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RESEARCH IN THE CHEMISTRY OF HETEROCYCLIC QUINONE IMINES.
11.* EFFECT OF BENZANNELATION ON THE OXIDATIVE CYCLIZATION OF DIARYLAMINO-N-ARYL-1,4-BENZOQUINONE MONOIMINES TO PHENAZINONE DERIVATIVES

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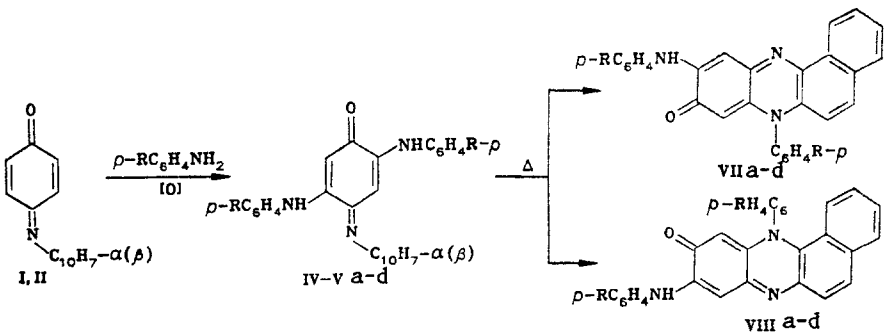
2,5-Diarylamino-N-α(β)-naphthyl-1,4-benzoquinone monoimines undergo oxidative cyclization to give benzannelated phenazinone derivatives. The effect of an N-aryl fragment on the ease of cyclization decreases in the order N-β-naphthyl > N-α-naphthyl > N-phenyl. 2-Arylamino-N-phenyl-1,4-naphthoquinone monoimines do not undergo oxidative cyclization to phenazinones.

It has been previously shown [2] that the cyclization of diarylamino-N-phenyl-1,4-benzoquinone monoimines is a simple and convenient method for the synthesis of phenazinone derivatives, which may be of interest as biologically active compounds [3]. Arylamino derivatives of benzannelated phenazinones can be obtained by the oxidative cyclization of the corresponding N-aryl-1,4-benzo(naphtho)quinone monoimines.

In the present research we examined the effect of annelation of the aromatic and quinone imine fragments in arylamino derivatives of quinone monoimines on oxidative cyclization to phenazinones. Arylamino derivatives of quinone monoimines are formed in the reaction of aromatic amines with N-α-naphthyl-1,4-benzoquinone monoimine (I), N-β-naphthyl-1,4-benzoquinone monoimine (II), and N-phenyl-1,4-benzoquinone monoimine (III). The reactions of the benzologs I and II of N-phenyl-1,4-benzoquinone monoimine with an annelated aromatic fragment with arylamines proceeds without pronounced differences from the reactions with nonannelated quinone imine. In the case of refluxing in ethanol the only products of nucleophilic arylamination of I and II are 2,5-diarylamino-N-α(β)-naphthyl-1,4-benzoquinone monoimines IVa-d and Va-d, which correspond to addition of the nucleophile to the C=C—C=N and C=C—C=O conjugated systems. The formation of the reduced form of the substrates indicates their participation in oxidation of the intermediately obtained adducts.



IV, V, VII, VIII a R=H, b R=CH_3O, c R=Br, d R=Cl

The PMR spectra of IVa-d and Va-d are similar to the spectra of the nonannelated analogs [2] and contain two singlet signals (1H, 1H) at 5.9-6.3 ppm belonging to the quinone imine 3-H and 6-H protons (compare with the PMR spectra of unsubstituted quinone imines I and II [4]), a multiplet of aromatic protons, and weak-fields signals of protons of amino groups. The structural similarity of the amino derivatives is also manifested in the common character of their electronic spectra (see Table 1).

*See [1] for Communication 10.
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TABLE 1. Characteristics of Benzoquinone Monoimines IV and V and Naphthoquinone Monoimines VI

Compound	Empirical formula	mp, °C	R_f*	λ_{max}, nm (log ε)	ν_{NH}, cm^{-1}	PMR spectrum, δ, ppm**				Yield, %
						quinoid protons		Ar(H)	NH	
						3-H	6-H			
IVa	$C_{28}H_{21}N_3O$	205	0,70	392 (4,24)	3268	6,11	6,23	7,0 ... 8,1	8,85	59
IVb	$C_{30}H_{25}N_3O_3$	188 ... 190	0,31	412 (4,18)	3290	5,92	6,04	6,6 ... 8,1	8,75	62
IVc	$C_{28}H_{19}Br_2N_3O$	226 ... 227	0,75	396 (4,19)	3280	6,00	6,13	6,65 ... 8,00	8,7	65
IVd	$C_{28}H_{19}Cl_2N_3O$	206 ... 208	0,72	394 (4,21)	3280	5,97	6,10	6,65 ... 8,00	8,7	54
Va	$C_{28}H_{21}N_3O$	220 ... 222	0,73	393 (4,22)	3282	6,19	6,28	6,9 ... 8,0	8,7	66
Vb	$C_{30}H_{25}N_3O_3$	194 ... 196	0,35	415 (4,14)	—	5,98	6,0	6,6 ... 8,0	8,6	57
Vc	$C_{28}H_{19}Br_2N_3O$	225 ... 227	0,79	396 (4,27)	—	6,13	6,22	6,8 ... 8,0	8,65	60
Vd	$C_{28}H_{19}Cl_2N_3O$	216 ... 217	0,74	396 (4,26)	3296	6,12	6,21	6,8 ... 8,0	8,65	55
VIa	$C_{22}H_{16}N_2O$	184	0,70	285 (4,40); 476 (3,83)	3296	6,69***	—	6,8 ... 8,7	—	65
VIb	$C_{23}H_{18}N_2O_2$	171 ... 173	0,33	280 (4,36); 491 (3,81)	3327	6,48***	—	6,8 ... 8,7	—	70
VIc	$C_{22}H_{15}BrN_2O$	214 ... 216	0,73	471 (3,85)	—	6,59***	—	6,8 ... 8,7	—	59
VId	$C_{22}H_{15}ClN_2O$	199 ... 201	0,70	287 (4,38)	—	6,62***	—	6,8 ... 8,7	—	61

*The eluents were chloroform for IVa-d and Va-d and chloroform—ethyl acetate (6:1) for VIa-d.

**For IVb: 3.71 (3H, s, OCH_3) and 3.84 ppm (3H, s, OCH_3); for Vb 3.67 (3H, s, OCH_3) and 3.82 ppm (3H, s, OCH_3); for VIb 3.77 ppm (3H, s, OCH_3).

***1H, s, 3-H.

TABLE 2. Characteristics of Phenazinones VII and VIII

Compound	Empirical formula	mp, °C	R_f*	λ_{max}, nm (log ε)	ν_{NH}, cm^{-1}	PMR spectru, δ, ppm			Yield, %
						quinoid protons		Ar(H)	
						11(8)-H	8(11)-H		
VIIa	$C_{28}H_{19}N_3O$	286...288	0,58	501 (4,49)	3240	7,47	5,43	6,8...8,5	62
VIIb	$C_{30}H_{23}N_3O_3$	322...324	0,42	503 (4,48)	3250	7,42	5,49	6,8...8,5**	65
VIIc	$C_{28}H_{27}Br_2N_3O$	360	0,81	505 (4,43)	3236	7,5	5,82	6,8...8,1	58
VIId	$C_{28}H_{17}Cl_2N_3O$	349...351	0,76	504 (4,54)	3230	7,5	5,83	6,8...8,1	60
VIIIa	$C_{28}H_{19}N_3O$	334...335	0,60	502 (4,43)	3314	—	—	—	66
VIIIb	$C_{30}H_{23}N_3O_3$	280...282	0,43	506 (4,29)	—	—	—	—	63
VIIIc	$C_{28}H_{17}Br_2N_3O$	340...342	0,83	504 (4,49)	—	(7,35)	(5,91)	7,0...8,2	61
VIIId	$C_{28}H_{17}Cl_2N_3O$	319...321	0,78	503 (4,44)	3280	(7,35)	(5,92)	7,0...8,2	57

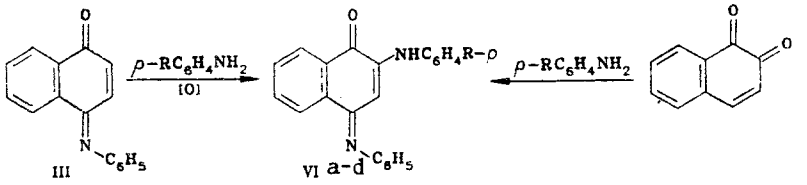
*Elution with chloroform—ethyl acetate (9:1).

**3.8 (3H, s, OCH_3) and 3.9 ppm (3H, s, OCH_3).

TABLE 3. Temperatures of the Exothermic Peaks (T_e) of Benzoquinone Monoimines IVa-c, Va-c, and Xa-c

Compound	T_e, °C	Compound	T_e, °C	Compound	T_e, °C
IVa	258	IVb	250	IVc	240
Va	252	Vb	243	Vc	233
Xa	289	Xb	272	Xc	255

In quinone monoimine III arylamines replace exclusively the hydrogen atom in the 2 position to give 2-arylamino-N-phenyl-1,4-naphthoquinone monoimines VIa-d.



VI a R=H, b R=CH_3O, c R=Br, d R=Cl

The independent synthesis of 2-anilino-N-phenyl-1,4-naphthoquinone monoimine (VIa) from 1,2-naphthoquinone and aniline by the method in [5] confirms the regio-orientation of the arylamination of III. The PMR spectra of all of the VI contain a singlet signal (1H, Table 1) at 6.3-6.7 ppm, the position of which corresponds to a 3-H proton (compare with unsubstituted quinone imine III [4]).

On heating in solution in DMF or in melts at 200-250°C benzoquinone monoimines IVa-d and Va-d undergo oxidative cyclization to benzannelated arylamino-N-arylphenazinones VIIa-d and VIIIa-d. The introduction of an oxidizing agent — by bubbling in air — increases the rate of conversion and the yields of cyclization products. In the case of Va-d two cyclization pathways corresponding to isomeric benzo[*a*]- or benzo[b]phenazinones are possible. The occurrence of intramolecular nucleophilic attack by the arylamino group in the 1 position of the naphthalene fragment follows from the identical character of VIIIa and the previously described 9-anilino-12-phenylbenzo[*a*]phenazin-10-one, obtained by independent synthesis [1].

The PMR spectra of VII and VIII (Table 2) differ little from one another and from the spectra of the corresponding IX derivatives [2] and contain two singlets of quinone imine protons (1H, 1H, $^5J_{1,4} = {}^5J_{4,1} = 0$ Hz) at 5.3-7.5 ppm, a multiplet of aromatic protons at 6.8-9.0 ppm, and a signal of the proton of an amino group (1H) in the weak-field part of the spectrum at 8-9 ppm.

Under similar conditions naphthoquinone monoimines VI do not undergo oxidative cyclization; this is due to the presence of an arylamino group in the 2 position rather than in the 3 position in VI.

The effect of the nature of the aromatic fragment in benzoquinone monoimines IV and V on the ease of cyclization was studied by differential thermal analysis (DTA). For comparison, we also studied the corresponding 2,5-diarylamino-N-phenyl-1,4-benzoquinone monoimines Xa-c, which were previously obtained [2]. One endothermic peak, which corresponds to melting, and an exothermic peak, which corresponds to cyclization, are observed on the DTA curves of IVa-c, Va-c, and Xa-c. It follows from the exothermic peaks that the ability to undergo cyclization decreases in the order V > IV > X, which corresponds to greater ease of cyclization and, consequently, greater electrophilic activity of the aromatic fragment in β-naphthylimine derivatives as compared with the corresponding α-naphthylimine and phenylimine derivatives (Table 3).

EXPERIMENTAL

The PMR spectra of solutions of the arylamino derivatives of the quinone imines in d_6-DMSO were recorded with a Perkin—Elmer 12B spectrometer (60 MHz) spectrometer, while the PMR spectra of solutions of the phenazinones in d_6-DMSO were recorded with a Bruker WP-80 spectrometer with tetramethylsilane (TMS) as the internal standard. The IR spectra of suspensions of the compounds in mineral oil were obtained with a UR-20 spectrometer. The electronic spectra of solutions in chloroform were obtained with a Specord UV-vis spectrophotometer. The DTA curves were recorded with a MOM derivatograph at a heating rate of 5°C/min in air; the sample masses were 50 mg. The course of the reactions and the individuality of the compounds were monitored by TLC on Silufol UV-254 plates with development with iodine vapors or in UV light.

The results of elementary analysis for C, H, Hal, and N were in agreement with the calculated values.

2,5-Diarylamino-N-α-naphthyl-1,4-benzoquinone Monoimines IVa-d. The arylamine (20 mmole) and 50 ml of ethanol were added to 2.33 g (10 mmole) of I in 50 ml of ethanol, and the mixture was refluxed with bubbling in of air until the conversion of the substrate was complete. The solvent was then removed by distillation, and the residue was chromatographed with a column packed with silica gel (40-100 μm) by elution with chloroform. Removal of the chloroform from the first (green-brown) fraction by distillation gave IVa-d. The second zone contained unchanged arylamine, while workup of the third (colorless) zone gave ~0.8 g of the reduced form of the substrate — p-hydroxyphenyl-α-naphthylamine.

2,5-Diarylamino-N-β-naphthyl-1,4-benzoquinone Monoimines Va-d. These compounds were obtained and isolated in the same way as IVa-d. Workup of the firs (green-brown), second, and third zones gave, respectively, Va-d, arylamines, and ~0.8 g of p-hydroxyphenyl-β-naphthylamine.

2-Arylamino-N-phenyl-1,4-naphthoquinone Monoimines VIa-d. A. A solution of 10 mmole of the arylamine in 30 ml of ethanol was added to 2.33 g (10 mmole) of III in 50 ml of ethanol, and the mixture was refluxed for 15 min with bubbling in of air. The solvent was then partially removed by distillation, and the resulting precipitate was removed by filtration and crystallized from ethanol—chloroform (2:1) to give red-brown crystals.

B. A solution of 3 ml of aniline in 30 ml of ethanol was added to 1.6 g (10 mmole) of 1,2-naphthoquinone in 50 ml of ethanol, after which the mixture was processed as indicated in method A to give 1.8 g (60%) of red-brown crystals of 2-anilino-N-phenyl-1,4-naphthoquinone monoimine (VIa) with mp 183-184°C (mp 179-180°C [5]).

10-Arylamino-7-arylbenzo[a]phenazin-9-ones VIIa-d. A. A solution of 5 mmole of IVa-d in 100 ml of DMF was refluxed for ~4 h with bubbling in of air until the conversion of starting quinone imine IV was complete. The solvent was then removed by distillation at reduced pressure, and the residue was chromatographed with a column packed with silica gel (40-100 μm) by elution with benzene—ethyl acetate (1:1). The crimson-red zone was collected, and the eluent was removed by distillation to give dark-red crystals of VIIa-d.

B. Finely ground powdered IVa-d were heated for 1 h at ~250°C with bubbling in of air, after which the melts were cooled, and VII were isolated as in method A.

12-Aryl-9-arylaminobenzo[a]phenazin-10-ones VIIIa-d. These compounds were obtained and isolated as in the preparation of VII from benzoquinone monoimines Va-d.

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