Mesoionic Purinone Analogs. II. A PPP π-SCF Variable Integral Study of Mesoionic Analogs Based Upon Six-Membered Ring Mesoionic Systems

R. A. Coburn, R. A. Carapellotti, and R. A. Glennon

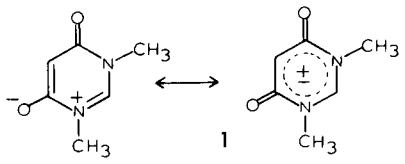
Department of Medicinal Chemistry, School of Pharmacy,
State University of New York at Buffalo, Buffalo, New York 14214

Received November 6, 1972

A large virtually unknown class of mesoionic structures which are isoconjugate to the purinones may be formulated as bicyclic derivatives of known six-membered ring mesoionic compounds. These mesoionic purinone analogs have been investigated *via* variable-electronegativity PPP-SCF treatments of their π-electron systems. The electronic structures of these analogs are compared with those of their covalent isomers and with other mesoionic purinone analogs.

Mesoionic purinone analogs are compounds having an isoconjugate relationship to the purinones, but which cannot be satisfactorily represented by any covalent or single dipolar valence bond structure. A number of these structures, which may be viewed as derivatives of known monocyclic five-membered ring mesoionic systems, were previously described (1). The chemical properties of several of these monocyclic systems were cited to support the hypothesis that many of these mesoionic purinone analogs may be expected to exhibit stabilities comparable to or greater than those of the monocyclic compounds. A number of molecular properties were anticipated to contrast with that implied by any single dipolar representation. The results of modified Hückel molecular orbital treatments of these systems have supported and detailed these contentions (1).

An even greater number of mesoionic purinone analogs may be formulated as ring-fused derivatives of the simple monocyclic six-membered ring mesoionic 1,3-dimethylpyrimidin-4,6-dione **1** (2). A number of alkyl and aryl substituted, as well as ring-fused, derivatives of this system have been reported (3). The results of a VESCF-MO



1

treatment of the π-system of the mesoionic xanthine, hypoxanthine and purin-2-one analogs based upon this six-membered ring mesoionic system will be described. For purposes of comparison, the mesoionic purinone analogs described earlier (1) will be referred to as Class I analogs and those formulated in this discussion will be referred to as Class II analogs.

Description of the Calculations.

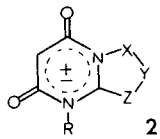
The well-known LCAO-SCF π-molecular orbital method developed by Pariser, Parr, and Pople was employed due to its theoretical justification and extensive application to heterocyclic systems (4). The use of the variable electronegativity method of Brown and Heffernan (5) is justified by the expectation that the variation in net charge among atoms in these molecules may be large. In this procedure the valence state ionization potential and electron affinity of each atom is quadratically related to the Slater effective nuclear charge of the atom. This procedure has been applied to other mesoionic systems by Sundaram and Purcell (6) with results which compare favorably with those obtained by the all-valence-electron CNDO/2 method (7).

Since ground state properties are of primary concern, core resonance integrals were not adjusted to give better predicted electronic absorption spectra, as this procedure compromises ground and excited state properties. Total π-electron energies were calculated by the standard method (4). The binding energy is the sum of the nuclear core repulsion energy (point charge approximation) and the total electronic energy.

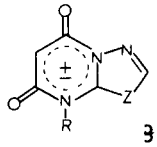
The necessity of representing these analogs with dipolar structures suggests a high degree of charge separation within the molecule. One index of such charge separation is the absolute sum of the net atomic charge densities, $\Sigma[Q]$. The dipole moment of the π-system, μ_π, depends in part upon this charge separation but also upon the geometrical distribution of charge and thus is a less

direct measure of this aspect of the ground state properties.

This method has been applied to the mesoionic analogs previously studied *via* the variable integral HMO method (1). Since the resultant ground state electronic structures were found to be quite similar to those already reported they will not be reported here. However, since the energy terms of the SCF procedure are more reliable, comparisons between all mesoionic analogs and covalent structures will refer only to SCF calculated terms.



2



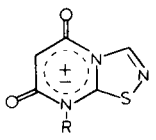
3

	X	Y	Z
2a	CH	CH	S
b	CH	CH	NR'
c	CH	CH	O
d	CH	S	CH
e	CH	NR'	CH
f	CH	O	CH
g	S	CH	CH
h	N	CH	CH
i	O	CH	CH

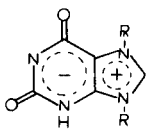
	Z
3a	S
b	NR'
c	O

Xanthine Analogs.

The Class II mesoionic xanthines, represented by the general structure **2**, may be formulated by the ring fusion of an electron-rich (pyrrole-type) five-membered ring heterocycle to the electron deficient portion of the known mesoionic 1,3-disubstituted pyrimidine-4,6-dione **1**. X, Y, and Z may be varied amongst CH, N, NR, S, and O as long as the resultant structure is isoelectronic with the π-system of xanthine. There are thirty-six such 14 π-electron structures; nine in which the five-membered ring contains two heteroatoms, eighteen in which the five-membered ring contains three heteroatoms, and nine in which the five-membered ring contains four heteroatoms.

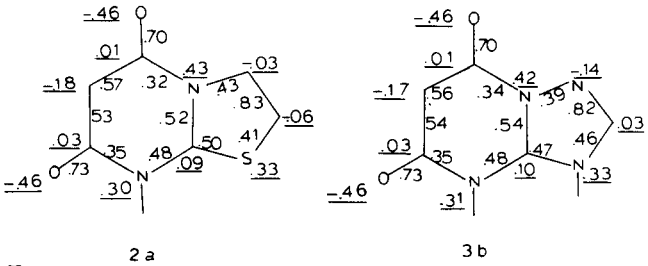


4



5

Quantum chemical studies have been completed on those xanthine analogs containing two heteroatoms in the five-membered ring, **2a-i**, and on several representative analogs containing three heteroatoms in the five-membered ring, **3a-c**, **4**. Comparisons of the results of this treatment with similar studies of Class I mesoionic purinone analogs and xanthine, itself, reveal several common features and a number of distinguishing characteristics.



2a 3b

Figure 1. Bond orders and charge densities (underlined) for mesoionic analogs **2a** and **3b**.

Bond order and charge density distributions which are representative of these xanthine analogs are given in Figure 1. Table I contains the calculated energy terms for these analogs as well as the absolute sum of the net charge densities ($\Sigma[Q]$) and the π-electron component of the dipole moment (μ_π). These latter two indices assist in the comparison of charge separation and polar character among the analogs and covalent isomers.

Analogs with Two Heteroatoms in the Five-Membered Ring (**2a-i**).

In general, the energies of the highest occupied molecular orbital (E_{HOMO}) are slightly higher than those of the Class I mesoionic purinones. In both series these values are considerably higher than the -9.58 eV E_{HOMO} of xanthine, indicating an increased ability of the mesoionic xanthines to function as electron donors. The stabilization of the lowest empty molecular orbitals also indicates an enhanced ability for these analogs to function as electron acceptors. The considerable decrease in energy separation between HOMO and LEMO orbitals appears to be one of the more significant features common to both classes of mesoionic xanthine analogs in distinguishing them from their covalent isomers.

The binding energies of these analogs are comparable to those of the Class I xanthines and the covalent isomers. Examples of analog **2a**, which has a lower value for this term, have been recently synthesized and the stability and classical aromatic properties of these compounds suggest that most of the other analogs can be expected to display comparable or greater stability, at least in a thermal sense (8).

It was of interest to examine the differences that may be expected within this series of xanthine analogs depending upon the position, in the five-membered ring, of the heteroatom which donates two electrons to the π-system. When this heteroatom is in the purine 9-position (**2a-c**), the C_7-C_8 bond order is very high, indicating a high degree of double bond character relative to that of the comparable bond in 2-acylaminothiazoles. The pmr vicinal coupling constant may be used as an indication of double-bond character (9). The H_7-H_8 proton coupling constant for **2a** (R = C_2H_5) in deuteriochloroform is found

TABLE I

π-SCF Energies and Charge Separation of Xanthine Analogs (a)

Structure	E_{Total}	E_{Bind}	E_{HOMO}	ΔE (b)	$\Sigma[Q]$	μ_π
2a	723.04	200.26	6.99	5.27	2.36	13.7
2b	751.66	208.69	7.03	5.65	2.35	13.4
2c	766.18	225.27	7.21	5.02	2.24	12.1
2d	720.46	199.58	7.00	4.55	2.53	13.9
2e	749.63	208.55	7.08	5.13	2.53	13.1
2f	764.39	224.27	6.82	3.03	2.21	12.9
2g	721.39	199.75	7.08	4.46	2.41	12.2
2h	751.28	206.22	7.15	4.80	2.43	12.0
2i	766.28	223.11	7.26	4.20	2.29	11.4
3a	726.71	202.64	7.00	5.20	2.46	13.9
3b	754.15	211.71	7.07	5.26	2.46	13.4
3c	770.31	227.64	7.25	5.00	2.44	12.5
4	726.12	203.34	7.15	4.85	2.57	12.7
5	746.75	216.56	6.96	4.97	2.48	16.6
Xanthine	753.48	221.20	9.58	8.26	2.41	3.7

(a) All energy terms are negative and in units of eV. (b) $E_{HOMO} - E_{LEMO}$.

to be 4.4 Hz while the corresponding coupling constant in 2-acetamidothiazole is 3.6 Hz, indicating higher C_7-C_8 double-bond character in the mesoionic analog than at the comparable positions in a 2-acetamidothiazole model.

Frontier charge densities, electrophilic superdelocalizability indices and localization energies predict the 1-position to be the most susceptible to electrophilic attack for all of the Class II xanthine analogs. Examples of such reactions on derivatives of **2a** support these predictions (8). Nucleophilic localization energies indicate that the two pseudocarbonyl groups should be most susceptible to nucleophilic attack. Nearly identical values for positions 2 and 6 (41.94 and 42.43 eV, respectively) were found for **2a**. Derivatives of **2a** have been found to undergo nucleophilic attack by amines at the 6-position (8).

When the two π-electron contributing heteroatom is in the 7-position (**2g-i**), the C_8-C_9 bond order is very high. With this heteroatom in the 8-position (**2d-f**), the average C_9-C_4 bond order is high (0.69) but not as high as the C_7-C_8 (0.86) or C_8-C_9 (0.80) bond orders of the two previously mentioned isomers. As the position of the heteroatom donating two π-electrons is varied, the change in bond order-charge distribution in the six-membered ring is negligible.

Although it is found that the pseudocarbonyl charge densities and bond orders of the Class I xanthine analogs were similar to the covalent model compounds, the analogs of this series have a lower average pseudocarbonyl bond order, 0.69 for C_2-O and 0.74 for C_6-O (0.78 and 0.81, respectively for xanthine), and a higher average electron density on oxygen, -0.44 for O_2 and -0.47 for O_6 (-0.37 and -0.42, respectively for xanthine). These predictions are supported by a study of the infrared spectra of several derivatives of **2a** (8). The true integrated absorption intensity of the carbonyl band can be used as a measurement of the polarity of the carbonyl group. The integrated absorption intensities of the carbonyl bands of these compounds fall within the range determined for sydnones which is very much higher than values observed for ketones, amides, or esters. On the other hand, the carbonyl band frequencies, 1690-1680 cm^{-1} and 1655-1630 cm^{-1}, suggest carbonyl bond orders similar or only slightly lower than those of covalent models.

Analogs with Three Heteroatoms in the Five-Membered Ring (**3a-c**, **4**).

In **2a**, replacement of C_7 by nitrogen (**3a**) has little

effect on the charge distribution or bond orders in the six-membered ring. Comparing the N_7 charge densities of **3a-c** with that of xanthine, it is found that the mesoionic purinones are more electron rich (-0.14 *vs* -0.125) at this position. Again the N_7-C_8 bond order indicates considerable double-bond character (av. .84) and the same positions are predicted for electrophilic (1-position) and nucleophilic attack (2- and 6-position).

If the nitrogen is moved to the 8-position (**4**) the change in the energy terms, charge distribution, (with the exception of the atoms being exchanged), and bond orders are negligible. Comparing **3b** with its Class I counterpart **5** and xanthine, it can be seen that the values of E_{HOMO} and E_{LEMO} are very similar to those of **5** and 2.51 eV higher and 0.49 eV lower, respectively, than those of xanthine. Although a low value of ΔE might indicate a possible tendency toward instability toward light or atmospheric oxygen, examples of **3a**, which have comparable or lower ΔE values, have been synthesized and found to be stable to these conditions (8).

TABLE II

Frontier Orbital Indices Related to Cycloaddition Reactions

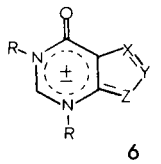
Frontier Orbital Eigenvectors

Structure	Position (a)	HOMO a	HOMO b	LEMO a	LEMO b
1		-.55	.13	-.42	-.75
10		.56	-.08	-.29	-.29
2a		-.57	.07	-.30	-.67
2d		.02	-.04	-.03	-.08
2g		-.56	.08	.32	.47

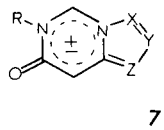
(a) Position a refers to positions: 5 in **1**, 3 in **10**, and 1 in **2a-g**. Position b refers to positons: 2 in **1**, 9a in **10**, 4 in **2a-g**.

A number of derivatives of monocyclic mesoionic pyrimidinones **1** as well as pyridine ring-fused derivatives of this structure (*i.e. anhydro* 2-hydroxy-1-methyl-4-oxopyrido[1,2-*a*]pyrimidinium hydroxide, **10**) have been reported by Potts and others to undergo 1,4-cycloaddition reactions (3). These additions are often followed by the loss of alkyl or aryl isocyanate to give α-pyridone derivatives. As a first approximation, examination of the frontier orbitals involved in the cycloaddition reaction has been shown by Fukui to be informative (9). The HOMO and LEMO orbitals of the mesoionic compounds can be seen to possess the required symmetry for overlap with the dipolarophile (Table II). Comparison of the eigenvectors of the orbitals at the reaction centers of the structures in Table II suggests that the cycloaddition reaction may be general for the entire series with the possible exception of structures **2d-f** in which the two electron contributing heteroatom is in the purine 8-position.

Reactions between derivatives of **2a** and acetylene dicarboxylic acid esters which are presumed to proceed *via* an initial 1,4-cycloaddition have been recently observed (8).



6



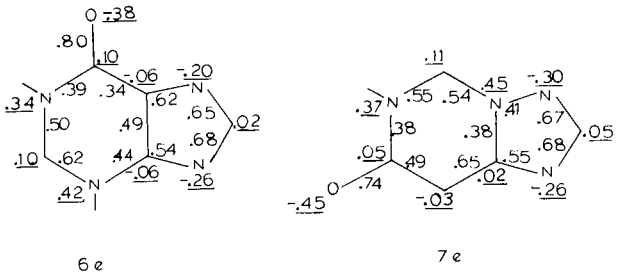
7

System	X	Y	Z
a	CH	CH	N
b	CH	N	CH
c	N	CH	CH
d	CH	N	N
e	N	CH	N
f	N	N	CH
g	N	N	N

Hypoxanthine Analogs.

Mesoionic hypoxanthine analogs may be formulated by the ring fusion of a five-membered ring to the exocyclic nitrogen of an imino derivative of **1** and the adjacent electron-rich carbon position (11). Positional isomerism of the imino nitrogen in the five-membered ring results in seven possible analogs, which are isoconjugate with hypoxanthine. These analogs are represented by the general structure **6**, where X, Y, and Z are varied between CH and divalent N. Reports of the synthesis of derivatives of **6e** and its conjugate acid have appeared (12,13).

Bond order and charge density distributions which are representative of the mesoionic hypoxanthine analogs are given in Figure 2. Table III contains the calculated energy terms and charge separation indices for these analogs.



6e **7e**

Figure 2. Bond orders and charge densities (underlined) for mesoionic analogs **6e** and **7e**.

TABLE III

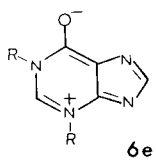
π-SCF Energies and Charge Separation of Hypoxanthine Analogs (a)

Structure	E_{Total}	E_{Bind}	E_{HOMO}	ΔE (b)	$\Sigma[Q]$	μ_π
Hypoxanthine	572.89	169.51	8.92	7.89	1.85	5.4
6a	574.55	169.88	8.81	6.19	1.89	9.4
6b	574.59	169.87	8.85	6.22	1.89	10.1
6c	574.67	172.70	8.79	6.22	1.88	10.0
6d	577.84	172.89	9.00	6.25	1.92	10.0
6e	577.99	172.53	8.92	6.21	1.95	10.0
6f	577.98	172.79	8.96	6.22	1.92	10.7
6g	581.57	175.66	9.11	6.22	1.95	10.7
8	578.91	172.37	7.63	5.91	1.97	11.1

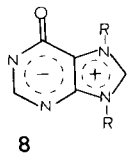
(a) All energy terms are negative and in units of eV. (b) $E_{HOMO} - E_{LEMO}$.

For all Class II hypoxanthine analogs, nucleophilic superdelocalizability and frontier orbital density indices predict nucleophilic attack to occur at C_2 (the position between the two most electron deficient centers). While localization energy calculations favor attack of the pseudocarbonyl carbon, several reports indicate derivatives of **6e** undergo attack by hydride and hydroxide ion at C_2 (13). Electrophilic localization energies indicate preferential electrophilic attack at C_7 in **6a** and **6d**, C_8 in **6e**, and at C_9 in **6b**, **6c**, and **6f**.

Comparisons between **6e** and its covalent isomer, hypoxanthine, indicate very similar calculated charge densities on the exocyclic oxygen atom (-0.384 **6e**, -0.391 hypoxanthine) and pseudocarbonyl bond orders (0.789 **6e**, 0.794 hypoxanthine), a similarity also noted in the Class I hypoxanthine analogs. Within the Class II hypoxanthine analogs, the average oxygen charge density is -0.383 and the average pseudocarbonyl bond order is 0.799. Such observations strongly support the feeling that the molecular properties of these mesoionic analogs are not adequately reflected by their valence bond representations typified in **6e**.



6e



8

The E_{HOMO} of **6e** is nearly identical to that of hypoxanthine and considerably lower than its Class I counterpart **8** (Table III). The E_{LEMO} calculated for **6e** is lower, relative to those of hypoxanthine and **8**, by 1.7 eV and 1.0 eV, respectively, indicating that **6e** possesses the greatest electron affinity. The average LEMO energy level for this series is -2.703 eV. The very slight increase in the $\Sigma[Q]$ term suggests little difference in the degree of charge spearation between hypoxanthine and many of these analogs in both classes.

Comparing this series with hypoxanthine, a very significant shift of electron density into the five-membered ring (0.6 *e*) of the mesoionic analogs is noted. In direct contrast, in Class I hypoxanthine analogs the five-membered ring is strongly electron deficient (0.6 *e*, on the average) in comparison to most of their covalent analogs. This is one of the more significant differences between Class I and Class II hypoxanthine analogs.

All the Class II hypoxanthine analogs show slightly higher calculated total energies and binding energies than hypoxanthine. Comparisons of dipole moments, however, show these mesoionic analogs to have nearly twice the dipole moment of hypoxanthine. The Class I hypoxanthine analog **8**, shows very similar total energy, binding energy, and dipole moment when compared to its Class II counterpart **6e**.

Purin-2-one Analogs.

The formulation of the Class II purin-2-ones, represented by the general structure **7** may be viewed as the ring fusion of an electron rich five-membered ring heterocycle between the imino function and the electron deficient nitrogen atom of a hypothetical mesoionic 1-substituted-4-iminopyrimidin-6-one. As in the hypoxanthine analogs, seven possible structures exist (**7a-g**) possessing 12 π-electrons.

In all cases nucleophilic attack, as determined by superdelocalizability and frontier orbital indices, is pre-

TABLE IV

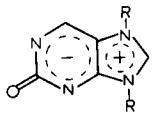
π-SCF Energies and Charge Separation of Purin-2-one Analogs (a)

Structure	E_{Total}	E_{Bind}	E_{HOMO}	ΔE (b)	$\Sigma[Q]$	μ_π
Purin-2-one	579.73	174.41	8.98	6.96	1.84	6.7
7a	579.34	165.05	7.84	4.81	1.86	6.9
7b	582.12	168.11	7.94	4.71	1.88	6.9
7c	579.87	164.38	7.89	4.90	1.90	5.6
7d	582.92	167.90	7.94	4.74	1.88	6.8
7e	582.93	167.32	8.10	5.02	2.07	6.3
7f	583.12	167.45	7.97	4.79	1.91	5.6
7g	586.60	170.48	8.21	4.96	2.0	6.2
9	575.25	173.82	7.28	5.11	1.83	4.4

(a) All energy terms are negative and in units of eV. (b) $E_{HOMO} - E_{LEMO}$.

dicted to occur at C_6 (position adjacent to the most electron deficient centers N_5 and N_1). Again, localization energy calculations favor attack of the pseudocarbonyl group. Electrophilic attack is predicted to occur at C_3 in all cases except **7b** and **7f** which favor attack at C_9.

Comparison of this series with purin-2-one shows only a slight shift of electron density into the five-membered ring (0.05-0.12 *e*) of the mesoionic analogs, whereas the Class I purin-2-one analogs show a significant shift of electron density out of the five-membered ring (0.56 *e*). Six of the analogs of this series have greater calculated total energies than purin-2-one, but have lower binding energies. In contrast to the comparison of hypoxanthine with the Class II hypoxanthine analogs, comparisons of the dipole moments of purin-2-one with those of its mesoionic analogs show striking similarities.



9

The Class II purin-2-ones shows very similar pseudocarbonyl charge densities and bond orders when compared with purin-2-one as did the Class II hypoxanthine and Class I purin-2-one analogs when compared to their covalent analogs. The E_{HOMO} of **7e** is slightly higher than purin-2-one and slightly lower than its Class I counterpart **9** (Table IV). The E_{LEMO} for **7e** is lower than both purin-2-one and **9**, an observation noted when similar comparisons were made in the hypoxanthine series. Very similar $\Sigma[Q]$ terms are noted between the Class I and Class II purin-2-one analogs and purin-2-one itself. The Class II purin-2-ones analogs show greater calculated total energies when compared to the Class II hypoxanthine analogs, yet show lower binding energies. Although similar charge separation terms are noted between these purin-2-one and hypoxanthine analogs, greatly different calculated dipole moments exist between the two series.

Conclusions.

Although this study of mesoionic purinone analogs has been systematic, it is not exhaustive. Many other analogs of potential interest are possible, such as the 1-aza derivatives of the Class II xanthine analogs (14). Thus, the number of such analogs is well over one hundred. The lack of knowledge concerning such a large class of structures, despite their close relationship to the important purinones, must rest with the peculiarities of their valence bond representations.

These studies have led to the predictions of reasonable stabilities for most of these analogs by comparison to known covalent structures. Although most of these analogs may be expected to be more polar than their covalent isomers the differences in many cases can be expected to be slight. These differences may be entirely obscured by the fact that the mesoionic analogs lack structural features (*i.e.* N-H or O-H groups) which give rise to physical properties commonly associated with highly polar compounds, such as high melting point and low lipid solubility. One of the most polar groups of analogs are the Class II xanthine analogs. Examination of the physical and molecular properties of derivatives of structures in this group is informative in establishing limits to these anticipated properties for the entire class (8).

Within the molecular orbital approach no fundamental difference exists between covalent and mesoionic structures. This difference is a product of a valence bond

framework of molecular notation. If faced with the problem of distinguishing covalent structures from mesoionic structures on the basis of the molecular orbital description of these systems, neither the polarity as evidenced by $\Sigma[Q]$ or dipole moment, nor the nature of the pseudocarbonyl groups is as good a criterion as the energy difference between highest occuppied and lowest empty molecular orbitals. This energy difference is significantly lower in all mesoionic structures.

The results of these studies which may have the greatest significance with respect to any anticipated biochemical properties of these analogs are the similarities in ground state properties of the analogs and the purinones, themselves. In addition, the general increase in electron affinity may be of importance since the purinones function as electron acceptors in nucleic acid base interactions.

EXPERIMENTAL

The semi-empirical self-consistent field π-molecular orbital calculations were performed using QCPE program 167 which was modified to include the variable electronegativity procedure and a Givens method of obtaining eigenvalues and eigenvectors. The parameterization followed that of Sundaram and Purcell (6). The two-center repulsion integrals were calculated using the method of Mataga-Nishimoto (15). Only the 3*p* orbital of sulfur was included by use of the quadratic function developed by Bossa (16) in relating the valence state ionization potential to the effective nuclear charge. The one-center repulsion integral for sulfur ($tr^2trtr\pi^2$) was given by $\delta_{ss} = 2.222Zs$, where Zs is the Slater effective nuclear charge of sulfur.

The core resonance integrals were evaluated by $B_{ij}^{SCF} = 1/2\ S_{ij}\ (Ii + Ij)$ where S_{ij} is the overlap integral between atoms i and j and I is the ionization potential. Penetration integrals and non-neighboring atom resonance integrals were neglected. The geometries employed were obtained through the use of the previously described $\omega\beta\omega a$ Hückel treatment (1), in which purinones of known geometry were used to construct bond order *vs.* bond length relationships for each bond type.

Acknowledgement.

The authors are grateful to the SUNY/Buffalo Computing Center for their donation of computing services. This work was partially supported by Public Health Service Training Grant 5-T01-GM00555 from the Division of Medical Sciences, Bethesda, Maryland.

REFERENCES

(1) R. A. Coburn, *J. Heterocyclic Chem.*, **8**, 881 (1971).

(2) M. Prystas, *Collect. Czech. Chem. Commun.*, **32**, 4241 (1967).

(3) K. T. Potts and M. Sorm, *J. Org. Chem.*, **36**, 8 (1967); **37**, 1422 (1971); T. Kappe and W. Lube, *Monatsch. Chem.*, **103**, 781 (1971); T. Maki, M. Sato, and M. Suzuki, *Chem. Commun.*, 999 (1972).

(4) R. G. Parr, "Quantum Theory of Molecular Electronic Structure," Benjamin, Inc., New York, 1963.

(5) R. D. Brown and M. L. Heffernan, *Trans. Faraday Soc.*, **54**, 757 (1958).

(6) K. Sundaram and W. P. Purcell, *Int. J. Quantum Chem.*, **2**, 145 (1968).

(7) J. E. Bloor, B. R. Gilson, and F. P. Billingsley, *Theoret. Chim. Acta*, **12**, 360 (1968).

(8) R. A. Coburn and R. A. Glennon, *J. Heterocyclic Chem.*, **10**, 487 (1973).

(9) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd Edition, New York, 1969, Chapter 4; V. F. Bystrov, *Russian Chem. Rev.*, English Translation, **41**, 281 (1972).

(10) K. Fukui, *Accts. of Chem. Res.*, **4**, 57 (1971).

(11) Simple imino derivatives of the six-membered ring mesoionic system represented by **1** have not yet been reported.

(12) L. B. Townsend and R. K. Robins, *J. Am. Chem. Soc.*, **84**, 3008 (1962).

(13) J. A. Montgomery, K. Hewson, S. J. Clayton, and H. J. Thomas, *ibid.*, **31**, 2202 (1966); Z. Neiman, *J. Chem. Soc.* (C), 91, 1970.

(14) A report is in preparation describing the synthesis and properties of a number of 1-aza derivatives of the Class II xanthine analogs.

(15) N. Mataga and K. Nishimoto, *Z. Phys. Chem.*, **13**, 140 (1957).

(16) M. Bossa, *J. Chem. Soc.* (B), 1182 (1969).