

配置와 形態에 관한 分子軌道函數論的 研究(第3報).  
Furan, Thiophene 및 Pyrrole 카르보닐  
化合物의 2-置換體의 形態

李 益 春 · 金 時 俊\*  
仁荷大學校 理科學 化學科  
\*漢陽大學校 教養學部 化學科

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MO Studies of Configuration and Conformation(III).  
Conformations of Some 2-Substituted Furan,  
Thiophene and Pyrrole Carbonyl Compounds

Ikchoon Lee and Shi Choon Kim\*

Department of Chemistry, College of Science, Inha University,  
Inchon, Korea

\*Department of Chemistry, College of General Studies,  
Hanyang University, Seoul, Korea

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要約. EHT 분자궤도함수법 계산으로 9가지 furan, thiophene 및 pyrrole의 2-치환체의 우세한 형태를 구명하였다. 계산 결과는 furan 유도체의 우세한 형태는 *trans* 형인데 이것은 주로 정전기적 상호작용에 의하여 안정화되어 있으며 thiophene 에서는 hetero 고리의 S 원자와 카르보닐 산소와의 전자적 혼쥬게이션이, 그리고 pyrrole 에서는 정전기적 및 혼쥬게이션 효과가 안정한 형태를 결정하는데 작용하고 있다. EHT 계산 결과는 실험결과와도 잘 일치된다.

**ABSTRACT.** Conformations of nine 2-substituted furan, thiophene and pyrrole compounds have been studied by EHT methods.

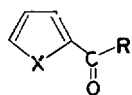
The preferred conformations of furan derivatives were *trans* form, which were mainly stabilized by electrostatic interactions. For thiophenes, electronic conjugation between the ring S and carbonyl oxygen was dominant, while for pyrroles both the electrostatic and conjugation effects were operative in determining the preferred conformations. Results of EHT calculation agreed well with experimentally determined preferences.

INTRODUCTION

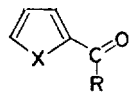
During the last few years, the conformational problems of 2-substituted pentatomic heterocycles

have attracted much attention. For example the conformational preference of 2-formyl furan has been the source of much controversy because of apparently contradictory results obtained by

different methods<sup>1</sup>. Experimental determination of preferred conformation becomes especially complicated since the conjugatively stabilized planar conformations are markedly medium dependent. Another notable example which has long been investigated but not yet unambiguously settled is the reasons for the different behavior of the conformation of 2-formyl thiophene, (*cis*-form preferred, i.e., 7(A), than that of the analogous 2-formyl furan (*trans*-form preferred, i.e., 1(B))<sup>2</sup>.



(A) *cis*



(B) *trans*

- (1) X=O, R=H (2) X=O, R=Cl (3) X=O, R=CH<sub>3</sub> (4) X=NH, R=H (5) X=NH, R=Cl (6) X=NH, R=CH<sub>3</sub> (7) X=S, R=H (8) X=S, R=Cl (9) X=S, R=CH<sub>3</sub>

Ritchie *et al.*,<sup>3</sup> studied the conformation of 2-substituted furan and thiophene carbonyl compounds by measuring dipole moments and molar Kerr constants in cyclohexane. They concluded that although *trans* form of the furan derivative is favored in cyclohexane, the corresponding thiophene exhibit a strong preference for the *cis*-conformation, and that for the furan this is readily explicable in terms of minimization of dipole-dipole interaction energy, while for the thiophene it may be indicative of a stabilizing interaction between the sulfur and carbonyl oxygen atoms. On the other hand the nucleophilic reactivities of 2-furoyl and 2-thenoyl chlorides were found to be greater than that of benzoyl chloride<sup>4</sup>. This has been attributed to the stabilization of developing positive charge at the carbonyl carbon atom in the transition state through conjugative interaction between

the electron-releasing ring hetero atom, O or S, and the carbonyl group<sup>4</sup>. Such an interaction is expected to be stronger for ring oxygen and sulfur in heterocycles than that for ring carbon in benzene.

In this paper we report on an MO theoretical studies of conformations of nine pentatomic heterocyclic compounds, (1)~(9), based on the extended Hückel (EHT) MO calculations.<sup>5</sup> We hope to establish the main contributing factors in determining the preferred conformations for these compounds.

## CALCULATIONS

**Molecular Geometry.** The geometries of 2-substituted furan, thiophene and pyrrole carbonyl compounds were assumed to be planar and were constructed from the probable bond angles and lengths, and dihedral angles<sup>6</sup>. The calculation of atomic cartesian coordinates of the molecular system was carried out with an aid of a modified version of Quantum Chemistry Program Exchange (QCPE) No 226 program with IBM 1130 computer. The coordinate system and numbering scheme are shown in Fig. 1, and bond lengths and bond angles used in these calculations are listed in Table 1.

**EHT Calculations.** The computer program for EHT calculation was obtained from QCPE (No 64). Input data in this program are the Slater orbital exponents  $Z$ , valence state ioniza-

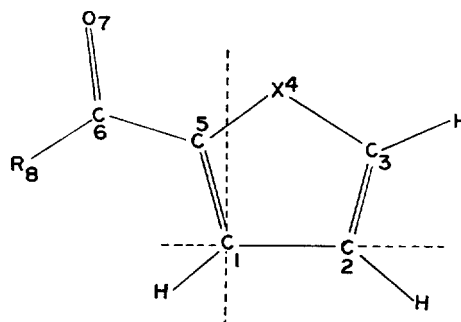


Fig. 1. Coordinate system and numbering scheme.

tion potential (VSIP),  $-I$  of AOs and cartesian coordinates of atom in molecules.  $Z$  and  $-I$  values used in this work are summarized in Table 2.

## RESULTS AND DISCUSSION

Results of relative EHT energies calculated are summarized in Table 3. Admittedly the energy differences between the two planar conformations are quite small in some cases. (e.g. (4)), but this is due to the inherent shortcom-

ings of the method used which is known to grossly exaggerate energies and atomic charges.

Table 3 shows that *trans*-forms are preferred for all the 2-substituted furans ((1)~(3)), which are consistent with the experimentally determined preferences. The pyrrole derivatives, the *cis*-form is favored with R=H, (4), while *trans*-forms are favored with R=Cl and CH<sub>3</sub>, (5) and (6). For thiophene derivatives, *cis*-forms are preferred except for R=CH<sub>3</sub>, (9), for which the EHT result predicts the *trans* preference while dipole moment measurements in cyclohexane gives the *cis* preference. In fact this is the only disagreement between our MO

Table 1. Bond lengths and angles used in atomic coordinate calculations.

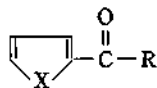
Bond length (Å) <sup>a</sup>		Bond angle <sup>a</sup>	
C <sub>1</sub> -C <sub>2</sub>	1.46	∠C <sub>1</sub> C <sub>2</sub> C <sub>3</sub>	103°
C <sub>2</sub> -C <sub>3</sub>	1.35	∠C <sub>2</sub> C <sub>3</sub> O <sub>4</sub>	112°
C <sub>3</sub> -O <sub>4</sub>	1.30	∠C <sub>3</sub> O <sub>4</sub> C <sub>5</sub>	107°
O <sub>4</sub> -C <sub>5</sub>	1.31	∠O <sub>4</sub> C <sub>5</sub> C <sub>1</sub>	113°
C <sub>5</sub> -C <sub>6</sub>	1.47	∠O <sub>4</sub> C <sub>5</sub> C <sub>6</sub>	120°
C <sub>6</sub> -C <sub>7</sub>	1.17	∠C <sub>5</sub> C <sub>6</sub> O <sub>7</sub>	123°
C <sub>6</sub> -C <sub>8</sub>	1.50	∠C <sub>5</sub> C <sub>6</sub> C <sub>8</sub>	115°
C <sub>1</sub> -C <sub>5</sub>	1.30	∠C <sub>5</sub> C <sub>6</sub> Cl	105°
C-Cl	1.77	∠C <sub>2</sub> C <sub>3</sub> S <sub>4</sub>	112°
C <sub>3</sub> -S <sub>4</sub>	1.74	∠C <sub>3</sub> S <sub>4</sub> C <sub>5</sub>	91°
C <sub>3</sub> -N <sub>4</sub>	1.42	∠C <sub>2</sub> C <sub>3</sub> N <sub>4</sub>	110°
C-H	1.08	∠C <sub>3</sub> N <sub>4</sub> C <sub>5</sub>	104°
N-H	1.03	∠C <sub>3</sub> N <sub>4</sub> H	128°
C <sub>6</sub> -H	1.09		

<sup>a</sup> from reference (6).

Table 2. The Slater orbital exponents,  $Z$ , and  $-VSIP$  used.

AO	$Z$	$-VSIP$
H 1s	1.00	-13.60
C 2s	1.59	-21.01
2p		-11.27
O 2s	2.24	-36.07
2p		-18.53
N 2s	1.92	-26.90
2p		-14.42
Cl 3s	2.20	-24.02
3p		-15.03
S 3s	1.97	-20.08
3p		-13.32

Table 3. Summary of relative total energies for *cis*- and *trans*-planar conformations of 2-substituted furan, pyrrole and thiophene.



X	O			NH			S			
	H	Cl	CH <sub>3</sub>	H	Cl	CH <sub>3</sub>	H	Cl	CH <sub>3</sub>	
R										
$\Delta E_2$ (kcal/mole)	<i>cis</i>	0	0	0	-1.0	0	0	-8.9	-2.3	0
	<i>trans</i>	-25.0	-3.0	-4.7	0	-6.4	-4.9	0	0	-3.7
(3) exptl. preference	<i>trans</i> 83±5%	—	<i>trans</i> 83±10%	<i>cis</i> <sup>*</sup> 100%	—	—	<i>cis</i> 73±10%	—	—	<i>cis</i> 61±10%

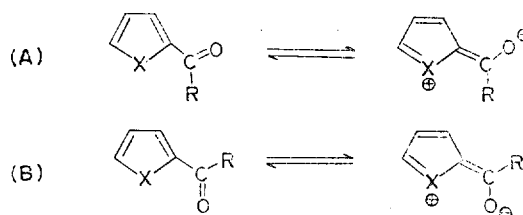
<sup>\*</sup>B.P. Roques and S. Combrisson, *Can. J. Chem.*, 51, 573 (1973).

results and dipole moment results available. It should be noted that these experimental values are obtained in cyclohexane solution while our MO results should correspond to the values in vapor phase for which no experimental results are available.

There are three main factors which are known to control the conformational preference in vapor phase; (1) electrostatic, (2) conjugative, and (3) steric interactions.

Drakenberg *et al.*<sup>7</sup>, reported that the electrostatic (e. s.) effects are of major importance in determining the most stable conformation of methylformate. We have carried out the similar calculation of e. s. energy,  $\sum_{i,j} q_i q_j / r_{ij}$ , where  $q_i$  is the formal charge of atom  $i$  and  $r_{ij}$  is the interatomic distances between atoms  $i$  and  $j$ . Results are summarized in Table 4, where relative e. s. energies,  $\Delta E_{cis-trans}$ , are shown. Thus e. s. energy tends to stabilize *trans*-conformation in all cases. Strikingly the relative e. s. energies differ quite markedly as the hetero atom changes; for furans, e. s. energy differences between the *trans* and *cis*-forms are  $\sim 10^2$  kcal, for pyrroles, they are  $\sim 10$  kcal, and finally for thiophenes, they are  $\sim 1$  kcal. It is therefore very likely that the preferred conformations of furan derivatives are mainly determined by e. s. interaction, while with pyrroles and thiophenes e. s. contribution may not be of major importance in determining preferred conformation. This could be the reason why 2-formyl pyrrole and thiophenes prefer *cis* conformations despite the small e. s. repulsions

in *cis* conformations. The pentatomic heterocycles are electron withdrawing by inductive effect and electron donating by resonance effect. The hetero atoms are clearly very strong resonance donors in these five-membered ring systems, an effect which completely overrides their inductive withdrawal<sup>8</sup>. Thus the  $\sigma^+$  values, which represent the electronic effects of substitution of O and S for CH=CH in the benzene ring, are  $-0.94$  and  $-0.84$  respectively<sup>8</sup>. This means that the following resonance stabilizations are operative in the molecules.



The results of our EHT calculations have shown that none of the compounds actually had positive formal charge on heteroatom except on the S atom of *trans*-2-thenoyl chloride, (8)B (+0.0023 electronic charge unit). This type of conjugative effect, however, should result in enhanced bond population of C<sub>5</sub>-C<sub>6</sub> bond. We have therefore compared bond populations of this bond in Table 4. It can be seen from this Table that bond populations of this bond are always larger, and hence more stabilizing, for preferred conformations (determined by total energies in Table 3) except for compounds (6) and (9) for which the differences in bond population between the

Table 4. Relative e. s. energies,  $\Delta E_{cis-trans}$  (kcal/mole), and bond populations for C<sub>5</sub>-C<sub>6</sub> bonds.

X	O			NH			S			
	H	Cl	CH <sub>3</sub>	H	Cl	CH <sub>3</sub>	H	Cl	CH <sub>3</sub>	
$\Delta E_{cis-trans}$	150.1	110.8	123.7	13.1	31.6	32.0	0.7	0.8	1.3	
bond popul of C <sub>5</sub> -C <sub>6</sub>	<i>trans</i>	0.9791	0.9743	0.9714	0.9852	0.9745	0.9663	0.9762	0.9708	0.9641
	<i>cis</i>	0.9706	0.9714	0.9698	0.9906	0.9707	0.9669	0.9958	0.9729	0.9647

*cis* and *rans* forms are insignificantly small. We can now see why the compounds (4), (7) and (8) have *cis* preferences despite the unfavorable e. s. interactions. (see above); the conjugative stabilization of *cis*-forms override the unfavorable e. s. effects for these compounds.

Kuzharov *et al.*,<sup>9</sup> attributed the *cis* preference of 2-formyl thiophene to the Coulomb interaction of the separated charges, i. e., negative on the carbonyl oxygen and positive on the sulfur atom. According to our MO results, however, sulfur atom had formal positive charge only in the case of *trans*-2-formyl thiophene, which is in fact a less stable form. We therefore conclude that the suggested e. s. interaction between sulfur and oxygen should not be present; it is not, in any case, required to explain the preference of the *cis*-conformation. The above hypothesis should thus be modified to state that the absence of or negligible e. g. repulsion is sufficient to prevent the existence of the *trans*-conformation in 2-formyl thiophene<sup>10</sup>. The dominant factor in determining preferred conformation in this case is rather the conjugative electronic effect. This is also true for the compounds (4) and (8), for which *cis*-conformations are stabilized by electronic conjugation in spite of the weak, unfavorable e. s. repulsion.

Finally inspection of molecular models show that there will be some steric crowding in *cis*-forms of 2-acetyl compounds, i. e., the compounds (3), (6) and (9). This effect will be somewhat smaller in (6), while the effects in (3) and (9) will be approximately equal. Thus consideration of steric effect alone will predict the *trans* preference for all the 2-acetyl compounds as we obtained from EHT energies in Table 3. With 2-acetyl thiophene, (9), all three, i. e., e. s., conjugative and steric interactions are small and therefore it may well be that the delicate balance of the three effects is

just enough give *trans* preference over the *cis* form.

### CONCLUSIONS

(1) The three 2-substituted furans, (1), (2) and (3), have preferred conformations of *trans* form due mainly to the e. s. stabilization, although conjugative and steric effects are also favorable.

(2) 2-formyl pyrrole has the *cis*-preference due to overriding conjugative effect over the unfavorable e. s. repulsion. Two other pyrrole derivatives have the *trans*-preferences, major contributing effects being relatively strong e. s. (for (5) & (6)) and conjugative (for (5)) interactions. For 2-acetyl pyrrole (6) some stabilizing effect can be expected from steric interaction.

(3) The main factor in determining *cis*-preferences of thiophene derivatives is the electron conjugation between the heteroatom, S, and the carbonyl oxygen. This effect overrides the weak unfavorable e. s. repulsion. The *trans*-preference of 2-acetyl thiophene may well be a result of delicate balance of the three contributing factors.

### ACKNOWLEDGMENT

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