

Jaume Capdevila and Enric Canadell*

Facultat de Química, Universitat de Barcelona, Pl. Imperial Tarraco, Tarragona, Spain

Received November 30, 1980

The conformational preferences for some 2-substituted furans and pyrroles have been studied by MINDO/3 and a qualitative model including solvent effects is proposed.

J. Heterocyclic Chem., **18**, 1055 (1981).

The conformational preferences for carbonyl substituted furans and pyrroles have been a subject of considerable discussion. It seems well established that furan-2-carbaldehyde preferentially adopts the *trans*-form (**1**) in the vapor phase and in nonpolar solvents (1), whereas the *cis*-isomer (**2**) is the most abundant species in dipolar solvents (2). However, pyrrole-2-carbaldehyde adopts the *cis*-form both in the vapor phase (3) and in polar and non-polar solvents (4). These and other related observations were first interpreted in terms of dipole-dipole interactions between the substituent and the heterocyclic ring but, as it has been pointed out (5), this interpretation is



open to criticism. Recently, several theoretical studies have been reported (5,6) but a simple rationalization of these apparently conflicting facts has not been proposed.

In order to provide some insight into the problem, we have performed MINDO/3 calculations (7) with complete optimization of geometries on a series of substituted-pyrroles and furans. Some results (8) are collected in Table I. It can be seen that the conformational preferences for furan-2-carbaldehyde and pyrrole-2-carbaldehyde are correctly predicted. By detailed inspection of the molecular orbitals obtained in the calculations a simple rationalization can be suggested.

Table I

Relative Energies of *cis*- and *trans*-Conformations of 2-Substituted Furans and Pyrroles. The Energies Are Those of Fully Minimized Geometries (kcal/mole).

R	X	E(<i>cis</i>)-E(<i>trans</i>)
CHO	NH	-1.5
CH=CH ₂	NH	-0.6
COCH ₃	NH	-1.9
CHO	O	1.3
CH=CH ₂	O	-1.0
COCH ₃	O	3.8

The PMO theory provides an elegant framework for the discussion of conformational problems (9); the molecules

are divided into several fragments and the interactions between the fragment orbitals in different conformations are considered. Furan-2-carbaldehyde is a good starting point for the analysis; the carbonyl group and the furan cycle are the convenient fragments here. Both σ and π type interactions are important but we shall focus our attention on the π interactions. The π orbitals of furan are as shown in Figure 1 (10).

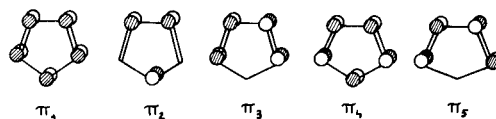


Figure 1. Schematic representation of π molecular orbitals of furan (10).

Clearly, only those orbitals with very different coefficients in C $_{\beta}$ and O will be important in determining a preference for *cis*- or *trans*- conformations. As π_2 does not have an appreciable coefficient in C $_{\alpha}$, only the interactions between π_3 , π_5 and the carbonyl orbitals are to be considered.

The four-electron destabilizing interaction **1** ($\pi_{CO} \rightarrow \pi_3$) will favor the conformation with lesser overlap between the fragment orbitals. As can be seen from the Figure 2, the positive secondary overlap between C $_{\beta}$ and O disfavors the *trans*-conformation.

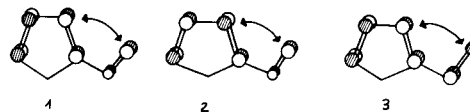


Figure 2. π -Type interactions in furan-2-carbaldehyde.

The two-electron stabilizing interactions **2** ($\pi_{CO} \rightarrow \pi_5$) and **3** ($\pi^*_{CO} \rightarrow \pi_3$) will favor the conformation with greater inter-fragment overlap. In both cases, there is a negative secondary overlap between C $_{\beta}$ and O in the *trans*-conformation and, consequently, the *cis*-conformation is favored by the two interactions. Let us

note that interactions **1** and **2** are more important than **3** in determining the conformational preference owing to the greater oxygen coefficient in π_{CO} .

Thus, the *cis*-conformation is clearly favored from π -orbital interactions. But there is a strong destabilizing interaction between the two σ lone pairs of the oxygens in the *cis*-conformation that outweighs the effect of π -orbital interactions. We conclude that the *trans*-conformation is favored.

According to the argument, the preference must be reversed by suppression of the σ -orbital interaction. We can accomplish this in several ways: a) By suppression of the heterocyclic lone pair. This is the case in pyrrole-2-carbaldehyde. Both the theoretical calculations (Table I) and the gas phase experimental results (1) indicate that the *cis*-conformation is favored. b) By suppression of the substituent lone pair. A possible example is 2-vinylfuran. Again, the *cis*-conformation is calculated to be the most stable. c) It can be argued that the results in a) and b) can be understood also on the basis of a weak intramolecular hydrogen bond. This is not the case in 2-vinylpyrrole, where the two lone pairs have been suppressed and, indeed, the calculations show that the *cis*-conformation is preferred.

The preference may also be reversed by an increase in the factors that create a bias for the *cis*-conformation in the π -interactions. In the case at hand, this is accomplished mainly by an increase in the positive secondary overlap in **1** and in the negative secondary overlap in **2**. This is precisely what would be obtained by the perturbing influence of a polar solvent.

In our qualitative model, the effect of the solvent may be modelled by the electric field of positive charges near the oxygens. Under this perturbation, there will be a mixing of the original orthogonal orbitals. The rules for this mixing have been worked out by Imamura and Hirano (11). When the perturbation is due to a positive charge, and assuming the initial orbitals (Ψ_i^0 , Ψ_j^0) are in phase at the nearest neighbor (r) of the charge, the perturbed orbital (Ψ_i) shows positive contributions from the initially higher energy orbitals (ϵ_i^0) and negative contributions from the initially lower energy orbitals (ϵ_j^0).

The magnitude of the mixing is proportional to the product of the coefficients C_i^0, C_j^0 , and inversely proportional to the difference $|\epsilon_i^0 - \epsilon_j^0|$. By application of these rules it is found that the oxygen coefficient in π_{CO} increases while the coefficients for C_β at the antisymmetric orbitals of the heterocycle are not changed. Then, the two important interactions **1** and **2** will now more strongly favor the *cis*-conformation. There is a decrease of the oxygen coefficient in π^*_{CO} and thus interaction **3** runs in opposite direc-

tion. But this is a less important interaction and furthermore, the effect of a small coefficient becoming smaller is largely dominated by that of a high-valued coefficient becoming higher. The result is a net increase in the preference for the *cis*-conformation when going from gas phase to polar solvents. This does not have major consequences for pyrrole-2-carbaldehyde but produces the aforementioned inversion in furan-2-carbaldehyde.

In short, a very simple electronic effect is the basis for the conformational preferences for these molecules, and we wish to emphasize that many other interesting problems, such as the effect of substituents on reactivity and conformational preferences, can be rationalized by similar arguments (12).

Acknowledgement.

We are greatly indebted to Drs. J. Oivella and R. Caballol for making available their computer programs, to Dr. J. Sueiras for a critical reading of the manuscript and to one of the referees for correcting the style of this manuscript.

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- (8) We have studied a long series of furans and pyrroles substituted at positions of 2 and 3, the substituents being CHO, COCH₃, COOH, CONH₂ and CHCH₃. Because our optimized MINDO/3 results are in reasonable agreement with the STO-3G results published by Radom, *et al.* (5, 6), the only results reported here are those useful for the qualitative reasoning. Details about the complete series of calculations may be obtained from the authors.
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