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Acivated Sterically Strained C=N Bond in N-Substituted *p*-Quinone Mono- and Diimines: XII.* Bromination of 4-Acylaminophenols

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Abstract—Exhaustive bromination of 4-acylaminophenols gives the corresponding 2-acylamino-3,5,6-tribromo-1,4-benzoquinones.

Fernando and Calder reported on the chlorination of 4-acetylaminophenol [2]; depending on the conditions, 4-acetylamino-2,3,5,6-tetrachlorophenol and 4-acetylimino-2,3,5,6-tetrachloro-2,5-cyclohexadienone were obtained [2]. We previously showed that the chlorination of 4-acylaminophenols could give rise to the corresponding 4-acylamino-2,3,6-trichlorophenols, 4-acylamino-2,3,5,6-tetrachlorophenols, and 4-acylimino-2,3,5,6-tetrachloro-2,5-cyclohexadienones [3]. 4-Acylimino-2,3,5,6-tetrachloro-2,5-cyclohexadienones attract interest due to the presence in their molecules of an activated sterically strained C=N bond, the bond angle C=N–C being estimated at 134° [4]. We have found no published data on bromination of 4-acylaminophenols, though analogous 4-acylimino-2,3,5,6-tetrabromo-2,5-cyclohexadienones should be characterized by even larger C=N–C bond angle (143°) due to considerable size of bromine atom [4]. We believed that quinone imines with a C=N–X bond angle of about 145° were unstable and that their synthesis was impossible [4]. For example, we did not succeed in obtaining 2,3,5,6-tetrachloro-4-chloroimino-2,5-cyclohexadienone with a presumed C=N–Cl angle of 143° [4].

In the previous study on the bromination of 4-acylaminophenols **I** we found that the main products were 2,6-dibromo- and 2,3,6-tribromo-4-acylaminophenols **II**–**IV** (Scheme 1) [5]. Further studies revealed formation of stable yellow substances as a result of profound bromination. These products were initially identified as 4-acylimino-2,3,5,6-tetrabromo-2,5-cyclohexadienones [5]. Their ^{1}H NMR spectra were consistent with the assumed structure, but the analytical data for bromine were underestimated. However, the high stability of these compounds and the presence in their molecules of C=N bond (i.e., there occurred no 1,2-addition typical of quinone imines with an activated sterically strained C=N bond, primarily in reaction with alcohols [6]) made the above assignment doubtful. The ^{13}C NMR spectra of the products contained 11 downfield signals (in the region δ_C 120–180 ppm), though 4-aroylamino-2,3,5,6-tetrabromo-2,5-cyclohexadienones should display 9 carbon signals.

In order to unambiguously establish the structure of the obtained compounds, we performed X-ray analysis of a single crystal of the bromination product derived from 4-benzoylaminophenol. The results showed that this compound is 2-benzoylamino-3,5,6-tribromo-1,4-benzoquinone (**Vb**) (see figure). Thus the final bromination products of 4-acylaminophenols **I** are the corresponding 1,4-benzoquinones **V** (Scheme 1). Presumably, 2-aroylamino-3,5,6-tribromo-1,4-benzoquinones **V** exists as *o*-quinone tautomers **B** rather than *p*-quinones **A**. In the ^{1}H NMR spectra of **Vb** and **Vc** in $CDCl_3$, we observed no signal from NH or OH proton due to exchange with traces of water in the solvent; therefore, we cannot distinguish between tautomers **A** and **B** on the basis of the ^{1}H NMR data.

Comparison of the X-ray diffraction data for compound **Vb** and other quinone imines, as well as for 2,6-di-*tert*-butyl-4-(4-nitrobenzoylamino)phenol (**VII**), unambiguously indicates *p*-quinoid structure of compound **Vb** (tautomer **A**). The C^2NC^7 angle in molecule **Vb** is 116.0°. The corresponding angle (C=N–C) in

* For communication XI, see [1].

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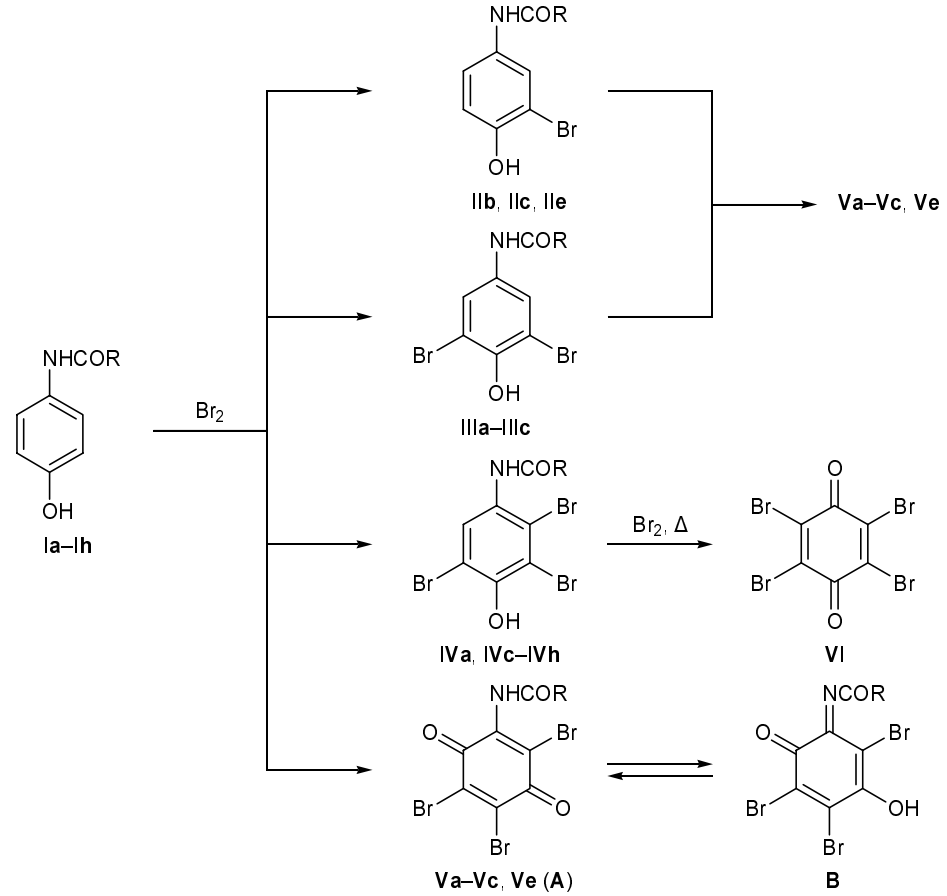
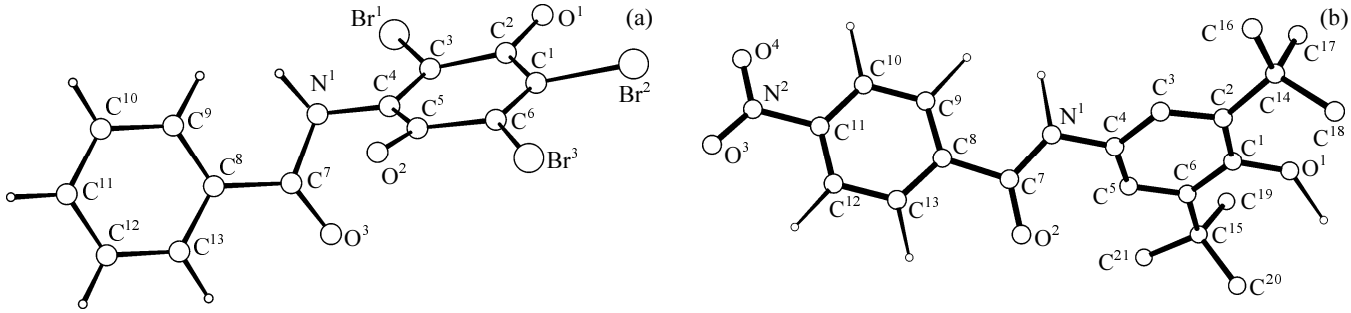
Scheme 1.



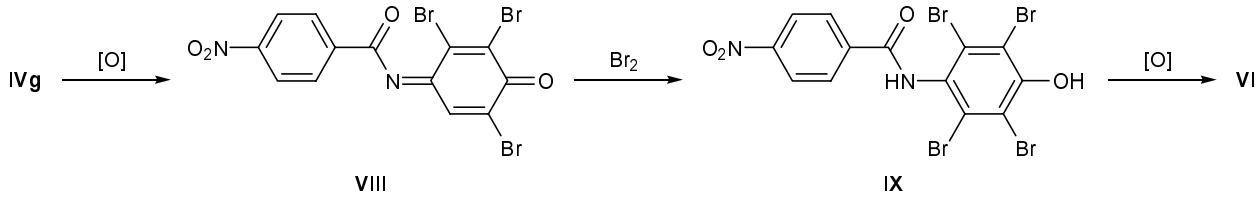
R = Me (**a**), Ph (**b**), 4-MeC_6H_4 (**c**), 3-MeC_6H_4 (**d**), 4-ClC_6H_4 (**e**), 2-ClC_6H_4 (**f**), 4-$O_2NC_6H_4$ (**g**), 4-FC_6H_4 (**h**).

2,6-di-*tert*-butyl-4-(4-chlorobenzoylamino)-2,5-cyclohexadienone is 124.6°, and in 2,6-dimethyl-4-[*N*-(phenylsulfonyl)benzimidoylamino]-2,5-cyclohexadienone, 124.1° [7]. The N–C^2 and N–C^7 bond lengths in molecule **Vb** are 1.36 and 1.39 Å, respectively, i.e., both these bonds are ordinary. The corresponding bond lengths in molecule **VII** are 1.43 and 1.35 Å. The ordinary C^7–N bond in 2,6-di-*tert*-butyl-4-(4-chlorobenzoylamino)-2,5-cyclohexadienone has a length of 1.40 Å, and in 2,6-dimethyl-4-[*N*-(phenylsulfonyl)benzimidoylamino]-2,5-cyclohexadienone, 1.38 Å [7]. The C=N bond in quinone imines is considerably shorter, 1.29 Å in both 2,6-di-*tert*-butyl-4-(4-chlorobenzoylamino)-2,5-cyclohexadienone and 2,6-dimethyl-4-[*N*-(phenylsulfonyl)benzimidoylamino]-2,5-cyclohexadienone [7].



Structure of the molecules of (a) 2-benzoylamino-3,5,6-tribromo-1,4-benzoquinone (**Vb**) and (b) 2,6-di-*tert*-butyl-4-(4-nitrobenzoylamino)phenol (**VII**) according to the X-ray diffraction data.

Scheme 2.



The lengths of the double C=O[1], C=O[2], and C=O[3] bonds in molecule **Vb** are 1.24, 1.21, and 1.21 Å, respectively. The quinone C=O bond in 2,6-di-*tert*-butyl-4-(4-chlorobenzoylamino)-2,5-cyclohexadienone and 2,6-dimethyl-4-[*N*-(phenylsulfonyl)benzimidoylamino]-2,5-cyclohexadienone is 1.22 Å long [7]. The aroyl C=O bond length in **VII** is 1.21 Å, and in 2,6-di-*tert*-butyl-4-(4-chlorobenzoylamino)-2,5-cyclohexadienone, 1.22 Å [7]. The C^1–O^1 bond length in molecule **VII** is 1.37 Å. Thus the X-ray diffraction data strictly correspond to structure **A** of compound **Vb**. Tautomer **A** is also more favorable according to the results of semiempirical quantum-chemical calculations (PM3): the enthalpies of formation of tautomers **A** and **B** are –21.19 and –19.53 kJ/mol, respectively.

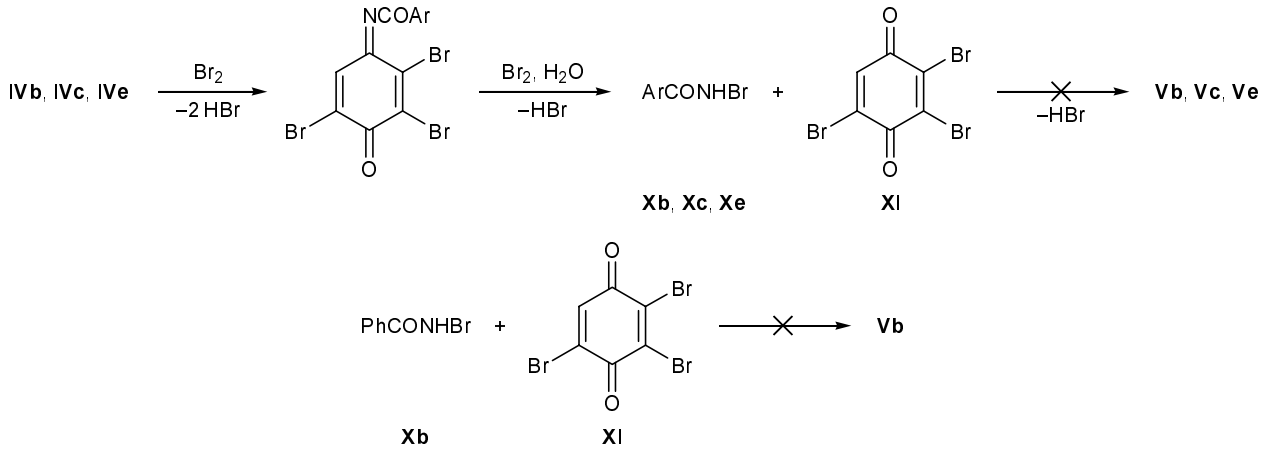
We did not succeed in obtaining 4-acylamino-2,3,5,6-tetrabromophenols by direct bromination of 4-acylaminophenols **I** (Scheme 1). 4-Acylamino-2,3,6-tribromophenols **IV** also failed to undergo bromination. Under more severe conditions (large excess of bromine, elevated temperature), 2,3,5,6-tetrabromo-1,4-benzoquinone (**VI**) was formed. 2,3,5,6-Tetrabromo-4-(4-nitrobenzoylamino)phenol (**IX**) was synthesized from 2,3,6-tribromo-4-(4-nitrobenzoylimino)-2,5-cyclohexadienone (**VIII**) according to Scheme 2. An attempt to oxidize compounds **IX** to 2,3,5,6-tetrabromo-4-(4-nitrobenzoylimino)-2,5-cyclohexadienone was unsuccessful; as a result, tetrabromobenzoquinone **VI** was obtained. These findings support the assumption that 4-acylimino-2,3,5,6-tetrabromo-2,5-cyclohexadienones are unstable due to increased C=N–C angle; therefore, they cannot be isolated.

Compounds **V** might be presumed to be formed from 4-aroylamino-2,3,6-tribromophenols **IV** through intermediate *N*-bromo benzamides **X** (Scheme 3); however, we failed to synthesize benzoquinone **Vb** from 2,3,6-tribromo-1,4-benzoquinone (**XI**) and *N*-bromobenzamide (**Xb**).

By acylation of 4-amino-2,3,6-tribromophenol with benzoyl chloride we obtained 4-benzoylamino-2,3,6-tribromophenol (**IVb**), and the latter was treated with bromine to isolate the corresponding quinone imine **XII**. Compound **XII** was also synthesized by oxidation of aminophenol **IVb** with lead tetraacetate (Scheme 4). Thus 4-aroylamino-2,3,6-tribromophenols **IV** are not intermediate products in the reaction sequence leading to quinones **V**.

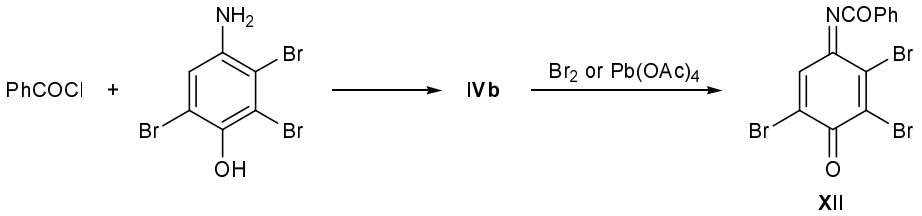
On the other hand, compounds **Va**–**Vc** are formed from intermediate 2,6-dibromo derivatives **IIIa**–**IIIc** (Scheme 1). Therefore, the most probable scheme of transformation of 4-aroylamino-2,6-dibromophenols **IIIa**–**IIIc** into 2-acylamino-3,5,6-tribromo-1,4-benzo-

Scheme 3.

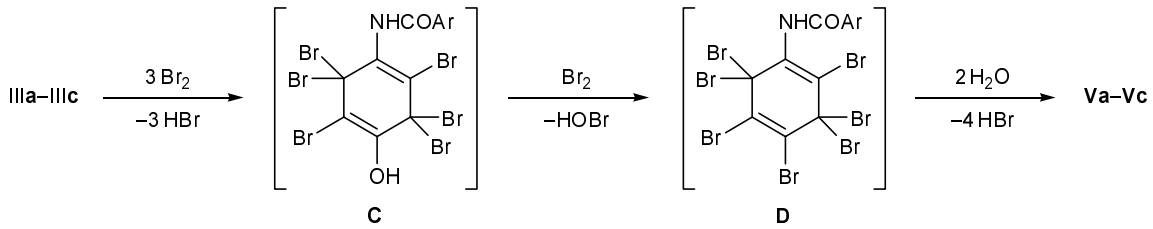


X, Ar = Ph (**b**), 4-MeC_6H_4 (**c**), 4-ClC_6H_4 (**e**).

Scheme 4.



Scheme 5.



quinones **Va**–**Vc** includes intermediate structures **C** and **D**, each containing two bromine atoms at the sp^3-hybridized carbon atoms (Scheme 5); structures **C** and **D** are analogous to those formed in some cases in the halogenation of phenols and quinones [8].

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^{13}C NMR spectra were measured on a Varian VXR-300 instrument operating at 75.4 MHz; the chemical shifts were determined relative to tetramethylsilane, and chloroform-*d* was used as solvent. The reaction mixtures were analyzed by thin-layer chromatography on Silufol UV-254 plates using benzene–hexane (10:1) as eluent; spots were visualized under UV light.

X-Ray analysis of single crystals of compounds **Vb** (0.37×0.43×0.50 mm) and **VII** (0.5×0.5×0.5 mm) was performed at room temperature on an Enraf–Nonius CAD-4 automatic four-circle diffractometer (λMoK_α irradiation, graphite monochromator, scan rate ratio $\omega/2\theta = 1.2$). The unit cell parameters and crystal orientation matrices were determined from 22 reflections with $12° < \theta < 13°$ (**Vb**) and $11° < \theta < 12°$ (**VI**). Total of 2797 reflections were measured for the single crystal of **Vb**, 2494 of which were symmetry-independent (R_{int} = 0.037). Monoclinic crystals; a = 13.258(1), b = 8.922(1), c = 13.695(1) Å; β = 119.02 (1)°; V = 1416.6(3) Å^3; Z = 4, d_{calc} = 2.18 g/cm^3; μ = 84.66 cm^{-1}; $F(000)$ = 876.08; space group $P2_1/n$. For compound **VII**, 3068 reflections were measured, 1609 of which were symmetry-independent (R_{int} = 0.088). Monoclinic crystals; a = 8.605(3), b = 12.872(4), c = 9.541(3) Å; β = 104.23(2)°; V = 1024.4(3) Å^3; Z = 2; d_{calc} = 1.194 g×cm^{-3}; μ = 0.83 cm^{-1}; $F(000)$ = 396; space group P_c.

The structures were solved by the direct method and were refined by the least-squares procedure in full-matrix anisotropic approximation using CRYSTALS software for **Vb** [9] and SHELXS and SHELXS-93 for **VII** [10, 11]. All hydrogen atoms were visualized objectively by difference synthesis of electron density and were included in the refinement procedure with fixed positional and thermal (U_{iso} = 0.08 Å^2) parameters. The absorption by the crystal was taken into account using the azimuthal scanning technique [12]. In the structure refinement of compound **Vb**, Chebyshev's weight scheme [13] was used with the following four parameters: 12.8, –18.0, 11.0, and –4.5; for compound **VII**, the following weight scheme was applied: $\omega = 1/[\sigma^2(F_0^2) + (AP)^2 + BP]$, where $P = (F_0^2 + 2F_c^2)/3$ (the coefficients A and B were calculated using SHELXS-93 software [11] and were 0.106 and 0.07, respectively). The final divergence factors were as follows: **Vb**: R = 0.053, R_w = 0.057, GOF = 1.101; **VII**: R = 0.054, R_w = 0.134, GOF = 1.026. The residual electron densities from the difference Fourier series were: **Vb**: 0.90, –0.62 $\bar{e}$/Å^3; **VII**: 0.16, –0.29 $\bar{e}$/Å^3.

4-Aroylamino-2,6-dibromophenols **IIIb** and **IIIc**, 4-benzoylamino-2,3,6-tribromophenol (**IVb**), and 2-aroylamino-3,5,6-tribromo-1,4-benzoquinones **Vb** and **Vc** were synthesized as described in [5]. 2,6-Di-*tert*-butyl-4-(4-nitrobenzoylamino)phenol (**VII**) was prepared by acylation of 4-amino-2,6-di-*tert*-butylphenol with *p*-nitrobenzoyl chloride in diethyl ether in the presence of triethylamine.

Bromination of 4-aroylamino-2,6-dibromophenols IIIb and IIIc. Bromine, 0.08 mol, was added

dropwise under vigorous stirring to a solution of 0.01 mol of compound **IIIb** and **IIIc** in 10 ml of DMF, maintaining the temperature at 70–80°C. The mixture was stirred for 3 h at that temperature, cooled to 20°C, and diluted with water. An oily material separated and crystallized within 24 h. The products, 2-aroylamino-3,5,6-tribromo-1,4-benzoquinones **Vb** and **Vc** were recrystallized from acetic acid; their properties coincided with those given in [5] for 4-aroylimino-2,3,5,6-tetrabromo-2,5-cyclohexadienones (erroneously identified). ^{13}C NMR spectrum, δ_C, ppm: **Vb**: 125.93 (C^3), 126.93 (C^8), 128.92 (C^{10}), 130.80 (C^9), 134.87 (C^{11}), 137.92 (C^5), 138.48 (C^6), 151.71 (C^2), 162.19 (C^7), 169.55 (C^4), 170.96 (C^1); **Vc**: 21.91 (Me), 124.27 (C^3), 125.84 (C^8), 129.69 (C^{10}), 130.93 (C^9), 137.96 (C^5), 138.50 (C^6), 146.12 (C^{11}), 151.93 (C^2), 162.24 (C^7), 169.66 (C^4), 171.04 (C^1).

Oxidation of 2,3,6-tribromo-4-(4-nitrobenzoylamino)phenol (IVg). Lead tetraacetate, 0.013 mol, was added under vigorous stirring to a solution of 0.01 mol of aminophenol **IVg** in 10 ml of acetic acid. When a solid separated, the mixture was cooled, and 1 ml of ethylene glycol was added. The yellow precipitate of 2,3,6-tribromo-4-(4-nitrobenzoylimino)-2,5-cyclohexadienone (**VIII**) was filtered off, washed with acetic acid, dried in air, and recrystallized from acetic acid. Yield 71%, mp 163–165°C. Found, %: Br 48.29; 48.74. $C_{13}H_5Br_3N_2O_4$. Calculated, %: Br 48.63.

2,3,5,6-Tetrabromo-4-(4-nitrobenzoylamino)-phenol (IX). A solution of 0.001 mol of compound **VIII** in 3 ml of a 1:5 DMF–AcOH mixture was heated to 70°C, and a solution of 0.02 mol of bromine in 5 ml of the same solvent was added under stirring. The mixture was stirred for several hours at 70°C and cooled to room temperature. The precipitate was filtered off and recrystallized from acetic acid. Yield 76%, yellowish crystals, mp 304–306°C. Found, %: Br 55.07, 55.49. $C_{13}H_6Br_4N_2O_4$. Calculated, %: Br 55.70.

Oxidation of 2,3,5,6-tetrabromo-4-(4-nitrobenzoylamino)phenol (IX). No oxidation occurred on treatment of aminophenol **IX** with an equimolar amount of lead tetraacetate in acetic acid at room temperature under stirring. Only initial aminophenol **IX** was recovered from the reaction mixture. The reaction with excess lead tetraacetate at elevated temperature resulted in decomposition of aminophenol **IX** with formation of tetrabromobenzoquinone **VI**.

Reaction of *N*-bromobenzamide with 2,3,5-tribromo-1,4-benzoquinone (XI). *a*. Sodium acetate, 0.01 mol, was added to a solution of 0.01 mol of compound **XI** in 5 ml of a 1:5 DMF–AcOH mixture, and 0.01 mol of *N*-bromobenzamide (**Xb**) was then added in portions under stirring. The mixture was heated for 1 h at room temperature. The same procedure was repeated at 80–90°C. By diluting the reaction mixture with water, in both cases we isolated mixtures of products containing initial quinone **XI**. No 2-benzoylamino-3,5,6-tribromo-1,4-benzoquinone (**Vb**) was detected.

b. The reaction was carried out in a similar way in diethyl ether in the presence of triethylamine. The results were the same as in *a*.

***N*-Benzoylamino-2,3,6-tribromophenol (IVb).** Benzoyl chloride, 0.01 mol, was added in small portions over a period of 30 min under stirring and cooling to a solution of 0.01 mol of 4-amino-2,3,6-tribromophenol and 0.011 mol of anhydrous sodium acetate in 10 ml of a 1:3 DMF–AcOH mixture. A part of the product separated from the mixture, and 50 ml of water was added to ensure more complete isolation. The precipitate was filtered off, washed with water, dried in air, and recrystallized from acetic acid. Yield 85%, light gray crystals, mp 187–188°C. Found, %: Br 53.17, 53.41. $C_{13}H_8Br_3NO_2$. Calculated, %: Br 53.28.

4-Benzoylimino-2,3,6-tribromo-2,5-cyclohexadienone (XII). *a*. A solution of 0.01 mol of aminophenol **IVb** in 3 ml of a 1:5 DMF–AcOH mixture was heated to 70°C, and a solution of 0.02 mol of bromine in 5 ml of the same solvent was added dropwise under stirring. After 24 h, the mixture was diluted with water, and an oily material separated and crystallized within 1 h. The product was filtered off and recrystallized from glacial acetic acid. Yield 61%, yellow crystals, mp 169–171°C. Found, %: Br 53.02, 53.46. $C_{13}H_6Br_3NO_2$. Calculated, %: Br 53.52. In the reaction of **IVb** with 0.08 mol of bromine (or more), tetrabromobenzoquinone **VI** was isolated from the reaction mixture.

b. Compound **IVb** was oxidized as described above for the oxidation of **IVg**. Yield 53%, yellow crystals. The product was identical to that obtained as described above in *a*.

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