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N-Aryltrifluoroacetimidoylphosphonates

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Abstract—By reaction of N-aryltrifluoroacetimidoyl chlorides with trialkyl phosphites the corresponding *N*-aryltrifluoroacetimidoylphosphonates $CF_3C(=NAr)P(O)(OR)_2$ existing as dynamic equilibrium mixture of *Z,E*-isomers [*Z*/*E* ~ (7–12):1] were prepared. By ^{19}F NMR spectroscopy kinetic and activation parameters of *Z*–*E* isomerization were evaluated. Reaction of imidoylphosphonates with O- or S-centered nucleophiles leads to the products of addition to C=N bond whereas cycloaddition with of nitrile oxide gives previously unknown phosphorylated oxadiazolines.

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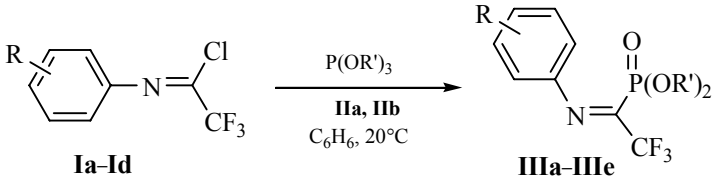
Imidoylphosphonates, the esters of iminophosphonic acids, remain comparatively poorly studied imines [1, 2]. At the same time, the presence of "oxidated" fragment of α-aminophosphonic acid [>P(O)C=N] capable of easy reductive functionalization opens new opportunities for preparing various biologically important derivatives of aminophosphonic acids. The latter, being phosphorus-containing analogs of natural amino acids, exhibit a large range of practically important properties [3, 4]. They are potential enzyme regulators and inhibitors of AIDS-protease, and due to that they are nowadays intensivsly studied. Imidoyl phosphonates containing trifluoromethyl group are especially interesting because the modifying effect of this group on chemical, physicochemical, and pharmacological properties of compounds is well known [5]. Previously we have developed methods for preparing N–H, *N*-alkyl, *N*-acyl, and *N*-phosphoryltrifluoroacetimidoylphosphonates and showed the possibility of their use for preparing biologically promising derivatives of phosphonotrifluotoalanine [1, 2, 6, 7]. The reported data concerning the synthesis of *N*-aryliminotrifluoroethylphosphonates [8–10] are scanty, their chemical properties are practically not studied, and ^1H and ^{31}P NMR spectral data are contradictory [8, 9]. In particular, the chemical shift of phosphorus reported in [8] for diethyl *N*-phenyliminotrifluoroethylphosphonate (δ_P 7.37) is not characteristic of trifluoroacetimidoylphosphonates (from –1 to –5 ppm [1, 11]).

In this work the synthesis of *N*-aryltrifluoroacetimidoylphosphonates is described and some of their chemical and physicochemical properties are studied. Most convenient approach to the target imidoylphosphonates is the reaction of synthetically available *N*-aryltrifluoroacetimidoyl chlorides [12] with phosphorous acid esters. We have found that the reaction of imidoyl chlorides **Ia–Id** with trialkyl phosphites **IIa, IIb** in benzene or ether solution leads to imidoyl phosphonates **IIIa–IIIe** in 80–94% yield (Scheme 1).

Scheme 1.



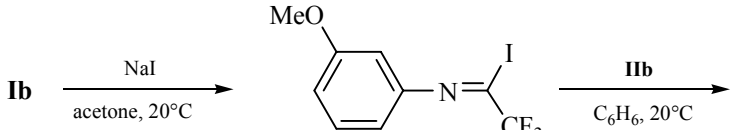
Ia–Id **IIIa–IIIe**

I, R = 4-MeO (**a**), 3-MeO (**b**), 4-CN (**c**), H (**d**); **II**, R' = Me (**a**), Et (**b**); **III**, R' = Me, R = 4-MeO (**a**), 3-MeO (**b**), 4-CN (**c**); R' = Et, R = H (**d**), 3-MeO (**e**).

Monitoring the process by ^{19}F and ^{31}P NMR spectroscopy shows that the reaction rate increases with the increase in the electron-acceptor properties of substituents R in the benzene ring: 4-CN > 4-Cl, 3-Cl, 3-MeO > H, 3-Me, 4-Me > 4-OMe. Reaction proceeds easily at room temperature (15–20°C) and requires no heating (compare with [8–10]).

It was interesting to study the possibility to use imidoyl iodides in this reaction. As is known, in some cases, for example for introduction of carboxy function to the imine carbon atom, their use is preferred [12], but these substances were not studied previously in the reactions with trivalent phosphorus compounds. We have for the first time investigated the reaction of imidoyl iodide **IV** with triethyl phosphite (Scheme 2). Reaction proceeds according to the Scheme analogous to that of corresponding imidoyl chloride **Ib**. It is the first example of the Arbuzov reaction for imidoyl iodides.

Scheme 2.



By the method of competing reactions we have evaluated relative reactivity of imidoyl iodide **IV** and the corresponding chloride **Ib** in the reaction with triethyl phosphite. It occurred that iodide reacts significantly faster ($k_{\mathbf{IV}}/k_{\mathbf{Ib}} \sim 3$), and the ratio of *E*–*Z* isomers of phosphonate **IIIe** prepared from imidoyl chloride **Ib** and iodide **IV** is the same.

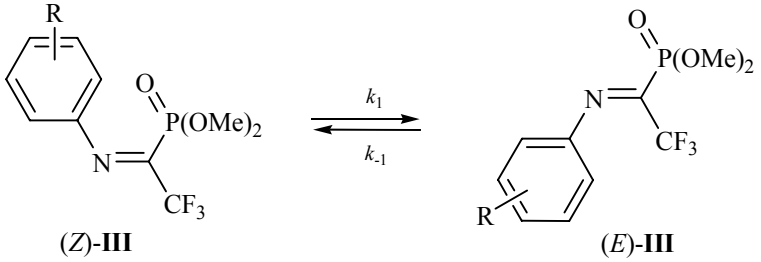
Imidoyl phosphonates **IIIa-e** are viscous light yellow liquids which can be distilled in a high vacuum without decomposition. The absorption band of C=N bond vibrations in the IR spectra appears at 1580–1610 cm^{-1}.

***Z-E* isomerizm of *N*-aryltrifluoroacetimidoylphosphonates.** Recently we have for the first time shown that some imidoyl phosphonates at room temperature exist as a mixture of *E*,*Z*- isomers and have established spectral properties permitting to distinguish these isomers [13–15]. It was established that NH and *N*-alkyltrifluoroacetimidoylphosphonates exist mainly in *Z*-form [*Z*/*E* ~ (6–10):1] [14, 15] while in the analogous benzimidoylphosphonates *E*-form is preferred [13]. Such difference was connected with large sterical demands of trifluoromethyl group (compare [6, 16]). Analogous data was observed later in [10]. We have found that *N*-trifluoroacetimidoylphosphonates **III** also exist mainly in *Z*-form [*Z*/*E* ~ (7–12):1]. Performed studies showed that the identification of isomers and evaluation of their ratio can be most conveniently carried out by ^{19}F and ^{31}P NMR spectroscopy. In the spectra of *Z*-isomers of imidoylphosphonates **III** chemical shifts of phosphorus (from 0.1 to –3.3 ppm) and fluorine (from –66.2 to –70.2 ppm) are located upfield as compared to the corresponding *E*-isomers (δ_P 1.5–4.8 ppm, δ_F –61 to –62 ppm). It follows from the obtained data that chemical shift of phosphorus in the compound **IIIa** (δ_P 7.37 ppm) reported in [8] is not correct.

The registration of NMR spectra of imidoylphosphonates **III** at elevated temperatures showed significant broadening of signals of both isomers indicating on the occurrence of dynamic process in the solution of these compounds. We consider it to be *Z*,*E*-isomerization. By ^{19}F NMR line-shape analysis we have for the first time calculated the rate constants of this process in compounds **III** at different temperatures (from –10 to –110°C). On the basis of these data using Eyring equation we have found activation and thermodynamic parameters of *Z*,*E*-isomerization in toluene-d_6 (see Scheme 3 and the table).

It follows from the data presented in the table that due to low activation barriers the isomerization relative to the C=N bond in *N*-aryltrifluoroacet-imidoylphosphonates **III** proceeds sufficiently fast at room temperature ($\tau_{1/2}$ 0.2–1.3 and 0.02–0.01 s for *Z*- and *E*-isomers of compounds **IIIa–IIIc** respectively). The increase in electron-donor properties of substituent R leads to significant and approximately equal acceleration of *Z*→*E* as well as of *E*→*Z* isomerization. Due to that the equilibrium constant only insignificantly varies in going from most electron-donor 4-MeO (σ_p –0.268) to most electron-acceptor 4-CN substituent (σ_p 0.66) in the phenyl ring (ΔG^0 6.3 and

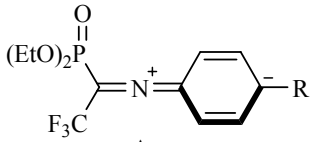
Scheme 3.



(*Z*)-**III** (*E*)-**III**

R= 4-MeO (**a**), 3-MeO (**b**), 4-CN (**c**).

5.8 kJ mol^{-1}). It is interesting to compare the results we obtained with the data [17] related to the the degenerate isomerization of *p*-substituted imines of hexafluoroacetone. These compounds can be regarded as the analogs of imidoylphosphonates **III** because trifluoromethyl and diethoxyphosphoryl groups have close polar characteristics (σ_I 0.38 and 0.37 respectively [18]). It occurred that isomerization barriers in compounds **IIIa–IIIc** are slightly higher than those in the imines of hexafluoroacetone ($\Delta G^{\#}$ 62.3–64.6 kJ mol^{-1}). At the same time the values of activation entropies for compounds **IIIa–IIIc** are positive, and for the imines of hexafluoroacetone are negative ($\Delta S^{\#}$ varies from –3.8 to –20.5 J mol^{-1} K^{-1}). Greatest differences are observed in the influence of substituents in *N*-phenyl ring on the rate of the process. The increase in the electron-acceptor properties of substituents leads to significant deceleration of *Z*→*E* isomerization for imines of hexafluoroacetone and to its acceleration for the compounds **IIIa–IIIc**. Roberts et al. [17] attribute the deceleration in the case of imines of hexafluoroacetone to the existence of the rotational "out of plane" mechanism of isomerization around the C=N bond. Accelerating effect of electron-acceptor substituents on the isomerization of compounds **III** agrees with the mechanism of "planar inversion" (compare [17, 19]) with the linear transition state of the type **A**.



A

The disappearance of sterical hindrances in going from *Z*- or *E*-configuration to the transition state **A** agrees with the positive value of activation entropies $\Delta S^{\#}$ (see the table). The important difference of compounds **III** from the imines of hexafluoroacetone is the nonequivalence of *Z*-and *E*-configurations, and

Activation and thermodynamic parameters of *Z,E*-isomerization of *N*-trifluoroacetimidoylphosphonates **IIIa–IIIc** (toluene-d_6, 298 K)

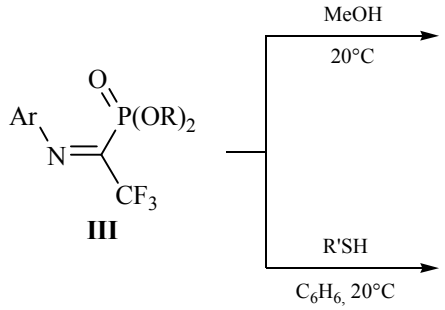
Substituent	4-MeO		3-MeO		4-CN	
	Z → *E*	*E* → *Z*	*Z* → *E*	*E* → *Z*	*Z* → *E*	*E* → *Z*
$\Delta H^{\neq}$, kJ mol^{-1}	81.9	73.4	75.1	68.6	70.1	64.6
$\Delta S^{\neq}$, J mol^{-1} K^{-1}	23.7	16.5	13.4	10.1	1.9	3.0
$\Delta G^{\neq}_{298}$, kJ mol^{-1}	74.8	68.5	71.6	65.6	69.5	63.8
ΔG^{o}_{298}, kJ mol^{-1}	6.3		6.0		5.8	
k_1 or k_{-1}, s^{-1}	0.5	1.7	4.1	6.0	20.1	41.5
$\tau_{1/2}$, s	1.3	0.4	0.2	0.1	0.03	0.02
K_{-1}/k_1	12.0		11.8		10.1	
ΔT[a]	271–370		246–364		234–306	
n[b]	13		14		15	

[a] Temperature range of measurements, K. [b] Number of points used for calculation of thermodynamic parameters.

hence *Z*,*E*-isomerization in this case is not degenerate. For all compounds studied by us *Z*-isomers are thermodynamically preferred at room temperature where the *N*-aryl substituent is *cis*-located in relation to more bulky phosphonyl group. Sterical constants R that we calculated according to [20] for $(MeO)_2P(O)$- and CF_3 groups are –2.07 and –1.39 respectively. As it follows from the table, the entropic factor favors more the *Z*→*E* isomerization than the reverse process. Assuming that the variations in entropy are connected mainly with the sterical influence of substituents at the C=N bond it may be suggested that sterical factors favor stabilization of *E*-isomer, and the preferred *Z*-configuration of compounds **III** is caused by electron effects of substituents. Indeed, the substitution of trifluoromethyl substituent (R_s = –1.36) with more bulky phenyl group (R_s = –2.39) is accompanied not by the increase, but by the considerable decrease in the content of *Z*-isomer. *Z*/*E* is 10:1 [14] and 1:17 [13] for *N*-methyltrifluoroacet- and *N*-methylbenzimidoylphosphonates respectively. Hence, the above assumption on the stercal stabilization of *Z*-configuration of trifluoroacetimidoylphosphonates [14] does not find experimental confirmation because our data show that sterically more hindered isomer is thermodynamically preferred for compounds **III**.

Chemical properties. The presence of two electron-acceptor groups at the imine carbon atom of imidoylphosphonates **III** causes sufficiently high electrophilicity of these compounds. The reactivity of compounds **III** with respect to nucleophilic reagents occupies intermediate position between the reactivity of *N*-acyl (*N*-phosphoryl, *N*-sulfonyl) and *N*-alkyltrifluoroacetimidoylphosphonates. They do not react at room temperature with dialkyl hydrogen phosphites but easily add O- and S-centered nucleophiles to give the adducts (**V, VI**) (see Scheme 4). Note that compounds **V** are sufficiently stable in pure state and in acetone solutions. At the same time while dissolved in $CDCl_3$ they partially dissociate to give the starting components.

Scheme 4.



V, Ar = Ph (**a**), 3-$MeOC_6H_4$ (**b**), R = Et (**a**), Me (**b**); **VI**, Ar = 4-$MeOC_6H_4$, R' = CH_2COOMe (**a**), 4-FC_6H_4 (**b**).

We have for the first time shown that trifluoroacetimidoylphosphonates in the reactions with dipolar compounds may act as dipolarophiles. For example, reaction of compounds **III** with nitrile oxides opens way to previously unknown phosphorylated oxadiazolines **VII** containing the fragment of aminophosphonic acid (Scheme 5).

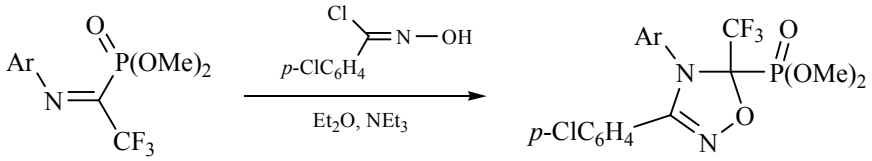
Hence, *N*-aryltrifluoroacetimidoylphosphonates exist in a form of *Z*–*E* isomers and are convenient building blocks for the synthesis of acyclic and heterocyclic derivatives containing pharmacophoric fragment of phosphonotrifluoroalanine.

EXPERIMENTAL

IR spectra were registered on an UR-20 spectrometer. NMR spectra were taken on spectrometers Varian VXR-300 (^1H), Bruker Avance DPX 500 (^1H, ^{13}C), and Varian Gemini-200 (^{31}P) with the working frequencies 299.95, 500.07, and 81.03 MHz respectively. Chemical shifts are presented relative internal TMS (^1H, ^{13}C), and external 85% phosphoric acid (^{31}P). All reactions were recorded in anhydrous conditions under argon.

Variable-temperature measurements of ^{19}F NMR spectra were carried out on a Varian VXR-300

Scheme 5.



IIIa–IIIc **VIIa–VIIc**

III, **VII**: Ar = 4-$MeOC_6H_4$ (**a**), 3-$MeOC_6H_4$ (**b**), 4-NCC_6H_4 (**c**).

spectrometer (282.2 MHz). Thermodynamic and activation parameters of the process of *Z*-*E* isomerization of compounds **III** were evaluated by the Eyring equation [12] on the basis of calculated values of rate constants of this process. The rate constants were evaluated by comparison of experimental and theoretical spectra using WINDMR program [22]. The calculations of rate constants were performed on the basis of line-shape analysis of trifluoromethyl groups were analyzed. For more correct evaluation of rate constants in the range of fast exchange the dependence of chemical shifts and population of corresponding isomers on temperature were taken into account. The relative error of evaluation of values of free activation energy was no more than 1%. Temperature-dependent ^{19}F NMR spectra were registered with the digital resolution 0.2 Hz per point. Accuracy of evaluation of temperature was 1 K.

Sterical constants R_s for $(MeO)_2P(O)$ and CF_3 groups at C=N bond were calculated according to the Eq. (1) [20].

$$R_s = 30\log\left(1 - \sum_{i=1}^{n} \frac{r_i^2}{4R_i^2}\right). \quad (1)$$

In the course of calculation the covalent radii of elements *r* presented in [23] were used. Parameter R_i, the distance between the *i*-atom and the reaction center, was evaluated from the optimized geometries of molecules calculated by quantum chemical methods (FireFly [24], PBE/6-311+G).

***N*-Aryltrifluoroacetylimidoylphosphonates (III)**. To a solution of the corresponding imidoyl chloride **I**, 10 mmol, in 5 ml of anhydrous benzene 10 mmol of triethyl phosphite was added with stirring. The obtained reaction mixture was stirred at 20°C for 24 h, evaporated under reduced pressure, and the residue was distilled in a vacuum.

***O,O*-Dimethyl-*N*-(4-methoxyphenyl)trifluoroacetimidoylphosphonate (IIIa)**. Yield 84%, mp 115–117°C (0.1 mm Hg). IR spectrum, ν, cm^{-1}: 1050 (C–O–P), 1275 (P=O), 1585 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.63 d (6H, $^3J_{PH}$ 11.4 Hz, POMe, *Z*), 3.83 s (3H, MeOAr), 3.98 d (6H, $^3J_{PH}$ 11.4 Hz, POMe, *E*), 6.93 d (2H, $^3J_{HH}$ 8.4 Hz, Ar), 7.13 d (2H, $^3J_{HH}$ 8.4 Hz, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 53.54 d ($^2J_{CP}$ 7 Hz, MeOP), 55.35 s (MeO), 113.88 s (C^3_{Ar}, C^5_{Ar}), 116.25 q.d (CF_3, $^1J_{CF}$ 180, $^2J_{PC}$ 47), 121.50 s (C^2_{Ar}, C^6_{Ar}), 139.92 d ($^3J_{CP}$ 14 Hz, C^1_{Ar}), 149.73 d.q ($^1J_{CP}$ 159 Hz, $^2J_{CP}$ 35 Hz, C=N), 159.14 s (C^4 Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –68.86 (*Z*-isomer), –61.75 (*E*-isomer). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 0.06 (*Z*-isomer), 4.78 (*E*-isomer). Calculated, %: C 42.46, H 4.21, N 4.50. $C_{11}H_{13}F_3NO_4P$. Found, %: C 42.52, H 4.19, N 4.55.

***O,O*-Dimethyl-*N*-(3-methoxyphenyl)trifluoroacetimidoylphosphonate (IIIb)**. Yield 84%, bp 124–126° C (0.1 mm Hg). IR spectrum, ν, cm^{-1}: 1040 (C–O–P), 1280 (P=O), 1590 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.58 d (6H, $^3J_{PH}$ 11.4, MeOP, *Z*), 3.82 s (3H, MeOAr), 3.97 d ($^3J_{PH}$ 11.4, MeOP, *E*), 6.56 s (1H, Ar), 6.58 d (1H, $^3J_{HH}$ 8.4 Hz, Ar), 6.78 d (1H, $^3J_{HH}$ 8.4. Ar), 6.30 t (1H, $^3J_{HH}$ 8.4, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 53.18 d ($^2J_{CP}$ 7 Hz, MeOP), 55.11 s (MeO), 104.21 s, 110.88 s, 113.02 s (C^2_{Ar}, C^4_{Ar}, C^6_{Ar}), 120.13 q.d ($^1J_{CF}$ 280 Hz, $^2J_{CP}$ 46 Hz, CF_3), 130.02 s (C^5_{Ar}), 149.35 d ($^3J_{CP}$ 13 Hz, C^1_{Ar}), 153.73 d.q ($^1J_{CP}$ 159 Hz, $^3J_{CP}$ 35 Hz, C=N), 160.05 s (C^3_{Ar}). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –69.95 (*Z*-isomer), –63.00 (*E*-isomer). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –0.78 (*Z*-isomer), 3.59 (*E*-isomer). Calculated, %: C 46.03; H 5.05; N 4.13. $C_{13}H_{17}NO_4P$. Found, %: C 45.86; H 5.11; N 4.12.

***O,O*-Dimethyl-*N*-(4-cyanophenyl)trifluoroacetimidoylphosphonate (IIIc)**. Yield 78%, bp 140–143°C (0.1 mm Hg). IR spectrum, ν, cm^{-1}: 1060 (C–O–P), 1280 (P–O), 1590 (C=N), 2170 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.66 d (6H, $^3J_{PH}$ 11.4 Hz),

MeOP, *Z*), 3.91 ($^3J_{PH}$ 11.4 Hz, *E*), 7.01 s (2H, $^3J_{HH}$ 7.8 Hz, Ar), 7.70 d (2H, $^3J_{HH}$ 7.8 Hz, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –70.20 (*Z*-isomer), –61.95 (*E*-isomer). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.0 (*Z*-isomer), 1.75 (*E*-isomer). Calculated, %: C 42.46; H 4.21; N 4.50. $C_{11}H_{13}F_3NO_4P$. Found, %: C 42.52; H 4.19; N 4.10.

***O,O*-Diethyl-*N*-phenyltrifluoroacetimidoylphosphonate (IIId)**. Yield 94%, bp 94–96°C (0.06 mm Hg). IR spectrum, ν, cm^{-1}: 1040 (C–O–P), 1285 (P=O), 1593 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.06 t (6H, $^3J_{HH}$ 6.8 Hz, $2CH_3$, *Z*), 1.32 t ($^3J_{HH}$ 6.8 Hz, $2CH_3$, *E*), 3.81 s (3H, MeO), 3.75-4.96 m (4H, $2CH_2$Me, *Z*), 4.93–4.3 m ($2CH_2$Me, *E*), 6.90 d (2H, $^3J_{HH}$ 7.3 Hz, Ph), 6.60 t (1H, $^3J_{HH}$ 7.3, Ph), 6.77 t (2H, $^4J_{HH}$ 7.3 Hz, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 15.90 d ($^4J_{CP}$ 6.5 Hz, CH_3), 63.66 d ($^3J_{CP}$ 6.7 Hz, CH_2), 118.18 s (C^3_{Ar}, C^5_{Ar}), 119.14 q.d ($^1J_{CF}$ 280 Hz, $^2J_{CP}$ 47 Hz, CF_3), 126.38 s (C^4_{Ar}), 128.64 s (C^2_{Ar}, C^6_{Ar}), 147.48 d ($^2J_{CP}$ 14 Hz, C^1_{Ar}), 153.15 d.q ($^1J_{CP}$ 160 Hz, $^2J_{CP}$ 35 Hz, C=N). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –69.17 (*Z*-isomer), –61.14 (*E*-isomer). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.0 (*Z*-isomer), 1.75 (*E*-isomer). Calculated, %: C 46.61; H 4.89; N 4.53. $C_{12}H_{13}NO_3P$. Found, %: C 46.45; H 4.94; N 4.60.

***O,O*-Diethyl-*N*-(3-methoxyphenyl)trifluoroacetimidoylphosphonate (IIIe)**. Yield 80%, bp 135–137°C (0.1 mm Hg). IR spectrum, ν, cm^{-1}: 1045 (C–O–P), 1270 (P=O), 1580 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.18 t (6H, $^3J_{HH}$ 7.2 Hz, $2CH_3$, *Z*), 1.42 t ($^3J_{HH}$ 7.2 Hz, $2CH_3$, *E*), 3.81 s (3H, MeO), 3.84–4.11 m (4H, $2CH_2$Me, *Z*), 4.24-4.39 m ($2CH_2$Me, *E*), 6.57 s (1H, Ar), 6.60 d (1H, $^2J_{HH}$ 8.5 Hz, Ar), 6.77 d (1H, $^3J_{HH}$ 8.5 Hz, Ar), 7.28 t (1H, $^3J_{HH}$ 8.5 Hz, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –69.60 (*Z*-isomer), –61.65 (*E*-isomer). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: –3.23 (*Z*-isomer), 1.48 (*E*-isomer). Calculated, %: C 45.75; H 5.61; N 4.10. $C_{13}H_{19}F_3NO_4P$. Found, %: C 45.83; H 5.53; N 4.12.

***N*-(3-Methoxyphenyl)trifluoroacetimidoyl iodide (IV)**. To a solution of 2.0 g of imidoyl chloride **Ib** in 20 ml of anhydrous acetone 3.9 g of anhydrous sodium iodide was added with stirring. After stirring for 5 h at 20°C the reaction mixture was left overnight. Then inorganic salts were filtered off, the filtrate was evaporated under a reduced pressure, and the residue was distilled in a vacuum. Yield 74%, bp 90–92°C (10 mm Hg). IR spectrum, ν, cm^{-1}: 1135, 1155 (C–F), 1715 (C=N).

^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.82 s (3H, MeO), 6.41 s (1H, Ar), 6.45 d (1H, $^3J_{HH}$ 8 Hz, Ar), 6.85 d (1H, $^3J_{HH}$ 8 Hz, Ar), 7.33 t (1H, $^3J_{HH}$ 8 Hz, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –70.57. Calculated, %: C 32.85; H 2.14; N 4.26. $C_9H_7F_3INO$. Found, %: C 32.92; H 2.19, N 4.24.

Phosphonates Va, Vb. A solution of 2 mmol of the corresponding imidoylphosphonate **III** in 3 ml of anhydrous methanol was stirred for 12 h at 20°C. Then the solvent was evaporated and the residue washed with petroleum ether.

***O,O*-Dimethyl-1-methoxy-1-(3-methoxyphenylamino)-2,2,2-trifluoroethylphosphonate (Va).** Yield 92%, mp 104–106°C. IR spectrum, ν, cm^{-1}: 1040 (C–O–P), 3340 (N–H). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.57 s (3H, MeOC), 3.77 s (3H, MeOAr), 3.84 d (3H, $^3J_{PH}$ 10.9 Hz, POMe), 3.87 d (3H, $^3J_{PH}$ 10.9 Hz, POMe), 6.48 d (1H, $^3J_{HH}$ 7.9 Hz, Ar), 6.76 d (1H, $^3J_{HH}$ 7.2 Hz, Ar), 6.83 m (2H, Ar, NH), 7.12 m (1H, Ar). ^{19}F NMR spectrum (acetone-d_6), δ_F, ppm: –71.41. ^{31}P NMR spectrum (acetone-d_6), δ_P, ppm: 16.46. Calculated, %: C 41.99; H 4.99, N 4.08. $C_{12}H_{17}F_3NO_5P$. Found, %: C 41.80, H 5.04, N 4.05.

***O,O*-Diethyl-1-methoxy-1-phenylamino-2,2,2-trifluoroethylphosphonate (Vb).** Yield 95%, mp 81–83°C. IR spectrum, ν, cm^{-1}: 1030 (C–O–P), 1280 (P=O), 3325 (N–H). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.55 s (3H, MeOC), 1.16 t (6H, $^3J_{HH}$ 7 Hz, $2CH_3$), 3.82 m (4H, $2CH_2$Me), 6.92 d (2H, $^3J_{HH}$ 7.3 Hz, Ph), 6.65 t (1H, $^3J_{HH}$ 7.3 Hz, Ph), 6.74 s (2H, $^3J_{HH}$ 7.3 Hz, Ph). ^{19}F NMR spectrum (acetone-d_6), δ_F, ppm: –71.22. ^{31}P NMR spectrum (acetone-d_6), δ_P, ppm: 13.75. Calculated, %: C 42.18, H 4.83, N 4.47. $C_{13}H_{15}F_3NO_4P$. Found, %: C 42.10, H 5.04, N 4.35.

Phosphonates VI. To a solution of 10.0 mmol of the corresponding imidoylphosphonate **III** in 5 ml of anhydrous benzene 10.0 mmol of methyl thioglycolate or 4-fluorophenol was added with stirring. The obtained reaction mixture was stirred for a day at 20°C, evaporated in a vacuum, and the residue was washed with hexane.

***O,O*-Dimethyl-1-(methoxycarbonylmethylthio)-1-(4-methoxyphenylamino)-2,2,2-trifluoroethylphosphonate (VIa).** Yield 85%, mp 76–77°C. IR spectrum, ν, cm^{-1}: 1020 (POC), 1755 (C=O), 3370 (N–H). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.60 d (1H, $^2J_{HH}$ 11.4 Hz, SCH_2), 3.68 s (3H, $^3J_{PH}$ 10.8 Hz, POMe), 3.77 s (3H, MeOAr), 3.82 d (1H, $^2J_{HH}$ 11.4 Hz, SCH_2), 3.92 d

(3H, $^3J_{PH}$ 10.8 Hz, POMe), 3.96 d (3H, $^3J_{PH}$ 10.8 Hz, POMe), 6.78 d (2H, $^3J_{HH}$ 8.4 Hz, Ar), 6.93 br s(1H, NH), 7.16 d (2H, $^3J_{HH}$ 8.4 Hz, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –67.01. ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 15.78. Calculated, %: C 40.29, H 4.59, N 3.36. $C_{14}H_{19}F_3NO_6PS$. Found, %: C 40.15, H 4.65, N 3.31.

***O,O*-Dimethyl-1-(4-methoxyphenylamino)-1-(4-fluorophenylthio)-2,2,2-trifluoroethylphosphonate (VIb).** Yield 82%, mp 69–71°C. IR spectrum, ν, cm^{-1}: 1035 (POC), 3410 (N–H). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.72 s (3H, MeOPC), 3.80 d (3H, $^3J_{PH}$ 10.5 Hz, POMe), 3.85 d (3H, $^3J_{PH}$ 10.5 Hz, POMe), 6.84 m (4H, ArF + ArOMe), 7.04 br (1H, NH), 7.26 m (4H, ArF + ArOMe). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –73.06 (3F), –117.2 (1F). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 16.32. Calculated, %: C 46.47, H 4.13, N 3.19. $C_{16}H_{18}F_4NO_4PS$. Found, %: C 46.15, H 4.20, N 3.30.

4,5-Dihydro-1,2,4-oxadiazoles (VIIa–VIIc). To a solution of 20 mmol of the corresponding imidoylphosphonate **I** and 22 mmol of triethylamine in 10 ml of anhydrous diethyl ether 22 mmol of 4-chlorophenylhydroxymoyl chloride was added with stirring at –20°C. The reaction mixture was left overnight at room temperature. The obtained precipitate was filtered off and washed with ether (2x3 ml). The filtrate was evaporated in a vacuum, and the residue was purified by chromatography on silica gel, elution with 2:1 ethyl acetate–hexane.

***O,O*-Dimethyl [4-(4-methoxyphenyl)-5-trifluoromethyl-3-(4-chlorophenyl)-4,5-dihydro-1,2,4-oxadiazol-5-yl]phosphonate (VIIa)**. Yield 74%, oil. IR spectrum, ν, cm^{-1}: 1015 (C–O–P), 1230 (P=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.57 d (3H, $^3J_{PH}$ 11.4 Hz, POMe), 3.77 s (3H, ArOMe), 3.89 d (3H, $^3J_{PH}$ 10.2 Hz, POMe), 6.79 d (2H, $^3J_{HH}$ 8.7 Hz, Ar), 7.20 d (2H, $^3J_{HH}$ 9.0 Hz, Ar), 7.24 d (2H, $^3J_{HH}$ 8.7 Hz, Ar), 7.30 d (2H, $^3J_{HH}$ 9.0 Hz, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 54.25 d ($^2J_{CP}$ 7 Hz, MeOP), 55.39 (MeOC), 55.51 d ($^2J_{CP}$ 7 Hz, MeOP), 96.70 d.q ($^1J_{CP}$ 183 Hz, $^2J_{CP}$ 34 Hz, C^5), 114.13 s (C^3, ArOMe), 121.79 s (C^1, ArCl), 121.82 q.d ($^2J_{CP}$ 36 Hz, $^1J_{CF}$ 290 Hz, CF_3), 128.47 d ($^2J_{CP}$ 1 Hz, C^1, ArOMe), 128.95, 128.95 s (C^2, C^3, ArCl), 131.17 s (C^2, ArOMe), 137.13 s (C^4, ArCl), 155.98 d ($^3J_{CP}$ 2 Hz, C^3), 159.36 s (C^4, ArOMe).^{19}F NMR spectrum ($CDCl_3$), δ_C, ppm: –78.47. ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 8.30. Calculated, %: C 46.52, H 3.69, N 6.03. $C_{18}H_{17}ClF_3N_2O_5P$. Found, %: C 46.45, H 3.74, N 6.09.

***O,O*-Dimethyl [4-(3-methoxyphenyl)-5-trifluoromethyl-3-(4-chlorophenyl)-4,5-dihydro-1,2,4-oxadiazol-5-yl]phosphonate (VIIb).** Yield 80%, oil. IR spectrum, ν, cm^{-1}: 1012 (C–O–P), 1230 (P=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.60 d (3H, $^3J_{PH}$ 11.4 Hz, POMe), 3.73 s (3H, ArOMe), 3.86 d (3H, $^3J_{PH}$ 10.8 Hz, POMe), 6.79–6.85 m (3H, Ar), 7.18 t (1H, $^3J_{HH}$ 7.8 Hz, Ar), 7.36 d (2H, $^3J_{HH}$ 8.4 Hz, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_C, ppm: –78.65. ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 8.07. Calculated, %: C 46.52, H 3.69, N 6.03. $C_{18}H_{17}ClF_3N_2O_5P$. Found, %: C 46.45, H 3.74, N 6.09.

***O,O*-Dimethyl [5-trifluoromethyl-3-(4-chlorophenyl)-4-(4-cyanophenyl)-4,5-dihydro-1,2,4-oxadiazol-5-yl]-phosphonate (VIIc).** Yield 76%, oil**.** IR spectrum, ν, cm^{-1}: 1010 (C–O–P), 1240 (P=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.60 d (3H, $^3J_{PH}$ 11.4 Hz, POMe), 3.87 d (3H, $^3J_{PH}$ 10.Hz, POMe), 7.21–7.38 m (6H, Ar), 7.59 d (2H, $^3J_{HH}$ 8.7 Hz, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_C, ppm: –78.96. ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 6.68. Calculated, %: C 47.03, H 3.07, N 9.14.$C_{18}H_{14}ClF_3N_3O_4P$. Found, %: C 47.20, H 3.02, N 9.05.

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