

# Theoretical Calculation of the Structure and Electronic Properties of Dihydrothymines and Dihydrouracils

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Extended Hückel type molecular orbital calculations were performed on a series of substituted 5,6-dihydropyrimidinediones. Substituents included the methyl, the hydroxy and the halogen groups. In most cases studied satisfactory agreement was obtained between the experimentally found and theoretically calculated conformational preferences for the various substituents.

The dipole moments of all the molecules were calculated and a qualitative relationship was found between the dipole moment component along the C—H bond and the chemical shift of the associated proton.

Es wurden Rechnungen nach dem erweiterten Hückelverfahren für Methyl-, Hydroxy- oder Halogen-substituierte 5,6-Dihydropyrimidindione mit meist befriedigenden Resultaten durchgeführt. Des weiteren ergab sich eine qualitative Beziehung zwischen der Komponente des Dipolmomentes entlang der CH-Bindung und der chemischen Verschiebung des entsprechenden Protons.

Les dérivés substitués en position 5 et 6 des 5,6-dihydropyrimidinediones ont été calculés par la méthode de Hückel étendue. Les substituents étudiés, comportent de méthyl, l'hydroxy et les halogènes. Le calcul rend bien compte des conformations préférentielle. Trouvées expérimentalement pour les différents molécules. Les moment dipolaires ont été calculés et on a trouvé une relation qualitative entre la composante du moment dipolaire le long des liaison C—H et le déplacement chimique du proton considéré.

## Introduction

Recently the study on the structure and electronic properties of uracil and thymine photodimers was performed using a molecular orbital approach for the determination of the preferred conformation in these molecules [1]. In order to establish if the saturated pyrimidine rings of these dimers exist in a planar or nonplanar conformation, the preferred conformations of 5,6-dihydrouracil (*DHU*) and 5,6-dihydrothymine (*DHT*) were also calculated.

These latter two molecules and their substituted derivatives are also of photobiological interest since one of the possible reaction paths in the photolysis of uracils and thymines leads to saturation of the C<sub>5</sub>—C<sub>6</sub> bond, for example by the addition of water across it [2]. These molecules are also of interest from a stereochemical view since the amount of puckering of the rings seems to be intermediate between that of cyclohexane and cyclohexene.

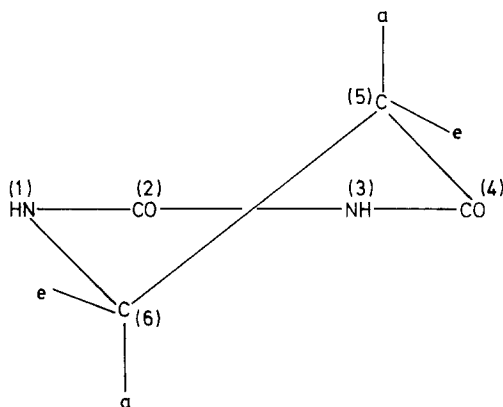
Some very interesting experimental data on the relative stability of the various conformers allows comparison of experimental and theoretical findings [3].

## Choice of Geometrical and Molecular Orbital Parameters

The experimental (*X*-ray) geometry has only recently become available for dihydrothymine [4]. It was shown that the molecule exists in the half-chair

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form. In the previous calculations [1] an assumption had to be made concerning the bond lengths and bond angles in the molecule. Since this assumed geometry differs from the experimental one primarily in the amount of puckering of the ring it is instructive to compare conformational differences employing both geometries. Experimentally the C<sub>5</sub> and C<sub>6</sub> atoms were found to be out of the plane of the other four coplanar ring atoms (see Fig. 1) by +0.42 Å and -0.31 Å whereas the corresponding values in the assumed geometry were +0.31 Å and -0.28 Å respectively. The details of the comparison of the two geometries were given in the previous work [1].



Unit vectors	$\hat{i}$	$\hat{j}$	$\hat{k}$
Assumed geometry			
C <sub>5</sub> axial	0.1170	0.9912	0.0612
C <sub>5</sub> equatorial	-0.0254	-0.3901	0.9204
C <sub>6</sub> axial	0.0258	-0.9897	0.1407
C <sub>6</sub> equatorial	0.8432	0.4085	0.3496
Experimental geometry			
C <sub>5</sub> axial	0.0041	0.9872	-0.1596
C <sub>5</sub> equatorial	0.7983	-0.2527	0.5467
C <sub>6</sub> axial	0.0509	-0.9848	0.1660
C <sub>6</sub> equatorial	0.7949	0.2896	-0.5332

5e, 5a, 6e, 6a = H dihydrouracil (DHU)  
 5e-Me or 5a-Me dihydrothymine (DHT)

Fig. 1. Dihydropyrimidinedione substituents and unit vectors

The bond lengths for the substituents were taken as follow: the C-H bond uniformly at 1.1 Å in the assumed and 1.0 Å in the experimental molecules; C-C bond distances of 1.54 Å in all cases; C-O equal to 1.42 Å, O-H at 0.97 Å, C-Br at 1.93 Å, C-Cl at 1.767 Å and C-F at 1.397 Å [5]. Substituents on the saturated carbon atoms were placed uniformly at tetrahedral angles in the plane perpendicularly bisecting the X-C-X angles. C-O-H angles of 105° were assumed. Substituted molecules were calculated only in the half chair forms shown to be preferred by DHT both experimentally and by the previous calculations.

The extended Hückel theory was chosen for the calculations because of its simplicity and relative ease of applicability to a large series of molecules [6]. This theory does not predict correct strain energies in the series of cycloalkanes (for a possible amelioration of the parameters for cyclic molecules see Ref. [7]). It does predict the correct relative energies of the cyclohexane and methyl cyclohexane conformers [6]. Since the same ring geometries are employed for all the different substituted molecules the internal ring strain remains constant for any one series with the same ring geometry. Differences in the energies of the conformers should be due to the effects of the substituents only.

The H, C, N and O parameters were described before along with the method [8]. Table 1 presents these parameters along with those for the halogens. The valence state ionization potentials for F and Cl were taken from Hinze and Jaffe [9]. The Br 4*p* parameter originates from Hinze also<sup>1</sup> and the 4*s* was obtained by a linear extrapolation assuming that a plot of *s* vs. *p* valence state ionization potentials is linear for the series F, Cl and Br. The parameters of the halogens other than F are in great doubt as the conformational and other electronic results will show. As a matter of fact the above values had to be changed in order to go along with experimental results. In particular the Slater orbital exponents had to be adjusted for Br to 1.70 and for Cl to 1.85. Qualitatively this amounts to a change in the overlap integrals between the halogens and the other atoms, the lowering of the Slater exponent increasing the "sphere of influence" of the atom. No full parametrization study was performed, but this was the parameter which had to be changed in order to be compatible with the other parameters utilized. Changes in the valence state ionization potentials appeared to have no measurable effect on conformational differences, whereas shifting the Slater exponent in some case reversed the axial or equatorial preference. Since a single *K* was used in the Wolfsberg-Helmholtz formula (footnote on Table 1) this more than likely could be the source of the problems with the halogens. Using a different *K* for each situation would make the method much more cumbersome.

Table 1. *Extended Hückel theory parameters*

Atom	Slater exponent	$\alpha 2s^a$ (eV)	$\alpha 2p^a$ (eV)
H	1.0	-13.60 (1s)	
C	1.625	-21.40	-11.40
N	1.950	-26.00	-13.40
O	2.275	-35.30	-17.76
F	2.600	-38.24	-20.86
Cl	2.033 <sup>b</sup>	-24.02 (3s)	-15.03 (3p)
Br	1.900 <sup>b</sup>	-19.20 (4s)	-13.10 (4p)

<sup>a</sup> Negative values of the valence state ionization potentials used to approximate the diagonal coulombic integrals of the type  $H_{ii} = \int \Phi_i H \Phi_i d\tau$  as suggested by Ref. [6]. The off-diagonal elements were calculated by the Wolfsberg-Helmholtz formula [J. chem. Physics **20**, 837 (1952)]

$$H_{ij} = 0.5 K S_{ij}(H_{ii} + H_{jj})$$

with  $K = 1.75$ .

<sup>b</sup> Unless otherwise indicated in which case the value of 1.85 for Cl and 1.70 for Br are employed.

<sup>1</sup> Private communication of Dr. J. Hinze to Madame A. Pullman.

### Conformational Energies

Fig. 1 shows the conformational assignment of the substituents in the dihydrouracil ring with the  $C_5$  and the  $C_6$  atoms out of the  $xz$  plane. The unit vectors are given for the various positions to show that the axial and equatorial directions are almost pure that is to say resembling those in cyclohexane more than the "quasi axial" and "quasi equatorial" directions associated with cyclohexene. In spite of this relationship comparison will not be made with hydrocarbons, but only with the dihydropyrimidinedione results obtained by *nmr* and infrared spectroscopy [3].

Table 2 gives the results of the energy calculations with the experimentally preferred position of the substituent indicated. The results of the calculations must be examined in the light of the following facts. No absolute minimization of the ring geometry was attempted for any of the molecules except for *DHU* and *DHT*, the results of which were reported before [1]. Since it was shown that the *DHU* and *DHT* molecules minimize at similar internal bond angles, all substituted molecules were assumed with this same set of geometrical conditions along with the experimental geometry that is to say the one found for *DHT*. There is, of course, a strong likelihood that the ring geometries do differ in the various cases, but on the basis of the results it can be assumed that the real values are not too different from at least one of the puckering angles employed. Indeed, the agreement is quite satisfactory for all cases in which the hydroxyl or the methyl groups are involved. One notable exception is *trans*-5,6-dihydroxy *DHU*. For this molecule *nmr* results indicated a diaxial structure [3] whereas the calculations consistently preferred the diequatorial form by a considerable (6 kcal/mole) energy difference. Due to the approximations involved and the lack of exact knowledge of the geometrical minima the energy differences between the conformers cannot be interpreted as the free energy differences between the two forms (implying an equilibrium constant). Qualitatively, however, the agreement between experiment and theory is again comforting. The experimental percentages of the conformers (as obtained in Ref. [10] from the infrared shifts of the hydroxyl peaks) are followed in a reasonable fashion by the differences in the total orbital energies of the conformers.

The halogen substituted forms present another problem. Table 2 gives the results on the halogens employing the revised Slater exponents of 1.70 for Br and 1.85 for Cl. With these parameters the agreement is reasonably good with a few exceptions. For instance 5-Br *DHU* prefers an axial bromine with the assumed geometry and an equatorial one with the experimental one. This could be due to the difference in puckering between the two forms, although the percentages of the conformers are very similar. The same factor of puckering could be playing a role in *trans*-5-bromo-6-hydroxy *DHU*. Experimentally the diaxial form seems to be the predominant one, a result confirmed by the assumed geometry with the experimental one giving equal stabilities to both forms. 5,5-Dibromo-6-hydroxy *DHU* is one of the few cases with absolute disagreement. Experimentally the hydroxy group seems to prefer the axial position whereas all the calculations prefer the equatorial position for this group (independent of the choice of bromine parameters).

Table 2. Energy of conformations and dipole moments of substituted dihydropyrimidinediones<sup>a</sup>

Molecule	Total orbital energy		% <sup>b</sup>	$\mu^c$ (D)	$\mu_{red}^d$ (D)	$\alpha^e$ (°)	$\beta^e$ (°)
	Assumed geometry	Experimental geometry (Kcal/mole)					
<i>DHU</i>	-20231.88	-20238.63		11.25	3.60	23.9	0.3
5-Methyl <i>DHU</i> ( <i>DHT</i> )							
Axial CH <sub>3</sub>	-22635.30	-22643.24		11.26	3.61	24.3	1.3
Equatorial CH <sub>3</sub> <sup>f</sup>	-22635.55	-22644.37		11.27	3.61	23.8	0.2
6-Methyl <i>DHU</i>							
Axial CH <sub>3</sub>	-22640.10	-22647.57		11.25	3.60	23.9	0.2
Equatorial CH <sub>3</sub> <sup>f</sup>	-22640.66	-22648.30		11.25	3.60	24.0	0.3
5-Hydroxy <i>DHU</i>							
Axial OH	-23639.73	-23647.25	5	10.10	3.24	36.6	-24.6
Equatorial OH <sup>f</sup>	-23644.54	-23650.46	95	12.59	4.03	45.0	8.9
6-Hydroxy <i>DHU</i>							
Axial OH <sup>f</sup>	-23653.60	-23658.63	60	13.00	4.16	39.0	15.1
Equatorial OH	-23652.87	-23657.09	40	6.87	2.18	21.1	14.0
5-Bromo <i>DHU</i>							
Axial Br <sup>f</sup>	-22248.43	-22255.20		11.24	3.60	25.2	-6.2
Equatorial Br	-22247.95	-22255.95		10.59	3.39	31.1	2.4
<i>Trans</i> -5-Bromo-6-hydroxy <i>DHU</i>							
Diaxial <sup>f</sup>	-25670.00	-25674.45		12.60	4.04	38.2	10.2
Diequatorial	-25668.72	-25674.46		6.35	2.04	33.4	18.7
5,5-Dibromo-6-hydroxy <i>DHU</i>							
Axial OH <sup>f</sup>	-27682.92	-27687.99	60	12.34	3.96	45.3	12.3
Equatorial OH	-27688.04	-27691.99	40	5.59	1.79	29.9	11.9
5-Bromo <i>DHT</i>							
Axial Br <sup>f</sup>	-24651.99	-24659.65		11.27	3.61	22.9	-6.4
Equatorial Br	-24650.99	-24658.87		10.59	3.39	31.7	3.5
<i>Trans</i> -5-Bromo-6-hydroxy <i>DHT</i>							
Diaxial (Br, OH) <sup>f</sup>	-28071.42	-28077.98		12.60	4.04	38.2	9.9
Diequatorial (Br, OH)	-28069.56	-28076.94		6.29	2.02	34.0	22.8
<i>Trans</i> -5-Chloro-6-hydroxy <i>DHT</i>							
Diaxial (Cl, OH) <sup>f</sup>		-28522.84		12.13	3.90	37.8	3.9
Diequatorial (Cl, OH)		-28522.58		6.12	1.96	44.3	26.1
<i>Cis</i> -5,6-Dihydroxy <i>DHU</i>							
5-Equatorial-6-axial <sup>f</sup>	-27064.53	-27069.37		15.61	5.00	55.7	19.8
6-Equatorial-5-axial	-27058.16	-27063.58		5.27	1.69	46.0	-29.3
<i>Trans</i> -5,6-dihydroxy <i>DHU</i>							
Diaxial <sup>f</sup>	-27057.52	-27062.28		11.03	3.53	52.2	-4.4
Diequatorial	-27064.66	-27068.48		9.33	2.99	53.5	22.3
<i>Cis</i> -6-hydroxy <i>DHT</i>							
Axial OH <sup>f</sup>	-26055.12	-26063.28		13.01	4.17	38.9	15.0
Equatorial OH	-26054.10	-26061.15		6.83	2.19	21.0	17.4
<i>Trans</i> -6-hydroxy <i>DHT</i>							
Diaxial	-26056.61	-26062.42		13.10	4.20	39.4	16.3
Diequatorial	-26055.66	-26062.05		6.92	2.22	21.3	13.6
<i>Cis</i> -5,6-Dihydroxy <i>DHT</i>							
5-Equatorial, 6-axial OH <sup>f</sup>	-29473.78	-29478.19	70	15.77	5.05	55.6	20.7
5-Axial, 6-equatorial OH	-29466.99	-29472.72	10	5.28	1.69	44.5	-28.3
5-Hydroxy <i>DHT</i>							
Axial OH		-26057.27	40	10.11	3.24	36.2	-24.1
Equatorial OH		-26059.79	60	12.71	4.07	45.0	9.8

<sup>a</sup> Starred conformations preferred experimentally (Ref. [3]).<sup>b</sup> Experimental percentages on the basis of infrared studies (Ref. [10]).<sup>c</sup> Computed from net atomic populations for molecules with experimental *DHT* type geometry.<sup>d</sup> Computed by using the reducing ratio of experimental dipole moment of 1,3-dimethyl-dihydrothymine to theoretical dipole moment of dihydrothymine.<sup>e</sup> Anlges defined in Fig. 2.<sup>f</sup> Preferred experimentally where such data is available.

The lowering of the Slater exponents for Br and Cl perhaps is not unjustifiable since Slater's rules of screening constants may be expected to hold less rigorously for third and fourth row elements in the periodic chart. The choice of valence state ionization potentials is also rather arbitrary for these elements. The parameters of Table 1 were, however, successfully applied in a calculation of preferred orientation of F and Cl in phosphorusfluorochlorides [11] by the extended Hückel theory. This latter study used a charge iterative version of the scheme. Such an iteration on the charges with a change in the Slater exponents along with changes in the diagonal matrix elements perhaps would improve the results with the halogen substituents. This approach will be tried on some of these molecules, but of course is much less feasible for such a large series.

Table 3. *Effect of halogen on conformational energy differences*

Molecule	Energy differences (Kcal/mole)		
	Halogen		
	F	Cl	Br
5-Halo <i>DHU</i> , Equatorial-Axial <sup>a</sup>	-3.7	-2.3	-0.8
<i>Trans</i> -6-Halo-6-hydroxy <i>DHU</i>			
Diequatorial-diaxial <sup>a</sup>	-7.8	-2.6	-1.7
5,5-dihalo-6-hydroxy <i>DHU</i>			
Equatorial OH-Axial <sup>a</sup> OH	-0.9	-2.8	-4.7
5-Halo <i>DHT</i>			
Equatorial halo-axial halo <sup>a</sup>	-4.3	-2.1	-0.8
<i>Trans</i> -5-Halo-6-hydroxy <i>DHT</i>			
Diequatorial-diaxial <sup>a</sup>	-6.8	-2.2	-1.3

<sup>a</sup> Preferred experimentally where such data is available.

In spite of the ambiguities inherent in the halogen parameters, it is interesting to compare the series of F, Cl and Br substituted molecules since definite trends may be observed. For this comparison only the parameters of Table 1 are employed with the assumed geometry for the dihydropyrimidinedione skeleton. Table 3 presents some of the conformational energy differences. The order of preference of equatorial over axial positions appears to be fluorine greater than chlorine in turn greater than bromine. The notable exception to any strict ordering is the reversal in the 5,5-dihalo-6-hydroxy molecules in which the axial hydroxy is preferred over the equatorial one experimentally and the calculations prefer the equatorial over the axial with this preference being more pronounced in bromine substitution than chlorine, than fluorine. It should be emphasised that these deductions are only generalities. What can be said though is that the lowering of some Slater exponents is necessary for agreement with experiment in the saturated (and puckered) heterocyclic rings and that indications are that halogen substitution tends to decrease the amount of puckering in the ring towards flatter ring geometries.

### Dipole Moments of Substituted Dihydropyrimidinediones

In the study on the structure of thymine photodimers [1] it was shown that while the dipole moments calculated from the extended Hückel theory net atomic

populations are always exaggerated in magnitude their directions are correct as was also shown by another study [12]. An empirical adjustment of the calculated dipole moment of uracil to the experimental value led to a correction factor which factor when applied to the calculated moments of the thymine dimers gave rather satisfactory agreement with the experimental values [13]. In Table 2 the calculated and reduced (obtained by multiplication of the calculated moment by the ratio of the experimental value for 1,3-dimethyldihydrothymine [13] to the calculated dipole moment of dihydrothymine) dipole moments are presented for the series of the molecules. All the values given in Table 2 pertain to structures calculated with the experimental *DHT* geometry. The angles  $\alpha$  and  $\beta$  are defined in Fig. 2 with the dipole in the chemical convention pointing from positive to

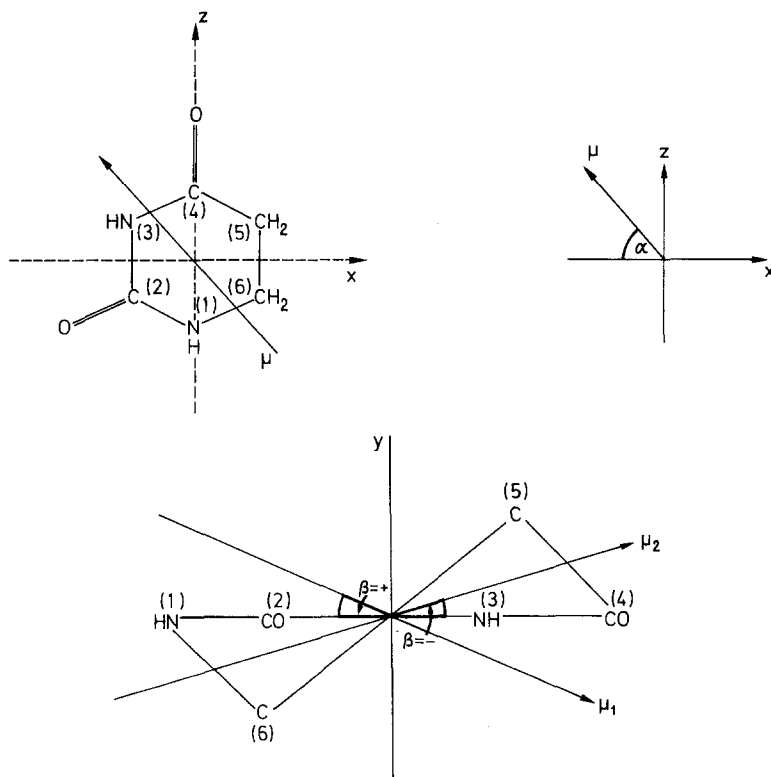


Fig. 2. Dipole moment direction in dihydropyrimidinediones

negative,  $\alpha$  being the angle of the moment in the planar part of the molecule and  $\beta$  the deviation of the direction of the dipole moment from the plane of the four coplanar ring atoms. The dipole moments follow simple intuitive ideas, not presenting any unusual characteristics. The hydroxyl group has the most profound effect on the total moment, in the 5-axial and 6-equatorial positions suppressing it whereas in the 5-equatorial and 6-axial positions augmenting the magnitude of the total dipole moment.

The dipole moments in the hydroxy and methyl substituted molecules are interesting to consider for another reason also, their effects and relationship to the chemical shifts of the protons in the axial and equatorial C–H bonds.

It was proposed by Buckingham [14] that the chemical shift for a proton of a C–H bond in a polar molecule is proportional to the field strength in the molecule and in turn to the dipole moment. Specifically, he stated [14] that “a field along the X–H bond draws the electrons in the enriched region between the nuclei away from the proton, thereby causing resonance to occur at lower magnetic field strengths, while a field in the H–X direction leads to resonance at higher fields”. Because of the approximate nature of the theory employed in calculation

Table 4. Dipole moment characteristics and chemical shifts in dihydropyrimidinediones

Molecule	Proton	Component of $\mu$ along C–H bond	Proton further downfield experimentally
5-Equatorial hydroxy <i>DHU</i>	6 equatorial	0.973	equatorial
	6 axial	–0.232	
6-Axial hydroxy <i>DHU</i>	5 equatorial	0.201	axial
	5 axial	0.358	
5-Equatorial methyl <i>DHU</i> ( <i>DHT</i> )	6 equatorial	0.943	equatorial
	6 axial	–0.024	
6-Equatorial methyl <i>DHU</i>	5 equatorial	0.506	equatorial
	5 axial	0.074	
5-Axial bromo <i>DHU</i>	6 equatorial	0.967	axial
	6 axial	–0.083	

of the dipole moments, no quantitative calculations were affected for this correlation. Qualitatively, however, this simple rule was obeyed in all cases involving hydroxyl or methyl substituents. The halogenated molecules again presented a problem, pointing out again lack of reliable knowledge of the parameters (only Br- and Cl-substituted molecules have been tried).

For physically observable properties which can be related to dipole moments the physical definition of dipole moments is invoked, that is the dipole pointing from negative to positive. In this latter definition the signs of the moments given in Table 2 must be reversed. In Table 4 some values of dipole moment components along the C–H bonds are compared with the chemical shift differences in the various molecules. In cyclohexanones axial protons, in general, absorb at lower fields than equatorial ones [15] in contrast to halocyclohexanes in which equatorial protons have signals at lower fields than do the axial ones [16]. In the case of cyclohexanones a reasoning similar to Buckingham's was chosen to rationalize the results [15] as was also suggested by Nofre *et al.* as a possibility to explain their results in the dihydropyrimidinediones [3]. These latter experimental values indicated that there was a pattern followed in changes in chemical shifts according to the type of neighboring atoms present. For example the relative shift of the 5-axial and 5-equatorial protons is reversed by a substitution of a 6-axial hydroxyl group by a 6-equatorial methyl one (both preferred conformationally as in Table 2). Thus the global dipole moment of the molecule may play a profound effect. From Table 4 it can be seen in a qualitative manner that the C–H bond along which



Table 5. Net atomic charges and atom-atom overlap populations in some dihydropyrimidinediones<sup>a</sup>

Molecule	Atom-atom overlap populations						Net charges						Substituent charges		
	C <sub>4</sub> -C <sub>5</sub>	C <sub>5</sub> -C <sub>6</sub>	N <sub>1</sub> -C <sub>6</sub>	N <sub>1</sub>	C <sub>4</sub>	C <sub>5</sub>	C <sub>6</sub>	C	O	Br					
<i>DHU</i>	0.813	0.700	0.639	-0.48	+1.31	-0.30	+0.01								
Equatorial <i>DHT</i>	0.836	0.727	0.638	-0.48	+1.30	-0.09	+0.00	-0.48							
6-Equatorial methyl <i>DHU</i>	0.811	0.733	0.661	-0.50	+1.31	-0.31	+0.21	-0.50							
5-Equatorial hydroxy <i>DHU</i>	0.823	0.725	0.637	-0.47	+1.29	+0.49	-0.01		-1.21						
5-Axial bromo <i>DHU</i>	0.807	0.729	0.640	-0.48	+1.30	-0.04	+0.00								
<i>Trans</i> -Diaxial-5-bromo-6-hydroxy <i>DHU</i>	0.805	0.761	0.687	-0.51	+1.31	-0.07	+0.75		-1.21					-0.06	
<i>Trans</i> -Diequatorial-5-bromo-6-hydroxy <i>DHU</i>	0.823	0.765	0.670	-0.50	+1.31	-0.06	+0.76		-1.20					-0.09	
5,5-Dibromo-6-axial hydroxy <i>DHU</i>	0.823	0.778	0.685	-0.51	+1.30	+0.19	+0.74		-1.21					-0.05 ax.	
5,5-Dibromo-6-equatorial hydroxy <i>DHU</i>	0.819	0.794	0.670	-0.50	+1.31	+0.19	+0.74		-1.22					-0.10 eq.	
5-Axial bromo <i>DHT</i>	0.832	0.757	0.639	-0.48	+1.29	+0.16	-0.02	-0.50						-0.10 eq.	
<i>Trans</i> -Diaxial-5-bromo-6-hydroxy <i>DHT</i>	0.829	0.788	0.686	-0.51	+1.29	+0.13	+0.73	-0.50	-1.21					-0.07	
6-Axial hydroxy <i>DHU</i>	0.810	0.745	0.688	-0.51	+1.32	-0.32	+0.76	-0.50	-1.21					-0.06	

<sup>a</sup> Using the experimental geometry with the Slater exponent Br = 1.70.

there is a greater component of the dipole moment leads to the chemical shift further downfield. Taking the scalar product of the bond vectors with the dipole moment vector the value which is algebraically larger will thus imply the chemical shift further downfield. Quantitative calculations on well known cases with more precise dipole moment approximations will be undertaken in the future.

### Electronic Indices of Selected Molecules

The charge densities and overlap populations in *DHU* and *DHT* have already been reported [1]. It is of interest to look at the effects of the different substituents in the ring skeleton. Table 5 presents these results for a few molecules. As expected, the major changes occur on the carbon atoms which have been saturated. The rest of the molecule remains almost unchanged, independent of substituents. Furthermore, the substituents have very similar charges and overlap populations

Table 6. Net atomic charges and atom-atom overlap populations in halogenated dihydropyrimidinediones<sup>a</sup>

Molecule	Overlap populations				Net changes				
	C <sub>4</sub> -C <sub>5</sub>	C <sub>5</sub> -C <sub>6</sub>	N <sub>1</sub> -C <sub>6</sub>	C <sub>5</sub> -X <sup>b</sup>	N <sub>1</sub>	C <sub>4</sub>	C <sub>5</sub>	C <sub>6</sub>	X
5-Axial fluoro <i>DHU</i>	0.807	0.768	0.657	0.307	-0.51	+1.32	+0.63	+0.04	-0.73
5-Axial chloro <i>DHU</i>	0.818	0.743	0.658	0.592	-0.52	+1.33	+0.21	+0.05	-0.29
5-Axial bromo <i>DHU</i>	0.835	0.747	0.657	0.564	-0.52	+1.32	+0.06	+0.05	-0.13
5-Equatorial fluoro <i>DHU</i>	0.845	0.736	0.655	0.312	-0.51	+1.30	+0.67	+0.05	-0.73
5-Equatorial chloro <i>DHU</i>	0.846	0.726	0.655	0.600	-0.52	+1.31	+0.24	+0.06	-0.31
5-Equatorial bromo <i>DHU</i>	0.855	0.730	0.654	0.577	-0.52	+1.31	+0.08	+0.06	-0.16

<sup>a</sup> Using "assumed" geometry with parameters of Table 1.

<sup>b</sup> Carbon-halogen bond.

in all the different positions. The following generalizations can be made: any substituent will increase the C<sub>5</sub>-C<sub>6</sub> overlap population, equatorial almost to the same extent as axial; substituents on the C<sub>6</sub> atom will increase the N<sub>1</sub>-C<sub>6</sub> overlap population and substituents on the C<sub>5</sub> will increase the C<sub>4</sub>-C<sub>5</sub> one.

Table 6 presents similar indices in the 5-halo *DHU*'s. The N<sub>1</sub>-C<sub>6</sub> bond is unaffected, as are the charges on N<sub>1</sub> and C<sub>4</sub>. On C<sub>6</sub> there is a slight increase of positive charge as compared to the same position in *DHU*. The C<sub>4</sub>-C<sub>5</sub> overlap population increases with substitution, less increase due to axial than to equatorial substituents. The C<sub>5</sub>-C<sub>6</sub> overlap population increases also with substitution with the axial leading to larger increase than the equatorial one. The overlap population in the C-X bond is slightly larger for the equatorial than for the axial substituents, as are the net positive charges on the C<sub>5</sub>-C<sub>6</sub> atoms. Halogen charges are almost identical in the two positions with the equatorial ones slightly more negative. In spite of the uncertainties in the Br and the Cl parameters, the halogen charges approximately correspond to accepted electronegativity differences.

*Acknowledgement.* The author would like to express his sincere thanks to Professor Bernard Pullman for many helpful and interesting discussions on quantum biochemistry throughout the author's stay at Laboratoire de Chimie Quantique. The hospitality and helpfulness of Professor and Madame Pullman and all the other research personnel at the Laboratory were also much appreciated.

Finally, financial support by the U.S. National Science Foundation in the form of a NATO Postdoctoral Fellowship for the year 1967-1968 is gratefully acknowledged.

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