SYNTHESIS AND STRUCTURE OF 2-HYDROXY-3-FORMYLBENZO[b]THIOPHENE AZOMETHINES[*]

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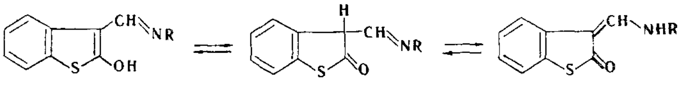
A number of 2-hydroxy-3-formylbenzo[b]thiophene azomethines and their derivatives, which model the individual tautomeric forms, were synthesized. As a result of a study of the electronic, vibrational, and PMR spectra, a ketone-amine structure, the stability of which is confirmed by quantum-mechanical calculations of the atomization energies of the individual tautomeric forms calculated by the Pariser–Parr–Pople (PPP) method within the Dewar σ, π parametrization, was assigned to these azomethines.

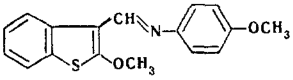
As a result of an investigation of the structures of 3-hydroxy(mercapto)-2-formylbenzo[b]thiophene and 3-hydroxy(mercapto)-2-formylbenzo[b] furanaryl- and alkylimines [1-3] we concluded that they exist in solution primarily in the form of ketone-amine and thione-amine tautomers, respectively. The aim of the present research was to establish the structures of potentially tautomeric 2-hydroxy-3-formylbenzo[b]thiophene imines (IA ⇌ IC), which have a mutual orientation of the heterocyclic sulfur atom and the tautomeric fragments that differs from that of 3-hydroxybenzo[b]thiophene derivatives [2]. In this connection, the problem of the effect of an annelated benzene ring on the structure of the previously investigated [4] mono-N-substituted 3-aminomethylene-4-thiolen-2-ones also seems of definite interest. With this end in mind, we synthesized a number of azomethines (Ia-*l*, Table 1) from 2-hydroxy-3-formylbenzo[b]thiophene and obtained their derivatives (II and III), which serve as models of the extreme tautomeric forms.

In order to evaluate the character of the IA ⇌ IC tautomeric equilibrium we recorded the electronic, vibrational, and PMR spectra of the compounds.

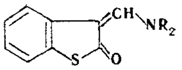


IA IB IC

R=Alk, Ar



II



III a, b

III a R=CH_3; b R=C_6H_5

We also formed a judgment regarding the relative stabilities of the tautomeric forms from quantum-mechanical calculations of their atomization energies.

The electronic absorption spectra of the arylazomethines (Ia-k) contain a characteristic long-wave absorption band at 405-420 nm, which appears in the spectrum of the alkylimine (I*l*) at ~370 nm. This band

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[*] Communication XVIII from the series "Benzoid–Quinoid Tautomerism of Azomethines and Their Structural Analogs." See [1] for communication XVII.

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TABLE 1. Compounds of the I and III Type

Compound	R	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	S	C	H	S	
Ia	C_6H_5	180—181	$C_{15}H_{11}NOS$	71,1	4,1	12,5	71,1	4,4	12,7	78
Ib	p-$H_3CC_6H_4$	186	$C_{16}H_{13}NOS$	71,6	5,0	12,0	71,9	4,9	12,0	87
Ic	m-$H_3CC_6H_4$	133	$C_{16}H_{13}NOS$	71,7	4,8	12,0	71,9	4,9	12,0	74
Id	p-ClC_6H_4	204	$C_{15}H_{10}ClNOS$	62,8	3,5	10,9	62,6	3,5	11,1	67
Ie	m-ClC_6H_4	185	$C_{15}H_{10}ClNOS$	62,3	3,5	11,0	62,6	3,5	11,1	63
If	p-$H_3COC_6H_4$	142	$C_{16}H_{13}NO_2S$	67,5	4,5	11,1	67,8	4,6	11,3	60
Ig	p-$H_5C_2OOCC_6H_4$	208	$C_{18}H_{15}NO_3S$	66,1	4,5	9,7	66,4	4,6	9,8	56
Ih	p-$H_3CCOC_6H_4$	243	$C_{17}H_{13}NO_2S$	69,4	4,7	10,7	69,1	4,4	10,9	48
Ii	p-$O_2NC_6H_4$	300	$C_{15}H_{10}N_2O_3S$	60,0	3,6	10,4	60,4	3,4	10,8	69
Ij	m-$O_2NC_6H_4$	262	$C_{15}H_{10}N_2O_3S$	60,5	3,4	10,8	60,4	3,4	10,8	30
Ik	m-HOC_6H_4	241—242	$C_{15}H_{11}NO_2S$	66,5	4,3	11,5	66,9	4,1	11,9	57
Il	CH_3	132	$C_{16}H_{13}NOS$	72,1	4,9	11,7	71,9	4,9	12,0	49
IIIa	$CH_2C_6H_5$	120—121	$C_{11}H_{11}NOS$	64,5	5,6	15,9	64,4	5,4	15,6	50
IIIb	C_6H_5	160	$C_{21}H_{15}NOS$	76,5	4,4	10,0	76,6	4,6	9,7	54

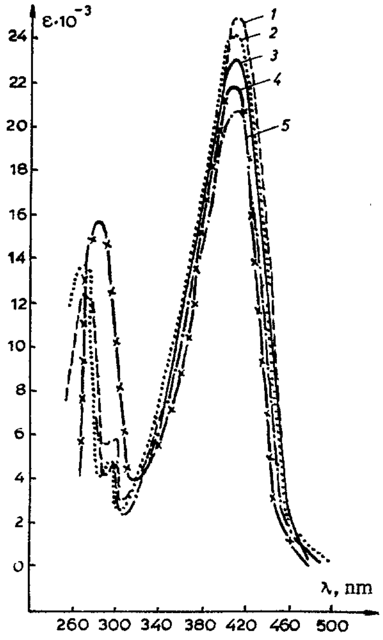


Fig. 1

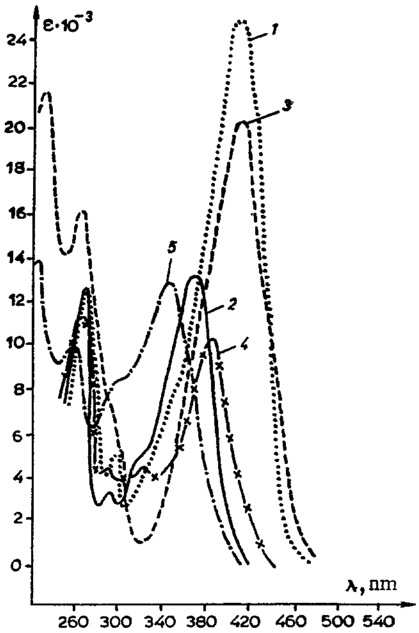


Fig. 2

Fig. 1. Electronic absorption spectra of 3-(N-phenylaminomethylene)-2(3H)-benzothiophenone (Ia): 1) in methanol; 2) in dimethylformamide; 3) in acetone; 4) in carbon tetrachloride; 5) in benzene.

Fig. 2. Electronic absorption spectra in methanol: 1) 3-(N-phenylaminomethylene)-2(3H)-benzothiophenone (Ia); 2) 3-(N-benzylaminomethylene)-2(3H)-benzothiophenone (Il); 3) 3-(N,N-diphenylaminomethylene)-2(3H)-benzothiophenone (IIIb); 4) 3-(N,N-dimethylaminomethylene)-2(3H)-benzothiophenone (IIIa); 5) 3-[N-(p-methoxyphenyl)iminomethylene]-2-methoxybenzo[b]thiophene (II).

is practically insensitive to a change in the polarity of the solvent, variation of the substituent in the benzene ring, and a change in the temperature, although its intensity increases in arylimines as compared with the alkylimine (Fig. 1 and Table 2). This means that compounds I exist in solution primarily in the form of one of three possible tautomeric forms. It is apparent from Fig. 2 that the spectra of I differ substantially from the spectrum of azomethine II, which models fixed benzoid form IA, and are similar to the spectra of IIIb (R $=C_6H_5$), which has a quinoid structure of the IC type. Consequently, azomethines I exist in solution primarily in quinoid form IC.

One may convince oneself of the accuracy of this conclusion by analyzing the data from the PMR and IR spectra. A characteristic pattern of splitting of the signals of the methylidyne protons, which is in agreement with structure IC, is observed in the PMR spectra of Ia and Il (Fig. 3, spectra a and c): at δ

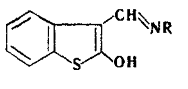
TABLE 2. Spectral Characteristics of I–III

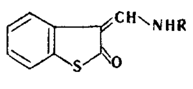
Compound	Solvent	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	IR spectra, ν, cm^{-1}	
			mineral oil	perfluorohydrocarbon
Ia	DMF	270 (13,8), 295 (4,7), 405 (24,2)	1585, 1605, 1650	2950, 3080, 3270
	Methanol	270 (12,2), 295 (5,4), 410 (25,1)		
	Benzene	— 295 (5,8), 410 (20,6)		
	Acetone	— — 405 (23,1)		
	CCl_4	280 (15,8) — 405 (22,0)		
Ib	DMF	270 (14,3), 293 (5,3), 405 (24,8)	1585, 1612, 1655	2930, 3060, 3240
	Methanol	270 (15,8), 295 (5,4), 410 (25,6)		
	Benzene	— 295 (6,2), 410 (22,2)		
Ic	DMF	270 (13,9), 293 (4,9), 405 (24,6)	1590, 1645	2950, 3070, 3245
	Methanol	270 (13,0), 295 (4,4), 410 (19,8)		
	Benzene	280 (8,5), 297 (6,8), 410 (21,2)		
Id	DMF	270 (11,6), 293 (4,3), 405 (18,9)	1585, 1630, 1660	2945, 3070, 3240
	Methanol	270 (11,5), 295 (4,2), 410 (25,0)		
	Benzene	— 295 (7,4), 407 (26,8)		
Ie	DMF	270 (14,8), 293 (7,4), 405 (23,3)	1597, 1650	2965, 3100, 3245
	Methanol	270 (13,4), 295 (3,8), 410 (25,0)		
	Benzene	280 (8,5), 295 (7,9), 410 (22,0)		
If	DMF	273 (13,8), 295 (6,3), 410 (24,5)	1595, 1620, 1655	2945, 3010, 3070, 3240
	Methanol	272 (9,7), 295 (3,9), 410 (25,9)		
	Benzene	— 295 (5,2), 415 (23,0)		
Ig	DMF	275 (14,8), 292 (8,4), 412 (31,3)	1582, 1610, 1655, 1710	2970, 3010, 3090, 3285
	Methanol	275 (10,0), 295 (5,6), 412 (30,7)		
	Benzene	285 (14,4), — 415 (27,1)		
Ih	DMF	270 (12,0), 290 (7,1), 415 (34,0)	1595, 1615, 1655	3010, 3070, 3245
	Methanol	— 293 (7,6), 420 (34,6)		
	Benzene	282 (15,1), 300 (11,5), 410 (42,8)		
Ii	DMF	270 (10,1), 295 (7,7), 438 (32,7), 530 (4,5)	1595, 1615, 1665	2940, 3085, 3230
Ij	DMF	270 (18,0), 290 (9,0), 402 (23,0)	1580, 1615, 1646	3110, 3235
Ik	DMF	270 (16,9), 293 (8,0), 408 (24,3)	1595, 1645	2950, 3030, 3080, 3170
Il	DMF	272 (12,2), 292 (3,5), 320 (5,1), 370 (13,0)	1600, 1645	3075, 3280
	Methanol	265 (12,7), 290 (3,2), 320 (5,9), 370 (13,4)		
	Benzene	280 (7,0), 293 (5,4), 328 (7,7), 370 (13,5)		
	Acetone	— — — 374 (15,6)		
IIIa	DMF	273 (16,2), 292 (7,2), 318 (6,9), 375 (15,9)	1583, 1650	2940, 3070
	Methanol	275 (11,5), 295 (4,3), 320 (4,3), 380 (10,2)		
	Benzene	292 (9,2), 297 (6,6), 330 (6,4), 385 (12,2)		
IIIb	DMF	270 (13,0), 290 (9,1), 408 (20,7)	1585, 1655	2940, 3075
	Methanol	262 (16,1), 295 (6,9), 410 (20,3)		
	Benzene	— 290 (10,6), 408 (21,6)		
II	Methanol	260 (9,1), 300 (8,2), 346 (13,0)	1585, 1610	

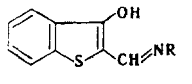
8.70 and 7.53 ppm, respectively, there are signals with J = 13.5 Hz, which is close in magnitude to the SSCC in the spectra of the quinoid tautomers of 2-formyl-3-hydroxy- and 2-formyl-3-mercaptobenzo[b]thiophene azomethines [1, 2]. Upon N-deuteration the proton of the methylidyne group gives a singlet (Fig. 3, spectrum b). At weaker fields at 11.20 ppm for Ia and 9.73 ppm for *Il* there are signals of NH protons that are characteristic for the >CH—NH system [4, 5]. The signals of the NH protons vanish after deuteration (Fig. 3, spectrum d).

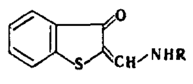
However, spin coupling of N^{15} and H nuclei with $J_{N^{15}H} = 93.4$ Hz appears in the spectrum of phenylimine Ia with N^{15}. Its magnitude, which does not change as the temperature is varied from 25 to 90°, constitutes evidence for the absence of proton exchange in the ketone–amine fragment [4, 6]. The PMR spectrum of benzylamine azomethine (*Il*) contains a doublet of protons of a benzyl group at δ 4.43 ppm with J = 6 Hz, which is close to the SSCC of the benzyl protons of anils with ketone- and thione-enamine structures [1, 7, 8].

TABLE 3. Differences in the Heats of Atomization of the Quinoid (C) and Benzoid (A) Tautomers of I and I' with Allowance for the Differences in the Solvation Energies ($\Delta\Delta H_a$)


I A

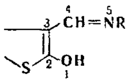

I C

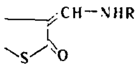

I'A

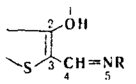

I'C

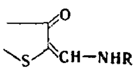
Compound type	R	$\Delta\Delta H_a$, kcal/mole		
		gas	ε=2,2	ε=48,9
I	H	8,4	19,4	27,2
	C_6H_5	5,8	16,8	24,6
I'	H	6,1	17,8	20,9
	C_6H_5	3,2	14,7	18,1

TABLE 4. Calculated Bond Lengths (Å) in the Hydroxyvinylimine and Amino-enone Fragments of the Benzoid and Quinoid Tautomers of I and I'


I A


I C


I'A


I'C

Compound type		R	Bond			
			1—2	2—3	3—4	4—5
I	A	H	1,371	1,362	1,461	1,289
		C_6H_5	1,371	1,363	1,458	1,296
	C	H	1,265	1,463	1,356	1,407
		C_6H_5	1,265	1,463	1,355	1,408
I'	A	H	1,372	1,362	1,460	1,288
		C_6H_5	1,372	1,363	1,456	1,296
	C	H	1,264	1,465	1,351	1,412
		C_6H_5	1,264	1,465	1,351	1,413

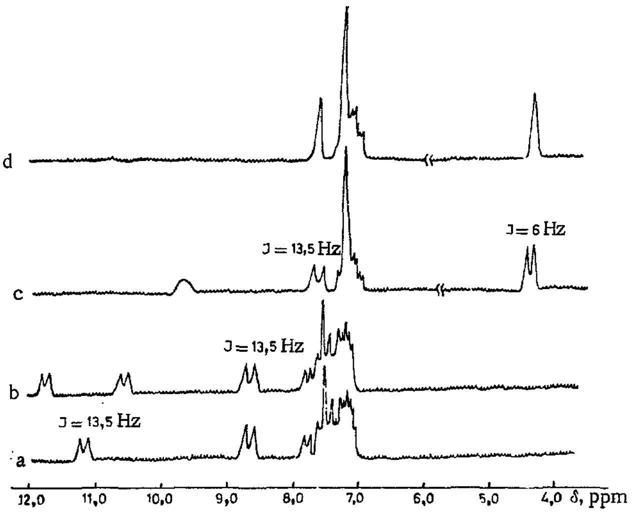
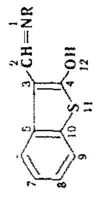
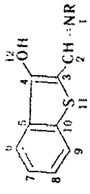


Fig. 3. PMR spectra of Ia in dimethyl sulfoxide (a, b) and of Il in methylene chloride (c, d): b) Ia with N^{15}; d) deuterated Il.

TABLE 5. Distribution of the π Charges in Molecules of I and I' in the Ground State

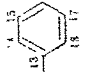


I A



I'A

R = H,



Compound type			Atom No.																	
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
I	A	H	−0,364	+0,312	−0,114	+0,079	−0,014	−0,002	−0,003	+0,040	−0,015	−0,026	+0,123	+0,019						
		C_6H_5	−0,371	+0,320	−0,117	+0,085	−0,015	−0,001	−0,002	+0,005	−0,014	−0,027	+0,126	+0,020	+0,099	−0,029	+0,008	−0,037	+0,009	−0,057
	C	H	+0,047	+0,127	−0,104	+0,421	−0,025	+0,004	−0,002	+0,010	−0,009	−0,019	+0,094	−0,546						
		C_6H_5	+0,066	+0,124	−0,100	+0,422	−0,027	+0,006	−0,002	+0,011	−0,009	−0,018	+0,095	−0,547	−0,007	+0,002	−0,008	−0,005	+0,006	−0,024
I'	A	H	−0,349	+0,297	−0,116	+0,076	−0,052	+0,026	−0,018	+0,025	−0,029	+0,011	+0,112	+0,018						
		C_6H_5	−0,354	+0,300	−0,120	+0,084	−0,055	+0,028	−0,018	+0,027	−0,030	+0,013	+0,112	+0,019	+0,105	−0,075	+0,039	−0,054	+0,019	−0,040
	C	H	+0,038	+0,080	−0,086	+0,422	−0,088	+0,087	−0,034	+0,048	−0,043	+0,035	+0,068	−0,528						
		C_6H_5	+0,061	+0,075	−0,082	+0,422	−0,089	+0,088	−0,034	+0,049	−0,043	+0,035	+0,069	−0,528	−0,009	−0,008	+0,015	−0,014	+0,016	−0,024

The examples of PMR spectra presented here, which are typical for all I, indicate practically complete shifting of the tautomeric equilibrium to favor the ketone-amine form and its high relative stability.

The data from the IR spectra enable us to definitively prefer form IC. The spectra of I and III (Table 2) contain an intense band at ~1650 cm^{-1}, which corresponds to the vibrations of a carbonyl group [2] and is absent in the spectra of an azomethine of the II type with an imine structure. For the latter, a band at 1610 cm^{-1}, which is affiliated with vibrations of the C=N bond [2] is characteristic. In addition, azomethines I have bands at 3240-3285 cm^{-1}, which are absent in the spectra of compounds with fixed benzoid and quinoid structures (II and III), in the region of NH stretching vibrations.

The stability of structure IC is confirmed by the results of quantum-mechanical calculations of the atomization energies of the individual tautomeric forms performed by means of the Pariser–Parr–Pople (PPP) method within the Dewar σ, π parametrization [9-11]. The results of the calculation predict the complete preferableness of the aminoenone form (IC), regardless of the substituent (R) attached to the nitrogen atom and the polarity of the solvent.

We also calculated the bond lengths of the hydroxyvinylimine and amino-enone fragments and the magnitudes of the π charges of the atoms in tautomeric forms IA and IC. It follows from Table 4 that, both in the case of the benzoid (IA) and quinoid (IC) tautomers the geometry of the indicated fragments is retained regardless of their orientation with respect to the ring heteroatom. The π charges undergo only slight changes on passing from the 3-hydroxy to the 2-hydroxy derivatives (Table 5).

Thus compounds I exist primarily in the form of tautomer IC. Neither variation of the structure of the amine component nor a change in the orientation of the keto-enamine fragment relative to the heteroatom shift the IA ⇌ IC equilibrium. A comparison of the data obtained with the results of investigations of the structures of the corresponding thiophenone derivative shows that annelation of the benzene ring does not have a substantial effect on the character of the tautomeric equilibrium in solution.

EXPERIMENTAL METHOD

2-Hydroxy-3-formylbenzo[b]thiophene (IV). This compound was obtained by alkaline hydrolysis of anil Ia [12], synthesized by condensation of thiooxindole [13] with diphenylformamidine [14, 15]. The product was purified by sublimation to give colorless crystals with mp 128-130° in 78% yield.

2-Methoxy-3-formylbenzo[b]thiophene (V). This compound was obtained in 72% yield by the Vilsmeier reaction [16]. The light-yellow needles had mp 59-60°.

Compounds I and IIIb (Table 1) were obtained by condensation of IV with the appropriate amines in alcohol and subsequent crystallization of the products from alcohols or dimethylformamide (DMF). The products were bright-yellow or orange crystals.

3-[N-(p-Methoxyphenyl)iminomethylene]-2-methoxybenzo[b]thiophene (II). This compound was obtained in 80% yield by reaction of equimolecular amounts of V with p-anisidine in ethanol. The product was obtained as yellow crystals with mp 116° (from alcohol). Found: C 69.0; H 5.2; S 11.1%. $C_{17}H_{15}NO_2S$. Calculated: C 68.7; H 5.1; S 10.8%.

3-(N,N-Dimethylaminomethylene)-2(3H)-benzothiophenone (IIIa). A 0.63-ml sample (7 mmole) of $POCl_3$ and a solution of 1 g (7 mmole) of thiooxindole in 7.5 ml of DMF were added successively dropwise at 0° to 0.55 ml (7 mmole) of DMF, after which the mixture was stirred at 0° for 1 h. The contents of the flask were transferred to a mixture of ice and sodium acetate, and the resulting precipitate was removed by filtration and recrystallized from benzene–petroleum ether to give bright-yellow needles.

The absorption spectra were recorded with a Specord UV-Vis recording spectrometer (German Democratic Republic). The IR spectra were obtained with a UR-20 spectrometer. The PMR spectra were recorded at 25° with a Tesla BS-407-C spectrometer (80 MHz). The concentrations of the substances in DMSO and methylene chloride were 15-20%, and the internal standard was hexamethyldisiloxane.

The method used to carry out the quantum-mechanical calculations was described in [1].

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