SYNTHESIS AND PROTON-ACCEPTOR CAPACITIES OF 5-ARYL-2-ACETYLTHIOPHENES AND 1-(5-ARYL-2-THIENYL)-1PROPENONES

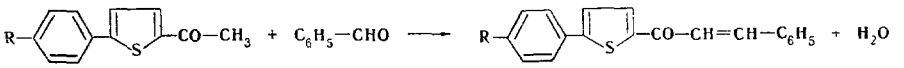
V. K. Polyakov, Z. P. Zaplyuisvechka,
L. P. Pivovarevich, Yu. N. Surov,
and S. V. Tsukerman

UDC 547.733.734:543.878

A number of 5-aryl-2-acetylthiophenes and 1-(5-aryl-2-thienyl)-3-phenyl-1-propenones were synthesized, and it was shown by means of their IR spectra that the 1-propenones are trans isomers with respect to the orientation of the substituents attached to the double bond and have an s-cis conformation. According to the data from the IR spectra of the H complexes of the investigated compounds with phenol, 5-aryl-2-acetylthiophenes have higher proton-acceptor capacities than acetophenones, 2-acetylthiophenes, and 4-acetyldiphenyl; a similar picture is also noted in a number of 1-propenones and 3-propenones. The transmission factors (π') obtained by Hammett correlation of the $\Delta\nu_{OH}$ values for 1,4-phenylene, 2,5-thienylene, and vinylene groupings are identical and are equal to 0.8. It is shown on the basis of a correlation with respect to an equation of the Yukawa–Zuno type that the thiophene ring transmits polar conjugation better than the benzene ring.

Until recently, of the 5-aryl-2-acetylthiophenes and the products of their condensation with aromatic and heterocyclic aldehydes, only 5-phenyl-2-acetylthiophene [1-3] and 1-(5-phenyl-2-thienyl)-3-phenyl-1-propenone [3] have been described. Since compounds of this type can be used as intermediates in organic synthesis, we decided to synthesize 5-phenyl-2-acetylthiophene derivatives containing substituents with different chemical natures in the benzene ring and to subject them to the Claisen–Schmidt reaction with benzaldehyde. On the other hand, we decided to investigate the IR spectra of these ketones and their H complexes with phenols in order to determine their relative proton-acceptor capacities in the step involving the formation of a hydrogen bond.

5-Aryl-2-acetylthiophenes were obtained by acylation of 2-arylthiophenes with acetyl chloride in benzene by means of stannic chloride (method B) and by condensation of arenediazonium chlorides with 2-acetylthiophene in the presence of cupric chloride (method B). In the first case the reaction proceeded quite smoothly at 20-25°C, and the final products were obtained in 63-70% yields (I-V, Table 1); however, this method cannot be used for the preparation of compounds containing a nitro group in the benzene ring (VII, VIII). When method B is used, side reactions with the formation of the corresponding phenols from the diazo compounds take place, and this leads to a considerable reduction in the yield of the product. The ketones that we obtained were subjected to condensation with benzaldehyde:



It was found that the reaction in this case proceeds under more severe conditions than in the preparation of the previously described thiophene analogs of chalcones with simpler structures [4, 5].

The proton-acceptor capacity of the investigated carbonyl compounds was characterized by means of the shifts in the stretching vibrations of the hydroxyl group of the phenol

A. M. Gor'kii Khar'kov State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1196-1202, September, 1976. Original article submitted March 4, 1975; revision submitted December 29, 1975.

TABLE 1. 2-Acetyl-5-(R-phenyl)thiophenes

Compound	R	mp, °C	Empirical formula	Found, %	Calc., %	Method A	
						meth. A	meth. B
I	H	119	$C_{12}H_{10}OS$	—	—	68	—
II	4-CH_3	121	$C_{13}H_{12}OS$	S 14,92	14,81	63	2
III	4-CH_3O	155	$C_{13}H_{12}O_2S$	S 13,64	13.79	66	8
IV	4-Cl	130	$C_{12}H_9ClOS$	S 13,47	13,56	70	12
V	4-Br	150	$C_{12}H_9BrOS$	S 11,18	11.03	69	13
VI	4-I	130	$C_{12}H_9IOS$	S 9,69	9.75	—	12
VII	3-NO_2	137	$C_{12}H_9NO_3S$	N 5,51	5,66	—	6
VIII	4-NO_2	170	$C_{12}H_9NO_3S$	N 5,74	5.66	—	14

TABLE 2. 1-[5-(R-Phenyl)-2-thienyl]-3-phenyl-1-propenones

Compound	R	mp, °C	Empirical formula	Found, %	Calc., %	Yield, %
IX	H	163	$C_{19}H_{14}OS$	—	—	97
X	4-CH_3	182	$C_{20}H_{16}OS$	S10,68	10,53	98
XI	4-CH_3O	183	$C_{20}H_{16}O_2S$	S 9,86	10,00	98
XII	4-Cl	176	$C_{19}H_{13}ClOS$	S 9,94	9,87	98
XIII	4-Br	185	$C_{19}H_{13}BrOS$	S 8,59	8,68	98
XIV	4-I	189	$C_{19}H_{13}IOS$	S 7,77	7,69	95
XV	3-NO_2	218	$C_{19}H_{13}NO_3S$	N 4.21	4,18	97
XVI	4-NO_2	236	$C_{19}H_{13}NO_3S$	N 4,29	4,18	97

during the formation of H complexes in ketone—phenol—carbon tetrachloride systems ($\Delta\nu_{OH}$) and also from data on the carbonyl frequencies ($\nu_{C=O}$) (Table 3). For comparison, we also measured the IR spectra of 1-(5-aryl-2-thienyl)-3-phenyl-3-propenones (XIV-XXII, Table 3) in carbon tetrachloride and of their H complexes with phenol.

A comparison of the $\Delta\nu_{OH}$ and $\nu_{C=O}$ values for 5-phenyl-2-acetylthiophene (I, Table 3 , acetophenone, and 2-acetylthiophene ($\Delta\nu_{OH}$, respectively, 190, 193 cm^{-1} and $\nu_{C=O}$ 1691.1 and 1672.2 cm^{-1} [6]) shows that the accumulation of aromatic rings leads to an increase in the proton-acceptor capacity. Replacement of the benzene ring in 4-acetyldiphenyl by a thiophene ring in turn increases the basicity of the methyl ketone (acetyldiphenyl: $\nu_{C=O}$ = 1688.3, $\Delta\nu_{OH}$ = 194 cm^{-1} [6]). The introduction of electron-donor substituents in the benzene ring of 5-phenyl-2-acetylthiophene leads to an increase in $\Delta\nu_{OH}$ and a decrease in $\nu_{C=O}$ (compare I with II and III, Table 3), whereas electron-acceptor substituents give rise to the opposite effect (compare I and IV-VIII). However, the effect of the substituent is not as clearly expressed as, for example, in the case of substituted acetophenones or 2-acetophenones or 2-acetylthiophenes [7]. Thus the introduction of a methoxy group in the benzene ring leads to an increase in $\Delta\nu_{OH}$ of 10 cm^{-1} (compare I with III), whereas this sort of change in the structure causes an increase of 14 cm^{-1} in the $\Delta\nu_{OH}$ value for acetophenones and 36 cm^{-1} for 2-acetylthiophenes [7]. A nitro group in the 3 or 4 position of the benzene ring (VII, VIII) has a much smaller electron-acceptor effect than in the acetophenone series, especially in the case of 2-acetylthiophenes [6].

A correlation analysis with the aid of the Hammett and Brown equations and an equation of the Yukawa—Zuno type [8] (Table 4) was made for the quantitative evaluation of the effect of substituents on the proton-acceptor capacity of the ketones and the carbonyl frequencies. It follows from the data in Table 4 that the $\Delta\nu_{OH}$ values correlate well with both the σ^- and σ^+ substituent parameters, but the correlation with respect to the Hammett equation is, nevertheless, better, judging from the r values. It is likely that the polar conjugation through the extended system consisting of the benzene and thiophene rings is somewhat weakened. This is confirmed by the fact that the m_r reaction constant in the equation of the Yukawa—Zuno type

$$\Delta\Delta\nu_{OH}=\Delta\Delta\nu_{OH}^{H}+m_0\sigma^0+m_r\sigma_R^-$$

for 5-aryl-2-acetylthiophenes, which characterizes the degree of the effect of polar conjugation in these systems on the proton-acceptor capacity of the carbonyl group, is smaller in absolute value than m_o (it indicates the relative degree of transmission via an inductive mechanism) (m_o = —63.3 ± 11.9, m_r = —16.5 ± 7.4, and r = 0.97), whereas, for example,

TABLE 3. Data from the IR Spectra of Heteroaromatic Ketones and Their H Complexes with Phenol

Substituent R	2-Acetyl-5-(R-phenyl)thiophenes			1-[5-(R-Phenyl)-2-thienyl]-3-phenyl-1-propenones				1-[5-(R-Phenyl)-2-thienyl]-3-phenyl-3-propenones			
	compound	$\nu_{C=O}$, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}	compound	$\nu_{C=O}$, cm^{-1}	$\nu_{C=C}$, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}	compound	$\nu_{C=O}$, cm^{-1}	$\nu_{C=C}$, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}
H	I	1669	198±2	IX	1660	1607	199±2	XVII	1666	1593	195±2
4-CH_3	II	1667	201±3	X	1660	1608	208±4	XVIII	1667	1592	212±2
4-CH_3O	III	1667	208±5	XI	1660	1609	212±3	XIX	1665	1593	214±2
4-Cl	IV	1670	183±6	XII	1660	1608	189±2	XX	1668	1595	195±2
4-Br	V	1669	174±4	XIII	1660	1609	187±2	XXI	1667	1598	202±1
4-I	VI	1670	171±6	XIV	1661	1609	168±5	—	—	—	—
3-NO_2	VII	1673	143±2	XV	1662	—	147±2	—	—	—	—
4-NO_2	VIII	1674	143±2	XVI	1662	—	146±1	XXII	1668	1605	151±1

TABLE 4. Data from a Correlation Analysis of the $\nu_{C=O}$ and $\Delta\nu_{OH}$ Values with Respect to the Hammett and Brown Equations

Equation y = mx + b	r*	S^*_m	S^*_b	S^*_{tot}	n*
5-Aryl-2-acetylthiophenes					
$\Delta\nu_{C=O}=7{,}8\sigma-1{,}1$	0,93	0,09	0,03	0,02	8
$\Delta\nu_{C=O}=5{,}0\sigma^+ +0{,}1$	0,98	0,06	0,01	0,01	8
$\Delta\Delta\nu_{OH}=-64{,}8\sigma+6{,}8$	0,98	1,8	0,6	1,7	8
$\Delta\Delta\nu_{OH}=-47{,}5\sigma^+ -15{,}5$	0,96	0,8	1,5	2,7	8
1-(5-Aryl-2-thienyl)-3-phenyl-1-propenones					
$\Delta\Delta\nu_{OH}=-66{,}7\sigma-3{,}1$	0,96	2,5	1,0	0,8	8
$\Delta\Delta\nu_{OH}=-48{,}5\sigma^+ +4{,}1$	0,93	2,1	3,1	2,9	8
1-(5-Aryl-2-thienyl)-3-phenyl-3-propenones					
$\Delta\Delta\nu_{OH}=-49{,}6\sigma+0{,}0$	0,95	3,7	1,5	2,7	5
$\Delta\Delta\nu_{OH}=33{,}4\sigma^+ -6{,}7$	0,88	4.7	2,4	4,5	5

*Symbols: r is the correlation coefficient, S_m, S_b, and S_{tot} are the mean square errors in the a and b parameters, and n is the number of points.

for substituted 2-acetylthiophenes, the ratio between m_o and m_r differs only slightly from unity (m_o = −59.5 and m_r = −44.7 [7]).

Transmission factor π' is frequently used for the characterization of the conductivity of electronic substituent effects by any fragment of the molecule [8]. Transmission factors π' for 1,4-phenylene and 2,5-thienylene bridges in the investigated systems, which were found to be identical and equal to 0.8, were determined by comparison of the reaction constants (m) obtained during correlation of the $\Delta\nu_{OH}$ values of 5-aryl-2-acetylthiophenes with respect to the Hammett equation (Table 4) with the values obtained for acetophenones and 2-acetylthiophenes [6]. The factors for the benzene ring (0.3) and the thiophene ring (0.5) were obtained by correlation of the carbonyl frequencies of the investigated compounds and comparison of them with the analogous data for acetophenones and 2-acetylthiophenes [6]. These values are in agreement with the literature data [9] and with the theoretical calculations of π' on the basis of the specific transmission factors of carbon and sulfur atoms [10, 11].

The difference in transmission factors π' obtained during a study of the hydrogen bonds ($\Delta\nu_{OH}$) and the carbonyl frequencies ($\nu_{C=O}$) is probably associated with the fact that primarily the magnitude of the electron density on the carbonyl oxygen atom affects the $\Delta\nu_{OH}$ values, whereas other factors such as, for example, interaction of the vibrations, the reduced masses, and the size of the angles at the carbonyl group [12] also affect the frequencies of the stretching vibrations of the carbonyl group.

A comparison of the m_o and m_r reaction constants in equations of the Yukawa–Zuno type for the investigated 5-aryl-2-acetylthiophenes with those obtained for acetophenones [6] made it possible to determine transmission factors π'_o and π'_r individually for transmission of the inductive effect and the polar conjugation. It was found that the thiophene ring

transmits the inductive effect approximately to the same degree as the benzene ring [$\pi_o'(T)$ = 1.0, $\pi_o'(B)$ = 1.1], whereas conductivity of the effects of polar conjugation is realized better by the thiophene ring (π_r' 0.6 and 0.4, respectively). Thus, the previously drawn conclusion [6, 13] regarding the better conductivity of polar conjugation by the thiophene ring as compared with the benzene ring are confirmed. In addition, it is apparent that the decrease in the transmission of the electronic effects by the molecular systems of 5-aryl-2-acetylthiophenes as compared with acetophenones or 2-acetylthiophenes is associated primarily with the decrease in the fraction of the conductivity of the conjugation effects (π_r' = 0.4 and 0.6), whereas the transmission of the inductive effect does not change appreciably (π_o' = 1.0). The decrease in the degree of polar conjugation in this system can be ascribed to the probable disruption of the coplanarity of the aromatic and heterocyclic rings.

The synthesized heterocyclic analogs of chalcones (IX-XVI) are trans isomers with respect to the orientation of the substituents attached to the aliphatic double bond, as evidenced by the presence in the IR spectra (KBr pellets) of peaks of medium intensity at 982-985 cm^{-1}, which are characteristic for the out-of-plane deformation vibrations of the hydrogen atoms of trans-vinylene groups. The characteristic vibrations of the carbonyl group appear at 1648-1652 cm^{-1} and those of the aliphatic double bonds show up at 1592-1600 cm^{-1}. Moreover, the intensity of $\nu_{C=C}$ is higher in all cases than that of $\nu_{C=O}$, and this indicates the s-cis orientation of the C=O and C=C bonds.

The $\Delta\nu_{OH}$ values for IX-XVII (Table 3) show that the transition from the corresponding acetyl derivatives to α, β-unsaturated ketones gives rise to a slight increase in the proton-acceptor capacity (+1=6 cm^{-1}). Substituents with different natures in the benzene ring of these chalcone analogs have the same effect as in the case of 5-aryl-2-acetylthiophenes.

To estimate the transmission of the electronic effects of substituents of the vinylene grouping we measure the $\nu_{C=O}$, $\nu_{C=C}$, and $\Delta\nu_{OH}$ values of phenol for isomeric unsaturated ketones — 1-(5-aryl-2-thienyl)-3-phenyl-1-propenones and 1-(5-aryl-2-thienyl)-3-phenyl-3-propenones. As seen from Table 3, the $\nu_{C=C}$ and $\nu_{C=O}$ values for XVIII-XXII are just as slightly sensitive to a change in the chemical structure of the ketones as in the case of 1-propenones. The $\Delta\nu_{OH}$ values for ketones XVII-XXII are generally somewhat higher than the values for IX-XVI. The high proton-acceptor capacity of 3-propenones as compared with 1-propenones can evidently be associated with the fact that steric hindrance to the formation of a hydrogen bond is eliminated as the carbonyl group becomes farther away from the heteroring. The existence of similar steric hindrance was also noted in [14].

The $\Delta\nu_{OH}$ values for unsaturated ketones IX-XVI and for the isomeric XVII-XXII satisfactorily correlate satisfactorily with the Hammett σ constants (Table 4). Satisfactory correlation also with respect to the Yukawa—Zuno equation is observed for ketones IX-XVI: $\Delta\Delta\nu_{OH} = (-66.0 \pm 9.8)\sigma^{\circ} - (16.6 \pm 5.2)\sigma_R^{+} - (2.8 \pm 7.8)$; r = 0.95. As in the case of 5-aryl-2-acetylthiophenes, transmission of the effect through the system of the benzene and thiophene rings via an inductive mechanism prevails. The transmission factor of the double aliphatic bond was estimated by comparison of the reaction constants in the Hammett equations (Table 4) for 1-propenones and 3-propenones and was found to be $\pi' = 0.8$; in general, this is in agreement with the literature data [15] and indicates rather high transmission of the electronic effects by the aliphatic double bond in the s-cis conformations of α, β-unsaturated ketones.

EXPERIMENTAL

5-Aryl-2-acetylthiophenes. Method A. A solution of 10 ml of stannic chloride in 10 ml of benzene was added dropwise with stirring at 20-25° to a benzene solution of 0.05 mole of 2-arylthiophene and 0.055 mole of acetyl chloride, after which the mixture was stirred for 4 h. The benzene was removed by steam distillation, and the residue was recrystallized from alcohol.

Method B. A 32-g (0.25 mole) sample of 2-acetylthiophene, 200 ml of acetone, and 10 g of cupric chloride in 20 ml of water were added to a cooled (to 0-5°) aqueous solution of arenediazonium chloride (0.25 mole), and the mixture was stirred at 20-30° for 6 h. The acetone, 2-acetylthiophene, and side-product phenol were removed by steam distillation, and the residue in the flask (a dark oil) began to crystallize on cooling. The product was purified successively from aqueous alcohol and alcohol.

1-(5-Aryl-2-thienyl)-3-phenyl-1-propenones. A 0.1-0.3-g sample of solid sodium hydroxide was added to a refluxing alcohol solution (50-100 ml) of 0.006 mole of 5-aryl-2-acetylthiophene and 0.006 mole of benzaldehyde, and the mixture was refluxed for 2-3 h. The precipitate on the filter was washed with 50 ml of 50% alcohol and, where necessary, recrystallized from acetic acid.

The 1-(5-aryl-2-thienyl)-3-phenyl-3-propenones were obtained as described in [16].

The IR spectra of carbon tetrachloride solutions of the compounds (0.01 mole) were scanned with a UR-20 spectrometer at a layer thickness of 0.1 cm. Carbon tetrachloride solutions containing 0.006 mole of phenol and 0.006 mole of the ketone with an absorbing-layer thickness of 2 cm were used to measure the $\Delta\nu_{OH}$ values.

LITERATURE CITED

1. W. Steinkopf and H. J. Petersdorf, Ann., 543, 119 (1940).
2. N. Gjos and S. Gronowitz, Acta Chem. Scand., 26, 1851 (1972).
3. A. E. Lipkin, N. I. Putokhin, and S. I. Borisov, Khim. Geterotsikl. Soedin., No. 4, 476 (1966).
4. V. F. Lavrushin, S. V. Tsukerman, and V. M. Nikitchenko, Url. Khim. Zh., 27, 379 (1961).
5. V. F. Lavrushin, S. V. Tsukerman, and V. M. Nikitchenko, Zh. Obshch. Khim., 31, 2845 (1961).
6. L. P. Pivovarevich, L. A. Kutulya, Yu. N. Surov, S. V. Tsukerman, and V. F. Lavrushin, Khim. Geterotsikl. Soedin., No. 7, 918 (1974).
7. L. P. Pivovarevich, L. A. Kutulya, Yu. N. Surov, S. V. Tsukerman, and V. F. Lavrushin, Reakts. Sposobn. Org. Soedin., 10, 119 (1973).
8. Yu. A. Zhdanov and V. I. Minkin, Correlation Analysis in Organic Chemistry [in Russian], Izd. Rostovskogo Univ. (1966).
9. A. Perjessy, P. Hrnčiar, R. Frimm, and L. Fišera, Tetrahedron, 28, 3781 (1972).
10. K. Bowden, Can. J. Chem., 41, 2781 (1963).
11. A. Perjessy and M. Zăcová, Coll. Czech. Chem. Commun., 36, 2944 (1971).
12. L. Bellamy, New Data on the Infrared Spectra of Complex Molecules [Russian translation], Mir, Moscow (1971).
13. L. A. Kutulya, L. P. Pivovarevich, V. G. Gordienko, S. V. Tsukerman, and V. F. Lavrushin, Reakts. Sposobn. Org. Soedin., 9, 1043 (1972).
14. S. V. Tsukerman, A. A. Sukhorukov, Yu. N. Surov, and V. F. Lavrushin, Teor. Eksp. Khim., No. 7, 674 (1971).
15. S. V. Tsukerman, Yu. N. Surov, and V. F. Lavrushin, Zh. Obshch. Khim., 40, 874 (1970).
16. L. Kovăč, L. Fišera, and R. Frimm, Chem. Zvesti, 27, 512 (1973).
17. V. K. Polyakov, Z. P. Zaplyuisvechka, and S. V. Tsukerman, Khim. Geterotsikl. Soedin., No. 1, 136 (1974).