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Double π- and σ-hydrogen bonding in formic acid complexes with pyrrole and imidazole: an *ab initio* and density functional theory study

Ruslan M. Minyaev,* Vladimir I. Minkin, Tatyana N. Gribanova and Andrey G. Starikov

Institute of Physical and Organic Chemistry, Rostov State University, 344090 Rostov-on-Don, Russian Federation.
Fax: +7 8632 434 66; e-mail: minyaev@ipoc.rsu.ru

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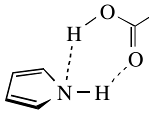
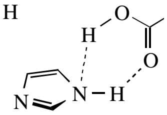
Ab initio [MP2(fu)/6-311++G**] and DFT (B3LYP/6-311++G**) calculations predict that the cyclic 1:1 complexes of formic acid with pyrrole or imidazole are stabilised by non-conventional double hydrogen σ- and π-bonds.

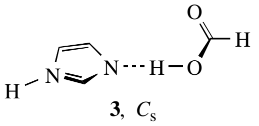
Conventional hydrogen bonds of the σ-type (X–H···Y, where X and Y are heteroatoms) play a crucial role in defining protein structure and biological functions.[1–3] During the last decade, non-conventional hydrogen bonds of the π-type were found to contribute to the secondary structure of important biological systems.[1,4,5] Although model structures with hydrogen π-bonds have been already studied, neither of these contained both σ- and π-type hydrogen bridges within a common associate. Here we report on the first computationally (*ab initio* and density functional theory calculations)[6,7] found examples of cyclic dimers with both σ- and π-hydrogen bonds formed by formic acid and five-membered nitrogen-containing heterocyclic bases. Pyrrole and imidazole rings are the building blocks of biologically important substances, and their interaction with carboxylic acids defines the structure and function of terminal parts of biologically important systems.[1–3]



1, C_s



2, C_1

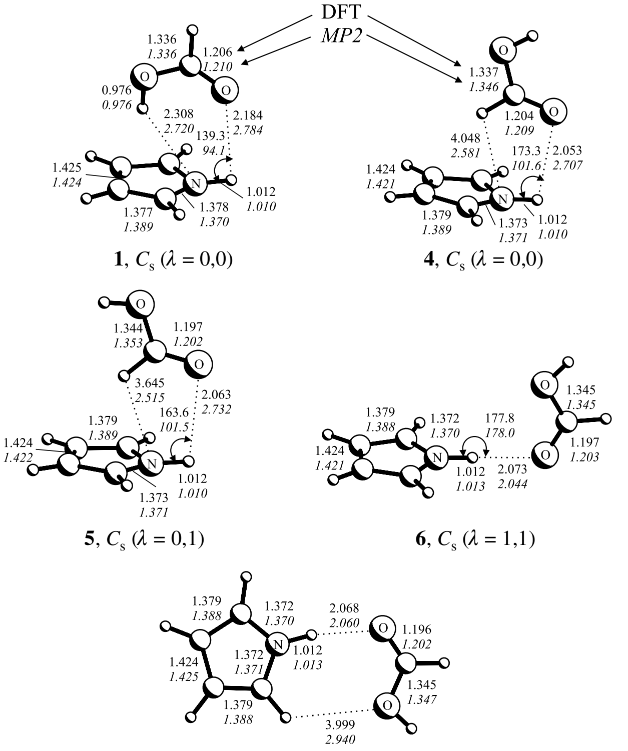


3, C_s

The calculations performed with the use of *ab initio* [MP2(fu)/6-311++G**] and density functional theory (B3LYP/6-311++G**) methods[4] reveal a series of stable H-complexes **1**–**3** formed by pyrrole and imidazole with formic acid, including those (**1** and **2**) with π-type H-bonds.

The geometrical structures found by calculations for H-complexes of pyrrole with formic acid are presented in Figure 1, and their energy characteristics are given in Table 1.

Figure 1 indicates that the intermolecular distances in stable π-complexes **1** and **4**, as predicted by *ab initio* and DFT calculations, are substantially different. On the other hand, both methods afford similar geometrical parameters for complex **7**



1, C_s (λ = 0,0)

4, C_s (λ = 0,0)

5, C_s (λ = 0,1)

6, C_s (λ = 1,1)

7, C_s (λ = 0,2)

Figure 1 Geometry parameters of complexes **1**, **4**–**7** calculated by DFT (B3LYP/6-311++G**) and *ab initio* [MP2(fu)/6-311++G**] methods. The bond lengths and angles are indicated in angström units and degrees, respectively. The molecular structures correspond to MP2 calculations.

Table 1 *Ab initio* [MP2(fu)/6-311++G**] and DFT (B3LYP/6-311++G**) data for compounds **1**, **4**–**7**.[a]

Structure, symmetry	Method	E_{tot} (a.u.)	ZPE (a.u.)	ΔE/kcal mol^{-1}	ΔE_{ZPE}/kcal mol^{-1}	ω_1/cm^{-1}
1, C_s	B3LYP/6-311++G**	–400.066881	0.117317	0	0	21
	MP2(fu)/6-311++G**	–399.130266	0.117878	0	0	14
4, C_s	B3LYP/6-311++G**	–400.065233	0.117171	1.03	0.94	18
	MP2(fu)/6-311++G**	–399.126153	0.117954	2.58	2.63	12
5, C_s	B3LYP/6-311++G**	–400.058256	0.116892	5.41	5.10	15
	MP2(fu)/6-311++G**	–399.120333	0.117709	6.23	6.13	*i*32
6, C_s	B3LYP/6-311++G**	–400.058223	0.116755	5.43	5.08	*i*19
	MP2(fu)/6-311++G**	–399.117789	0.11687	7.83	7.18	*i*21
7, C_s	B3LYP/6-311++G**	–400.058523	0.116756	5.24	4.89	16
	MP2(fu)/6-311++G**	–399.118377	0.116349	7.46	6.50	*i*52
Pyrrole	B3LYP/6-311++G**	–210.230579	0.082187	—	—	477
	MP2(fu)/6-311++G**	–209.679777	0.081500	—	—	364
cis-Formic acid	B3LYP/6-311++G**	–189.827770	0.033700	0	0	630
	MP2(fu)/6-311++G**	–189.418928	0.034183	0	0	634
trans-Formic acid	B3LYP/6-311++G**	–189.820508	0.033321	4.51	4.32	510
	MP2(fu)/6-311++G**	–189.411537	0.033789	4.63	4.39	524

[a] E_{tot} are total energies (1 a.u. = 627.5095 kcal mol^{-1}); ZPE is the harmonic zero-point correction; ω_1 is the smallest harmonic vibration frequency; ΔE are relative energies; ΔE_{ZPE} is the relative energy including the harmonic zero-point correction.

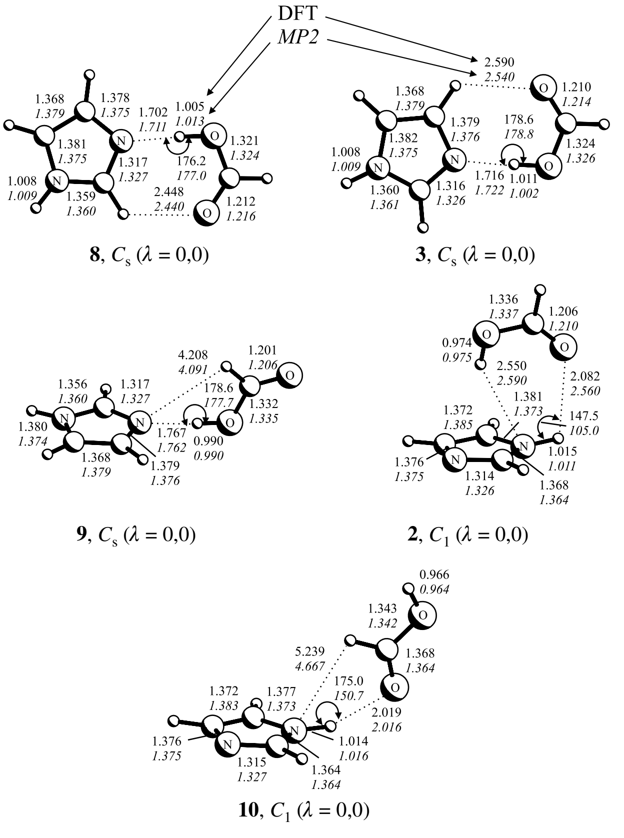
Table 2 *Ab initio* and DFT data for compounds **2**, **3**, **8**–**10**.[a]

Structure, symmetry	Method	E_{tot} (a.u.)	ZPE (a.u.)	ΔE/kcal mol^{-1}	ΔE_{ZPE}/kcal mol^{-1}	ω_1/cm^{-1}
2, C_1	B3LYP/6-311++G**	–416.118345	0.105922	5.43	5.08	23
	MP2(fu)/6-311++G**	–415.166049	0.106769	7.83	7.18	39
3, C_s	B3LYP/6-311++G**	–416.130267	0.106455	1.15	0.94	52
	MP2(fu)/6-311++G**	–415.175332	0.106660	1.01	2.63	18
8, C_s	B3LYP/6-311++G**	–416.132093	0.106546	0	0	62
	MP2(fu)/6-311++G**	–415.176938	0.106780	0	0	24
9, C_1	B3LYP/6-311++G**	–416.124038	0.106195	5.41	5.10	28
	MP2(fu)/6-311++G**	–415.168935	0.106778	6.23	6.13	28
10, C_1	B3LYP/6-311++G**	–416.111786	0.105448	5.24	4.89	13
	MP2(fu)/6-311++G**	–415.156998	0.106246	7.46	6.50	16
Imidazole	B3LYP/6-311++G**	–226.282844	0.070847	—	—	517
	MP2(fu)/6-311++G**	–225.734737	0.070671	—	—	416
cis-Formic acid	B3LYP/6-311++G**	–189.827770	0.033700	0	0	630
	MP2(fu)/6-311++G**	–189.418928	0.034183	0	0	634
trans-Formic acid	B3LYP/6-311++G**	–189.820508	0.033321	4.51	4.32	510
	MP2(fu)/6-311++G**	–189.411537	0.033789	4.63	4.39	524

[a] See Table 1 for notations.

(although predict different types of the stationary points) with the ordinary σ-type of the H-bond. Of special interest is that complex **7** is predicted by DFT calculations to be less energy stable than **1**. The stabilization of π-H-complex **1** compared to the isolated monomers calculated without taking into account BSSE (basis set superposition error) and ZPE (zero point energy) was found to be 5.35 (DFT) or 19.80 (MP2) kcal mol^{-1}. These values changed to 4.46 (DFT) and 18.43 (MP2) kcal mol^{-1} when ZPE values were accounted for. The complexation does not affect significantly the geometrical characteristics of components of complex **1** (changes in the bond lengths are in the range 0.003–0.007 Å). The charge transfer 0.060e (DFT) or 0.016e (MP2) is observed from formic acid to pyrrole.

For the complexes of imidazole with formic acid, the order of stability of σ- and π-type H-complexes is inverted as compared with the above complexes of pyrrole. According to the calculations, complexes **3**, **8**–**10** with usual σ-H-bonds are more stable than complex **2** with additional π-H-bonding. At the same time, the latter also corresponds to a local minimum on the PES. Energy characteristics and geometrical structures found by calculations for all stable complexes of imidazole with formic acid are presented in Table 2 and Figure 2, respectively.



8, C_s (λ = 0,0)

3, C_s (λ = 0,0)

9, C_s (λ = 0,0)

2, C_1 (λ = 0,0)

10, C_1 (λ = 0,0)

Figure 2 Geometry parameters of complexes **2**, **3**, **8**–**10** calculated by *ab initio* [MP2(fu)/6-311++G**] and DFT (B3LYP/6-311++G**) methods. The bond lengths and angles are indicated in angström units and degrees, respectively.

In complex **2**, the π-H-bond is formed by the basic nitrogen and the hydroxyl hydrogen of the acid, whereas σ-type H-bonding occurs when the acidic hydrogen at the HN centre of imidazole forms a bridge to the carbonyl oxygen of the acid. Imidazole units in various biological systems participate in different proton relay chains. Considering the small energy difference found by calculations for the H-complexes of σ- (**3**, **8**–**10**), and π-type (**2**), we may assume that the latter can play a certain role in the function of some proton relay systems.

The energies of formation of the most stable complex **8** from the monomers calculated without taking into account BSSE and ZPE are 13.48 (DFT) and 14.60 (MP2) kcal mol^{-1}, respectively; with accounting for ZPE, the values are 12.22 (DFT) and 13.41 (MP2) kcal mol^{-1}, respectively. Under complexation, the geometrical characteristics of imidazole and formic acid in complex **8** change within the range 0.003–0.008 Å. An insignificant charge transfer of 0.062e (DFT) or 0.081e (MP2) is characteristic of complex **8**.

Note that the DFT calculations give considerably higher values of the bend NH···O angles in π-H-complexes **1**, **2**, **4**, **5** and **10**, which can be explained by the fact that DFT methods underestimate weak intermolecular π-interactions and overestimate σ-interactions.[8] Therefore, the MP2 results appear more reliable. As for other structures, the DFT method gives the same results as MP2 calculations.

In conclusion, the calculations demonstrated that both σ- and π-type hydrogen bonding can occur in the H-complexes of nitrogen-containing heterocycles with carboxylic acids. Therefore, it can play an important role in various effects associated with hydrogen transfer reactions in biological systems.

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