ELECTRONIC STRUCTURES AND ELECTROPHILIC SUBSTITUTION IN 2-(4-R-2-QUINOLYL)THIOPHENES AND 5-(4-R-2-QUINOLYL)-2,2'-DITHIENYLS

P. L. Trakhtenberg, M. N. Zemtsova,
A. N. Gusarov, V. P. Zvolinskii,
and A. E. Lipkin

UDC 541.42'65:547.734'831

The electronic structures and reactivity indexes (RI) of 2-(4-R-2-quinolyl)thiophenes and 5-(4-R-2-quinolyl)-2,2'-dithienyls (R = H, COOH, $COOC_2H_5$, and $NHCOCH_3$) and their protonated forms were calculated by the Pariser—Parr—Pople (PPP) method. The peculiarities of the geometrical and π-electron structures were established. The calculated reactivity indexes are compared with experimental data on the electrophilic substitution reactions of the investigated compounds. A qualitative agreement between the calculated values and the experimental data was established. It is shown that quinoline derivatives of thiophene are less reactive than the corresponding dithienyl compounds in electrophilic substitution reactions.

Quinoline derivatives of thiophene and 2,2'-dithienyl are of interest as biologically active compounds [1-3]. Information regarding their electronic structures is necessary for the interpretation and prediction of the various physicochemical properties of these compounds. In the present research we investigated the geometries, electronic structures, and reactivities in electrophilic substitution of 2-(4-R-2-quinolyl)thiophenes [R = H (I), COOH (II), $COOC_2H_5$ (III), and $NHCOCH_3$ (IV)] and 5-(4-R-2-quinolyl)-2,2'-dithienyls [R = H (V), COOH (VI), $COOC_2H_5$ (VII), and $NHCOCH_3$ (VIII)].

In connection with the fact that the investigated electrophilic substitution reactions proceed in proton-donor media or with the formation of protonic acids, the nitrogen-protonated forms of these compounds were examined during the study of the reactivities of the 2-(4-R-2-quinolyl)thiophenes and 5-(4-R-2-quinolyl)-2,2'-dithienyls.

The electronic structures were calculated by the Pariser—Parr—Pople (PPP) method. To determine the relative orientation of the quinoline and thiophene fragments in the 2-(2-quinolyl)thiophene (I) and 5-(2-quinolyl)-2,2'-dithienyl (V) molecules and their protonated forms (IX and XIII) we calculated the heats of atomization and the bond lengths of these molecules by the PPP method with Dewar's parametrization [4-6]. Proceeding from the calculated heats of atomization of the cis and trans conformations (I, IX) it may be stated that the cis conformation is more favorable (the differences from the trans conformation are 1.5 and 3.2 kcal/mole for the basic and protonated forms, respectively). The cis,trans conformation is more favorable in the case of 5-(2-quinolyl)-2,2'-dithienyls (V, XIII) (the differences are, respectively, 0.2, 1.1, and 0.7 for the unprotonated cis,cis, trans,trans, and trans,cis forms, whereas they are 0, 2.1, and 1.7 kcal/mole for the protonated forms). These differences are extremely insignificant and do not go beyond the limits of the accuracy of the Dewar method. The bond lengths for the energetically more favorable conformations of I, V, IX, and XIII are presented in Fig. 1. It should be noted that the slight changes in the bond lengths due to protonation of the system involve primarily the quinoline fragment and, to a very small extent, involve the thiophene fragment. The results of calculation of the geometry of the thiophene ring are in complete satisfactory agreement with the data in [7] (R_{S-C_2} 1.714 Å, $R_{C_2-C_3}$ 1.370 Å, and $R_{C_3-C_4}$ 1.423 Å). The calculated geometrical characteristics of the quinoline and thiophene fragments were also adopted for the substituted quinoline derivatives of thiophene (II, III, and IV), 2,2'-dithienyl (VI, VII, and VIII), and their nitrogen-protonated forms (X-XVI), assuming that the perturbations exerted

---

V. V. Kuibyshev Kuibyshev Polytechnic Institute, Kuibyshev 443645. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 751-754, June, 1979. Original article submitted February 18, 1978; revision submitted January 5, 1979.

0009-3122/79/1506-0608$07.50

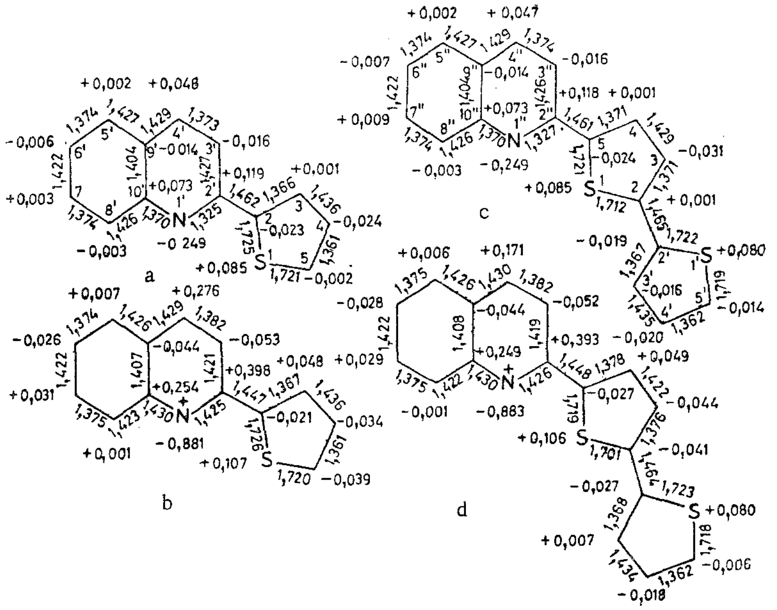


Fig. 1. Calculated bond lengths (Å) and π charges for the most energetically favorable conformations of 2-(2-quinolyl)thiophene (a), its protonated form (b), 5-(2-quinolyl)-2,2'-dithienyl (c), and its protonated form (d).

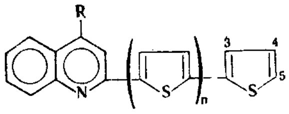
by the substituents are insignificant; this was confirmed by control calculations. The geometrical and other parameters of the substituents were selected from the data in [8, 9].

To calculate the reactivity indexes (RI) we used the Mataga–Nishimoto–Forster parameters and the geometrical characteristics calculated for unsubstituted systems. An analysis of the reactivity indexes of 2-(2-quinolyl)thiophene showed that the thiophene ring is more reactive in electrophilic substitution reactions; all of the carbon atoms of the quinoline ring are considerably less active. Similar calculations were made for the entire series of investigated compounds (II-XVI). It was correspondingly established for the 2,2'-dithienyl compounds that the thiophene ring that is not bonded to the quinoline fragment is the most reactive ring.

We used data on the localization energy during electrophilic substitution as the decisive criterion in the estimation of the reactivities of the various atoms of the thiophene ring (the calculated π-electron charges on the atoms presented in Fig. 1 are the most reliable reactivity indexes in the discussion of the orientation of electrophilic substitution of the investigated series of compounds). It was established from a comparison of the localization energies that the most reactive center of the molecule is the C_5 ($C_{5'}$) atom. The localization energies for the protonated forms indicate the same specificity of entry of the electrophilic agent.

The estimates made on the basis of the localization energies are in agreement with the experimental data on the electrophilic substitution reactions (nitration, acetylation, and formylation) of quinoline derivatives of thiophene and 2,2'-dithienyl published in [1, 2, 13, 14]. Thus 5-(4-R-2-quinolyl)-2,2'-dithienyls are nitrated by copper nitrate salts at 8-10°C to give 5'-nitro and 3'-nitro derivatives in 88-98% yields. 5-Formyl-5'-(4-R-2-quinolyl)-2,2'-dithienyls are formed in 50-92% yields in the formylation of quinoline derivatives of 2,2'-dithienyl derivatives by dimethylformamide (DMF) in the presence of a tenfold excess of phosphorus oxychloride at 96°C. The acetylation of VI and VII with acetic anhydride in polyphosphoric acid (PPA) at 50°C leads to the formation of 5'-acetyl derivatives in up to 50% yields. An appreciable decrease in the reactivity is observed on passing to thiophene compounds. Thus the nitration of II and III is realized when there is a considerable excess of the nitrating agent present at 20°C after 72 h, and the 5-nitro derivative is formed (in 92% yield). 5-Nitro-2-(2-quinolyl)thiophene was isolated only in the case of nitration with a mixture of concentrated nitric and sulfuric acids at –3°C after 3 h (the nitro product was obtained in 82% yield). We were unable to realize the formyla-

TABLE 1. Calculated Characteristics of the Reactivities of Compounds of the



Series

Neutral form	Protonated form	R	n	Atom No.	L_E, eV		Specificity, S_E	ΣQ_π of thiophene*	
					neutral form	protonated form		neutral form	protonated form
I	IX	H	0	3 4 5	11,707 12,739 10,389	11,841 12,591 10,498	5>3>4	0,037	0,140
II	X	COOH	0	3 4 5	11,771 12,805 10,461	11,841 12,591 10,540	5>3>4	0,035	0,140
III	XI	$COOC_2H_5$	0	3 4 5	11,771 12,798 10,452	11,871 12,629 10,529	5>3>4	0,035	0,134
IV	XII	$NHCOCH_3$	0	3 4 5	11,791 12,776 10,465	14,627 13,064 13,078	4>5>3	0,037	0,406
V	XIII	H	1	3 4 5	11,006 12,654 10,193	11,056 12,625 10,232	5>3>4	0,011	0,036
VI	XIV	COOH	1	3 4 5	11,166 12,690 10,245	11,095 —† 10,247	5>3	0,013	0,034
VII	XV	$COOC_2H_5$	1	3 4 5	11,059 12,686 10,149	11,087 —† 10,239	5>3	0,012	0,039
VIII	XVI	$NHCOCH_3$	1	3 4 5	11,056 12,671 10,231	13,054 —† 10,757	5>3	0,012	0,196

*This is the overall effective charge of the thiophene ring in which the reaction center is located.

†A self-consistent solution for the fragment of the molecule is not observed in the case of localization of the electron pair on the given atom.

tion and acetylation of the quinoline derivatives of thiophene under more severe conditions. The starting compounds were isolated in all cases.

The sharp decrease in the reactivities of the acetyl amines under conditions involving a proton-donor medium is legitimate, as evidenced by the localization energies (L_E) of the protonated forms XII and XVI presented in Table 1. We were unable to realize the acetylation and formylation of IV and VIII.

The division of the compounds into two characteristic groups with respect to reactivies, viz., thiophene compounds and 2,2'-dithienyl compounds, is not disrupted when the overall effective charge of the thiophene ring, in which the reaction center is located, is used as the deciding criterion (Table 1).

On the whole, a comparison of the results of the calculations with the experimental data makes it possible to conclude that the estimates obtained by the PPP method are acceptable and, consequently, that the premises placed at the foundation of the selection of the computational model in accordance with the PPP method are legitimate.

LITERATURE CITED

1. M. N. Zemtsova and A. E. Lipkin, Khim. Geterotsikl. Soedin., No. 1, 183 (1973).
2. M. N. Zemtsova, P. L. Trakhtenberg, A. E. Lipkin, and T. B. Ryskina, Khim.-Farm. Zh., No. 8, 13 (1973).
3. M. Martin-Smith and S. T. Reid, J. Med. Pharm. Chem., 1, 515 (1959).
4. M. J. S. Dewar and G. J. Gleicher, J. Am. Chem. Soc., 87, 685 (1965).
5. A. L. H. Chang and M. J. S. Dewar, J. Am. Chem. Soc., 87, 756 (1965).

6. M. J. S. Dewar and T. Morita, J. Am. Chem. Soc., 91, 769 (1969).
7. A. G. H. Wachters and D. W. Davies, Tetrahedron, 20, 2841 (1964).
8. K. Nishimoto and N. Z. Mataga, Phys. Chem., 13, 140 (1957).
9. J. Leska and P. Zahkadnik, Coll. Czech. Chem. Commun., 38, 3365 (1973).
10. K. Nishimoto and L. S. Forster, Theoret. Chim. Acta, 4, 155 (1965).
11. K. Nishimoto, Theoret. Chim. Acta, 7, 207 (1967).
12. V. I. Minkin, B. Ya. Simkin, and L. P. Olekhnovich, Int. J. Sulfur Chem., 3A, 249 (1973).
13. M. N. Zemtsova and A. E. Lipkin, Khim. Geterotsikl. Soedin., No. 6, 770 (1972).
14. P. L. Trakhtenberg, Z. I. Nuzhdina, and A. E. Lipkin, Khim. Geterotsikl. Soedin., No. 6, 773 (1972).

TAUTOMERISM OF 2-ARYLAMINO- AND 2-BENZYLAMINOTHIAZOLINE

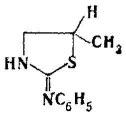
I. N. Azerbaev,* L. A. Tsoi,
S. T. Cholpankulova, and V. I. Artyukhin

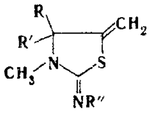
UDC 547.789.1.07:543.422.25.4.6

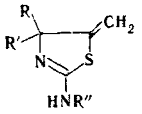
It was established by means of the IR, UV, and PMR spectra that 2-arylamino-4,4-dialkyl-5-methylenethiazolines have the 2-aryliminothiazolidine structure in the crystalline state and in solutions, whereas the 2-benzylamino derivatives can exist in both the amino and imino forms.

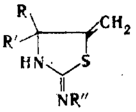
The problem of the structure of 2-aminothiazolines has been discussed repeatedly [1, 2]. It has been shown that 2-alkylaminothiazolines exist in the amino form, while 2-acylamino derivatives exist in the iminothiazolidine form. The data on the tautomerism of 2-arylaminothiazolines are contradictory. Thus Ramsh and co-authors have proved the existence of 2-phenylamino-4-thiazolidone in the form of a mixture of two tautomeric species [3], whereas an imino structure is assigned to this compound in [4].

The possibility of obtaining thiazolidines with a fixed imino structure (IIa-IXa) enabled us to investigate the effect of an N-aryl substituent on the amine—imine equilibrium. We investigated IIb-IXb (Table 1), which were obtained by the method in [5].


I


II a–IX a


II b-IX b
A


II b-IX b
B

The structures of IIb-IXb were determined by spectral methods.

IR Spectra

We investigated only the intense absorption bands in the 1500-1700 cm^{-1} region (Table 2). As a rule, the spectra of the investigated compounds in the crystalline state (in KBr) in this region contain three intense bands at 1590, 1610-1620, and 1640-1670 cm^{-1} due to the stretching vibrations of the methylene group, the phenyl ring, and the C=N bond [6]. To assign the absorption of the methylene bond and the phenyl ring we made an analysis of the spectra of I and II. Compounds IIa, b ($R = R' = CH_3$, $R'' = C_2H_5$) [5] do not contain a phenyl ring, and we assigned the absorption at 1610 cm^{-1} to the absorption of the methylene bond. Compound I [7] does not contain a methylene bond, and its spectrum does not contain a band at 1610 cm^{-1}; we therefore assigned the band at 1590 cm^{-1} to the absorption of the phenyl ring. The intensity of the absorption band at 1610 cm^{-1} is lower than the intensities of

---

*Deceased.

Institute of Chemical Sciences, Academy of Sciences of the Kazakh SSR, Alma-Ata 480100. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 755-760, June, 1979. Original article submitted August 30, 1978.