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Orientation in Electrophilic Substitution of — I — M Substituted Thiophenes

II. Correlations between Localization Energy Differences and Reactivity Ratios

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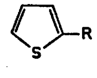
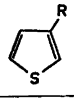
Localization energies for electrophilic attack on the various positions in certain 2- and 3-monosubstituted thiophenes have been calculated with the ω-technique. The calculated orientations as obtained with the *p*- and the *d*-models of thiophene are compared with recent experimental results.

In Part I the orientations have been obtained in the nitration of —I—M type monoderivatives of thiophene.[1] The isomer ratios at +75°C are given in Table 1. According to earlier MO calculations concerning 2- and 3-nitrothiophene the reactivity order for the different positions was predicted to be $5 \gg 4 > 3$ and $5 > 2 \gg 4$, respectively,[2] after consideration of the HMO localization energies as obtained employing the Longuet-Higgins *d*-model for thiophene.[3] From the experimental data now available (Table 1) it is seen, that the reactivity orders for the positions are $5 \geq 4 \gg 3$ and $5 > 2 > 4$ for 2- and

Table 1. GLC isomer ratios (x_i/x_j) in nitration[1] (+75°C) of 2-R- and 3-R-thiophenes.

	R	x_5/x_4	x_5/x_3	x_5/x_2
	CHO	0.84 ± 0.02	19 ± 2	—
	CN	2.06 ± 0.04	23 ± 2	—
	NO$_2$	0.90 ± 0.06	118 ± 25	—
	CHO	7.5 ± 0.8	—	5 ± 1
	CN	11.0 ± 0.7	—	5.8 ± 0.2
	NO$_2$	15.6 ± 0.3	—	8.3 ± 0.2

3-substituted thiophene, respectively. In view of recent criticism of the thiophene *d*-model[4] it is of interest to see if better agreement can be obtained between calculated and experimentally obtained reactivity ratios if the calculations are based on the so-called *p*-model. In the latter case the sulfur atom contributes its $3p$ electrons to the π-cloud.

The present calculations have been carried out with the ω-technique using $\omega = 1.25$ throughout,[5] including overlap between nearest neighbors with the value $S_0 = 0.25$ for the carbon-carbon π-overlap integral. Exchange integrals have been approximated as proportional to the overlap integrals. The calculations include both the *d*- and the *p*-thiophene models and are made self-consistent with respect to the charge densities.

The computations were carried out with an ω-technique program for the IBM 7090 digital computer.

RESULTS AND DISCUSSION

Benzene derivatives. —I—M substituent model. The model for the —I—M substituent was chosen to be of the form —X=Y, where the atoms X and Y are contributing one electron each to the π-framework. The parameter values are (in the usual notation) $h_X = h_Y = 1$, $k_{C_X-X} = 0.5$, $k_{XY} = 1$ which with $h_{C_X} > 0.3$ give *meta* direction as well as deactivation to the benzene nucleus when the localization energies of the respective Wheland complexes are considered. The set of parameters suggested by Matlow and Wheland[6] and Roberts and Streitwieser[7] for a —I—M substituent could not be used in the present calculations since neither *meta*-orientation nor deactivation was obtained.

The ionization potentials obtained for $h_{C_X} = 0.4$, 0.5, 0.6 were found to be 9.52, 9.68, and 9.10 eV. The values for the Coulomb and the exchange integrals used to compute the IP's were -10.12 and -2.5 eV, respectively, obtained from the ionization potential fitting procedure of ethylene and benzene.[8] The electron impact ionization potentials for benzaldehyde and benzonitrile are 9.82 and 9.95 eV, respectively.[9] This together with comparison of the *m:o* and *m:p* ratios with the respective localization energy differences suggest the application of $h_{C_X} = 0.4$ for CHO, $h_{C_X} = 0.5$ for CN, and $h_{C_X} = 0.6$ for NO_2, the other parameter values being kept unchanged. Variation of the overlap integrals for the XY-group showed that (with $h_{C_X} = 0.5$), $k_{C_X-X} \leq 0.6$ and $k_{XY} \geq 0.7$ are required to achieve simultaneously *meta* direction and deactivation. The ionization potentials did not vary much and remained around 9.6 eV for these variations.

In the present cases the transition states in the electrophilic substitution are probably "late" because of the deactivating character of the substituents. Therefore it is to be expected that the Wheland complexes are reasonably good models for the transition states. Thus the relation $-RT \ln (k_i/k_j) = E_i - E_j$ where the indices i and j refer to different aromatic positions (E is the calculated localization energy in β_0-units. Note that β_0 is a negative quantity.) should yield a straight line, when the logarithms of the *m:o* and *m:p* ratios are plotted against the differences of the corresponding localization energies. The slope

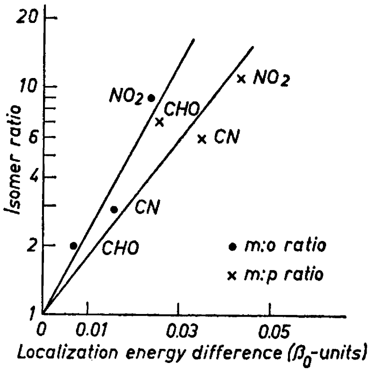


Fig. 1. Semilogarithmic plot of the isomer ratios (corrected for statistical factor) obtained in the nitrations (+75°C) of benzaldehyde, benzonitrile, and nitrobenzene *versus* the differences of the localization energies. Substituent parameters for C_6H_5XY: $h_X=h_Y=1$, $k_{Cx-X}=0.5$, $k_{X=Y}=1$; $h_{Cx}=0.4$ (CHO), $h_{Cx}=0.5$ (CN), $h_{Cx}=0.6$ (NO_2).

should give a value for β_0, the exchange integral, which is about -2.5 eV.[10] In Fig. 1 this relation is shown for the isomer ratios obtained in the nitration * of benzaldehyde, benzonitrile, and nitrobenzene. It is seen that two lines may be drawn through the points and the origin which correspond to the β_0-values -2.6 and -1.8 eV. In view of the approximations involved these are acceptable limits for β, and it is concluded that for the present purpose, the parameter values derived for the XY-group are reasonable.

Thiophene models. For thiophene it is desirable that the salient properties of the directing effects of the substituents of the present type as applied to the heterocycle should be reproduced within this framework. Thus the 5:4 ratios of the 2-R cases should be calculated to be near unity and for the 3-R cases the observed order of substituent influence on the fraction of 5-substitution as well as the reactivity order should be predicted.

Assuming as a first approximation that the substituent parameters developed in the benzene cases may be used unchanged, the set corresponding to the nitrile substituent was used to investigate the effect of different thiophene models on the calculated localization energy differences (Table 2). The influence of different thiophene models on the ionization potentials has not been investigated, since such experimental data are not available for —I—M thiophenes.

With respect to the thiophene *p*-model, there is some uncertainty as to which parameter values are to be used for the sulfur coulomb integral ($\alpha_S=\alpha_0+h_S\beta_0$) and for the carbon-sulfur exchange integral ($\beta_{C-S}=k_{C-S}\beta_0$). Thus according to the literature h_S and k_{C-S} values range from 0 to 1 and from 0.5 to 1, respectively. In the present case variation of k_{C-S} from 0.5 to 1 changed the E_5-E_4 energy difference (for the nitrile substituent in 2-position) from about 0.2 to about -0.03 β_0-units for a given value of h_S. This energy difference increased with about 0.02 β_0-units when h_S was changed from 0 to 1 for a given value of k_{C-S}. The E_5-E_3 energy difference was always between

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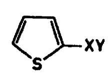
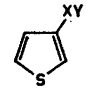
* The isomer ratios for benzonitrile and nitrobenzene appearing in Fig. 1 are averages of the values obtained for nitrations in sulfuric acid[11a,b] (extrapolated to +75°C) and for those in trifluoroacetic acid[11c] at +75°C. The isomer ratios in the aldehyde case are only those obtained in trifluoroacetic acid at +75°C.[11c]

Table 2. Differences in localization energies (in β_0-units) for different thiophene models.

	E_5-E_4		E_5-E_3		E_5-E_2	
	p	d	p	d	p	d
	0.0527	0.1364	0.0717	0.1604	—	—
	0.0042 *	0.0954 *	0.0237 *	0.1186 *		
	0.0762	0.1811	—	—	−0.0136	0.0142
	0.0314 *	0.1386 *			−0.0161 *	0.0135 *

Parameters —XY: $h_{C_X}=0.5$; $h_X=h_Y=1$; $k_{C_X-X}=0.5$; $k_{XY}=1$
p-model $h_S=0.5$; $k_{C-S}=0.8$
d-model $h_S=0$; $k_{C-S}=0.8$; $k_{S-S}=1$
Values marked with an asterisk are obtained with $h_{C\alpha}=0.05$ (see text).

0.01 and 0.03 β_0-units larger than E_5-E_4 except for $h_S=0$, $k_{C-S}=0.5$, when E_5-E_3 became less than E_5-E_4. With respect to the 3-XY case the variations above invariably resulted in that E_5-E_2 was <0, thus predicting that the 2-position in a 3-substituted thiophene of the present kind should be more reactive than the 5-position in electrophilic substitution.

Thus the E_5-E_4 difference is strongly dependent on the value of k_{C-S}. It seems, however, that a reasonable choice of k_{C-S} could be made on the basis of bond length ratios. Hence k_{C-S} may simply be assumed to be equal to the C—C/C—S bond length ratio which according to Bak *et al.*[12] is 0.81 for thiophene.

The differences in localization energies obtained with $h_S=0.5$ and $k_{C-S}=0.8$ appear in Table 2. Taking $\beta_0\sim-2$ eV (from the benzene results) the rate ratio $k_5:k_4\sim35$ at 75°C is obtained for the 2-XY case.

In the case of the thiophene d-model the parameter values used by Longuet-Higgins[3] (*i.e.*, $h_S=0$, $k_{C-S}=0.8$, $k_{S-S}=1$) have been used in the present work without any change, in this manner the essential feature of this model of depicting thiophene (and derivatives) as a kind of perturbation of benzene (and benzene derivatives) is preserved. It should be noted that this treatment of thiophene itself reproduces its ionization potential correctly with $\omega=1.25$.[8]

The energy differences obtained with the d-model and with the nitrile parameters are given in Table 2. With respect to the E_5-E_2 difference of the 3-XY case it is seen that the d-model makes the qualitatively correct prediction which was not the case of the p-model (see above). With respect to the 2-XY case, however, the d-model predicts a $k_5:k_4$ ratio of the order of 10^5.

Although the value for the $k_5:k_4$ ratio obtained with the p-model is undeniably more reasonable, both models tend to overestimate the "activating" influence of sulfur. It may be argued that this defect may be remedied through adjustment of the carbon-sulfur exchange integral but in the present case this is a questionable procedure. Instead it seems more instructive to consider the difference in hybridization of the α- and β-carbons of the thiophene ring system, since the NMR coupling constants ($J^{13}{}_{\text{C-H}}$) are reported to be 184.5 cps for the α-carbon and 167.5 cps for the β-carbon in thiophene.[13] Assuming that the coupling constant measures the fraction *s*-character of the carbon-hydrogen bond [14] the result implies that there is more *s*-character in the α-carbon-hydrogen bond than in the β-carbon-hydrogen bond. Since increase of the *s*-character of a bond will lead to relatively higher electronegativity of the carbon atom in that bond [15] one may conclude that the α-carbons will appear more electronegative than the β-carbons in the carbon-hydrogen bonds of thiophene.

Hence, the calculations above were carried out with a perturbation of the Coulomb integral of the α-carbons with $+0.05\ \beta_0$, whereas the β-carbons were unperturbed, implying the same degree of hybridization for the latter as for a benzene carbon.

The results of these calculations for the nitrile substituent are given in Table 2, from which is seen that the applied perturbation decreases all the energy differences, in particular the E_5-E_4 difference.

Although the *p*-model results are quite reasonable, the fact that the reverse order (from that actually observed) is predicted for the 3-XY case will make that model less suitable for this type of thiophene derivative. On the other hand the *d*-model predictions show considerable quantitative deviation from the observed orientations.

As in the *p*-model case the overestimation of the reactivity of the α positions in the *d*-model is to a certain extent due to the probably too low value assigned to the carbon-sulfur exchange integral.

Since increase of $k_{\text{C-S}}$ will make the resemblance of the thiophene system to benzene closer, a necessary consequence is that the differences between the positions will show a steady decrease. For example, if $k_{\text{C-S}}$ for the *d*-model is chosen as 0.9 the E_5-E_4 values in Table 2 for the *d*-model (perturbed at C_α) are reduced with 90 and 60 %, respectively, for 2-XY and 3-XY cases. The E_5-E_3 value is similarly reduced with 75 % whereas the E_5-E_2 value is practically unchanged. Thus the quantitative deviations of the *d*-model may be reduced by increasing the carbon-sulfur exchange integral, but rather drastic increases have to be made (*i.e.*, $k_{\text{C-S}}$ close to unity) if the correction to the α-carbon Coulomb integral discussed above is not applied. On the other hand this perturbation has to be increased substantially if the "normal" value of $k_{\text{C-S}}$ (*i.e.* $=0.8$) for the *d*-model should be retained. As mentioned before this value is in agreement with that obtained from the ionization potential of thiophene. The latter, however, does not seem to be too sensitive for a change of $k_{\text{C-S}}$ since almost the same I.P. is calculated with the *d*-model for $k_{\text{C-S}}=0.8$ or 0.9. For the present purpose it is felt, however, that $k_{\text{C-S}}=0.8$ should be retained for the *d*-model and that this model as well as the *p*-model should be understood as extreme structural descriptions of the prevailing state of affairs.

Thus, none of the models may be abandoned in the present context, each having its special merits. The *p*-model, as appears from Table 2, provides a description of the reactivity ratios for 2-R-thiophenes which seems to be in fair quantitative agreement with the observed ratios. The *d*-model, although suffering more from the overestimation of the α-carbon reactivity than does the *p*-model, provides the qualitatively correct orientation for 3-R-thiophenes. It seems, that in both cases more reasonable reactivity ratios are predicted if account is made for the fact that the two different kinds of ring carbon may not be identical with respect to their degree of hybridization. The treatment in this respect merely illustrates the trend, however.

In view of the foregoing it should not be surprising if an analysis, not suffering from the parameterization necessarily involved with the present type of MO description, should reveal that the true π-contribution of the sulfur atom is one where the degree of *d*-character of the 3*p*-electrons is changing from a minimum for 2-substituted thiophenes to a maximum for 3-substituted thiophenes (and thiophene itself). The above statements may then as applied to the Wheland structures be considered as a reflection of the conclusion reached by Bielefeld and Fitts [16] with respect to the ground state of thiophene. They found in a detailed SCF MO analysis that the 3*d* atomic orbitals on sulfur participated only slightly but that this participation had a marked effect on the charge densities and the electronic spectrum of thiophene. Lucken [17] also found that equally good predictions of spin densities in the radical anions of the nitrothiophenes were obtained with the *p*- and the *d*-model.

In the following, however, the 2-XY cases will be treated according to the *p*-model and the 3-XY cases to the *d*-model. It is emphasized, that the treatment pertains only to the —I—M substituents and to the results given in Part I. The artificial division in *p*- and *d*-models thus serves to illustrate in the following the validity of the approach used in Fig. 1 for the thiophene system.

Correlation between reactivity ratios and localization energy differences. In Fig. 2 are shown the correlations for the thiophene cases obtained in the same manner as those in Fig. 1, employing for the reactivity ratios the values given in Table 1, and assigning to the thiophene derivatives the same substituent parameters as developed for the benzene derivatives. The localization energies were calculated using the α-carbon perturbation discussed above. From the figure appears that the calculated ratios of the 2-XY cases (*p*-model) and the

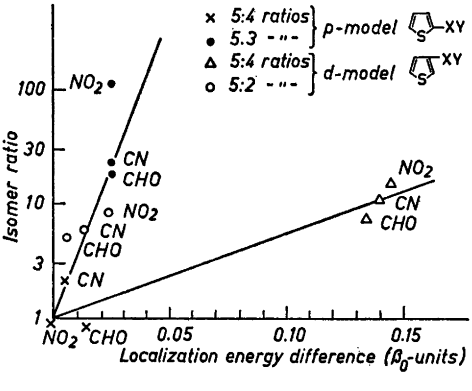


Fig. 2. Semilogarithmic plot of the isomer ratios obtained in the nitrations (+75°C) of thiophene derivatives (Table 1) *versus* the differences in localization energies. Substituent parameters are the same as in Fig. 1. Thiophene model parameters are those given in Table 2 (with α-carbon perturbation).

calculated 5:2 ratios of the 3-XY cases (*d*-model) correlate with the real orientations in such a manner that a correlation line may be drawn from which $\beta_0 \sim -3.8$ eV is obtained. This correlation does not, however, include the 5:4 ratios of the 3-XY cases (*d*-model). These are grouped separately on a line which indicates $\beta_0 \sim -0.5$ eV.

Compared to the β_0-values obtained in the benzene cases the latter value shows then that the prediction of the 5:4 ratios in the 3-XY cases is in poor quantitative agreement with the observed orientations. It is felt, however, that this discrepancy is chiefly due to the possibly too low value assigned to the carbon-sulfur exchange integral of the *d*-model. Thus increasing $k_{\text{C-S}}$ should improve the quantitative correlation for the 5:4 ratios, but the 5:2 ratios would remain unchanged since these ratios show hardly any dependence at all for a change of $k_{\text{C-S}}$. Although the quantitative prediction with respect to the 5:4 ratios is poor, the qualitative correlation is correct for the orientation as well as for the order of substituent influence for the 3-XY cases.

The reactivity ratios in the 2-XY cases (*p*-model) are predicted to be fairly close to those actually observed as reflected in the β_0-value (~ -3.8 eV). The deviation with respect to the benzene β_0-values is not too serious when the approximations necessarily involved are considered. There is, however, one significant qualitative deviation with respect to the prediction of 5:4 ratios which is due to 2-thiophenealdehyde (*cf.* Fig. 2).

The calculated value should imply a 5:4 ratio of about 6 whereas the observed value in fact is less than unity (Table 1). No such discrepancy is found in the benzaldehyde and 3-thiophenealdehyde cases. Thus the effect of the aldehyde substituent in 2-position is different from the one where this group occupies the 3-position or a benzene position. That such a difference exists has been shown by Gronowitz and Rosenberg[18] who found that the carbonyl stretching frequency in 2-thiophenealdehyde was shifted 18 cm^{-1} lower than that of the 3-isomer, which was interpreted as due to stronger conjugation between the aldehyde group and the ring for the 2-isomer. For the present purpose it is sufficient then to state that if $k_{\text{Cx-X}}$ is increased from the "normal" value of 0.5 to 0.6 the energy difference $E_5 - E_4$ decreases from 0.0136 β_0 to 0.0101 β_0, other parameters being the same for the 2-thiophenealdehyde *p*-model. Although this decrease is not sufficient to bring the 5:4 ratio below unity, the trend is in agreement with the findings of Gronowitz and Rosenberg. It must be remembered that the parameters of the thiophene ring are by no means defined sharply and small changes in h_{S} and $k_{\text{C-S}}$ together with the one in $k_{\text{Cx-X}}$ above may well bring the $E_5 - E_4$ difference to become less than zero.

It is important, however, to note that when this change of $k_{\text{Cx-X}}$ is applied to the *d*-model calculation of 2-thiophenealdehyde it will increase the energy difference in question.

Finally, with respect to the *p*-model treatment of the 3-XY cases, it may be sufficient to note that the $E_5 - E_4$ energy differences showed hardly any dependence at all upon a change of substituent parameters and, as already mentioned above, that, the $E_5 - E_2$ energy difference was found to be opposite to the one implied from the reactivity ratios.

In summarizing it is concluded that the *p*-model treatment of the 2-substituted thiophenes is satisfactory on the whole, predicting the reactivity order to be $5 \sim 4 > 3$ which is in quantitative agreement with the experimentally found order for the nitrile and nitro substituents. The deviation due to 2-thiophenealdehyde may also be accounted for, qualitatively, with this treatment. The *d*-model calculations of the 3-substituted thiophenes predict the reactivity order to be $5 > 2 \gg 4$ which is qualitatively in agreement with experimentally found order for the three substituents in question. The model also provides the correct order of substituent influence with respect to the 5:4 and 5:2 ratios to be $CHO < CN < NO_2$.

With respect to the deviations and discrepancies it is felt that those are chiefly due to the shortcomings of each of the thiophene models, rather than to a significant difference in the substituent interaction compared to the corresponding benzene derivatives, with the exception of 2-thiophenealdehyde. The failure of the present treatment to interpret the reactivity ratios obtained with one single thiophene model, could imply that the degree of *d*-character of the sulfur $3p\pi$ orbital is dependent on whether or not the α-carbon is substituted.

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