SYNTHESIS IN THE PHENOTHIAZINE SERIES

XXVI.* ELECTRONIC ABSORPTION SPECTRA OF SEVERAL PHENOTHIAZINE DERIVATIVES

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The UV spectra of 18 phenothiazine derivatives and seven diphenylamine derivatives having similar substituents in the corresponding positions of the benzene ring are presented. The interrelationship between the structure and the character of absorption in the UV region is discussed.

A study of the absorption spectra of phenothiazine derivatives is of theoretical and practical interest since these compounds have assumed great importance in medical practice; one of the current practical problems is raising the stability of these substances, particularly in solutions, to the action of UV radiation in sunlight.

The absorption spectra of phenothiazine derivatives have not yet been studied systematically. Individual data on attempts to apply UV absorption spectra for the analysis of several medicinal forms containing these derivatives are presented in [1, 2]. A comparison of the UV spectra of aminazine, propazine, dinezin, and diprazin has shown [3] that replacement of hydrogen in the 10 position of phenothiazine by dialkylaminoalkyl substituents only slightly (by 1 to 2 nm) shifts the short-wave maximum of phenothiazine (254 nm) to the long-wave side. Branching of the side chain in the diprazin molecule also leads to a certain bathochromic shift (2 nm). A more pronounced bathochromic shift (5 nm) is induced by the introduction of chlorine into the 2 position, as occurs in the spectrum of aminazine. The long-wave maximum (at 320 nm for phenothiazine) in the spectra of these compounds is shifted hypsochromically and more appreciably (by 11 nm).

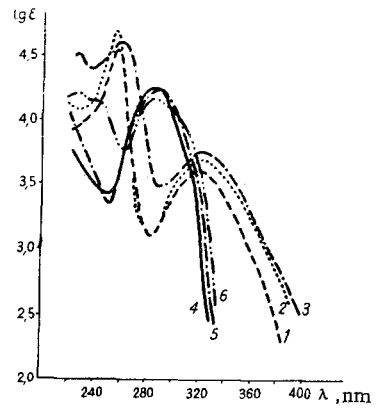

Fig. 1. UV spectra of compounds: 1) I; 2) IV; 3) VII; 4) XIX; 5) XXI; 6) XXII.

We have compared the electronic absorption spectra of individual phenothiazine and diphenylamine derivatives and have compared the results with several previously reported results.

The UV absorption spectra of substituted phenothiazine derivatives and similarly substituted diphenylamine derivatives are presented in Fig. 1. Despite several differences in the position of the maxima and minima and in the absorption intensities, two rays of curves which correspond to the diphenylamine or phenothiazine derivatives are clearly visible. Phenothiazine and its derivatives have absorption minima at the sites where the absorption maxima of diphenylamine and its derivatives are located. The absorption curves of these phenothiazine derivatives, like the curve of phenothiazine itself, have two maxima: a short-wave maximum near 254 nm, and a long-wave maximum near 320 nm. Attention was drawn to this property of phenothiazine in [3].

*For Communication XXV see [7].

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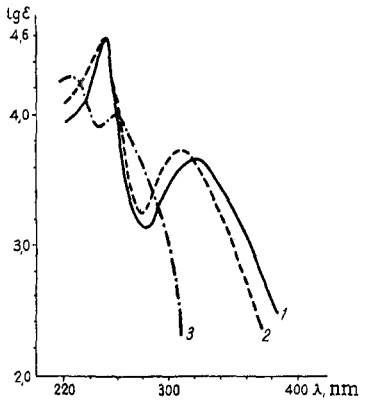

Fig. 2. UV spectra of compounds: 1) I; 2) II; 3) III.

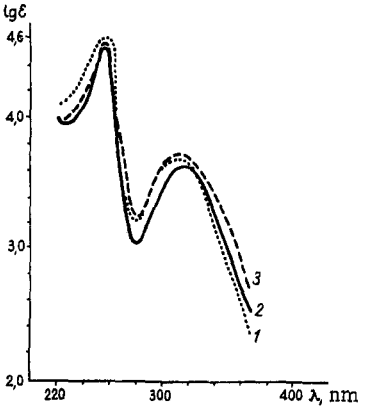

Fig. 3. UV spectra of compounds: 1) II; 2) V; 3) VI.

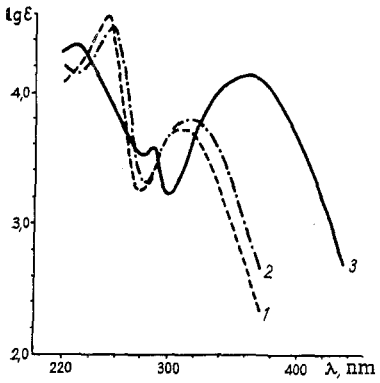

Fig. 4. UV spectra of compounds: 1) II; 2) IX; 3) VIII.

Fig. 5. UV spectra of compounds: 1) IX; 2) XI; 3) X.

The character of the absorption spectra of the diphenylamine derivatives is determined to a significant degree by interaction of the $2p_z$ electrons of the nitrogen atom with the π system of benzene rings. The development of two absorption bands on passing from diphenylamine derivatives to phenothiazine derivatives attests to the appearance of the possibility of electron transfer from one benzene ring to another (through the sulfur atom), i.e., the creation of a new chromophoric system; it depends on two electronic ground states of the new tricyclic π-electron system of phenothiazine. Closing the phenothiazine ring apparently leads to delocalization of the π electrons over the entire ring.

The curves of the UV absorption spectra of phenothiazine (1), 10-methylphenothiazine (2), and 10-acetylphenothiazine (3) are presented in Fig. 2. Transition from compound I to II is in no way reflected in the short-wave maximum, while the long-wave maximum is shifted to the short-wave side by 8 to 14 nm. A similar hypsochromic shift of the long-wave maximum was observed [3] on passing from phenothiazine to 10-dialkylaminoalkyl substituents. The curve of compound III presents an absolutely different picture: both maxima are markedly shifted to the short-wave region (by 26 and 60 nm, respectively) as a result of conjugation of the carbonyl oxygen atom with the unshared electron pair of nitrogen.

Introduction of chlorine into the 10-methylphenothiazine molecule affects the absorption curve rather slightly (Fig. 3): the short-wave maximum is shifted bathochromically by 2 to 4 nm, while the long-wave maximum is shifted hypsochromically by 6 to 8 nm. The position of chlorine in the 2- and 3-chloro-10-methylphenothiazines affects only the intensities of the minimum at 278 nm.

Introduction of a nitro group into the 3 position of 10-methylphenothiazine markedly changes the shape of the absorption curve (Fig. 4): the short-wave maximum is shifted hypsochromically by 24 nm and decreases somewhat in intensity; the long-wave maximum is shifted to the long-wave side by 50 nm with an appreciable increase in intensity. In addition, a new maximum appears at 286 nm (log ε 3.38). These

TABLE 1. UV Spectra of Phenothiazine and Diphenylamine Derivatives

Compound	Substance	Short-wave λ				Long-wave λ				Δλ max (in comparison with phenothiazine)			
										short-wave		long-wave	
		min	max	min	max	min	max	min	max	hyps.	bath.	hyps.	bath.
I	Phenothiazine		254			284	320			–	–	–	–
II	10-Methylphenothiazine		254			278	306-12					8-14	
III	10-Acetylphenothiazine		228	248	259					26		60	
IV	2-Chlorophenothiazine	230	256			286	326				2		6
V	2-Chloro-10-methylphenothiazine	226	256			280	314				2	6	
VI	3-Chloro-10-methylphenothiazine	224	258			280	312				4	8	
VII	2-Aminophenothiazine	234	256			288	320				2		
VIII	3-Nitro-10-methylphenothiazine		230	280	286	298			362	24			40-45
IX	3-Amino-10-methylphenothiazine	232	256			282	316				2	4	
X	3-Amino-10-methylphenothiazine S-oxide		232	252	284			344	370	22			50
XI	3-Amino-10-methylphenothiazine S,S-dioxide		226	248	281	336			363	28			40-45
XII	2-Amino-10-methylphenothiazine	234	256			284	315				2	5	
XIII	Methyl phenothiazine-2-carbamate	236	260			290	324				6		4
XIV	Methyl 10-methylphenothiazine-2-carbamate	232	258			282	313				4	7	
XV	Methyl 10-methylphenothiazine-3-carbamate	230	260			282	312				4	8	
XVI	2-Chloro-10-methylphenothiazine S,S-dioxide		232	256	272	288	296	318	330	22			10
XVII	3-Chloro-10-methylphenothiazine S,S-dioxide		222	254	274	290	302	318	339	32			19
XVIII	2-Phthalimidophenothiazine	242	260	296	324		324						4
XIX	Diphenylamine	248											
XX	3-Phthalimidodiphenylamine		220	260	286								
XXI	3-Chlorodiphenylamine	250	285		286								
XXII	3-Aminodiphenylamine		224	260	282								
XXIII	3-Amino-N-acetyldiphenylamine		226	278	296								
XXIV	Methyl diphenylamino-3-carbamate		229	257	286								
XXV	Methyl N-methyldiphenylamino-4-carbamate		250		297								

changes in the absorption spectrum occur due to migration of an electron from the aromatic ring to the NO_2 group, as occurs in the case of nitrobenzene as compared with benzene [5]. The three maxima in the spectrum of 3-nitro-10-methylphenothiazine (VIII) are apparently explained as follows: a) 365 nm is local excitation of the nitro group; b) 286 nm is the primary local excitation of the phenothiazine chromophore; c) 230 nm is absorption associated with electron transfer [6].

Reduction of the nitro group to the amino group markedly changes the curve and makes it extremely close to the curve of 10-methylphenothiazine.

Transition from the absorption spectrum of 3-amino-10-methylphenothiazine (IX) to the spectrum of the S-oxide of this compound (X) attests to an appreciable change in the phenothiazine chromophore (Fig. 5). Further transition to an even more oxidized compound, 3-amino-10-methylphenothiazine S,S-dioxide (XI), does not change the shape of the absorption of the new compound so markedly.

A more profound interpretation of the spectra of the compounds discussed here requires additional experimental data as well as the application of quantum-chemical methods of calculating the π-electron structures.

EXPERIMENTAL

Compounds V and XVI were obtained for the first time. Compound V was obtained by methylation of IV, in analogy with [4], and had mp 81-83°. Found %: Cl 14.04; N 5.83; S 12.96. $C_{13}H_{10}ClNS$. Calculated %: Cl 14.32; N 5.65; S 12.94. Compound XVI was obtained by oxidation of IV with hydrogen peroxide in glacial acetic acid by refluxing for 2 h and had mp 157-158.5° (from alcohol). Found %: Cl 12.71; N 5.03; S 11.73. $C_{13}H_{10}ClNO_2$. Calculated %: Cl 12.67; N 5.01; S 11.46.

The remaining compounds are indicated in Table 1 and were synthesized by previously described methods.

The UV absorption spectra were obtained by N. D. Solokhina with an SF-4 spectrophotometer. Concentrations from $1 \cdot 10^{-3}$ to $2 \cdot 10^{-5}$ in alcohol were used with a layer thickness d of 0.5 cm. The data are presented in Table 1.

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