STUDY OF THE PROPERTIES AND STRUCTURE OF 6-SUBSTITUTED 2-THIONOLEPIDINES

D. I. Biskupskaya and A. V. Voropaeva

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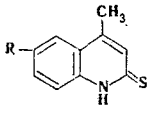
It has been shown that 2-thioquinolones are weaker conjugate acids and bases than 4-thioquinolones [1]. The UV spectra of solutions and the IR spectra of crystalline 6-substituted 2-thionolepidines confirm the predominance of the thione structure. It was found that 2-thioquinolones exist in the form of a dipolar ion. In contrast to 2-thiopyridones, 2-thioquinolones form derivatives of only the thiol form with methyl iodide, diazomethane, and acrylonitrile. The pK_a $(-H)^+$ values are correlated with the σ_J constants.

We have previously [1] reported the effect of substituents in the 6 position of 4-thionoquinaldines on their acid–base properties and reactivity in reactions with electrophilic reagents. In the present study we have obtained a number of 2-thionolepidine derivatives.



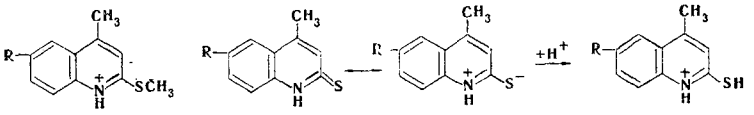
R=H; OCH_3; Cl; NO_2

We have studied their acid–base properties and reactions with methyl iodide, diazomethane, and acrylonitrile. The 2-thionolepidines were obtained from the corresponding chlorolepidines [2-5] by reaction with sodium thiosulfate [6]. The structure of the 2-thionolepidines was confirmed by spectral data (Tables 1 and 2).

The UV spectrum of an alcohol solution of thionolepidine I is similar to the spectrum of model compound XII, which has a fixed thione structure.

According to modern concepts, mesomerism of the thione ⟷ zwitterion type is characteristic for thiones. The synthesized 2-thionolepidines apparently are no exception in this respect. The absorption curves of solutions of III and its S-methyl derivative (IV) in concentrated hydrochloric acid (Fig. 1) are similar. This indicates that the proton adds to the sulfur atom to give cation B, which is identical to methylthiolepidinium cation A, thereby confirming the presence of a zwitterion.

Mesomerism apparently explains the insignificant effect of the chemical nature of the substituent on the pK_a $(+H)^+$ values in the investigated 6-substituted 2-thionolepidines and the considerable effect on the pK_a $(-H)^+$ values, which differ by more than two orders of magnitude in the order $OCH_3 > Cl > NO_2$. A similar regularity was also observed among 4-thionoquinaldines [1].



A B

2-Thionolepidines and 4-thionoquinaldines are interesting objects for a study of both localization of the proton and transmission of the substituent effect.

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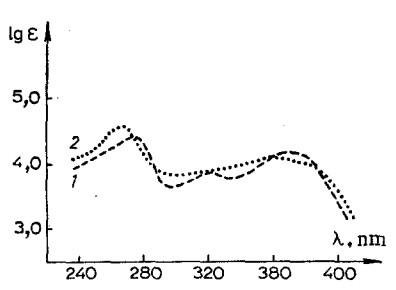

Fig. 1

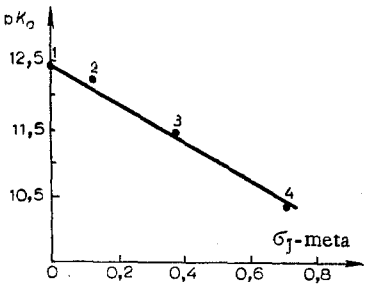

Fig. 2

Fig. 1. Absorption spectra in concentrated HCl: 1) 2-thiono-6-methyllepidine (III), 2) 2-methylthio-6-methoxylepidine (IV).

Fig. 2. Correlation of the pK_a $(-H)^+$ of 2-thionolepidines with the σ_J-meta constants (in 70% aqueous ethanol): 1) H; 2) OCH_3; 3) Cl; 4) NO_2 ($r = 0.994$, $\rho = -2.914$, $-\log K_0 = 12.53$, and $S_0 = 0.12$).

TABLE 1. 2-Thionolepidines and Their S-Alkylation Products

Compound	Name	mp, °C	R_f	Empirical formula	Found, %		Calc., %		Yield, %
					N	S	N	S	
I	4-Methyl-2-thioquinolone	266—267	0,16	$C_{10}H_9NS$	7,9	18,3	8,0	18,3	75
II[a]	4-Methyl-2-methylthioquinoline	35—35,5	0,82	$C_{11}H_{11}NS$	7,2	17,0	7,4	16,9	83
III	4-Methyl-6-methoxy-2-thioquinolone	275—276	0,27	$C_{11}H_{11}NOS$	6,8	15,7	6,8	15,6	74
IV[a]	4-Methyl-6-methoxy-2-methylthio-quinoline	103—104	0,81	$C_{12}H_{13}NOS$	6,6	14,7	6,4	14,6	77
V	4-Methyl-6-chloro-2-thioquinolone	273—275	0,30	$C_{10}H_8NSCl$ c	6,5	15,4	6,7	15,3	85
VI[a]	4-Methyl-6-chloro-2-methylthio-quinoline	60—61	0,86	$C_{11}H_{10}NSCl$ d	6,2	14,5	6,3	14,4	82
VII	4-Methyl-6-nitro-2-thioquinolone	281—282	0,04	$C_{10}H_8N_2O_2S$	12,8	14,7	12,7	14,5	84
VIII[a]	4-Methyl-6-nitro-2-methylthio-quinoline	157—158	0,84	$C_{11}H_{10}N_2O_2S$	12,1	13,4	12,0	13,7	86
IX[b]	4-Methyl-6-methoxy-2-cyano-ethylthioquinoline	94—95	0,72	$C_{14}H_{14}N_2OS$	10,9	12,8	10,8	12,8	87
X[b]	4-Methyl-2-cyanoethylthioquin-oline	70—71	0,88	$C_{13}H_{12}N_2S$	12,3	14,2	12,3	14,0	85
XI[b]	4-Methyl-6-nitro-2-cyanoethyl-thioquinoline	202—203	0,81	$C_{13}H_{11}N_3O_2S$	15,2	11,8	15,4	11,7	82
XII	1,4-Dimethyl-2-thioquinolone	138—140	0,65	$C_{11}H_{11}NS$	7,3	17,1	7,4	16,9	—

a) The 2-methyl derivatives were reprecipitated from the minimum amount of ethanol by the addition of water; b) the 2-cyanoethylthioquinolines were recrystallized from acetone; c) Found: Cl 16.8%. Calculated: Cl 16.9%. d) Found: Cl 16.0%. Calculated: Cl 15.9%.

We were unable to calculate the tautomer ratio by the Ebert method for 2-thionolepidines as we did for 4-thionoquinaldines in [1], since the pK_a $(+H)^+$ values for 2-thionolepidines and their S-methyl derivatives are close. We made a qualitative judgement of the localization of the proton in 2-thionolepidines from data from the UV and IR spectra, on the basis of which we confirmed the predominance of the thione form. The UV spectra of thionolepidines I and XII are close and differ from the spectra of their S-alkyl derivatives (II, X) with respect to the presence of absorption maxima in the long-wave portion of the spectrum (390, 405 nm) (Table 2), which are characteristic for the thione structure [7]. Intense bands are observed in the IR spectra of thionolepidines I, III, and VII in the region of the characteristic frequencies of C = S groups (1400-1500 cm^{-1}), and, in addition, there are one or two bands at 1600-1620 cm^{-1}. In addition to this, there are broad bands of a hydrogen bond at 2800-3120 cm^{-1} and at 3400-3550 cm^{-1}, which can be assigned to vibrations of the $\overset{+}{N}-H$ bond. There is no absorption in the region of the S−H stretching vibrations (2600 cm^{-1}). This is also in agreement with the results obtained by Yu. N. Sheinker [8], whose papers were devoted to a study of the structure and tautomerism of hydroxy, mercapto, and amino derivatives of nitrogen heterocyclic compounds by means of their spectra.

TABLE 2. pK Values and UV and IR Spectra of 2-Thioquinolones and Their Derivatives

Compound	$pK_a(+H)^+$	$pK_a(-H)^+$	UV spectra		IR spectra, cm^{-1}	
			λ_{max}, nm	lg ε	1400—1650	2600—3600
I	2,80	12,42	220, 280, 390	4,48; 4,32; 4,10	1400m 1488m 1480w, 1587—1620s	2830—3000s 3200m 3400—3600m
II	3,38		215, 255, 340	4,62, 4,45; 3,76		
III	2,95	12,32	225, 295, 395	4,57; 4,33; 4,06	1400m, 1438—1463m 1508 m, 1600s	2920s 3120m 3200m 3400—3600m
IV	2,95		220, 260, 345	4,50; 4,36; 3,77		
V	2,54	11,48	230, 285, 400	4,20; 3,96; 4,10		
VI	2,54		227, 300	4,31; 4,02		
VII	2,91	10,43	*, 283, 417	4,21; 4,33	1440 w, 1492m 1530m, 1620s	2900—3100s 3140m 3400—3600m
VIII	2,98		*, 266, 356	4,41; 4,47		
IX			215, 260, 350	4,48; 4,34; 3,67		
X			215, 255, 355	4,56; 4,49; 3,75		
XI			225, 255, 300	4,29; 4,44; 4,07		
XII			220, 285, 405	4,43; 4,05; 4,29		

*The spectra were recorded from dimethylformamide solutions.

Although the problem of the applicability of correlation analysis to quinoline derivatives was discussed in a number of papers [9], the transmission of the effect of substituents of the benzene ring of quinoline on the reaction centers in the 2 and 4 positions of the pyridine ring of quinaldine and lepidine has not been investigated. We verified the applicability of correlation analysis to the investigated systems. The σ_m and σ_p constants of Jaffe were used for the correlation. The ionization constants with respect to splitting out of a proton correlate excellently with the σ_m substituent constants (Fig. 2) but not with σ_p.

This indicates primarily that the character of the transmission of the electronic effect of the substituent is inductive. We used the method of least squares to calculate the correlation coefficient (r), the reaction constant (ρ), $-\log K_0$ (the pK_a of the unsubstituted compound), and the standard error (S_0).

2-Thionolepidines are weaker conjugate acids and bases than the corresponding 4-thionoquinaldines. This difference is manifested in reactions with methyl iodide, diazomethane, and acrylonitrile, with which 2-thionolepidines react considerably more slowly. For example, 2-methyl-6-nitro-4-thioquinolone is alkylated quantitatively by diazomethane after 20 min, while 4-methyl-6-nitro-2-thioquinolone undergoes 25% alkylation after several days.

In contrast to 4-cyanoethylthioquinolines [1], products IX-XI do not form picrates; this also may apparently be explained by their weak basicity.

EXPERIMENTAL

The purity of the products was monitored by chromatography in a loose layer of activity-II aluminum oxide in chloroform. The IR spectra of KBr pellets were recorded with a UR-10 spectrophotometer. The UV spectra of alcohol solutions (dimethylformamide solutions in the case of VII and VIII, in view of their low solubility in alcohol) of the compounds were recorded with an SF-4 spectrophotometer. The ionization constants were determined by the method in [11] in 70% aqueous ethanol at 20°. The scatter in the results did not exceed ±0.06 pK_a units. The pH values were measured with an LPU-01 potentiometer.

2-Thionolepidines I, III, V, and VII were obtained by the method in [1]. The hydriodide of II had mp 230-231°. Found: N 4.5; I 42.0%. $C_{11}H_{11}NS \cdot HI$. Calculated: N 4.6; I 41.9%. The hydriodide of IV had mp 235-236°. Found: N 4.4; I 38.4%. $C_{12}H_{13}NOS \cdot HI$. Calculated: N 4.2; I 38.1%.

1,4-Dimethyl-2-thioquinolone XII was synthesized by the method in [12].

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