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Quantum-Chemical Study of the Relative Stability of Conformers of 1,4-Dihydropyrazine and 1,4-Dihydro-1,4-diphosphinine

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Abstract—Spatial and electronic structure of the molecules of 1,4-dihydropyrazine and 1,4-dihydro-1,4-dihydrophosphinine was studied by the non-empirical method G2. The boat conformation with the *syn*-orientation of the lone electron pairs was shown to be the most preferable form for both molecules.

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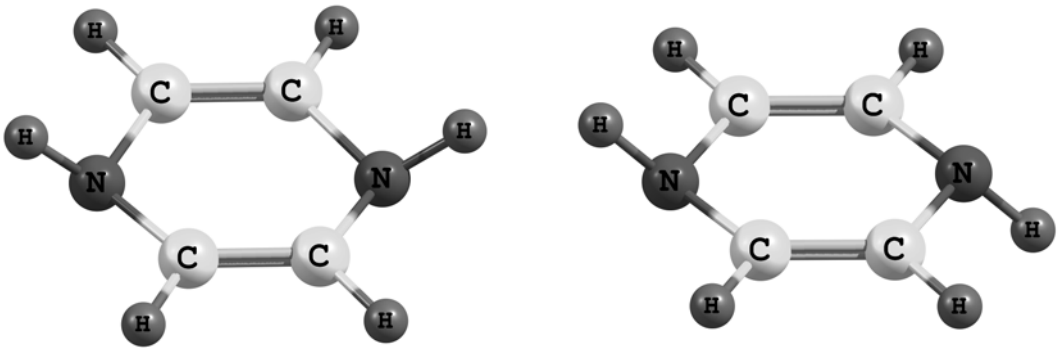
Compounds containing the 1,4-dihydropyrazine ring in the molecule can adopt either the planar structure of the dihydropyrazine fragment with D_{2h} symmetry or nonplanar structure with the C_{2h} or C_{2v} symmetry. The type of symmetry may vary depending on steric and electronic requirements of the substituent. However, it is essential to know the original type of symmetry affected by the substituents. Therefore, the question of the preferable by energy form of the molecule of 1,4-dihydropyrazine is principal in spite of the fact that the synthesis of the unsaturated compound was not described. Understanding of the structure of simple fundamental building blocks allows a better knowledge of structural peculiarities of biochemically important molecules like luciferins [1–4] and riboflavins [5, 6] containing the 1,4-dihydropyrazine ring.

1,4-Dihydropyrazine (**I**) and its derivatives were theoretically studied in [7–12] in various approximations. According to calculations, the molecule of 1,4-dihydropyrazine can exist in two forms with the *syn*– and *anti*-orientation of the lone electron pairs (Fig. 1). Earlier, the stability of the conformers was estimated at the MNDO [7], INDO/S [8], HF and MP2 [10] levels. The highest levels of calculations were B3LYP/6-31G* [11] and MP2/6-31G* [10]. The relative stability of the *syn*- and *anti*-forms according to these methods is different. From B3LYP calculations, the *anti*-



syn, C_{2v} *anti*, C_{2h}

Fig. 1. Most stable conformations of 1,4-dihydropyrazine (**I**).

Total (au) and relative (kcal mol^{-1}) energies of 1,4-dihydropyrazine (**I**) and 1,4-dihydro-1,4-diphosphinine (**II**)

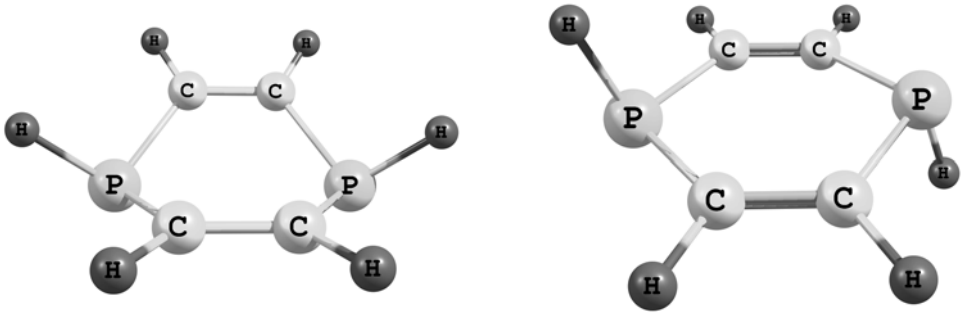
Method/basis set	Total energy				$\Delta E_{syn\text{-}anti}$
	I		**II**		
	syn C_{2v}	*anti* C_{2h}	*syn* C_{2v}	*anti* C_{2h}	
MP2(Full)/6-31G(d)	–264.648109	–264.64773	–837.21948	–837.21838	0.238(0.690)[b]
MP4SDQ/6-311G(d,p)	–264.805907	–264.80554	–837.27628	–837.27486	0.230(0.891)
QCISD(T)/6-311G(d,p)	–264.847201	–264.84651	–837.31703	–837.31577	0.434(0.960)
MP4/6-311+G(d,p)	–264.830783	–264.82946	–837.29745	–837.29589	0.830(0.979)
MP4SDTQ/6-311+G(d,p)	–264.861475	–264.85979	–837.32426	–837.32276	1.057(0.941)
MP4/6-311G(2df ,p)	–264.957283	–264.95701	–837.43491	–837.43309	0.171(1.142)
MP2/6-311+G(3df,2p)	–264.938792	–264.93703	–837.38760	–837.38544	1.106(1.355)
G1	–265.035633	–265.03452	–837.52355	–837.52305	0.697(0.314)
G2MP2	–265.032290	–265.03101	–837.51346	–837.51282	0.803(0.402)
G2	–265.037611	–265.03638	–837.52379	–837.52323	0.772(0.351)
B3LYP/6-31G(d)[a]	–265.475384	–265.47544	–	–	–0.041
MP2/6-31G(d)	–264.644583	–264.64263	–	–	1.224

[a] From [11]. [b] Relative stability of the conformers of 1,4-dihydro-1,4-diphosphinine (**II**) is given in parentheses.

conformer is 0.04 kcal mol^{-1} more stable, whereas MP2 suggests the *syn*-conformer of 1,4-dihydropyrazine to be preferable by 1.22 kcal mol^{-1}.

The goal of this study was to estimate the relative stability of the conformers of 1,4-dihydropyrazine using a high-level G2 method [13] as implemented in the Gaussian 03 program package [14].

To establish the dependence of the relative stability of the conformers on the method and the basis set used we have performed the calculations in different basis sets and by different methods (see the table). All calculations indicate that the syn-conformer of 1,4-dihydropyrazine is preferable, the value of ΔE varying from 0.17 to 1.22 kcal mol^{-1}. The analysis of the calculated vibrational parameters of 1,4-dihydropyrazine (**I**) in the *syn*- and *anti*-conformations has shown the absence of imaginary frequencies. The G1 and G2 calculations gave similar relative stabilities falling in the range 0.70–0.80 kcal mol^{-1}, which can be considered as reference points. Note that the deviation of the results of other calculations from the reference values is due to several reasons, the main one being non-balanced method and basis set. Both too restricted or too extended basis is bad, and gives underestimated or overestimated values of the relative energy stability



syn, C_{2v} *anti*, C_{2h}

Fig. 2. Most stable conformations of 1,4-dihydro-1,4-diphosphinine (**II**).

of the conformers. The most close to the reference value result is given by MP4/6-311+G(d,p) calculations (0.83 kcal mol^{-1}, see the table). Therefore, the theoretical assessment of the relative stability of the conformers gives as the preferable (with small energy gap) the *boat* conformation with the *syn*-orientation of the nitrogen lone electron pairs in the molecule of 1,4-dihydropyrazine (**I**). The relative population of the conformers is 79% *syn* versus 21% *anti* from the G2 method. The four-fold predominance of the *syn*-conformation of **I** is due to its geometrical structure. The bond angle C–N–C is 111.7° and 112.7° in the *syn*- and *anti*-conformers, respectively. In spite of a smaller bond angle, the Bayer strain in the *syn*-conformer is not higher than in the *anti*-conformer. The presence of a folding angle of ca. 12° along the N–N axis allows avoiding the possible strains at a smaller valence angle, which is reflected in such characteristics as nuclear-nuclear repulsion and electron-nuclear attraction. Thus, for the C_{2h} symmetry, the value of E is 224.498 au versus 224.915 au for the C_{2v} symmetry. A small increase in the internuclear repulsion is outweighed by the electron-nuclear attraction: $E_{e\text{-}n}$ is equal to –1066.938 and –1067.776 au, respectively. The kinetic energy has the values of 264.406 (C_{2h}) and 264.408 (C_{2v}) au.

For comparison, the molecule of 1,4-dihydro-1,4-diphosphinine **II**, which is structurally similar to 1,4-dihydropyrazine **I** (Fig. 2) was calculated. The character of filling outer electronic shells of the nitrogen and phosphorus atoms is identical, s^2p^3, they differ only in the size of the shell. For molecule **II**, the *boat* conformation with the *syn*-orientation of the phosphorus lone electron pairs is also preferable. The relative population of the conformers is 64% *syn* and 36% *anti* (from the G2 calculations). The angle of folding along the P–P axis is 26°. The pyramidality of the nitrogen atom in the *syn*- and anti-conformers is only slightly different, the sum of the bond angles around the nitrogen atom is 334° and 337°, respectively. The pyramidality of the phosphorus atom is much larger. The sum of the angles for the *syn*- and *anti*-conformers is 298° and 301°, respectively, so, the difference with the nitrogen atom is more than 30°.

Therefore, 1,4-dihydropyrazine (**I**) and 1,4-dihydro-1,4-diphosphinine (**II**) have similar spatial and electronic structure with small energy preference of the *syn*-conformer. The C_{2v} symmetry of the molecules allows more effective electron-nuclear attraction as compared to the C_{2h} form. The relative population of the conformers is indicative of the shift of the equilibrium toward the *syn*-conformer. We performed the MP2/6-311++G(d,p) analysis of the potential energy surface for the *syn*-*anti* transition via the structure with planar nitrogen (phosphorus) atom. The barrier of the inversion was estimated by scanning the NNH (PPH) angle in the H–N–N–H (H–P–P–H) plane from the value characteristic of the *syn*-conformer to that for the *anti*-conformer with the step of 6° and full optimization of other geometric parameters. The calculated barrier to inversion on the nitrogen atom was 3 kcal mol^{-1}, and on the phosphorus atom, 29 kcal mol^{-1}. This allows a conclusion on an easy nitrogen inversion in molecule **I** and impossibility of interconversion of the two forms of compound **II**.

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