METHYL DERIVATIVES OF THIOPHENE

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Theoretical data obtained by simple HMO calculation of methyl derivatives of thiophene were correlated with experimental data on reactivity, as well as with the NMR spectroscopy data.

This paper is part of a complex study of the behaviour of furan[1] and thiophene nuclei in dependence on the substitution with methyl groups. Using simple HMO approximation, indexes of chemical reactivity were calculated for all the positions of the compounds $I-IX$ investigated, *i.e.* the values of π-electron densities, free valences, superdelocalisabilities, and localisation energies.
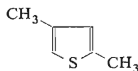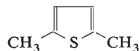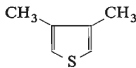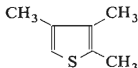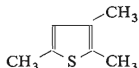

The values of π-electron densities were correlated with the shifts of corresponding hydrogens in the proton magnetic resonance spectrum. The indexes of chemical reactivity were compared with the available data on electrophilic, nucleophilic and radical substitution on the thiophene nucleus.

EXPERIMENTAL

Calculations

The calculation of all substances was carried out using a standard program (author Dr V. Kvasnič-ka) and the computers NE 803B and Tesla 200. The coulombic and exchange integrals were approximated according to the conventional equations

$$\alpha_x = \alpha_C + h_X\beta_{CC}, \quad \beta_{CX} = k_{CX}\beta_{CC},$$

where h_X and k_{CX} are empirical parameters. The choice of parameters was carried out on the basis of an earlier published study on sulfur heterocycles[2]. It was found that all models recommended give a correct qualitative picture of the reactivity of the substances investigated. In the case of correlations, however, the best results were afforded by the model in which the following parameters were used.

$$h_S = 1\cdot0, \quad k_{CS} = 0\cdot8, \quad h_{CH_4} = 2\cdot0, \quad k_{C-CH_3} = 0\cdot7, \quad \alpha_C = 0\cdot0, \quad \beta_{CC} = 1\cdot0.$$

Material

Thiophene (*I*) was dried and fractionated before use. Applying the methods described in literature 2-methylthiophene[3] (*II*), 3-methylthiophene[4] (*III*) and 2,5-dimethylthiophene[5] (*IV*) were prepared. For the preparation of other methylthiophenes see[6].

TABLE I
PMR spectra, Correlation of the Chemical Shifts of Hydrogen Atoms with π-Electron Densities q

Substance	Position	q	δ, Hz	Substance	Position	q	δ, Hz
I	2 = 5	1·066	735·54	*IV*	4	1·141	677·14
	3 = 4	1·126	712·99		5	1·095	697·46
II	3	1·172	675·90	*V*	3	1·188	656·88
	4	1·125	689·52		5	1·142	663·86
	5	1·094	708·14	*VI*	3 = 4	1·142	652·52
III	2	1·113	692·58	*VII*	2 = 5	1·112	687·89
	4	1·143	688·62	*VIII*	5	1·142	664·58
	5	1·065	722·52	*IX*	4	1·188	642·64

RESULTS

Proton magnetic resonance spectra were measured on a 100 MHz instrument Varian XL-100-15. The values of chemical shifts were determined by extrapolation to zero dilution in $CDCl_3$ at 30°C. Thus an accuracy of $\pm 0\cdot01$ Hz was achieved. The values

so obtained are listed in Table I. The resulting correlation may be expressed by the relation:

$$\delta = -651{\cdot}77\,q - 1421{\cdot}12 \quad r = 0{\cdot}8546\,.$$

This dependence is statistically significant when testing at the 99.9% level of significance. It may be stated that in comparison with an analogous study in the furan series[1] a decrease in the decomposition of the data to α and β protons of the

TABLE II

Comparison of Calculations with Chemical Reactivity

Type of reaction	Substance	Reactivity of positions on the basis of			Reaction, reference
		superdelocalisability	localisation energy	experiment	
S_E	I	$2 > 3$	$2 > 3$	$2 > 3$	exchange H-D, H-T[7,8], cleavage C—Si[9] alkylation[10], nitration[7,11]
	II	$5 > 3 > 4$	$5 > 3 > 4$	$5 > 3 > 4$	alkylation[10] nitration[12]
	III	$2 > 5 > 4$	$2 > 5 > 4$	$2 > 5 > 4$	acylation[14,13], bromination[4]
	IV	$5 > 4$	$5 > 4$	$5 > 4$	acylation[3,15], halogenation[16]
	V	$5 > 3$	$5 > 3$	$5 > 3$	acylation[3,15], halogenation[17]
	VI	$3 = 4$	$3 = 4$	$3 = 4$	acylation[3,18], chloromethylation[19]
	VII	$2 = 5$	$2 = 5$	$2 = 5$	acylation[3,20]
	VIII	5	5	5	acylation[3]
	IX	4	4	4	acylation[3]
S_N	I	$2 > 3$	$2 > 3$	$2 > 3$	metalation[21-23]
	II	$5 > 3 > 4$	$5 > 3 > 4$	$5 > 3 > 4$	metalation[24]
	III	$5 > 2 > 4$	$5 > 2 > 4$	$5 > 2 > 4$	metalation[25]
	IV	$5 > 4$	$5 > 4$	$5 > 4$	metalation[16]
S_R		free valence			
	I	$2 > 3$	$2 > 3$	$2 > 3$	methylation[27], benzylation[26], phenylation[28,29]
	II	$5 > 3 > 4$	$5 > 3 > 4$	$5 > 3 > 4$	methylation[27], phenylation[30]
	III	$2 > 5 > 4$	$2 > 5 > 4$	$2 > 5 > 4$	methylation[27], phenylation[31]
	V	$5 > 3$	$5 > 3$	$5 > 3$	methylation[27]
	VI	$3 = 4$	$3 = 4$	$3 = 4$	methylation[27]

heterocyclic nucleus took place, which is in agreement with the aromaticity of both systems.

Experimental data on the reactivity of the compounds studied are relatively abundant in the field of electrophilic substitution. From the data on nucleophilic substitution the results of metalation reactions were also employed even though their mechanism is not quite unambiguously proved. Similarly as in the methylfurans series[1] the data from this study also indicate that the superdelocalisabilities give absolute qualitative information on the sequence of reactivity of single positions of the thiophene nucleus. π-Electron densities[2] may also be used for the reactivity in nucleophilic reactions, and in the case of radical reactions free valences can be applied. In the case of radical reactions the results of the brominations of thiophene derivatives with N-bromo-succinimide in the presence of a radical initiator were not taken into account for reasons already discussed[1,27]. The results thus obtained are summarized in Table II.

In conclusion it way be stated that the simple HMO method gives a reasonable picture of the reactivity and the properties of the compounds studied in spite of all the simplifications which it comprizes. In view of its simplicity and the fact that it is not too exacting with respect to the time of computation it is suitable for a first orientation of an organic chemist when studying the properties of aromatic and heterocyclic systems.

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