CONCLUSIONS

1. The aminal and aminalacetal of α-chloro-β-dimethylaminoacrolein were synthesized and their reactions with ketones and β-dicarbonyl compounds were investigated.

2. Dienylic δ-dimethylamino-γ-chloroketones, ketoesters, and diesters were obtained.

3. Dynamic equilibria between δ-dimethylamino-γ-chlorodienones and the corresponding 3-chloro-2-dimethylamino-2H-pyrans are established as a result of valence isomerization.

4. The position of the dienone-2H-pyran equilibrium depends upon the solvent. An increase in the specific solvating ability of the solvent shifts the equilibrium in favor of the δ-aminodienone form.

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HETEROCYCLIZATION OF N-SUBSTITUTED 2-AMINO-3-ACETYLENYL-1,4-NAPHTHOQUINONES

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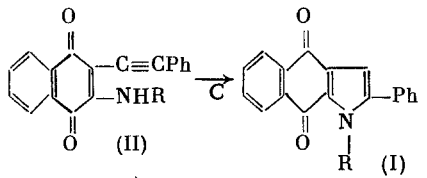
Many naturally occurring and synthetic indolequinones possess high biological activity [1]. The methods available for the synthesis of these heterocyclic quinone compounds include thermal and photochemical intramolecular cyclization reactions of azido- and aminoquinones containing vicinal ethylene, tosylhydrazone, and active methylene substituents, as well as photocycloaddition reactions with conjugated dienes [1-4].

We have found that 1,2-disubstituted benzindolequinones (I) can be prepared via the base-catalyzed cyclization of 2-amino-3-acetylenyl-1,4-naphthoquinones (II), which have been previously described [5].



R = Me (a), Ph (b), CH_2Ph (c), $CH_2CH{=}CH_2$ (d), CH_2CH_2OH (e), CH_2CH_2OAc (f), Ac (g)

The reactions are carried out with heating in pyridine or mesitylene in the presence of catalytic amounts of KOH (1.5-6 wt.%, relative to (II)). The cyclization of IIg was carried out using PhC≡CCu instead of KOH as catalyst. The product yields of (I) ranged from 25-82% and are presented in Table 1.

Addition of base to a solution of the starting material (II) results in a deep coloration of the solution, which is characteristic of 2-substituted naphthoquinones containing an active hydrogen atom in the α position of the substituent; the color change is probably due to deprotonation of this acidic group. Intramolecular addition to the triple bond of (II), which is normally deactivated to nucleophilic attack [5], is apparently facilitated by the formation

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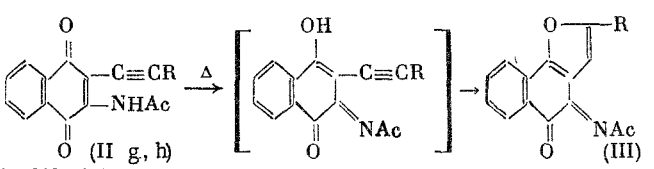
TABLE 1. N-Substituted 2-Phenylbenz[f]indole-4,9-diones (I)

Compound	Yield, %	mp, °C	Found/Calcd., %			Molecular formula	PMR spectrum ($CDCl_3$) δ, ppm
			C	H	N		
(Ia)	82	146,5–147,5 (возгон.)	79,20 / 79,43	4,38 / 4,56	4,87 / 4,88	$C_{19}H_{13}NO_2$	4,05 (CH_3), 6,81 (H^3), 7,4–7,5 m(Ph), 7,6–7,7 m ($H^{6,7}$), 8,1–8,2 m ($H^{5,8}$)
(Ib)	74	211,5–212 (возгон.)	82,31 / 82,50	4,18 / 4,33	3,92 / 4,01	$C_{24}H_{15}NO_2$	7,02 (H^3), 7,1–7,5 m (Ph, PhN), 7,6–7,7 m ($H^{6,7}$), 8,00–8,07 m and 8,15–8,22 m ($H^{5,8}$)
(Ic)	74	163,5–164 (Me_2CO – октан)	82,43 / 82,62	4,62 / 4,72	3,86 / 3,85	$C_{25}H_{17}NO_2$	5,74 (CH_2), 6,87 (H^3), 7,1–7,5 m (Ph, $PhCH_2$), 7,6–7,7 m ($H^{6,7}$), 8,0–8,2 m ($H^{5,8}$)
(Id)	52 *	137,5–138 (Me_2CO)	80,46 / 80,49	4,86 / 4,83	4,62 / 4,47	$C_{21}H_{15}NO_2$	4,90 d (H, H)C=C(H), 5,18 d (H, H)C=C(H), 5,06 m (CH_2N), 6,04 m ($CH=CH_2$), 6,82 (H^3), 7,46 (Ph), 7,6–7,7 m ($H^{6,7}$), 8,1–8,2 m ($H^{5,8}$)
(Ie)	44 *	134–134,5 (эфир – гексан)	75,68 / 75,70	4,89 / 4,76	4,62 / 4,41	$C_{20}H_{13}NO_3$	2,33 br. t (OH), 3,94 q (CH_2O), 4,60 t (CH_2N), 6,76 (H^3), 7,48 (Ph), 7,6–7,7 m ($H^{6,7}$), 8,05–8,15 m ($H^{5,8}$)
(If)	78	152–152,5 (эфир)	73,41 / 73,53	4,87 / 4,77	3,83 / 3,90	$C_{22}H_{17}NO_4$	1,82 (CH_3), 4,33 t (CH_2O), 4,77 t (CH_2N), 6,79 (H^3), 7.4–7,5 m (Ph), 7,6–7,7 m ($H^{6,7}$), 8,1–8,2 m (^{5,8})
(Ig)	25 †	177–177,5 ($CHCl_3$ – EtOH)	75,85 / 76,18	4,03 / 4,16	4,46 / 4,44	$C_{20}H_{13}NO_3$	2,61 (CH_3), 6,87 (H^3), 7,3–7,5 m (Ph), 7,65–7,75 m ($H^{6,7}$), 8,1–8,2 m ($H^{5,8}$)

*In mesitylene; yields in pyridine were 29.5% (Id), 32.7% (Ie).
†In DMSO in the presence of PhC≡CCu.

and three-dimensional proximity of the highly charged nucleophilic center. In contrast, the well-known cyclization of o-aminoacetylenic aromatic compounds in the presence of Cu(I) salts [6] does not involve initial deprotonation of the amino group, and probably takes place via a different mechanism. The cyclization of (II) is not catalyzed by salts such as CuCl and CuI. It is reasonable to assume, therefore, that PhC≡CCu acts as a base, in a manner analogous to KOH, in these reactions.

The acetylaminoquinones (IIg, h) appear to be significantly stronger NH acids than the other compounds; upon heating to 80-110°C in the absence of catalysts, these compounds undergo cycloisomerization to give the 4-acetylamino-5-oxonaphtho[4,3-b]furans (III) in high yield. It cannot be excluded that the reactive forms of (IIg, h) are actually the tautomeric hydroxyl acetylamino derivatives of o-naphthoquinone.



R = Ph (g), CMe_2OH (h).

The structures of the products (I) and (III) were assigned on the basis of their elemental analyses, which identified them as isomers of the starting aminoacetylenes (II), and by

means of their spectral data. The IR spectra of (I) and (III) do not contain stretching bands associated with NH or disubstituted acetylenic groups, which appear at 3345-3375 and 2200-2210 cm^{-1}, respectively, in the starting materials (II). Instead of a broad signal for the NH group at δ 6.4-6.7 ppm as in (II), the PMR spectra of (I) and (III) contain narrow singlets at δ 6.56-7.02 ppm, corresponding to the protons (H^3) on the unsubstituted ring of the aromatic heterocyclic product. The spectra of (I) retain a symmetrical pattern for the four protons of the benzindole ring at δ 8.0-8.2 and 7.6-7.7 ppm, which is typical of substituted 1,4-naphthoquinones (for comparison with (II), see [5]); this substantiates the p-quinone structure of these compounds and, by extension, their designation as members of the benz[f]indole-4,9-dione series. The involvement of the unshared pair of electrons on the nitrogen atom in the aromatic π-system in (I) is implied by the fact the colors of (I) are significantly less intense relative to their aminoquinone counterparts (II): compounds (I) are yellow substances, whereas (II), with the exception of (IIg), are various shades of deep red, thanks to a "push–pull" conjugation effect. In contrast to (I), the 4-acetylamino-5-oxonaphtho[4,3-b]furans (III), which contain a conjugated N=C–C=O group, exist as raspberry-colored crystals. The assignment of the o-quinone structure of compounds (III) is based on their PMR spectra, in which the low-field region (δ ∿ 8 ppm) contains a signal for only one proton (H^6) [in contrast to (I) and (II)], which is situated in a peri position with respect to the C=O group.

EXPERIMENTAL

PMR spectra of $CDCl_3$ solutions were recorded on a Varian XL-200 spectrometer; IR spectra in $CHCl_3$ solutions were taken on a UR-20 spectrophotometer.

2-N-Allylamino-3-phenylethynyl-1,4-naphthoquinone (IId). A mixture of 650 mg 2-amino-3-phenylethynyl-1,4-naphthoquinone [5] and 670 mg powdered KOH in 24 ml DMFA at 20°C was treated with 675 mg of allyl bromide, stirred 5 min, diluted with 50 ml of ether, and poured into a mixture of 150 ml water and 200 ml ether. The ether solution was washed five times with water and dried over $CaCl_2$. The residue remaining after removal of the ether was dissolved in 30 ml of acetone; 30 ml of octane was added, and the acetone was evaporated *in vacuo*. Yield 510 mg (68.5%) of (IId), mp 150-150.5°C (ether). Found: C 80.48; H 4.94; N 4.38%. $C_{21}H_{15}NO_2$. Calculated: C 80.49; H 4.83; N 4.47%. PMR spectrum (δ, ppm): 4.69 m (CH_2), 5.25-5.35 m ($C\underline{H}_2$=CH), 5.95-6.15 m (CH=CH_2), 6.53 br (NH), 7.3-7.5 m (Ph), 7.62 t and 7.73 t ($H^{6,7}$), 8.04 d and 8.15 d ($H^{5,8}$).

2-N-(2'-Acetoxyethyl)amino-3-phenylethynyl-1,4-naphthoquinone (IIf). A mixture of 0.60 g of (IIe) [5] in 20 ml of Ac_2O was heated at the boiling point 2-3 min, poured into water, and the resulting precipitate was removed by filtration. Chromatography on Al_2O_3 (activity II; 100 cm^3, 40 × 80 mm) with benzene–ether (4:1) gave 0.50 g (73.5%) (IIf), mp 158-158.5°C (Me_2CO). Found: C 73.27; H 5.07; N 3.88%, $C_{22}H_{17}NO_4$. Calculated: C 73.53; H 4.77; N 3.90%. IR spectrum (ν, cm^{-1}): 2200 (C≡C), 1650, 1680, 1750 (C=O), 3360 (NH).

2-N-Acetylamino-3-phenylethynyl-1,4-naphthoquinone (IIg). A mixture of 200 mg 2-amino-3-phenylethynyl-1,4-naphthoquinone [5] and 1 ml of Ac_2O was stirred vigorously and 0.04 ml conc. H_2SO_4 was added; the thickened reaction mixture was diluted with 5 ml of ether, and the resulting precipitate was removed by filtration and washed with 5 ml ether and water. Yield (IIg) 150 mg (65%), mp 186-187°C (dec., EtOH; when the sample was heated rapidly (∿3°/sec), the mp was ∿219-221°C). Found: C 76.17; H 4.06; N 4.40%. $C_{29}H_{13}NO_3$. Calculated: C 76.18; H 4.16; N 4.44%. IR spectrum (ν, cm^{-1}): 2205 (C≡C), 1665, 1720 (C=O), 3375 (NH).

1-Methyl-2-phenylbenz[f]indole-4,9-dione (Ia). A mixture of 300 mg (IIa) and 5 mg powdered KOH in 3 ml of pyridine was boiled for 2 min, until the red color had faded to yellow, cooled, and 100 mg $NaHCO_3$, followed by 10 ml water, was added with stirring. The resulting precipitate was removed by filtration, washed with water, 1% HCl, and finally water again, and then dried. After filtration through a layer of Al_2O_3 (activity II; 50 cm^3, 28 × 80 mm) in benzene the material was dissolved in $CHCl_3$; the chloroform was replaced with octane to give 246 mg (Ia), whose yield and physical constants are recorded in Table 1.

Compounds (IIb-f) were cyclized in an analogous manner, using more dilute solutions [20-50 ml pyridine and 5-27 mg KOH/300 g (II)], and general reaction times of 2-16 min, 40 min for (IId) and 3 h for (IIe).

When the reactions were carried out in refluxing mesitylene, the cyclization times were shortened, to 20 min for (IId) and 30 min for (IIe), and the yields were increased to 52 and 44%, respectively (see Table). Yields of (Ia, b, and f) ranged from 58-74%.

1-Acetyl-2-phenylbenz[f]indole-4,9-dione (Ig). A mixture of 400 mg (IIg) and 10 mg PhC≡CCu in 16 ml DMSO was heated at 140°C 10 min, diluted with $CHCl_3$, washed repeatedly with water, and finally dried over Na_2SO_4. The chloroform solution was concentrated *in vacuo* to ~10 ml, filtered to remove precipitated side products, and chromatographed on silica gel (25 × 120 mm) with $CHCl_3$ to give 100 mg (Ig) (see Table 1). The product (Ig) was recrystallized as described above for (Ia) from $CHCl_3$–EtOH.

The following compounds were obtained in a similar manner in the presence of PhC≡CCu: (Ia), in 52.5% yield, (Ib), in 60% yield, and (Id), in 26.7% yield, from a mixture of pyridine and dioxane (1:2) at 100°C; (If), in 33.4% yield, (Ie), in 21.9% yield, and (Ig), in 20% yield, from pyridine at 115°C.

2-(1'-Hydroxy-1'-methylethyl)-4-N-acetylamino-5-oxonaphtho[4,3-b]furan (IIIh). A solution of 0.40 g (IIh) in 40 ml of toluene was refluxed 7 min (TLC-monitor: Silufol, ether), the solvent was removed, and the residue was triturated with 5 ml ether and filtered; yield (IIIh) 0.30 g (75%), mp 149.5-150.5°C (dec., C_6H_6). Found: C 68.72; H 5.04; N 4.67%. $C_{17}H_{15}NO_4$. Calculated: C 68.68; H 5.09; N 4.71%. IR spectrum (ν, cm^{-1}): 1635, 1680, 1705 (C=O, C=N), 3605 (OH). PMR spectrum (δ, ppm): 1.61 (CH_3COH), 2.28 (CH_3C=O), 3.63 (OH), 6.56 (H^3), 7.2-7.7 m (H^{7-9}), 7.96 d (H^6).

2-Phenyl-4-N-acetylamino-5-oxonaphtho[1,2-b]furan (IIIg) was obtained in an analogous manner (benzene, 80°C, 17 min) in quantitative yield, mp 182-183°C (dec., C_6H_6). Found: C 76.08; H 4.32; N 4.19%. $C_{20}H_{13}NO_3$. Calculated: C 76.18; H 4.16; N 4.44%. IR spectrum (ν, cm^{-1}): 1635, 1685 sh, 1705 (C=O). PMR spectrum (δ, ppm): 2.39 (CH_3), 7.02 (H^3), 7.35-7.85 m (Ph, H^{7-9}), 8.04 d (H^6).

CONCLUSIONS

1. 2-N-Alkyl(aryl)amino-3-acetylenyl-1,4-naphthoquinones undergo cyclization reactions in the presence of KOH or PhC≡CCu to give corresponding 1,2-disubstituted benz[f]indole-4,9-diones.

2. 2-N-Acetylamino-3-acetylenyl-1,4-naphthoquinones are cyclized in neutral solvents at 80-110°C to the corresponding 2-substituted 4-N-acetylamino-5-oxonaphtho[4,3-b]furans.

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