Synthesis of ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates, exhibiting plant growth-regulating properties

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A convenient method for the synthesis of high-boiling-point α-(trifluoromethyl)styrenes was proposed. The regioselective synthesis of a series of ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates was conducted by the reaction of ethyl nitroacetate with α-(trifluoromethyl)styrenes in the presence of 1,4-diazabicyclo[2.2.2]octane as a catalyst. The effect of the resulting compounds on seed germination and root formation was studied.

Key words: α-(trifluoromethyl)styrenes, ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates, ethyl nitroacetate, 1,3-cycloaddition, nitrile oxide, plant growth regulator, metsulfuron-methyl.

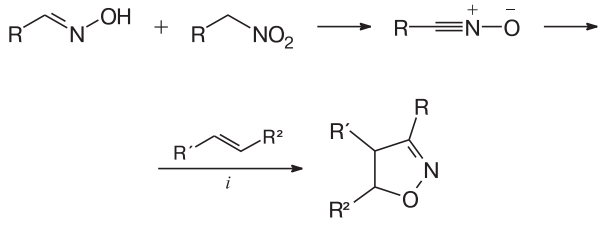
The synthesis and study of heterocyclic systems based on 4,5-dihydroisoxazole is one of the rapidly developing directions of the search for practically useful compounds. The interest to the representatives of this series is due to their wide use as building blocks in the total synthesis of natural compounds[1] and to the results of applied biomedical and agrochemical studies.[2] Numerous 4,5-dihydroisoxazole derivatives exhibit antifungal and antiviral activities,[3,4] are promising as anticancer agents,[5,6] while their agrochemical potential was confirmed by patents.[7—9] Thus, 5,5-diaryl-substituted ethyl 4,5-dihydroisoxazole-3-carboxylates (in particular, ethyl 5,5-diphenyl-4,5-dihydroisoxazole-3-carboxylate, the trade name Isoxadiphenethyl) is patented by a number of companies as agrochemical agents: pesticides, herbicides, or antidotes of the vegetation period in the composition of disinfectants.[10—12] The practical significance of compounds with a 4,5-dihydroisoxazole skeleton stimulates the search for new methods of their synthesis and functionalization, as well as a productive synthetic application.

The introduction of fluorine atoms into organic molecules for several decades has been used as an efficient strategy for broadening the range of their potential physiological action.[13] In the case of 4,5-dihydroisoxazole, the introduction of polyfluoroalkyl groups at position 5 led not only to the appearance of specific properties, but also to the enhancement of the biological effects.[14]

The purpose of the present work is the development of an approach to the synthesis of a series of new ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates and the study of their growth-regulating properties on corn seeds and seedlings.

One of the main strategies in the design of isoxazole skeleton is a 1,3-dipolar cycloaddition involving alkenes and generated *in situ* nitrile oxides[15] (Scheme 1).

Scheme 1



i. 1,3-Cycloaddition.

In this work, we used the condensation of 1,1-disubstituted alkenes with ethyl nitroacetate in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) as a catalyst.[16] The starting α-(trifluoromethyl)styrenes were obtained using two synthetic schemes. According to one of them, the corresponding 1-aryl-1-methyl-1-(trifluoromethyl)-carbinols (**1a**,**b**) were subjected to high-temperature dehydration with phosphorus pentoxide (the Tarrant method[17,18]) to obtain low-boiling-point and very volatile styrenes, namely α-(trifluoromethyl)-*para*-methylstyrene

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 1, pp. 0099—0103, January, 2019.

(**2a**) and α-(trifluoromethyl)styrene (**2b**) (with a boiling point below 170 °C) (Scheme 2). However, the high-boiling-point α-(trifluoromethyl)styrenes (with a boiling point above 170 °C) cannot be obtained by this method with a satisfactory yield. Therefore, the high-boiling-point styrenes were synthesized by the Wittig reaction from the corresponding 2,2,2-trifluoroacetophenones. We found that the reflux of 2,2,2-trifluoroacetophenone derivatives (**1c—e**) (1 equiv.), methyltriphenylphosphonium bromide or iodide (1.25 equiv.), and potassium carbonate (1.7 equiv.) in anhydrous 1,2-dimethoxyethane for 5 h afforded α-(trifluoromethyl)-*para*-chlorostyrene (**2c**), α-(trifluoromethyl)-*para*-bromostyrene (**2d**), and α-(trifluoromethyl)-2,4-dichlorostyrene (**2e**) in high yields (Scheme 2). This version of Wittig reaction is very practical, does not require strong bases (in particular, organolithium ones) and cryogenic temperatures for generation of methylenetriphenylphosphorane (*cf.* Refs 19 and 20).

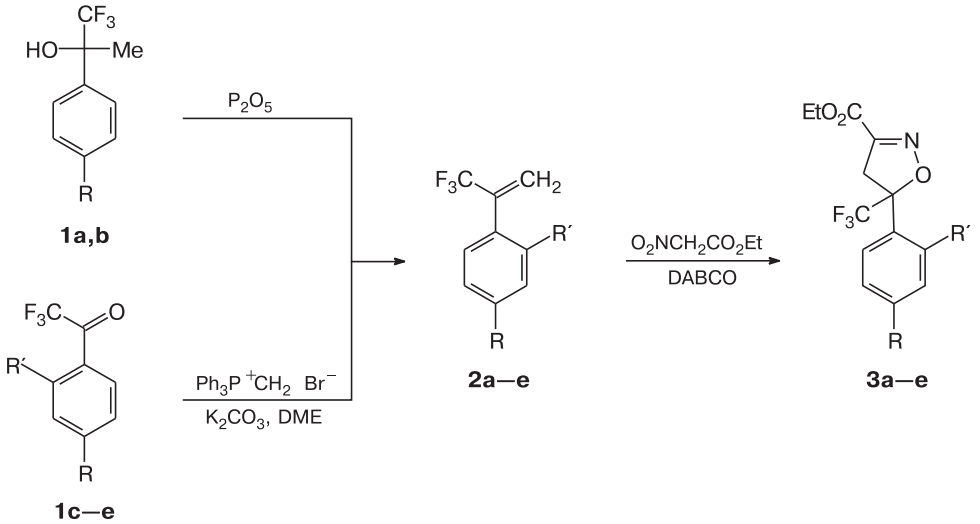
The condensation of the obtained α-(trifluoromethyl)-styrenes (1 equiv.) with ethyl nitroacetate (2 equiv.) was carried out in anhydrous EtOH at 80 °C in the presence of catalytic amounts of DABCO (0.1 equiv.) for 80 h until complete conversion of the initial alkene. The reaction progress was monitored by TLC. The target products, ethyl 5-aryl-5-(trifluoromethyl)-1,2-dihydroisoxazole-3-carboxylates (**3a—e**), were isolated in 65—75% yields after the removal of the solvent from the reaction mixture and purification by column chromatography on silica gel. The compounds were identified by ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy, mass spectrometry, and elemental analysis. The mass spectra were characterized by the low-abundant peaks of molecular radical cations, which underwent fragmentation under electron ionization following two pathways of the 1,2-dihydroisoxazole ring decomposition. The main direction was the formation of the $[RR^1C_6H_3CO]^+$ ion in all the cases with 100% abundance; the side fragmentation pathway gave the $[RR^1C_6H_3{-}C{=}CH_2]^+$ ions of medium or low abundance. The ^{1}H NMR spectra, in addition to the characteristic signals for the aromatic and ethyl groups of protons, exhibited doublets in the region of δ 4.0—3.6 from the diastereotopic protons of the CH_2 group of the 1,2-dihydroisoxazole ring forming the AB-system. As expected, the ^{19}F NMR spectra of **3a—e** exhibited the singlets from the (trifluoromethyl) groups in the region of δ −80—81.

Considering the possibility of using the compounds obtained in agrochemistry, we evaluated their effect on the germination of corn seeds and studied the antidote effect against such powerful phytotoxicants as sulfonylureas.

The tests of the antidote activity of ethyl 5,5-diphenyl-4,5-dihydroisoxazole-3-carboxylate (the Isoxadifen-ethyl agent) and its fluoro analogs **3a—e** were carried out against the herbicide Zinger, SP (60% metsulfuron-methyl) (see Experimental and Table 1).

From Table 1, it is seen that none of the compounds tested in treatment of seed, including the reference Isoxadifen-ethyl, removed the toxic effect of the herbicide, *i.e.*, they did not possess the properties of antidotes (safeners). At the same time, they were active as plant growth regulators, with compounds **3d** and **3e** significantly exceed-

Scheme 2



Compounds **2**, **3**	R	R′	Yield (%) **2**	Yield (%) **3**
a	Me	H	75	70
b	H	H	74	65
c	Cl	H	78	67
d	Br	H	77	70
e	Cl	Cl	73	75

Table 1. Comparison of growth-regulating and antidote activity (against herbicide Zinger, SP) of ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates **3a—e** and antidote Isoxadiphen-ethyl (IE)

Agent	Dose of agent, g t^{-1} of seeds	Sprouts		Roots	
		*d**/cm	Δ*d*** (%)	*d**/cm	Δ*d*** (%)
IE	1	3.1	11.4	11.3	−7.6
	10	3.4	2.9	12.4	−18.1
IE + Zinger, SP	1 + 2.5	2.2	37.1	2.7	74.3
	10 + 2.5	2.2	37.1	2.6	75.2
3a	1	3.8	−8.6	11.0	−4.8
	10	2.8	20.0	11.4	−8.6
3a + Zinger, SP	1 + 2.5	2.2	37.1	2.7	74.3
	10 + 2.5	2.0	42.9	2.8	73.3
3b	1	3.6	−2.9	11.4	−8.6
	10	3.2	8.6	12.1	−15.2
3b + Zinger, SP	1 + 2.5	2.0	42.9	2.4	77.1
	10 + 2.5	1.7	51.4	2.6	75.2
3c	1	2.9	17.1	8.8	16.2
	10	3.7	−5.7	12.6	−20.0
3c + Zinger, SP	1 + 2.5	2.2	37.1	2.4	77.1
	10 + 2.5	2.2	37.1	2.9	72.4
3d	1	3.8	−8.6	11.1	−5.7
	10	3.6	−2.9	13.3	−26.7
3d + Zinger, SP	1 + 2.5	2.1	40.0	2.9	72.4
	10 + 2.5	2.1	40.0	2.9	72.4
3e	1	3.6	−2.9	12.3	−17.1
	10	2.9	17.1	14.0	−33.3
3e + Zinger, SP	1 + 2.5	1.9	45.7	2.5	76.2
	10 + 2.5	1.8	48.6	2.5	76.2
Zinger, SP	2.5	1.8	48.6	2.5	76.2
Distilled water (control)	10 L t^{-1} of seeds	3.5	0	10.5	0

* Average length (*d*) of 35 measurements.

** Reduction in length (Δ*d*) is given as a percentage of control, negative values mean stimulation of the maize plant growth as compared to control.

ing the reference in this activity. Apparently, it is reasonable to continue the comparison on vegetative plants.

Thus, we developed a convenient method for the synthesis of previously unknown ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates by the DABCO-catalyzed reaction of α-(trifluoromethyl)styrenes with ethyl nitroacetate. The availability of new heterocycles is also determined by the feasibility and efficiency of the method for obtaining high-boiling-point α-(trifluoromethyl)styrenes using a modified Wittig reaction. It was shown that ethyl 5-aryl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylates can be used as plant growth regulators.

Experimental

^1H and ^{19}F NMR spectra were recorded on a Bruker-Avance^{TM}400 spectrometer (400.13 MHz for ^1H and 376.50 MHz with proton decoupling for ^{19}F). The proton chemical shifts were determined using the residual signal of chloroform and DMSO (δ 7.26 and 2.50, respectively) and recalculated relative to the $SiMe_4$ signal. The ^{19}F chemical shifts were determined using trifluoroacetic acid as an external standard and recalculated relative to the signal of $CFCl_3$. Melting points were determined on a Boetius heating stage and were not corrected. Elemental analysis was performed on a vario Micro cube CHNS-O analyzer. Mass spectra were recorded on a Kratos MS-890 spectrometer with an ionizing potential of 70 eV.

Column chromatography was performed on silica gel with a particle size of 0.06—0.20 mm (Merck Kieselgel 60). TLC plates (Merck Kieselgel 60 F254) were used to detect substances and monitor reaction progress. A 4 : 1 mixture of light petroleum ether (PE, fraction 40—70)—AcOEt was used as an eluent.

1,1,1-(Trifluoromethyl)-2-phenylpropan-2-ol and 1,1,1-(trifluoromethyl)-2-(*para*-tolyl)propan-2-ol were obtained by the Grignard reaction of methylmagnesium iodide with 2,2,2-trifluoroacetophenone and 2,2,2-trifluoro-4′-methylacetophenone, respectively.[21] The reagents were mixed at −15 °C, the reaction was carried out with stirring for 16 h.

1-Methyl-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (2a). 1,1,1-(Trifluoromethyl)-2-(*para*-tolyl)propan-2-ol (8.37 g, 41 mmol) and phosphorus pentoxide (7.52 g, 53 mmol) were mixed in a distillation apparatus with a 8-cm dephlegmator. The distillation flask was placed in a Horst heating mantle with a tem-

perature controller and heated to 450 °C by an electronic counter. At first, the liquid with a boiling point of 165 °C was distilled off; at the end of the distillation, the boiling point of the distilled liquid rose to 180 °C. A total of 5.86 g of the liquid was collected, which was re-distilled to obtain a colorless liquid (5.65 g, 74%) with b.p. 164—166 °C. ^{1}H NMR ($CDCl_3$), δ: 7.38 (d, 2 H, Ph, J = 7.8 Hz); 7.22 (d, 2 H, Ph, J = 7.8 Hz); 5.94 (m, 1 H, CH=); 5.77 (m, 1 H, CH=); 2.40 (s, 3 H, CH_3). ^{19}F NMR ($CDCl_3$), δ: –64.77 (s, CF_3).

(3,3,3-Trifluoroprop-1-en-2-yl)benzene (2b) was obtained similarly from 1,1,1-(trifluoromethyl)-2-phenylpropan-2-ol. B.p. 150—152 °C. The yield was 75%. ^{1}H NMR ($CDCl_3$), δ: 7.55—7.47 (m, 2 H, Ph); 7.46—7.38 (m, 3 H, Ph); 5.99 (m, 1 H, CH=); 5.80 (m, 1 H, CH=). ^{19}F NMR ($CDCl_3$), δ: –64.76 (s, CF_3).

1-Chloro-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (2c). Anhydrous 1,2-dimethoxyethane (45 mL) was added to a mixture of methyltriphenylphosphonium bromide (6.43 g, 18 mmol) and anhydrous potassium carbonate (3.45 g, 25 mmol). A solution of 2,2,2-trifluoro-4′-chloroacetophenone (3.13 g, 15 mmol) in 1,2-dimethoxyethane (5 mL) was added to the resulting suspension, which was refluxed for 5 h. TLC in the system PE—AcOEt (10 : 1) showed a complete conversion of the starting ketone. The reaction mixture was cooled and poured into water (200 mL). The resulting heterophase system was extracted with light petroleum ether (3×40 mL), the organic phases were combined, washed with brine, and dried with $MgSO_4$. Petroleum ether was distilled off using a Vigreux column, the residue was distilled to obtain compound **2c** (2.44 g, 78%) as a colorless liquid with b.p. 63—65 °C (12 Torr). ^{1}H NMR ($CDCl_3$), δ: 7.47—7.34 (m, 4 H, Ph), 6.00 (m, 1 H, CH=); 5.80 (m, 1 H, CH=). ^{19}F NMR ($CDCl_3$), δ: –64.92 (s, CF_3).

1-Bromo-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (2d) was obtained similarly from 2,2,2-trifluoro-4′-bromoacetophenone and methyltriphenylphosphonium iodide. A colorless liquid with b.p. 75—77 °C (12 Torr). The yield was 77%. ^{1}H NMR ($CDCl_3$), δ: 7.55 (d, 2 H, Ph, J = 8.6 Hz); 7.35 (d, 2 H, Ph, J = 8.6 Hz); 6.00 (m, 1 H, CH=); 5.80 (m, 1 H, CH=). ^{19}F NMR ($CDCl_3$), δ: –64.92 (s, CF_3).

2.4-Dichloro-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (2e) was obtained similarly from 2,2,2-trifluoro-2′,4′-dichloroacetophenone and methyltriphenylphosphonium iodide. A colorless liquid purified by column chromatography on silica gel, eluent PE—AcOEt (10 : 1). The yield was 73%. ^{1}H NMR ($CDCl_3$), δ: 7.51 (s, 1 H, Ph); 7.35—7.25 (m, 2 H, Ph); 6.25 (s, 1 H, CH=); 5.67 (s, 1 H, CH=). ^{19}F NMR ($CDCl_3$), δ: –66.85 (s, CF_3).

Synthesis of ethyl 5-*para*-tolyl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylate (3a) (general procedure). A solution of styrene (**2a**) (1.86 g, 10 mmol), ethyl nitroacetate (2.66 g, 20 mmol), and DABCO (0.11 g, 1 mmol) in anhydrous ethanol (40 mL) was heated for 80 h at 80 °C in a sealed tube. Then, the solvent was removed from the reaction mixture, the residue was purified by column chromatography on silica gel, eluent PE—AcOEt (4 : 1) to obtain **3a** as a colorless powder. The yield was 2.1 g (70%), m.p. 49 °C (Et_2O). ^{1}H NMR ($CDCl_3$), δ: 7.43 (d, 2 H, Ph, J = 8.0 Hz); 7.26 (d, 2 H, Ph, J = 8.0 Hz); 4.38 (q, 2 H, CH_2, J = 7.1 Hz); 3.94 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 3.63 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 2.40 (s, 3 H, CH_3); 1.39 (t, 3 H, CH_3, J = 7.1 Hz). ^{19}F NMR ($CDCl_3$), δ: –80.28 (s, CF_3). ^{13}C NMR ($CDCl_3$), δ: 14.03 (CH_3), 21.13 (CH_3—Ar), 42.67 (C(4)); 62.60 (OCH_2); 90.0 (q, C(5), J = 30.8 Hz); 123.75 (q, CF_3, J = 283.9 Hz); 126.27, 129.43, 131.75, 139.77, 151.16 (C(3)), 159.50 (C=O). MS (EI, 70 eV), m/z (I_{rel} (%)): 301 $[M]^+$ (7), 256 $[M - OC_2H_5]^+$ (8), 232 $[M - CF_3]^+$ (35), 210 $[M - C_7H_7]^+$ (13), 186 $[C_{10}H_9F_3]^+$ (50), 119 $[CH_3C_6H_4CO]^+$ (100), 117 $[C_9H_9]^+$ (53), 91 $[C_7H_7]^+$ (29). Found (%): C, 55.96; H, 4.75; N, 4.72. $C_{14}H_{14}F_3NO_3$. Calculated (%): C, 55.82; H, 4.68; N, 4.65.

Compounds **3b—e** were obtained similarly as colorless powders.

Ethyl 5-phenyl-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylate (3b). The yield was 1.95 g (65%), m.p. 32 °C (Et_2O). ^{1}H NMR ($CDCl_3$), δ: 7.55 (m, 2 H, Ph); 7.55—7.44 (m, 3 H, Ph); 4.38 (q, 2 H, CH_2, J = 7.1 Hz); 3.97 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 3.65 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 1.39 (t, 3 H, CH_3, J = 7.1 Hz). ^{19}F NMR ($CDCl_3$), δ: –80.18 (s, CF_3). ^{13}C NMR ($CDCl_3$), δ: 14.02 (CH_3); 42.72 (C(4)); 62.63 (OCH_2); 89.9 (q, C(5), J = 30.8 Hz); 123.5 (q, CF_3, J = 283.9 Hz); 126.37, 128.78, 129.68, 134.75, 151.20 (C(3)), 159.43 (C=O). MS (EI, 70 eV), m/z (I_{rel} (%)): 287 $[M]^+$ (14), 242 $[M - OC_2H_5]^+$ (10), 218 $[M - CF_3]^+$ (31), 214 $[M - CO_2C_2H_5]$ (29), 190 $[M - Ph + HF]^+$ (29), 172 $[C_9H_7F]^+$ (49), 164 $[M - Ph + OC_2H_5]^+$ (7), 105 $[PhCO]^+$ (100), 103 $[C_8H_7]^+$ (50), 77 $[Ph]^+$ (30). Found (%): C, 54.28; H, 4.28; N, 4.91. $C_{13}H_{12}F_3NO_3$. Calculated (%): C, 54.26; H, 4.21; N, 4.87.

Ethyl 5-(4-chlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylate (3c). The yield was 2.1 g (67%), m.p. 51 °C (Et_2O). ^{1}H NMR ($CDCl_3$), δ: 7.50—7.43 (m, 4 H, Ph); 4.38 (q, 2 H, CH_2, J = 7.1 Hz); 3.96 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 3.61 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 1.39 (t, 3 H, CH_3, J = 7.1 Hz). ^{19}F NMR ($CDCl_3$), δ: –80.19 (s, CF_3). ^{13}C NMR ($CDCl_3$), δ: 14.02 (CH_3), 42.75 (C(4)), 62.74 (OCH_2), 89.52 (q, C(5), J = 30.8 Hz); 123.48 (q, CF_3, J = 283.9 Hz); 127.86, 129.06, 133.20. 135.99. 151.19 (C(3)), 159.27 (C=O). MS (EI, 70 eV), m/z (I_{rel} (%)): 321 $[M]^+$ (11); 276 $[M - OC_2H_5]^+$ (8), 252 $[M - CF_3]^+$ (26), 248 $[M - CO_2C_2H_5]^+$ (14), 206 $[C_9H_6F_3Cl]^+$(68), 139 $[ClC_6H_4CO]^+$ (100), 137 $[ClC_8H_6]^+$ (41), 111 $[C_6H_4Cl]^+$ (11). Found (%):C, 48.52; H, 3.58; N, 4.44. $C_{13}H_{11}ClF_3NO_3$. Calculated (%): C, 48.54; H, 3.45; N, 4.35.

Ethyl 5-(4-bromophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylate (3d). The yield was 2.56 g (70%), m.p. 44 °C (Et_2O). ^{1}H NMR ($CDCl_3$), δ: 7.60 (d, 2 H, Ph, J = 8.4 Hz), 7.42 (d, 2 H, Ph, J = 8.4 Hz); 4.38 (q, 2 H, CH_2, J = 7.1 Hz); 3.96 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 3.60 (d, 1 H, CH_2, AB-system, J = 18.2 Hz); 1.39 (t, 3 H, CH_3, J = 7.1 Hz). ^{19}F NMR ($CDCl_3$), δ: –80.17 (s, CF_3). ^{13}C NMR ($CDCl_3$), δ: 14.03 (CH_3); 42.71 (C(4)); 62.75 (OCH_2); 89.6 (q, C(5), J = 30.8 Hz); 123.4 (q, CF_3, J = 283.9 Hz); 124.23, 128.1, 132.04, 133.74, 151.18 (C(3)), 159.27 (C=O). MS (EI, 70 eV), m/z (I_{rel} (%)): 365 $[M]^+$ (13), 320 $[M - OC_2H_5]^+$ (5), 296 $[M - CF_3]^+$ (21), 250 $[C_9H_6BrF_3]^+$ (38), 183 $[C_6H_4BrCO]^+$ (100), 181 $[C_8H_6Br]^+$ (13). Found (%): C, 42.71; H, 3.12; N, 3.88. $C_{13}H_{11}BrF_3NO_3$. Calculated (%): C, 42.65; H, 3.03; N, 3.82.

Ethyl 5-(2,4-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazole-3-carboxylate (3e). The yield was 2.67 g (75%), m.p. 74 °C (Et_2O). ^{1}H NMR ($CDCl_3$), δ: 7.82 (d, 1 H, Ph, J = 8.7 Hz); 7.51 (d, 1 H, Ph, J = 2.1 Hz); 7.38 (dd, 1 H, Ph, J = 8.7 Hz, J = 2.1 Hz); 4.40 (q, 2 H, CH_2, J = 7.1 Hz); 4.06 (d, 1 H, CH_2, AB-system, J = 18.9 Hz); 3.93 (d, 1 H, CH_2, AB-system, J = 18.9 Hz); 1.40 (t, 3 H, CH_3, J = 7.1 Hz). ^{19}F NMR ($CDCl_3$), δ: –80.02 (s, CF_3). ^{13}C NMR ($CDCl_3$), δ: 14.05 (CH_3); 41.62 (C(4)); 62.75 (OCH_2); 88.79 (q, C(5), J = 30.8 Hz); 123.63 (q, CF_3, J = 283.9 Hz); 127.57, 130.17, 131.23, 132.69, 136.72,

152.14 (C(3)), 159.22 (C=O). MS (EI, 70 eV), m/z (I_{rel} (%)): 310 $[M - OC_2H_5]^+$ (3), 286 $[M - CF_3]^+$ (11), 240 $[C_9H_5Cl_2F_3]^+$ (11), 173 $[C_7H_3Cl_2O]^+$ (100), 171 $[Cl_2C_8H_5]^+$ (15). Found (%): C, 43.80; H, 2.79; N, 3.89. $C_{13}H_{10}Cl_2F_3NO_3$. Calculated (%): C, 43.85; H, 2.83; N, 3.93.

Biological tests. The seeds of Krasnodar 291 AMB maize were treated with a mixture of Isoxadifen-ethyl or each of the fluoro analogs **3a—e** (at concentrations of 1 g t^{-1} and 10 g t^{-1}) with the herbicide Zinger, SP (at a concentration of 2. 5 g t^{-1} in all experiments). For comparison, maize seeds were also treated with a mixture of Isoxadifen-ethyl (at concentrations of 1 g t^{-1} and 10 g t^{-1}) with Zinger, SP (at a concentration of 2.5 g t^{-1} in all experiments). As a control, the seeds were treated with the herbicide Zinger, SP at a concentration of 2.5 g t^{-1}. The tests for the growth-regulating activity of fluoro analogs **3a—e** were carried out in two concentrations: 1 g t^{-1} and 10 g t^{-1} of seeds (see Table 1). For comparison, corn seeds were also treated with Isoxadifen-ethyl at concentrations of 1 g t^{-1} and 10 g t^{-1}. Seeds treated with distilled water were used as a control. The procedure for the preparation of test compound solutions and their mixtures with herbicides is described in the work.[22]

Structural studies were carried out using equipment of the X-Ray Structural Center of the A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 15-29-05793).

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Received June 29, 2018;
in revised form September 25, 2018;
accepted October 16, 2018