formation. The present paper, then, provides a firm foundation for the continuing research of Salem and colleagues[6] on the subject of sudden polarizations.

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Conformations, Stabilities, and Charge Distributions in 2- and 3-Monosubstituted Thiophenes. An ab Initio Molecular Orbital Study

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Abstract: Ab initio molecular orbital theory with the STO-3G basis set is used to determine the equilibrium geometry for thiophene and to study the conformations, stabilities, and charge distributions of several monosubstituted thiophenes. The conformational preferences are rationalized in terms of orbital interactions and electrostatic interactions. The stabilizing effect of substituents attached to thiophene, furan, and benzene rings is compared. As with the furyl group, the thienyl group usually prefers to act relative to phenyl as a π-electron donor and σ-electron acceptor and it is stabilized by substituents characterized as being π-electron acceptors and σ-electron donors. These effects are greater at the 2 than at the 3 position. Differences between the thiophene and furan derivatives are discussed.

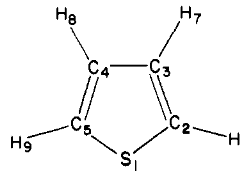
Introduction

The conformational problem which arises when an asymmetric planar substituent is attached to an unsaturated five-membered ring has attracted continued theoretical and experimental interest.[1-7] The preference between the two possible planar conformations of the resulting monosubstituted heterocycles is often strongly medium dependent because of their differing polarities. In these circumstances, the conformational preference in the absence of solvent is of some importance. Ab initio molecular orbital theory provides a means of determining such intrinsic conformational preferences. Detailed ab initio studies have previously been reported for monosubstituted furans[1,2] and pyrroles.[2,3] In this paper, we present the results of a similar though less extensive study for 2- and 3-substituted thiophenes, Th-Z, with Z = H, CHO, OH, $CHCH_2$, CH_3, CN, NO_2, F, and Li. In addition to the conformational preferences that are of interest for some of these molecules, we examine in all cases the effect of the substitutent on stability and charge distribution. Extensive comparison is made with the previously reported results for monosubstituted furans[1] and monosubstituted benzenes.[8]

Computational Aspects and Results

Standard LCAO SCF molecular orbital theory was employed using a modified version of the GAUSSIAN 70 system of programs.[9,10] Unless otherwise specified, calculations were carried out at the STO-3G minimal basis set level of theory.[11,12] Some calculations were carried out with the split-valence 44-31G set.[13] Although there is some debate in the literature as to the importance of inclusion in the basis set of d-type functions on sulfur, we note that both STO-3G and 44-31G basis sets have been successfully employed in previous studies[14-16] of the structures and energies of sulfur-containing molecules.

As a first step in the present study, the geometry of thiophene (**1**) was fully optimized subject only to a C_{2v} symmetry constraint. The optimized structure and comparative experimental data[17-19] are shown in Table I.



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For the substituted thiophenes, the geometry of the thiophene nucleus was taken from the STO-3G fully optimized structure while standard bond lengths and angles[20] were used for the substituent groups. Only cis and trans conformations were considered in this work; the cis form is defined as having the heaviest (i.e., generally nonhydrogen) atom of a substituent group cis to the ring sulfur atom (cf. **2** and **3**). For a methyl

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Table I. Comparison of Theoretical (STO-3G) and Experimental Structures for Thiophene[a]

structural parameter	Harshbarger and Bauer[b] data set 1	Harshbarger and Bauer[b] data set 2	Bak[c] et al.	Bonham and Momany[d]	STO-3G
S_1-C_2	1.718 (4)	1.716 (4)	1.714 (1)	1.714 (4)	1.732
C_2-C_3	1.370 (4)	1.366 (4)	1.370 (2)	1.370 (6)	1.335
C_3-C_4	1.442[e]	1.442[e]	1.424 (2)	1.419 (7)	1.454[e]
C_2-H_6	1.075 (15)	1.070 (12)	1.078 (2)	1.092 (8)	1.079
C_3-H_7			1.081 (1)		1.080
$C_2S_1C_5$	92.0 (0.3)	91.8 (0.3)	92.2 (0.1)	92.2 (0.2)	90.4
$S_1C_2C_3$	112.0 (0.3)	112.1 (0.3)	111.5 (0.3)	111.4 (0.2)	112.8
$S_1C_2H_6$	121.0 (3.0)	121.0 (3.0)	119.8 (0.8)		120.4
$C_3C_4H_8$	123.0 (6.0)	117.0 (9.0)	124.3 (0.1)		123.2

[a] Bond lengths in ångstroms, bond angles in degrees. The figures given in parentheses are reported standard deviations. [b] From ref 17. [c] From ref 18. [d] From ref 19. [e] A dependent parameter shown for comparison.

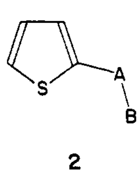
Table II. Calculated Total Energies (hartrees) for 2- and 3-Substituted Thiophenes[a]

molecule	conformation	energy
thiophene		−545.092 32
2-formylthiophene	SCCO cis	−656.319 34
	SCCO trans	−656.318 21
	SCCO cis[b]	−656.322 89
	SCCO trans[b]	−656.321 53
	SCCO cis[c]	−663.156 74
	SCCO trans[c]	−663.155 59
2-hydroxythiophene	SCOH trans	−618.928 96
	SCOH cis	−618.925 42
2-vinylthiophene	SCCC cis	−621.034 00
	SCCC trans	−621.032 54
	SCCC cis[d]	−621.036 28
	SCCC trans[d]	−621.034 72
2-methylthiophene	SCCH trans	−583.677 43
	SCCH cis	−583.676 03
2-cyanothiophene		−635.646 67
2-nitrothiophene		−745.783 05
2-fluorothiophene		−642.548 90
2-lithiothiophene		−551.816 05
3-formylthiophene	C_2CCO trans	−656.318 58
	C_2CCO cis	−656.318 48
3-hydroxythiophene	C_2COH cis	−618.927 58
	C_2COH trans	−618.926 88
3-vinylthiophene	C_2CCC trans	−621.031 20
	C_2CCC cis	−621.030 76
3-methylthiophene	C_2CCH cis	−583.677 29
	C_2CCH trans	−583.675 90
3-cyanothiophene		−635.647 19
3-nitrothiophene		−745.785 55
3-fluorothiophene		−642.549 06
3-lithiothiophene		−551.809 28

[a] Standard geometry for substituent, except as noted. [b] Partly optimized geometry: cis, S_1C_2C = 121.6°, C_2CO = 124.5°, C_2CH = 113.7°, C_2-C = 1.502, C-H = 1.104, C-O = 1.222; trans, S_1C_2C = 121.3°, C_2CO = 123.7°, C_2CH = 114.9°, C_2-C = 1.503, C-H = 1.104, C-O = 1.222. [c] Single 44-31G calculation on the STO-3G optimized geometry. [d] Partly optimized geometry: cis, C_2CC = 126.0°; trans, C_2CC = 126.2°.

substituent, the cis conformation has a methyl C-H bond cis to the ring sulfur.

Previous related calculations[1,3,8] have shown that use of the standard geometric model gives rise to unrealistic steric repulsions for the vinyl substituent. We have therefore optimized the C_2—C=C bond angle of 2-vinylthiophene, the corresponding C-H bond being kept on the bisector of this angle. The resulting flexible rotor model is expected to give, as evidenced by previous work,[21] a reasonable description of conformational behavior. We find here that, although optimization of the C_2—C=C bond angle leads to a widening of about 6°, it has only a small effect on the calculated trans-cis energy difference.



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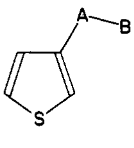
S_1C_2AB *cis*



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C_2C_3AB *cis*

For 2-formylthiophene, an even more extensive optimization has been carried out since this molecule is of particular interest and we wished to ensure that our conclusions were not dependent on the choice of geometric model. Structural parameters related to the CHO substituent, i.e., C_2-C, C-O, C-H, S_1C_2C, C_2CO, and C_2CH, were fully optimized using the STO-3G basis set. A single 44-31G calculation[13] was then carried out at the STO-3G optimized geometry in order to examine the basis set dependence of the results. Interestingly, although the total energies and values of the structural parameters are significantly different, the energy difference between cis and trans conformations is not sensitive to our choice of geometric model or basis set.

Calculated total energies are shown in Table II. The energy differences between trans and cis conformations of substituted thiophenes are compared with corresponding values for substituted furans in Table III. Finally, charge distributions derived using the Mulliken approach[22] are reported. The calculated π-electron distributions are displayed in Figure 1 while total σ and π charges (q_σ and q_π, respectively) donated to the ring by the substituent are presented in Table IV.

Discussion

A. Comparison with Experimental Structural Data. Our fully optimized structure for thiophene is compared with the microwave structure[18] and electron diffraction structures[17,19] in Table I.[23] Agreement between experimental and theoretical bond lengths is generally good. The largest error (about 0.035 Å) occurs for the C_2-C_3 double bond, which, characteristically of STO-3G calculations,[24] is underestimated by the theory. For bond angles, agreement between theoretical and experimental values is also satisfactory with the largest deviation being 1.8° in the $C_2S_1C_5$ angle.

B. π-Electron Distributions. We note initially that our STO-3G π-electron distribution for thiophene itself (Figure 1) agrees qualitatively with the results of previous ab initio calculations[25,26] which employed extended basis sets including polarization functions and were based on the microwave structure.[18] The total π-electron density is greater at the 2 position than at the 3 position and this is related to the enhanced conjugative interaction in the 2-substituted thiophenes.

There appear to be no previously reported ab initio studies

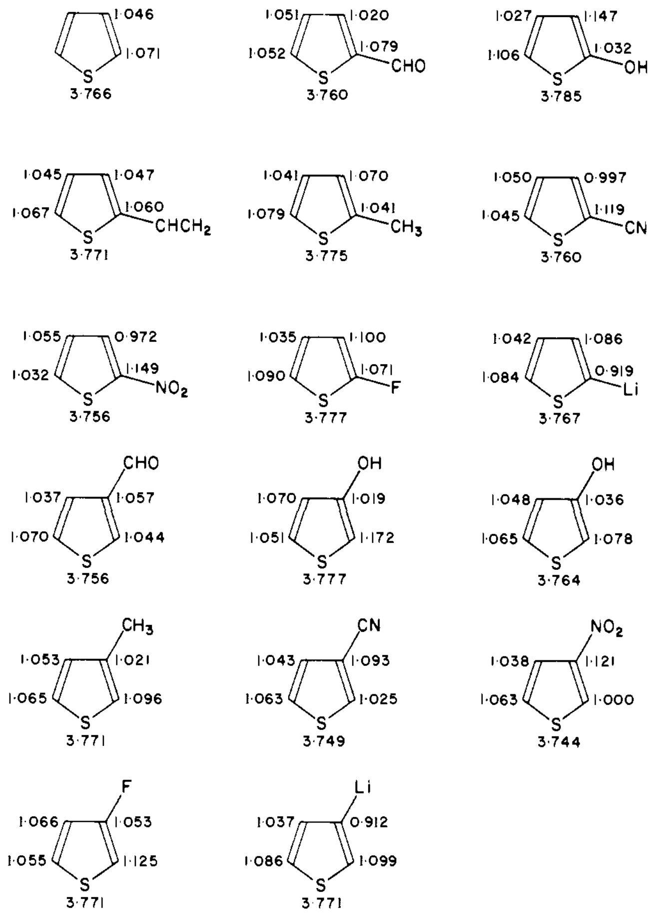


Figure 1. π-Electron populations in substituted thiophenes.

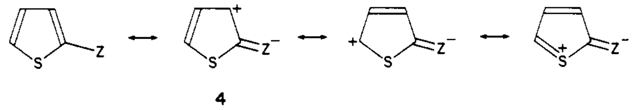
Table III. Calculated Trans-Cis Energy Differences (kJ mol^{-1}) for 2- and 3-Substituted Thiophenes and Furans

substituent	thiophene	furan
2-CHO	+2.97	−4.15
	+3.57[a]	
	+3.02[b]	
2-OH	−9.29	+5.80
2-CH=CH$_2$	+3.83	+3.04
	+4.10[a]	+2.24[a]
2-CH$_3$	−3.68	−2.47
3-CHO	−0.26	+0.01
3-OH	+1.84	−0.57
3-CH=CH$_2$	−1.16	−2.03
		−1.68[a]
3-CH$_3$	+3.65	+3.11

[a] Partially optimized. [b] Single 44-31G calculations on the STO-3G optimized geometry.

on substituted thiophenes. Our calculated STO-3G π-electron distributions for substituted thiophenes are depicted in Figure 1. These show some interesting features, with several of the effects being similar to those in corresponding benzene,[8] pyrrole,[3] and furan[1] derivatives.

We begin with π-electron distributions in thiophenes substituted by π-electron-withdrawing substituents (e.g., Z = CHO, NO$_2$, and CN). These indicate electron delocalization compatible with the valence structures shown in **4** and **5**. A point of interest is that enhanced π-electron donation from the ring heteroatom which occurs to a slight extent in the 2-substituted thiophenes in this class does not appear to occur for the corresponding 2-substituted furans. We also note that π-electron donation from the ring sulfur induced by π-electron-withdrawing substitutents is greater in the 3 position than in the 2 position.



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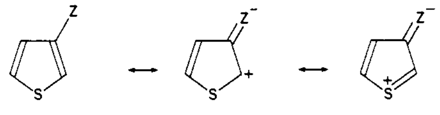

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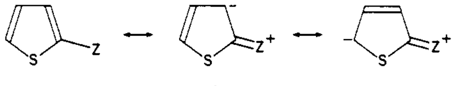
The π-electron populations for thiophenes substituted with π-electron donor substituents (Z = OH, F, CH$_3$) show π-electron donation into the ring in accordance with the valence structures shown in **6** and **7**. As with the corresponding furans,



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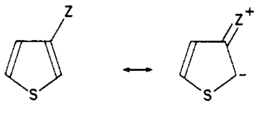

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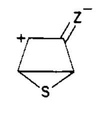
there is an increased π-electron density on the ring heteroatom compared with the unsubstituted molecule. This may be attributed to the retardation of electron delocalization from that atom caused by the presence of the strong π-donor substituent.

As with styrenes and vinylfurans, vinyl substitution in thiophene does not cause a significant π-electron redistribution in the ring. For the lithio substituent, the main effect is a polarization of the π-electrons in the adjacent double bond.

One general point of interest in the 3-substituted derivatives is the enhanced π-electron density at the 2 and 4 positions for π-donor substituents (e.g., OH, F) and reduced π-electron density at the 2 and 4 positions for π-acceptor substituents (e.g., CHO, NO$_2$). This is analogous to the effects observed in the ortho positions of corresponding benzene derivatives. However, for the thiophenes, it is difficult to rationalize the results in terms of the normal valence structures (as shown in **5** and **7**). An additional contributing structure which will account for this aspect of the charge distribution has been suggested previously[27] and involves bonding across C$_2$–C$_5$ as shown, for example, in **8** for a π-accepting Z. Our calculations



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do not provide support for this suggestion since the computed overlap population for C$_2$···C$_5$ is negative.

C. Electronic Nature of the Thiophene Ring. Total σ and π charges (q_σ and q_π, respectively) donated to the ring by the substituent are compared with the values obtained for the corresponding substituted benzenes and substituted furans in Table IV. In general, we find that q_σ values in the substituted thiophenes decrease and q_π values increase relative to their values in corresponding substituted benzenes. We may thus characterize the thiophene ring as being a σ-electron acceptor and π-electron donor, relative to benzene.

Comparison with the substituted furans shows that the q_σ

Table IV. Calculated Total π and σ Charges Donated to the Ring by the Substituent Z[a]

substituent (-Z)	PhZ[b]		2-FuZ[c]		3-FuZ[c]		2-ThZ		3-ThZ	
	q_σ	q_π	q_σ	q_π	q_σ	q_π	q_σ	q_π	q_σ	q_π
-H	−0.063	0	−0.082	0	−0.072	0	−0.071	0	−0.063	0
-CHO	−0.001	0.032	−0.029	0.038	−0.014	0.037	−0.018	0.038	−0.004	0.037
-OH	0.185	−0.102	0.153	−0.094	0.162	−0.085	0.169	−0.098	0.175	−0.089
$-CHCH_2$	0.003	0.006	−0.028	0.006	−0.012	0.011	−0.010	0.011	−0.002	0.008
$-CH_3$	−0.007	−0.008	−0.035	−0.007	−0.019	−0.006	−0.018	−0.007	−0.008	−0.006
-CN	0.104	0.022	0.070	0.027	0.088	0.026	0.092	0.028	0.100	0.027
$-NO_2$	0.227	0.031	0.198	0.034	0.213	0.032	0.216	0.037	0.225	0.034
-F	0.215	−0.080	0.183	−0.071	0.192	−0.067	0.196	−0.073	0.203	−0.069
-Li	−0.266	0.092	−0.290	0.091	−0.260	0.094	−0.266	0.101	−0.246	0.095

[a] q_σ and q_π are the total σ and π charges, respectively, donated to the ring by the substituent Z. A negative sign corresponds to electron donation. [b] From ref 8. [c] From ref 1.

Table V. Stabilization Energies Calculated for Thiophene and Furan Derivatives

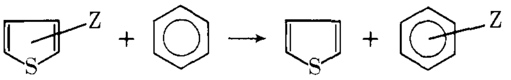
substituent (-Z)	stabilization energy, kJ mol^{-1} [a]			
	2-ThZ	3-ThZ	2-FuZ[b]	3-FuZ[b]
-CHO	4.4	2.4	5.1	1.7
-OH	−5.0	−8.7	6.9	−14.9
$-CHCH_2$	18.2	10.9	29.1	16.6
	11.1[c]		18.5[c]	8.4[c]
$-CH_3$	3.6	3.2	13.6	4.6
-CN	2.9	4.3	−4.7	0.6
$-NO_2$	−6.4	0.2	−18.5	−10.1
-F	−7.2	−6.8	3.2	−13.8
-Li	36.7	17.4	43.4	28.6

[a] Except as noted, results are based on unoptimized geometries. [b] From ref 1. [c] Calculated results based on optimized geometries.

values for the thiophenes are consistently more positive (or less negative), i.e., thiophene is a poorer σ-electron acceptor than furan. On the other hand, q_π values for the thiophenes are either more positive (in the case of π-electron accepting substituents) or more negative (in the case of π-electron donor substituents) than for the furans, i.e., thiophene is both a stronger π-electron acceptor and a stronger π-electron donor than is furan.

D. Stabilization Energies. Some care must be taken in analyzing energetic data in ab initio calculations since heats of reaction are not always well described. For instance, although good agreement with experiment is generally obtained, even with the minimal STO-3G basis set, for heats of isodesmic reactions[28] involving acyclic molecules alone, unsatisfactory values are obtained for reactions involving comparisons of cyclic and acyclic structures.[24b,28,29] The only substituted thiophenes for which comparative gas-phase experimental enthalpies of formation are available[30] are the 2- and 3-methylthiophenes. Our calculated energy difference between these isomers is 0.22 kJ mol^{-1}, in qualitative agreement with the experimental 0.92 kJ mol^{-1}, the 2-methyl derivative being lower in energy.

In this paper, our energetic data are analyzed in terms of substituent stabilization energies, which are defined as the energy changes (ΔE_{SE}) in formal reactions of the type (1).



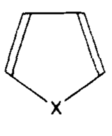
(1)

ΔE_{SE} is a measure of the stabilizing effect of a substituent Z on the thiophene ring compared with its effect in benzene. Similar reactions have previously been defined for pyrrole and furan derivatives.[1-3] Reactions of this type are not only isodesmic but also conserve ring type. We might therefore expect to get good stabilization energies (ΔE_{SE}) even with STO-3G calculations.

Results obtained in this manner are shown in Table V. Also included in Table V are the corresponding results for furan derivatives.[1] In the light of the tendency of the thiophene ring to act as a stronger π-electron donor and a stronger σ-electron acceptor than the benzene ring, we might expect that substituents which are π-electron acceptors and σ-electron donors will stabilize the thiophene nucleus while those acting as π-electron donors and σ-electron acceptors will destabilize the thiophene nucleus. In addition, we would expect the effects to be more pronounced at the 2 than at the 3 position. Indeed, we find positive values of ΔE_{SE} for the σ-electron donor, π-electron acceptor Li substituent, and negative values for the substituents F and OH, which are π-electron donors and σ-electron acceptors. For the remaining substituents, the σ- and π-electron effects either have opposing stabilization properties (e.g., CN, NO_2) or are not sufficiently large to warrant a prediction, on these grounds alone, of the stabilization energy. In all cases, there are, of course, other contributions to the stabilization energy which should be considered. The absolute magnitudes of the stabilization energies are generally greater for the 2-substituted than 3-substituted derivatives, as expected in the absence of specific effects. A notable exception is the hydroxy substituent and this will be discussed further below.

A comparison of stabilization energies for substituted thiophenes with corresponding substituted furans (Table V) is of interest and may be largely interpreted in terms of the lower electronegativity of S (2.5) than 0 (3.5).[31] This property has already revealed itself in the increased q_σ values for the thiophene derivatives (vide supra). For strong σ-electron-withdrawing groups (CN, NO_2, OH, F), it would be expected to lead to less unfavorable σ interaction and, in the absence of other effects, to less negative values of ΔE_{SE}. This is observed for CN and NO_2. For OH and F substitutents, the positive values of ΔE_{SE} in the 2-furan derivatives have been rationalized in terms of a compensating hyperconjugative interaction of the in-plane lone pair at oxygen with the bond to the electronegative group, and in the case of the hydroxy substituent to intramolecular hydrogen bonding as well. We conclude from the ΔE_{SE} values in Table V that both these effects are greatly diminished in the thiophenes.

E. Conformational Analysis. 1. Dipole Moment Considerations. In earlier papers,[1-3] we were able to rationalize the preferred conformations of a variety of heterocyclic derivatives largely in terms of dipole-dipole interactions between the component ring and the substituent. It is therefore instructive as a first step in this work to compare the experimental dipole moments[32] and appropriate dipole directions for several five-membered rings[32,33] as shown in **9**. The dipole direction of a conjugated five-membered ring (**9**) may be analyzed in terms of (a) the possible π-type interaction (**10**) between the filled p_π (or pseudo-p_π) orbital of X and the lowest unoccupied molecular orbital (LUMO) of the butadiene fragment[34] and



(a) $X = CH_2$, ↑ 0·42D
(b) $X = NH$, ↑ 1·74D
(c) $X = O$, ↓ 0·72D
(d) $X = S$, ↓ 0·53D

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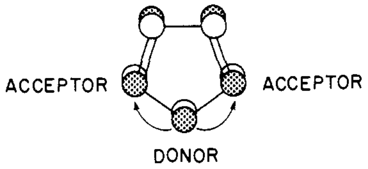

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(b) the electronegativity and inherent dipole moment of the group X. For cyclopentadiene, both effects act in the same direction, producing a dipole directed from X into the ring. For pyrrole, the π effect dominates and the observed dipole direction is the same as in cyclopentadiene. For furan, a combination from the in-plane lone pair on oxygen and the polar C–O bonds leads to a σ component of the dipole moment in the opposite direction and slightly larger than the π component. As a result, the dipole moment of furan is not only smaller than that in pyrrole but also operates in the reverse direction. Finally, the dipole moment in thiophene is in the same direction as in furan but is slightly smaller, presumably owing to the lower electronegativity of S compared with O.

2. Conformational Preferences. We now look at the preferred conformations in substituted thiophenes. In the past few years, the conformational preferences of substituted thiophenes have received considerable attention in the literature.[5-7,35-43] However, most attention has been focused on 2-substituted carbonyl compounds. The microwave spectrum[35a] of 2-formylthiophene was initially interpreted as favoring the trans isomer in the gas phase, but a subsequent analysis[35b] indicates the predominance of the cis form. Other physical methods such as NMR investigations,[37-40] IR spectroscopy,[41] dipole moment measurements,[42] and molar Kerr constants[5] have been employed and suggest that the cis conformation is also the more stable form in solution. X-ray analysis shows that the cis conformation also exists in the solid state for 2-formyl-4-bromothiophene and 2-acetyl-4-bromothiophene.[38,43] Our calculations indicate, in fact, that the cis form is favored over the trans by about 3.0–3.6 kJ mol^{-1} in the gas phase. We also find that the cis form of 2-vinylthiophene is favored by about 4.1 kJ mol^{-1}, which is consistent with the NMR spectra of *trans*-2-(2-thienyl)ethylene.[36] No other experimental results are currently available for comparison with our results shown in Table III.

By way of contrast, let us compare results for substituted thiophenes and furans. Both experimentally and theoretically, the cis form of 2-formylthiophene is favored, as opposed to the trans in 2-formylfuran.[1] Since thiophene and furan have the same dipole direction, the simple picture in terms of dipolar interaction between a five-membered ring and a substituent breaks down here. Apparently, there are other factors involved in this case. Furthermore, although STO-3G and 44-31G calculations give an opposite dipole direction for thiophene (STO-3G, ↑ 0.13 D; 44-31G, ↓ 0.90 D), they both correctly favor the cis form. This result suggests that the preference is dictated by features common to both methods and is not dominated by dipole interactions between the component thiophene ring and the CHO functional group. A stabilizing interaction between the sulfur and oxygen atoms has previously been proposed.[38,40,44] Another point of interest is that the more stable cis form of 2-formylthiophene is more polar than the trans. Thus, the preference for the cis form in the gas phase should be even more pronounced in solution through reaction field stabilization. This contrasts with the situation for 2-formylfuran, where the conformational preference is reversed in moving from gas to solution phase.[2,5]

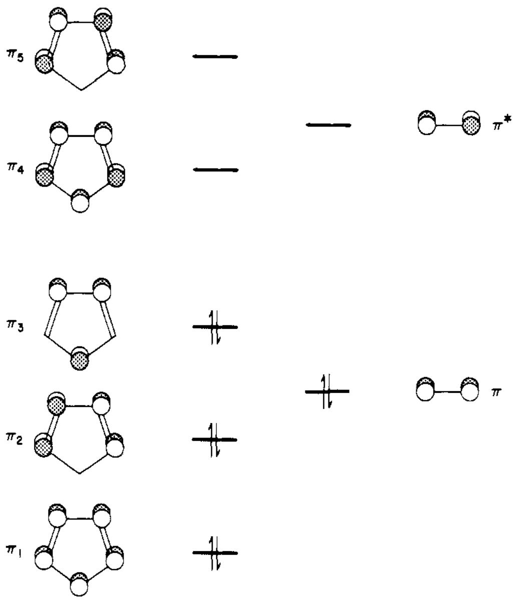
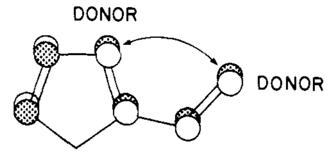


Figure 2. Interacting orbitals of thiophene and a double bond.

For 2-hydroxythiophene, the preferred conformation is predicted to be trans while the cis is predicted to be more stable in 2-hydroxyfuran. Again, the explanation of conformational preference in terms of dipolar interaction alone breaks down here. On the other hand, 2-vinyl-, 2-methyl-, 3-vinyl-, and 3-methylthiophene each have the same conformational preference as the corresponding furan. The conformational energy differences for 3-formylfuran, 3-formylthiophene, and 3-hydroxyfuran are very small; 3-hydroxythiophene appears to favor the cis conformation.

3. Orbital Interactions. In order to rationalize the preferred conformations, we consider both orbital and electrostatic interactions. We begin with orbital interactions which will dictate the preferred conformation for weakly polar or nonpolar substituents. The relevant orbitals of thiophene and a double bond are shown in Figure 2. For a double-bonded substituent (such as $CHCH_2$ or CHO) at the 2 position, the orbital interactions which are expected on the basis of qualitative considerations to be most important in influencing the conformational preferences are the four-electron destabilizing in-



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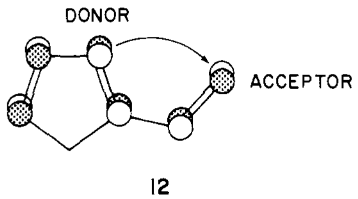

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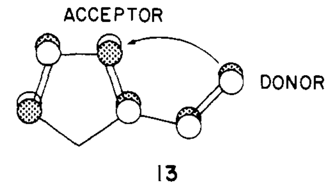

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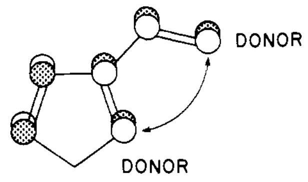
teraction between π_2 and π (**11**) and the two-electron stabilizing interactions between π_2 and π^* (**12**) and between π and π_5 (**13**). All these interactions are relatively unfavorable for the trans conformation and hence lead to a preference for the cis conformation for these systems. For a double-bonded substituent at the 3 position, the interactions which are likely to differentiate between cis and trans conformations are the four-electron destabilizing interaction between π_2 and π (**14**) and the two-electron stabilizing interactions between π_2 and π^* (**15**) and between π and π_4 (**16**). In this case, all the interactions favor the trans conformation. Similar orbital interaction arguments may be used for methyl substituents by considering the π_{CH_3} and $\pi^*_{CH_3}$ group orbitals leading to a preference for the trans conformation at the 2 position and the cis at the 3 position.



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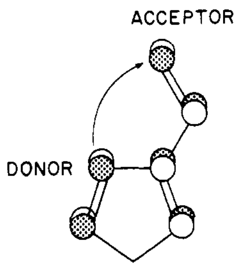

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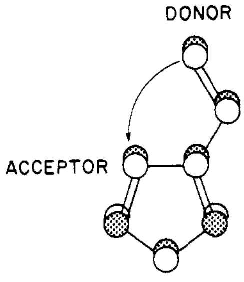

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An alternative rationalization of the conformational predictions produced by the detailed orbital analysis above comes from recognizing initially that the carbon-carbon bonds in the thiophene ring (as in furan[1]) may be distinguished as having more (C_2-C_3, C_4-C_5) or less (C_3-C_4) double-bond character. In addition, we note from known conformational data that a single bond of a substitutent generally prefers to eclipse an adjacent double bond while a double bond of a substituent prefers to be trans to an adjacent double bond. The conformational preferences (e.g., trans for 2-methylthiophene and 3-vinylthiophene, cis for 3-methylthiophene and 2-vinylthiophene) follow immediately.

4. Electrostatic Interactions. Electrostatic interactions become important for more polar substituents. There are two simple mathematical expressions which are commonly used in the literature to account for electrostatic interactions. These are the point-charge interaction model and the dipole-dipole interaction model.[49,50] Both models are approximations and will be accurate only if the interacting dipoles or point charges are reasonably far apart. Here, we have adopted the point-charge model to calculate electrostatic interactions with the hope of obtaining a qualitatively correct picture. Point charges are taken from our ab initio calculations and are located at the corresponding atomic centers. The coulombic interactions were calculated according to the equation

$$E_{es} = \sum \frac{q_i q_j}{r_{ij}} \qquad (2)$$

where r_{ij} is the interatomic distance between atoms i and j with net charges q_i and q_j, respectively. The summation was taken over all atomic pairs with the exception of interactions between two bonded atoms and interactions between atoms bound to a common atom. The relative electrostatic energies obtained in this manner are shown in Table VI.

Table VI. Calculated Trans-Cis Electrostatic Energy Differences (kJ mol^{-1})

substituent (-Z)	thiophene 2-ThZ	3-ThZ	furans 2-FuZ	3-FuZ
-CHO	6.0,[a] 8.8[b]	2.3	−5.9	2.1
-OH	−4.7	−0.1	8.5	−0.1
-CHCH$_2$	0.9[a]	0.0	−0.6[a]	0.4
-CH$_3$	−0.1	−0.2	0.5	−0.1

[a] Calculated results based on optimized geometries. [b] On the basis of single 44-31G calculations on the STO-3G optimized geometries.

As can be seen from Table VI, a significant electrostatic contribution to the conformational preference occurs only for the 2- and 3-formyl and the 2-hydroxy derivatives. For 2-hydroxyfuran, the main contributions which are responsible for the electrostatic energy difference between cis and trans conformations are provided by the attractive interactions of the hydroxy hydrogen with O_1 and C_3. The net result is a preference, on electrostatic grounds, of the cis form by 8.4 kJ mol^{-1}. The main contribution to the electrostatic energy difference between the two conformations of 2-hydroxythiophene also comes from interactions with the hydroxy hydrogen. However, while the C_3···H-O interaction is still attractive, the S_1···H-O interaction in this case is repulsive. This leads to an overall preference for the trans form of 2-hydroxythiophene by 4.6 kJ mol^{-1} from electrostatic interactions.

In looking closely at the electrostatic interactions of 2-formylfuran, we find that the electrostatic interaction between O_1 and the formyl groups (CHO) favors the trans form by 5.4 kJ mol^{-1}. The interaction between H_7 and CHO also favors the trans form (by 0.8 kJ mol^{-1}), but its effect is largely counterbalanced by the interaction between C_3 and CHO, which favors the cis by 1.7 kJ mol^{-1}. Since all of the other electrostatic contributions are approximately of equal magnitude in the two forms, the net result is that the trans is stabilized relative to the cis by 5.9 kJ mol^{-1} owing to electrostatic interactions. For 3-formylfuran, the interaction between O_1 and CHO becomes much less important, although the trans is still preferred (by 1.3 kJ mol^{-1}). The major factors which account for the energy difference between the two conformations are the interaction between C_4 and CHO and the interaction between C_2 and CHO. Both interactions favor the cis form by about 2.0 kJ mol^{-1} each. This leaves the cis form being favored by 2.1 kJ mol^{-1} for electrostatic interactions.

According to STO-3G calculations, the electrostatic interactions between S_1 and CHO in 2-formylthiophene strongly disfavor the trans form (by 7.5 kJ mol^{-1}) because of the close proximity of S_1 and O in the cis form. The C_3···CHO interactions also disfavor the trans (by 1.7 kJ mol^{-1}), because both C_3 and H are positively charged. However, the above two interactions are counterbalanced somewhat by the H_7···CHO interaction which favors the trans by 2.5 kJ mol^{-1}. After some other small contributions are added up, the cis form is favored by 5.9 kJ mol^{-1}. A similar analysis applies to the results obtained by 44-31G calculations. A point of interest is that, although the charge distributions are quite different for the STO-3G and 44-31G calculations, the calculated differences in electrostatic energies are quite similar. This gives some confidence to our analysis based on the STO-3G calculations.

As with 3-formylfuran, the interaction between S_1 and CHO becomes much less important when the formyl group is located at the 3 position of thiophene, but the interaction still favors the cis form (1.7 kJ mol^{-1}). However, the contributions to the electrostatic energy difference between the two conformations are different for 3-formylfuran and 3-formylthiophene. The interaction between the formyl group and the next-neighbor carbons as well as the interaction between the formyl groups and the second-next-neighbor hydrogens are all important now. The C_2···CHO interaction favors the trans by 3.8 kJ mol^{-1} while the C_4···CHO favors the cis by 1.7 kJ mol^{-1}. The H_6···CHO interaction favors the cis by 3.8 kJ mol^{-1} but is compensated somewhat by the H_8···CHO interaction, which favors the trans by 0.8 kJ mol^{-1}. The net result is the cis being favored by 2.1 kJ mol^{-1}.

5. Rationalization of Conformational Preferences. On the basis of our orbital interaction and electrostatic interaction models, the calculated results can be easily interpreted. For the CH_3 and $CHCH_2$ substituents, the electrostatic interaction energies are about the same for planar cis and trans conformations, and consequently orbital interactions will dictate the preferred conformations. Indeed, the calculated trends are consistent with predictions on the basis of orbital interactions for 2-methylthiophene, 3-methylthiophene, 2-methylfuran, 3-methylfuran, 2-vinylthiophene, 3-vinylthiophene, 2-vinylfuran, and 3-vinylfuran.

For 3-hydroxythiophene and 3-hydroxyfuran, the difference in electrostatic interaction energy between cis and trans conformations is small, and the preferred conformation should also be controlled by orbital interactions. The trans form of 3-hydroxythiophene is indeed favored, which is in agreement with considerations of orbital interactions. However, the cis form of 3-hydroxyfuran is calculated to be slightly more stable than the trans, which disagrees with predictions based on orbital interactions. It is possible that the discrepancy is due to the use of standard geometries. For the related vinyl alcohol molecule, geometry optimization is found to be important in reproducing the experimentally observed preference for a C=COH syn conformation.[51]

The trans form of 2-hydroxythiophene is strongly favored by electrostatic and orbital interactions and it is in fact the preferred (by 9.3 kJ mol^{-1}) conformation. In contrast, the cis form of 2-hydroxyfuran is strongly favored over the trans by electrostatic interactions (8.5 kJ mol^{-1}) but is disfavored by orbital interactions; the net result is that the cis form is only 5.8 kJ mol^{-1} more stable than the trans.

For 2-formylthiophene and 2-formylfuran, the preferred conformations also appear to be determined by electrostatic interactions. The small cis-trans energy difference in 2-formylfuran is expected since the trans form, favored by electrostatic interactions, is opposed by orbital interactions. On the other hand, the small trans-cis energy difference in 2-formylthiophene is less expected since both electrostatic and orbital interactions favor the cis form. For 3-formylthiophene and 3-formylfuran, electrostatic interactions prefer the cis (by about 2 kJ mol^{-1}) while orbital interactions prefer the trans. The full calculations do now show a strong conformational preference for either of these molecules.

Conclusions

Several important points should be noted from this study.

(1) The STO-3G structure for thiophene is in reasonable agreement with experimental data.

(2) The STO-3G dipole moment for thiophene is very small but is in the opposite direction to that found experimentally. The 44-31G dipole moment is somewhat too large in magnitude but is in the correct direction.

(3) Despite the poor calculated dipole moments, the theoretical conformational predictions for monosubstituted thiophenes are in qualitative agreement with the currently available experimental data for these systems.

(4) The thienyl group prefers to act, relative to phenyl, as a π-electron donor and a σ-electron acceptor. This leads to the most favorable interactions (i.e., largest stabilization energies) for substituents (e.g., Li) which are π-electron acceptors and σ-electron donors.

(5) Comparison with results for the corresponding substituted furans shows that conformational preferences in substituted thiophenes are the same for nonpolar or weakly polar substituents but may be strikingly different for strongly polar substituents. These differences may be attributed to the lower electronegativity of sulfur compared with oxygen. This property is also reflected in the calculated charge distributions, which show that thiophene is a weaker σ-electron acceptor than furan,

(6) The conformational preferences are readily rationalized through a consideration of orbital and electrostatic interactions.

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Theoretical Exploration of the Photochemical Rearrangement of Oxaziridines

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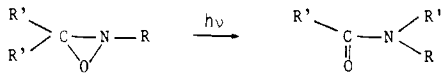
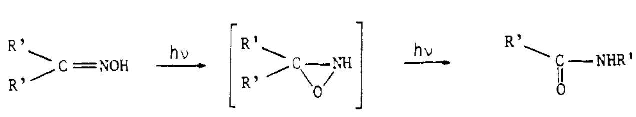
Abstract: The mechanism of the thermal and photochemical rearrangements of oxaziridines into amides has been explored through ab initio calculations using double-ζ plus diffuse basis sets and extensive CI. The lowest singlet excited state of the oxaziridine ring results from an $n_{\pi} \rightarrow \sigma^*_{NO}$ excitation and undergoes the breaking of the NO bond. The H(C) migration does not occur simultaneously; it should proceed on the ground state surface after deexcitation in the open geometry. The regioselectivity of the reaction would be due to an important barrier for the migration of the H atom in syn position with respect to the N lone pair.

Since their discovery by Emmons,[2] oxaziridines have drawn a great deal of attention in view of their practical and theoretical interest.[3-5]

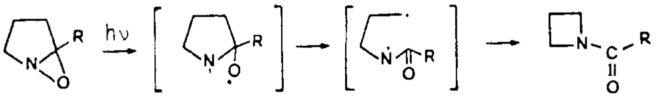
Oxaziridines are photolabile[3b,6] and in the singlet state, the major pathway for their decomposition is the rearrangement into amides with migration of one of the carbon substituents



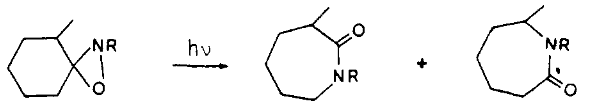
to nitrogen.[7] This reaction is consistent with the suggestion that oxaziridines are intermediates in the photochemical conversion of oximes into the corresponding amides.[7] According to Suginome et al.,[8f] this photo-Beckmann rearrangement may be understood in terms of a rather simple scheme; singlet excited cycloalkanone oximes "are rapidly transformed into intermediate oxaziridines. These oxaziridines undergo excitation to a singlet state and this is reorganized to give lactams without a further intermediate".



However, in the case of fused bicyclic oxaziridines, several authors[6b,c] suggested that the rearrangement proceeds with a biradical intermediate via homolytic cleavage of the N-O bond.

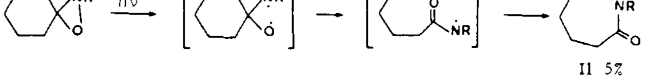


But this free-radical mechanism is also brought into question by the results concerning the photochemical ring expansion of spiro oxaziridines.[6d,9,10] The experimental data show that this reaction is highly stereoselective[9,10] and regioselective.[9,10]



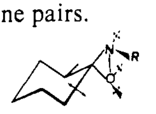
I 95% II 5%

In thermal reactions the degree of stereoselectivity is slightly lower but the lactam I is always the main product.[10c] The regioselectivity observed rules against free-radical intermediates; should a radical mechanism be involved, the photolysis of spiro oxaziridines would be expected to give preferential cleavage of the C-C bond to the more highly substituted carbon atom



II 5%

leading to the more stable free radical and to lactam II. Another remarkable feature[10] appears in the rearrangement of the oxaziridines; the regioselectivity seems to be controlled by stereoelectronic requirements. The steric orientation of the nitrogen lone pair has not been considered so far. In fact, one may notice[10] that the C-C bond which undergoes fragmentation lies quasi-antiperiplanar to the nitrogen lone pair and to one of the oxygen lone pairs.



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