

### Molecular Orbital Calculations of the Acid-catalysed Hydrogen Exchange in Substituted Thiophenes

L. KLASINC and K. HUMSKI

"Rudjer Bošković" Institute, Zagreb, Yugoslavia

(Z. Naturforsch. 25 b, 324—325 [1970]; eingegangen am 17. Januar 1970)

Continuing the early work of MELANDER, OLSSON and coworkers<sup>1</sup> who studied the heterogeneous acid catalysed hydrogen exchange in thiophene, determinations of the dedeuteration<sup>2</sup> and detritiation<sup>3</sup> rates of a number of substituted thiophenes in homogeneous conditions were recently carried out. The relative rates are strongly dependent on the substitution in the thiophene ring. SHATENSHTEIN et al.<sup>2</sup> showed that in mixtures of acetic and fluoroacetic acid the ratio of the dedeuteration rates of 5-methoxythiophene-2-d and thiophene-3-d is about  $10^{10}$  under same conditions. The relative exchange rates are not much dependent on the reaction conditions. A ratio of 200 was observed<sup>2</sup> for the dedeuteration rates of 5-methylthiophene-2-d and

thiophene-2-d in 33.3 mole-% trifluoroacetic acid, 66.7 mole-% acetic acid at 25°. Detritiation of the tritium analogs at the same temperature in 44.5 mole-% and 27.9 mole-% trifluoroacetic acid gave ratios of 206 and 202, respectively<sup>3</sup>. This suggests that the exchange rate is primarily a function of the electronic configuration. Such an assumption was previously made by MELANDER<sup>4</sup> who thus explained the ratio of exchange rates for the 2- and 3-position in thiophene. Now having more data available concerning the homogeneous acid catalysed hydrogen exchange of different positions in substituted thiophenes, we thought it worthwhile to see whether the measured relative rates correlate with theoretical quantities reflecting the electronic structure and reactivity of these compounds to-

$$\begin{array}{ll} \alpha_S = \alpha + 0.93 \beta & \alpha_3 = \alpha - 0.02 \beta \\ \alpha_{CH_3} = \alpha - 0.1 \beta^* & \alpha_{OCH_3} = \alpha + 1.9 \beta \\ \beta_{CS} = 0.5 \beta & \beta_{C-OCH_3} = 0.8 \beta \end{array}$$

Table 1. Coulomb and Resonance Integrals.  
\* Inductive.

Substitution in thiophene	Deuterium position	Free valence index	Superdelocalisation index, $S_r(E)$	Wheland's localisation energy, $L_r^+$	Exchange rate * $\log k_{relative}$
none	2	0.523	1.364	1.734	0
	3	0.391	1.046	2.289	-3.40
	3	0.393	1.133	2.220	(-2)
2-CH <sub>3</sub>	4	0.392	1.056	2.283	(-3)
	5	0.532	1.457	1.688	+2.30
	2	0.532	1.449	1.689	+2.53
3-CH <sub>3</sub>	4	0.391	1.049	2.281	(-3)
	5	0.524	1.373	1.729	+1.08
	3	0.423	1.418	2.038	(0)
2-OCH <sub>3</sub>	4	0.389	1.074	2.281	(-3)
	5	0.556	1.742	1.579	+6.20
	2	0.572	1.724	1.549	+6.05
3-OCH <sub>3</sub>	4	0.404	1.065	2.253	(-3)
	5	0.522	1.392	1.726	(1)
	3	0.461	1.490	2.123	(-2)
2-(2'-thienyl) 1	4	0.381	1.050	2.131	(-3)
	5	0.553	1.762	1.662	(+5)
	3	0.447	1.379	2.219	(-2)
2-(3'-thienyl) 2	4	0.383	1.052	2.475	(-4)
	5	0.547	1.667	1.711	(+4)
	2'	0.595	1.818	1.572	(+6)
	4'	0.421	1.087	2.378	(-3)
	5'	0.519	1.366	1.829	(+1)
3-(3'-thienyl) 3	2	0.582	1.700	1.642	(+5)
	4	0.417	1.076	2.397	(-3)
	5	0.520	1.369	1.822	(+1)

Table 2. Reactivity indices in correlation to relative rates of the acid-catalysed hydrogen exchange in substituted thiophenes.

\* From Ref. 2 Predicted values are given in parentheses.

<sup>1</sup> K. HALVARSON and L. MELANDER, Ark. Kemi 8, 29 [1956]; B. OSTMAN and S. OLSSON, 15, 275 [1960].

<sup>2</sup> A. I. SHATENSHTEIN, A. G. KAMRAD, I. O. SHAPIRO, Y. I. RANNEVA, and E. N. ZVYAGINTSEVA, Dokl. Acad. Nauk SSSR 168, 364 [1966]; A. I. SHATENSHTEIN, N. N.

MASDESIEVA, Y. I. RANNEVA, I. O. SHAPIRO, and A. I. SEREBRYANSKAYA, Teor. Eksp. Khim. 3, 343 [1967].

<sup>3</sup> A. R. BUTLER and C. EABORN, J. chem. Soc. [London], Ser. B 1968, 370.

<sup>4</sup> L. MELANDER, Ark. Kemi 8, 361 [1955].

wards protons. Such correlation would also confirm the generally accepted assumption that acid catalysed exchange in thiophenes proceeds via equilibria in which protonated thiophene cations are formed. Stable cations from thiophene protonated exclusively in the 2-position have been observed<sup>5</sup>. We applied the molecular orbital theory within the framework of the Hückel method on thiophene and 2- and 3-methyl, and 2- and 3-methoxy thiophenes as well as on 2,2'-dithienyl (**1**), 2,3'-dithienyl (**2**) and 3,3'-dithienyl (**3**). The empirical parameters used in the calculation are shown in Table 1. Similar parameters for thiophene have been used by SAPPENFIELD and KREEVOY<sup>6</sup>.

We calculated for the ground state the free valence indices, electrophilic superdelocalisabilities and Wheeland's localisation energies for an electrophilic attack. The results are listed in Table 2. Following the "isolated molecule approximation" a correlation of the free valence indices and electrophilic superdelocalisabilities with observed exchange rates for the position of the proton exchange is expected. On the other hand if the formation of the corresponding protonated thiophene cation is important a correlation with Wheeland's electrophilic localisation energies should be found. In fact, all of these quantities correlate well with the observed relative exchange rates. The close relationship of these quantities enables us to make

some predictions of the relative exchange rates for the less reactive positions in these compounds. It also allows to find out the relative rates of deuterium exchange in the case of the dithienyls which were not determined. KELLOG, SCHAAP and WYNBERG<sup>7</sup> recently reported the complete analysis of the kinetically controlled products of the electrophilic bromination and deuteration of **1**, **2**, and **3**. So the results of deuterium-hydrogen exchange reactions of **1**, **2**, and **3** carried out for 5 hours in refluxing deuterioacetic acid are as follows: **1** showed 60% exchange in 5,5'-positions, **2** 22% in 5-position and 40% exchange in 2'-positions and **3** about 60% exchange in the 2,2'-positions. Same positions in all three compounds were quantitatively brominated within matter of minutes at room or slight elevated temperatures using the brominating agent *N*-bromo-succinimide (NBS) in mixed chloroform-acetic acid solvent. Other reaction conditions and longer times were used to form 2',5',5-tribromo-**2** and 2,2',5,5'-tetrabromo-**3**. The results of our calculation are in agreement with the above experimental data, indicating that the deuterium exchange found proceeds with about the same rate as in the case of methoxythiophenes, whereas the less reactive positions (being brominated after longer time) react about  $10^3$ – $10^4$  times slower. All predictions (in parenthesis) for the relative rates of deuterium exchange together with the observed relative exchange rates<sup>2</sup> are shown in Table 2.

<sup>5</sup> H. HOGEVEEN, Recueil Trav. chim. Pays-Bas **85**, 1072 [1966].

<sup>6</sup> D. S. SAPPENFIELD and M. KREEVOY, Tetrahedron [London] **19** (Suppl. 2), 157 [1963].

<sup>7</sup> R. M. KELLOG, A. P. SCHAAP, and H. WYNBERG, J. org. Chem. **34**, 343 [1969].