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Halogenation of N-Substituted *para*-Quinone Monoimine and *para*-Quinone Monooxime Esters: VI.* Regular Trends in Chlorination and Bromination of *N*-Arylsulfonyl-1,4-benzoquinone Monoimines Alkyl-Substituted in the Quinoid Ring

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Abstract—Reactions of halogens with *N*-arylsulfonyl-1,4-benzoquinone monoimines occur with the formation of a halogenonium ion that either transforms into a carbocation where the first halogen atom adds to the carbon in the *ortho*-position relative to the carbonyl carbon, or the halogenonium ion adds directly the second halogen atom.

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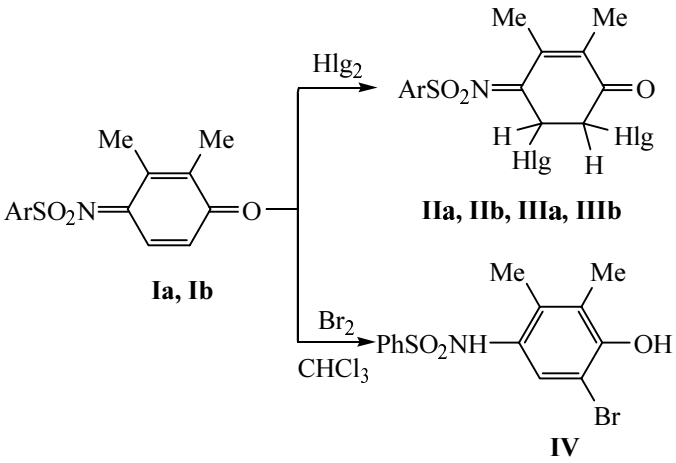
This research continues the investigation of the halogenation processes of *N*-arylsulfonyl-1,4-benzoquinone monoimines alkyl-substituted in the quinoid ring. In the preceding publications of this series [1–3] the features of the halogenation of various *N*-aroyl(arylsulfonyl)oximino-2,5-cyclohexadien-1-ones and *N*-arylsulfonyl-1,4-benzoquinone monoimines were considered, the main reaction paths and regularities were revealed.

As the last object for the study in this series we selected *N*-arylsulfonyl-2,3-dimethyl-1,4-benzoquinone monoimines **Ia** and **Ib** in order to establish finally the halogenation mechanism of *N*-arylsulfonyl-1,4-benzoquinone monoimines. Similarly to *N*-arylsulfonyl-3-methyl-1,4-benzoquinone monoimines [3] quinone imines **Ia** and **Ib** exist in solution in the form of a single isomer but to the *anti*-bond C=C of the quinoid ring in these compounds one more substituent, Me group, is attached, even more increasing the steric hindrance to the halogen addition across this bond. Therefore the halogen addition should occur strictly regiospecifically at the C=C bond of the quinoid ring lacking substituents.

The halogenation of quinone imines **Ia** and **Ib** was performed in various solvents ($CHCl_3$, CH_3CO_2H, CH_3CO_2H–DMF mixture, 5:1), and at different ratios quinone imine **I**–halogen. Depending on the experimental conditions the halogenation of quinone imines **Ia** and **Ib** gave rise mainly to stable 4-arylsulfonylimino-5,6-dihalo-2,3-dimethyl-2-cyclohexen-1-ones **IIa, IIb, IIIa**, and **IIIb**, and only at the bromination in $CHCl_3$ *N*-phenylsulfonyl-4-amino-6-bromo-2,3-dimethylphenol (**IV**) was isolated (Scheme 1).

The chlorination of 4-arylsulfonylamido-2,3-dimethylphenols **Va** and **Vb** depending on the experimental

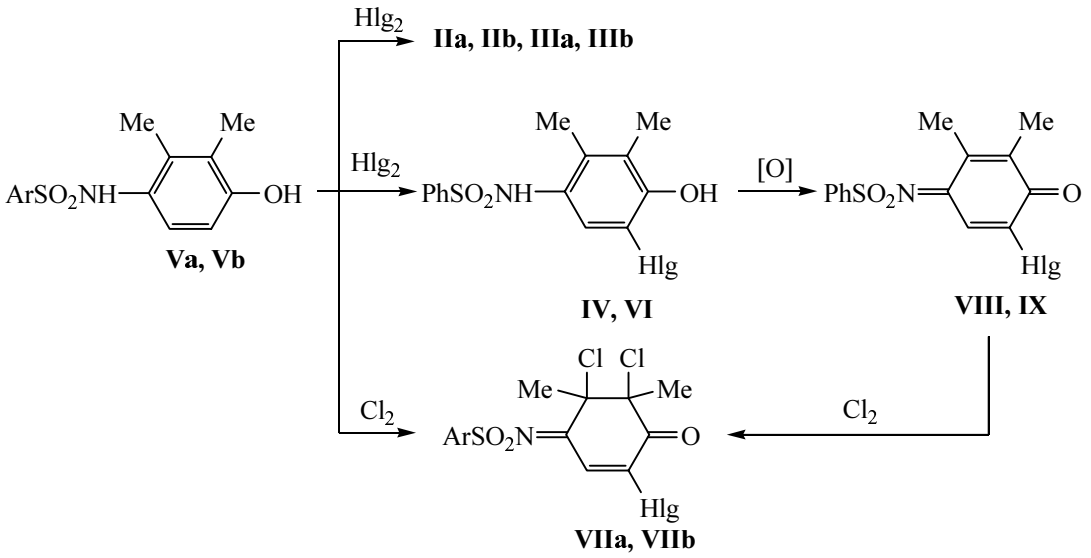
Scheme 1.



Ar = Ph (**a**), 4-MeC_6H_4 (**b**); Hlg = Cl (**II**), Br (**III**).

* For communication V, see [1].

Scheme 2.



Ar = Ph (**a**), 4-MeC_6H_4 (**b**); Hlg = Cl (**VI, VIII**), Br (**IV, IX**).

conditions afforded 4-arylsulfonylimino-2,3-dimethyl-5,6-dichloro-2-cyclohexen-1-ones **IIa** and **IIb**, 4-phenylsulfonylamido-2,3-dimethyl-6-chlorophenol (**VI**), and 4-arylsulfonylimino-5,6-dimethyl-2,5,6-trichloro-2-cyclohexen-1-ones **VIIa** and **VIIb** (Scheme 2).

Aminophenol **VI** was obtained only in chloroform at the ratio substrate **Va**–chlorine 1:1. In this case the electrophilic substitution is likely to occur (the chlorine enters into the *meta*-position with respect to the most electron-withdrawing group). Then under the action of the second chlorine molecule aminophenol **VI** is oxidized to give quinone imine **VIII**, and the next chlorine molecule adds to form a compound of cyclohexene structure **VIIa**. The latter stage was proved by an independent synthesis, the chlorination of quinone imine **VIII**. Compound **VIII** was obtained by oxidation of aminophenol **VI** with lead tetraacetate. In the same way was synthesized quinone imine **IX**.

In CH_3CO_2H and the mixture DMF–CH_3CO_2H, 1:5, the aminophenols **Va** and **Vb** are oxidized with chlorine to the corresponding quinone imines, add a single chlorine molecule forming compounds of cyclohexene structure **IIa** and **IIb** (which were isolated at the ratios initial susbtance–chlorine 1:1, 1:2), eliminate an HCl molecule, and add the second molecule of Cl_2 furnishing compounds **VIIa** and **VIIb**. This scheme is supported by the fact, that the reduced form **VI** is not isolated in the reactions carried out in CH_3CO_2H and the mixture DMF–CH_3CO_2H, 1:5.

The bromination of aminophenols **Va** and **Vb** in $CHCl_3$ or CH_3CO_2H yielded only aminophenol **IV**, in the mixture DMF–CH_3CO_2H, 1:5, at the ratio initial compound–bromine 1:1 formed aminophenol **VI**; and at the ratio 1:5 compounds of cyclohexene structure **IIIa** and **IIIb** were obtained. The structure of aminophenols **IV** and **VI** was confirmed by the ^{1}H NMR spectra recorded after oxidation of the aminophenols to the corresponding quinone imines **VIII** and **IX** for the ^{1}H NMR spectra of the latter were more informative. The signal from the H^5 atom of quinone imines **VIII** and **IX** is observed in the spectra as a singlet in a downfield region characteristic of hydrogen atoms in the *ortho*-position with respect to the imine carbon.

The structure of aminophenols **IV** and **VI** was confirmed by their independent synthesis by hydrohalogenation of quinone imines **I**. The compounds obtained were identical to aminophenols **IV** and **VI** prepared by the halogenation.

In order to prove the last stages of the chlorination and to obtain products with a higher extent of the bromination we performed the halogenation of aminophenols **IV** and **VI**, and quinone imines **VIII** and **IX** (Scheme 3). We succeeded to obtain by bromination of aminophenol **IV** a compound of cyclohexene structure **X** which we failed to isolated at the bromination of aminophenol **Va**.

The halogenation of quinone imines **VIII** and **IX** provided mixtures of compounds **VIIa, XI** and **X, XII** respectively. Thus the halogen molecule added both at

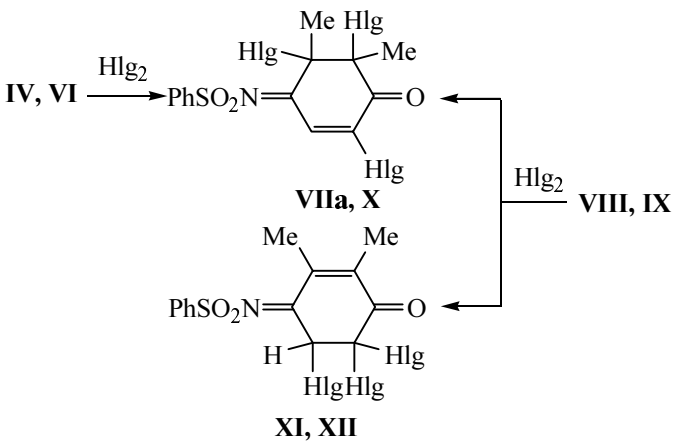
the C=C linked to a halogen atom and to the C=C bond with two methyl substituents notwithstanding the steric hindrances (Scheme 3).

Calculations by PM3 method show that in quinone imine **Ia** the bond C^5=C^6 is less polarized and therefore more active (see the table), and at the same time as in the case of *N*-arylsulfonyl-3-methyl-1,4-benzoquinone monoimines [3] it is more sterically accessible. Hence the steric and electronic factors operate in the same direction, and therefore the halogen addition products obtained from quinone imines **I** resulted from the reaction only at the C^5=C^6 bond. In quinone imine **VIII** the difference in polarization of the C^2=C^3 and C^5=C^6 bonds is less pronounced (see the table), and besides a substituent, chlorine atom, is attached to the C^5=C^6 bond. Accordingly the chlorination of quinone imine **VIII** gave rise to products of chlorine addition to either of the C=C bonds of the quinoid ring, compounds **VII** and **XI**.

The composition and structure of compounds synthesized were proved by elemental analysis, IR, ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectra were registered only for compounds of the quinoid and cyclohexene structure since they were more informative. To confirm the structures of compounds **IIa** and **VIIa** we recorded their ^{13}C NMR spectra.

Thus based on experiments reported here and in [1–3] the following regular trends can be formulated for the halogens reactions with *N*-arylsulfonyl-1,4-benzoquinone monoimines. *para*-Benzoquinone monoimines existing as a single isomer due to steric hindrance to the nitrogen inversion add a halogen molecule predominantly to the *syn*-bond C=C of the quinoid ring; introduction to this bond of a bulky substituent (*i*-Pr group) does not block the reaction across the bond. Nonsymmetrically substituted *p*-benzoquinone monoimines where inversion of the nitrogen occurs add the halogen atm regiospecifically exclusively to the less sterically hindered C=C bond of the quinoid ring. Introduction of substituents of different character (donors or acceptors) into the quinoid ring of the *p*-benzoquinone monoimines where the nitrogen atom undergoes inversion results in the halogen addition to the bond linked to a donor substituent. The

Scheme 3.



Hlg = Cl (**VII, XI**), Br (**X, XII**).

stability of the cyclohexene structures arising from the halogen addition to the C=C bond of the quinoid ring depends on the configurational stability of the nitrogen atom: the configurationally rigid compounds are stable, the configurationally labile, unstable. A firm stage sequence of the halogen addition to *p*-benzoquinone monoimines was established. The cyclohexene structures, products of a single halogen molecule addition to the C=C bond of the quinoid ring, were isolated for the first time. Depending on the nature of the solvent these structures may undergo either a prototropic rearrangement into an aminophenol, or they suffer a regioselective dehydrohalogenation affording two quinone imines. Aminophenols obtained as a result of the prototropic rearrangements are oxidized with a halogen molecule followed by a halogen or a hydrogen halide molecule addition, and the quinone imines either add a halogen molecule with subsequent dehydrohalogenation etc., or add a hydrogen halide molecule and further are oxidized by a halogen molecule etc. The reaction of *N*-arylsulfonyl-4-aminophenols with halogens occurs either as an electrophilic substitution or the initial aminophenol is oxidized into quinone imine. Further transformations are similar to those described above.

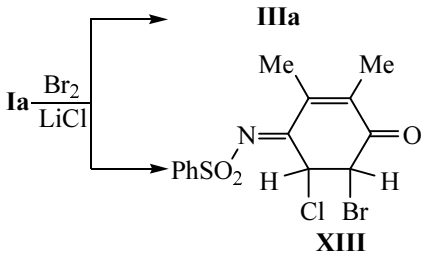
To elucidate the halogenation mechanism of N-arylsulfonyl-1,4-benzoquinone monoimines we carried out the bromination of quinone imine **Ia** in the presence of LiCl.

Atomic charges (q, e.u.) on C^2, C^3, C^5, and C^6 of quinoid ring in quinone imines **Ia** and **VIII** calculated by PM3 method

Compd. no.	qC^2	qC^3	Δq_1[a]	qC^5	qC^6	Δq_2[b]	Δq[c]
Ia	–0.142	–0.059	0.083	–0.127	–0.137	0.01	0.073
VIII	–0.0149	–0.054	0.096	–0.133	–0.193	0.060	0.036

[a] $\Delta q_1 = |qC^2 - qC^3|$; [b] $\Delta q_2 = |qC^5 - qC^6|$; [c] $\Delta q = \Delta q_1 - \Delta q_2$.

Scheme 4.

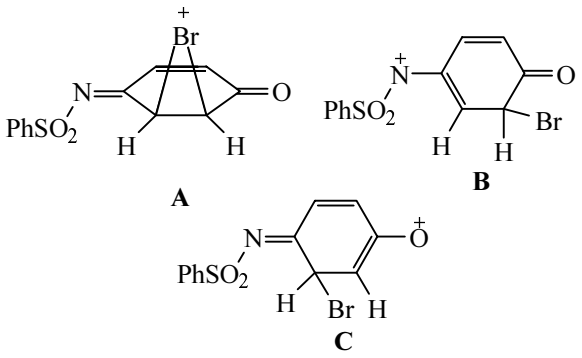


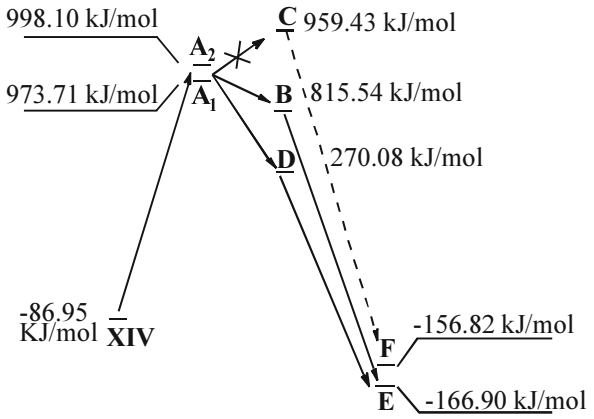
The resulting product was a mixture of isomers **IIIa** and **XIII** (Scheme 4).

The structure of compounds obtained was established from the ^{1}H NMR spectra considering the chemical shifts of atoms H^5 and H^6 in 6-bromo-2,3-dimethyl-4-phenylsulfonylimino-5-chloro-2-cyclohexen-1-one (**XIII**) as compared to those in the spectra of 5,6-dibromo-2,3-dimethyl-4-phenylsulfonylimino-2-cyclohexen-1-one (**IIIa**) and 2,3-dimethyl-4-phenyl-sulfonylimino-5,6-dichloro-2-cyclohexen-1-one (**IIa**). The ratio of compounds **IIIa** and **XIII** in the mixture obtained was in the range 45:55.

Thus at the bromination of quinone imine **Ia** in the presence of Cl^- ions the main reaction product is the cyclohexene structure containing a chlorine atom at the C^5 (*ortho*-position relative to the imine carbon atom) and a bromine atom at C^6 (*ortho*-position with respect to the carbonyl carbon). In bromination of *p*-benzoquinone monooximes esters in the presence of LiCl a cyclohexene structure was obtained with a bromine atom at C^5 (*ortho*-position with respect to oximine carbom atom) and a chlorine atom attached to C^6 (*ortho*-position with respect to the carbonyl carbon) [2].

According to the classical theory of a bromine molecule addition to a C=C bond a π-complex forms in the first stage transforming into a bromonium ion **A**. Then depending on the reaction conditions this ion either directly reacts with a bromide anion or initially converts into cation **B** or **C** that in its turn adds the bromide anion.





Energy diagram of the bromination process of *N*-phenylsulfonyl-1,4-benzoquinone monoimine (**XIV**) in the presence of Cl^- ions.

We carried out by the PM3 procedure the geometry optimization for the above ions of *N*-phenylsulfonyl-1,4-benzoquinone monoimine (**XIV**). Bromonium ion $\mathbf{A_1}$ with a bromine atom attached to the *syn*-bond C=C of the quinoid ring has a lower enthalpy of formation than bromonium ion $\mathbf{A_2}$ with a bromine atom added to the *anti*-bond C=C with respect to the substituent at the nitrogen; thus bromonium ion $\mathbf{A_1}$ is more energetically feasible (see the figure). This result is well consistent with the experiment: The halogen addition occurs mainly at the the *syn*-bond C=C of the quinoid ring.

The optimization of bromonium ion **A** finally leads to cation **B**. The comparison of enthalpy of formation for cations **A**–**C** demonstrated that from the energy viewpoint carbocation **B** is the most favorable (see the figure), and its structure corresponds to that of the final reaction product.

Therefore the experimental data and calculations suggest, that the bromination of benzoquinone monoimines presumable proceeds via bromonium ion **A** subsequently transforming into cation **B** that has the smallest enthalpy of formation among the ions considered, or exclusively through bromonium ion **A** not involving other cations, namely, along the most energetically favorable pathway (see the figure). The intermediate structure **D** (Cl^- ion attached to the bromonium ion) posseses the smallest enthalpy of formation among the species considered. The optimization of intermediate structure **D** (*cis*-configuration) gives finally compound **E**.

The least possible route is the bromination through intermediate cation **C** for its enthalpy of formation is the largest, and compound **F** that should have formed in this case as a result of bromination was not isolated.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from KBr pellets. ^1H and ^{13}C were registered on a spectrometer Varian VXR-300 (^1H 300, ^{13}C 75.4 MHz) in $CDCl_3$ relative to TMS.

The reaction mixtures were analyzed by TLC on Silufol UV-254 plates (eluent benzene–ethyl acetate, 10:1, development under UV irradiation).

Quinone imines Ia, Ib and aminophenols Va, Vb were synthesized by procedures from [4]. Recrystallization from CH_3CO_2H. Yield of compound **Ia** 87%, mp 97–99°C. Found, %: N 4.95, 5.02. $C_{14}H_{13}NO_3S$. Calculated, %: N 5.09. Yield of compound **Ib** 84%, mp 86–88°C. Found, %: N 4.82, 4.91. $C_{15}H_{15}NO_3S$. Calculated, %: N 4.84. Yield of compound **Va** 92%, mp 206–207°C. Found, %: N 4.97, 5.07. $C_{14}H_{15}NO_3S$. Calculated, %: N 5.05. Yield of compound **Vb** 88%, mp 212–214°C. Found, %: N 4.75, 4.87. $C_{15}H_{17}NO_3S$. Calculated, %: N 4.81. ^1H NMR spectra, δ, ppm: **Ia**: 2.06 br.s (3H, Me^3), 2.05 br.s (3H, Me^2), 6.64 d (1H, H^6), 8.14 d [1H, H^5, $J(H^5, H^6)$ 10.2 Hz], 7.56–8.04 m (5H, Ph); **Ib**: 2.04 br.s (3H, Me^2), 2.05 br.s (3H, Me^3), 6.62 d (1H, H^6), 8.15 d [1H, H^5, $J(H^5, H^6)$ 10.5 Hz], 2.47 s (3H, Me β Ts), 7.36–7.92 d.d (4H, Ts).

Chlorination of quinone imines Ia, Ib, VIII, and aminophenols Va, Vb, VI. Through a solution of 2 mmol of compound **Ia, Ib, Va, Vb, VI,** or **VIII** in 3 ml of $CHCl_3$, CH_3CO_2H, DMF, or a mixture DMF–CH_3CO_2H, 1:5, was passed a stream of dry chlorine at a rate 15–20 ml/min at 25–30°C. The ratio initial substance–chlorine was controlled by the weight gain, and it was varied in the range 1:1–1:3. In several hours the reaction products were filtered off. All compounds obtained were recrystallized from acetic acid.

2,3-Dimethyl-4-phenylsulfonylimino-5,6-dichloro-2-cyclohexen-1-one (IIa). Yield 85%, mp 156–157°C. ^1H NMR spectrum, δ, ppm: 2.07 br.s (3H, Me^2), 2.10 br.s (3H, Me^3), 4.58 d (1H, H^6), 6.32 d [1H, H^5, $J(H^5,H^6)$ 3.3 Hz], 7.56–8.06 m (5H, Ph). ^{13}C NMR spectrum, δ, ppm: 13.71 (Me^3), 15.75 (Me^2), 50.79 (C^5), 55.14 (C^6), 141.54 (C^2), 144.05 (C^3), 168.41 (C^4), 187.11 (C^1). Found, %: Cl 20.40, 20.55. $C_{14}H_{13}Cl_2NO_3S$. Calculated, %: Cl 20.48.

2,3-Dimethyl-4-tosylimino-5,6-dichloro-2-cyclohexen-1-one (IIb). Yield 80%, mp 107–108°C. ^1H NMR spectrum, δ, ppm: 2.06 br.s (3H, Me^2), 2.09 br.s (3H, Me^3), 4.57 d (1H, H^6), 6.34 d [1H, H^5, $J(H^5$, H^6) 3.3 Hz], 7.37–7.94 d.d (4H β Ts), 2.47 s (3H, Me, Ts). Found, %: Cl 19.28, 19.36. $C_{15}H_{15}Cl_2NO_3S$. Calculated, %: Cl 19.68.

2,3-Dimethyl-4-phenylsulfonylamido-6-chlorophenol (VI). Yield 68%, mp 198–199°C. Found, %: Cl 11.39, 11.43. $C_{14}H_{14}ClNO_3S$. Calculated, %: Cl 11.37.

5,6-Dimethyl-4-phenylsulfonylimino-2,5,6-trichloro-2-cyclohexen-1-one (VIIa). Yield 75%, mp 117–118°C. ^1H NMR spectrum, δ, ppm: 1.88 s (3H, Me^6), 1.98 s (3H, Me^5), 8.34 s (1H, H^3), 7.57–8.03 m (5H, Ph). ^{13}C NMR spectrum, δ, ppm: 19.55 (Me^3), 20.94 (Me^2), 70.44 (C^3), 72.93 (C^2), 128.74 (C^5), 141.77 (C^6), 167.24 (C^4), 181.66 (C^1). Found, %: Cl 28.10, 28.15. $C_{14}H_{12}Cl_3NO_3S$. Calculated, %: Cl 27.94.

5,6-Dimethyl-4-tosylimino-2,5,6-trichloro-2-cyclohexen-1-one (VIIb). Yield 82%, mp 132–133°C. ^1H NMR spectrum, δ, ppm: 1.87 s (3H, Me^6), 1.97 s (3H, Me^5), 8.35 s (1H, H^3), 7.37–7.94 d.d (4H, Ts), 2.47 s (3H, Me, Ts). Found, %: Cl 27.02, 27.10. $C_{15}H_{14}Cl_3NO_3S$. Calculated, %: Cl 26.95.

2,3-Dimethyl-*N*-phenylsulfonyl-6-chloro-1,4-benzoquinone monoimine (VIII). Yield 68%, mp 127–128°C. ^1H NMR spectrum, δ, ppm: 2.05 q (3H, Me^2), 2.12 q (3H, Me^3), 8.37 s (1H, H^5), 7.57–8.04 m (5H, Ph). Found, %: Cl 11.40, 11.45. $C_{14}H_{12}ClNO_3S$. Calculated, %: Cl 11.44.

2,3-Dimethyl-4-phenylsulfonylimino-5,6,6-trichloro-2-cyclohexen-1-one (XI). ^1H NMR spectrum, δ, ppm: 2.07 d (3H, Me^2), 2.17 d (3H, Me^3), 6.61 s (1H, H^5), 7.57–8.06 m (5H in Ph).

Bromination of quinone imines Ia, Ib, IX, and aminophenol IV, Va, Vb. To a solution of 2 mmol of compound **Ia, Ib, IV, Va, Vb,** or **IX** in 3 ml of $CHCl_3$, CH_3CO_2H, DMF, DMF–CH_3CO_2H, 1:5, was added dropwise at stirring a solution of bromine in the appropriate solvent to the desired ratio initial compound–bromine (1:1, 1:3, 1:5, 1:8). The reaction products obtained in several hours were filtered off, washed with acetic acid, and recrystallized from acetic acid.

5,6-Dibromo-2,3-dimethyl-4-phenylsulfonylimino-2-cyclohexen-1-one (IIIa). Yield 75%, mp 138–139°C. ^1H NMR spectrum, δ, ppm: 2.07 br.s (3H, Me^2), 2.11 br.s (3H, Me^3), 4.76 d (1H, H^6), 6.43 d [1H, H^5, $J(H^5$, H^6) 3.3 Hz], 7.56–8.06 m (5H, Ph). Found, %: Br 36.83, 36.94. $C_{14}H_{13}Br_2NO_3S$. Calculated, %: Br 36.73.

5,6-Dibromo-2,3-dimethyl-4-tosylsulfonylimino-2-cyclohexen-1-one (IIIb). Yield 81%, mp 127–128°C.

^{1}H NMR spectrum, δ, ppm: 2.06 br.s (3H,Me^2), 2.10 br.s (3H, Me^3), 4.76 d (1H, H^6), 6.45 d [1H, H^5, J(H^5, H^6) 3.6 Hz], 7.36–7.95 d.d (4H, Ts), 2.47 s (3H, Me, Ts). Found, %: Br 35.48, 35.55. $C_{15}H_{15}Br_2NO_3S$. Calculated, %: Br 35.58.

6-Bromo-2,3-dimethyl-4-phenylsulfonylamidophenol (IV). Yield 90%, mp 200–201°C. Found, %: Br 22.45, 22.54. $C_{14}H_{14}BrNO_3S$. Calculated, %: Br 22.43.

6-Bromo-2,3-dimethyl-*N*-phenylsulfonyl-1,4-benzoquinone monoimine (IX). Yield 67%, mp 127–128°C.

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