TABLE 2. Characteristics of the Synthesized Compounds

Compound	bp, °C (mm)	n_D^{20}	d_4^{20}	Found, %				Empirical formula	Calc., %				Yield, %
				C	H	N	S		C	H	N	S	
IIa	148—150 (0,25)	1,5569	1,1096	61,4	7,8	5,8	12,7	$C_{13}H_{19}NO_2S$	61,6	7,6	5,5	12,6	80
IIb	141—142 (0,3)	1,5740	1,1706	62,6	8,1	5,5	11,7	$C_{14}H_{21}NO_2S$	62,9	7,9	5,2	12,0	35
IIc	164—165 (0,18)	1,5379	1,0703	62,5	8,1	4,6	10,0	$C_{17}H_{27}NO_3S$	62,7	8,4	4,3	9,8	32
IIc'	172—173 (0,25)	1,5121	1,0648	64,3	8,7	4,1	9,3	$C_{19}H_{31}NO_3S$	64,6	8,8	4,0	9,1	30
IIIa	154 (0,1), 34—35*	—	—	63,6	6,5	6,5	15,2	$C_{11}H_{13}NOS$	63,7	6,3	6,8	15,5	55
IIIb	106 (0,05)	1,5670	—	65,5	6,8	6,2	14,0	$C_{12}H_{15}NOS$	65,1	6,8	6,3	14,5	50
IIIc	161—162 (0,1), 45*	1,5531	—	64,7	7,7	4,8	11,2	$C_{15}H_{21}NO_2S$	64,5	7,6	5,0	11,5	52
IIId	164—165 (0,1)	1,5365	—	65,7	7,7	4,9	10,6	$C_{16}H_{23}NO_2S$	65,5	7,9	4,8	10,9	45

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*Melting point.

Compound IIId was similarly synthesized.

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RESEARCH IN THE CHEMISTRY OF HETEROCYCLIC QUINONEIMINES.

3.* OXIDATIVE CYCLIZATION OF 2,5-DIARYLAMINO-SUBSTITUTED 1,4-BENZOQUINONE-4-PHENYLIMINES — SIMPLE METHOD FOR THE PREPARATION OF 2-ARYLAMINO-5-ARYL-3-PHENAZINONES

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UDC 547.864.6'86.5.7'867.6'869.
2'567.5.07:542.943:543.422

2,5-Diarylamino-1,4-benzoquinone-4-phenylimines, which are formed in the reaction of 1,4-benzoquinone-4-phenylimine with aromatic amines, are converted under oxidative conditions to products of intramolecular oxidative cyclization, viz., 2-arylamino-5-aryl-3-phenazinones.

In a series of studies devoted to the chemistry of 3-phenoxazinones, 3-phenothiazinones, and 3-phenazinones it was established that in the reaction of these compounds with various O-, S-, and N-nucleophiles substitution of hydrogen may occur in both the quinoneimine and aryl parts of the molecules [1-4].

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*See [4] for Communication 2.

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	mp,[a] °C	R_f[b]	PMR spectrum, ppm			IR spectrum, NH, cm^{-1}	Electronic spectra, λ_{max}, nm (log ε)	Found, %			Empirical formula	Calculated, %			Yield, %
			quinoid protons	NH	Ar(H)			C	H	N		C	H	N	
IIIa	203—204	0,58	6,12; 6,21	9,10	7,1—8,1	3240, 3276	284 (4,40), 392 (4,27)	78,6	5,3	11,4	$C_{24}H_{19}N_3O$	78,9	5,2	11,5	65
IIIb	199—201	0,40	5,85; 5,97	8,80; 9,64	6,9—8,0	3222, 3245	280 (4,34), 410 (4,23)	73,3	5,2	9,9	$C_{26}H_{23}N_3O_3$	73,4	5,4	9,9	70
IIIc	185—186	0,60	6,00; 6,11	8,85; 9,70	6,9—8,0	3323, 3363	284 (4,40), 400 (4,27)	79,4	5,9	10,8	$C_{26}H_{23}N_3O$	79,4	5,9	10,7	43
IIId	233—235	0,69	6,10; 6,17	9,10; 9,95	7,1—8,2	3204, 3249	291 (4,48), 397 (4,29)	55,4	3,5	8,4	$C_{24}H_{17}N_3Br_2O$[c]	55,1	3,3	8,0	57
IIIe	200—201	0,68	5,86; 5,92	8,66; 9,26	6,9—8,1	3210, 3253	289 (4,43), 394 (4,23)	66,9	4,2	10,0	$C_{24}H_{17}N_3Cl_2O$[d]	66,4	4,0	9,7	58
Va	257—258	0,69	5,37; 7,21	8,79	7,3—8,3	3255	279 (4,69), 468 (4,51)	79,2	4,8	11,4	$C_{24}H_{17}N_3O$	79,3	4,7	11,6	55
Vb	317—318	0,56	5,40; 7,19	8,80	7,3—8,2	3268	282 (4,67), 471 (4,42)	73,7	4,9	9,6	$C_{26}H_{21}N_3O_3$	73,7	5,0	9,9	59
Vc	295—297	0,74	5,35; 7,03	8,50	7,1—8,2	3275	281 (4,67), 470 (4,41)	79,7	5,5	10,9	$C_{26}H_{21}N_3O$	79,7	5,4	10,7	51
Vd	327—328	0,60	5,37; 7,22	8,93	7,4—8,3	3280	281 (4,68), 470 (4,52)	55,0	3,1	7,9	$C_{24}H_{15}N_3Br_2O$[e]	55,3	2,9	8,1	56
Ve	314—315	0,56	5,34; 7,09	8,69	7,3—8,3	3270	280 (4,62), 471 (4,44)	66,8	3,7	9,5	$C_{24}H_{15}N_3Cl_2O$[f]	66,7	3,5	9,7	60

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[a] Crystallization solvents: chloroform—ethanol (IIIa-e) and chloroform (Va-e). [b] Chromatographic solvents: benzene—ethyl acetate (9:1) for IIIa-e, benzene—ethyl acetate (1:1) for Va-c, and benzene—ethyl acetate (6:1) for Vd, e. [c] Found: Br 30.6%. Calculated: Br 30.5%. [d] Found: Cl 15.9%. Calculated: Cl 16.3%. [e] Found: Br 30.1%. Calculated: Br 30.7%. [f] Found: Cl 16.4%. Calculated: Cl 16.4%.

In the present research we investigated the reactions of a model compound, viz., 1,4-benzoquinone-4-phenylimine, with arylamines. Little study has been devoted to the reactivities of N-arylquinonemonoimines [5]. Thus the reactions with arylamines remain virtually uninvestigated.

We have established that, regardless of the conditions, 1,4-benzoquinone-4-phenylimine (I) reacts with arylamines IIa-e to give 2,5-diarylamino derivatives IIIa-e, the formation of which can be regarded as 1,4-nucleophilic addition with subsequent oxidation of the resulting adducts.

As a consequence of a decrease in the oxidation potential of the quinoneimine when electron-donor arylamino substituents are introduced, the starting quinoneimine acts as an oxidizing agent, as evidenced by the formation in all cases of p-hydroxydiphenylamine. Air oxygen also participates in the oxidation of the adducts; this follows from the yields of disubstitution products in reactions carried out in an air (see Table 1) and argon (33%) atmospheres.

Singlet signals of two quinoneimine protons at 5.8-6.2 ppm are observed in the PMR spectra of 2,5-diarylamino derivatives III; this indicates that the two substituents are para-oriented with respect to one another. The PMR spectrum also contains signals of two NH protons at 8.6-10.0 ppm and a multiplet of aromatic protons at 6.9-8.2 ppm with an overall integral intensity of 13 (15 for IIIa) proton units. The characteristic absorption bands of two amino groups at 3200-3400 cm^{-1} are present in the IR spectra.

An analysis of the electronic spectra of IIIa-e shows that the introduction of arylamino substituents in the quinoneimine fragment is accompanied by a significant hypsochromic shift of the absorption band in the visible region of the spectrum [1,4-benzoquinone-4-phenylimine; λ_{max} = 460 nm (in chloroform)].

Thus, in contrast to heterocyclic quinoneimines, quinoneimine I does not form products of substitution in the aromatic ring; this constitutes evidence for weak activation of the latter by the negative inductive and mesomeric effects of the quinoneimine part. The development of an electrophilic center in the aromatic ring of heterocyclic derivatives is evidently due to an increase in the mesomeric effect of the quinoneimine fragment owing to the development of coplanarity of the molecule in the case of additional bonding of the fragments through heterobridges. Moreover, it may be assumed that the effect indicated above and the positive mesomeric effect of the heteroatom lead to an increase in the aromatic character of the quinoid ring, which is expressed in a decrease in its activity in addition reactions [2].

The reactions of quinoneimine I with bisnucleophiles proceed somewhat differently.

The reaction of quinoneimine I with o-aminophenol leads to a product of oxidative self-condensation of the latter, viz., 2-amino-3-phenoxazinone (IV), the formation of which is also observed in the action of other oxidizing agents on o-aminophenol [6-8].

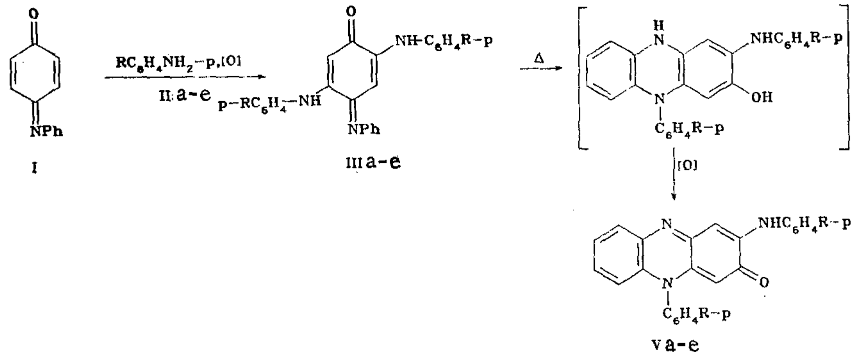
Complex mixtures of unidentifiable products are formed with bisnucleophiles that are readily oxidized by the starting quinoneimine to p-quinoneimines, viz., p-aminophenol and p-phenylenediamine.

When 2,5-diarylamino-1,4-benzoquinone-4-phenylimines IIIa-e are heated in the presence of air oxygen or $K_3Fe(CN)_6$, they undergo intramolecular oxidative cyclization to give 2-arylamino-5-aryl-3-phenazinones (Va-e) in good yields (Table 1).

The formation of cyclization products is the result of intramolecular nucleophilic substitution of the hydrogen atom in the ortho position of the aromatic ring of N-arylquinoneimines IIIa-e by the spatially close arylamino residue. Rather severe oxidation conditions are required for this substitution because of the low reactivity of the aromatic ring.

The cyclization evidently proceeds through 5,10-dihydrophenazine derivatives, as in the cyclization of amino derivatives of indophenols [9, 10].

The structures of the cyclization products are confirmed by the PMR spectra, in which singlet signals of two protons of the quinoid ring at 5.3-5.4 (1H) and 7.0-7.2 ppm (1H), a signal of the NH proton at 8.5-9.0 ppm, and a multiplet of aromatic protons at 7.1-8.3 ppm are present. The IR spectra display an absorption band of an NH group at 3250-3280 cm^{-1}. A bathochromic shift of the maximum of the absorption band relative to starting quinoneimines IIIa-e is observed in the spectra of the visible region of Va-e.



II, III, V a R=H, b R=OCH_3, c R=CH_3, d R=Br, e R=Cl

The identical character of Va and 2-phenylamino-5-phenyl-3-phenazinone obtained by alternative synthesis [11] constitutes evidence for the phenazine structure of the compounds obtained.

Thus, the smooth nucleophilic substitution of a hydrogen atom in 1,4-benzoquinone-4-phenylimine by aromatic amines and subsequent oxidative cyclization make it possible to regard this sequence of reactions as a possible method for the synthesis of compounds of the phenazinone series, viz., 2-arylamino-5-aryl-3-phenazinones.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in d_6-DMSO were recorded with a Perkin-Elmer R12B spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of mineral oil suspensions were recorded with a UR-20 spectrometer. The electronic spectra of solutions in chloroform were recorded with a Specord UV-vis spectrophotometer. The course of the reactions and the purity of the compounds obtained were monitored by thin-layer chromatography (TLC) on Silufol UV-254 plates with development by iodine vapors.

1,4-Benzoquinone-4-phenylimine (I) was obtained by oxidation of p-hydroxydiphenylamine by the method in [12].

2,5-Diarylamino-1,4-benzoquinone-4-phenylimines (IIIa-e). A solution of 10 mmole of the arylamine in 25 ml of ethanol was added at room temperature to 0.92 g (5 mmole) of quinoneimine I in 25 ml of ethanol. At the end of the reaction (2-3 h), which was judged from disappearance of the spot of the starting quinoneimine on the thin-layer chromatogram, the solvent was removed by distillation, and the residue was dissolved in chloroform and chromatographed with a column packed with silica gel (40/100) by elution with chloroform. The first zone was eluted, the solvent was removed by distillation, and the residue was crystallized from ethanol—chloroform (2:1).

Reaction of 1,4-Benzoquinone-4-phenylimine with o-Aminophenol. A solution of 0.54 g (5 mmole) of o-aminophenol in 15 ml of ethanol was added to 0.46 g (2.5 mmole) of quinoneimine I in 15 ml of ethanol. At the end of the reaction (25 min), the solvent was removed by distillation, and the residue was chromatographed by elution with chloroform—ethyl acetate (1:1) to give 0.09 g (51%) of 2-amino-3-phenoxazinone with mp 250°C and R_f 0.46 [benzene—ethyl acetate (1:1)]. PMR spectrum: 6.43, 6.46 (two s, quinoid protons); 6.85 (broad s, 2H, NH_2); 7.8-8.0 ppm (aromatic protons). Electronic spectrum, λ_{max} (log ε): 429 nm (4.43). Found: C 68.2; H 3.9; N 12.9%. Calculated: C 67.9; H 3.9; N 13.2%.

2-Arylamino-5-aryl-3-phenazinones (Va-e). A) A 2-mmole sample of $K_3Fe(CN)_6$ was added to 1 mmole of IIIa-e in 25 ml of DMF, and the mixture was refluxed for 5 h. The solvent was removed by distillation, and the residue was chromatographed with a column packed with silica gel (40/100) by elution with benzene—ethyl acetate (1:1). The red zone was collected, and the eluent was removed by distillation to give Va-e in the form of red crystals that were only slightly soluble in organic solvents.

B) A finely powdered sample of IIIa-e was heated with the passage of air at 250°C for 1 h, after which the melt was cooled, dissolved in chloroform, and chromatographed.

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RESEARCH IN THE CHEMISTRY OF HETEROCYCLIC QUINONEIMINES. 4.* EFFECT OF MODE OF ACTIVATION OF THE REAGENTS ON THE REACTION OF 3-PHENOTHIAZINONE WITH ALKANETHIOLS

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UDC 547.869.2:542.953:543.422

2-Alkylthio- and 2,4-dialkylthio-3-phenothiazinones were obtained in the case of activation of 3-phenothiazinone in reactions with alkanethiols. Activation of the reagent by means of a charge accelerates the reaction significantly and is accompanied by the additional formation of 1,2-dialkylthio-3-phenothiazinones.

It is known that the mode of activation of the reagents may have a substantial effect on both the rate of a reaction and its regioselectivity [2, 3]. Depending on the type of nucleophile, the substitution of a hydrogen atom in a series of heterocyclic quinoneimines may proceed under conditions of activation of either the substrate or the reagent. In a number of cases only one of the indicated modes of activation proves to be effective. Thus 3-phenothiazinone does not react with alcohols but forms alkoxy derivatives smoothly with alkoxides [4].

The high nucleophilic reactivities of thiols and thiolate anions with respect to various substrates [5] in conjunction with the possibility of subsequent transformations of the resulting alkylthio derivatives makes them advantageous as reagents in the study of the various nucleophilic processes [2].

We have investigated the reaction of 3-phenothiazinone with a number of aliphatic thiols and the corresponding thiolates. Under conditions of activation of the substrate (H^+) the reaction of 3-phenothiazinone (I) with thiols proceeds smoothly at 0°C. The initially formed mixture of colorless products of addition and reduction of 3-phenothiazinone is oxidized in air to mono- and dialkylthio-3-phenothiazinones and starting I. The principal products of the reaction of 3-phenothiazinone with thiols are 2-alkylthio-3-phenothiazinones (II). For example, in the case of octanethiol (an eight- to tenfold excess) the ratio of 2-octylthio-3-phenothiazinone and 2,4-dioctylthio-3-phenothiazinone is ∿8:1. The overall yield

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*See [1] for Communication 3.

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