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Transformations of *gem*-Dichloroarylcyclopropanes in the Reaction with $NOCl·2SO_3$. Synthesis of 3-Aryl-5-chloroisoxazoles

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Abstract—Nitrosation with complex $NOCl·2SO_3$ of *gem*-dichloroarylcyclopropanes containing acceptor substituents in the aromatic ring proceeded chemo- and regioselectively affording 3-aryl-5-chloroisoxazoles in high yields. The presence of donor substituents complicated the reaction by the occurrence of competing processes.

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Cyclopropanes play an important role in the organic synthesis. The high activity of the cyclopropane ring originating from the angular and torsion strain underlies its capability to the ring opening with the formation of addition products. This allows a successful 1,3-bifunctionalization of the carbon skeleton containing a cyclopropane fragment [1]. In some events the opening of the three-membered ring is accompanied by the subsequent cyclization leading to the formation of versatile carbocyclic or heterocyclic systems [2]. Among diverse reactions the nitrosation of cyclopropanes acquires ever-growing importance since it provides a possibility to obtain a wide spectrum of nitrogen- and [NO]-containing heterocyclic compounds [3]. In particular, the nitrosation of arylcyclopropanes provided isoxazolines in high yields [4, 5].

We formerly introduced a new efficient nitrosation reagent, a complex $NOCl·2SO_3$, exhibiting a high chemoselectivity and reactivity in the synthesis of isoxazolines from arylcyclopropanes containing both donor and acceptor substituents in the aromatic ring [6]. At the nitrosation of *gem*-dichloroalkylcyclopropanes of diverse structures with the complex $NOCl·2SO_3$ we obtained regioisomeric alkyl-5-chloroisoxazoles in high yields [7].

The nitrosation of aryl-*gem*-dihalocyclopropanes was studied before, but good yields were obtained only at the use as the nitrosation reagent of nitrosonium tetrafluoroborate [8]. With the other nitrosation systems the reaction gave ambiguous results furnishing either the products of the small ring opening [9, 10] or the other heterocyclic compounds, e.g., isoxazoline and azetine *N*-oxide like in the case of *cis*-2,3-diphenyl-1,1-dichlorocyclopropane [11].

It seemed interesting to explore the behavior of monoaryl-*gem*-dichlorocyclopropanes in the reaction with the complex $NOCl·2SO_3$ with the goal to reveal the factors governing the chemoselectivity and regiochemistry of the process, and to know the synthetic opportunities of the reagent and the prospects of its application to the synthesis of arylisoxazoles. The derivatives of isoxazoline and isoxazole are convenient synthons and important structural elements of a number of drugs [12].

The reaction of 2-aryl-1,1-dichlorocyclopropanes **Ia–Ih** with the complex $NOCl·2SO_3$ was carried out

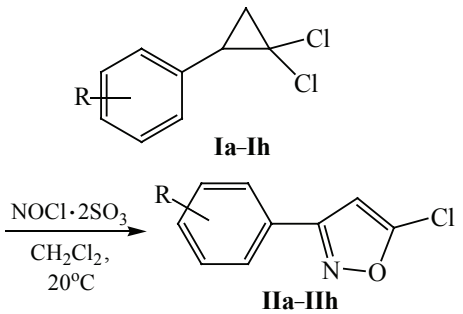


Table 1. Conversion of 2-aryl-1,1-dichlorocyclopropanes effected by $NOCl·2SO_3$ in dichloromethane at 20°C.

Compound no.	R	Reagents ratio	Time, h	Conversion, %[a]	Reaction products (yield, %)
Ia	3-Cl	1 : 2	24	100	**IIa** (87)
Ib	3-Br	1 : 1	24	100	**IIb** (85)
Ic	3-NO_2	1 : 1	24	100	**IIc** (87)
Id	4-NO_2	1 : 1	24	50	**IId** (45)
		1 : 3	24	100	**IId** (95)
Ie	2-NO_2	1 : 1	24	15	**IIe** (15)
		1 : 2	6 days	60	**IIe** (60)
		1 : 2	10 days	100	**IIe** (80)
If	4-Cl	1 : 1	24	100	**IIf** (55), **IIIf** (10), **IVf** (10), **Vf** (8)
Ig	4-Br	1 : 1	48	100	**IIg** (50), **IIIg** (30), **IVg** (10), **Vg** (5)
Ih	H	1 : 1	0.5[b]	100	**IIh** (20)[c], **IVh** (5), **VI** (45)[a]

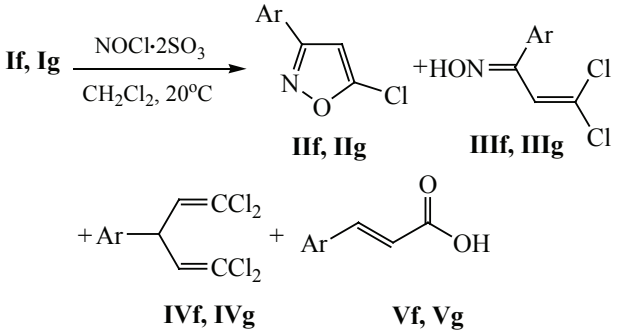
[a] According to the data of ^1H NMR spectra of the reaction mixtures.
[b] Considerable tarring was observed.
[c] Isoxazole **IIh** was isolated by chromatography in a 15% yield.

in dichloromethane at room temperature varying the reagents ratio. The results are listed in Table 1. All reaction products were isolated as individual compounds by column chromatography and were characterized by ^1H and ^{13}C NMR spectra which for already described compounds were consistent with the published data [8].

The data of Table 1 show that in the case of compounds with acceptor substituents in the aromatic ring (a halogen atom in the meta-position with respect to the small ring or a nitro group in any position of the benzene ring) the reaction proceeds chemo- and regioselectively affording in high yields the corresponding 3-aryl-5-chloroisoxazoles **IIa–IIe**.

meta-Substituted arylcyclopropanes **Ia–Ic** proved to be the most reactive and were quantitatively converted into the corresponding 3-aryl-5-chloroisoxazoles **IIa–IIc** within 24 h at the equimolar reagents ratio (Table 1). The presence of an acceptor substituent in the *ortho*-position with respect to the small ring essentially affected the reaction rate: the conversion of cyclopropane **Ie** under the comparable conditions was only 15%, and at the double excess of $NOCl·2SO_3$ it was 60% in 6 days and only in 10 days it reached 90%. The degree of conversion of the *para*-nitrosubstituted cyclopropane **Id** in comparable conditions also was lower than that of *meta*-isomer **Ic**, but at the excess of the reagent the conversion was considerably higher.

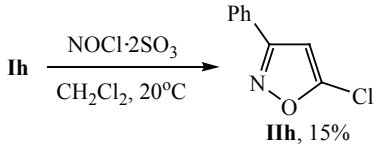
In the case of *para*-halosubstituted *gem*-dichloroarylcyclopropanes **If, Ig** the yields of isoxazoles **IIf, IIg** did not exceed 55%. Alongside the isoxazoles formed acyclic nitrosation products, oximes **IIIf, IIIg**, and also small quantities of 3-arylpentadienes **IVf, IVg**, and the corresponding cinnamic acids **Vf, Vg**.



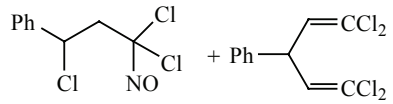
The structures of oximes **IIIf, IIIg** was established from the data of NMR and IR spectroscopy and of elemental analysis. It should be noted that the formation of analogous oxime was found earlier at the nitrosation of bicyclo[3.1.0]hexane [7]. ^1H NMR spectra of isoxazoles **II** and oximes **III** are resembling each other: a set of proton signals of the aromatic ring and a singlet in the region of ~6.5 ppm and belonging to the sole proton outside of the benzene ring are observed. ^{13}C NMR spectra of 5-chloroisoxazoles **II** alongside the carbon signals from the benzene ring atoms contain three characteristic carbon signals of the heterocycle atoms: a strong upfield signal of

HC= in the region of 100.0 ppm and two signals of quaternary carbon atoms at 155.0 (ClCO) and 162.0 (C=N) ppm. In the ^{13}C NMR spectra of oximes **III** the signal of the carbon atom C^2H= is located in the region characteristic of the sp^2-hybridized carbon (~123 ppm). Two other quaternary atoms of the carbon backbone also are present in the appropriate characteristic regions: ~130 and 160 ppm (see EXPERIMENTAL). Besides the IR spectra of oximes contain the absorption band of the stretching vibrations of the hydroxy group at 3500–3100 cm^{-1}.

The reaction of 2-phenyl-1,1-dichlorocyclopropane (**Ih**) with the complex $NOCl{\cdot}2SO_3$ completed within 30 min (cyclopropane conversion 100% according to ^1H NMR data). However the transformation proceeded along several routes giving a complex mixture of substances. The main compound observed in the ^1H NMR spectrum of the reaction mixture (45%) was the product of 1,3-addition to the small ring whose spectral characteristics (chemical shifts of aliphatic protons [3.72 d.d (1H, CH_2, ^2J 15.5, ^3J 6.2 Hz), 3.96 d.d (1H, CH_2, ^2J 15.5, ^3J 7.5 Hz), 5.17 d.d (1H, CH, ^3J 7.5, ^3J 6.2 Hz)] and the signals of the corresponding carbon atoms in the ^{13}C NMR spectrum (51.7, 57.5, 118.9 ppm) coincided with the data published for 1-nitroso-3-phenyl-1,1,3-trichloropropane (**VIh**) [13]. The yield of 3-phenyl-5-chloroisoxazole (**IIh**), according to ^1H NMR data, did not exceed 20%. The products of small ring opening turned out to be unstable and decomposed during the chromatography on silica gel. They proved also to be unstable in the comparable conditions (CH_2Cl_2, 20°C) within 24 h, in the ^1H NMR spectrum a signal of the proton of the isoxazole ring at 6.51 ppm was observed and a large number of signals of the aromatic protons belonging to tarry substances.



IIh, 15%



IVh, 5%

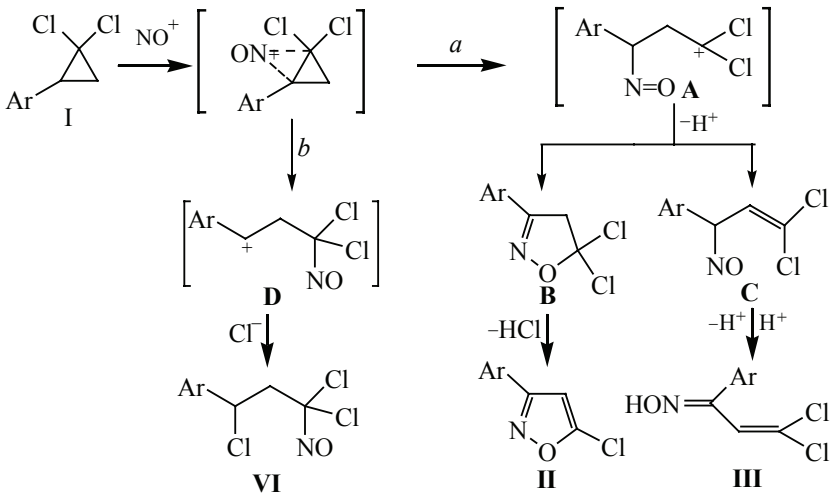
Also 3-phenylpentadiene (**IVh**) was isolated in a small quantity (~5%). The composition and structure of compounds **IVe–IVh** were established from elemental analysis, ^1H and ^{13}C NMR and mass spectra. The aliphatic part of the ^1H NMR spectra contained two signals belonging to three coupled protons: triplet (~4.8 ppm) and doublet (~6.0 ppm) with the ratio of the integral intensities of 1:2. The ^{13}C NMR spectrum contained only seven signals indicating the presence of symmetry elements in the molecule. The signal of one carbon atom appeared in the aliphatic part of the spectrum at 45.6 ppm, all other signals were observed in the region from 120 to 140 ppm characteristic of sp^2-hybridized carbon atoms, therewith three among them corresponded to CH= carbons as was established by NMR Apt-experiment (for compound **IVg**). The data of mass spectra indicated the polychloro substitution in compounds **IVf–IVh**. For instance, the distribution of the lines intensity in the molecular ion cluster and the fragmentation character corresponded to the presence in pentadienes **IVf, IVh** of five and four chlorine atoms, and in compound **IVg** of one bromine and four chlorine atoms.

The analysis of published data on the transformations of *gem*-dihaloarylcyclopropanes showed that in some events at the use of nitration mixtures 3-aryl-5-haloisoxazoles were obtained. In particular, at the treatment of 1,1-dichloro- and 1,1-dibromo-2-phenylcyclopropanes with sodium nitrate in sulfuric acid alongside the products of the nitration of the aromatic ring 2-(4-nitrophenyl)-5-chloro- and 2-(4-nitrophenyl)-5-bromoisoxazoles respectively were isolated in good yields (50–65%) [9]. Yet among the reaction products no isoxazoles were found without a nitro group in the aromatic ring. It was experimentally proved that first the nitration occurred of the aromatic ring and then the nitrosation of the small ring resulting in the isoxazole.

In [14] at the treatment of 2-(4-nitrophenyl)-1,1-dichlorocyclopropane with the nitration mixture the 2-(4-nitrophenyl)-5-chloroisoxazole was isolated in an 81% yield. Yet the positive result was obtained in this single case.

Thus the analysis of the published data and our own experimental findings permits a conclusion that the nitrosation of 2-aryl-1,1-dichlorocyclopropanes containing acceptor substituents in the aromatic ring proceeds chemoselectively with the formation of 3-aryl-5-chloroisoxazoles. In the presence of donor substituents the reaction is complicated by the occurrence of the competing processes with the formation of acyclic products of 1,3-addition [10, 13]. Here the key moment is apparently the possibility of the formation as intermediate in the reaction with an electrophilic species of dichloromethyl or benzyl carbocations.

Scheme 1.



Scheme 1 describes these processes. As follows from the structure of the reaction products, the primary coordination of the nitrosonium cation proceeds at the C^1–C^2 bond of the small ring, and the subsequent interaction with the atom C^1 or C^2 is governed apparently by the electronic factors.

At the realization of the route *a* the arising intermediate **A** is stabilized due to the positive mesomeric effect of the halogen atoms. Similar examples were described in the literature [15]. Further possible transformations of intermediate **A** are presented in the scheme by structures **B** and **C**. The ring closure and the formation of structure **B** is a result of the intramolecular nucleophilic attack of the oxygen atom of the nitroso group on the carbocation center. The presence of a halogen atom, a potential good leaving group, leads finally to the formation of isoxazole **II**. The elimination of a proton from structure **C** and the isomerization of the nitroso group into the oxime gives compound **III**.

The attack of the nitrosonium cation on the atom C^1 (route *b*) is favored by the formation as an intermediate of the benzyl carbocation **D**. Therewith in the absence of acceptor groups the aromatic ring is capable of the efficient stabilization of carbocation **D**, and this reaction rout prevails in the case of compound **Ih**. The subsequent reaction with a nucleophile (Cl^-) results in the formation of the acyclic products of 1,3-addition to the small ring **VI**.

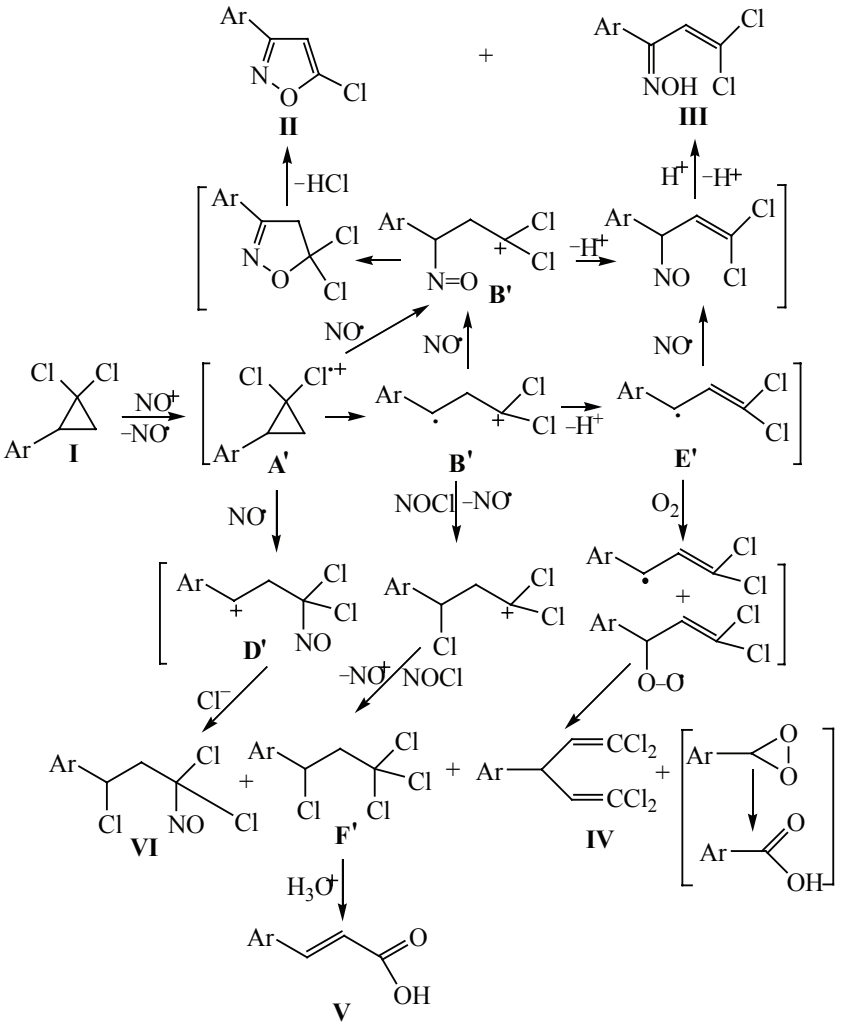
However the scheme of the electrophilic mechanism cannot rationalize all the multitude of the reaction products obtained at the nitrosation of compounds **If–Ih**.

The nitrosonium salts are known to be capable of one-electron oxidation of aromatic substrates [16]. Formerly in [5, 17] the theory of the SET-mechanism was considered with respect to arylcyclopropanes. We believe that in the event of the nitrosation of compounds **If–Ih** with the complex $NOCl{\cdot}2SO_3$ also the primary one-electron oxidation of substrates with the nitrosonium cation is possible with the formation of a cation-radical **A'** (Scheme 2) and its open form **B'** which being in the solvent cage in the direct proximity to the nitrogen(II) oxide lead to the formation of intermediates **C'** and **D'** and further of the final reaction products **II, VI** respectively. Radical **E'** may govern both the formation of oximes **III** and of structure **IV**. Intermediates **F'** may control the appearance among the reaction products of the cinnamic acid derivatives in the course of the subsequent hydrolysis of the reaction mixture [18].

We tried to vary the reaction conditions in order to suppress the side processes and to increase the isoxazoles yield. The changes in the temperature regime did not give the desired result. Decreasing the temperature considerably reduced the reaction rate. 2-Aryl-1,1-dichlorocyclopropanes as a whole proved to be less active than aryl- or 1-aryl-2-halocyclopropanes [19] and did not undergo nitrosation at 0°C save compound **Ih**.

To examine the influence of the solvent polarity on the course of the reaction we applied acetonitrile beside the dichloromethane, and this significantly increased the selectivity of the reaction with respect to isoxazole. However the yields of the target products did not exceed

Scheme 2.



50%, and therewith the reproducibility of the results was poor. The reaction in acetonitrile at higher temperature (50–80°C) was accompanied with fast discoloration of the reaction mixture apparently due to the decomposition of $NOCl·2SO_3$.

Note that the reagent we employed, $NOCl·2SO_3$, is a solid hygroscopic substance. It forms a suspension in dichloromethane and partially dissolves in the course of the reaction. In acetonitrile the reagent dissolves completely. In this case probably equilibrium is established due to the partial decomposition of the complex: $NOCl·2SO_3 \leftrightarrows NOCl + 2SO_3$

At the use of acetonitrile the equilibrium can be considerably shifted to the right because acetonitrile is capable of reacting with sulfur trioxide forming cyclic compounds [20].

Accounting for this possibility we carried out a series of reactions with the complex $NOCl·2SO_3$ in acetonitrile in the presence of the double excess of nitrosyl chloride with respect to the reagent to suppress this process (Table 2).

In this case with the cyclopropanes containing acceptor substituents we got lower yields of isoxazoles although the time of the reaction was increased. This was apparently due still to the decomposition of the reagent. Yet the isoxazole yields in reactions with arylcyclopropanes **Ih, Ii** with the donor substituents in the aromatic ring rose. Presumably, the nitrosation rate of the active substrates is higher that the rate of the reagent decomposition.

Nitrosation of alkyl-*gem*-dichlorocyclopropanes with the complex $NOCl·2SO_3$ resulted in the formation of a mixture of regioisomeric alkyl-5-chloroisoxazoles [7],

Table 2. Conversion of 2-aryl-1,1-dichlorocyclopropanes effected by $NOCl·2SO_3$ in acetonitrile in the presence of excess nitrosyl chloride, $NOCl·2SO_3$–NOCl 1:(1.5–2.0)

Compound no.	Temperature, °C	Time, h	Yield of reaction products, %	
			I	**II**
Ib	20	144	30	60
Id	20	44	70	25
Ie	20	44	80	19
If	20	72	50	40
Ih	20	24	–	70
Ii[a]	–20	24	–	35

[a] R = 4-Tol.

whereas in the case of aryl-*gem*-dichlorocyclopropanes notwithstanding the nature of the nitrosation reagent [8] the reaction occurred regioselectively giving exclusively 3-aryl-5-chloroisoxazoles. The high regioselectivity at the nitrosation of the *gem*-dichloroarylcyclopropanes is probably due to the considerable loosening of the 1,2-disubstituted bond owing to the influence of the aromatic ring and consequently to its higher reactivity. Yet it cannot be excluded that the primary coordination of the reagent occurs at the aromatic ring of the *gem*-dichloroarylcyclopropanes in keeping with the theory of the SET-mechanism. This assumption is supported by the fact that the reaction of the 2-benzyl-1,1-dichlorocyclopropane with the complex $NOCl·2SO_3$ first of all afforded the products of sulfochlorination in the aromatic ring and only with the excess of the reagent occurred the subsequent nitrosation of the small ring giving isoxazolylarylsulfochlorides [21]. In this case the carbon atom of the cyclopropane ring linked to the aryl substituent turns out to be the nearest reaction center for the nitrosation species, and at the realization of the SET-mechanism (Scheme 2) structure **B'** is the most stabilized intermediate favoring the direction of the attack of the nitrosation species on the benzyl position.

Therefore the performed research showed that the nitrosation of 2-aryl-1,1-dichlorocyclopropanes with the complex $NOCl·2SO_3$ in dichloromethane of the substrates containing acceptor susbstituents in the aromatic ring proceeds chemo- and regioselectively leading to the formation in high yields of 3-aryl-5-chloroisoxazoles. The transformation of 2-aryl-1,1-dichlorocyclopropanes with the substituents having positive electronic effect in the aromatic ring proceeds ambiguously. This was ratuionalized from the position of the theory of SET-mechanism. At the presence in the aromatic ring of donor substituents the selectivity of the reaction with respect to isoxazole can be increased by changing the solvent for a more polar one, e.g., acetonitrile.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were registered on spectrometers Varian XR-400 and Bruker Avance-400 (400 MHz) from solutions of compounds in $CDCl_3$ (internal reference HMDS). IR spectra were recorded on a spectrophotometer UR-20. Mass spectra were taken on a GC-MS instrument Finnigan MAT SSQ 7000, ionizing energy 70 eV, quartz column OV-1 (25 m), temperature programming as follows: 70°C (2 min), heating rate 20 deg/min, 280°C (10 min). Melting points were measured in open capillaries heated in a block. TLC was carried out on Silufol UV-254 plates, development under UV irradiation. All used solvents were purified and dried according to standard procedures [22].

High resolution mass spectra were registered on an instrument Bruker micrOTOF II by the method of electrospray ionization [23]. The measurements were performed on positive (voltage on the capillary 4500 V) or negative (voltage on the capillary 3200 V) ions. Range of mass scanning *m/z* 50–3000 Da, external and internal calibration (Electrospray Calibrant Solution, Fluka). The samples were admitted by a syringe as a solution in acetonitrile, methanol, or water, flow rate 3 μl/min. Spraying gas nitrogen (4 l/min), interface temperature 180°C.

2-Aryl-1,1-dichlorocyclopropanes **Ia–Ic, If–Ii** [24] were obtained by cyclopropanation of the appropriate alkenes with dichlorocarbene by Makosza reaction in keeping with procedure [25].

gem-Dihalonitrophenylcyclopropanes **Id, Ie** were obtained by nitration of *gem*-dichlorophenylcyclopropane with nitronium tetrafluoroborate in acetonitrile. To a slurry of 6.9 g (0.052 mol) of NO_2BF_4 in 50 ml of anhydrous acetonitrile at 0°C was added dropwise a solution of 9.35 g (0.05 mol) of 2-phenyl-1,1-dichlorocyclopropane in 10 ml of acetonitrile, then the mixture was stirred for 4 h at room temperature. The mixture was poured into 200 ml of water, the product was extracted into ethyl acetate (3 × 50 ml). The combined organic solutions were washed with water, dried with anhydrous Na_2SO_4, and evaporated. The isomeric nitro derivatives **Id, Ie** were separated by column chromatography on silica gel (Silica gel 40/100 μm, eluent EtOAc–petroleum

ether, 1 : 10). Characteristics of 2-(2-nitrophenyl)- and 2-(4-nitrophenyl)-1,1-dichlorocyclopropanes **Id, Ie** were consistent with the published data [26].

Nitrosation of *gem*-dichloroarylcyclopropanes with the complex $NOCl{\cdot}2SO_3$. General procedure. *a*. To a slurry of $NOCl{\cdot}2SO_3$ in 10 ml of dichloromethane at 20°C was added *gem*-dichloroarylcyclopropane in 2 ml of dichloromethane. The part of precipitate immediately dissolved, and the solvent turned colored. On the completion of the reaction (at equimolar reagents ratio the complex totally dissolved, at the excess of the nitrosation reagent, TLC monitoring) the reaction mixture was neutralized with the sodium carbonate solution and washed with water. The water solutions were extracted with dichloromethane (3 × 10 ml), the organic solutions were combined and dried with sodium sulfate. The solvent was evaporated, the residue was chromatographed on a column packed with silica gel.

b. To 1.5 mmol of $NOCl{\cdot}2SO_3$ was added 2.0–3.0 mmol of NOCl as a solution in 3–5 ml of anhydrous acetonitrile cooled to –20°C. The reagent partially or totally dissolved and the solvent turned deep red-brown. To the obtained solution at –20°C was added 1.0 mmol of *gem*-dichloroarylcyclopropane in 2 ml of anhydrous acetonitrile, the flask was tightly stoppered and maintained at 20°C for a desired time. At the completion of the reaction the mixture was neutralized with sodium carbonate solution and washed with water. The water solutions were extracted with ethyl actate (3 × 10 ml), the organic solutions were combined and dried with sodium sulfate. The solvent was evaporated, the residue was chromatographed on a column packed with silica gel (yields given in Table 2).

5-Chloro-3-(3-chlorophenyl)isoxazole (IIa). ^{1}H NMR spectrum, δ, ppm: 6.40 s (1H), 7.42 d (1H, ^3J 8.5 Hz), 7.46 t (1H, ^3J 8.5 Hz), 7.66 d (1H, ^3J 8.5 Hz), 7.77 s (1H).

3-(3-Bromophenyl)-5-chloroisoxazole (IIb). R_f 0.48 (EtOAc–petroleum ether, 1:10). ^{1}H NMR spectrum, δ, ppm: 6.48 s (1H), 7.34 t (1H, $H^5{}_{arom.}$, ^3J 7.9 Hz), 7.60 d.d.d (1H, $H^{4(6)}{}_{arom.}$, ^3J 7.9, ^4J 1.9, ^4J 1.0 Hz), 7.68 d.d.d (1H, $H^{6(4)}{}_{arom.}$, ^3J 7.9, ^4J 1.9, ^4J 1.0 Hz), 7.91 t (1H, $H^2{}_{arom.}$, ^4J 1.9 Hz). ^{13}C NMR spectrum, δ, ppm: 99.6 (C^4), 123.1 (CBr), 125.2 ($C_{arom.}$), 129.6 ($C_{arom.}$), 130.1 (CHt), 130.6 ($C_{arom.}$), 133.6 ($C_{arom.}$), 155.6 (C^5), 163.0 (C^3).

3-(3-Nitrophenyl)-5-chloroisoxazole (IIc). R_f 0.64 (EtOAc–petroleum ether, 1:5), mp 143°C (147°C [13]). IR spectrum (from film), ν, cm^{-1}: 1540, 1360 (NO_2). ^{1}H NMR spectrum, δ, ppm: 6.62 s (1H, H^4), 7.69 t (1H, $H^5{}_{arom.}$, ^3J 8.0 Hz), 8.15 d.t (1H, $H^{4(6)}{}_{arom.}$, ^3J 8.0, ^4J 1.2 Hz), 8.33 d.d.d (1H, $H^{6(4)}{}_{arom.}$, ^3J 8.0, ^4J 1.2, ^4J 2.0 Hz), 8.59 t (1H, $H^2{}_{arom.}$, ^4J 2.0 Hz). ^{13}C NMR spectrum, δ, ppm: 99.7 (C^4), 121.7 ($C_{arom.}$), 125.1 ($C_{arom.}$), 129.9 (CHt), 130.3 ($C_{arom.}$), 132.2 ($C_{arom.}$), 148.7 (CNO_2), 156.3 (C^5), 162.3 (C^3). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 224 (21), 189 (100) $[M - Cl]^+$, 143 (75) $[M - Cl - NO_2]^+$, 115 (14) $[M - Cl - NO_2 - CO]^+$, 88 (10), 76 (48), 63 (10), 50 (23), 28 (22). Found, %: C 48.21; H 2.34; N 12.31. $C_9H_5ClN_2O_3$. Calculated, %: C 48.11; H 2.23; N 12.47. *M* 224.60

3-(4-Nitrophenyl)-5-chloroisoxazole (IId). R_f 0.69 (EtOAc–petroleum ether, 1:5), mp. 170°C (169.9–171.3°C [13]). ^{1}H NMR spectrum, δ, ppm: 6.60 s (1H, H^4), 7.98 d ($2H_{arom.}$, ^3J 8.8 Hz), 8.36 d ($2H_{arom.}$, ^3J 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 99.9 (C^4), 124.3 (2CH), 127.6 (2CH), 134.1 (CHt), 149.1 (CNO_2), 156.4 (C^5), 162.3 (C^3).

3-(2-Nitrophenyl)-5-chloroisoxazole (IIe). R_f 0.38 (EtOAc–petroleum ether, 1:7). ^{1}H NMR spectrum, δ, ppm: 6.33 s (1H, H^4), 7.67–7.77 m ($3H_{arom.}$), 8.07 d ($1H_{arom.}$, ^3J 8.6 Hz). ^{13}C NMR spectrum, δ, ppm: 102.1 (C^4), 123.5 (CHt), 124.8 ($C_{arom.}$), 131.2 ($C_{arom.}$), 131.6 ($C_{arom.}$), 133.3 ($C_{arom.}$), 148.3 (CNO_2), 155.2 (C^5), 161.9 (C^3). Found, %: C 48.04; H 2.45; N 12.31. $C_9H_5ClN_2O_3$. Calculated, %: C 48.11; H 2.23; N 12.47.

3-(4-Chlorophenyl)-5-chloroisoxazole (IIf). R_f 0.71 (EtOAc – petroleum ether, 1:5), mp 107°C (106–107°C [27]). ^{1}H NMR spectrum, δ, ppm: 6.46 s (1H, H^4), 7.43 d ($2H_{arom.}$, ^3J 8.3 Hz), 7.69 d ($2H_{arom.}$, ^3J 8.3 Hz). ^{13}C NMR spectrum, δ, ppm: 99.5 (C^4), 126.6 (CHt), 127.9 ($2C_{arom.}$), 129.3 ($2C_{arom.}$), 136.7 (CCl), 155.4 (C^5), 163.2 (C^3). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 213 (48), 178 (100) $[M - Cl]^+$, 150 (60) $[M - Cl - CO]^+$, 123 (20) $[M - Cl - CO - HCN]^+$, 111 (20) $[C_6H_4Cl]^+$, 75 (23) $[C_6H_3]^+$. $C_9H_5Cl_2NO$. Calculated *M* 213.08.

3-(4-Bromophenyl)-5-chloroisoxazole (IIg). R_f 0.55 (EtOAc–petroleum ether, 1:5), mp 108°C. ^{1}H NMR spectrum, δ, ppm: 6.48 s (1H, H^4), 7.63 d ($2H_{arom.}$, ^3J 8.8 Hz), 7.66 d ($2H_{arom.}$, ^3J 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 99.5 (C^4), 125.0 (CBr), 127.1 (CHt), 128.1 ($2C_{arom.}$), 132.3 ($2C_{arom.}$), 155.5 (C^5), 163.3 (C^3). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 257, 259 (33), 222, 224 (100) $[M - Cl]^+$, 194, 196 (40) $[M - Cl - CO]^+$, 154, 156 (16) $[M - C_3H_2NOCl]^+ = [C_6H_3Br]^+$, 115 (49) $[C_6H_4C_2HN]^+$, 102 (34) $[C_6H_4CN]^+$, 88 (29) $[C_6H_4C]^+$, 75 (76) $[C_6H_3]^+$, 63 (41) $[C_5H_3]^+$, 50 (83) $[C_4H_2]^+$. $C_9H_5BrClNO$. Calculated

M 258.50.

3-Phenyl-5-chloroisoxazole (IIh). R_f 0.63 (EtOAc–petroleum ether, 1:10), mp 47–48°C (46–48°C [27]). ^{1}H NMR spectrum, δ, ppm: 6.45 s (H^4), 7.45 m ($3H_{arom.}$), 7.75 m ($2H_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 99.6 (C^4), 126.6 ($2C_{arom.}$), 128.2 (CHt), 129.0 ($2C_{arom.}$), 130.6 ($C^4_{arom.}$), 155.1 (C^5), 164.2 (C^3).

3-(4-Methylphenyl)-5-chloroisoxazole (IIi). ^{1}H NMR spectrum, δ, ppm: 2.43 s (3H, CH_3), 6.48 s (1H, H^4), 7.30 d ($2H_{arom.}$, ^3J 7.9 Hz), 7.68 d ($2H_{arom.}$, ^3J 7.9 Hz). ^{13}C NMR spectrum, δ, ppm: 21.4 (CH_3), 99.5 (C^4), 125.3 (CHt), 126.5 ($2C_{arom.}$), 129.7 ($2C_{arom.}$), 140.9 ($C^4_{arom.}$), 154.9 (C^5), 164.2 (C^3).

1-(4-Chlorophenyl)-3,3-dichloroprop-2-en-1-one oxime (IIIf). R_f 0.80 (EtOAc–petroleum ether, 1 : 1), mp 102–104°C. IR spectrum (mull in mineral oil), ν, cm^{-1}: 3400–3200 (OH), 1670 (C=N), 1600 (C=C), 1550 and 1500 ($C_{arom.}$). ^{1}H NMR spectrum, δ, ppm: 6.50 s (1H, H^2), 7.29 d ($2H_{arom.}$, ^3J 8.7 Hz), 7.50 d ($2H_{arom.}$, ^3J 8.7 Hz), 8.01 br.s (1H, OH). ^{13}C NMR spectrum, δ, ppm: 121.4 ($2C_{arom.}$), 122.9 (H<u>C</u>=CCl_2), 129.1 ($2C_{arom.}$), 130.1 ($C^4_{arom.}$), 133.7 (=CCl_2), 135.7 ($C^1_{arom.}$), 160.0 (C=NOH). Found $[M + H]^+$ 249.9590. $C_9H_6Cl_3NO$. Calculated *M* 248.9588.

1-(4-Bromophenyl)-3,3-dichloroprop-2-en-1-one oxime (IIIg), isomers mixture by GC-MS data, R_f 0.28 (EtOAc–petroleum ether эфandp, 1:5), mp. 128°C. IR spectrum, ν, cm^{-1}: 3500–3100 (OH), 1680 (C=N), 1510, 1580. ^{1}H NMR spectrum, δ, ppm: 6.49 s (1H, CH=CCl_2), 7.45 br.s ($4H_{arom.}$), 7.83 br.s (1H, OH). ^{13}C NMR spectrum, δ, ppm: 117.8 ($C^4_{arom.}$, Br), 121.7 ($2C_{arom.}$), 123.0 (H<u>C</u>=CCl_2), 132.1 ($2C_{arom.}$), 133.6 (=CCl_2), 136.2 ($C^1_{arom.}$), 159.8 (C=NOH). Mass spectrum, *m/z* (I_{rel}, %): 293, 295 (22) $[M]^+$, 171, 173 (100) $[M - Cl_2C{=}CH{-}CH{=}N]^+$, 123 (60) $[Cl_2C{=}CH{-}CH{=}NH]^+$, 63 (31) $[C_5H_3]^+$. Found, %: C 36.75; H 1.99; N 4.79. $C_9H_6BrCl_2NO$. Calculated, %: C 36.60; H 2.03; N 4.75. *M* 294.96.

1,1,5,5-Tetrachloro-3-(4-chlorophenyl)penta-1,4-diene (IVf). R_f 0.77 (ethyl acetate–petroleum ether, 1:10). IR spectrum (from film), ν, cm^{-1}: 3050–2870, 1620 (C=C), 1490 ($C_{arom.}$), 1100, 1025, 915, 870, 840. ^{1}H NMR spectrum, δ, ppm: 4.80 t (1H, ^3J 9.4 Hz), 5.99 d (2H, ^3J 9.4 Hz), 7.16 d ($2H_{arom.}$, ^3J 8.5 Hz), 7.35 d ($2H_{arom.}$, ^3J 8.5 Hz). ^{13}C NMR spectrum, δ, ppm: 45.5 (CH), 123.6 ($2CCl_2$), 128.1 ($2C_{arom.}$), 128.4 ($2C_{arom.}$), 129.2 (2CH=), 130.7 ($C^4_{arom.}$Cl), 137.5 ($C^1_{arom.}$). Mass spectrum, *m/z* (I_{rel}, %): 316 (3) $[M]^+$·, 279 (35) $[M - Cl]^+$, 243(60) $[M - Cl - HCl]^+$, 219 (25) $[M - CH{=}CCl_2]^+$, 209 (22) $[M - 3Cl]^+$, 187 (100), 183 (60) $[M - CH{=}CCl_2 - HCl]^+$, 173 (12) $[M - 3Cl - HCl]^+$, 149 (35) $[M - CH{=}CCl_2 - 2Cl]^+$, 86 (50), 84 (70). $C_{11}H_7Cl_5$. Calculated *M* 316.43.

3-(4-Bromophenyl)-1,1,5,5-tetrachloropenta-1,4-diene (IVg). R_f 0.65 (petroleum ether). ^{1}H NMR spectrum, δ, ppm: 4.79 t (1H, ^3J 9.5 Hz), 5.99 d (2H, ^3J 9.5 Hz), 7.10 d ($2H_{arom.}$, ^3J 8.2 Hz), 7.49 d ($2H_{arom.}$, ^3J 8.2 Hz). ^{13}C NMR spectrum, δ, ppm: 45.6 (CH), 121.5 (CBr), 123.7 ($2CCl_2$), 128.0 ($2C_{arom.}$), 128.8 ($2C_{arom.}$), 132.2 (2CH=), 138.0 ($C^1_{arom.}$). Mass spectrum, *m/z* (I_{rel}, %): 360 (30) $[M]^+$·, 323 (25) $[M - Cl]^+$, 287 (12) $[M - Cl - HCl]^+$, 244 (40), 205 (100), 203 (80) $[M - C_6H_4Br]^+$, 149 (35), 74 (18). Found, %: C 36.41; H 2.06. $C_{11}H_7CrCl_4$. Calculated, %: C 36.57; H 1.94. *M* 360.89.

3-Phenyl-1,1,5,5-tetrachloropenta-1,4-diene (IVh). R_f 0.61 (petroleum ether). ^{1}H NMR spectrum, δ, ppm: 4.85 t (1H, ^3J 9.6 Hz), 6.05 d (2H, ^3J 9.6 Hz), 7.25– 7.39 m ($5H_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 46.1 (CH), 123.1 ($2CCl_2$), 127.1 ($2C_{arom.}$), 127.5 ($C^4H_{arom.}$), 128.6 ($2C_{arom.}$), 129.1 (2CH=), 139.1 ($C^1_{arom.}$). Mass spectrum, *m/z* (I_{rel}, %): 281 (8) $[M]^+$·, 247 (100), 245 (88) $[M - Cl]^+$, 209 (68) $[M - Cl - HCl]^+$, 175 (40) $[M - 3Cl]^+$, 148 (73), 139 (28) $[M - 3Cl - HCl]^+$, 125 (56), 115 (70) $[M - 2Cl - C{=}CCl_2]^+$, 75 (35), 62 (37), 51 (38). $C_{11}H_8Cl_4$. Calculated *M* 281.99.

4-Bromocinnamic acid (VI). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.57 d (1H, CH=, ^3J 16.1 Hz), 7.57 d (1H, CH=, ^3J 16.1 Hz), 7.61 d ($2H_{arom.}$, ^3J 8.5 Hz), 7.67 d ($2H_{arom.}$, ^3J 8.5 Hz), 12.40 br.s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 120.6 (CH=), 124.0 (C^4Br), 130.6 ($2C_{arom.}$), 132.3 ($2C_{arom.}$), 134.0 (C^1), 143.1 (CH=), 167.9 (COOH) [28].

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