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Halogenation of N-Substituted *p*-Quinone Imines and *p*-Quinone Oxime Esters: III.* Regioselectivity in the Halogenation of *N*-Aroyl(arylsulfonyl)oxyimino-2,5-cyclohexadienones

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Abstract—Halogenation of 4-aroyl(arylsulfonyl)oxyimino-2,5-cyclohexadienones is not accompanied by change of the configuration at the nitrogen atom. *p*-Benzoquinone oxime ethers and esters take up halogens in a regioselective fashion at the *syn*-C=C bond of the quinoid ring. The main factor responsible for regioselective addition of halogens is configuration at the nitrogen atom, which determines the stability of intermediate halogenonium ion.

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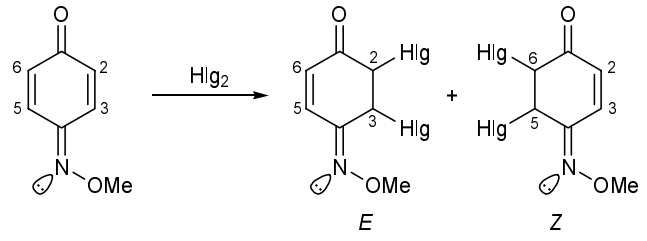
Analysis of the results of our preceding studies on the chlorination and bromination of *p*-benzoquinone oxime esters [1–7] showed that the main problem to be solved is nonequivalence of the double C=C bonds in the quinoid ring [6]. Baldwin and Norris [8] studied halogenation of *p*-benzoquinone *O*-methyloximes using ^{1}H NMR spectroscopy and found that halogen atoms add at both C=C bonds of the quinoid ring to give mixtures of two isomeric products, the *E* isomer prevailing (Scheme 1). The major isomer is formed via halogen addition at the C=C bond located *cis* with respect to the MeO group (C^2=C^3 in Scheme 1). Thus the authors demonstrated higher reactivity of the quinoid C=C bond in the *cis* position with respect to the substituent on the nitrogen atom. In the ^{1}H NMR spectrum of *p*-benzoquinone *O*-methyloxime, the coupling constant for protons in positions *2* and *3* is larger than that for 5-H and 6-H ($J_{2,3} > J_{5,6}$). According to [8], this is the result of stereoelectronic effects. The interaction $n(N) \rightarrow \sigma^*(C–C)$ is characterized by a small antibonding contribution, which leads to extension of the antiperiplanar C^3–C^4 bond and hence weakens orbital overlap between C^3 and C^4. The degree of conjugation along the N=C^4–C^5=C^6–C^1=O bond sequence increases, thus facilitating addition at the C^2=C^3 bond.

Scheme 1.



Perrin and Engler [9] disproved the above assumption on the basis of the results of PM3 semiempirical calculations. According to [9], the C–C bond in the *anti* position with respect to the lone electron pair (LEP) on the nitrogen atom is shorter by 3–4 mÅ than the *syn*-C–C bond. The assumption involving extension of the antiperiplanar C–C bond was additionally and finally refuted by our previous publication [6], where X-ray diffraction data for 4-benzoyloxyimino-2,6-dimethyl-2,5-cyclohexadienone were given. We found that the *anti*-C–C bond has almost the same length as that located in the *syn* position with respect to the nitrogen: C^4–C^5 1.450, C^3–C^4 1.449 Å.

Comparison of the results obtained by halogenation of quinone oximes and quinone methides showed that lone electron pair on the nitrogen cannot induce nonequivalence of the quinoid double C=C bonds since quinone methides lack nitrogen atom at all [9]. It was presumed [9] that the reactivity of the *syn*-C=C bond is

* For communication II, see [1].

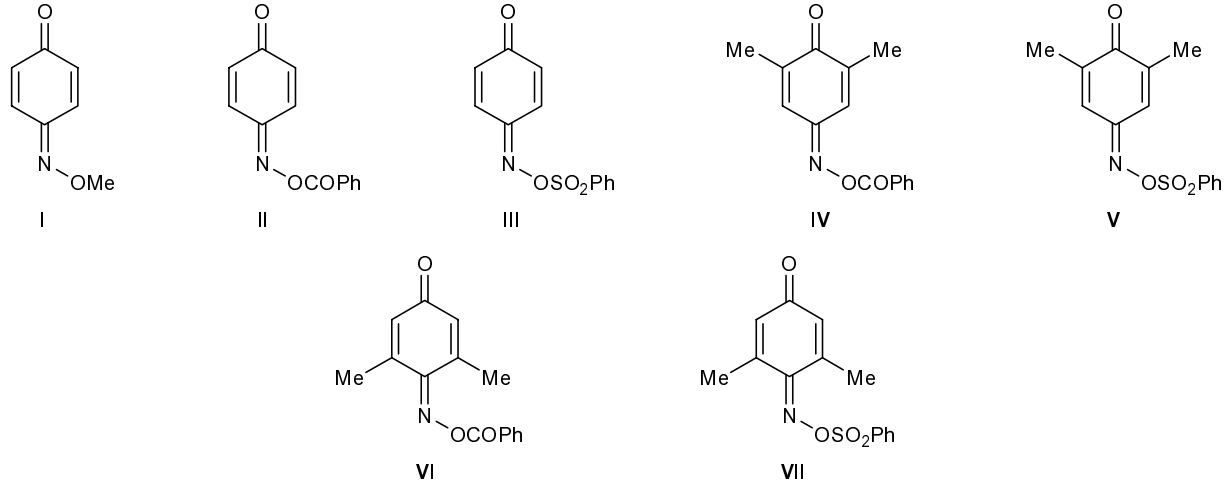
determined by steric factor. According to MMX calculations, the hydrogen atom on C^3 in *p*-benzoquinone *O*-methyloxime appears spatially close to the oxygen atom of the hydroxyimino group: the distance between these atoms is shorter than the sum of their van der Waals radii. Addition of a halogen atom to carbon atom at the *syn*-C=C bond leads to $sp^2 \rightarrow sp^3$ rehybridization of that carbon atom, and the hydrogen atom attached thereto is forced out from the quinoid ring plane, i.e., the *syn*-addition becomes more favorable. If this assumption were valid, the fraction of the isomer formed by halogen addition at the *syn*-C=C bond of 3,5-dimethyl-*p*-benzoquinone oxime ethers (esters) would be much greater than in the halogenation of compounds having no substituents in the quinoid ring, for in the former case hydrogen atom in the *ortho* position with respect to the oxime group is replaced by a bulkier methyl group. However, the isomer ratio in the halogenation of 4-aroyl(arylsulfonyl)oxyimino-2,6(3,5)-dimethyl-2,5-cyclohexadienones [6] is the same as in the halogenation of unsubstituted *p*-benzoquinone oxime esters (90:10) [3].

We can conclude that the problem concerning nonequivalence of double C=C bonds in the quinoid ring in the halogenation of *p*-quinone oxime esters (ethers) remains so far unresolved; i.e., factors determining this nonequivalence are not clear.

In the preceding study [1], analysis of a lot of experimental data led us to conclude that the direction of halogen addition to *p*-benzoquinone oxime esters is strongly affected by electron density distribution over the quinoid ring (together with other factors). In order to elucidate this effect we used as model structures symmetrically substituted *p*-benzoquinone oxime esters **I**–**VII**. Insofar as the substituents at different C=C bonds in the quinoid ring are similar, influence of steric factor on the reaction direction may be neglected. The geometric parameters of molecules **I**–**VII** were optimized by the PM3 semiempirical methods. As initial parameters we used those obtained by X-ray analysis [2, 6]. X-Ray diffraction study of a single crystal of 3-methyl-4-phenylsulfonyloxyimino-2,5-cyclohexadienone was performed in the present work (Fig. 1), and the results were used in the geometry optimization of arylsulfonyloxyimino derivatives.

First of all, we were interested in charges on the C^2, C^3, C^5, and C^6 atoms, taking into account that halogens add just at the C^2=C^3 and C^5=C^6 bonds. Nonequivalence of these bonds was characterized by differences in the charges between C^2 and C^3 and between C^5 and C^6 atoms, Δq_1 and Δq_2, respectively (see table). The calculations showed that the electron density in the quinoid ring is distributed nonuniformly over the C^2=C^3 and C^5=C^6 bonds. The C^2=C^3 bond located in the *syn*-position with respect to the substituent on the nitrogen in compounds **I**–**VII** is less polarized that the *anti*-C^5=C^6 bond. This pattern may be rationalized in terms of the interaction $n_p(O) \rightarrow \pi^*(N{=}C) \rightarrow \pi^*(C{=}C)$ in the parent *p*-benzoquinone oxime molecule. The *s-trans* configuration corresponding to the $n_p(O) \rightarrow \pi^*(N{=}C) \rightarrow \pi(C^5{=}C^6)$ interaction is energetically more favorable than *s-cis* [$n_p(O) \rightarrow \pi^*(N{=}C) \rightarrow \pi^*(C^2{=}C^3)$] [10]. The maximal partial negative charge should be localized on C^6, which is confirmed by the calculations. The interaction $n_\sigma(N) \rightarrow \sigma^*(C{-}C)$ also affects electron density distribution in the quinoid ring; this interaction should give rise to greater partial negative charge on C^3, as compared to C^5. This is also consistent with the results of calculations.

According to [3, 6, 8], halogens add to *p*-benzoquinone oxime esters **I**–**VII** mainly at the *syn*-C^2=C^3



Charges on the C^2, C^3, C^5, and C^6 atoms in the quinoid ring of compounds **I**–**IX** and **XXI**–**XXVI**, calculated by the PM3 method

Compound no.	qC^2	qC^3	Δq_1[a]	qC^5	qC^6	Δq_2[b]	Δq[c]
Z-**I**	–0.172	–0.063	0.109	–0.04	–0.19	0.15	–0.041
Z-**II**	–0.166	–0.075	0.091	–0.038	–0.183	0.145	–0.054
Z-**III**	–0.175	–0.059	0.116	–0.044	–0.185	0.141	–0.025
Z-**IV**	–0.135	–0.094	0.041	–0.059	–0.149	0.09	–0.049
Z-**V**	–0.143	–0.078	0.065	–0.063	–0.154	0.091	–0.026
Z-**VI**	–0.189	–0.037	0.152	–0.008	–0.201	0.193	–0.041
Z-**VII**	–0.186	–0.022	0.164	–0.01	–0.197	0.187	–0.023
Z-**VIIIa**	–0.141	–0.08	0.061	–0.042	–0.188	0.146	–0.085
E-**VIIIa**	–0.148	–0.065	0.083	–0.058	–0.180	0.122	–0.039
Z-**IXa**	–0.130	–0.093	0.037	–0.038	–0.190	0.152	–0.115
E-**IXa**	–0.144	–0.062	0.082	–0.080	–0.165	0.085	–0.003
E-**XXI**	–0.205	–0.005	0.200	–0.079	–0.162	0.083	0.117
E-**XXII**	–0.200	–0.012	0.188	–0.065	–0.172	0.107	0.081
E-**XXIII**	–0.205	0.003	0.208	–0.096	–0.209	0.113	0.095
E-**XXIV**	–0.202	–0.005	0.197	–0.079	–0.217	0.138	0.059
E-**XXVa**	–0.211	0.003	0.214	–0.104	–0.128	0.024	0.19
E-**XXVc**	–0.204	–0.011	0.193	–0.086	–0.138	0.052	0.141
E-**XXVIa**	–0.207	–0.04	0.167	–0.094	–0.126	0.032	0.135
E-**XXVId**	–0.2032	–0.012	0.1912	–0.08	–0.136	0.056	0.1352

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

bond which is less polarized (the order of that bond is higher). Therefore, the calculated charges on the carbon atoms in the quinoid ring may be used to estimate the regioselectivity in reactions of halogens with *p*-benzoquinone oxime esters. In keeping with the experimental data, the isomer ratio varies from 20:80 to 10:90, the *syn*-addition products prevailing. The same follows from the calculations.

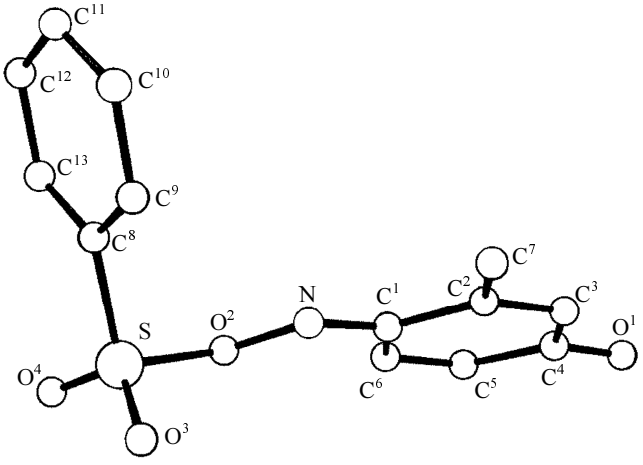
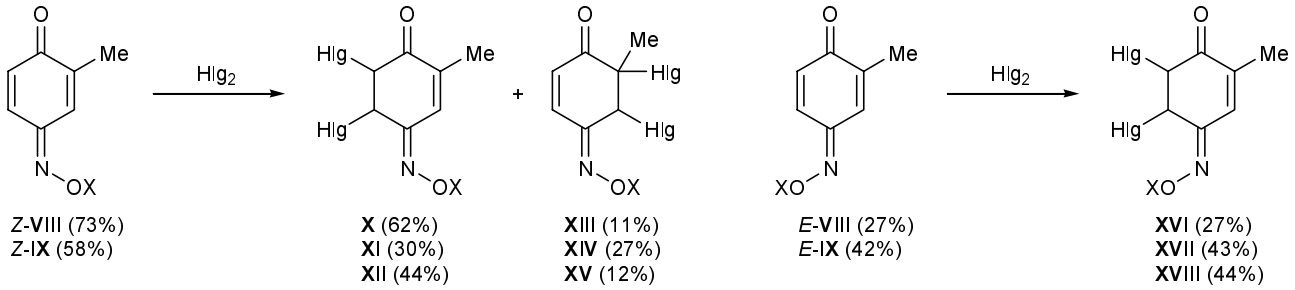


Fig. 1. Structure of the molecule of 3-methyl-4-phenylsulfonyloxyimino-2,5-cyclohexadienone (**XXII**) according to the X-ray diffraction data.

Different polarizations of the quinoid C=C bonds may also be a factor responsible for the observed difference in the ^1H–^1H coupling constants $J_{2,3}$ and $J_{5,6}$ [3, 6, 8]. In the general case, vicinal coupling constants $^3J_{HH}$ depend on various factors, such as C–C and C–H bond lengths, HCC angle, and polarity of bonds; more polar bond should be characterized by smaller $^3J_{HH}$ value [11]. Compounds **I**–**VII** showed a good correlation between the coupling constants $J_{2,3}$ and $J_{5,6}$ [3, 8], on the one hand, and polarizations of the C^2=C^3 and C^5=C^6 bonds estimated by PM3 calculations in the present work, on the other.

In the halogenation of 2-methyl-1,4-benzoquinone oxime esters, both electronic and steric factors must be taken into account while predicting the reaction direction. As with unsubstituted analogs, electron density distribution over the quinoid ring may be estimated by

Scheme 2.



Z-**VIII** (73%)
Z-**IX** (58%)

X (62%)
XI (30%)
XII (44%)

XIII (11%)
XIV (27%)
XV (12%)

E-**VIII** (27%)
E-**IX** (42%)

XVI (27%)
XVII (43%)
XVIII (44%)

VIII, **X**, **XIII**, **XVI**, X = $PhSO_2$; **IX**, **XI**, **XII**, **XIV**, **XV**, **XVII**, **XVIII**, X = PhCO; **X**, **XI**, **XIII**, **XIV**, **XVI**, **XVII**, Hlg = Cl; **XII**, **XV**, **XVIII**, Hlg = Br.

PM3 calculations. According to the calculations, introduction of a methyl group into the 2-position appreciably changes the electron density distribution. Unlike unsubstituted *p*-benzoquinone oxime esters **II** and **III**, the methyl-substituted C=C bond in 2-methyl-1,4-benzoquinone oxime esters **VIII** and **IX** is less polarized, regardless of the orientation of the acyl ($ArSO_2O$ or ArCO) group ($\Delta q_2 > \Delta q_1$; see table). Orientation of the substituent on the nitrogen atom affects only the magnitude of the differences Δq_2 and Δq_1.

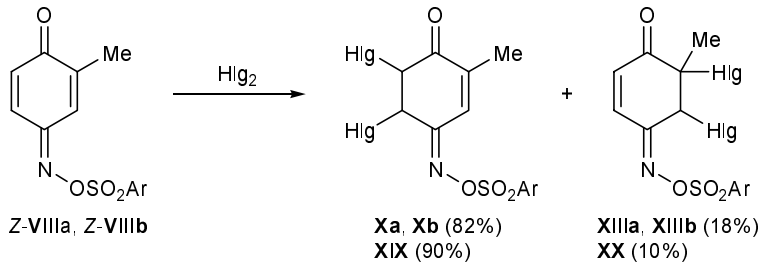
In order to verify the results of calculations we performed halogenation of 4-arylsulfonyloxyimino-2-methyl-2,5-cyclohexadienone (**VIII**) and 4-benzoyloxyimino-2-methyl-2,5-cyclohexadienone (**IX**) in acetic acid and in chloroform. The reaction conditions were selected in such a way that undesirable side processes (e.g., dehydrohalogenation) be avoided. Gaseous chlorine was used as chlorinating agent, and the bromination was performed using a solution of bromine in appropriate solvent. The products were isolated by precipitation from the reaction mixture with water and were not subjected to recrystallization to avoid loss of some isomers. In our early studies [1, 4, 5], the halogenation products were analyzed after crystallization, which may result in loss of some compounds or change in the isomer ratio. When the reaction was carried out in chloroform, the products were isolated by complete removal of the solvent. The product mixtures were analyzed by ^{1}H NMR spectroscopy. It should be noted that asymmetric substitution pattern in 2-methyl derivatives **VIII** and **IX** made it possible to unambiguously assign signals to particular isomers on the basis of the known data for individual isomers [1, 4, 5]. The results of reactions of compounds **VIII** and **IX** with halogens are shown in Scheme 2.

The chlorination of quinone oximes **VIII** and **IX** led to formation of mixtures of products, each containing three compounds: **X**, **XIII**, and **XVI** from **VIII** and **XI**, **XIV**, and **XVII** from **IX**. The addition of chlorine to the *Z* isomers of **VIII** and **IX** involved both double C=C bonds of the quinoid ring, while their *E* isomers took up chlorine only at the unsubstituted C=C bond. Moreover, the *E*:*Z* isomer ratios in the chlorination products of both compound **VIII** and **IX** remain the same as in the initial oximes within experimental error (73:27 for phenylsulfonyl derivatives and 58:42 for benzoyl derivative).

We succeeded in obtaining bromination products only from benzoyl derivative **IX**. The bromination of *O*-phenylsulfonyloxime **VIII** resulted in formation of a noncrystallizable oily material whose composition cannot be determined. Treatment of *O*-benzoyloxime **IX** with bromine in both acetic acid and chloroform gave a mixture of compounds **XII**, **XV**, and **XVIII**; their structure and ratio were analogous to the structure and ratio of the chlorination products. The average percentage of each isomer (from several runs) is given in Scheme 2. Like in the chlorination, the ratio of the *Z*- and *E*-isomeric bromination products was almost the same as in initial compound **IX** within experimental error (56:44).

Goncharova [12] proposed a mechanism for halogenation of *p*-benzoquinone oxime esters, according to which addition of a negatively charged halogen atom to double-bonded carbon atom gives an intermediate capable of changing its configuration via rotation about the C=N bond and the ratio of isomeric products is determined by steric factor. This means that the *E*:*Z* isomer ratio may change during the halogenation process. Our experimental data showed the reverse; however, the possibility for rotation about the C=N bond still cannot be ruled out. Norris and Sternhell [13] believed that under certain conditions *p*-benzoquinone oxime esters are capable of undergoing *Z*–*E* isomerization via rotation about the ordinary C–N

Scheme 3.



VIII, **X**, **XIII**, Ar = Ph (**a**), 4-MeC_6H_4 (**b**); **XIX**, **XX**, Ar = Ph; **X**, **XIII**, Hlg = Cl; **XIX**, **XX**, Hlg = Br.

bond which appears as a result of protonation of initial quinone oxime and that equilibrium establishes after a time. It might be presumed that the halogenation process also involves some equilibrium between the isomers. Therefore, the results of halogenation of compounds **VIII** and **IX** cannot be regarded as a rigorous proof for the absence of rotation about the C=N bond during the process.

In order to elucidate the true pattern, it was reasonable to perform halogenation of an individual isomer. By repeated recrystallizations we succeeded in isolating pure *Z* isomers of 4-arylsulfonyloxyimino-2-methyl-2,5-cyclohexadienones *Z*-**VIIIa** and *Z*-**VIIIb** which were subjected to halogenation in different solvents (CCl_4, $CHCl_3$, and AcOH). The product mixtures were isolated by complete precipitation with water and were analyzed by ^{1}H NMR spectroscopy. Both chlorination and bromination of compounds *Z*-**VIIIa** and *Z*-**VIIIb** gave mixtures of two isomeric products formed by halogen addition at one or another double C=C bond (Scheme 3). The ratio of products **Xa** and **XIIIa** was the same as in the chlorination of a mixture of *Z*-**VIIIa** and *E*-**VIIIa** (Scheme 2) within experimental error. No compounds which could be formed from the corresponding *E* isomers were detected. Thus we have obtained a convincing proof that the halogenation of *p*-benzoquinone oxime esters in carbon tetrachloride, chloroform, and acetic acid is not accompanied by *E*–*Z* isomerization at the nitrogen atom.

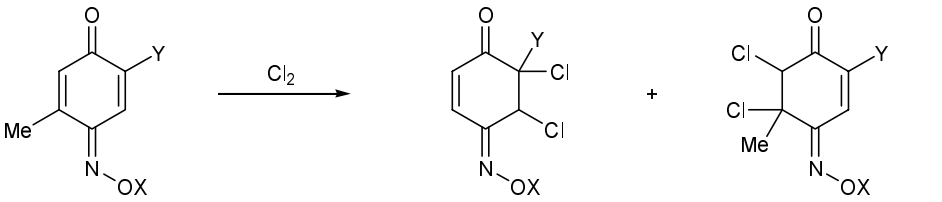
The experimental data indicate that halogens add mainly at the unsubstituted double bond (C^5=C^6) in the quinoid ring (Schemes 2, 3). Obviously, the main factor determining the reaction direction is spatial accessibility of one or another C=C bond, while charge distribution over the double-bonded carbon atoms is less significant.

The chlorination of phenylsulfonyloxyimino derivative *Z*-**VIII** gives on the average 62% of dichlorocyclohexenone **X** formed by addition of chlorine at the unsubstituted C=C bond; the fraction of product **XI** obtained from benzoyl analog *Z*-**IX** is 30%. This means that the C^2=C^3 bond in the *Z* isomer of **IX** is more reactive (Scheme 2) than in *Z*-**VIII**. According to the calculations, molecule *Z*-**IX** is characterized by a stronger difference in the C=C bond polarizations, as compared to *Z*-**VIII**; i.e., the C^2=C^3 bond in *Z*-**IX** should be more active than the corresponding bond in *Z*-**VIII** (see table), which is fully consistent with the experimental data. In this case, the electronic factor is more important, for steric effects due to the presence of methyl group in both compounds are similar. The differences in the charges on carbon atoms in the quinoid ring of *E*-**VIII** and *E*-**IX** are considerably smaller than in the corresponding *Z* isomers. Therefore, halogen addition to the *E* isomers is governed mainly by steric factor, and only the unsubstituted double C=C bond in the quinoid ring is involved (Scheme 2).

We previously reported on regioselective halogenation of 4-benzoyloxyimino-3-methyl-2,5-cyclohexadienone (**XXI**) and 3-methyl-4-phenylsulfonyloxyimino-2,5-cyclohexadienone (**XXII**) [2, 4, 5]. The results of PM3 calculations showed that, unlike 2-methyl-1,4-benzoquinone oxime esters *E*-**VIII** and *E*-**IX**, the unsubstituted C^5=C^6 bond in 3-methyl-substituted analogs (which is located *syn* with respect to the substituent on the nitrogen atom) is less polarized, i.e., $\Delta q_1 > \Delta q_2$ (see table). Thus both electronic and steric factors in quinone oximes **XXI** and **XXII** act in the same direction, and addition products at the C^2=C^3 bond are formed.

Chlorine addition to 4-benzoyloxyimino-6-chloro-3-methyl-2,5-cyclohexadienone (**XXIII**) and 2-chloro-5-methyl-4-phenylsulfonyloxyimino-2,5-cyclohexadienone (**XXIV**) occurs predominantly at the chloro-substituted C=C bond [2]. According to the calculations, the Cl–C=C bond in molecules **XXIII** and **XXIV** is less polarized than the methyl-substituted

Scheme 4.



XXVa–XXVd
XXVIa, **XXVIb**, **XXVId**

XXVIIa, **XXVIIb** (90%)
XXVIIc, **XXVIId** (68%)
XXIXa, **XXIXb**, **XXIXd** (42%)

XXVIIIa, **XXVIIIb** (10%)
XXVIIIc, **XXVIIId** (32%)
XXXa, **XXXb**, **XXXd** (58%)

XXV, **XXVII**, **XXVIII**, Y = Me; **XXVI**, **XXIX**, **XXX**, Y = *i*-Pr; X = PhCO (**a**), 4-$O_2NC_6H_4CO$ (**b**), 4-$MeC_6H_4SO_2$ (**c**), 3-$O_2NC_6H_4SO_2$ (**d**).

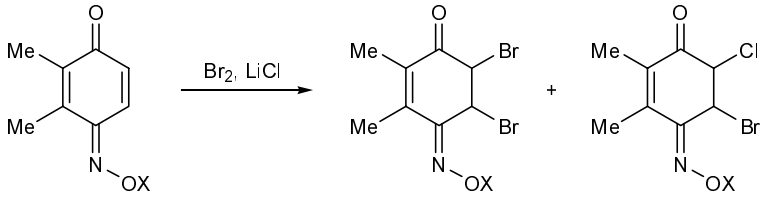
double bond (see table). The sizes of chlorine atom and methyl group are almost similar; therefore, the reaction direction is determined mainly by electronic effect. We previously presumed [7] that chlorine addition to quinone oximes containing both methyl group and chlorine atom in the quinoid ring occurs mainly at the methyl-substituted double bond. By contrast, compounds **XXIII** and **XXIV** take up chlorine at the less polarized (more reactive) chloro-substituted double bond, in keeping with the calculation data.

2,5-Dialkyl-1,4-benzoquinone oxime esters **XXV** and **XXVI**, as well as previously studied 3-methyl-1,4-benzoquinone oxime esters **XXI** and **XXII**, exist in solution as a single isomer but, unlike the latter, they have an alkyl substituent at the *syn*-C=C bond. By halogenation of 4-aroyl(arylsulfonyl)oxyimino-2,5-dialkyl-2,5-cyclohexadienones **XXV** and **XXVI** we isolated products of halogen addition at both C=C bonds of the quinoid ring [2, 4, 5], but the products were analyzed after crystallization which could lead to loss of some isomers or change in their ratio. In the present work we performed chlorination of 4-aroyl(arylsulfonyl)oxyimino-2,5-dimethyl-2,5-cyclohexadienones **XXVa**–**XXVd** and 4-aroyl(arylsulfonyl)oxyimino-2-isopropyl-5-methyl-2,5-cyclohexadienones **XXVIa**, **XXVIb**, and **XXVId**, and the products were completely precipitated from the reaction mixture with water. In the reactions with **XXV** and **XXVI** (Scheme 4), chlorine adducts at both C=C bonds of the quinoid ring were formed (**XXVIIa**–**XXVIId**, **XXVIIIa**–**XXVIIId**, **XXIXa**, **XXIXb**, **XXIXd**, **XXXa**, **XXXb**, and **XXXd**). Signals in the ^1H NMR spectra of the reaction mixtures were assigned on the basis of published data for individual isomers [4, 5]. As follows from the isomer ratios given in Scheme 4, aroyl derivatives **XXVIIa** and **XXVIIb** give rise to a greater fraction of adducts at the *syn*-C=C bond (90%), as compared to arylsulfonyl derivatives **XXVIIc** and **XXVIId** (68%).

PM3 calculations showed an appreciable contribution of electron density distribution over the quinoid ring to the regioselectivity of chlorine addition to 2,5-dialkyl-1,4-benzoquinone oxime esters **XXV** (see table). The difference in the polarizations of the $C^2=C^3$ and $C^5=C^6$ bonds in aroyloxyimino derivative **XXVa** is greater than that found for arylsulfonyloxyimino analog **XXVc**; i.e., the former should give rise to a greater fraction of chlorine adduct at the *syn*-C=C bond. In fact, this is confirmed by the experimental data.

Quinone oxime esters **XXVIa**, **XXVIb**, and **XXVId** are characterized by similar differences in the charges on C^2/C^3 and C^5/C^6, regardless of the substituent on the nitrogen atom. From the viewpoint of electron density distribution, the *syn*-C=C bond (isopropyl-

Scheme 5.



XXXIa, **XXXIb**

XXXIIa, **XXXIIb**

XXXIIIa, **XXXIIIb**

X = $PhSO_2$ (**a**), PhCO (**b**).

substituted) should be more reactive. The ratio of the chlorine addition products is on the average 58:42, the major product being that formed via addition at the less reactive (according to the charge distribution pattern) methyl-substituted double bond, which may be due to steric effect of the bulky isopropyl group.

Thus estimation of electron density distribution over the C^2/C^3 and C^5/C^6 atoms of the quinoid ring makes it possible to predict the predominant direction of halogen addition to *p*-benzoquinone oxime esters; however, the mechanism of halogen addition remains unclear. Therefore, we performed bromination of 4-benzoyloxyimino- and 4-phenylsulfonyloxyimino-2,3-dimethyl-2,5-cyclohexadienones **XXXIa** and **XXXIb** in the presence of chloride ions. Compounds **XXXIa** and **XXXIb** were taken as substrates, taking into account that the presence of two substituents at one double bond should hamper bromine addition at that bond. As source of Cl^- ions we used a solution of lithium chloride in acetic acid. In each case, the reaction afforded a mixture of two products (Scheme 5). The structure of the products was determined by ^1H NMR spectroscopy using previously reported data for dibromocyclohexenones **XXXIIa** and **XXXIIb** and dichlorocyclohexenones **XXXIVa** and **XXXIVb** [7]. The ratio of compounds **XXXII** and **XXXIII** in the product mixtures ranged from 20:80 for sulfonyl derivatives to 30:70 for aroyl analogs.

Thus the major product in the bromination of quinone oxime esters **XXXI** in the presence of chloride ions has bromochlorocyclohexenone structure with the bromine atom attached to C^5 (*ortho* position with respect to the oxime moiety) and the chlorine atom attached to C^6 (*ortho* position with respect to the carbonyl carbon atom). According to the classical concepts of bromine addition to double C=C bonds, the first step involves formation of a π complex which is converted into bromonium ion like **A**. Depending on the conditions, ion **A** either reacts directly with bromide ion or is converted first into cation **B** or **C** which then takes up bromide ion. We performed PM3 optimization of geometric parameters of structures **A**–**C** derived from 4-phenylsulfonyloxyimino-2,5-cyclohexadienone (**III**). Optimization of cation **C** led finally to structure **B**. From the viewpoint of thermodynamics, cation **B** is the most favorable (it has the lowest enthalpy of formation); however, it cannot produce the product obtained experimentally. It should be noted that bromonium ion $\mathbf{A}^1$ formed via interaction of Br^+ with the *syn*-C=C bond has a lower enthalpy of formation than ion $\mathbf{A}^2$ resulting from bromine addition to the *anti*-C=C bond. This is consistent with the experimental data.

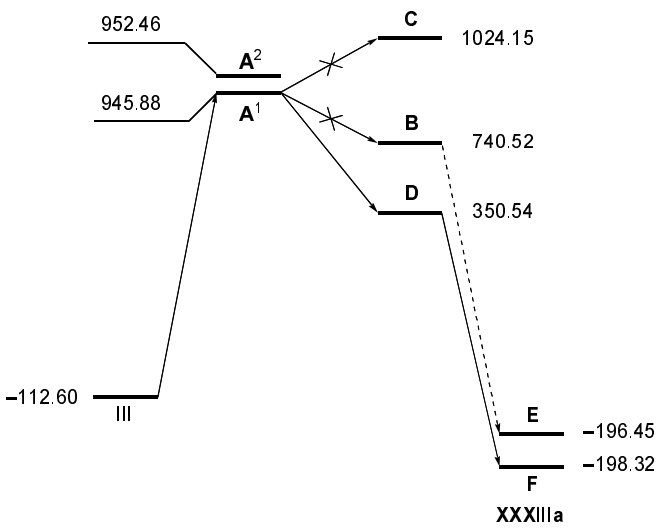
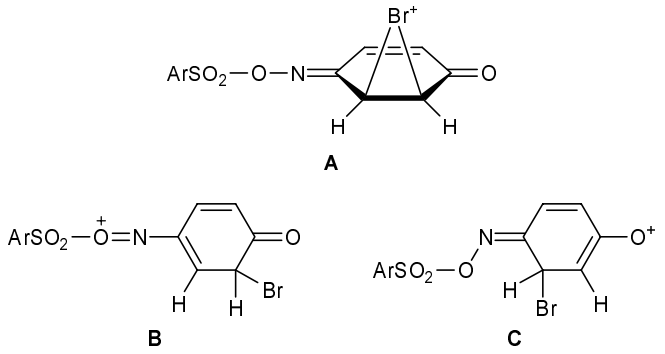
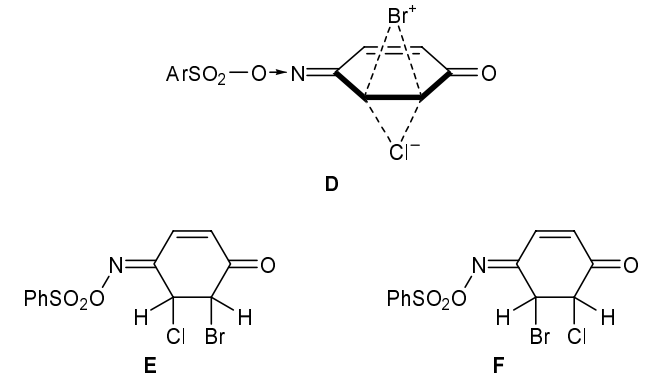


Fig. 2. Energy diagram for the bromination of 4-phenylsulfonyloxyimino-2,5-cyclohexadienone (**III**) in the presence of chloride ions (given are the corresponding enthalpies of formation, kJ/mol).



The experimental data suggest that the bromination process should involve intermediate bromonium ion **A** or its subsequent transformation into cation **C**. Insofar



as the enthalpy of formation of ion **C** is even greater than that of **A**, this path is unfavorable from the energy considerations (Fig. 2). Most probably, halide ion Hlg^- adds directly to bromonium ion **A**. Optimization of the corresponding intermediate structure **D** (*cis* configuration), which is characterized by a lower enthalpy of formation than **B** and **C**, gives eventually structure **F** (**XXXIIIa**). Furthermore, the enthalpy of formation of cyclohexene structure **F** is lower than that calculated for isomeric structure **E**.

Taking into account published data and the results of our experiments performed in the present work, we can formulate the following general relations holding in the halogenation of *p*-benzoquinone oxime esters: (1) the process is not accompanied by change of configuration of the nitrogen atom in *p*-benzoquinone oxime esters; (2) addition of halogens occurs predominantly at the *syn*-C=C bond in the quinoid ring, i.e., configuration at the nitrogen atom is the crucial factor determining the regioselectivity of the process; (3) charge distribution over carbon atoms of the quinoid ring and orders of the C=C bonds, calculated by the PM3 method, may be used to predict the direction of halogen addition to *p*-benzoquinone oxime esters; (4) nonequivalence of the quinoid C=C bonds in the halogenation originates from their different polarizations and orders, which determine the stability of intermediate bromonium ion; (5) methyl substitution at the *anti*-C=C bond leads to addition of halogens exclusively at the *syn*-C=C bond, while isopropyl substitution at the *syn*-C=C bond does not prevent halogen addition at that bond; and (6) the nature of solvent, halogen, or substituent on the nitrogen atom does not affect the reaction direction to an appreciable extent.

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^{1}H NMR spectra were measured on a Varian VXR-300 instrument (300 MHz) using chloroform-*d* as solvent and tetramethylsilane as reference. The reaction mixtures were analyzed by TLC on Silufol UV-254 plates using benzene–ethyl acetate (10:1, by volume) as eluent; spots were visualized under UV light.

X-Ray analysis of 3-methyl-4-phenylsulfonyloxyimino-2,5-cyclohexadienone (XXII). A single crystal of **XXII**, 0.42×0.33×0.28 mm, was examined at 293(2) K on an Enraf–Nonius CAD-4 automatic four-circle diffractometer (λCuK_α irradiation, λ = 1.54178 Å, graphite monochromator, scan rate ratio $\omega/2\Theta$ 1.2). The unit cell parameters and orientation matrix were determined from 22 reflections with $30° < \Theta < 32°$. Monoclinic crystals; $C_{13}H_{11}NO_4S$; M 277.29; a = 19.711(4), b = 9.890(2), c = 15.298(8) Å; $\alpha = \gamma = 90°$, β = 118.62(2)°; V = 2618 Å^3; Z = 8; d_{calc} = 1.407 g×cm^{-3}; space group $C2/c$; μ = 23.03 cm^{-1}. Absorption coefficient 2.303 mm^{-1}; $F(000)$ = 1152; spherical segment $0 \le h \le 20$, $0 \le k \le 10$, $-16 \le l \le 14$; limiting Θ value 56°. Total of 1892 reflections were measured, 1706 of which were symmetry-independent (R_{int} = 0.0183); 1700 reflections were used in the refinement procedure [1511 reflections with $I > 2\sigma(I)$; 173 refined parameters, 9.83 reflections per parameter]. The structure was solved by the direct method and was refined by the least-squares procedure in full-matrix anisotropic approximation using SHELXS and SHELXL-93 software [14, 15]. Chebyshev's weight scheme $\omega = 1/[\sigma^2(F_o^2) + (AP)^2 + BP]$ where $P = (F_o^2 + 2F_c^2)/3$ was applied; the coefficients A and B were calculated using program [15] and were 0.083 and 1.398, respectively. All hydrogen atoms were visualized objectively from the difference synthesis of electron density and were involved in the calculation with fixed positional and thermal parameters (U_{iso} = 0.08 Å^2). The final divergence factors were $R_1(F)$ = 0.0441 and $R_w(F^2)$ = 0.1187; GOF = 1.035. The residual electron density from the Fourier difference series was 0.17 and –0.28 $\bar{e}$/Å^3. All calculations were performed using a PC-AT/486.

4-Aroyloxyimino- and 4-arylsulfonyoxyimino-2,5-cyclohexadienones **VIIIa**, **VIIIb**, **IXa**, **IXb**, **XXVa**–**XXVd**, **XXVIa**, **XXVIb**, and **XXVId** were synthesized by acylation of the corresponding 1,4-benzoquinone oximes with aroyl or arenesulfonyl chlorides in diethyl ether in the presence of triethylamine according to the procedure described in [16].

Chlorination of 4-aroyloxyimino- and 4-arylsulfonyloxyimino-2-methyl-2,5-cyclohexadienones VIIIa, VIIIb, and IX. Dry chlorine was passed at a flow rate of 15–20 ml/min through a solution of 2 mmol of compound **VIIIa**, **VIIIb**, or **IX** in 3 ml of chloroform or acetic acid, maintained at 25–30°C, until complete saturation. After several hours, the solution in acetic acid was diluted with water until complete precipitation, and the precipitate was filtered off. The solution in chloroform was evaporated to dryness. The products thus isolated were analyzed by ^{1}H NMR spectroscopy without preliminary recrystallization.

Compounds **Xa** and **XVa** were reported in [1]. ^{1}H NMR spectrum, δ, ppm: **Xb**: 7.31 q (3-H), 4.94 q (5-H), 4.49 d (6-H), 2.06 d (2-Me), $J_{5,6}$ = 3, $J_{3,5}$ = 2.1, J(CH_3, 3-H) = 1.5 Hz; **XI**: 7.51 q (3-H), 5.28 q (5-H), 4.61 d (6-H), 2.15 d (2-Me), $J_{5,6}$ = 3.3, $J_{3,5}$ = 2.1, J(CH_3, 3-H) = 1.5 Hz; **XIIIa**: 6.95 d.d (3-H), 5.50 d (5-H), 6.41 d (2-H), 1.84 s (6-Me), $J_{2,3}$ = 10.2, $J_{3,5}$ = 2.1 Hz; **XIIIb**: 6.95 d.d (3-H), 5.49 d (5-H), 6.40 d (2-H), 1.84 s (6-Me), $J_{2,3}$ = 9.9, $J_{3,5}$ = 1.8 Hz; **XIV**: 7.29 d.d (3-H), 5.63 d (5-H), 6.51 d (2-H), 1.95 s (6-Me), $J_{2,3}$ = 10.2, $J_{3,5}$ = 1.8 Hz; **XVI**: 6.82 q (3-H), 5.47 q (5-H), 4.40 d (6-H), 2.02 d (6-Me), $J_{5,6}$ = 3, $J_{3,5}$ = 2.1, J(CH_3, 3-H) = 1.5 Hz.

Bromination of 4-aroyloxyimino- and 4-arylsulfonyloxyimino-2-methyl-2,5-cyclohexadienones VIIIa, VIIIb, and IX. A solution of 6 mmol of bromine in chloroform or acetic acid was added dropwise under stirring to a solution of 2 mmol of compound **VIIIa**, **VIIIb**, or **IX** in 3 ml of the same solvent. The solution in acetic acid was diluted with water until complete precipitation, and the precipitate was filtered off. The solution in chloroform was evaporated to dryness. The products thus isolated were analyzed by ^{1}H NMR spectroscopy without preliminary recrystallization.

Compounds **XII** and **XVIII** were described in [1]. ^{1}H NMR spectrum, δ, ppm: **XV**: 7.25 d.d (3-H), 5.85 d (5-H), 6.51 d (2-H), 2.12 s (6-Me), $J_{2,3}$ = 10.5, $J_{3,5}$ = 1.5 Hz; **XIX**: 7.27 q (3-H), 5.11 d.d (5-H), 4.70 d (6-H), 2.07 d (2-Me), $J_{3,5}$ = 2.1, $J_{5,6}$ = 2.7, J(CH_3, 3-H) = 1.2 Hz; **XX**: 6.91 d.d (3-H), 5.71 d (5-H), 6.49 d (2-H), 2.03 s (6-Me), $J_{2,3}$ = 10.5, $J_{3,5}$ = 2.1 Hz.

Chlorination of 4-aroyloxyimino- and 4-arylsulfonyloxyimino-2,5-dialkyl-2,5-cyclohexadienones XXVa–XXVd, XXVIa, XXVIb, and XXVId. Gaseous chlorine was passed at a flow rate of 15–20 ml/min through a solution of 0.3 g of compound **XXVa**–**XXVd**, **XXVIa**, **XXVIb**, or **XXVId** in 3 ml of acetic acid, dimethylformamide, or DMF–AcOH mixture (1:1, 3:1, or 5:1), heated to 70–80°C, until complete saturation. The mixture was diluted with water, and the precipitate was filtered off and analyzed by ^{1}H NMR spectroscopy without preliminary recrystallization.

Compounds **XXVIIa**, **XXIXb**, **XXIXd**, **XXXa**, **XXXb**, and **XXXd** were described in [2, 5, 7]. ^{1}H NMR spectrum, δ, ppm: **XXIXa**: 6.29 q (2-H), 5.73 s (5-H), 2.69–2.77 m (6-H), 2.32 d (3-Me), 1.12–1.20 d.d (6H, Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIIb**: 6.39 q (2-H), 5.62 s (5-H), 2.36 d (3-Me), 1.92 s (6-Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIIc**: 6.24 q (2-H), 5.52 s (5-H), 2.09 d (3-Me), 1.82 s (6-Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIId**: 6.28 q (2-H), 5.52 s (5-H), 2.10 d (3-Me), 1.84 s (6-Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIIIa**: 7.50 q (3-H), 4.48 s (6-H), 2.19 s (5-Me), 2.14 d (2-Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIIIb**: 7.45 q (3-H), 4.49 s (6-H), 2.18 s (5-Me), 2.16 d (2-Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIIIc**: 7.31 q (3-H), 4.36 s (6-H), 2.07 s (2-Me), 1.91 d (5-Me), J(CH_3, 2-H) = 1.2 Hz; **XXVIIId**: 7.29 q (3-H), 4.38 s (6-H), 2.08 s (2-Me), 1.93 d (5-Me), J(CH_3, 2-H) = 1.2 Hz.

Bromination of 4-aroyloxyimino- and 4-arylsulfonyloxyimino-2,3-dimethyl-2,5-cyclohexadienones XXXIa and XXXIb. Anhydrous lithium chloride, 0.14 g, was added to a solution of 2 mmol of compound **XXXIa** or **XXXIb** in 2 ml of acetic acid, and a solution of 2 mmol of bromine in acetic acid was then added dropwise under stirring. The mixture was diluted with water until complete precipitation, and the precipitate was filtered off and analyzed by ^{1}H NMR spectroscopy without preliminary recrystallization.

Compounds **XXXIIa** and **XXXIIb** were described in [7]. ^{1}H NMR spectrum, δ, ppm: **XXXIIIa**: 5.61 d (5-H), 4.47 d (6-H), 2.00 s (2-Me), 2.08 s (3-Me), $J_{5,6}$ = 2.7 Hz; **XXXIIIb**: 5.81 d (5-H), 4.58 d (6-H), 2.10 s (2-Me), 2.37 s (3-Me), $J_{3,5}$ = 2.4 Hz.

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