4-Hydroxy	 -248.91 5.07 (0.07) 6.24 (0.13) 7.17 (1.11) 7.24 (0.99)	 -248.14 4.38 (0.26) 5.47 (0.38) 6.73 (0.18) 7.41 (0.49)	 -246.23 4.56 (0.08) 5.29 (0.49) 6.44 (0.20) 7.31 (1.04)
2,6-Dihydroxy	 -357.19 4.92 (0.12) 6.17 (0.18) 7.06 (1.13) 7.21 (0.91)	 -356.98 4.20 (0.18) 5.70 (0.09) 6.63 (1.39) 6.97 (0.11)	 -360.29 4.05 (0.32) 5.72 (0.20) 6.58 (0.63) 7.17 (0.42)
	 -360.48 4.39 (0.36) 5.41 (0.36) 6.82 (0.08) 7.23 (0.50)	 -358.57 4.79 (0.04) 5.30 (0.53) 6.07 (0.20) 7.10 (1.19)	 -360.58 5.17 (0.45) 5.97 (0.14) 6.30 (0.37) 7.18 (0.77)
Purine derivatives			
None  -336.87	4.79 (0.18) 5.45 (0.34) 6.35 (0.45) 6.84 (0.49)		
2-Hydroxy	 -453.49 4.62 (0.24) 5.36 (0.41) 6.28 (0.33) 6.74 (0.64)	 -454.42 3.55 (0.23) 4.97 (0.23) 5.55 (0.36) 6.02 (0.18)	 -458.36 4.14 (0.31) 5.27 (0.33) 6.05 (0.29) 6.42 (0.53)
6-Hydroxy	 -458.19 4.83 (0.10) 5.22 (0.45) 6.27 (0.46) 6.65 (0.58)	 -458.68 4.35 (0.25) 5.26 (0.19) 5.70 (0.11) 6.46 (0.68)	 -457.09 4.28 (0.39) 5.10 (0.35) 5.81 (0.03) 6.34 (0.22)
8-Hydroxy	 -456.24 4.69 (0.22) 5.31 (0.41) 6.30 (0.38) 6.73 (0.41)	 -459.89 4.69 (0.25) 5.60 (0.16) 6.32 (1.06) 6.71 (0.06)	
2,6-Dihydroxy	 -585.29 4.68 (0.18) 5.17 (0.47) 6.22 (0.35) 6.61 (0.74)	 -588.24 4.34 (0.45) 4.97 (0.40) 5.77 (0.04) 6.54 (0.23)	 -589.84 4.60 (0.24) 5.30 (0.19) 5.70 (0.16) 6.12 (0.50)
	 -593.95 5.06 (0.31) 5.36 (0.45) *6.05 (0.00)* *6.61 (0.36)*	 -590.86 4.34 (0.26) 5.23 (0.30) *5.99 (0.54)* *6.45 (0.52)*	 -590.26 3.56 (0.29) 4.84 (0.36) *5.55 (0.34)* *6.09 (0.02)*
2,8-Dihydroxy	 -580.08 4.52 (0.26) 5.26 (0.50) 6.24 (0.24) 6.67 (0.56)	 -581.73 3.58 (0.25) 4.97 (0.20) 5.38 (0.50) 6.08 (0.16)	 -586.42 4.01 (0.31) 5.25 (0.36) 5.83 (0.49) 6.30 (0.26)
	 -584.74 4.53 (0.29) 5.60 (0.27) 6.23 (0.83) 6.60 (0.25)	 -587.01 3.84 (0.21) 5.09 (0.20) 5.85 (1.44) 6.27 (0.09)	 -591.18 3.80 (0.37) 5.38 (0.13) 5.69 (0.50) 6.09 (0.12)
6,8-Dihydroxy	 -586.88 4.73 (0.15) 5.13 (0.50) 6.21 (0.33) 6.59 (0.64)	 -585.35 4.16 (0.44) 4.96 (0.38) 5.76 (0.04) 6.13 (0.21)	 -587.73 4.19 (0.26) 5.13 (0.17) 5.70 (0.17) 6.30 (0.50)
	 -593.55 4.69 (0.17) 5.51 (0.21) 6.17 (0.95) 6.54 (0.33)	 -593.60 3.29 (0.61) 3.71 (0.26) 5.35 (0.07) 5.77 (0.26)	 -592.10 4.22 (0.21) 4.81 (0.25) 5.89 (0.26) 6.04 (0.19)

a) *ΔE* is singlet-singlet transition energy in eV.
b) *f* is oscillator strength.
c) The valence-state ionization potential and electron affinity are taken as follows:

	=C-	=N-	$-\overset{\vert}{N}-$	=O	-O-
Ionization potential (eV)	11.16	14.12	28.72	17.28	34.75
Electron affinity (eV)	0.03	1.78	11.96	2.01	13.57

The two-center Coulomb integral is evaluated with the Nishimoto-Mataga formula. Parametrization for the evaluation of the core-resonance integral by the variable-β method is as follows:

$$\beta_{C-C} = -0.51\ P_{C-C} - 2.04,$$
$$\beta_{C-N} = -0.53\ P_{C-N} - 2.24,$$
$$\beta_{C-O} = -0.56\ P_{C-O} - 2.44.$$

d) Numerals under the structural formula are π-electronic energies in eV.

supported by the present calculations of the electronic transitions and energies. In the case of the 6-isomer, the predominance of the keto-form -CO-NH-, can not be confirmed by the calculated results. As regards the dihydroxypurines, the calculated data of the electronic spectra of diketo-forms satisfy the relative sequence of the observed first-transition energies. Moreover, the π-electronic energies support the predominance of diketo-forms.

In conclusion, the variable β-P-P-P calculation of the π-electronic transitions and energies was found to be rather useful for the prediction of the predominant tautomers of the compounds in the title.

The calculations were performed on a HITAC 5020-E computer at the University of Tokyo. The author wishes to thank Professor Yukio Akahori for his useful suggestions.