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Quantum-Chemical Investigations on the Functionalized 1H-Pyrimidines

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Conformational analysis and quantum-chemical calculations were carried out by means of the methods MMP2 and SCF MO LCAO in the CNDO/2 and MNDO approximation for the series of compounds being functionalized 1H- pyrimidines. The analysis of the electron density distribution depending on the substituents' nature was done on the basis of the data obtained.

Introduction

We have written before about one simple synthesis of the functionalized 1H- Pyrimidines¹. These compounds are of interest for practice as perspective biologically active preparations²⁻⁵. It is important to investigate their electronic structure with the aim of receiving information on the electron distribution in the systems and its dependence on the nature of substituents. This allows for deeper understanding of the processes occurring in the molecules and gives possibility of purposeful synthesis of new compounds with the properties given beforehand.

In the present communication we give the results of theoretical investigations of 8 compounds being products of the five-membered heterocyclic 2,3-diones reacting with NH- nucleophiles (ureas and thioureas). General scheme of the reaction and the common skeleton of the compounds investigated are shown in Figure 1.

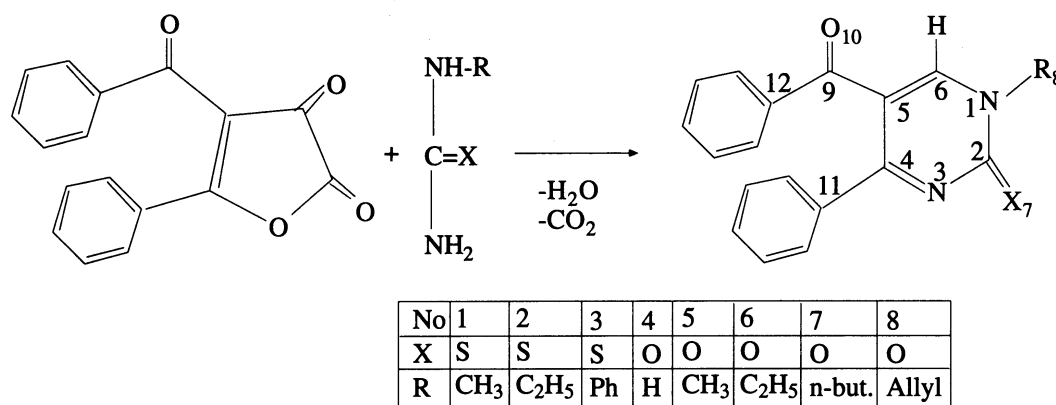


Figure 1. General scheme of the reaction and the skeleton of the compounds investigated

Methodology

At the first stage we optimized the geometry of the molecules by the MMP2* method for molecular mechanics⁶. The optimized values of atomic coordinates were used for further quantum-chemical calculations. Systematic calculations were made by the method MO LCAO SCF in the CNDO/2** and MNDO*** approximations⁷. The CNDO/2 method has been systematically parameterized for the most part of the periodical system⁸. The standard parameters^{9,10} and programs^{11,12} were used in the MNDO-calculations.

Results and Discussion

In Table 1 optimized geometrical characteristics calculated by means of MMP2 and MNDO methods are given for the molecules 1-8.

The spatial disposition of atoms for the molecules 1-8 is shown in Figure 2. The same numeration of atoms in molecular skeletons is used for comparative analysis. The experimental data on X-ray analysis obtained earlier are shown¹³ for compound 1 only. The comparison of the structural parameters (bond lengths, valent and dihedral angles) demonstrates satisfactory coincidence of the theoretical and experimental values. Underestimated theoretical values of the $C_2 = S_8$ bond lengths (1.61 Å) for the compounds 1-3 in comparison with the data given in¹³ (1.65 Å) and averaged data of the Cambridge Structural Database (CSD)¹⁵ (1.66 Å) attract attention. Comparative analysis of the bond lengths has shown that their values calculated by the MNDO method are a little higher than the analogous ones calculated by means of the MMP2 method.

The resting bond lengths in molecules 1-8 correlate satisfactory with the data of CSD¹⁵. As it is seen from the values of the dihedral angles given, the pyrimidine cycle planarity does not depend on the nature of atom X and substitutor R.

The comparison of the structural parameters obtained (bond lengths, valent and torsion angles) with the data known from the publications^{13,14} tells us about their satisfactory agreement. 124 functions were taken as the valency maximal base for calculations. The self-consistent energy values and wave functions were obtained as a result. Based on the data, the rest of the electron structure parameters necessary for analyzing the electron density distribution in the systems was calculated. The accuracy of self-consistency is equal to 0.005 electron charge unit (\bar{e}).

In Table 2 the effective charge distributions in the pyrimidine cycle and on the atoms adjusted are given (the CNDO/2 method). Analogous charge distributions on atoms are obtained by means of the MNDO method and not given here thereby. The data analysis (Table 2) showed that the charges in the atomic group $N_1 - C_2(X_7) - N_3$ depend on X_7 .

A small positive charge is on N_1 when $X = S$, but for $X = O$ this charge varies in the limits of -0.18/-0.22 \bar{e} . This is due to the ability of O_7 (comparing with S_7) of stronger polarization of the nearby atoms and bonds. As a consequence, there is a greater positive charge (0.39 \bar{e}) on C_2 . For the compounds with the same R_8 there is a greater negative charge on S_7 than on O_7 . For the rest of atoms the changes in their charge are inconsiderable. The analysis of the electron density distributions on bonds is given in Table 3 in the form of the Wiberg's indices W_{ij} . Index W_{ij} may be considered as a quantum- chemical analogue

* Molecular Mechanics Program

* Complete Neglect of Differential Overlap

** Modified Neglect of Diatomic Overlap

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Table 1. Optimized structural parameters of the compounds investigated

Geometr.paramet.	Compounds																CSD**		
	1		2		3		4		5		6		7		8				
	MMP2	MNDO	MMP2	MNDO	MMP2	MNDO	MMP2	MNDO	MMP2	MNDO	MMP2	MNDO	MMP2	MNDO	MMP2	MNDO			
$N_1 - C_2$	1.39	1.43	1.39	1.36	1.36	1.36	1.34	1.36	1.35	1.37	1.35	1.35	1.40	1.35	1.40	1.35	1.40	1.35	
$N_1 - C_6$	1.34	1.39	1.35	1.37	1.38	1.38	1.36	1.36	1.37	1.37	1.37	1.37	1.37	1.37	1.37	1.37	1.37	1.37	1.37
$N_1 - R_8$	1.48	1.48	1.48	1.46	1.38	1.38	0.96	1.00	1.46	1.47	1.47	1.47	1.48	1.47	1.48	1.46	1.49	1.46	1.49
$C_2 - N_3$	1.36	1.40	1.38	1.37	1.37	1.37	1.41	1.41	1.41	1.42	1.41	1.41	1.40	1.41	1.40	1.41	1.40	1.41	1.39
$C_2 = X_7$	1.61	1.61	1.65	1.61	1.61	1.61	1.21	1.22	1.21	1.23	1.21	1.21	1.22	1.21	1.22	1.21	1.22	1.22	1.66
$N_3 - C_4$	1.31	1.32	1.32	1.31	1.32	1.32	1.28	1.32	1.28	1.29	1.28	1.28	1.31	1.28	1.31	1.28	1.33	1.33	1.33
$C_4 - C_5$	1.41	1.41	1.41	1.43	1.43	1.43	1.35	1.37	1.35	1.38	1.35	1.35	1.37	1.35	1.37	1.35	1.41	1.39	1.39
$C_4 - C_{11}$	1.49	1.49	1.49	1.43	1.43	1.43	1.36	1.39	1.36	1.41	1.36	1.36	1.38	1.36	1.38	1.36	1.39	1.45	1.45
$C_5 - C_6$	1.39	1.38	1.38	1.38	1.38	1.38	1.35	1.38	1.35	1.41	1.35	1.35	1.39	1.35	1.39	1.35	1.37	1.36	1.36
$C_5 - C_9$	1.48	1.51	1.49	1.43	1.44	1.44	1.48	1.50	1.48	1.52	1.48	1.48	1.51	1.48	1.48	1.51	1.50	1.48	1.48
$C_9 = O_{10}$	1.21	1.23	1.23	1.21	1.21	1.21	1.21	1.22	1.21	1.23	1.21	1.21	1.22	1.21	1.22	1.21	1.23	1.22	1.22
$C_9 - C_{12}$	1.47	1.51	1.48	1.42	1.42	1.43	1.36	1.41	1.36	1.41	1.36	1.41	1.41	1.36	1.41	1.37	1.41	1.44	1.44
$\langle N_1, C_2, N_3$	127.3	120.4	117.3	119.4	116.9	116.9	155.4	116.5	115.9	116.2	115.9	115.9	116.8	115.9	116.8	116.0	117.5	117.5	117.5
$\langle C_2, N_3, C_4$	117.5	123.2	121.3	125.5	127.3	127.3	126.8	121.8	127.3	127.6	127.4	127.4	127.3	127.3	126.0	127.4	124.9	124.9	124.9
$\langle N_3, C_4, C_{11}$	108.4	108.4	114.6	114.4	113.2	113.2	115.8	114.9	115.9	115.1	115.9	115.1	115.8	115.6	115.6	119.8	119.5	119.5	119.5
$\langle C_5, C_9, O_{10}$	114.7	114.7	119.0	116.4	113.4	113.4	119.9	121.5	119.8	117.6	120.1	120.1	118.4	119.9	118.4	119.9	119.4	119.4	119.4
$\langle N_1, C_2, X_7$	120.0	122.4	121.3	124.9	124.4	124.4	120.5	124.3	122.8	122.4	123.0	122.9	123.1	122.8	123.1	122.8	123.2	123.2	123.2
$\langle N_3, C_4, C_5$	119.3	120.1	123.2	117.2	118.2	116.6	115.2	122.1	121.4	120.1	114.9	115.1	114.9	115.1	114.9	115.1	117.3	117.3	117.3
$\langle C_4, C_5, C_6$	120.2	119.0	115.2	116.2	113.3	117.3	122.2	117.2	118.3	119.4	122.2	121.3	122.1	121.3	122.2	121.3	118.7	118.7	118.7
$\langle N_1, C_2, N_3, C_4$	179.5	-179.5	-179.1	0.19	0.194	0.90	0.00	-0.128	2.40	2.59	1.79	1.79	-0.14	-2.19	0.08	0.56	0.56	0.56	0.56
$\langle C_2, N_3, C_4, C_{11}$	-171.7	-179.1	-178.8	-171.2	-169.9	-169.9	-179.7	0.02	179.8	178.9	-179.7	-179.3	178.5	-179.1	179.4	179.8	179.8	179.8	179.8
$\langle C_4, C_5, C_9, O_{10}$	161.6	-72.8	-72.1	163.0	-20.1	164.4	-17.6	-79.2	-78.2	-77.9	-77.5	-77.1	-98.0	-98.3	-93.6	-95.7	-95.7	-95.7	-95.7
$\langle X_7, C_2, N_1, C_6$	179.8	-177.4	-176.9	-179.2	-179.2	177.3	180.0	179.8	176.6	177.1	-177.3	-179.3	-	179.7	179.7	179.3	179.3	179.3	179.3

* X-Ray

** Cambridge structural Database

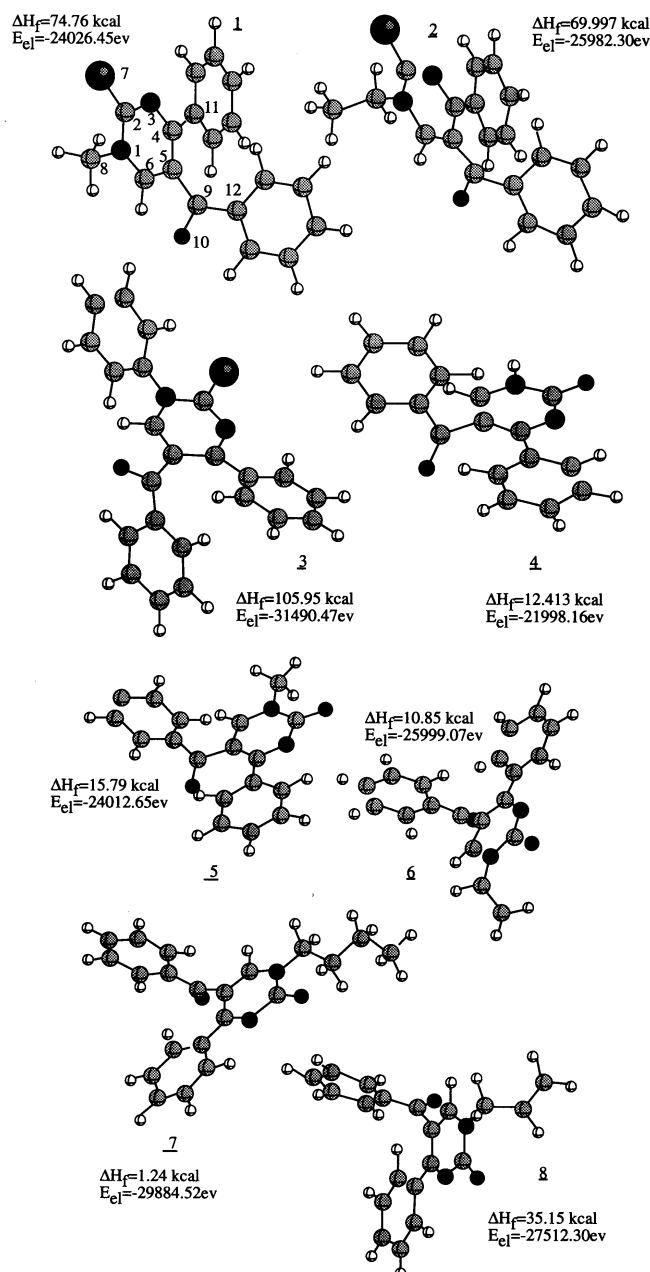


Figure 2. The spatial disposition of atoms, heats of formation and total energies (calculated by MNDO) for the molecules 1-8

of the bond (i-j) multiplicity and characterizes the strength of the bond. When varying X_7 , we can see the difference in the values of W_{ij} for the bonded atoms $N_1 - C_2(X_7) - N_3$. Rather great values of W_{ij} are observed for the bond $N_1 - C_2$ when $X = S$. On the other hand, the bond $C_2 - X_7$ is more strong in the compounds with $X_7 = O$. It should be noted that all the bonds in the cycle are delocalized due to the π -electron system presence. The ordinary bonds with the cycle ($N_1 - R_8$ and $C_5 - C_9$) are weaker than the formers. Further information on the compounds features may be obtained after the frontier orbitals analysis.

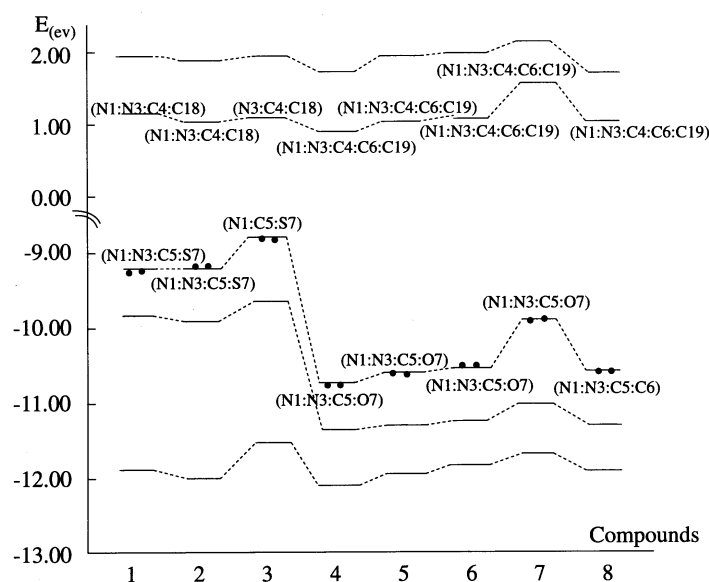
The highest occupied and the lowest unoccupied molecular orbital analysis (HOMO and LUMO, respectively, see figure 3) has shown that they are formed by the orbitals of the pyrimidine cycle's atoms mainly. By this, the orbitals of the negatively charged atoms for HOMO, and the orbitals of the positively charged atoms form LUMO, as a rule. Therefore, a molecule will demonstrate donor (acceptor) features when participating in the reaction by the HOMO (the LUMO, respectively).

Table 2. Effective charges on atoms for the systems calculated

Atom	Comp.							
	1	2	3	4	5	6	7	8
N_1	0.04	0.03	0.04	-0.19	-0.18	-0.21	-0.21	-0.22
C_2	0.29	0.29	0.32	0.40	0.39	0.38	0.40	0.38
N_3	-0.25	-0.26	-0.28	-0.24	-0.25	-0.25	-0.23	-0.23
C_4	0.18	0.19	0.16	0.20	0.21	0.22	0.21	0.21
C_5	-0.13	-0.12	-0.16	-0.15	-0.12	-0.12	-0.13	-0.11
C_6	0.18	0.17	0.18	0.15	0.13	0.13	0.14	0.13
X_7	-0.47	-0.47	-0.48	-0.35	-0.34	-0.34	-0.36	-0.34
R_8	0.08	0.11	0.12	0.03	0.09	0.12	0.11	0.12
C_9	0.27	0.28	0.25	0.24	0.26	0.26	0.27	0.26
O_{10}	-0.32	-0.33	-0.31	-0.25	-0.28	-0.28	-0.30	-0.28
C_{11}	0.00	0.01	-0.01	-0.01	-0.00	0.00	0.01	0.00
C_{12}	0.00	0.00	-0.00	-0.06	-0.04	-0.04	0.01	-0.04
$\mu(\text{Deb.})$	7.92	7.61	8.10	5.95	5.93	5.81	6.04	5.50

Table 3. The Wiberg's indices for the pyrimidine skeleton bonds

Atom	Comp.							
	1	2	3	4	5	6	7	8
$N_1 - C_2$	1.15	1.20	1.20	1.05	1.04	1.04	1.11	1.04
$N_1 - C_6$	1.29	1.25	1.26	1.18	1.16	1.16	1.20	1.15
$N_1 - R_8$	1.00	0.97	1.03	0.98	1.01	1.01	0.98	0.96
$C_2 - N_3$	1.28	1.26	1.25	1.10	1.10	1.10	1.11	1.10
$C_2 = X_7$	1.31	1.29	1.28	1.71	1.71	1.71	1.64	1.71
$N_3 - C_4$	1.50	1.52	1.53	1.58	1.58	1.57	1.56	1.58
$C_4 - C_5$	1.23	1.18	1.18	1.16	1.15	1.15	1.18	1.16
$C_4 - C_{11}$	1.04	1.08	1.07	1.08	1.08	1.09	1.09	1.09
$C_5 - C_6$	1.51	1.54	1.54	1.64	1.65	1.65	1.62	1.65
$C_5 - C_9$	1.03	1.06	1.06	0.98	0.98	0.98	0.99	1.00
$C_9 = O_{10}$	1.77	1.75	1.77	1.81	1.80	1.80	1.78	1.80
$C_9 = C_{12}$	1.07	1.06	1.06	1.08	1.08	1.08	1.08	1.08

**Figure 3.** Energy levels in “active zone” and atoms contained in HOMO/LUMO with a maximal weight

The energy levels disposition for the molecular orbitals entering into “the active zone” (the three last occupied and the two first free MO) is presented in Figure 3. From the picture we see that the energy levels for the occupied orbitals in the compounds 1-3 ($X_7 = S$) are higher by their disposition than the corresponding orbitals in their oxygen analogues. This indicates the higher stability of the compounds 4-8 containing oxygen in the position of X_7 . The HOMO is nonbonding by its nature orbital including the

atomic orbitals of X_7 with the greatest weight. For the compounds 1-3 the closest (by its energy) to the HOMO occupied orbital belongs to a free electron pair of sulfur and is a nonbonding orbital thereby. In contrast to this, the same orbital for the compounds 4-8 is analogous by its structure to the LUMO.

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