Synthesis of new η^6-(arene) chromium tricarbonyl complexes of isoxazolidines by 1,3-dipolar cycloaddition

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The 1,3-dipolar cycloaddition products of *C*,*N*-disubstituted nitrones and different *in situ* prepared mono-*N*-substituted nitrones to η^6-(styrene) chromium tricarbonyl and η^6-(ethyl cynnamate) chromium tricarbonyl were synthesized and characterized by HPLC, IR, ^{1}H NMR spectroscopy, and mass spectrometry. The resulted isoxazolidines were produced with a full regioselectivity and high stereoselectivity reached 100% in most cases.

Key words: nitrone, η^6-(arene) chromium tricarbonyl, isoxazolidine, 1,3-dipolar cycloaddition.

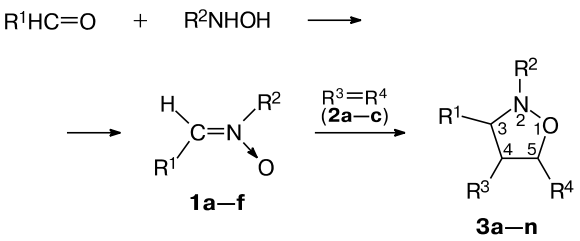
It is known that the 1,3-dipolar cycloaddition reactions are universal methods for the synthesis of various five-membered heterocyclic compounds.[1—3] For example, the reactions of nitrones with substituted alkenes result in the formation of a wide variety of isoxazolidines, which are five-membered heterocycles containing the N—O bond.[4—6] Isoxazolidines are starting compounds in the synthesis of many natural compounds, such as alkaloids,[4,7—9] amino acids,[10—12] and amino sugars.[13,14] Depending on the nature of reagents, cycloaddition of nitrones to different dipolarophiles can proceed both regioselectively and non-regioselectively,[6] which often affords a mixture of C(4)- and C(5)-substituted isoxazolidines. For this reason, the one of the main research problems is to improve the selectivity of 1,3-dipolar cycloaddition, *i.e.*, to achieve the predominant formation of any given isomer. From this viewpoint, unsaturated arene chromium tricarbonyl complexes seem to be very attractive, wherein the chromium tricarbonyl groups can influence significantly the changes in the electronic properties of the substrate and the structures of the products formed.[15,16] The important factor is the ability of the chromium tricarbonyl moiety to block one side of the arene ligand, which can be used in the diastereoselective syntheses of various compounds.[17,18]

Since isoxazolidines are synthesized under relatively mild conditions suitable for the preparations of arene chromium tricarbonyl complexes, we decided to study the 1,3-dipolar cycloaddition of different nitrones to substituted alkenes containing arene chromium tricarbonyl groups.

Results and Discussion

A series of simple mono-*N*-substituted nitrones **1a—c** were used as dipoles in the performed syntheses (Scheme 1),

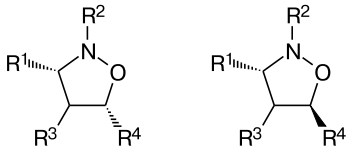
Scheme 1



1a—f **3a—n**

1: R^1 = H, R^2 = Ph (**a**), Bu^t (**b**), Me (**c**), R^1 = Ph, R^2 = Me (**d**), Ph (**e**), Bu^t (**f**)
2: R^3 = H, R^4 = Ph (**a**), Ph[Cr(CO)$_3$] (**b**), R^3 = CO_2Et, R^3 = Ph[Cr(CO)$_3$] (**c**)

3	R^1	R^2	R^3	R^4
a	H	Ph	H	Ph[Cr(CO)$_3$]
b	H	Bu^t	H	Ph[Cr(CO)$_3$]
c	H	Me	H	Ph[Cr(CO)$_3$]
d	H	Ph	H	Ph
e	H	Bu^t	H	Ph
f	H	Me	H	Ph
g	Ph	Me	H	Ph
h	Ph	Ph	H	Ph
i	Ph	Bu^t	H	Ph
j	Ph	Me	H	Ph[Cr(CO)$_3$]
k	Ph	Ph	H	Ph[Cr(CO)$_3$]
l	Ph	Bu^t	H	Ph[Cr(CO)$_3$]
m	Ph	Ph	CO_2Et	Ph[Cr(CO)$_3$]
n	Ph	Bu^t	CO_2Et	Ph[Cr(CO)$_3$]



cis-**3** *trans*-**3**

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which were impossible to isolate in pure form due to their instability; therefore, these substances were obtained *in situ* from formaldehyde and *N*-substituted hydroxylamine.[19] The stable C,*N*-disubstituted nitrones[20—22] **1d—f** were served as the dipole components. Styrene **2a**, η^6-(styrene) chromium tricarbonyl[23] (**2b**), and η^6-(ethyl cinnamate) chromium tricarbonyl[24] (**2c**) acted as dipolarophiles in the reactions.

All isoxazolidines obtained were isolated in pure form and characterized by the physicochemical analysis methods; their main characteristics are given in Table 1.

In all cases, the 1,3-dipolar cycloaddition between nitrones and dipolarophiles, including coordinated ones, yielded isoxazolidines containing either phenyl group or phenylchromium tricarbonyl group at the C(5) carbon atom of the heterocyclic ring, which evidences a high regioselectivity of the processes. For example, the reaction of nitrone **1a** with η^6-(styrene) chromium tricarbonyl **2b** afforded the C(5)-substituted isoxazolidine **3a**. The signals in the ^{1}H NMR spectrum of this compound, *viz.*, doublet of doublets of doublets (1 H, 2.35—2.45), multiplet (1 H, 2.62—2.77), triplet (1 H, 3.70), and doublet of doublets (2 H, 4.95), suggest that the phenyl chromium tricarbonyl group is located at the C(5) carbon atom (Fig. 1). The spectrum of the corresponding C(4)-substituted isomer would display two doublets of doublets for the methylene protons at the C(3) and C(5) carbon atoms due to their spin-spin coupling with the proton at C(4) and one multiplet for the proton at C(4) resulting from the coupling with the protons at C(3) and C(5).

Such a high regioselectivity of the 1,3-dipolar cycloaddition can be explained by two major factors. The first factor is based on the consideration of polarities of 1,3-dipole and dipolarophile and the second one is related to the calculation of electron populations of the HOMO and LUMO of reacting molecules. It is assiumed that the closer the frontier orbitals are arranged to each other by the energy and orbital symmetry, the stronger the interaction of reacting components and the higher the process regioselectivity.[25,26] The quantum chemical calculation data for a series of the 1,3-dipolar cycloaddition reactions suggest the predominant formation of the C(5)-substituted isoxazolidines. The increase in the yield of the C(5)-substituted products can be explained by either an increase in the HOMO energies or a decrease in the LUMO energies of reacting substances.[27]

The reaction products of nitrones **1b** and **1c** with η^6-(styrene) chromium tricarbonyl **2b** are isoxazolidines **3b** and **3c**, respectively. For their non-coordinated analogs **3e**,**f**, 1,3-dipolar cycloaddition also results in the exclusive formation of the C(5)-substituted products, which suggests that the regioselectivity remains unchanged upon introduction of the chromium tricarbonyl group to the dipolarophile molecule.

The interesting feature of the IR spectra of all prepared isoxazolidines containing the phenyl chromium tricarbonyl group at the C(5) atom of the heterocyclic ring is considerable band splitting (E) of degenerate carbonyl vibrations (C≡O). This splitting appears to be caused by the C_{3v} symmetry violation, which is caused by the spatial interaction of the $Cr(CO)_3$ group with the oxygen atom at the α-position relative to the η^6-(arene) chromium tricarbonyl fragment. We have observed such splitting earlier by the example of η^6-(1-phenylethanol) chromium tricarbonyl[28] (Fig. 2).

Thus, we showed that the reaction of mono-*N*-substituted nitrones with coordinated dipolarophiles affords the η^6-(arene) chromium tricarbonyl complexes of isoxazolidines, the high regioselectivity of the reaction remaining unchanged upon introduction of the chromium tricarbonyl group to the alkene molecule.

The effect of the $Cr(CO)_3$ group on the stereoselectivity of 1,3-dipolar cycloadditon, namely, on the yield of the *cis* and *trans* isomers, was studied by the example of the reaction of stable *C*,*N*-disubstituted nitrones **1d—f** with the α,β-unsaturated arene chromium tricarbonyl complexes **2a—c** (see Scheme 1). According to the studies of German scientists,[29] the reaction of *C*-phenyl-*N*-methyl nitrone (**1d**) with styrene **2a** results in a mixture of the *C*(5)-substituted *cis* and *trans* isomers in a ratio of *cis*-**3g** : *trans*-**3g** = 67 : 33, while cycloaddition of *C*,*N*-diphenylnitrone (**1e**) to styrene **2a** affords a mixture of adducts *cis*-**3h** and *trans*-**3h** in the ratio of 90 : 10 (Table 2).

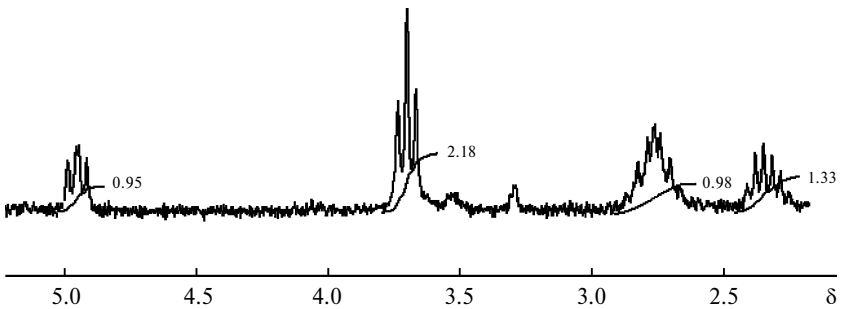

Fig. 1. A fragment of the ^{1}H NMR spectrum of complex **3a** (in the spectrum, the integral intensities of the signals are given).

Table 1. Some characteristics* of isoxazolidines **3a—d**

Dipole (nitrone) **1**	Dipolarophile **2**	Isoxazolidine **3**	R^1	R^2	R^3	R^4	M.p./°C	Yield (%)	ν(C≡O)/cm^{-1}
1a	**2b**	**3a**	H	Ph	H	Ph[Cr(CO)$_3$]	115—116	45	1950, 1886, 1865
1b	**2b**	**3b**	H	Bu^t	H	Ph[Cr(CO)$_3$]	103—105	47	1963, 1888, 1864
1c	**2b**	**3c**	H	Me	H	Ph[Cr(CO)$_3$]	Oil	44	1962, 1878, 1866
1a	**2a**	**3d**	H	Ph	H	Ph	61—62	69	—
1b	**2a**	**3e**	H	Bu^t	H	Ph	Oil	72	—
1c	**2a**	**3f**	H	Me	H	Ph	Oil	41	—
1d	**2a**	*cis*-**3g**	Ph	Me	H	Ph	Oil	64	—
1d	**2a**	*trans*-**3g**	Ph	Me	H	Ph	Oil	31	
1e	**2a**	*cis*-**3h**	Ph	Ph	H	Ph	99—100	85.5	—
1e	**2a**	*trans*-**3h**	Ph	Ph	H	Ph	—	9.5	
1f	**2a**	*cis*-**3i**	Ph	Bu^t	H	Ph	57—58	80	—
1d	**2b**	*cis*-**3j**	Ph	Me	H	Ph[Cr(CO)$_3$]	90—92	66	1953, 1887, 1876
1d	**2b**	*trans*-**3j**	Ph	Me	H	Ph[Cr(CO)$_3$]	112—113	14	1956, 1895, 1878
1e	**2b**	*cis*-**3k**	Ph	Ph	H	Ph[Cr(CO)$_3$]	111—113	45	1973, 1904, 1858
1f	**2b**	*cis*-**3l**	Ph	Bu^t	H	Ph[Cr(CO)$_3$]	103—105	47	1960, 1890, 1873
1e	**2c**	*cis*-**3m**	Ph	Ph	CO_2Et	Ph[Cr(CO)$_3$]	91—93	5	1970, 1910, 1884
1f	**2c**	*cis*-**3n**	Ph	Bu^t	CO_2Et	Ph[Cr(CO)$_3$]	82—84	21	1962, 1910, 1878

* Data for isoxazolidines *cis*-**3g**, *trans*-**3g**, *cis*-**3h**, and *trans*-**3h** are taken from Ref. 29.

The conducted reactions between nitrones and coordinated dipolarophiles revealed that introduction of chromium tricarbonyl group into the alkene molecule favors an increase in the process stereoselectivity. For example, the reaction of *C*-phenyl-*N*-methyl nitrone **1d** with η^6-(styrene) chromium tricarbonyl **2b** afforded a mixture of isomers *cis*-**3j** and *trans*-**3j**, which were separated by column chromatography. The ratio of *cis*-**3j** : *trans*-**3j** was found to be 83 : 17, while the ratio of *cis*-**3g** : *trans*-**3g** was 67 : 33. The structure of complex *cis*-**3j** was proved by X-ray diffraction study: the coordinated and free phenyl substituents are on the same side from the five-membered ring (Fig. 3, Table 3). The structures of isomers *cis*-**3j** and *trans*-**3j** were confirmed by comparison of their ^{1}H NMR spectra with those of the non-coordinated analogs.[29]

The reactions of *C*,*N*-diphenylnitrone (**1e**) and *C*-phenyl-*N*-*tert*-butylnitrone (**1f**) with the coordinated dipolarophiles result in the formation of only *cis*-isomers (see Table 2). One of the reasons of so high stereoselectivity is strengthening of the interaction between the free and coordinated phenyl rings.[15] This conception is confirmed by the fact that a charge-transfer complex can form as shown in Ref. 30 (see Fig. 4, *a*).

In summary, based on the experimental data obtained one can conclude that the 1,3-dipolar cycloaddition reactions between nitrones and different alkenes containing the phenyl chromium tricarbonyl group proceed under sufficiently mild conditions to form the corresponding C(5)-substituted isoxazolidines, which evidences high regioselectivities of the reactions. It was established that introduction of the chromium tricarbonyl group to the dipolarophile molecules increases considerably the stereoselectiviy of 1,3-dipolar cycloaddition, which, in some cases, reached 100%, which can be used in various diastereoselective syntheses.[16—18]

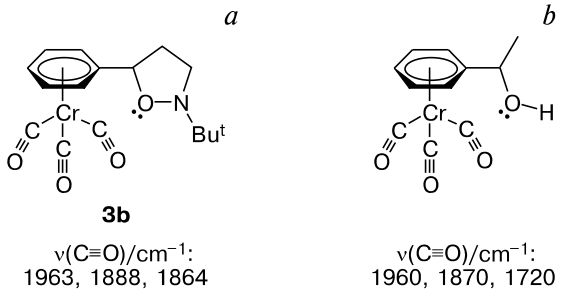

Fig. 2. Intramolecular interaction of the Cr(CO)$_3$ group with the oxygen atoms in the molecules of compound **3b** (*a*) and η^6-(1-phenylethanol) chromium tricarbonyl (*b*).

Table 2. Ratio of the *cis*- and *trans*-isomers of isoxazolidines **3g—n** in the 1,3-dipolar cycloaddition reactions

Nitrone (dipole)	Dipolarophile	Product	*Cis*-**3** : *trans*-**3** ratio
1d	**2a**	**3g**	67 : 33*
1e	**2a**	**3h**	90 : 10*
1f	**2a**	**3i**	100 : 0
1d	**2b**	**3j**	83 : 17
1e	**2b**	**3k**	100 : 0
1f	**2b**	**3l**	100 : 0
1e	**2c**	**3m**	100 : 0
1f	**2c**	**3n**	100 : 0

* Data from Ref. 29.

Table 3. Selected bond lengths and bond angles in the structure of complex *cis*-**3j**

Bond	*d*/Å	Bond	*d*/Å	Angle	ω/deg
N(1)—O(4)	1.4786(18)	Cr(1)—C(3)	1.8454(18)	N(1)—C(12)—C(11)	101.62(13)
N(1)—C(12)	1.472(2)	Cr(1)—C(7)	2.2137(18)	C(12)—C(11)—C(10)	102.98(14)
C(11)—C(12)	1.534(2)	Cr(1)—C(8)	2.2172(17)	O(4)—C(10)—C(11)	105.79(13)
C(10)—C(11)	1.544(2)	Cr(1)—C(5)	2.2210(17)	C(10)—O(4)—N(1)	104.02(12)
O(4)—C(10)	1.436(2)	Cr(1)—C(6)	2.2225(17)	C(12)—N(1)—O(4)	101.29(12)
Cr(1)—C(2)	1.8375(18)	Cr(1)—C(9)	2.2286(16)	C(2)—Cr(1)—C(1)	87.59(8)
Cr(1)—C(1)	1.8402(19)	Cr(1)—C(4)	2.2295(16)	C(2)—Cr(1)—C(3)	87.82(8)
				C(1)—Cr(1)—C(3)	89.64(9)

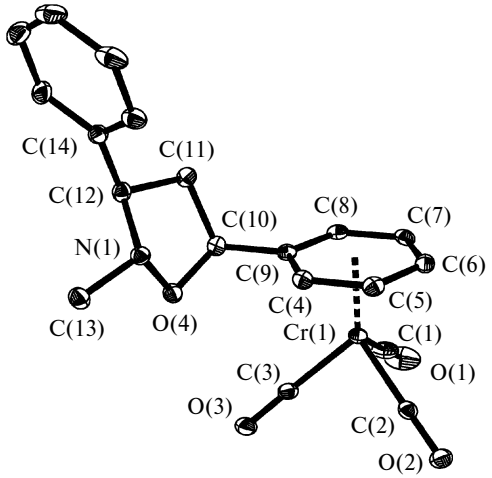

Fig. 3. Molecular structure of complex *cis*-**3j** (the hydrogen atoms are not shown).

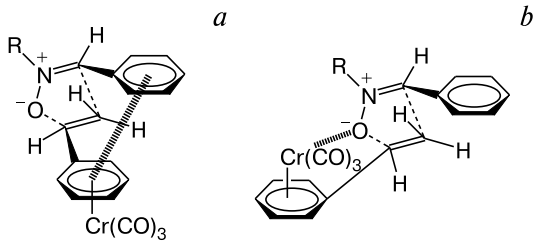

Fig. 4. Transition states of the 1,3-dipolar cycloaddition reactions leading to the formation of the isoxazolidine *cis*- (*a*) and *trans*-isomers (*b*).

Experimental

All solvents were distilled over sodium metal under atmospheric pressure.[30] *N*-Phenyl- and *N*-*tert*-butylhydroxylamines were prepared by reduction of the corresponding nitro compounds.[20,31] For the synthesis of *C*-phenyl-*N*-methylnitrone (**1d**), *N*-methylhydroxylamine hydrochloride (Sigma—Aldrich) was used. *C*,*N*-Disubstituted nitrones **1d**—**f** were synthesized by condensation of benzaldehyde with the corresponding hydroxylamines.[20—22] η⁶-(Styrene) chromium tricarbonyl (**2b**) and η⁶-(ethyl cinnamate) chromium tricarbonyl (**2c**) were synthesized according to the published procedures.[23,24] 2-Methyl-5-phenylisoxazolidine (**3f**) was prepared from styrene, formaldehyde, and *N*-methylhydroxylamine according to a known procedure.[19]

To remove the stabilizer, styrene was washed with a 10% aqueous solution of sodium hydroxide and water, dried, and distilled (b.p. 48—49 °C (10 Torr)). Ethyl cinnamate was synthesized according to a known procedure.[32] The products were isolated and purified by column chromatography on silica gel (Acros, 0.035—0.070 mm). High-performance liquid chromatography was performed on a Knauer Smartline 5000 chromatograph with a S 2600 PDA detector, Diaspher-110-C16 column, 5 m, 4.6×250 mm, the eluent was acetonitrile—water (84 : 16). The UV spectra of eluates were recorded in the range of 200—500 nm. IR spectra were recorded on a Infralum FT-801 spectrometer in the range of 480—4600 cm^{-1} in suspension with KBr or in films on ZnSe glass plates. ^1H NMR spectra were recorded on Bruker DPX 200 and Bruker Avance DPX 400 spectrometers (200 and 400 MHz, respectively) in acetone-d_6. Mass spectrometric studies were performed on a Trace GC Metra/PS QII instrument in the positive ion mode, electron impact ionization (70 eV), *m*/*z* range of 28—500, TR5MS capillary column (60000×0.25 mm), the flow rate of helium was 1 mL min^{-1}, temperature programming from 60 to 300 °C at the heating rate of 15 deg min^{-1}, and on a Bruker Microflex LT instrument by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI MS).

The synthesis and isolation of 2,5-disubstituted (**3a**—**c**), as well as isolation of 2,3,5-trisubstituted (**3j**—**n**) η⁶-(arene) chromium tricarbonyl complexes were performed under an argon atmosphere.

Synthesis of the 2,5-disubstituted isoxazolidines 3a—f (general procedure).[19] To a mixture of the corresponding dipolarophile **2a**,**b** (0.014 mol), 37% aqueous formaldehyde (0.020 mol), and dioxane (15 mL), a solution of the *N*-substituted hydroxylamine (0.012 mol) in dioxane (5 mL) was added dropwise with vigorous stirring at room temperature. The reaction mixture was kept for 16 h, concentrated, and extracted with ethyl acetate, the organic layer was dried with calcium chloride. The solvent was removed under reduced pressure. The target products were isolated by column chromatography of a viscous residue and subsequent recrystallization from a hexane—ethyl acetate mixture.

η⁶-(5-Phenyl chromium tricarbonyl)-2-phenylisoxazolidine (3a). The yield was 45%, m.p. 115—116 °C. Found (%): Cr, 13.97. $C_{18}H_{15}NO_4Cr$. Calculated (%): Cr, 14.40. MS (MALDI MS), *m*/*z* (I_{rel} (%)): 399.9 $[M + K]^+$ (30), 333.0 $[M - CO]^+$ (25), 277.1 $[M - 3\ CO]^+$ (35), 221.1 $[M - Cr(CO)_3 - 4\ H]^+$

(100). IR (KBr), ν/cm^{-1}: 1950, 1886, 1865 (ν(C≡O)); 1177, 1036 (ν(N—O, C—O)); 763, 664, 633 (ω(C_{Ar}—H)). ^{1}H NMR (200 MHz), δ: 2.35 (ddd, 1 H, $H_2C(4)$, J = 12.6 Hz, J = 6.4 Hz, J = 6.2 Hz); 2.62—2.77 (m, 1 H, $H_2C(4)$); 3.70 (t, 1 H, HC(5), J = 7.1 Hz); 4.95 (dd, 2 H, $H_2C(3)$, J = 7.8 Hz, J = 6.2 Hz); 5.49—5.90 (m, 5 H, C(5)PhCr); 6.95 (t, 1 H, *p*-PhN, J = 7.1 Hz); 7.12 (d, 2 H, *m*-PhN, J = 7.7 Hz); 7.26 (d, 2 H, *o*-PhN, J = 7.3 Hz).

η^6-(5-Phenyl chromium tircarbonyl)-2-*tert*-butylisoxazolidine (3b) was synthesized at 55 °C (bath temperature). The yield was 47%, m.p. 103—105 °C. Found (%): C, 56.80; H, 5.81; Cr, 14.93. $C_{16}H_{19}NO_4Cr$. Calculated (%): C, 56.30; H, 5.57; Cr, 15.25. MS (MALDI MS), m/z (I_{rel} (%)): 379.9 $[M + K]^+$ (100), 352.0 $[M + K - CO]^+$, 313.1 $[M - CO]^+$ (28), 257.1 $[M - 3\ CO]^+$ (39). IR (KBr), ν/cm^{-1}: 3155, 2976, 2927 (ν(C—H)); 1963, 1888, 1864 (ν(C≡O)); 1457 (ν(C—C)); 1233, 1031 (ν(N—O, C—O)); 814, 662, 633 (ω(C_{Ar}—H)).

η^6-(5-Phenyl chromium tricarbonyl)-2-methylisoxazolidine (3c) was synthesized at 55 °C (bath temperature). The yield was 44%. MS (MALDI MS), m/z (I_{rel} (%)): 337.9 $[M + K]^+$ (100), 309.9 $[M + K - CO]^+$ (17), 270.9 $[M - CO]^+$ (22). IR, ν/cm^{-1}: 2959, 2916, 2849 (ν(C—H)); 1962, 1878, 1866 (ν(C≡O)); 1457, 1424 (ν(C—C)); 1290, 1026 (ν(N—O, C—O)); 819, 662, 631 (ω(C_{Ar}—H)). ^{1}H NMR (400 MHz), δ: 2.21 (m, 1 H, $H_2C(4)$); 2.62 (br.s, 1 H, $H_2C(4)$); 2.67 (br.s, 3 H, NCH_3); 2.84 (br.s, 1 H, $H_2C(3)$); 3.21—3.43 (m, 1 H, $H_2C(3)$); 4.90 (br.s, 1 H, HC(5)); 5.45—5.79 (m, 5 H, C(5)PhCr).

2,5-Diphenylisoxazolidine (3d). The yield was 69%, m.p. 61—62 °C. IR (KBr), ν/cm^{-1}: 2985, 2959, 2917 (ν(C—H)); 1596 (ν(C—C_{Ar})); 1284, 1176 (ν(N—O, C—O)); 1024 (ν(C—N)); 761, 698, 669 (ω(C_{Ar}—H)). ^{1}H NMR (200 MHz), δ: 2.45—2.10 (m, 1 H, $H_2C(4)$); 2.68 (ddd, 1 H, $H_2C(4)$, J = 14.8 Hz, J = 12.1 Hz, J = 7.9 Hz); 3.93—3.52 (m, 2 H, $H_2C(3)N$); 5.18 (t, 1 H, HC(5)Ph, J = 7.5 Hz); 6.99 (t, 1 H, *p*-PhN, J = 7.2 Hz); 7.13 (d, 2 H, *o*-PhN, J = 7.7 Hz); 7.19—7.66 (m, 7 H, Ph).

2-*tert*-Butyl-5-phenylisoxazolidine (3e). The yield was 72%. Found (%): C, 76.62; H, 9.60. $C_{13}H_{19}NO$. Calculated (%): C, 76.10; H, 9.27. MS (EI, 70 eV), m/z (I_{rel} (%)): 205.0 $[M]^+$ (20), 190.0 $[M - CH_3]^+$ (50), 117.2 $[PhC_2O]^+$ (100), 104.0 $[PhCHCH_2]^+$ (68), 77.2 $[Ph]^+$ (28), 57.0 $[Bu^t]^+$ (26). IR (KBr), ν/cm^{-1}: 2971, 2925, 2855 (ν(C—H)); 1604 (ν(C—C_{Ar})); 1361, 1232 (ν(N—O, C—O)); 830, 757, 698 (ω(C_{Ar}—H)).

Synthesis of 2,3,5-trisubstituted isoxazolidines 3i—n (general procedure). The corresponding *C*,*N*-disubstituted nitrone **1d—f** (0.002 mol), dipolarophile **2a—c** (0.002 mol) and toluene (3 mL) were placed into a 20 mL glass tube. The tube was degassed and sealed *in vacuo*. The reaction mixture was heated for 40 h at 105 °C. The tube was opened, the content was filtered through a glass filter, the filtration residue was washed with toluene, and the solvent was evaporated *in vacuo*. The reaciton products were isolated from a viscous residue by column chromatography and recrystallized from hexane to yield the target products.

2-*tert*-Butyl-3,5-diphenylisoxazolidine (3i). The yield was 80%, m.p. 57—58 °C. Found (%): C, 80.97; H, 8.30. $C_{19}H_{23}NO$. Calculated (%): C, 81.14; H, 8.19. IR (KBr), ν/cm^{-1}: 3055, 2977, 2926 (ν(C—H)); 1579 (ν(C—C_{Ar})); 1447 (ν(C—C)); 1222, 1193 (ν(N—O, C—O)); 1028 (ν(C—N)); 842, 753, 699 (ω(C_{Ar}—H)). ^{1}H NMR (200 MHz), δ: 1.12 (s, 9 H, Bu^t); 2.35 (dt, 1 H, HC(4), J = 10.0 Hz, J = 12.0 Hz); 2.94 (dt, 1 H, HC(4), J = 6.0 Hz, J = 12.0 Hz); 4.46 (dd, 1 H, HC(3), J = 7.0 Hz, J = 10.0 Hz); 5.13 (dd, 1 H, HC(5), J = 5.0 Hz, J = 10.0 Hz); 7.16—7.52 (m, 10 H, Ph).

η^6-(5-Phenyl chromium tricarbonyl)-2-methyl-3-phenylisoxazolidine (*trans*-3j and *cis*-3j) were synthesized at 80 °C (bath temperature).

Isomer *cis*-**3j**. The yield was 66%, m.p. 90—92 °C. IR (KBr), ν/cm^{-1}: 1953, 1887, 1876 (ν(C—O)); 1384 (ν(C—C)); 1292, 1150 (ν(N—O, C—O)); 1011 (ν(C—N)); 761, 662, 633 (ω(C_{Ar}—H)). ^{1}H NMR (400 MHz), δ: 2.29 (ddd, 1 H, HC(4), J = 12.6 Hz, J = 9.5 Hz, J = 6.3 Hz); 2.57 (s, 3 H, CH_3N); 3.22—3.29 (m, 1 H, HC(4)); 3.71 (t, 1 H, HC(3), J = 8.2 Hz); 4.98 (dd, 1 H, HC(5), J = 8.5 Hz, J = 6.3 Hz); 5.52—5.59 (m, 1 H, C(5)-*m*-PhCr); 5.66 (d, 2 H, C(5)-*o*-PhCr, J = 3.8 Hz); 5.71 (t, 1 H, C(5)-*m*-PhCr, J = 6.4 Hz); 5.95 (d, 1 H, C(5)-*p*-PhCr, J = 6.3 Hz); 7.29 (d, 1 H, *p*-PhC(3), J = 7.0 Hz); 7.34 (t, 2 H, *m*-PhC(3), J = 7.3 Hz); 7.39 (d, 2 H, *o*-PhC(3), J = 7.3 Hz).

Isomer *trans*-**3j**. The yield was 14%, m.p. 112—113 °C. IR (KBr), ν/cm^{-1}: 1956, 1895, 1878 (ν(C≡O)); 1384 (ν(C—C)); 1290, 1150 (ν(N—O, C—O)); 1037(ν(C—N)); 706, 661, 633 (ω(C_{Ar}—H)). ^{1}H NMR (400 MHz), δ: 2.59 (s, 3 H, NCH_3); 2.62—2.69 (m, 1 H, HC(4)); 2.74 (d, 1 H, HC(4), J = 9.5 Hz); 3.13 (d, 1 H, HC(3), J = 5.3 Hz); 4.93 (t, 1 H, HC(5), J = 7.2 Hz); 5.57—5.71 (m, 3 H, C(5)PhCr); 5.73—5.83 (m, 2 H, C(5)PhCr); 7.30 (d, 1 H, *o*-PhC(3), J = 7.0 Hz); 7.36—7.52 (m, 4 H, *o*-, *m*-, *p*-PhC(3)).

η^6-(5-Phenyl chromium tricarbonyl)-2,3-diphenylisoxazolidine (3k). The yield was 42%, m.p. 111—113 °C. IR (KBr), ν/cm^{-1}: 2987, 2923, 2893 (ν(C—H)); 1973, 1904, 1858 (ν(C≡O); 1650 (ν(C—C_{Ar})); 1489 (ν(C—C)); 1261, 1127 (ν(N—O, C—O)); 1027 (ν(C—N)); 802, 664 (ω(C_{Ar}—H)). ^{1}H NMR (400 MHz), δ: 2.37 (td, 1 H, HC(4), J = 7.2 Hz, J = 8.8 Hz, J = 12.4 Hz); 3.37 (td, 1 H, HC(4), J = 7.2 Hz, J = 6.0 Hz, J = 15.0 Hz); 5.00 (t, 2 H, HC(3)Ph,HC(5)Ph, J = 7.0); 5.50—5.80 (m, 4 H, *o*-, *m*-, *p*-C(5)PhCr); 5.85 (d, 1 H, *o*-C(5)PhCr, J = 6.0 Hz); 6.94 (t, 1 H, *p*-PhN, J = 7.2 Hz); 7.11 (d, 2 H, *o*-PhN, J = 3.8 Hz); 7.26 (m, 3 H, *m*-PhN, *p*-PhC(3)); 7.40 (m, 2 H, *m*-PhC(3)); 7.58 (d, 2 H, *o*-PhC(3), J = 7.4 Hz).

η^6-(5-Phenyl chromium tricarbonyl)-2-*tert*-butyl-3-phenylisoxazolidine (3l). The yield was 47%, m.p. 103—105 °C. IR (KBr), ν/cm^{-1}: 2961, 2925, 2855 (ν(C—H)); 1960, 1890, 1873 (ν(C≡O)); 1632 (ν(C—C_{Ar})); 1458 (ν(C—C)); 1261, 1120 (ν(N—O, C—O)); 1091 (ν(C—N)); 802, 662 (ω(C_{Ar}—H)). ^{1}H NMR (400 MHz), δ: 1.08 (s, 9 H, Bu^t); 2.19 (dt, 1 H, HC(4), J = 9.0 Hz, J = 12.0 Hz); 3.16 (dt, 1 H, HC(4), J = 7.0 Hz, J = 12.0 Hz); 4.49 (dd, 1 H, HC(3), J = 6.0 Hz, J = 9.0 Hz); 4.88 (dd, 1 H, HC(5), J = 7.0 Hz, J = 9.0 Hz); 5.58 (m, 2 H, *m*-C(5)PhCr); 5.63 (d, 1 H, *o*-C(5)PhCr, J = 4.0 Hz); 5.71 (t, 1 H, *p*-C(5)PhCr, J = 6.0 Hz); 5.99 (d, 1 H, *o*-C(5)PhCr, J = 6.0 Hz); 7.32 (m, 3 H, *m*-, *p*-PhC(3)); 7.48 (d, 2 H, *o*-PhC(3), J = 7.0 Hz).

η^6-(5-Phenyl chromium tricarbonyl)-2,3-diphenyl-4-ethylcarboxyisoxazolidine (3m). The yield was 5%, m.p. 91—93 °C. IR (KBr), ν/cm^{-1}: 2958, 2919, 2852 (ν(C—H)); 1970, 1910, 1884 (ν(C≡O)); 1734 (ν(C=O)); 1649, 1457 (ν(C—C_{Ar})); 1261, 1172 (ν(N—O, C—O)); 1089 (ν(C—N)); 801, 664, 631 (ω(C_{Ar}—H)).

η^6-(5-Phenyl chromium tricarbonyl)-2-*tert*-butyl-3-phenyl-4-ethylcarboxyisoxazolidine (3n). The yield was 21%, m.p. 82—84 °C. IR (KBr), ν/cm^{-1}: 2967, 2922, 2874 (ν(C—H)); 1962, 1910, 1878 (ν(C≡O)); 1733 (ν(C=O)); 1650, 1456 (ν(C—C_{Ar})); 1269 (ν(N—O, C—O)); 1092 (ν(C—N)); 799, 662, 631 (ω(C_{Ar}—H)). ^{1}H NMR (400 MHz), δ: 1.09 (s, 9 H, Bu^t); 1.19 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.0 Hz); 3.36 (dd, 1 H, HC(4), J = 7.0 Hz,

J = 9.0 Hz); 4.16 (s, 2 H, $OC\underline{H}_2CH_3$, J = 7.0 Hz); 4.62 (d, 1 H, HC(3), J = 9.0 Hz); 5.15 (d, 1 H, C(5)H, J = 7.0 Hz); 5.63 (m, 3 H, *o*-, *m*-C(5)PhCr); 5,75 (t, 1 H, *p*-C(5)PhCr, J = 6.0 Hz); 6.11 (d, 1 H, *o*-C(5)PhCr, J = 6.0 Hz); 7.30 (m, 3 H, *p*-, *m*-Ph); 7.47 (dd, 2 H, *o*-Ph, J = 2.0 Hz, J = 8.0 Hz).

X-ray diffraction study of complex *cis*-3j. The crystals ($C_{19}H_{17}NO_4Cr$, M = 375.34) are monoclinic (space group $P2(1)/c$, at 100 K: a = 10.3424(7), b = 7.1473(5), c = 23.9375(16) Å, α = 90, β = 95.692(10), γ = 90°, V = 1760.7(2) Å^3, Z = 4, d_{calc} = 1.416 g cm^{-3}, μ = 6.72 cm^{-1}) and were obtained by crystallization from hexane. The intensities of 19 268 reflections (3458 independent reflections, R_{int} = 0.0243) were measured on a Smart Apex diffractometer (graphite monochromator, λ(Mo-Kα) = 0.71073 Å, 100 K). The account of absorption was performed by the SADABS program.[33] The structure were solved by the direct method and refined by the full-matrix least-squares method over F^2_{hkl} with the anisotropic thermal parameters for all non-hydrogen atoms. The hydrogen atoms were placed into the geometrically calculated positions and refined in the riding model. The final divergence factors were R_1 = 0.0300 ($I > 2\sigma(I)$), wR_2 = 0.0805 (refinement over F_{hkl}^2 for all independent reflections). All calculations were performed on PC using the SHELXTL software.[34] The full tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters are deposited in the Cambridge Crystallographic Data Center (CCDC 913412).

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References

1. R. Huisgen, *Angew. Chem., Int. Ed.*, 1968, **7**, 321.
2. R. Huisgen, *J. Org. Chem.*, 1968, **33**, 2291.
3. R. Huisgen, *Helv. Chim. Acta*, 1967, **50**, 2421.
4. J. J. Tufariello, *Acc. Chem. Res.*, 1979, **12**, 396.
5. J. J. Tufariello, in *1,3-Dipolar Cycloaddition Chemistry*, Ed. A. Padwa, John Wiley and Sons, New York, 1984, Vol. **2**, p. 83.
6. P. N. Confalone, E. M. Huie, *Org. React.*, 1988, **36**, 1.
7. G. A. Schiehser, J. D. White, G. Matsumoto, J. O. Pezzanite, J. Clardy, *Tetrahedron Lett.*, 1986, **27**, 5587.
8. A. E. McCaig, R. H. Wightman, *Tetrahedron Lett.*, 1993, **34**, 3939.
9. A. Goti, F. Cardona, A. Brandi, S. Picasso, P. Vogel, *Tetrahedron: Asymmetry*, 1996, **7**, 1659.
10. D. Kiers, D. Moffat, K. Overton, *J. Chem. Soc., Chem. Commun.*, 1988, 654.
11. D. Kiers, D. Moffat, K. Overton, R. J. Tomanek, *Chem. Soc., Perkin Trans. 1*, 1991, 1041.
12. C. M. Tice, B. Ganem, *J. Org. Chem.*, 1983, **48**, 5048.
13. A. Vasella, R. Voeffray, *J. Chem. Soc., Chem. Commun.*, 1981, 97.
14. A. Vasella, R. Voeffray, *Helv. Chim. Acta*, 1982, **65**, 1134.
15. C. Mukai, I. J. Kim, W. J. Cho, M. Hanaoka, *Tetrahedron Lett.*, 1990, **31**, 6893.
16. M. Rosillo, G. Dominguez, J. Perez-Castells, *Chem. Soc. Rev.*, 2007, **36**, 1589.
17. F. Rose-Munch, E. Rose, in *Modern Arene Chemistry*, Ed. D. Astruc, Willy-VCH, 2003, p. 368.
18. S. E. Gibson, H. Ibrahim, *Chem. Commun.*, 2002, **21**, 2465.
19. E. J. Fornefeld, A. J. Pike, *J. Org. Chem.*, 1979, **44**, 835.
20. K. Heusler, P. Wieland, Ch. Meystre, *Org. Synth.*, 1973, **5**, 1124.
21. C. Mukai, I. J Kim, W. J. Cho, M. Kido, M. Hanaoka, *J. Chem. Soc., Perkin Trans. 1*, 1993, 2495.
22. W. D. Emmons, *J. Am. Chem. Soc.*, 1957, **79**, 5739.
23. M. D. Raush, G. A. Moser, E. S. Zaiko, A. L. Lipman, *J. Organomet. Chem.*, 1970, **23**, 185.
24. N. B. Valetova, A. N. Artemov, D. F. Grishin, *Izv. Vyssh. Uchebn. Zaved., Khimiya and Khim. Tekhnologiya*, 2007, **50**, No. 9, 80 (in Russian).
25. K.N. Houk, *J. Am. Chem. Soc.*, 1972, **94**, 8953.
26. K. N. Houk, A. Bimanand, D. Mukherjee, J. Sims, Y.-M. Chang, D. C. Kaufman, N. L. Domelsmith, *Heterocycles*, 1977, **7**, 293.
27. J. P. Freeman, *Chem. Rev.*, 1983, **63**, 241.
28. I. V. Bodrikov, I. I. Grinval´d, A. N. Artemov, L. I. Bazhan, I. Yu. Kalagaev, *Zh. Obshch. Khim.*, 2010, **80**, 24 [*Russ. J. Gen. Chem.* (*Engl. Transl.*), 2010, **80**, 20].
29. R. Huisgen, R. Grashey, H. Hawk, H. Seidl, *Chem. Ber.*, 1968, **101**, 2548.
30. W. J. Bland, R. Davis, J. L. A. Durrant, *J. Organomet. Chem.*, 1982, **234**, C20.
31. C. Weygand, *Organisch-Chemische Experimentierkunst*, 2. Auflage, Johann Ambrosius Barth, Leipzig, 1948, 824 S.
32. V. V. Shpanova, V. S. Volodina, *Preparativnaya organicheskaya khimiya* [*Preparative Organic Chemistry*], Ed. N. S. Wulfson, Goskhimizdat, Moscow, 1959, p. 594 [*Preparatyka organiczna*, Panstwowe wydawnictwa techniczne, Warszawa, 1954, 1187 s.]
33. G. M. Sheldrick, *SADABS*, 1997, Bruker AXS, Inc., Madison (WI), USA.
34. G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, **64**, 112.

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