

## Quantum-chemical modeling of the stacking mechanism for the 1H-4H proton transfer in pyridine derivatives. A DFT study

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### ABSTRACT

The stacking mechanism of the 1H-4H proton transfer in 4-pyridone, 4-pyridinthione and p-amino-pyridine are constructed. For quantitative description of this process by means of the quantum-chemical method density functional theory (DFT) the activation energy ( $\Delta E^\ddagger$ ), reaction energy ( $\Delta E$ ) and tautomeric equilibrium constant ( $K_T$ ) has been calculated. The results of calculations have shown, that the values of the energetical and kinetical characteristics, from the point of view of chemical reactions, in reasonable limits varies, that allows one to make the conclusion in favour of competence of the offered stacking mechanism for the 1H-4H proton transfer in pyridine derivatives. It is a new one-stage synchronous and unique mechanism for the 1H-4H proton transfer.

**Keywords:** Pyridine derivatives; Proton transfer; Stacking mechanism; DFT calculations

### INTRODUCTION

The proton transfer through intermolecular hydrogen bonds is fundamental process among chemical and biochemical reactions. Cyclic-dimeric and trimeric mechanisms of tautomeric transformations in pyridines by quantum-chemical<sup>1-7</sup> methods has been studied. Cyclic-dimeric mechanism well works in case of a intermolecular proton transfer in ortho - position whereas for meta - and para - position the process is comes through separate stages with the large expenses of energy, that does this mechanism less probable. The tautomerism of 2-pyridone, and 4-pyridone has been investigated by ab initio calculations and was shown, that 4-hydroxypyridine more stable than 4-pyridone<sup>2</sup>. The effect of the dimerization,

by hydrogen-bond (HB) complexation, on the tautomerism of 2-hydroxypyridine and a series 2-aminopyridines has been carried using ab initio methods. The results obtained for 2-hydroxypyridine fit satisfactorily with the experimental data and show that the 2-pyridone/2-pyridone homodimer complex is the most stable [5].

### RESULTS AND DISCUSSION

With the purpose of search of the mechanism of a protons transfer in para - position in pyridine derivatives the quantum-chemical model of the stacking mechanism was constructed, in which the flatness of molecules are located in parallel and trans – configuration along the relation to each other.

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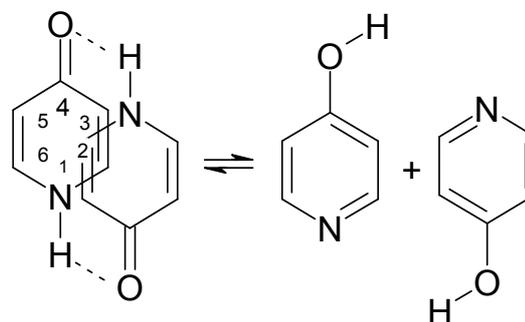
The possibility of the existence of the offered mechanism is based on the principle of molecular dynamics, according to which molecules carry out not only translational but oscillatory and rotary motions. For the purpose of creating of the favourable condition 1H-4H proton transfer the stacking model was constructed (Figure 1-3). In the further the process proceeds in a mode of complete optimization of geometry and the molecules interacted with small expenses of energy.

The idea about stacking interaction between parallel located flat molecules imidazole It has been suggested by Teterin and Nikolenko on based data of NMR<sup>1</sup>H spectrometry<sup>7</sup>. Besides the stacking mechanism was used for study of the 1H-4H rearrangement in 4-azaindole<sup>8</sup>.

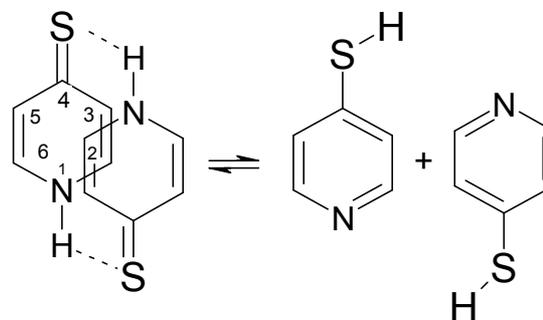
The activation energy ( $\Delta E^\ddagger$ ) and the energy reaction ( $\Delta E$ ) for 1H-4H proton transfer in pyridine derivatives by means stacking mechanism and tautomeric equilibrium constant ( $K_T$ ) has been calculated by quantum-chemical method of density functional theory (DFT)<sup>9</sup>, using the three-parameter functional B3LYP<sup>10-13</sup>. Calculations were performed using software "Priroda"<sup>14</sup> in regime of the reaction coordinate. The results of the calculations is given in table 1. From the table it is seen, that the highest values of the energy activation ( $\Delta E^\ddagger$ ) and energy reaction ( $\Delta E$ ) and low values of the of tautomeric equilibrium constant ( $K_T$ ) for the p-amino-pyridine (3) is characteristic. Hence, in this derivative of pyridine probability of the 1H-4H proton transfer in process of tautomeric transformation is relatively low. The further analysis shows that the activation energy and reaction energy of the proton transfer in 4-pyridone (1) and 4-pyridinthione (2) is lowest, and the tautomeric equilibrium constant has highest values versus p-amino-pyridine. Consequently, the proton transfer in 4-

pyridone and 4-pyridinthione more easily occurs. On a figure 4 as an example the diagram of dependence of energy of proton transfer in 4-pyridone from coordinate of reaction is given.

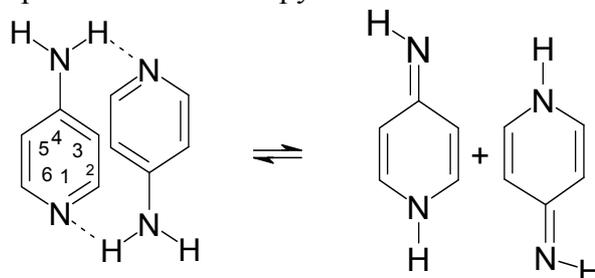
The qualitative correlation between the energetical characteristics and constant of tautomeric equilibrium is observed. In particular, with increase of reaction energy ( $\Delta E$ )  $K_T$  is decreased that is in the consent with representation of tautomeric equilibria constant.



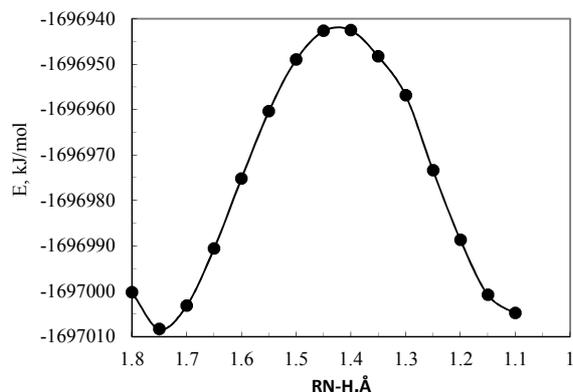
**Fig. 1.** Stacking mechanism of the 1H-4H proton transfer in 4 – pyridine.



**Fig. 2.** Stacking mechanism of the 1H-4H proton transfer in 4-pyridinthione.



**Fig. 3.** Stacking mechanism of the 1H-4H proton transfer in para-amino-pyridinthione.



**Fig. 4.** Proton transfer energy in 4-pyridone ( $E$ ) vs reaction coordinate ( $R_{NH}$ ) (For example).

**Table 1.** Values of activation ( $\Delta E^\ddagger$ ), reaction energy ( $\Delta E$ ), and tautomeric equilibrium constant ( $K_T$ )

| # | Pyridine derivatives | $\Delta E^\ddagger$ , kJ/mol | $\Delta E$ , kJ/mol | $K_T$ |
|---|----------------------|------------------------------|---------------------|-------|
| 1 | 4-pyridone           | 65.8                         | 3.5                 | 0.13  |
| 2 | 4-pyridinthion       | 38.5                         | 30.9                | 0.07  |
| 3 | p-aminopyridine      | 91.7                         | 75.2                | 0.05  |

## CONCLUSION

On the basis of the general analysis of the calculated results it is shown that the values of the activation energy ( $\Delta E^\ddagger$ ), energy reaction ( $\Delta E$ ) for the proton transfer and the tautomeric equilibrium constant ( $K_T$ ) change in quite reasonable limits with point of view of chemical reactions. This allows one to make the conclusion about the competence of the stacking mechanism for the proton transfer in the researched pyridine derivatives. It is a new one-stage synchronous and unique mechanism for the 1H-4H proton transfer. In our opinion the offered mechanism of stacking of proton transfer can be generalized and for other organic reactions, in which the geometry of molecules does

not allow to carry out process of a proton transfer with one stage.

## ACKNOWLEDGMENTS

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