

## The Direction of the Dipole Moments of Furan, Thiophen, and Pyrrole: A Controversial Question

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The report that the dipole moment in the five-membered heterocyclic rings, furan, thiophene, and pyrrole has the positive pole on the heteroatom is contradicted with arguments based on reactivity data, theoretical calculations and moment values of substituted derivatives.

In actuality, the dipole moment in furan and thiophene is directed from the ring (positive pole) to the heteroatom (negative pole).

The direction of the dipole moments (1) of furan (0.67 D), thiophene (0.53 D), and pyrrole (1.80 D) depends on the relative importance of the inductive (electron withdrawing) and the opposing conjugative (electron releasing) effects exerted by the heteroatoms.

Recent literature on heterocyclic chemistry (2) reports that, in these three fundamental five-membered rings, the dipole moment is directed from the positive heteroatom towards the C(3)-C(4)-bond. The main argument in favor of this hypothesis is based on the high reactivity of these compounds toward electrophilic substitution, which is considered an indication of a high ground state electron density at the ring carbons.

Such an argument must be handled with prudence since the reactivity data refers to both reactants and the transition states, whereas the dipole moments are properties of the ground states only. However, a critical examination of all the reactivity data (not only of electrophilic substitutions but also of other reactions) makes the above argument invalid. Moreover, an examination of the moment values of substituted derivatives and the theoretical

calculations lead to the conclusion that the statements reported in the literature (2) are not correct, with regard to furan and thiophene.

### Aromatic Substitutions.

Furan is much more reactive than thiophene with regard to electrophilic substitution (3) (Table I), although the electron density on the carbon atoms is surely lower in the former ring. In fact, the inductive electron attracting effect of oxygen (because of the greater electronegativity of this atom) is much greater than that of the sulfur atom and, on the other hand, the electron releasing conjugative effect should be less important in furan than in thiophen, as shown by the larger degree of "bond fixation" observed in the furan ring. Other factors must be mainly responsible for the high reactivity of furan, *i.e.* low localization energies. That the reactivity is not directly related to the ground state electron distribution is also confirmed by the fact that furan and thiophene are more reactive than benzene also in nucleophilic substitutions, although in these latter reactions the electronic require-

TABLE I

Relative Reactivities of Furan, Thiophene, and Pyrrole in Electrophilic Substitutions

Compound	Acetylation (a)	Trifluoroacetylation (b)	Formylation	Bromination
Thiophene	1	1	1	1
Furan	11.9	$1.4 \times 10^2$	$1.0 \times 10^2$	$1.2 \times 10^2$
Pyrrole	---	$5.3 \times 10^7$	-----	$5.9 \times 10^8$

(a) Tin tetrachloride-catalyzed acetylation by acetic anhydride. Ref. 4. (b) Reaction with trifluoroacetic anhydride in dichloroethane. Ref. 5. (c) Reaction with phosgene and dimethylformamide in chloroform. Ref. 6. (d) Relative rates of bromination at position 5 of the 2-methoxycarbonyl derivatives in acetic acid. Ref. 7.

ments are opposite. For example, halogenderivatives of furan react about ten times as fast as the corresponding benzene derivatives in the reaction with methoxide ions (8). Also, in substitutions activated by nitro groups, the furan and thiophene rings are far more reactive than the benzene ring (Table II).

TABLE II

Relative Reactivities of the Benzene, Thiophene, and Furan Rings toward Nucleophilic Substitution of the Bromonitroderivatives (a)

Compound	k/k <sub>0</sub>
1-Bromo-4-nitrobenzene	1
2-Bromo-5-nitrothiophene	4.7 x 10 <sup>2</sup>
2-Bromo-5-nitrofuran	8.9 x 10 <sup>4</sup>

(a) Reaction with piperidine in ethanol, ref. 9.

#### Side Chain Reactivities.

The pK<sub>a</sub>'s of the 2- and 3-carboxylic acids of thiophene, furan, and pyrrole are reported in Table III. While

TABLE III

Ionization Constants of the Carboxylic Acids in Water, at 25°

Acid	pK <sub>a</sub>	Ref.
Benzoic acid	4.21	10
2-Furoic acid	3.16	11
3-Furoic acid	3.95	12
2-Thiophenecarboxylic acid	3.53	11
3-Thiophenecarboxylic acid	4.10	13
2-Pyrrolecarboxylic acid	4.45	11
3-Pyrrolecarboxylic acid	5.07	14

pyrrole carboxylic acids, as the alkoxy and amino-substituted benzoic acids, are weaker, thiophene and furan-carboxylic acids, like the chloro and bromobenzoic acids, are stronger than the unsubstituted benzoic acid.

Quantitative data on other side-chain reactions of derivatives of furan, thiophene, and pyrrole confirm this particular behavior (15).

#### Molecular Orbital Calculations.

All recent theoretical calculations of the electron distributions (16-20), which include the contribution of the sigma electrons, agree that in thiophen and furan the heteroatoms are negatively charged with respect to the carbon atoms.

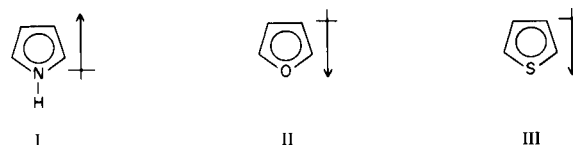
#### Dipole Moments of Derivatives.

In recent years, several research groups (20-24) have determined the dipole moments of many thiophen and furan derivatives bearing a substituent at the α- or the β-position. The agreement between experimental moment values and those calculated on the basis of vector additivity can be obtained only on the assumption that the dipole moments of the unsubstituted thiophene and furan are directed from the pentagonal ring to the heteroatom.

For pyrrole the situation is different. In fact, the dipole moment of pyrrole (1.80 D) is larger than that of the tetrahydro derivative (1.57 D): only if the directions of the dipole moments of pyrrole and tetrahydropyrrole are opposite, does this difference become understandable.

#### Conclusions.

To summarize, in pyrrole (I) the mesomeric π-moment overcomes the electrostatic σ-moment, leading to a charge



distribution similar to that of anisole or aniline. This hypothesis is confirmed by the fact that pyrrole itself is a weak acid and that the basic center is not the nitrogen atom but the α-carbon (25).

For furan (II) and thiophene (III), all the available data favor an opposite situation, similar to that of the halobenzenes, in which the inductive effect is prevailing and the dipole moment is directed from the ring (positive pole) to the heteroatom (negative).

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