gem-Dichloro(alkyl)cyclopropanes in reactions with $NOCl \cdot 2SO_3$: synthesis of alkyl-5-chloroisoxazoles

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Nitrosation of *gem*-dichloro(alkyl)cyclopropanes with the complex $NOCl \cdot 2SO_3$ gave regioisomeric alkyl-5-chloroisoxazoles in high yields; a similar reaction with 1,2-bis(*gem*-dichlorocyclopropyl)ethane afforded the corresponding bis(5-chloroisoxazoles). The reactivities of *gem*-dichlorobicyclo[n.1.0]alkanes depend on their spatial structures, sharply decreasing with an increase in the number of the methylene units in the bicyclic molecule.

Key words: *gem*-dichloro(alkyl)cyclopropanes, nitrosation, the complex $NOCl \cdot 2SO_3$, alkyl-5-chloroisoxazoles, synthesis.

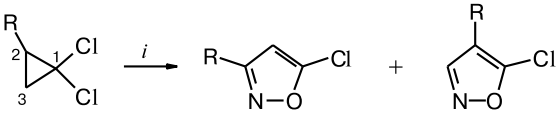
Addition of carbenes to olefins is a common route to cyclopropanes.[1] Generation of dihalocarbenes under the conditions of phase-transfer catalysis with their subsequent cycloaddition to olefins has offered a nearly complete solution of the problem of cyclopropane ring formation.[2] Considerable achievements in this area of organic chemistry have been made by involving various olefins (including structurally exotic ones[2,3]) in this reaction, which substantially extended its synthetic scope. As a result, a large number of various *gem*-dihalocyclopropanes are available for organic chemists. At present, the study of their chemical properties for comprehensive use of their synthetic potential in organic synthesis is a problem of prime importance. *gem*-Dihalocyclopropanes have been employed[3] as starting materials for the synthesis of both cyclopropane derivatives and organic compounds of other classes by means of transformation of the cyclopropane ring. For instance, it has been reported[4] that *gem*-dihalo(aryl)cyclopropanes react with nitrosonium tetrafluoroborate to give isoxazoles. However, the possibility of obtaining isoxazoles from *gem*-dihalo(alkyl)cyclopropanes has been demonstrated only with 7,7-dichloronorcarane as an example; the yield of the corresponding isoxazole was 43%.

Taking into account that various *gem*-dihalocyclopropanes are easily accessible and that isoxazoles are of practical value as compounds with a broad spectrum of biological activity, we studied the nitrosation of *gem*-dichloro(alkyl)cyclopropanes under the action of $NOCl \cdot 2SO_3$. Earlier,[5,6] this complex has been successfully employed for the synthesis of isoxazolines from arylcyclopropanes.

The objects of our present study included cyclopropanes and biscyclopropanes containing a linear alkyl substituent and a number of bi- and tricycloalkanes containing one or two three-membered rings.

We found that 2-(*n*-butyl)-1,1-dichloro- (**1a**) and 1,1-dichloro-2-(*n*-hexyl)cyclopropanes (**1b**) react with $NOCl \cdot 2SO_3$ in CH_2Cl_2 with a 100% conversion to give mixtures of isomeric 3-alkyl- (**2a,b**) and 4-alkyl-5-chloroisoxazoles (**3a,b**) in high yields (**2a** : **3a** = 1 : 1.5; **2b** : **3b** = = 1 : 1.2) (Scheme 1). The first step of this transformation is an electrophilic attack of the nitrosating agent at the cyclopropane ring with cleavage of one of its bonds.[4,6]

Scheme 1



1a,b **2a,b** **3a,b**

2a : **3a** = 1 : 1.5 (90%)
2b : **3b** = 1 : 1.2 (77%)

R = Bu^n (**a**), *n*-C_6H_{13} (**b**)
i. $NOCl \cdot 2SO_3$, CH_2Cl_2.

Regioisomers **2a** and **3a** and regioisomers **2b** and **3b** were separated by column chromatography and characterized using ^1H and ^{13}C NMR spectroscopy and mass

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Table 1. ^{13}C NMR spectra ($CDCl_3$) of substituted 5-chloroisoxazoles

Compound	δ			
	C(3)	C(4)	C(5)	The other C atoms
2a	165.9	100.8	154.2	13.7 (Me), 22.2 (CH_2), 26.1 (CH_2), 30.0 (CH_2)
2b	166.3	101.0	154.2	14.0 (Me), 22.5 (CH_2), 26.4 (CH_2), 27.9 (CH_2), 28.7 (CH_2), 31.4 (CH_2)
3a	152.5	113.9	150.8	13.7 (Me), 21.7 (CH_2), 22.1 (CH_2), 31.2 (CH_2)
3b	152.8	114.1	150.8	14.0 (Me), 22.0 (CH_2), 22.5 (CH_2), 28.6 (CH_2), 29.0 (CH_2), 31.4 (CH_2)
5	164.9	101.2	154.7	25.5 (CH_2), 26.7 (CH_2), 28.6 (CH_2), 29.8 (CH), 60.8 (CCl_2)
6	152.7	112.9	151.5	21.2 (CH_2), 26.6 (CH_2), 29.8 (CH), 29.9 (CH_2), 60.7 (CCl_2)
7	164.2	101.2	152.6	24.5 (2 CH_2)
8*	164.0 (RC=N)	101.1 (=CH)	155.1	20.3 (CH_2), 26.0 (CH_2)
	152.6 (HC=N)	112.2 (=CR)	152.4	
9	152.4	112.0	151.9	21.9 (2 CH_2)
11a	176.1	119.6	145.1	21.4 (CH_2), 24.4 (CH_2), 30.5 (CH_2)
11b	162.7	110.0	148.7	18.5 (CH_2), 21.9 (CH_2) 22.0 (2 CH_2)
11c	167.0	114.8	149.3	23.5 (CH_2), 27.0 (CH_2), 27.9 (CH_2), 28.3 (CH_2), 31.8 (CH_2)
14	164.7	112.8	151.4	19.6 (CH_2), 22.9 (CH_2), 23.5 (CH_2), 23.7 (CH_2), 33.1 (CH), 33.3 (CH), 64.6 (CCl_2)

* For assignment of the signals for the quaternary C atoms in isomer **8**, the δ_C values of the isoxazole ring in compounds **2**, **3**, **7**, and **9** were taken into account.

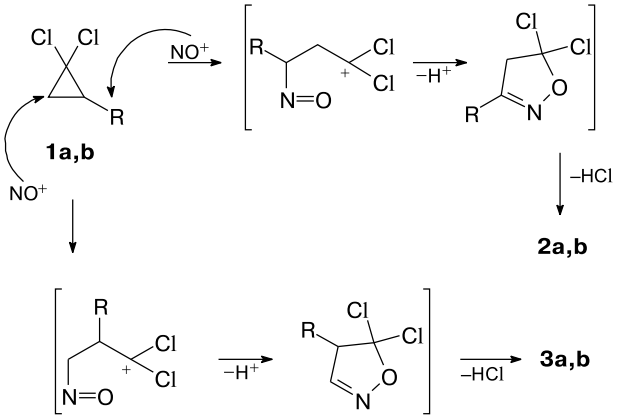
spectrometry. The structure of the isomers was determined and the signals for the isomers were assigned from the ^1H and ^{13}C NMR spectra (Table 1).

For instance, in the ^1H NMR spectrum of isoxazole **2a**, the signal for the H atom of the heterocycle (CH=CCl) appears at δ 6.02. The ^{13}C NMR spectrum contains signals for the C(4), C(5), and C(3) atoms of the isoxazole ring at δ 100.8, 154.2, and 165.9, respectively (see Table 1). In addition, the two lower-field signals are quaternary; this confirms the attachment of the *n*-butyl substituent to the C(3) atom of the heterocycle.

The ^1H NMR spectrum of isomer **3a** shows a signal for the H atom of the heterocycle (HC=N) at δ 8.15; in the ^{13}C NMR spectrum, the signals for the C(4), C(5), and C(3) atoms of the isoxazole ring appear at δ 113.9, 150.8, and 152.5, respectively. Since the signal for the C(4) atom is quaternary, the butyl substituent is attached to this atom. Note that the signals attributed to the C(4) and C(3) atoms in isomer **3a** are shifted downfield and upfield, respectively, by 13 ppm compared to those for isomer **2a**.

Thus, the nitrosation of 2-alkyl-1,1-dichlorocyclopropanes **1a,b** with $NOCl \cdot 2SO_3$ is not regioselective, yielding isomeric 5-chloroisoxazoles **2a,b** and **3a,b**. An attack of the electrophilic species NO^+ results in cleavage of both the C(1)—C(2) and C(1)—C(3) bonds of the cyclopropane ring. The latter pathway is slightly preferred, which follows from the somewhat higher fractions of C(3)-unsubstituted isoxazoles **3a,b** in mixtures with their isomers **2a,b**; *i.e.*, the nitrosonium cation preferably attacks the more sterically accessible site of the cyclopropane ring (Scheme 2).

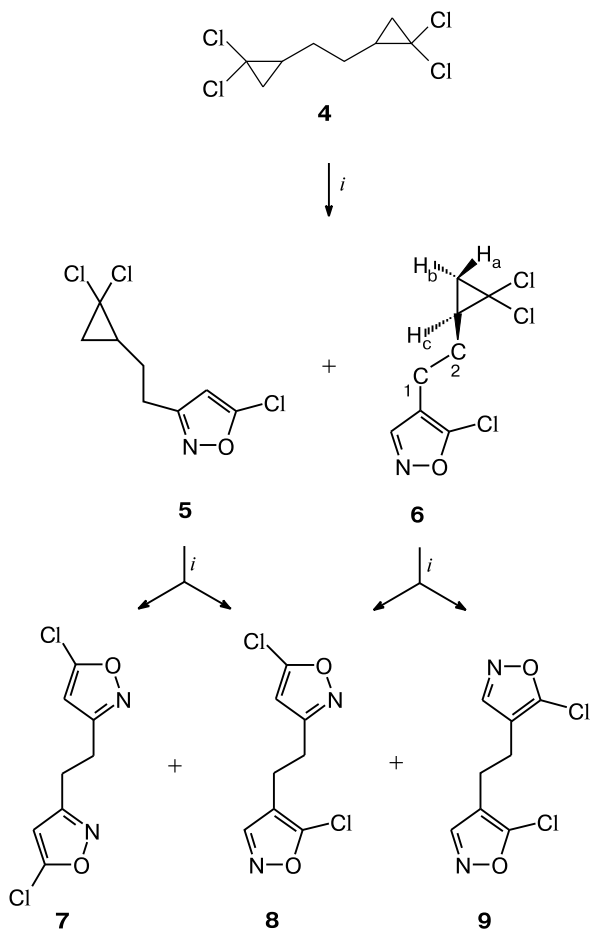
Scheme 2



We also studied nitrosation of 1,2-bis(2,2-dichlorocyclopropyl)ethane (**4**) with $NOCl \cdot 2SO_3$ and found that the reaction proceeds through the opening of one or both of the cyclopropane rings and affords isomeric mono- (**5**, **6**) and bisisoxazoles (**7**—**9**) in a total yield of 85% (Scheme 3).

The isoxazoles were separated by column chromatography on silica gel; their structures were determined using ^1H and ^{13}C NMR spectroscopy. The signals for the protons of the cyclopropane ring in isomer **6** were assigned

Scheme 3



i. $NOCl \cdot 2SO_3$, CH_2Cl_2.

from the coupling constants found in a selective homodecoupling experiment with irradiation of the ^1H NMR signals at δ 1.13, 1.83, and 2.64 (see Experimental).

Note that the ratio of mono- (**5**, **6**) and dinitrosation products (**7**—**9**) depends on the ratio of the starting reagents. For instance, when the molar ratio **4** : $NOCl \cdot 2SO_3$ is 1 : 2 (20 °C, 24 h), the ratio of the isoxazoles in the final mixture is **5** : **6** : **7** : **8** : **9** = 34 : 27 : 5 : 19 : 15 (^1H NMR); compound **4** (9%) is recovered. For **4** : $NOCl \cdot 2SO_3$ = 1 : 4 (20 °C, 120 h), the ratio of the same isoxazoles is 26 : 7 : 11 : 32 : 24. Note that isomers **7** and **9** can be obtained only from isoxazoles **5** and **6**, respectively, while isomer **8** can be a product from both.

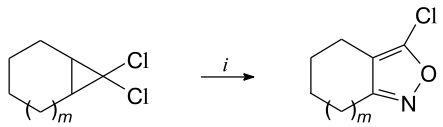
Cyclopropylethylisoxazoles **5** and **6** were isolated in the individual state by column chromatography. Their reactions with an excess of $NOCl \cdot 2SO_3$ gave bisisoxazoles **7** and **8** (from **5**) and **8** and **9** (from **6**) in quantitative yields: **7** : **8** = 1.4 : 1 and **8** : **9** = 1 : 0.8 (^1H NMR).

An analysis of the isomer ratios in mixtures of isoxazoles **5**—**9**, as well as the preferential formation of 4-alkyl-5-chloroisoxazoles (isomers **3a,b**, see Scheme 1), suggests that bisisoxazole **8** is mainly obtained from isomer **6** (*i.e.*, the latter is more reactive than isomer **5**).

However, the presence of one isoxazole ring generally does not prevent the formation of the second ring in compounds **7**—**9**.

We studied nitrosation of polycyclic *gem*-dichlorocyclopropanes with *gem*-dichlorobicyclo[n.1.0]alkanes as examples. We found that the nitrosation of bicycloalkanes **10a**—**d** gives 5-chloro-3,4-cycloalkylisoxazoles **11a**—**d**. The yields of the isoxazoles from 6,6-dichlorobicyclo[3.1.0]hexane **10a** and 7,7-dichlorobicyclo[4.1.0]heptane **10b** are high, though noticeably decreasing with an increase in the number of methylene units in the starting bicycloalkane (Scheme 4).

Scheme 4

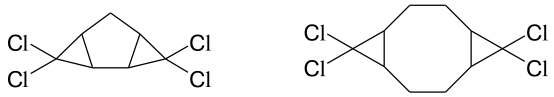


i. $NOCl \cdot 2SO_4$, CH_2Cl.

Compound **10,11**	*m*	Yield (%) of compound **11**
a	0	90
b	1	70
c	2	30
d	3	10

The yield of isoxazole **11c** from 8,8-dichlorobicyclo[5.1.0]octane **10c** was 30%; the unreacted residue of compound **10c** was recovered intact. Cyclopropane **10c** was also inert under other reaction conditions ($NOCl \cdot 2SO_3$, CH_3NO_2, 20 °C, 24 h or $NOBF_4$, CH_3CN, 20 °C, 24 h). In the case of 9,9-dichlorobicyclo[6.1.0]nonane **10d**, the yield of isoxazole **11d** was only 10%; however, the consumption of compound **10d** was considerable (up to 50%).

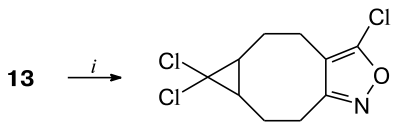
The possibility of the formation of two isoxazole fragments in one molecule prompted us to study the nitrosation of tricycloalkanes **12** and **13**.



Insofar as bicyclohexane **10a** is very highly reactive, 3,3,7,7-tetrachlorotricyclo[4.1.0.$0^{2,4}$]heptane (**12**) could be expected to be also reactive in nitrosation. However, the latter was inert under standard reaction conditions ($NOCl \cdot 2SO_3$, CH_2Cl_2, 20 °C, 24 h). Nor did it react with $NOCl \cdot 2SO_3$ in boiling CH_2Cl_2 or chloroform for 8 and 70 h, respectively; compound **12** was fully recovered from the reaction mixture.

5,5,10,10-Tetrachlorotricyclo[7.1.0.0^{4,6}]decane (**13**) as a 9 : 1 mixture of *cis*- and *trans*-isomers (^{1}H NMR) was kept with a twofold excess of $NOCl \cdot 2SO_3$ in CH_2Cl_2 at 25—30 °C for five days. The degree of its conversion into isoxazole **14** was 75% (^{1}H NMR), only one cyclopropane ring being involved (Scheme 5). The starting compound **13** was recovered in 15% yield (*cis* : *trans* = 1 : 2). By extending the reaction time to 55 days, we produced no effect on the composition of the reaction mixture or the yield of isoxazole **14**.

Scheme 5



14 (75%)

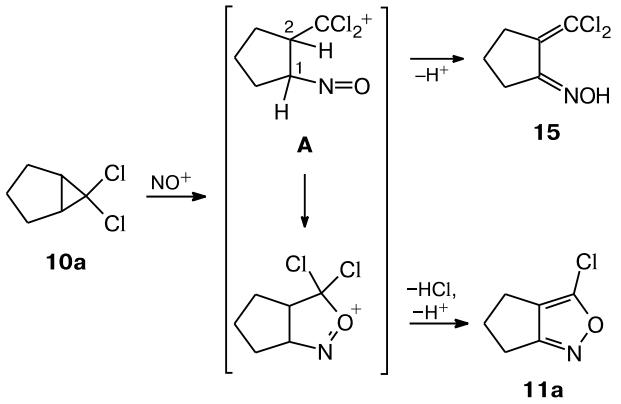
i. $NOCl \cdot 2SO_3$ (2 equiv.), CH_2Cl_2, 25—30 °C, 5 days.

The lower reactivities of tricyclo- (**12**, **13**) and some bicycloalkanes (**10c,d**) are probably due to their spatial structures. Tricycloheptane **12** obtained from cyclopentadiene by the Makosza reaction is known to exist as one stereoisomer with the *anti*-configuration of the cyclopropane rings*. Apparently, the *anti*-arrangement of the cyclopropane fragments additionally shielded by the Cl atoms makes the reactive site less accessible for the nitrosating agent. As for tricyclodecane **13**, it has been reported[9] to be a 3 : 1 mixture of *cis*- and *trans*-isomers.

The steric factor may be another plausible reason for the lower reactivities of larger bicycloalkanes **10c**,**d**. Apparently, the molecule takes the most favorable conformation, in which the reactive site (the cyclopropane ring) is shielded by the carbon framework.

Note that the opening of the cyclopropane ring in bicyclo[n.1.0]alkanes can occur by cleavage of both the exocyclic and endocyclic C—C bonds. It is known that the decrease in the number *n* of methylene units in bicyclo[n.1.0]alkanes makes the endocyclic bond more liable to cleavage because of increased strain in the molecule; this reaction pathway usually becomes appreciable for bicyclo[3.1.0]hexane.[10—13] In our case, the nitrosation of bicycloalkanes was regioselective, with cleavage of the exocyclic bond only. The intermediate cation **A** (Scheme 6) can be stabilized either by cyclization that results from a nucleophilic attack of the O atom of the nitroso group and finally leads to isoxazole **11a** or by abstraction of the C(2)H proton with simultaneous isomerization of the nitroso group into an oxime one. Indeed, in the case of bicyclohexane **10a**, we isolated unsaturated oxime **15** in 5% yield; its structure and molecular formula were determined from ^{1}H and ^{13}C NMR, IR, and mass spectra and elemental analysis data.

Scheme 6



To sum up, we demonstrated that the nitrosation of 2-alkyl-1,1-dichlorocyclopropanes with $NOCl \cdot 2SO_3$ affords regioisomeric 3- and 4-alkyl-5-chloroisoxazoles in high yields; bis(5-chloroisoxazolyl) derivatives were obtained from 1,2-bis(dichlorocyclopropyl)ethane. The nitrosation of *gem*-dichlorobi- and -tricycloalkanes containing the cyclopropane ring is regioselective; however, the yields of the resulting isoxazoles largely depend on the spatial structure of the substrate molecule.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on Varian-XR-400 and Bruker Avance-400 instruments (400 (^{1}H) and 100 MHz (^{13}C)) in $CDCl_3$ with HMDS as the internal standard. IR spectra were recorded on a UR-20 instrument (Nujol or thin film). Mass spectra were measured on a Finnigan MAT SSQ 7000 GC-MS spectrometer (ionizing energy 70 eV, OV-1 quartz capillary column (25 m), programmed temperature rise from 70 °C (2 min) to 280 °C (10 min) at a heating rate of 20 deg min^{-1}) and a Finnigan MAT ITD-700 GC-MS spectrometer (Varian 3400 chromatograph, HP-101 quartz capillary column (25 m), programmed temperature rise from 80 °C (1 min) to 290 °C (10 min) at a heating rate of 10 deg min^{-1}). For chlorine-containing ions, the *m*/*z* ratios are cited for the ^{35}Cl isotope. Melting points were determined in open capillaries placed on a heating block. The course of the reactions was monitored, and the purity of the compounds was checked, by TLC on Silufol-UV plates; spots were visualized under UV light. All the solvents used were purified and dehydrated according to standard procedures.[14]

gem-Dichlorocyclopropanes (**1a,b**, **4**, **10a—d**, **12**, and **13**) were prepared from appropriate alkenes by the Makosza reaction.[8] Their physicochemical constants agree with the literature data.[8,9,15—17] The ^{1}H and ^{13}C NMR spectra of the starting reagents that are unavailable from the literature are given in Table 2. The ^{13}C NMR spectra of the 5-chloroisoxazoles obtained are given in Table 1.

* The spectroscopic characteristics of compound **12** are in full agreement with the literature data.[7,8]

Table 2. ^{1}H and ^{13}C NMR spectra ($CDCl_3$) of compounds **1a,b**, **10a—d**, and **13***

Compound	NMR, δ (*J*/Hz)	
	^{1}H	^{13}C
1a	0.96 (t, 3 H, Me, ^3J = 7.0); 1.06 (dist.t, 1 H, ^3J = 4.4); 1.42 (quint, 2 H, CH_2, ^3J = 7.0); 1.45—1.65 (m, 6 H)	14.1 (Me), 22.4 (CH_2), 26.8 (CH_2), 30.1 (CH), 30.81 (CH_2), 30.84 (CH_2), 61.5 (CCl_2)
1b	0.92 (t, 3 H, Me, ^3J = 6.8); 1.05 (m, 1 H); 1.33 (m, 6 H, 3 CH_2); 1.44—1.64 (m, 6 H)	14.1 (Me), 22.6 (CH_2), 26.8 (CH_2), 28.6 (CH_2), 29.0, 30.4 (CH_2), 30.9, 31.8, 61.6 (CCl_2)
10a	1.63—1.80 (m, 2 H); 1.95—2.10 (m, 4 H); 2.10—2.13 (m, 2 H)	25.1 (CH_2), 27.7 (2 CH_2), 38.2 (2 CH), 68.2 (CCl_2)
10b	1.22 (m, 2 H); 1.34 (m, 2 H); 1.63—1.76 (m, 4 H); 1.96 (m, 2 H)	18.9 (2 CH_2), 20.2 (2 CH_2), 25.8 (2 CH), 67.4 (CCl_2)
10c	1.10—1.40 (m, 5 H); 1.66 (m, 2 H); 1.82 (m, 2 H); 1.90 (dm, 1 H, ^2J = 13.5); 2.15 (m, 1 H); 2.19 (m, 1 H)	26.5 (2 CH_2), 28.3 (2 CH_2), 32.3 (2 CH), 33.9 (CH_2), 68.2 (CCl_2)
10d	1.22 (m, 2 H); 1.34—1.52 (m, 6 H); 1.55—1.71 (m, 4 H); 2.05 (dm, 2 H, ^2J = 14.1)	23.2 (2 CH_2), 26.3 (2 CH_2), 28.0 (2 CH), 32.4 (2 CH_2), 65.2 (CCl_2)
13-*cis*	1.63 (m, 4 H); 1.74 (m, 4 H); 2.21 (m, 4 H)	21.3 (4 CH_2), 31.0 (4 CH), 66.0 (CCl_2)
13-*trans*	1.25 (m, 4 H); 1.73 (m, 4 H); 2.30 (m, 4 H)	21.9 (4 CH_2), 34.4 (4 CH), 65.3 (CCl_2)

* The ^{1}H and ^{13}C NMR spectra of compounds **4**, **12**, and *cis*-**13** have been cited in Refs 8 and 9.

Nitrosation of *gem*-dichlorocyclopropanes with the complex $NOCl \cdot 2SO_3$ (general procedure). An appropriate *gem*-dichlorocyclopropane (1.0 mmol) in CH_2Cl_2 (2 mL) was added at 20 °C to a suspension of $NOCl \cdot 2SO_3$ (1.2—1.5 mmol*) in CH_2Cl_2 (10 mL). The reaction mixture was stirred for 24 h, neutralized with $NaHCO_3$, and washed with water. Organic material was extracted from the aqueous fractions with CH_2Cl_2 (3×10 mL). The organic extracts were combined, dried with Na_2SO_4, and concentrated. The products were isolated by column chromatography on SiO_2 (40—100 μm, AcOEt—light petroleum as an eluent).

3-*n*-Butyl-5-chloroisoxazole (2a). Yield 36%, colorless oil with a pungent odor. R_f 0.60 (AcOEt—light petroleum, 1 : 15). ^{1}H NMR, δ: 0.97 (t, 3 H, Me, ^3J = 7.4 Hz); 1.42 (sextet, 2 H, CH_2, ^3J = 7.4 Hz); 1.65 (quint, 2 H, CH_2, ^3J = 7.6 Hz); 2.66 (t, 2 H, CH_2, ^3J = 7.6 Hz); 6.02 (s, 1 H, CH=). MS, *m/z* (I_{rel} (%)): 159 $[M]^{+\cdot}$ (1), 144 $[M - Me]^+$ (0.6), 130 $[M - Et]^+$ (13), 124 $[M - Cl]^+$ (25), 117 $[M - C_3H_6]^+$ (100), 96 $[M - Cl - Et]^+$ (13), 82 $[M - Cl - C_3H_6]^+$ (15), 68 $[C_3H_2NO]^+$ (40), 55 (20), 44 (42), 41 (75).

4-*n*-Butyl-5-chloroisoxazole (3a). Yield 54%, colorless oil with a pungent odor. R_f 0.40 (AcOEt—light petroleum, 1 : 15). ^{1}H NMR, δ: 0.97 (t, 3 H, Me, ^3J = 7.4 Hz); 1.38 (sextet, 2 H, CH_2, ^3J = 7.4 Hz); 1.57 (quint, 2 H, CH_2, ^3J = 7.6 Hz); 2.40 (t, 2 H, CH_2, ^3J = 7.6 Hz); 8.15 (s, 1 H, CH=). MS, *m/z* (I_{rel} (%)): 159 $[M]^{+\cdot}$ (39), 144 $[M - Me]^+$ (3), 130 $[M - Et]^+$ (23), 124 $[M - Cl]^+$ (57), 116 $[M - Pr]^+$ (100), 96 $[M - Cl - Et]^+$ (33), 82 $[M - Cl - C_3H_6]^+$ (18), 68 $[C_3H_2NO]^+$ (18), 55 (24), 41 (38). **2a + 3a**. Found (%): C, 52.72; H, 6.22; N, 8.62. $C_7H_{10}ClNO$. Calculated (%): C, 52.66; H, 6.27; N, 8.78.

5-Chloro-3-*n*-hexylisoxazole (2b). Yield 35%, colorless oil with a pungent odor. R_f 0.74 (AcOEt—light petroleum, 1 : 10). ^{1}H NMR, δ: 0.90 (dist.t, 3 H, Me, ^3J = 6.8 Hz); 1.28—1.42 (m, 6 H, 3 CH_2); 1.65 (quint, 2 H, CH_2, ^3J = 7.6 Hz); 2.64 (t, 2 H, CH_2, ^3J = 7.6 Hz); 6.03 (s, 1 H, CH=). MS, *m/z* (I_{rel} (%)): 188 $[M + H]^+$ (100), 152 $[M - Cl]^+$ (24), 130 $[M - Bu^n]^+$ (4), 117 $[M + H - Am^n]^+$ (22), 108 (4), 96 $[M + H - Cl - Bu^n]^+$ (11), 82 (15), 68 (7), 55 (11).

5-Chloro-4-*n*-hexylisoxazole (3b). Yield 42%, colorless oil with a pungent odor. R_f 0.55 (AcOEt—light petroleum, 1 : 10). ^{1}H NMR, δ: 0.89 (dist.t, 3 H, Me, ^3J = 6.9 Hz); 1.30 (m, 6 H, 3 CH_2); 1.55 (quint, 2 H, CH_2, ^3J = 7.6 Hz); 2.38 (t, 2 H, CH_2, ^3J = 7.6 Hz); 8.16 (s, 1 H, CH=). MS, *m/z* (I_{rel} (%)): 188 $[M + H]^+$ (100), 152 $[M - Cl]^+$ (37), 124 (13), 116 $[M - Am^n]^+$ (10), 95 $[M - Cl - Bu^n]^+$ (25), 82 (35), 67 (18), 55 (50). **2b + 3b**. Found (%): C, 57.65; H, 7.54; N, 7.67. $C_9H_{14}ClNO$. Calculated (%): C, 57.60; H, 7.47; N, 7.47.

5-Chloro-3-[2-(2,2-dichlorocycloprop-1-yl)ethyl]isoxazole (5). Yield 22%, colorless oil. R_f 0.69 (AcOEt—light petroleum, 1 : 6). ^{1}H NMR, δ: 1.14 (m, 1 H); 1.65 (m, 2 H); 1.94 (m, 2 H, CH_2); 2.85 (dt, 1 H, CH_2, ^2J = 14.8 Hz, ^3J = 7.5 Hz), 2.89 (dt, 1 H, CH_2, ^2J = 14.8 Hz, ^3J = 7.5 Hz); 6.10 (s, 1 H). MS, *m/z* (I_{rel} (%)): 240 $[M + H]^+$ (3), 204 $[M - Cl]^+$ (3), 168 $[M - Cl - HCl]^+$ (1), 116 $[C_3HNOClCH_2]^+$ (4), 108 (100). Found (%): C, 40.09; H, 3.20; N, 5.69. $C_8H_8Cl_3NO$. Calculated (%): C, 39.92; H, 3.33; N, 5.82.

5-Chloro-4-[2-(2,2-Dichlorocycloprop-1-yl)ethyl]isoxazole (6). Yield 22%, colorless oil. R_f 0.58 (AcOEt—light petroleum, 1 : 6). ^{1}H NMR, δ: 1.13 (t, 1 H_a, $^2J_{a,b} \approx J_{a,c}$ = 6.8—7.3 Hz); 1.57 (ddt, 1 H_c, $^3J_{a,c}$ = 7.3 Hz, $^3J_{b,c}$ = 10.3 Hz); 1.64 (dd, 1 H_b, $^2J_{a,b}$ = 6.8 Hz, $^3J_{b,c}$ = 10.3 Hz); 1.83 (q, 2 H, C(2)H_2, ^3J = 7.3 Hz); 2.61 and 2.66 (both dt, 1 H each, C(1)H_2, ^2J = 14.9 Hz, ^3J = 7.3 Hz); 8.24 (s, 1 H). MS, *m/z* (I_{rel} (%)): 240 $[M + H]^+$ (2), 204 $[M - Cl]^+$ (17), 175 $[M - NOCl]^+$ (46), 142 (25), 115 $[C_3NOClCH_2]^+$ (59), 107 (100), 86 (56), 79 (85). Found (%): C, 39.87; H, 3.45; N, 5.75. $C_8H_8Cl_3NO$. Calculated (%): C, 39.92; H, 3.33; N, 5.82.

5-Chloro-3-[2-(5-chloroisoxazol-3-yl)ethyl]isoxazole (7), m.p. 41—42 °C. R_f 0.56 (AcOEt—light petroleum, 1 : 3). ^{1}H NMR, δ: 3.08 (s, 4 H, 2 CH_2), 6.09 (s, 2 H, CH=). MS, *m/z*

* For cyclopropanes **4** and **13**, the molar ratios of cyclopropane to $NOCl \cdot 2SO_3$ are 1 : 2 and 1 : 4.

(I_{rel} (%)): 233 $[M + H]^+$ (0.4), 197 $[M - Cl]^+$ (7), 169 $[M - Cl - CO]^+$ (100), 133 (36), 106 (27), 78 (18), 67 (32). Found (%): C, 41.10; H, 2.69; N, 12.13. $C_8H_6Cl_2N_2O_2$. Calculated (%): C, 41.20; H, 2.58; N, 12.02.

5-Chloro-3-[2-(5-chloroisoxazol-4-yl)ethyl]isoxazole (8), colorless oil. R_f 0.50 (AcOEt—light petroleum, 1 : 3). ^{1}H NMR, δ: 2.83 (t, 2 H, ^3J = 7.3 Hz); 2.94 (t, 2 H, ^3J = 7.3 Hz); 6.04 (s, 1 H, CH=); 8.21 (s, 1 H, CH=). MS, *m/z* (I_{rel} (%)): 233 $[M + H]^+$ (0.3), 197 $[M - Cl]^+$ (65), 169 $[M - Cl - CO]^+$ (100), 142 (63), 116 $[C_3HNOClCH_2]^+$ (25), 80 $[C_3NOCH_2]^+$ (30), 63 (21). Found (%): C, 41.08; H, 2.37; N, 12.19. $C_8H_6Cl_2N_2O_2$. Calculated (%): C, 41.20; H, 2.58; N, 12.02.

5-Chloro-4-[2-(5-chloroisoxazol-4-yl)ethyl]isoxazole (9), m.p. 57—58 °C. R_f 0.35 (AcOEt—light petroleum, 1 : 3). ^{1}H NMR, δ: 2.69 (s, 4 H, 2 CH_2); 8.16 (s, 2 H, CH=). MS, *m/z* (I_{rel} (%)): 232 $[M]^{+\cdot}$ (10), 116 $[C_3HNOClCH_2]^+$ (100), 79 (95), 61 (23), 44 (30), 36 (57). Found (%): C, 41.08; H, 2.63; N, 12.15. $C_8H_6Cl_2N_2O_2$. Calculated (%): C, 41.20; H, 2.58; N, 12.02.

3-Chlorocyclopent[*c*]isoxazole (11a). Yield 90%, colorless oil with a pungent odor. R_f 0.51 (AcOEt—light petroleum, 1 : 5). IR, ν/cm^{-1}: 2970, 2880, 1650, 1400, 1125, 1030. ^{1}H NMR, δ: 2.50 (quint, 2 H, ^3J = 7.2 Hz); 2.63 (t, 2 H, ^3J = 7.2 Hz); 2.83 (t, 2 H, ^3J = 7.2 Hz). MS, *m/z* (I_{rel} (%)): $[M]^{+\cdot}$ 143 (21), 115 $[M - C_2H_4]^+$ (14), 108 $[M - Cl]^+$ (18), 80 $[M - Cl - C_2H_4]^+$ (62), 63 (16), 53 (100). Found (%): C, 50.01; H, 4.25; N, 9.89. C_6H_6ClNO. Calculated (%): C, 50.17; H, 4.18; N, 9.76.

3-Chloro-4,5,6,7-tetrahydrobenz[*c*]isoxazole (11b). Yield 70%, m.p. 36 °C (*cf.* Ref. 4: 34.2—35.8 °C). R_f 0.62 (AcOEt—light petroleum, 1 : 6). IR, ν/cm^{-1}: 2960, 2940, 2875, 1630, 1450, 1420, 1215, 1160, 765. ^{1}H NMR, δ: 1.70 (m, 4 H, 2 CH_2); 2.37 (t, 2 H, CH_2, ^3J = 6.3 Hz); 2.65 (t, 2 H, CH_2, ^3J = 6.3 Hz). MS, *m/z* (I_{rel} (%)): 157 $[M]^{+\cdot}$ (100), 130 $[M - C_2H_3]^+$ (36), 122 $[M - Cl]^+$ (36), 115 $[M - C_3H_6]^+$ (30), 100 (40), 94 $[M - Cl - C_2H_4]^+$ (11), 80 $[M - Cl - C_3H_6]^+$ (55), 67 $[C_3HNO]^+$ (3).

3-Chlorocyclohept[*c*]isoxazole (11c). Yield 30%, R_f 0.56 (AcOEt—light petroleum, 1 : 10). IR, ν/cm^{-1}: 2960, 2940, 2875, 1630, 1450, 1420, 1215, 1160, 765. ^{1}H NMR, δ: 1.67 (m, 2 H); 1.74 (m, 2 H); 1.85 (m, 2 H); 2.48 (m, 2 H); 2.78 (m, 2 H). MS, *m/z* (I_{rel} (%)): 171 $[M]^{+\cdot}$ (30), 143 $[M - C_2H_4]^+$ (5), 136 $[M - Cl]^+$ (27), 108 $[M - Cl - C_2H_4]^+$ (27), 81 (41), 80 $[M - Cl - C_4H_8]^+$ (36), 67 $[C_3HNO]^+$ (26), 55 (44), 41 (100). Found (%): C, 55.75; H, 5.67; N, 8.22. $C_8H_{10}ClNO$. Calculated (%): C, 55.98; H, 5.83; N, 8.16.

3-Chlorocyclooct[*c*]isoxazole (11d). Yield 10%, R_f 0.66 (AcOEt—light petroleum, 1 : 6). ^{1}H NMR, δ: 1.65, 1.75, 1.85 (m, 8 H); 2.50 (m, 2 H); 2.80 (m, 2 H). MS, *m/z* (I_{rel} (%)): 185 $[M]^{+\cdot}$ (63), 150 $[M - Cl^+]$ (100), 122 $[M - Cl - C_2H_4]^+$ (67), 95 (37), 80 $[M - Cl - C_5H_{10}]^+$ (34).

3,6,6-Trichlorocyclopropa[5,6]cyclooct[1,2-*c*]isoxazole (14). Yield 75%, m.p. 75—77 °C. R_f 0.48 (AcOEt—light petroleum, 1 : 3). IR, ν/cm^{-1}: 2960, 2940, 2875, 1630, 1450, 1420, 1215, 1160, 765. ^{1}H NMR, δ: 1.53 (m, 1 H); 1.61 (m, 1 H); 1.76 (m, 2 H); 2.46 (m, 3 H); 2.74 (m, 2 H); 3.05 (ddd, 1 H, ^3J = 3.6 Hz, ^3J = 8.0 Hz, ^2J = 11.7 Hz). Found (%): C, 45.10; H, 3.82; N, 5.03. $C_{10}H_{10}Cl_3NO$. Calculated (%): C, 45.11; H, 3.76; N, 5.26.

2-Dichloromethylidenecyclopentanone oxime (15). Yield 5%, m.p. 135—136 °C. R_f 0.26 (AcOEt—light petroleum, 1 : 6). IR, ν/cm^{-1}: 3500—3200 (OH), 1590 (C=N). ^{1}H NMR, δ: 1.85 (quint, 2 H, CH_2, ^3J = 7.6 Hz); 2.73 (t, 2 H, CH_2, ^3J = 7.6 Hz); 2.79 (t, 2 H, CH_2, ^3J = 7.6 Hz); 8.69 (br.s, 1 H, OH). ^{13}C NMR, δ: 20.8, 29.7, 35.2, 134.0 (C=); 151.0 (=CCl_2); 160.1 (C=N). MS, *m/z* (I_{rel} (%)): 179 $[M]^{+\cdot}$ (30), 163 (5), 134 (10), 108 (23), 89 (100), 80 (93), 73 (42), 63 (35), 54 (84). Found (%): C, 40.10; H, 4.16; N, 7.57. $C_6H_7Cl_2NO$. Calculated (%): C, 40.00; H, 3.90; N, 7.80.

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References

1. W. Kirmse, *Carbene Chemistry*, Academic Press, New York, 1964.
2. W. P. Weber, G. W. Gokel, *Phase Transfer Catalysis in Organic Synthesis*, Springer, Berlin, 1977, 280 pp.
3. N. S. Zefirov, I. V. Kazimirchik, K. L. Lukin, *Tsikloprisoedinenie dikhlorkarbena k olefinam* [*Cycloaddition of Dichlorocarbene to Olefins*], Nauka, Moscow, 1985, 152 pp. (in Russian).
4. S.-T. Lin, S.-H. Kuo, F.-M. Yang, *J. Org. Chem.*, 1997, **62**, 5229.
5. O. B. Bondarenko, A. Yu. Gavrilova, L. G. Saginova, N. V. Zyk, N. S. Zefirov, *Izv. Akad. Nauk, Ser. Khim.*, 2003, 741 [*Russ. Chem. Bull., Int. Ed.*, 2003, **52**, 778].
6. O. B. Bondarenko, A. Yu. Gavrilova, L. G. Saginova, N. V. Zyk, *Zh. Org. Khim.,* 2009, **45**, 230 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2009, **45**, 218].
7. E. V. Dehmlow, *Tetrahedron*, 1972, **28**, 175.
8. W. Kuhn, H. Marschall, P. Weyerstahl, *Chem. Ber.*, 1977, **110**, 1564.
9. L. F. Fieser, D. H. Sachs, *J. Org. Chem.*, 1964, **29**, 1113.
10. R. T. LaLonde, M. A. Tobias, *J. Am. Chem. Soc.*, 1964, **86**, 4068.
11. R. T. LaLonde, J. J. Batelka, *Tetrahedron Lett.*, 1964, **5**, 445.
12. F. R. Jensen, D. B. Patterson, S. E. Dinizo, *Tetrahedron Lett.*, 1974, **15**, 1315.
13. P. H. Atkinson, R. C. Camble, G. Dixon, W. I. Noall, P. S. Rutledge, P. D. Woodgate, *J. Chem. Soc., Perkin Trans. 1*, 1977, 230.
14. A. J. Gordon, R. A. Ford, *The Chemist´s Companion: A Handbook of Practical Data, Techniques, and References*, Wiley, New York, 1972, 537 pp.
15. W. E. von Doering, A. K. Hoffmann, *J. Am. Chem. Soc.*, 1954, **76**, 6162.
16. D. Reinhard, P. Weyerstahl, *Chem. Ber.*, 1977, **110**, 138.
17. C. M. Starks, *J. Am. Chem. Soc.*, 1971, **93**, 195.

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