

## Evaluation of the intramolecular hydrogen bond enthalpy by means of specialized quantum chemical methods

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**Abstract:** By means of the MNDO/H, I-MNDO, MNDO/HB and MNDO/M methods, the values of the enthalpy of intramolecular hydrogen bond (IHB) formation for series of substances have been computed. The applicability of these methods for a semi-quantitative estimation of the IHB enthalpy in compounds with a planar quasicycle has been shown.

**Keywords:** intramolecular hydrogen bond, enthalpy, quantum chemical evaluation, organic compounds with a planar quasicycle.

### INTRODUCTION

An extensive number of physicochemical properties of chemical compounds, as well as their reactivity, analytical properties, biological activity depend on the presence of intramolecular hydrogen bonds (IHB) and their thermodynamic parameters.<sup>1–10</sup> For the directive synthesis of compounds, the quantum chemical evaluation of the IHB energy (enthalpy) is of great interest.

Appropriate models for studying IHB are organic molecules with a planar quasicycle. They are widely distributed and play a very important role in chemistry,<sup>1,4,5,8,9,11</sup> being promising building blocks for the construction of supramolecular structures with specific receptor properties. For planar quasicyclic systems, the effect of IHB on thermodynamics can be isolated in an explicit form. When evaluating the IHB enthalpy, it would be correct to use the difference in the enthalpy of formation of a conformer with an IHB and that of a rotamer without an IHB, with all other specific interactions being the same as those in the molecule with an IHB (dihedral angle comprising the X–H bond, which takes part in the X–H···Y IHB, changes from 0 to 180°).<sup>12,13</sup>

For the initial selection of the compounds – "candidates" – to a directive synthesis, with subsequent refinement by means of the *ab initio* (non-empirical) or DFT (Density Functional Theory) methods, it seems promising to use a simplified preliminary semi-quantitative estimation of the IHB enthalpy on the basis of spe-

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cially parameterized semi-empirical methods from the MNDO (Modified Neglect of Differential Overlap) group.

The above group includes the methods MNDO/H,<sup>14,15</sup> I-MNDO,<sup>16</sup> MNDO/HB<sup>17,18</sup> and MNDO/M,<sup>19</sup> which have been shown to be quite adequate in describing the thermodynamics of intermolecular hydrogen bonds.<sup>14–20</sup> The examples of their use for studying IHB are of an exclusive character.<sup>21</sup>

The aim of the present work consisted in establishing the possibility of the evaluation of the IHB formation enthalpy in organic compounds with a planar quasicycle by means of the MNDO/H, I-MNDO, MNDO/HB and MNDO/M methods.

#### RESULTS AND DISCUSSION

The correctness of the use of the above quantum chemical methods was confirmed by reproducing the experimental values of standard gaseous-phase heats of formation of the substances (Table I). It is interesting to note that the heat of formation of salicylic aldehyde computed by all the methods is in agreement with the experimental value for the liquid state. Obviously, in liquid salicylic aldehyde, the intermolecular interactions are relatively weak.

TABLE I. Standard gaseous-phase heats of formation ( $\Delta H_f$ ) of the compounds; to obtain the values in  $\text{kJ mol}^{-1}$  multiply by 4.184

2-Hydroxybenzoic (salicylic) aldehyde	
Method of computation	$\Delta H_f/\text{kcal mol}^{-1}$
MNDO/H	-63.19
I-MNDO	-64.63
MNDO/HB	-61.93
MNDO/M	-64.86
Experiment <sup>22*</sup>	-67.2
*Liquid state	
2-Hydroxy-2,4,6-cycloheptatriene-1-one (tropolone)	
Method of computation	$\Delta H_f/\text{kcal mol}^{-1}$
MNDO/H	-43.07
I-MNDO	-43.34
MNDO/HB	-43.80
MNDO/M	-46.03
Experiment <sup>23</sup>	-37.23
2-Methoxyphenol (guaiacol)	
Method of computation	$\Delta H_f/\text{kcal mol}^{-1}$
MNDO/H	-68.29
I-MNDO	-68.34
MNDO/HB	-68.64
MNDO/M	-71.36
Experiment <sup>22</sup>	-65.38

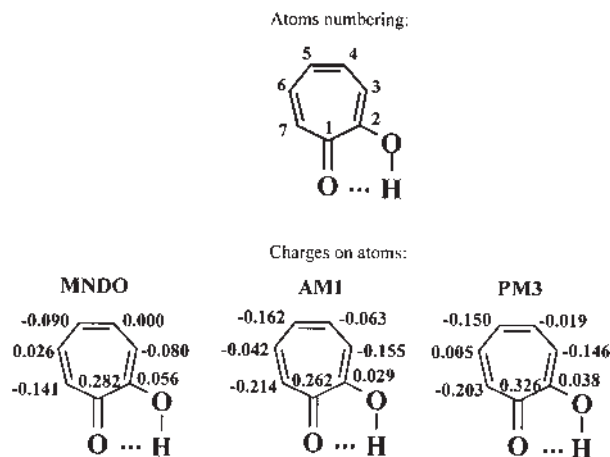


Fig. 1. Mulliken charges on the atoms in the tropolone molecule.

The adequacy of the said methods with respect to the problem to be solved also follows from the correlation between the regioselectivity of electrophilic substitution reactions in a series of tropolones and the electron density distribution (computed using methods of the same group) in the molecule of the origin substance of this series. The charges on the atom (Fig. 1) conform with the occurrence of the reactions of azo coupling, nitrosation, nitration, sulphonation, halogenation, hydroxylation, hydroxymethylation of tropolones with the involvement of the positions 3, 5 and 7 of the cycle.<sup>24-26</sup>

The values of the IHB enthalpies computed by means of the programs from the MNDO 90 package<sup>20</sup> are presented in Table II (IR means infrared spectroscopy, GLC is gas-liquid chromatography).

As can be seen, the aforesaid methods in general reproduce quite well the enthalpies of IHB formation in different compounds. For thiomalonaldehyde and 2-hydroxybenzenethiol, the "experiment", which data are referred to when comparing the results of semi-empirical evaluations, means the computations using the DFT method in the B3LYP version (the papers<sup>33,34</sup> report on the computing procedure in detail and substantiate the assurance of the computations of the IHB enthalpy by the DFT methods).

In the course of the optimization of the geometry of the tropolone molecule it was possible to avoid the "falling" of the system into an alternative energy minimum, which corresponds to a non-planar conformation and is an artefact of the MNDO-group methods.

In analytical chemistry, the procedure of the relativation of the systematic errors is commonly used when the analytical determination is performed in respect to a somewhat other object, and the result of the analysis is evaluated by a difference, thus the systematic errors of measurement are mutually subtracted.<sup>35</sup> Obviously, the above procedure is universal, *i.e.*, is applicable to different kinds of measure-

TABLE II. Experimental and computed values of the enthalpies of formation ( $\Delta H$ ) of intramolecular hydrogen bonds; to obtain the values in  $\text{kJ mol}^{-1}$ , multiply by 4.184

Compound	Hydrogen bond	$-\Delta H_{\text{exper}}$ $\text{kcal mol}^{-1}$	Experimental method, conditions, literature	$-\Delta H_{\text{theor}}/\text{kcal mol}^{-1}$	
				MNDO/H	MNDO/HB
Acetylacetone*	O-H...O	9.26	IR, $\text{CCl}_4$ <sup>27</sup>	9.37	7.82
4-Methoxy-2-hydroxybenzaldehyde	O-H...O	6.25	*** <sup>28,29</sup>	7.88	7.29
2-Nitrophenol	O-H...O	8.00	GLC <sup>30</sup>	9.99	7.85
1,2-Dihydroxybenzene (pyrocatechol)	O-H...O	4.7	GLC <sup>31</sup>	4.28	3.33
2-Hydroxy-1,4-naphthoquinone	O-H...O	2.98	IR, $\text{CCl}_4$ <sup>27</sup>	2.84	3.27
2-Methyl-3-hydroxy-1,4-naphthoquinone	O-H...O	3.07	IR, $\text{CCl}_4$ <sup>27</sup>	4.51	4.94
2-Benzyl-3-hydroxy-1,4-naphthoquinone	O-H...O	3.11	IR, $\text{CCl}_4$ <sup>27</sup>	2.30	2.06
2-Hydroxy-2,4,6-cycloheptatriene-1-one (tropolone)	O-H...O	8.45	IR, $\text{CCl}_4$ <sup>27</sup>	5.62	6.35
3-Methyltropolone	O-H...O	8.19	IR, $\text{CCl}_4$ <sup>27</sup>	7.64	7.08
8-Hydroxyquinoline	O-H...O	6	IR, $\text{CCl}_4$ <sup>32</sup>	6.32	4.06
Thiomalonaldehyde**	S-H...O	2.736 <sup>***</sup>	B3LYP/6-311++G(d,p)	3.45	4.42
2-Hydroxybenzenethiol	S-H...O	1.805 <sup>***</sup>	B3LYP/6-311++G(d,p)	3.29	6.15

\* In the enolic form; \*\* In the thioenolic form; \*\*\* Our computations; \*\*\*\* Chromatography on paper

ments and theoretical estimations, including quantum chemical computations. Relativation of the errors of the differential evaluation of the energetic characteristics of IHB for 2-nitrophenol leads to satisfactory agreement between the calculated and experimental values of the IHB enthalpy, in spite of the poor reproduction of the heats of formation of nitro compounds by the MNDO computing scheme.<sup>36–40</sup>

TABLE III. Relationship between the experimental and computed values of the enthalpy of intramolecular hydrogen bonds

Method	$\Delta H_{\text{exper}} = b\Delta H_{\text{theor}}$	
	$b$	$r$
MNDO/H	0.9440±0.1366	0.8685
I-MNDO	0.8494±0.1363	0.8474
MNDO/HB	0.9907±0.2144	0.6871
MNDO/M	0.7333±0.1389	0.7676

The semi-empirical nature of the MNDO-group methods results sometimes in the over estimation or underestimation of the IHB enthalpy. Thus, the MNDO/M method overestimates the IHB enthalpy in the cases of 4-methoxy-2-hydroxybenzaldehyde, 2-hydroxy-1,4-naphthoquinone, 2-methyl-3-hydroxy-1,4-naphthoquinone, and underestimates it for the molecule of 8-hydroxyquinoline. The MNDO/HB method overestimates the IHB enthalpy in the 2-hydroxythiophenol molecule.

Table II is in essence a recommendation for choosing a given method from the MNDO group with the purpose of the computation of the IHB enthalpy in compounds from one or other series.

When using the MNDO/H and I-MNDO methods, the interrelationship between the computed and experimental values of the IHB enthalpy tends to linearization, although a true linear dependence is not the case in point (Table III; the number of compounds  $m = 12$ ;  $r$  is the correlation coefficient). It can not be rigorously concluded therewith that any method, in general, gives better or worse results as compared to the others. On the one hand, for MNDO/HB, the slope  $b$  of the dependence  $\Delta H_{\text{exper}} = b\Delta H_{\text{theor}}$  is essentially closer to unity. However, on the other hand, the confidence limits concerning the slope are considerably greater in this case than in the other ones, and the correlation coefficient is the lowest among the data of all the methods. Thus, for each series of compounds, only the testing of all the specialized methods considered in this work on a species – selected representative of the sample – as an example would enable a decision to be made between the methods.

The studies carried out show the principal applicability of the MNDO/H, I-MNDO, MNDO/HB, MNDO/M methods for *a priori* semi-quantitative evaluation of the heat of IHB formation in compounds with a planar quasicycle, including preliminary estimations before proceeding to more sophisticated quantum chemical methods and forthcoming planned synthesis.

## ИЗВОД

ПРОЦЕНА ЕНТАЛПИЈЕ ИНТРАМОЛЕКУЛСКИХ ВОДНИЧНИХ ВЕЗА  
ОДРЕЂЕНИМ КВАНТНОХЕМИЈСКИМ МЕТОДАМА

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Применом метода MNDO/H, I-MNDO, MNDO/HB, MNDO/M су израчунате вредности енталпије интрамолекулских водничних веза серије различитих супстанци. Показано је да се методе могу применити у одређивању енталпије интрамолекулских водничних веза планарних квазициклических једињења.

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