AMINATION OF N-ARYL-1,4-NAPHTHOQUINONEIMINES BY SECONDARY ALIPHATIC AMINES

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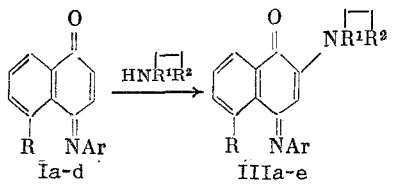
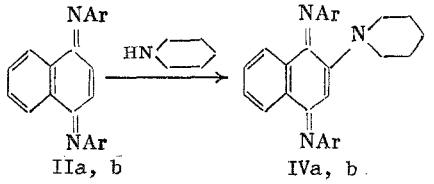
In contrast to quninoneimines which contain an arylsulfonyl group attached to the nitrogen atom [1], the reactions of N-aryl-1,4-naphthoquinoneimines have been studied very little. The only thing that is known is that N-aryl-1,4-naphthoquinoneimines react with aromatic amines to give 2-arylamino-N-aryl-1,4-naphthoquinone-4-imines [2]. In the present paper we have examined the amination of various N-aryl-1,4-naphthoquinone-4-imines and N,N'-diaryl-1,4-naphthoquinonediimines with secondary aliphatic amines.

We have found that, in contrast to the behavior of N-phenylsulfonyl-1,4-naphthoquinone-4-imine, which reacts readily with piperidine and morpholine in the absence of catalyst [3], the direct introduction of a piperidine moiety to N-aryl-1,4-naphthoquinone-4-imines (Ia, b) and N,N'-diaryl-1,4-naphthoquinoneimines (IIa, b) can take place only under conditions for the synthesis of aminoquinones [4], i.e., in the presence of Cu^{2+} salts. This is apparently due to the greater electron withdrawing characteristics of a phenylsulfonyl group attached to the imine nitrogen, compared with a N-phenyl group in paraquinoneimines [5]. In the amination of compounds (Ia, b), the dialkylamino group is introduced into the ortho position with respect to the carbonyl group, as evidenced by the presence of absorption bands at ca. 460 nm in the visible spectra of compounds (IIIa, b); at the same time, introduction of a dialkylamino group in the ortho position relative to an N-arylimino group in an N,N'-diaryl-1,4-naphthoquinonediimine (IIa, b) leads to a hypsochromic shift of the long wavelength maximum to ca. 400 nm, due to steric factors. An analogous observation has been made in the case of amino derivatives of N,N'-diaryl-1,4-benzoquinonediimines [1].



Ia-d IIIa-e

R = H, Ar = Ph (Ia); R = H, Ar = $C_6H_4CH_3$-p (Ib); R = OH, Ar = Ph (Ic); R = OH, Ar = $C_6H_4CH_3$-p (Id); R = H, Ar = Ph, $R^1R^2 = (CH_2)_5$ (IIIa); R = H, Ar = $C_6H_4CH_3$-p, $R^1R^2 = (CH_2)_5$ (IIIb); R = OH, Ar = $C_6H_4CH_3$-p, $R^1R^2 = (CH_3)_2$ (IIIc); R = OH, Ar = = Ph, $R^1R^2 = (CH_2CH_2)_2O$ (IIId); R = OH, Ar = $C_6H_4CH_3$-p, $R^1R^2 = (CH_2)_5$ (IIIe)



IIa, b IVa, b

Ar = Ph (IIa), (IVa); Ar = $C_6H_4CH_3$-p (IIb), (IVb).

Compounds (Ic, d), which contain a hydroxyl group in the 5 position, react with dimethylamine, morpholine, and piperidine in the absence of catalyst. This is probably due to the fact that in 5-hydroxy-1,4-naphthoquinone [6], there is a strong intramolecular hydrogen bond of the type —OH···N=C, which activates the naphthoquinoneimine molecule toward reactions with nucleophiles. In addition, it has also been found that as the reaction time is increased, the reaction does not stop at the formation of 5-hydroxy-2-dialkylamino-N-aryl-1,4-naphthoquinoneimines (IIc-e), but rather proceeds further to give a mixture of

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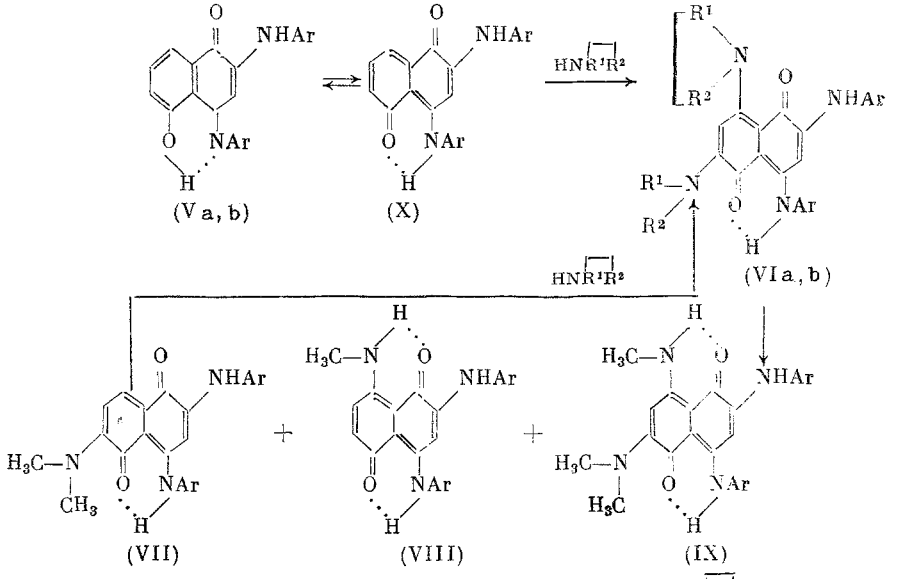
TABLE 1

Compound	Reaction time, h	Yield, %	mp; °C (solvent)	Found, %			Molecular formula	Calcd., %			IR spectrum, ν, cm^{-1}	Electronic spectrum in the visible region λ_{max}, nm (log ε)
				C	H	N		C	H	N		
(IIIa)	4	80	113–114 heptane	79,43	6,51	8,60	$C_{21}H_{20}N_2O$	79,72	6,37	8,85	1660(C=O) 1600(C=N)	461(3,83)
(IIIb)	4	69	99–100 ethanol	79,70	6,91	8,58	$C_{22}H_{22}N_2O$	79,97	6,72	8,47	1660(C=O) 1600(C=N)	465(3,83)
(IIIc)	1,5	74	115–116 heptane	74,75	5,76	9,09	$C_{19}H_{18}N_2O_2$	74,49	5,92	9,14	1660(C=O) 1600(C=N)	468(4,00), 590(3,48)
(IIId)	1,5	62	147–149 hexane	72,09	5,40	8,33	$C_{20}H_{18}N_2O_3$	71,84	5,43	8,38	1660(C=O) 1610(C=N)	440(4,00), 590(2,90)
(IIIe)	2	75	145–146 heptane	76,07	6,34	7,85	$C_{22}H_{22}N_2O_2$	76,27	6,40	8,09	1660(C=O) 1600(C=N)	465(4,00), 587(3,20)
(IVa)	4	65	135–136 heptane	83,19	6,52	10,75	$C_{27}H_{25}N_3$	82,84	6,43	10,73	1610(C=N) 1590(C=N)	390(4,01)
(IVb)	4	62	126–127 heptane	82,88	7,10	10,01	$C_{29}H_{29}N_3$	83,01	6,96	10,03	1620(C=N) 1600(C=N)	415(4,23)
(VIa)	48	40*	199–200 benzene	70,39	5,79	10,81	$C_{30}H_{30}N_4O_4$	70,57	5,92	10,97	3320(NH) 1630, 1590	† 438(4,13), 609(4,21), 648(4,34)
(VIb)	24	42	205–206 benzene	74,17	6,49	12,23	$C_{28}H_{30}N_4O_2$	73,98	6,65	12,33	3330(NH) 1630, 1580	† 454(4,14), 592(4,19), 641(4,38)
(VII)		20	225–227 hexane–benzene	75,85	6,19	10,20	$C_{26}H_{26}N_3O_2$	75,89	6,12	10,21	3290(NH) 1600	435(3,94), 634(4,05), 676(4,02)
(VIII)		20	274–275 benzene	75,09	5,67	10,58	$C_{25}H_{22}N_3O_2$	75,55	5,83	10,57	3290(NH) 1640, 1620, 1600	† 336(3,88), 530(3,85), 555(3,90), 608(4,23), 658(4,48)
(IX)		9	248–250 hexane–benzene	73,85	6,38	12,43	$C_{27}H_{28}N_4O_2$	73,61	6,41	12,72	3330(NH) 1600	435(4,22), 576(4,29), 621(4,47)

*40% starting material was recovered.
†In $CHCl_3$.

highly colored organic compounds. In the case of treatment of 5-hydroxy-2-arylamino-N-aryl-1,4-naphthoquinone-4-imines (Va, b) with dimethylamine and morpholine, amination products of the second ring, namely, compounds (VI)-(IX) have also been isolated. It should be noted in this context that N-aryl-1,4-naphthoquinone-4-imines which do not contain a hydroxyl group in the 5-position [1], as well as 5-hydroxy-1,4-naphthoquinone [7], react with nucleophiles at the quinone ring only. The ability of 5-hydroxy-N-aryl-1,4-naphthoquinone-4-imines to form amination products at both rings is probably associated with the possible existence of compounds (Va, b) in two tautomeric forms: 5-hydroxy-1,4-quinone-imino form (V) and 4-arylamino-1,5-naphthoquinoid form (X), as a result of migration of a proton between the nitrogen and oxygen atoms. This assumption is supported by the presence of a low intensity shoulder at ca. 600 nm, in addition to the intense absorption maximum at ca. 450 nm, in the visible spectra of compounds (Va, b) in EtOH solution. The first band corresponds to an intramolecular charge transfer (ICT) band of the OH form (V), which is similar in structure to 2-dialkylamino-N-aryl-1,4-naphthoquinone-4-imines (IIa, b), which also absorb in this region (Table 1); the second band, the shoulder with a maximum at ca. 600 nm, is probably an ICT band of the tautomeric NH form. A similar equilibrium has been observed in the case of 1-hydroxyanthraquinone-9-imines [8]. Since 1,4-naphthoquinone is energetically much more favored than 1,5-naphthoquinone [9], in the starting materials (Va, b) the equilibrium should be shifted strongly in the direction of the OH tautomer; in contrast, however, as the reaction proceeds and amination products are formed, the equilibrium is shifted constantly to the side of the anaquinoid form (X).



Ar = Ph (V a); Ar = $C_6H_4CH_3$-*p* (V b), (VII), (VIII), (IX); Ar = Ph, $\overline{R^1R^2}$ = $(CH_2CH_2)_2O$ (VI a); Ar = $C_6H_4CH_3$-*p*, $\overline{R^1R^2}$ = $(CH_3)_2$ (VI b).

The structures of the products were established based on their analytical and spectral data (Tables 1, 2). Products (VI)-(IX) all contain a 1,5-naphthoquinone structure, as evidenced from the IR spectra of these compounds, in which the C=O stretching vibrations have been shifted to lower frequency (1630-1600 cm^{-1}), just as has been observed in the spectra of other quinones which contain carbonyl groups in two different rings; their electronic spectra are also similar to the spectra of previously prepared ana-naphthoquinones [10]. The main products of the reaction of 5-hydroxy-2-arylamino-N-aryl-1,4-naphthoquinone-4-imines (Va, b) with dimethylamine and morpholine are 6,8-bis(dimethylamino)-2,4-bis(phenylamino)-1,5-naphthoquinone (VIa) and 6,8-bis(morpholino)-2,4-bis(p-toylamino)-1,5-naphthoquinone (VIb), respectively.

The PMR spectrum of compound (VIb) contains in addition to the methyl group singlets and aromatic proton multiplet, signals due to the protons of two different amino groups (8.38 and 15.16 ppm) and singlets at 6.11 and 6.73 ppm, corresponding to the protons attached to the C^7 and C^3 carbon atoms of the naphthoquinone nucleus. 6-Dimethylamino-2,4-bis(p-toylamino)-1,5-naphthoquinone (VII) is an intermediate product in the formation of compound (VIb); its structure is confirmed by the presence of two doublets with J = 9 Hz at 6.65 and 7.70 ppm, as well as of a singlet at 6.56 ppm in the PMR spectrum.

TABLE 2

Compound	PMR spectrum, δ, ppm (in $CDCl_3$)
(VIb)	2,29 s (3H, CH_3), 2,36 s (3H, CH_3), 3,10 s (6H, $2CH_3$), 3,21 s (6H, $2CH_3$), 6,11 s (1H, H^7), 6,73 s (1H, H^3), 7,06—6,36 m (8H, H_{arom}), 8,38 s (1H, NH), 15,46 s (1H, NH)
(VII)	2,29 s (3H, CH_3), 2,36 s (3H, CH_3), 3,17 s (6H, $2CH_3$), 6,56 s (1H, H^3), 6,65 d (1H, H^7, $J_o = 9$ Hz), 6,96—7,22 m (8H, H_{arom}), 7,70 d (1H, H^8, $J_o = 9$ Hz), 7,85 s (1H, NH), 16,95 s (1H, NH)
(VIII)	2,30 s (3H, CH_3), 2,35 s (3H, CH_3), 3,19 d (3H, CH_3, $J = 5$ Hz), 6,80 s (1H, H^3), 7,00—7,20 m (10H, H_{arom}), 8,01 s (1H, NH), 11,72 s (1H, NH), 15,18 s (1H, NH)
(IX)	2,28 s (3H, CH_3), 2,33 s (3H, CH_3), 3,12 d (3H, CH_3, $J = 5$ Hz), 3,26 s (6H, $2CH_3$), 5,77 s (1H, H^7), 6,81 s (1H, H^3), 7,00—7,34 m (8H, H_{arom}), 8,22 s (1H, NH), 12,30 m (1H, NH), 14,01 s (1H, NH)

In the case of the reaction of (Vb) with dimethylamine, two products characterized by dealkylation of a dimethylamino group in the peri-position relative to the carbonyl group were isolated: 8-monomethylamino-2,4-bis(p-tolylamino)-1,5-naphthoquinone (VIII) and 6-dimethylamino-8-monomethylamino-2,4-bis(p-tolylamino)-1,5-naphthoquinone (IX). Compound (VIII) is obtained from the first formed 8-dimethylamino-2,4-bis(p-tolylamino)-1,5-naphthoquinone, which readily loses a methyl group during the course of the reaction, as well as during chromatographic purification; consequently, it was not isolated in pure form. Compound (VIb) is more stable, but is converted rapidly to the demethylated product (IX) upon heating in pyridine; this process probably occurs in a similar fashion to the dealkylation of dialkylamino groups located in the peri-position to a carbonyl group in the anthraquinone series [11].

Chromatographic control of the reaction of 5-hydroxy-2-arylamino-N-aryl-1,4-naphthoquinone-4-imines (Va, b) with morpholine and piperidine also indicated the presence of alkylamination products similar to compounds (VI)-(IX); because of their instability, however, they were not isolated.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrophotometer for KBr pellets or $CHCl_3$ solutions, while electronic spectra were obtained on a Specord UV-VIS spectrophotometer for EtOH solutions, and PMR spectra (200 MHz) were obtained on a Bruker WP-200 SY instrument. TLC analyses on Silufol plates were carried out with $CHCl_3$; preparative chromatography was conducted on L grade (100-250 μm) SiO_2 columns from Chemapol (Czech. SSR). Reaction times, yields, melting points, elemental analyses, as well as IR and electronic absorption spectral data are summarized in Table 1; PMR spectra of compounds (VI)-(IX) are given in Table 2.

Starting materials were prepared according to known methods: N-aryl-1,4-naphthoquinone-4-imines (Ia, b), [12]; N,N'-diaryl-1,4-naphthoquinonediimines (IIa, b), [13]; 5-hydroxy-N-aryl-1,4-naphthoquinone-4-imines (Ic, d) and 5-hydroxy-2-arylamino-1,4-naphthoquinone-4-imines (Va, b), [10].

Reaction of N-Aryl-1,4-naphthoquinone-4-imines (Ia, b) and N,N'-Diaryl-1,4-naphthoquinonediimines (IIa, b) with Piperidine. A mixture of 5 mmoles piperidine and 5 mmoles $Cu(OAc)_2 \cdot H_2O$ in 30 ml EtOH was treated with 1 mmole of (Ia, b) or (IIa, b) and heated to 60-70°C with air bubbling. 5% HCl was added and the resulting precipitate was removed by filtration, washed with water, and dried. The product was chromatographed on a SiO_2 column with petroleum ether—benzene (1:1) eluent. Compounds (IIIa, b) or (IVa, b) were obtained.

Reaction of 5-Hydroxy-N-aryl-1,4-naphthoquinone-4-imines (Ic, d) with Secondary Aliphatic Amines. A mixture of 1 mmole (Ic, d) in 15 ml of 10% solution of the appropriate amine in pyridine was stirred at ∿20°C while air was bubbled through the solution. The mixture was poured onto water, and the precipitate was filtered, washed with water, and dried. Upon chromatography on SiO_2, the main dark red fraction containing compounds (IIIc-e) was eluted with a C_6H_6—$CHCl_3$ (7:3) mixture.

Reaction of 2-Arylamino-5-hydroxy-1,4-naphthoquinone-4-imines (Va, b) with Dimethylamine or Morpholine. a) A mixture of 1 mmole (Va) and 15 ml of a 10% solution of morpholine in pyridine was stirred at ∿20°C with air bubbling through the solution. The mixture was

poured into water, the precipitate was filtered, washed with water, and dried. Upon chromatography on SiO_2 under vacuum, the following were isolated: starting material (Va) upon elution with a C_6H_6–$CHCl_3$ (2:1) mixture, and compound (VIa) by elution with a 1:1 mixture. There remained on the column two small zones, which were blue and green, respectively.

b) A mixture of 1 mmole (Vb) and 15 ml 10% Me_2NH solution in Py was stirred at ~20°C as air was bubbled through the solution. The mixture was worked up as described above. Chromatography on a SiO_2 column under vacuum with a mixture of C_6H_6–$CHCl_3$, as the concentration of $CHCl_3$ was varied in a gradient from 30 to 100%, gave the following compounds in order of successive elution: (VII), (IX), (VIII), and (VIb).

Reaction of 6-Dimethylamino-2,4-bis(p-tolylamino)-1,5-naphthoquinone (VII) with Dimethylamine. A mixture of 1 mmole (VII) and a solution of Me_2NH in Py was maintained as described above for 24 h. Workup and chromatography were also analogous to the above procedure. Yield, 0.4 g (80%) of compound (VIb) and 0.05 g (10%) of compound (IX).

6-Dimethylamino-8-monomethylamino-2,4-bis(p-tolylamino)-1,5-naphthoquinone (IX). A mixture of 0.1 g 6,8-bis(dimethylamino)-2,4-bis(p-tolylamino)-1,5-naphthoquinone (VIb) in 5 ml Py was heated at 120°C for 10 h. It was worked up and chromatographed as described above. Yield of compound (IX), 0.06 g (60%).

CONCLUSIONS

1. N,N'-Diaryl-1,4-naphthoquinonediimines and N-aryl-1,4-naphthoquinone-4-imines react with dialkylamines in the presence of Cu^{2+} salts at the double bond of the quinoid ring.

2. 5-Hydroxy-N-aryl-1,4-naphthoquinone-4-imines undergo amination at both rings of the naphthoquinone moiety in the absence of catalyst, and the dialkylamino group which is located peri to the carbonyl group can undergo subsequent dealkylation.

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