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π-Nonbonded Interactions Involving Heteroatoms[*]

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Ab initio calculations were performed on systems containing various basic π fragments and glycines to generalize the π-nonbonded interaction (π-NBI) method of determining relative conformational and configurational stability of organic molecules. It was found that the relative stability of conformational isomers can be determined in general by the simple application of the π-NBI method, but the method is not applicable to the geometrical isomerism in which stronger structural factors are involved. The π-NBI effect of a crowded π-structure ($n\pi/m$) is maximum for the system in which n is equal to m. In crowded structures containing heteroatoms, P^{π}_{ij} values of $4N+1$ system may become negative, but this sign reversal does not invalidate the predictions based on the π-NBI method.

Introduction

Precise knowledge of the molecular structure is a prerequisite for undertaking any analysis or interpretation of chemical phenomena pertaining to a molecule. Conformational and configurational isomerisms due to rotation about single and double bonds respectively in an organic molecule are of considerable interest and have been extensively investigated both computationally and experimentally.

With the recent advance in experimental technique, experimental data on small rotational barriers and conformational energy differences are becoming increasingly available, and provided tests for theoretical computational approaches to the subject.

Theoretically molecular orbital method has proved highly successful in predicting quantitatively correct molecular conformations and configurations through computations involving use of improved and extended sets of basis functions.[1] It has been shown that the MO approaches can even deal with molecular structural features which are difficult to determine experimentally.[2]

In spite of these high level quantitative MO calculations and extensive studies on the analysis of the origin of the conformational and configurational energy differences, simple

and expedient method of determining relative conformational and configurational stabilities of organic molecules is scarce. In this respect, the method of π-nonbonded interaction (π-NBI)[3] developed by us based on the frontier molecular orbital (FMO) approximation is useful; one needs only to count π electrons contained in crowded π structures within each conformational or configurational isomers in order to determine their relative stabilities. According to our analysis $4N + 2$ and $4N + 1$ π electron systems are stabilizing, whereas $4N$ and $4N - 1$ systems are destabilizing, the effect being stronger with the former respectively. It was also found that the effect of composite π structures in a conformer is additive.[3c,4] In a formal quantum mechanical sense, a one-electron factor which is responsible for nonbonded attractive or repulsive interactions and a steric factor consisting of two-electrons and internuclear repulsive factors can be distinguished.[5] The π-NBI is reflected in the former since it concerns through-space interaction between nonbonded end atoms in a crowded structure.[3b] Thus the π-NBI is especially important in alkanes in which conjugated π structures are provided by pseudo π group orbitals of $-CH_2$ or $-CH_3$,[6] since conformational stabilities are dominated by the one-electron factor due to small changes in the steric factor.[3b]

In this report, we attempted to generalize the π-NBI method of determining relative conformational and configurational stabilities of organic molecules by extending applications to systems with heteroatoms, with localized π structures (alken-

es) and with end atoms other than the $-CH_2$(or $-CH_3$).

Computation

All computations were performed using Gaussian-70 program with STO-3G basis set. Standard geometries[7] were used for basic fragment π structures. Geometries for glycine and glycine methyl ester were 4-21G optimized values of Schäfer et al[8]. The isoconjugate π structure was given to the nonplanar amine group ($-NH_2$) as given to the methylene ($-CH_2$) group.[9] The same notation[3,4] of ($n\pi/m$) was used to denote a crowded structure formed with n π-electrons on m centers.

Results and Discussion

Terminal π centers likely to be found in the ($n\pi/m$) structures of simple organic molecules are methyl, amine (sp³), ammonium, hydroxyl, amide (sp^2), carbanion (sp^2) and ethylene groups as shown in Figure 1. First three of these contribute ($2\pi/2$) while the next three ($2\pi/1$). The last, ethyl-
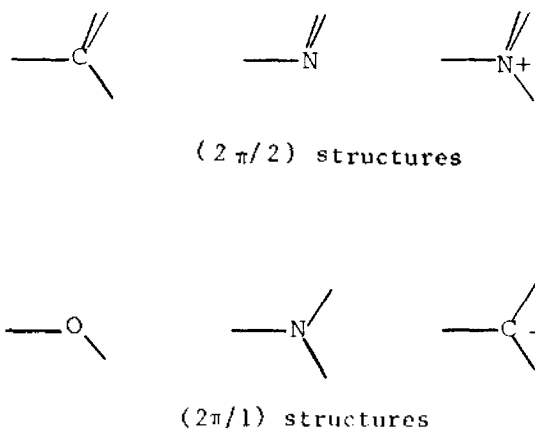

(2 π/ 2) structures

(2π/ 1) structures

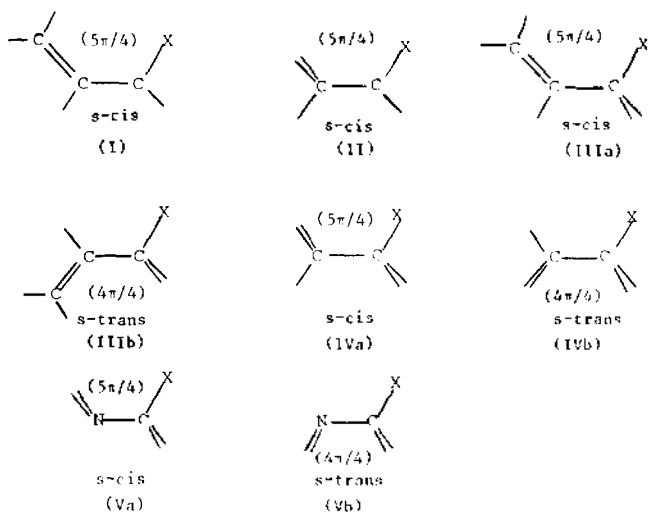**Figure 1.** Isoconjugate π structures of terminal groups (basic π fragments, X).

Figure 2. Some hypothetical systems containing isoconjugate π structures with ($2\pi/1$), sp², centers, X.

ene, contribute also ($2\pi/2$) but this fragment may be different from other ($2\pi/2$) terminal systems in that it has a pure π orbital which can be considered as somewhat localized unless the ethylene fragment forms a part of alternant hydrocarbon chain.

Interrelationship between the two numbers n and m of ($n\pi/m$) systems is also likely to affect the π-NBI; a ($2\pi/1$) structure should have less delocalization compared with a ($2\pi/2$) system.

We first consider some hypothetical systems shown in Figure 2. Rotation about the C–C single bond gives two conformationally significant structures s-cis and s-trans, for each of these systems (I)$\sim$(V). Each system has a stabilizing ($5\pi/4$) structure in s-cis form, which will be converted to a destabilizing ($4\pi/3$) or ($4\pi/4$) structure in s-stans form.

In systems (I) and (II), 180° rotation of s-cis form about the C–C single bond to s-trans destroys weakly stabilizing ($5\pi/4$) structure present in the s-cis but does not create any new crowded π structure in the s-trans.

We would therefore expect that s-cis forms of (I) and (II) will be more stable than the s-trans forms. STO-3G results in Table 1 show that the total energy differences between s-cis and s-trans forms are in general quite small, except for (I) with $X=NH_2$ for which the s-cis is less stable but has more favorable π-NBI over the s-trans.

In system (III), a weakly stabilizing ($5\pi/4$) structure present in the s-cis is lost and a destabilizing ($4\pi/4$) structure is formed in the s-trans. Here again s-trans forms are more stable (Table 2) for $X=-NH_2$ and CH_2^-, which are contrary to what we would expect from the π-NBI effect. The π overlap population between the two terminal centers, $P_{ij}{}^\pi$, of ($5\pi/4$) structure is however positive (i. e., attractive and hence stabilizing) and the total π overlap population is greater ($\Delta P_{tot}{}^\pi > 0$) for the s-cis indicating favorable π-NBI effect. The $P_{ij}{}^\pi$ for the ($4\pi/4$) structures in the s-trans forms

TABLE 1: Relative energies (kcal/mol) of s-cis Conformer with with Respect to s-trans for Structures (I) and (II). Positive Values Correspond to Destabilization

Compound X / E_{rel}	I		II	
	$-OH$	$-NH_2(sp^2)$	$-OH$	$-NH_2(sp^2)$
ΔE_T	0.4	2.9	0.2	-0.2
$\Delta(2\sum_\pi \varepsilon_i)$	43.2	-23.1	1.2	4.3
$\Delta(2\sum_\pi \varepsilon_i)$	4.2	-2.0	1.9	0.0
$\Delta(V_{nn}-V_{ee})$	-42.8	26.0	-1.0	-4.5

TABLE 2: Relative Energies (kcal/mol) and Populations of s-cis Conformer with Respect to s-trans for Structure (III). P^π_{ij} for ($4\pi/4$) in s-trans was $\sim -10^{-2}$

E_{rel} / X	$-OH$	$-NH_2(sp^2)$	$-CH_2^-(sp^2)$
ΔE_T	-1.0	6.5	10.3
$\Delta(2\sum_\pi \varepsilon_i)$	62.8	-9.4	221.6
$\Delta(2\sum_\pi \varepsilon_i)$	8.0	-0.4	31.7
$\Delta(V_{nn}-V_{ee})$	-63.8	-15.9	-211.3
$P^\pi_{ij}\times10^4$	1.2	1.2	4.2
ΔP^π_{tot}	0.01	0.01	0.05

was negative (repulsive and hence destabilizing) as expected of the structure.

In system (IV) and (V), ethylene group in (III) has been replaced by a pseudo π group $-CH_3$ or $-NH_2$. In the system (V), one terminal group is formed by an isoconjugate π structure of $-NH_2(sp^3)$, which has characteristic π group orbital as shown by methylene group.[6a] In both systems again, the s–*cis* form contains a $(5\pi/4)$ structure, while the s–*trans* has a $(4\pi/4)$. Tables 3 and 4 show that for all the compounds investigated the s–*cis* form is preferred rather than the s–*trans* due to favorable π–NBI in the former. The $P_{ij}{}^\pi$ and $\Delta P_{tot}{}^\pi$ values are also as expected from the crowded π structures present in each conformer.

We can therefore conclude that the systems having a terminal π lone pair (sp^2 center) behave normally as far as π–NBIs are concerned, except when the systems have an ethylene group on the other terminal, *i. e.*, when both ends of crowded π structure are sp^2 centers.

Recently the same type of s–*cis* preference relative to s–*trans* has been shown for simple alcohols, amines and ethers which contain similar isoconjugate π structures, using geometry optimized 4–21G computations.[2] The results agreed well with predictions based on π–NBI as well as with experiment.[10] One conclusion drawn from these studies is that in a π crowded sytem a terminal p_π orbital formed with two hydrogen atoms of methylene[11] or amine group, interact through space with another terminal X which is a π electron-rich $(2\pi/1)$ center (Figure 3). One example of such system is provided with acetic acid, in which another heteroatom, a carbonyl oxygen, is involved, Relative energies and populations are given in Table 5 for the two conformers of acetic acid. Since the s–*cis* form contains a $(5\pi/4)$ structure with a terminal pseudo π group orbital, it is expected to be preferred rather than the s–*trans* form as confirmed by calculations given in Table 5.

However the $P_{ij}{}^\pi$ value for $(5\pi/4)$ structure is negative although it is numerically smaller than that for $(4\pi/4)$ structure. The sign reversal of $P_{ij}{}^\pi$ for $(5\pi/4)$ structure is due to the approximation we adopted; in the FMO approximation, the sign of $P_{ij}{}^\pi$ is judged by using the AO coefficient of two end atoms i and j in the π-HOMO.[3a] Strictly however $P_{ij}{}^\pi$ should be given as a sum of individual overlap population, $P_{ij}{}^\pi(\Psi_n{}^\pi)$, for occupied π orbitals, Ψ_n, so that $P_{ij}{}^\pi = \sum_{n=1}^{occ} P_{ij}{}^\pi (\Psi_n{}^\pi)$ For the $(5\pi/4)$ structure $\Psi_3{}^\pi$ is the π-HOMO which is singly occupied. Furthermore the $(5\pi/4)$ crowded π-system in the s–*cis* conformer of acetic acid contains a strong electron-withdrawing group, *i.e.*, $-C=O$, within the structure, and hence AO coefficients of end atoms, i and j, for $\Psi_3{}^\pi$ will be numerically reduced. As a result contribution of $P_{ij}{}^\pi(\Psi_3{}^\pi)$ to $P_{ij}{}^\pi$ becomes smaller enabling the observed sign reversal of $P_{ij}{}^\pi$ to occur for $(5\pi/4)$ structure. This situation will be remedied when the electron-withdrawing group is removed as in ethanol. The results in Table 6 show that products of terminal AO coefficients, $P_{ij}{}^\pi$, for occupied orbitals are indeed influenced by the introduction of carbonyl group in acetic acid in the direction toward negative $P_{ij}{}^\pi$ value.

The sign reversal of $P_{ij}{}^\pi$ for $(5\pi/4)$ structure however does

TABLE 3: Relative Energies (kcal/mol) and Populations of s–cis Conformers with Respect to s–trans for Structure (IV)

E_{rel} \ X	—OH	—NH₂(sp²)	—CH₂⁻(sp²)
ΔE_T	−2.7	−3.7	−22.9
$\Delta(2\sum_\pi \varepsilon_i)$	−10.9	−5.4	−88.1
$\Delta(2\sum_\sigma \varepsilon_i)$	−0.1	−1.8	−3.4
$\Delta(V_{nn} - V_{ee})$	8.2	1.7	65.2
$P_{ij}{}^\pi \times 10^4$	1.0	1.5	5.3
$\Delta P_{tot}{}^\pi$	0.01	0.01	0.05

TABLE 4: Relative Energies (kcal/mole) and Populations of s–cis Conformers with Respect to s–trans for Structure (V)

E_{rel} \ X	—OH	—NH₂(sp²)	—CH₂⁻(sp²)
ΔE_T	−6.1	−2.5	−10.0
$\Delta(2\sum_\pi \varepsilon_i)$	−33.9	−88.3	−8.7
$\Delta(2\sum_\sigma \varepsilon_i)$	−6.1	−17.7	1.6
$\Delta(V_{nn} - V_{ee})$	27.8	85.8	−1.3
$P_{ij}{}^\pi \times 10^4$	1.3	2.1	2.6
$\Delta P_{tot}{}^\pi$	0.01	0.01	0.02

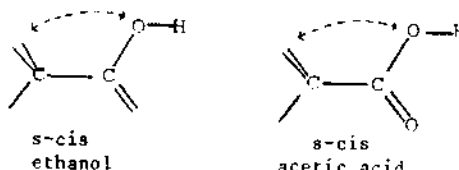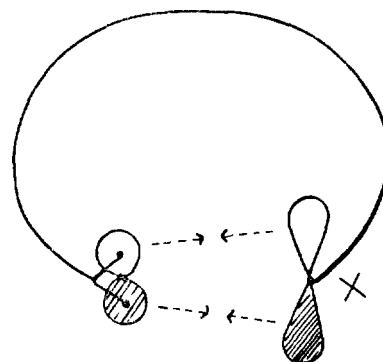**Figure 3.** Strong through–space interaction between $-CH_2$ (or-NH_2) group orbital which have two nuclei within one p_x orbital and large p_x orbital of X which have two π electrons in one center $(2\pi/1)$.

TABLE 5: Relative Energies (kcal/mol) and Populations for s–cis and s–trans Conformers of Acetic Acid

conformer E_{rel}	s–*cis*	s–*trans*
ΔE_T	−0.4	0.0
$\Delta(2\sum_\pi \varepsilon_i)$	−2.5	0.0
$\Delta(2\sum_\sigma \varepsilon_i)$	−0.5	0.0
$\Delta(V_{nn} - V_{ee})$	2.1	0.0
$P_{ij}{}^\pi \times 10^4$	−5.8	−15.0

not invalidate our qualitative prediction, using π–NBI method, of preference for the conformer with a $(5\pi/4)$ structure, s–*cis*, relative to the conformer with a destabilizing $(4\pi/4)$, s–*trans*.

Next we will examine conformational stabilities of glycine and glycine methyl ester as shown in Figures 4 and 5. Two

TABLE 6: Terminal AO Coefficients for Occupied π MOs of Ethanol and Acetic Acid

s-cis
ethanol

s-cis
acetic acid

| Compound	AO	$\Psi_1{}^\pi$	$\Psi_2{}^\pi$	$\Psi_3{}^\pi$(HOMO)	$P_{ij}{}^\pi$
Ethanol	H_2	−0.192	0.376	−0.069	
	$P_z(0)$	−0.266	−0.294	−0.913	1.0×10^{-4}
Acetic acid	H_2	−0.306	0.276	0.084	
	$P_z(0)$	−0.315	−0.606	0.676	-5.8×10^{-4}

TABLE 7: Relative Energies (kcal/mol) Obtained by Various Basis Sets and Experiment *in Debye

Conformer	$\Delta E_T(STO\text{-}3G)$	$\Delta E_T(4\text{-}31G)$[14]	$\Delta E_T(4\text{-}21G)$[8a]	$\Delta E_T(\exp.)$[13]	$\Delta(2\sum \varepsilon_i)$	$P^\pi{}_{tot}$	μ^{*8a}
VI	0.0	0.0	0.0	0.0	0.0	0.9156	1.10
VII	1.1	2.2	2.2	1.4±0.43	116.1	0.0966	6.54
VIII	1.9	2.6	1.9	—	14.1	0.9139	1.76

stable forms of glycine, (VI) and (VII) have been detected by Brown et al.[12] and Suenram et al.[13] using gas phase microwave spectra. On the other hand another conformer (VIII) has been suggested by Pople[14] as one of the local minima in the potential energy map constructed from 4-31G computations. This conformer (VIII) was found to be the third most stable form according to the ab initio MO calculations of Schäfer et al.[15] The conformational stability predicted by the π-NBI method is (VI)>(VIII)>(VII) as can be judged by the additive effect of composite π structures shown in Figure 4.

The STO-3G computational results obtained are summarized in Table 7 together with other literature data. Reference to Table 7 indicates that there is an agreement as to the most stable conformer which is (VI), but the relative stability of the other two forms, (VII) and (VIII) are not decisive and depends on the basis set used in the computation. However the relative stability obtained, (VIII) > (VII), from the results of 4-21G geometry optimized computation without any geometrical constraints agrees well with our prediction based on the π-NBI effect. Experimentally the conformer (VII) has larger electric dipole moment giving the larger transition intensity to (VII) in the microwave spectrum although the actual amount of (VII) present is very small compared to (VI).[8a]

The MO theoretical calculation of Schäfer et al[8b] on glycine methyl ester gave four local minima, (IX~XII), which have symmetry planes. The conformations are shown in Figure 5 together with composite π crowded structures in each forms. Our STO-3G results are presented in Table 8, again with relevant literature data. The relative order of stability predicted[16] with our π-NBI method, (IX)>(X)>(XI)>(XII), agrees with that obtained by the ab initio calculations in Table 8. In this compound there are no clear cut trends in one-electron factors $(\Delta 2\sum \varepsilon_i)$ and in hyperconjugative π delocalization effect, $P_{tot}{}^\pi$, due to the complex involvements of fragments and heteroatoms. However as we have already pointed out above, general trend of relative stability agrees

(VI)   (VII)   (VIII)
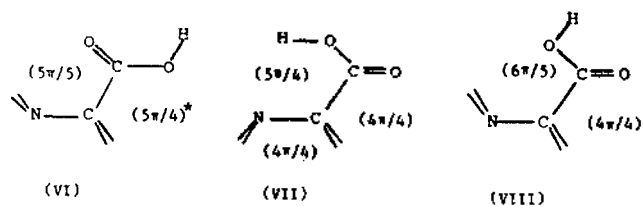
Figure 4: Conformations with composite π structures of the glycine. $*P_{ij}{}^\pi = -6.5 \times 10^{-4}$.

(IX)   (X)   (XI)   (XII)
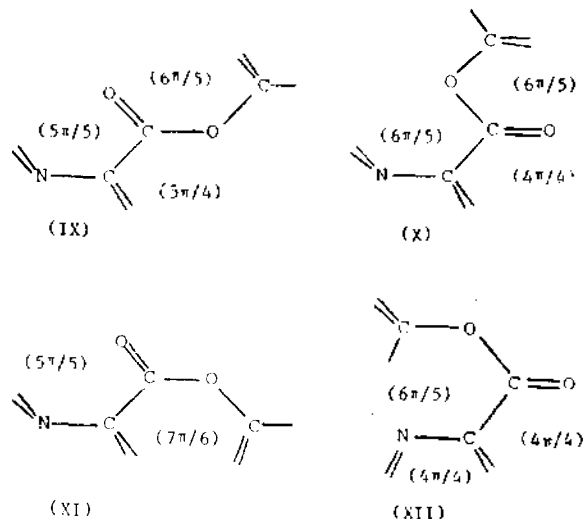
Figure 5: Conformations with composite π structures of glycine methyl ester.

TABLE 8: Relative Energies (kcal/mol) Obtained by Various Basis Sets and Total π Overlap Populations.

Conformer	$\Delta E_T(STO\text{-}3G)$	$\Delta E_T(4\text{-}21G)$[8b]	$\Delta(2\sum \varepsilon_i)$	$P_{tot}{}^\pi$
IX	0.0	0.0	0.0	1.2799
X	0.7	2.0	−1.9	1.2784
XI	7.4	10.7	−111.1	1.2791
XII	22.0	18.5	269.9	1.2710

well with the results of quantitative MO calculations. The forms (XI) and (XII) were not detected in gas electron diffrac-

tion spectra reported by Klimkowski *et al.*,[17] for the two are high energy conformers being unstable by 10 or more kcal/mol. The most stable form obtained from the spectra was the conformer (IX), which was confirmed again by MO constrained electron diffraction.[17]

The P_{ij}^{π} values of (5π/4) structures containing carbonyl groups in various conformers of glycine and glycine methyl ester above had negative values of $\sim -6.5 \times 10^{-4}$.

Lastly we should point out limitations in the applications of π-NBI method: since the π-nonbonded interactions involved in conformational and/or configurational problems are small, the method will not be applicable to geometrical isomerism. One such example is the relative stabilities of geometrical isomers of alkyl substituted alkenes recently reported by Whangbo *et al.*[18] In this type of geometrical isomerism, greater energetic contribution controlling the stability other than the π-NBI are involved and hence the π-NBI method is not expected to work.

Conclusions

(i) The relative stability of conformational isomers can be determined in general by the simple application of the π-NBI method, but the method is not applicable to the geometrical isomerism.

(ii) The π-NBI effect of a crowded π-structure $(n\pi/m)$ is maximum in the system with $n = m$; the effects are $(5\pi/5)$ $(5\pi/4)$ and $(6\pi/6) > (6\pi/5)$, etc.

(iii) In crowded structures containing heteroatoms, P_{ij}^{π} values of $4N + 1$ system may become negative, but this sign reversal does not invalidate the predictions based on the π-NBI method.

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(16) Composite π structures show that relative stability is expected to be (IX) $>$ (X) $>$ (XI) $>$ (XII), since π structures involved are: (IX) all three, (5π/4), (5π/5), and (6π/5) are stabilizing; (X) two stabilizing, 2 $\times$ (6π/5) and one destabilizing, (4π/4); (XI) one stabilizing, (5π/5) and one destabilizing, (7π/6); (XII) two destabilizing, 2 $\times$ (4π/4) and one stabilizing, (6π/5).

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