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STRUCTURE AND REACTIVITY OF URACIL DERIVATIVES. THERMODYNAMIC STABILITY OF 5-DIAZOURACIL

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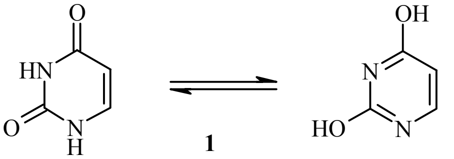
The equilibrium position in the electrocyclization of certain model diazo compounds has been calculated using ab initio calculations based on RHF/6-31G with full optimization of the geometry. It was shown that on reducing the NN bond length the position of equilibrium is displaced towards the acyclic isomer. This effect is expressed to the greatest extent in α-diazocarbonyl systems to which 5-diazouracil derivatives belong. An unusual polarized electron distribution was apparent for 5-diazouracil itself, which does not correspond with the classical Lewis structure.

Keywords: azo compounds, diazo compounds, pyrimidinedione, uracil.

Uracil **1** and its derivatives occupy an important place in bioorganic and pharmaceutical chemistry, diazo substituted systems, *viz*. the salt-like **2** or the electrically neutral **3,** have attracted constant interest for several years [1,2].



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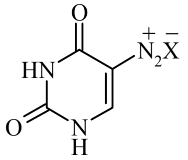

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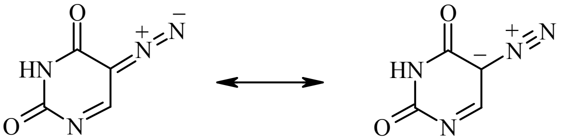

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The latter, in essence, may be considered as derivatives of the α-diazocarbonyl compounds **4**, the kinetic and thermodynamic stability of which is determined by the inclination towards electrocyclic isomerization **4a** ⇄ **4b** [3].

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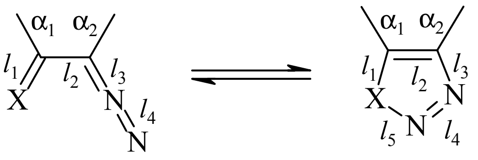


4a **4b**

The experimental data on processes of such type are extremely few and contradictory for structurally similar systems [3]. Thus in acyclic compounds **4a** when X = O the possibility of isomerization into the 1,2,3-oxadiazole form **4b** is proposed, however it has not been discovered synthetically until now [3].

However on going over to the isoelectronic α-diazoimine (X = NH) the triazole–diazoimine equilibrium occurs as a component of the general scheme of *syn–anti* isomerization [3]. Inclusion of the central carbon atoms in a ring of conjugated bonds also favors to the **4a** $\rightleftarrows$ **4b** equilibrium, and in the gas phase the cyclic oxadiazole isomer proves to be approximately 4 kJ/mole more stable than the diazocarbonyl isomer [3].

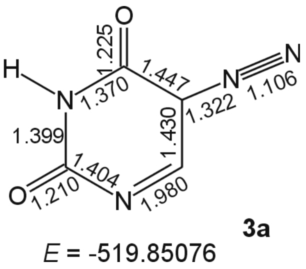
In the present work we have carried out an investigation on equilibria in isoelectronic systems **4a** $\rightleftarrows$ **4b** by *ab initio* calculations with full optimization of the geometry in the RHF/6-31G basis with the GAUSSIAN 94 program [4] (see Table 1). We also note that such an isomerization is an individual case of one of the four basic types of electrocyclic reactions used for the synthesis of five-membered heterocycles [1].

All the calculated model forms of **4** correspond to minima of the potential energy surfaces (PES) (Hesse matrices for them were determined positively). At the same time the bicyclic form does not generally exist as stable one on the PES for the initial 5-diazouracil, which corresponds to the mentioned tendency for the models (see Table 1) towards destabilization of the closed forms on going to a more electronegative X centers. It is evident that the relative destabilization of the cyclic systems **4b** is in agreement with the reduction in bond length of the NN bond (l_4). The most important characteristics calculated by us for 5-diazouracil are given in the structure **3a**, which evidently corresponds to an unusually strongly polarized electron distribution (calculated dipole moment μ = 5.9 D) and the practically triple NN bond in the diazo group. The α-diazocarbonyl fragment O=C–C–NN of 5-diazouracil is therefore geometrically extremely close to the model **4a** for X = O (Table 1). It is evident that the possible structures with localized bonds (type 3) usually proposed in the literature for 5-diazouracil do not correspond to the calculated electron distribution, and consequently discussion of reaction mechanisms involving this pyrimidine base may be adequate only on the basis of quantum-chemical calculations at a high level.

TABLE 1. The Most Important Geometric and Energy Characteristics of Isomers **4a** and **4b** Calculated Using RHF/6-31G (bond lengths l_i, Å, angles α_i, deg, total energies *E*, arbitrary units)

X	Isomers **4a**						
	l_1	l_2	l_3	l_4	α_1	α_2	*E*
CH_2	1.330	1.456	1.287	1.135	113	122	-224, 62230
NH	1.270	1.442	1.299	1.121	114	124	-240, 60940
S	1.696	1.396	1.333	1.107	114	126	-583, 10053
O	1.225	1.434	1.312	1.114	114	125	-260, 44448

	Isomers **4b**							
	l_1	l_2	l_3	l_4	l_5	α_1	α_2	*E*
CH_2	1.497	1.327	1.444	1.242	1.480	128	131	-224, 63598
NH	1.353	1.361	1.372	1.283	1.346	132	130	-240, 63895
S	1.766	1.340	1.398	1.232	1.862	127	128	-583, 09435
O	1.345	1.342	1.393	1.240	1.442	134	132	-260, 41347



3a

The *ab initio* calculations have therefore shown not only an unusual electron distribution in 5-diazouracil, not contributing in principle within the framework of classical structural concepts, but also the high thermodynamic stability of the heterocycle in its probable isomerization reactions.

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