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Studies on the Tautomers of Purines and Pyrimidines. II. Variable β-SCF-CI Calculations on the Tautomers of Amino- and Hydroxy-substituted Purines and Pyrimidines

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Variable β-SCF-CI calculations on the π-electronic transitions and π-electronic energies were performed over a number of possible tautomers of the purines and pyrimidines substituted with potential amino- or hydroxy-groups. The theoretical results, in particular on the monohydroxy-derivatives, were in good accord with the experimental informations about the preferable tautomers. On the whole, the theoretical data on the electronic transitions were found to be rather useful for classification of various tautomers into predominant and rare forms.

The purine and pyrimidine bases carrying potential amino- or hydroxy-groups have attracted a number of chemists because of the tautomerism in solution. One of the prevailing methods for guessing the predominant tautomers is to compare the ultraviolet (UV) spectrum of a given compound with that of reference compounds whose tautomerism has been blocked by the introduction of alkyl groups. In recent years, theoretical insights into the tautomerism of biochemical purines and pyrimidines have been gained by means of semi-empirical SCF-CI methods.[2] The works indicate that the P-P-P method, combined with any adjustable approximations, can afford to visualize variations of the π-electronic transitions over various tautomers. In this work, the above-mentioned merit of the P-P-P method has been explored more generally with a view of grasping the structure-spectrum correlations over a number of alternative tautomers of the compounds in the title.

Result

The π-electronic transitions were calculated using the variable β-SCF method[3] combined with the CI treatment including all singly excited configurations. The variable β-approximation was adopted for taking account of the effect of the remarked π-bond localization to the π-bonding interactions. Particular requirement for this procedure is associated with the keto- and/or imino-tautomers in which the ring-distances are altered to a large extent. The parametrizations used herein are analogous to that in a previous calculation on purines and pyrimidines.[4]

The experimental data of the transition energies of pyrimidine are fairly well reproduced by the theoretical data, provided that the second weak band is reduced to $n \rightarrow \pi^*$ on the basis of the assignment by Clark and Tinoco.[5] This good result can be derived only after coupling the variable β-method.

1) Location: *Oshika, Shizuoka-shi.*
2) See for example A. Pullman and B. Pullman, *Advan. Quant. Chem.*, 4, 267 (1968); B. Pullman, *Quant. Asp. Heterocycl. Compd. Chem. Biochem., Proc. Int. Symp.*, 2, 292 (1969).
3) K. Nishimoto and L.S. Forster, Theoret. Chim. Acta, 4, 155 (1966).
4) M. Kamiya and Y. Akahori, *Nippon Kagaku Zasshi*, 92, 118 (1971).
5) L.B. Clark and I. Tinoco, Jr., *J. Am. Chem. Soc.*, 87, 11 (1965).

Since earlier works on the spectroscopic studies of hydroxypyrimidines,[6-8] the predominant forms of the 2-, 4-, and 2,4-derivatives have been considered to be the keto-forms. Comparison of the experimental and theoretical data on the electronic transitions suggests that such is the case with the 2- and 4-derivatives. The predominance of the diketo-form of the 2,4-derivative is also supported in terms of the π-energy. On the whole, the increase of the absorption intensity of the first band due to the poly-substitutions is well reproduced by the theoretical data restricted to the diketo-forms.

As concerns aminopyrimidines, agreement between the experimental and theoretical data is not so good with respect to the transition energies. But the relative sequence of the first transition energies is fairly well reproduced by the theoretical data on the amino-tautomers. The imino-tautomers but for the 2,4(6)-diimino-form yield poor results in terms of the transition energies. In contrast to the other P-P-P calculations not using the variable β-procedure, these calculations serve to visualize that the iminotautomers exert large bathochromic shifts upon the first transitions.

The calculations on purines were performed on the basis of the N(9)H form of purine because the majority of biochemical purines exist essentially as the derivatives of this form and because the theoretical data on the electronic transitions of this form is in good accord with the experimental data.

As is known from the spectroscopic study by Mason,[9] the predominant forms of the

Table I. Experimental UV data of purines and pyrimidines

		ΔE ($\varepsilon_{max} \times 10^{-3}$)
Pyrimidine derivatives	none	5.12(2.0), 5.90(1.0), 6.53(6.0)[a]
	2-hydroxy	4.14(4.6), 5.77(10.0)[b]
	4-hydroxy	4.77(3.7), 5.59(7.4)[c]
	2,6-dihydroxy	4.77(9.0)[d]
	2,4,6-trihydroxy	4.77(25.0)[d]
	2-amino	4.25(3.2), 5.53(13.5)[c]
	4-amino	4.63(3.5), 5.30(12.0)[b]
	5-amino	4.16(3.1), 5.25(11.0)[e]
	2,4-diamino	4.64(5.4)[d]
	4,5-diamino	4.29(7.2), 5.04(7.8)[f]
	4,6-diamino	4.77(6.5)[d]
	2,4,5-triamino	4.09(5.4), 5.30–5.34(8.3)[f]
	2,4,6-triamino	4.59(14.4)[d]
	4,5,6-triamino	3.26(0.2), 4.47(7.8)[f]
Purine derivatives	none	4.68(6.9), 5.17(3.0), 6.20(18.1), 6.59(21.1)[a]
	2-hydroxy	3.94(4.9), 5.21(2.9)[f]
	6-hydroxy	4.98(10.5)[f]
	8-hydroxy	4.47(11.2), 5.28(3.2)[f]
	2,6-dihydroxy	4.64(7.9)[f]
	2,8-dihydroxy	4.00(5.0), 5.39(7.9)[f]
	6,8-dihydroxy	4.43(5.7), 4.82(12.0)[f]
	2,6,8-trihydroxy	4.26(11.9), 5.28(9.8)[d]
	2-amino	4.06(6.0), 5.25(5.0)[f]
	6-amino	4.76(12.6), 5.96(18.7), 6.70(15.8)[f]
	8-amino	4.38(14.4), 5.14(3.2)[f]

ΔE is transition energy in eV obtained from spectra in neutral solution.
a) L.B. Clark *et al.*, J. Am. Chem., Soc., **87**, 11 (1965). *b*) M.P.V. Boarland *et al.*, J. Chem. Soc., **1952**, 3716.
c) D.J. Brown *et al.*, J. Chem. Soc., **1953**, 331. *d*) L.F. Cavalieri *et al.*, J. Am. Chem. Soc., **72**, 2587 (1950).
e) N. Whittaker, J. Chem. Soc., **1951**, 1565. *f*) S.F. Mason, J. Chem. Soc., **1954**, 2071.

6) M.P.V. Boarland and J.F.W. McOmie, *J. Chem. Soc.*, **1952**, 3716.
7) D.J. Brown and L.N. Short, *J. Chem. Soc.*, **1953**, 331.
8) J.R. Marshall and J. Walker, *J. Chem. Soc.*, **1951**, 1004.
9) S.F. Mason, *J. Chem. Soc.*, **1954**, 2071.

2- and 8-hydroxypurines are considered to be the keto-form type of -CO-NH-, but the 6-hydroxypurine is likely to exist largely in the enol-form, in aqueous solution, which might contain an OH···N(7) hydrogen-bond. The theoretical data both on the electronic transitions and electronic energies support the above-mentioned result about the 2- and 8-isomers. The somewhat exceptional indication about the 6-isomer appears not to be so unreasonable so far as the present calculations are concerned.

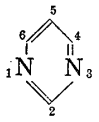
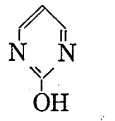
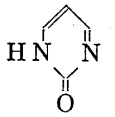
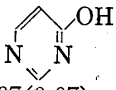
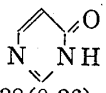
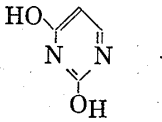
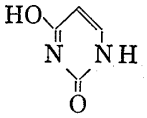
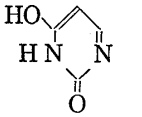
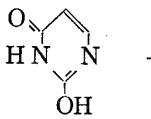
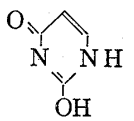
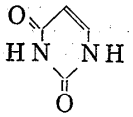
As regards dihydroxypurines, the theoretical data on the diketo-forms well satisfy the relative sequence of the experimental values of the first transition energies. Moreover, the π-electronic energies support the predominance of the diketo-forms. The predominance of the amino-forms of aminopurines is suggested in general only by the calculations on the electronic transitions.

In conclusion, this work serves to exhibit that when the variable β-method is included, the P-P-P-CI calculations on a number of alternative tautomers of purines and pyrimidines are rather available for classification of the tautomers into predominant and rare forms.

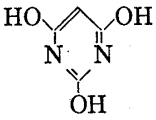
The calculations were performed using a HITAC 5020-E computer at the Computation Center of the University of Tokyo.

TABLE II. Theoretical UV Data of Purines and Pyrimidines

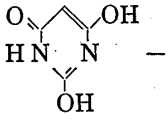
Pyrimidine derivatives

none	ΔE (f)		
 −151.20	5.16(0.07) 6.49(0.09) 7.44(1.09) 7.49(1.11)		
2-hydroxy	 −248.99	 −248.08	
	4.95(0.13) 6.31(0.26) 7.36(1.05) 7.51(0.96)	4.08(0.22) 5.77(0.18) 6.76(0.70) 7.18(0.52)	
4-hydroxy	 −248.91	 −248.14	 −246.23
	5.07(0.07) 6.24(0.13) 7.17(1.11) 7.24(0.99)	4.38(0.26) 5.47(0.38) 6.73(0.18) 7.41(0.49)	4.56(0.08) 5.29(0.49) 6.44(0.20) 7.31(1.04)
2,6-dihydroxy	 −357.19	 −356.98	 −360.29
	4.92(0.12) 6.17(0.18) 7.06(1.13) 7.21(0.91)	4.20(0.18) 5.70(0.09) 6.63(1.39) 6.97(0.11)	4.05(0.32) 5.72(0.20) 6.58(0.63) 7.17(0.42)
	 −360.48	 −358.57	 −360.58
	4.39(0.36) 5.41(0.36) 6.82(0.08) 7.23(0.50)	4.79(0.04) 5.30(0.53) 6.07(0.20) 7.10(1.19)	5.17(0.45) 5.97(0.14) 6.30(0.37) 7.18(0.77)

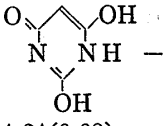
2,4,6-trihydroxy


−475.85

4.91(0.10)
6.10(0.10)
6.90(1.06)
6.92(1.14)


−479.74

4.27(0.29)
5.21(0.36)
6.55(0.37)
7.15(0.61)


−481.15

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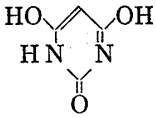
5.18(0.39)
5.96(0.35)
6.83(1.16)


−479.66

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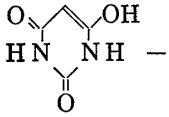
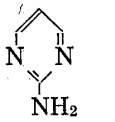
6.55(1.29)
6.88(0.12)


−483.84

5.04(0.58)
5.70(0.13)
6.41(0.26)
7.13(0.67)

2-amino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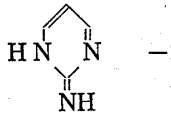
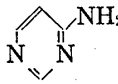
6.15(0.36)
7.30(0.95)
7.44(0.80)


−243.67

3.69(0.17)
5.48(0.30)
6.41(0.75)
6.96(0.29)

4-amino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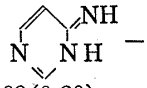
7.00(1.00)
7.15(0.86)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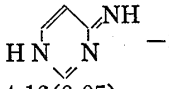
5.25(0.51)
6.49(0.13)
7.08(0.43)


−241.93

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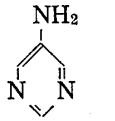
4.99(0.65)
6.38(0.16)
7.06(0.78)

5-amino


−239.11

4.75(0.14)
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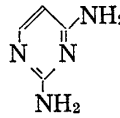
7.27(0.67)
7.32(0.94)

2,4-diamino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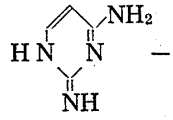
6.75(1.11)
7.02(0.67)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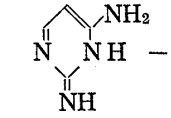
5.42(0.18)
6.15(1.27)
6.68(0.12)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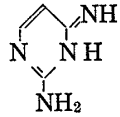
5.36(0.29)
6.15(0.68)
6.91(0.26)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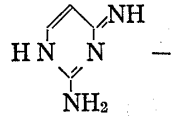
6.45(0.16)
6.89(0.36)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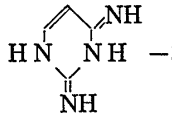
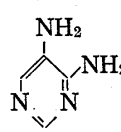
4.97(0.68)
5.93(0.20)
6.79(0.97)


−351.57

4.90(0.39)
5.46(0.20)
5.87(0.42)
6.52(0.78)

4,5-diamino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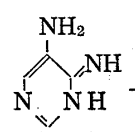
6.83(1.05)
6.99(0.63)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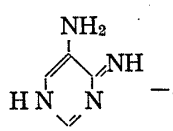
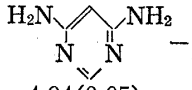
4.00(0.36)
4.76(0.39)
6.00(0.07)
6.84(0.07)

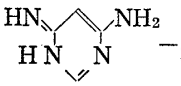

−344.04

3.95(0.13)
4.78(0.41)
5.95(0.22)
6.49(0.94)

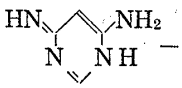
4,6-diamino


−337.59

4.94(0.05)
5.95(0.01)
6.54(1.20)
6.69(0.87)

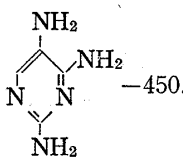

−342.65

3.82(0.16)
5.01(0.49)
5.98(0.34)
7.03(0.56)

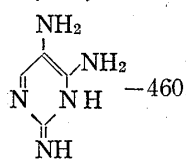

−344.05

3.98(0.08)
4.83(0.53)
6.10(0.32)
6.61(0.85)

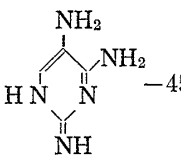
2,4,5-triamino


−450.30

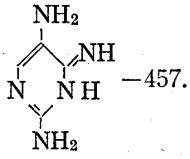
4.46(0.21)
5.54(0.35)
6.72(0.99)
7.02(0.58)


−460.42

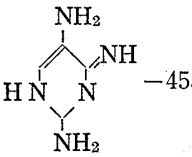
3.47(0.30)
5.08(0.13)
5.76(0.84)
6.71(0.19)


−457.30

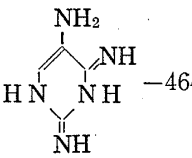
3.70(0.16)
5.12(0.08)
5.90(1.41)
6.51(0.06)


−457.14

3.98(0.48)
4.69(0.33)
6.14(0.04)
6.71(0.16)

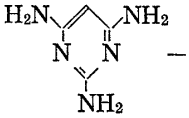

−455.37

4.23(0.11)
4.82(0.43)
5.55(0.29)
6.32(0.99)

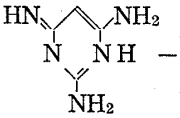

−464.55

4.44(0.40)
5.23(0.23)
5.69(0.38)
6.55(0.54)

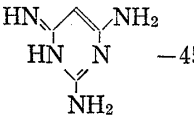
2,4,6-triamino


−446.10

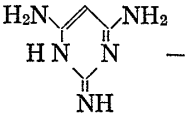
4.80(0.11)
5.93(0.10)
6.61(1.09)
6.61(1.06)


−455.18

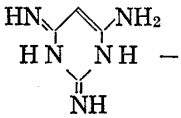
3.95(0.26)
4.94(0.46)
6.17(0.28)
6.63(0.67)


−456.55

4.26(0.05)
4.87(0.57)
5.68(0.35)
6.45(0.95)

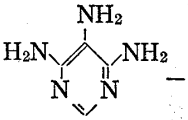

−455.10

3.85(0.22)
5.32(0.19)
6.06(1.26)
6.51(0.11)

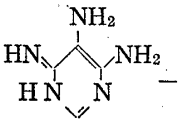

−455.37

4.76(0.61)
5.34(0.09)
5.77(0.31)
6.47(0.78)

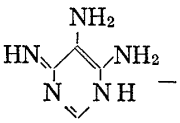
4,5,6-triamino


−457.02

4.60(0.15)
5.42(0.15)
6.48(0.95)
6.62(0.88)


−460.49

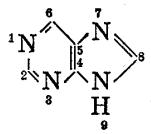
3.71(0.29)
4.54(0.44)
5.74(0.12)
6.67(0.03)


−461.88

3.66(0.14)
4.55(0.37)
5.94(0.37)
6.21(0.85)

Purine derivatives

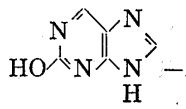
none


−336.87

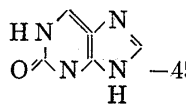
ΔE in eV (f)

4.79(0.18)
5.45(0.34)
6.35(0.45)
6.84(0.49)

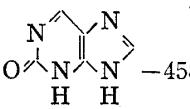
2-hydroxy


−453.49

4.62(0.24)
5.36(0.41)
6.28(0.33)
6.74(0.64)

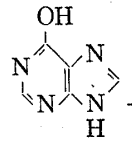

−454.42

3.55(0.23)
4.97(0.23)
5.55(0.36)
6.02(0.18)

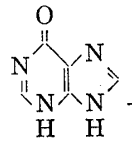

−458.36

4.14(0.31)
5.27(0.33)
6.05(0.29)
6.42(0.53)

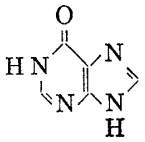
6-hydroxy


−458.19

4.83(0.10)
5.22(0.45)
6.27(0.46)
6.65(0.58)

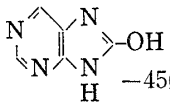

−458.68

4.35(0.25)
5.26(0.19)
5.70(0.11)
6.46(0.68)

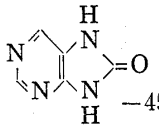

−457.09

4.28(0.39)
5.10(0.35)
5.81(0.03)
6.34(0.22)

8-hydroxy

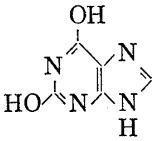

−456.24

4.69(0.22)
5.31(0.41)
6.30(0.38)
6.73(0.41)

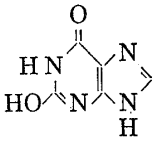

−459.89

4.69(0.25)
5.60(0.16)
6.32(1.06)
6.71(0.06)

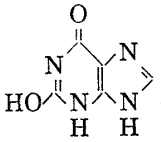
2,6-dihydroxy


−585.29

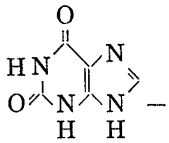
4.68(0.18)
5.17(0.47)
6.22(0.35)
6.61(0.74)


−588.24

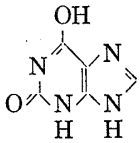
4.34(0.45)
4.97(0.40)
5.77(0.04)
6.54(0.23)


−589.84

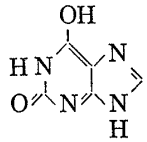
4.60(0.24)
5.30(0.19)
5.70(0.16)
6.12(0.50)


−593.95

5.06(0.31)
5.36(0.45)
6.05(0.00)
6.61(0.36)

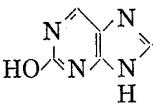

−590.86

4.34(0.26)
5.23(0.30)
5.99(0.54)
6.45(0.52)

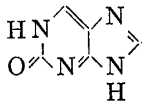

−590.26

3.56(0.29)
4.84(0.36)
5.55(0.34)
6.09(0.02)

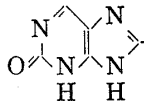
2,8-dihydroxy


−580.08

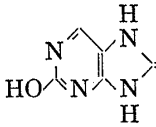
4.52(0.26)
5.26(0.50)
6.24(0.24)
6.67(0.56)


−581.73

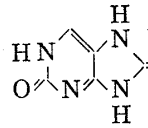
3.58(0.25)
4.97(0.20)
5.38(0.50)
6.08(0.16)


−586.42

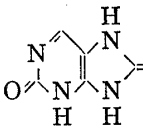
4.01(0.31)
5.25(0.36)
5.83(0.49)
6.30(0.26)


−584.74

4.53(0.29)
5.60(0.27)
6.23(0.83)
6.60(0.25)

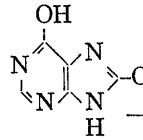

−587.01

3.84(0.21)
5.09(0.20)
5.85(1.44)
6.27(0.09)

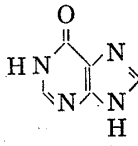

−591.18

3.80(0.37)
5.38(0.13)
5.69(0.50)
6.09(0.12)

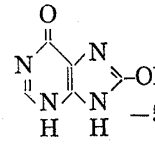
6,8-dihydroxy


−586.88

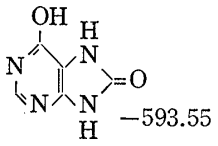
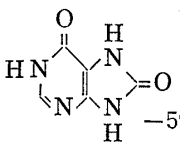
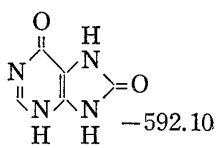
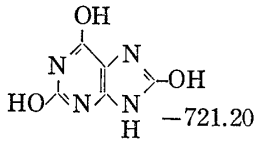
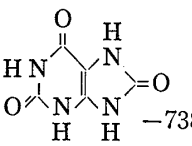
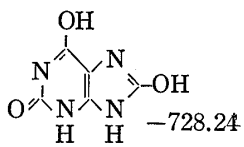
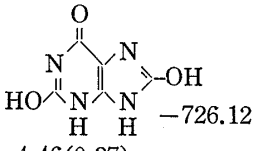
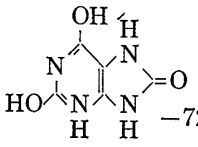
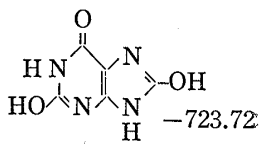
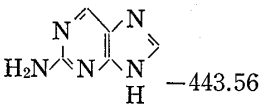
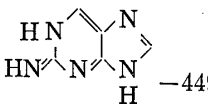
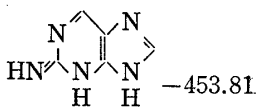
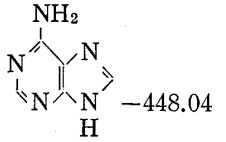
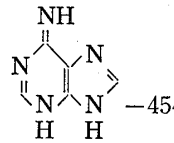
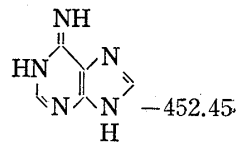
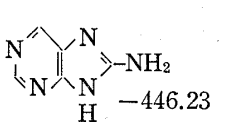
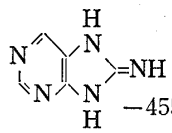
4.73(0.15)
5.13(0.50)
6.21(0.33)
6.59(0.64)


−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	 −593.60	 −592.10
	4.69(0.17) 5.51(0.21) 6.17(0.95) 6.54(0.33)	3.29(0.61) 3.71(0.26) 5.35(0.07) 5.77(0.26)	4.22(0.21) 4.81(0.25) 5.89(0.26) 6.04(0.19)
2,6,8-trihydroxy	 −721.20	 −738.33	 −728.24
	4.58(0.02) 5.11(0.56) 6.16(0.20) 6.58(0.79)	4.51(0.41) 5.43(0.37) 6.03(0.21) 6.18(0.04)	4.23(0.26) 5.24(0.34) 5.81(0.65) 6.34(0.28)
	 −726.12	 −728.88	 −723.72
	4.46(0.27) 5.17(0.15) 5.69(0.22) 6.10(0.64)	4.56(0.22) 5.53(0.34) 6.13(0.65) 6.51(0.29)	4.23(0.49) 4.85(0.43) 5.71(0.06) 6.32(0.18)
2-amino	 −443.56	 −449.84	 −453.81
	4.55(0.25) 5.29(0.44) 6.26(0.28) 6.66(0.68)	3.19(0.16) 4.77(0.30) 5.32(0.41) 5.94(0.00)	3.87(0.28) 5.03(0.40) 5.77(0.22) 6.20(0.56)
6-amino	 −448.04	 −454.14	 −452.45
	4.79(0.11) 5.12(0.44) 6.19(0.56) 6.55(0.51)	4.09(0.21) 5.06(0.31) 5.44(0.13) 6.21(0.64)	4.03(0.30) 4.95(0.43) 5.65(0.04) 6.04(0.30)
8-amino	 −446.23	 −455.28	
	4.65(0.25) 5.24(0.43) 6.24(0.34) 6.68(0.39)	4.56(0.31) 5.37(0.15) 6.04(0.94) 6.38(0.01)	

ΔE is singlet-singlet transition energy.
f is oscillator strength.
As concerns trisubstituted purines, the theoretcial data are given for the best six tautomers which were selected on the basis of the first transition energy.
The valence-state ionization potential and electron affinity are taken as follows:

	=C-	=N-	-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:
$\beta_{C-C}=-0.51\ P_{C-C}-2.04$, $\beta_{C-N}=-0.53\ P_{C-N}-2.24$, $\beta_{C-O}=-0.56\ P_{C-O}-2.44$.
The initial values of bond length were all taken as 1.39 Å
Figures given under the structural formula are total π-energies in eV.