

## Direct Phenylamination of 6-Aminonaphthacenequinones Promoted by Metal Salts

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Received April 11, 2000

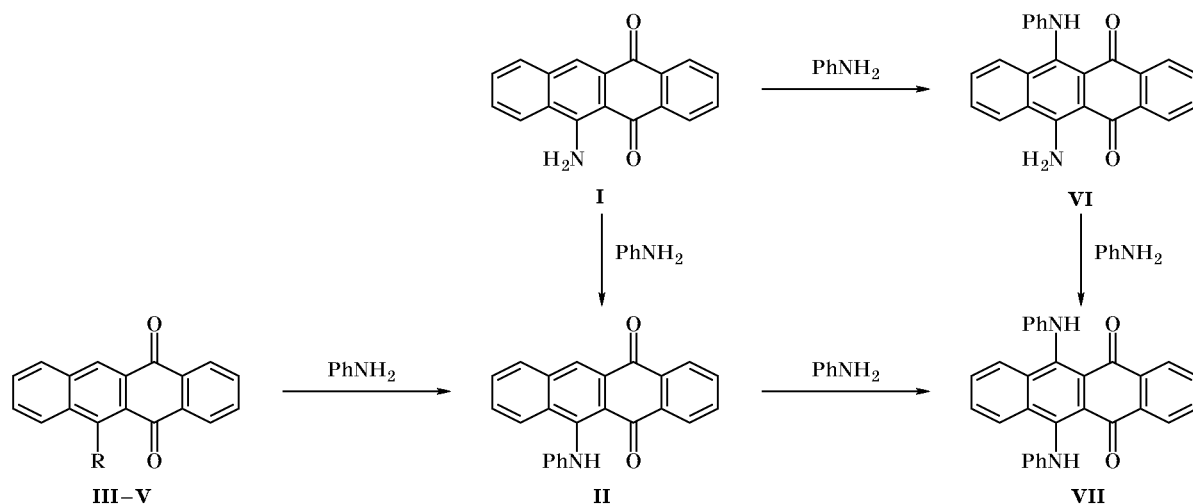
**Abstract**—6-Amino-5,12- and -5,11-naphthacenequinones react with aniline in the presence of cobalt, copper, and manganese salts, resulting in replacement of hydrogen in the *peri*-position with respect to the carbonyl group by phenylamino group and formation of 11- and 12-phenylamino-6-amino(phenylamino)-5,12- and -5,11-naphthacenequinones.

Phenylamino group can be introduced into the *peri*-position with respect to the carbonyl group of 5,12-(*para*) and 5,11-(*ana*)naphthacenequinones via nucleophilic replacement of halogen [1, 2] or phenoxy group [3, 4] by aniline residue. Substitution of the hydroxy group in 6-hydroxy- and 6,11-dihydroxy-5,12-naphthacenequinones by aniline in the presence of boric acid is accompanied by reorganization of the *para*-quinoid structure into *ana*-quinoid with formation of 6-phenylamino- and 6,12-bis(phenylamino)-5,11-naphthacenequinones, respectively [2, 5, 6]. Highly

reactive unsubstituted *ana*-naphthacenequinone reacts [2] with aniline directly to form product of hydrogen replacement by phenylamino group [7], 6-phenylamino-5,11-naphthacenequinone. We have found that an analogous reaction can be effected with less reactive *p*-naphthacenequinone: Its 6-hydroxy derivative reacts with aniline in the presence of copper acetate, yielding 6-hydroxy-11-phenylamino-5,12-naphthacenequinone [8].

The present communication reports on the results of our study on the possibility of direct phenylamination

Scheme 1.



III, R = NHBu; IV, R = morpholino; V, R = NHAc.

**Table 1.** Melting points and spectral parameters of 6-aminonaphthacenequinone derivatives **III**, **IV**, **VI**, **VII**, **X**, and **XI**

Comp. no.	mp, °C	Electron absorption spectrum (toluene), $\lambda_{\max}$ , nm (log $\epsilon$ )	IR spectrum (KBr), $\nu$ , $\text{cm}^{-1}$			
			C=O	C=C <sub>arom</sub>	C=C-C=C <sub>quinoid</sub>	C-H
<b>III</b>	159–160 <sup>a</sup>	382 sh (3.58) 395 (3.62) 504 (4.07)	1656	1620 1580	1288	2960, 2928 2868
<b>IV</b>	242–243 <sup>b</sup>	391 (3.67) 447 (3.55)	1672 1656	1610 1596 1580	1272	2968 2956 2888 2852
<b>VI</b>	252–253 <sup>b</sup>	442 (3.80) 544 (4.16) 571 sh (4.11)	1652 1620	1600 1584	1272 1256	3404 (NH)
<b>VII</b>	255–256, <sup>a</sup> 244–246 (AcOH) [5]	463 (3.98) 566 (4.13) 595 sh (4.08)	1652	1620 1576	1266	
<b>X</b>	235.5–236.5 <sup>b</sup>	547 (4.29) 586 (4.43) 546 (4.33) 585 (4.48) <sup>c</sup> 542 (4.28) 580 (4.41) <sup>d</sup>	1652 1636	1616 1592	1336	3408 (NH)
<b>XI</b>	314–315, <sup>b</sup> 314–315 [8]	571 (4.36) 611 (4.48) 571 (4.44) 611 (4.57) <sup>c</sup> 562 (4.01) 601 (4.13) <sup>d</sup>	1652	1590 1576	1328	

<sup>a</sup> From benzene–hexane.<sup>b</sup> From chloroform–hexane.<sup>c</sup> In CCl<sub>4</sub>.<sup>d</sup> In MeOH.

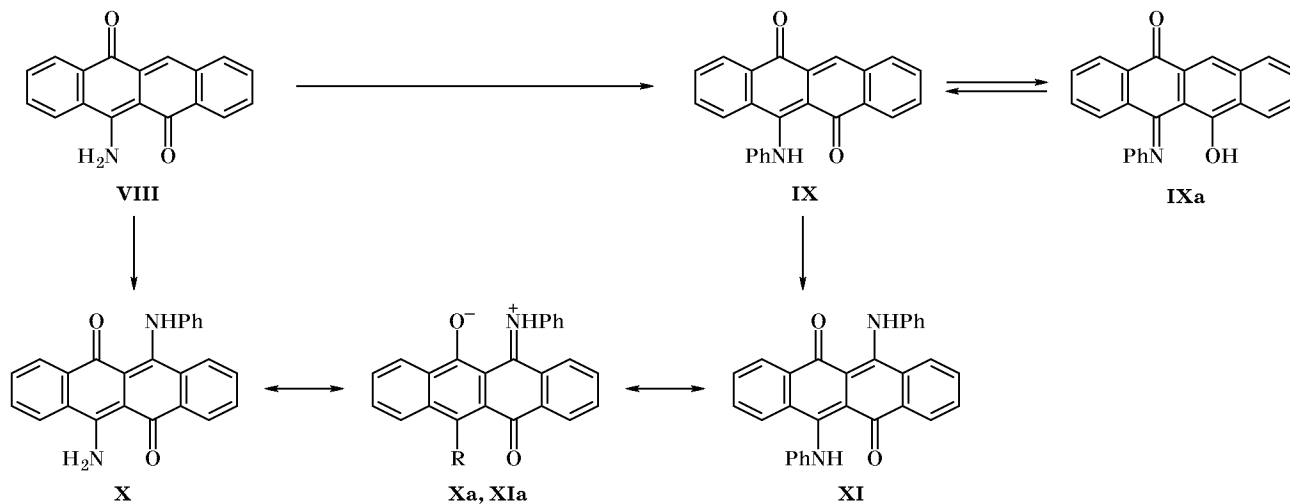
of 6-amino derivatives of *para*- and *ana*-naphthacenequinones. We found that heating of 6-amino-5,12-naphthacenequinones **I**–**V** in aniline in the presence of metal salts results in replacement of hydrogen in the *peri*-position with respect to the carbonyl group by phenylamino group with formation of the corresponding 11-phenylamino derivatives **VI** and **VII** (Scheme 1). The structure of products **VI** and **VII** was proved by independent synthesis and spectral data. The melting points and IR and electron spectral parameters of **VI** and **VII**, as well as of previously unknown naphthacenequinones **III** and **IV**, are given in Table 1.

Preliminarily, we have found that prolonged heating of *p*-aminonaphthacenequinones **I** and **II** in aniline in the absence of metal salt does not result

in introduction of phenylamino group into the naphthacene core, and initial compounds **I** and **II** were quantitatively recovered from the reaction mixture. Among the examined salts, manganese acetate showed the highest activity in the direct phenylation of naphthacenequinones **I** and **II** (Table 2). Metal salts promote not only phenylation of *p*-aminonaphthacenequinone (**I**) but also its transamination, as follows from the presence in the reaction mixture of 6-phenylamino-5,12-naphthacenequinone (**III**). In addition, the transformation of 6-amino-5,12-naphthacenequinone (**I**) into phenylamino derivative **VI** is accompanied by formation of 6,11-bis(phenylamino)naphthacenequinone **VII** whose yield attains ~13% in the presence of cobalt nitrate. The yield of **VII** decreases to 1.5% when the reaction is carried out in the



Scheme 2.



**Xa**, R = NH<sub>2</sub>; **XIa**, R = NHPh.

transamination of 6-butylaminonaphthacenequinone **III** and subsequent replacement of hydrogen by phenylamino group in 6-phenylamino-5,12-naphthacenequinone (**II**). The ability of 6-butylaminonaphthacenequinone **III** to undergo transamination is likely to be responsible for its transformation into **II**, which occurs in 50% yield by the action of aniline even in the absence of manganese acetate.

6-Morpholino-5,12-naphthacenequinone (**IV**) failed to react with aniline to give hydrogen replacement product. Heating of **IV** in boiling aniline for a short time both in the presence and in the absence of manganese acetate resulted in transamination and formation of 6-phenylaminonaphthacenequinone **II** in high yield.

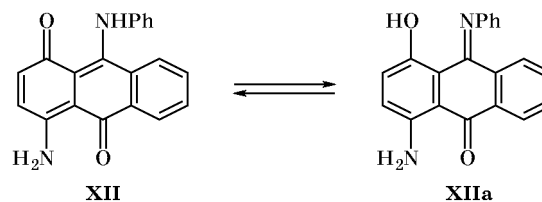
The reaction of 6-acetylaminonaphthacenequinone **V** with aniline and manganese acetate gave 10% of 6-amino-11-phenylaminonaphthacenequinone **VI** as a result of direct phenylation and hydrolysis of the acetyl amino group. In the absence of manganese acetate less than 1% of **VI** was obtained, and unchanged initial compound **V** was recovered from the mixture in high yield.

Unlike *para* isomers **I** and **II**, *ana*-aminonaphthacenequinones **VIII** and **IX** react with aniline in the absence of metal salts to afford 5–9% of 6-amino-12-phenylamino-5,12-naphthacenequinone (**X**) and 6,12-bis(phenylamino)-5,12-naphthacenequinone (**XI**) (Scheme 2). However, the predominant process is transamination of **VIII**, which leads to formation of 6-phenylamino-5,11-naphthacenequinone (**IX**) in 40% yield. Further heating of the reaction mixture results

in complete conversion of **IX** into 6,12-bis(phenylamino)-5,11-naphthacenequinone (**XI**). Direct phenylation products **X** and **XI** were formed in high yield and at a higher rate (as compared to the corresponding *para* analogs **I** and **II**) when *ana*-aminonaphthacenequinones **VIII** and **IX** were treated with aniline in the presence of manganese acetate. Likewise, *ana*-phenylaminonaphthacenequinone **IX** readily reacts with aniline in the presence of copper acetate, but the yield of the product is smaller. Zinc acetate turned out to be ineffective in the phenylation of **IX**. The yield of target product **XI** was poor, and the process was accompanied by formation of 6-hydroxynaphthacenequinone via hydrolysis of *ana*-phenylaminonaphthacenequinone **IX**.

Reduction of the amount of manganese acetate from 2 mol to 0.1 mol leads to insignificant decrease of the yield of product **XI** in the phenylation of *ana*-phenylaminonaphthacenequinone **IX**, while in the reaction with *para*-phenylamino derivative **II** increase in the yield of product **VII** is observed. These data suggest some difference in the mechanisms of direct phenylation of *para*- and *ana*-phenylaminonaphthacenequinones **II** and **IX**.

Scheme 3.



6-Phenylamino-5,11-naphthacenequinone (**IX**) [9] and 4-amino-9-phenylamino-1,10-anthraquinone (**XII**) [10] are capable of undergoing tautomeric transformations via proton migration between the phenylamino group and carbonyl oxygen atom in the *peri* position (Scheme 3). By contrast, *ana*-aminonaphthacenequinones **X** and **XI** are incapable of prototropic transformations, as follows from their spectral data: The spectral curves of compounds **X** and **XI** do not change their shape on variation of the solvent polarity. In going from a less polar solvent to more polar, compound **X** and, to a greater extent, *ana*-diphenylaminonaphthacenequinone **XI** exhibit a negative solvatochromism, i.e., the long-wave absorption maxima of **X** and **XI** shift to shorter wavelengths, and their intensity decreases (Table 1). This means [11] that the ground state of molecules **X** and **XI** is more polar than the excited state; therefore, it is described better by dipolar structures **Xa** and **XIa** (Scheme 2). The predominant contribution of dipolar structures is likely to result from the lower energy of the *para*-quinonimine structure relative to *ana*-quinoid.

Thus, direct phenylation promoted by metal salts can be effected with 6-amino- and 6-phenylaminonaphthacenequinones having both *para*- and *ana*-quinoid structure. This reaction can be used as a method for introduction of phenylamino group into the *peri*-position with respect to the carbonyl group of 6-amino- and 6-phenylaminonaphthacenequinone derivatives.

## EXPERIMENTAL

The electron absorption spectra were measured on a Specord M-40 spectrophotometer. The IR spectra were obtained on a Specord M-80 spectrometer in KBr. The melting points were determined with the aid of a PTP device (TU 25-11-1144-76).

6-Amino-5,12-naphthacenequinone (**I**), 6-phenylamino-5,12-naphthacenequinone (**II**) [1], 6-amino-5,11-naphthacenequinone (**VIII**) [12], 6-phenylamino-5,11-naphthacenequinone (**IX**) [3], and 6,11-bis(phenylamino)-5,12- and 6,12-bis(phenylamino)-5,11-naphthacenequinones **VII** and **XI** [5] were synthesized and purified by known methods. Their properties were consistent with published data. Cobalt, manganese, copper, and zinc salts (crystal hydrates) of pure or analytical grade were used without additional purification.

**6-Butylamino-5,12-naphthacenequinone (III).** A mixture of 0.207 g of 6-chloro-5,12-naphthacenequinone and 7 ml of butylamine was refluxed for 1.5 h. It was then cooled and poured into 10% hydro-

chloric acid, and the precipitate was filtered off, washed with water, dried, and subjected to column chromatography on aluminum oxide (Brockman activity grade II) using chloroform as eluent. The major fraction (crimson) was evaporated, and the residue was recrystallized from benzene-hexane. Yield 0.195 g (85%), dark red crystals.

**6-Morpholino-5,12-naphthacenequinone (IV)** was synthesized in a similar way, but the reaction time was 10 min. Recrystallization from chloroform-hexane gave compound **IV** in 89% yield; brownish-yellow crystals.

**6-Acetylamino-5,12-naphthacenequinone (V)** was synthesized by acylation of 6-amino-5,12-naphthacenequinone (**I**) with acetic anhydride, following the procedure described in [4] for preparation of 6-acetylamino-11-phenoxy-5,12-naphthacenequinone. mp 250–251°C (from benzene); published data [13]: mp 249 and 254°C (from benzene).

**6-Amino-11-phenylamino-5,12-naphthacenequinone (VI) (independent synthesis).** A mixture of 0.044 g of 6-amino-11-phenoxy-5,12-naphthacenequinone [4] and 5 ml of aniline was refluxed for 0.5 h. It was then cooled and poured into 10% hydrochloric acid, and the precipitate was filtered off, washed with water, dried, and subjected to chromatography on porous quartz (50–150 μm) using chloroform as eluent. The major fraction (violet) was evaporated, and the residue was recrystallized from chloroform-hexane. Yield 0.042 g (95%), dark violet needles with a greenish tinge. The electron absorption and IR spectra, melting point, and  $R_f$  value coincided with those found for compound **VI** obtained by direct phenylation of naphthacenequinone (**I**).

**6-Amino-12-phenylamino-5,11-naphthacenequinone (X) (independent synthesis).** Compound **X** was synthesized from 6-amino-12-(4-ethylphenoxy)-5,11-naphthacenequinone which was obtained by acid-catalyzed isomerization of the corresponding *para* isomer prepared by the procedure reported in [14]. A mixture of 0.3 g of 6-amino-12-(4-ethylphenoxy)-5,11-naphthacenequinone, 50 ml of aniline, and 250 ml of ethanol was refluxed for 2 h. The solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel (40–100 μm) using chloroform as eluent. The major fraction (dark violet) was evaporated, and the residue was recrystallized first from benzene and then from ethanol. Yield 0.25 g (90%). Found, %: C 79.57; H 4.54; N 7.60.  $C_{24}H_{16}N_2O_2$ . Calculated, %: C 79.10; H 4.43; N 7.69. The electron absorption and IR spectra, melting point, and  $R_f$  value coincided with those

found for compound **X** obtained by direct phenylation of aminonaphthacenequinone (**VIII**).

**Direct phenylation of 6-aminonaphthacenequinone derivatives I–V, VIII, and IX (general procedure).** A mixture of  $10^{-4}$  mol of compound **I–V**, **VIII**, or **IX**,  $2 \times 10^{-4}$  mol of appropriate metal salt hydrate, and aniline was refluxed under continuous stirring. It was then cooled and poured into 10% hydrochloric acid, and the precipitate was filtered off, washed with water, dried, and subjected to chromatography on porous quartz (50–150  $\mu\text{m}$ ) using chloroform as eluent. Fractions containing the phenylation products were collected and evaporated. Each product was additionally purified by chromatography on silica gel (40–100  $\mu\text{m}$ ) using benzene as eluent. The solvent was distilled off from the eluate, the residue was dissolved in chloroform, the solution was filtered from mechanical impurities through a folded filter, the filtrate was transferred to a porcelain evaporating dish and was evaporated on a water bath, and the residue was dried at 90–95°C and weighed. The yield of each reaction product was calculated from the results of 2–3 parallel runs (Table 2).

**Reaction of 6-amino-11-phenylamino-5,12-naphthacenequinone (VI) with aniline in the presence of cobalt nitrate.** The reaction was carried out following the above procedure. The mixture was refluxed for 6 h. By chromatographic treatment we isolated 18% of 6,11-bis(phenylamino)-5,12-naphthacenequinone (**VII**) and 44% of unreacted initial compound **VI**.

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