

Evaluation of Self-Association Energies of 2-Pyridone Tautomers by Modified MNDO Methods

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Abstract : We have carried out the molecular orbital calculations supported by the modified MNDO methods (MNDO/H, Modified MNDO and AM1) to study the self-associations of formic acid, 2-pyridone and its tautomer, 2-pyridinol. The greater self-association energy of 2-pyridone than that of 2-pyridinol was shown in all the methods. The calculated self-association energies of formic acid and 2-pyridone by the MNDO/H method were well compatible with the experimental values. However, the difference in energy between two tautomers of 2-pyridone was too small to reproduce the experimentally known values. On the other hand, it was found that the Modified MNDO method was invalid for the doubly hydrogen-bonded systems. The AM1 method have been shown to give a proper account of the tautomeric features of 2-pyridone, although the calculated energies of hydrogen-bonding were only about a half the experimental values.

Keyphrases : molecular orbital, modified MNDO, MNDO/H, AM1, hydrogen bond, self-association, tautomerism, 2-pyridone, 2-pyridinol, formic acid

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Nowadays, many theoreticians (*ab initio*-ists) use nonempirical *ab initio* calculations with extended basis sets for various studies of organic and inorganic molecules. The semiempirical molecular orbital calculations, despite of their known limitations, are also useful for posterio-ists and widely being used in gaining insight into a wide range of chemical problems due in part to short amount of computer time for those of large molecules and systematic studies of structurally related molecules.

However, one of the disappointing features of all the current semiempirical molecular orbital calculations is its failure to evaluate weak intermolecular interaction such as hydrogen bond, although these methods have provided many reliable results for other chemical problems.

The defects of the MINDO/3¹⁾ and MNDO²⁾ methods for the evaluation of hydrogen-bonding interactions have already been demonstrated on the model hydrogen-bonded systems between small

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molecules.^{3,4)} It is known, however, that the CNDO/2⁵⁾ method could give a satisfactory account of relative energetics of hydrogen bonding within a certain limitation for the hydrogen-bonded structures set on specific association orientations,⁶⁾ although there are the abundant documented failures.⁷⁾ In order to improve the defects in hydrogen-bonded systems, the reformalized schemes of the CNDO/2 and MINDO/3 methods (CNDO/2H and MINDO/3H) had been proposed.⁸⁾ However, those methods are intended for investigating only neutral systems.

Recently, in the MNDO scheme several methods have been proposed for evaluation of hydrogen bond, which involve modifications of the core-core repulsion function, and are referred to as the MNDO/H,⁹⁾ AM1,¹⁰⁾ I-MNDO¹¹⁾ and Modified MNDO¹²⁾ methods. Among these methods, the MNDO/H and Modified MNDO methods have given fairly accurate results in energy for various hydrogen-bonded systems of small molecules, *e. g.* hydrogen bonds among H₂O, NH₃, HF and those ionic species, and the results were even superior to those of *ab initio* STO-4-31G. The I-MNDO scheme is a special method to calculate only (H₂O)_n clusters. The AM1 method derived from the MNDO scheme is, at present, the most reliable semiempirical method in calculating a wide variety of chemical systems involving weak interactions.

We have recently reported the quantum chemical study for the tautomeric properties of 2-pyridones and found that the self-association is important in the tautomeric equilibria.¹³⁾ The electronic nature of hydrogen bonding on these compounds, however, is not fully understood. As part of our continuing work on the tautomeric properties of 2-pyridones, we have carried out the modified MNDO calculations for the hydrogen-bonded dimers of 2-pyridone and its tautomer, 2-pyridinol, and the results were compared with the experimental values. As far as we are aware, this is the first attempt for these methods to be applied for systems containing doubly hydrogen-bonded structure such as those reported herein.

Calculations

In order to perform the MNDO/H⁹⁾ and the Modified MNDO¹²⁾ calculation, the original MNDO program¹⁴⁾ was modified to use the new core-core repulsion function for atomic pairs taking part in formation of hydrogen bonds. That is to say, in the original MNDO method the following function is used for core-core repulsion between the cores of atom *A* and *B*

$$E_{AB} = Z_A Z_B (AA | BB) (1 + f(R_{AB}))$$

where Z_A and Z_B are core electric charges; $(AA | BB)$ is a two-center two-electron repulsion integral; R_{AB} is an interatomic distance; $f(R_{AB})$ is an empirical function. In the modified MNDO methods, new expressions $f(R_{AB})$ are used for atomic pairs taking part in formation of hydrogen bonds and are listed in Table I, together with the parameters involved in the expressions. Thus, in these modified MNDO calculations, hydrogen-bonded atomic pairs must be specified in advance, and otherwise the MNDO, MNDO/H and Modified MNDO methods gave the identical results on nonhydrogen-bonded molecules.

The MNDO²⁾ and AM1¹⁰⁾ methods were employed with the original parameters. The full geometry optimizations were started from standard bond lengths and bond angles,¹⁵⁾ and from hydrogen-bond lengths of 2.8 Å for N--O and 2.7 Å for O--O.

All calculations were carried out on a FACOM M-382 computer at the Computation Center of Nagoya University.

Table I. Functions for Core-Core Repulsions in Modified MNDO Methods

Method	Function, $f(R_{AB})$	Parameter		
		N	O	H
MNDO	$R_{XH} \exp(-a_X R_X) + \exp(-a_H R_{XH})$ for the pairs N-H and O-H	$a : 2.861342$	3.160604	2.544134
MNDO/H	$\exp(-a R_{XH})$ for the hydrogen bonds X---H-Y (X, Y=N, O, F)	$a : 2.0$	2.0	
Modified MNDO	$\sum_{i=1}^2 A_{Xi} \exp(-C_X(R_{XH}-B_{Xi})^2)$ for the pairs X-H and X'-H in the hydrogen bond X--H-X' (X=N, O)	$A_{X1} : 0.259$ $A_{X2} : 0.060$ $B_{X1} : 0.341$ $B_{X2} : 0.046$ $C_X : 1.700$	0.289 7.077 0.327 -1.117 2.000	

Results and Discussion

We have first examined the validity of these methods on the self-association of formic acid, since this compound has well been studied experimentally and theoretically.¹⁶⁾ The results are shown in Table II. The MNDO method with the full geometry optimization gave quite unreasonable results, *i. e.* the destabilization by 1.1 kJ/mol and the intermolecular O--O distance of 4.076 Å. Also, the calculation with a fixed O--O distance of 2.703 Å showed destabilization by as much as 64.5 kJ/mol.

Among the modified MNDO methods, the MNDO/H calculation with specifying the intermolecular H--O hydrogen bonds gave the self-association energy of 61.4 kJ/mol in good agreement with the experimental values^{17,18)} and rather shorter O--O distance of 2.520 Å compared with the experimental value of 2.703 Å.¹⁷⁾ On the other hand, the Modified MNDO method gave the unrealistic large value of 170.0 kJ/mol for the self-association energy and the symmetric O--H-O hydrogen-bond structure. The Modified MNDO method permits to study hydrogen transfer reactions, and gave more reliable values for hydrogen-bond energies and for barrier heights of proton transfers for small molecular systems than the 4-31G *ab-initio* method.¹²⁾ In this respect, the Modified MNDO method seems to be superior to the MNDO/H method. However, in this study the defect of the Modified MNDO method for the cyclic doubly hydrogen-bonded system was disclosed.

The AM1 result for the hydrogen bond of formic acid had been described in the original report of the AM1 method.¹⁰⁾ Although the AM1 method represents a real improvement over the MNDO

Table II. Self-Association Energies ΔE and Distances R_{XY} of Hydrogen Bond X-H-Y

Dimer system	Method of calculation	R_{XY} (Å)		ΔE (kJ/mol)	
		calcd.	expt.	calcd.	expt.
Formic acid	MNDO	4.076	2.703 ^{a)}	1.1	-59.0, ^{a)} -57.3 ^{b)}
	MNDO (fixed O--O distance)	2.703		64.5	
	MNDO/H	2.520		-61.4	
	Modified MNDO	2.537		-170.0	
	AM1	3.062		-26.0	
2-Pyridone	MNDO	4.091	2.796 ^{c)}	-8.2	-65.3, ^{d)} -36.2, ^{e)}
	MNDO/H	2.549		-73.6	-36.2, ^{f)} -66.5 ^{g)}
	Modified MNDO	2.560		-309.4	
	AM1	3.039		-44.2	
2-Pyridinol	MNDO	4.373	2.757 ^{h)}	-2.5	
	MNDO/H	2.513		-70.0	
	Modified MNDO	2.559		-227.5	
	AM1	3.577		-9.9	

a) Ref. 17. b) Ref. 18. c) Ref. 22. d) Ref. 25. e) Ref. 26. f) Ref. 27. g) Ref. 28. h) Ref. 24.

method for many chemical systems, especially for those including weak molecular interactions, the calculated hydrogen bond energies had been only about a half the experimental value.

Thus, we have concluded that the MNDO/H method gives the most accurate self-association energies of formic acid among the methods examined.

It has already abundantly documented that reproducing the tautomeric energies of 2-pyridones is extremely difficult. It is not until 1980s' that the tautomeric energy differences are reproduced with the accuracy of 10 kJ/mol.¹⁹⁾ The tautomeric energy difference of monomeric 2-pyridone is as small as 1.7 kJ/mol.²⁰⁾ So, the tautomeric equilibria in solution strongly depend on the self-association abilities of both tautomeric forms, and the exclusive existence of the pyridone form in solutions is due to the great self-association and solvation ability of the pyridone form. The self-associated dimeric structures of 2-pyridones were known by the X-ray studies of 2-pyridone²¹⁾ and 5-chloro-2-pyridone,²²⁾ and for 2-pyridinols by those of 6-chloro-²³⁾ and 6-bromo-2-pyridinol.²⁴⁾ There are a number of conflicting reports concerning the self-association energy for 2-pyridone (36-67 kJ/mol),^{16,25-28)}

For 2-pyridone, the MNDO calculations again gave quite unreasonable results for the self-association energy and the geometry, whereas the MNDO/H calculation gave the self-association energy of 73.6 kJ/mol for 2-pyridone and 70.0 kJ/mol for 2-pyridinol. The calculated value for 2-pyridone was in good agreement with the experimental value, but the difference from the value for the pyridinol form seems to be too small in comparison with the experimentally known tautomeric features, *i.e.* the exclusive existence of 2-pyridone form due to the greater stabilization by the

self-association in solution.^{13,20)} In the calculated geometries shown in Fig. 1, the intermolecular N--O distances were slightly shorter than the experimental values in both tautomeric forms. The Modified MNDO method again gave unrealistic strong self-association energies of 309.4 kJ/mol for 2-pyridone and of 227.5 kJ/mol for 2-pyridinol. The hydrogen bonds calculated by the AM1 method were rather weak in the energy and

the hydrogen-bond lengths were too long, and in the comparison between both tautomers the much weaker self-association ability for 2-pyridinol was shown. This large difference in the self-association energy between the tautomers seems to be consistent with the exclusive existence of the pyridone form in a solution. Also, the AM1 method gave a fairly accurate value of -2.0 kJ/mol for the tautomeric energy difference between the monomeric tautomers. These calculated results for the self-associations of 2-pyridone tautomers were on the whole those as expected from the results for formic acid.

Thus, it may be concluded that the AM1 method gives the best account of the tautomeric features of 2-pyridone among the methods examined and that the MNDO/H method does not reproduce the difference in the self-association energy between the tautomers in spite of the accurate evaluation of the self-association energy of 2-pyridone. This failing in the MNDO/H method may be due to the use of the same values as the parameters of nitrogen and oxygen atoms in the modified expression for the core-core repulsion.

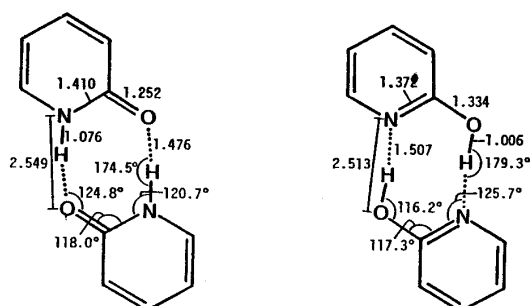


Fig. 1. MNDO/H Geometries

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