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To the 80th Anniversary of B.I. Ionin

N-(R-Cyclopropyl)fluorobenzimidoyl Phosphonates

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Abstract—Reaction of *N*-(R-cyclopropyl)benzimidoyl chloride with triethyl phosphite has yielded the corresponding *N*-(R-cyclopropyl)-substituted benzimidoyl phosphonates existing predominantly in the *E*-configuration [*E* : *Z* ≈ (8–10) : 1] at room temperature. ^{19}F NMR spectroscopy allowed determination of inductive and resonance σ-constants of *N*-(R-cyclopropyl)-substituted imidoyl chloride and imidoyl phosphonate groups for the first time.

Keywords: imidoyl phosphonate, imidoyl chloride, cyclopropyl, *E*/*Z*-isomerism, σ-constant
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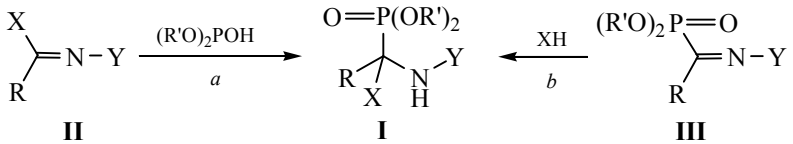
Imidoyl phosphonates (esters of iminophosphonic acids) have been a scarcely studied type of imines [1–3]. At the same time, the presence of "oxidized" fragment of α-aminophosphonic acid [>P(O)C=N] capable of reductive modification opens a wide range of applications of these compounds for synthesis of a variety of biologically important aminophosphonic acid derivatives. Being the phosphorus analogs of natural amino acids, such derivatives have revealed a complex of practically important properties [4, 5]: they may act as enzyme regulators and HIV-protease inhibitors, and have been hence intensively studied. The majority of synthetic routes leading to aminophosphonates **I** include a key stage of phosphites addition non-phosphorylated imine **II**. We have proposed another synthetic strategy; in contrast to conventional preparations via the Kabachnik–Fields and the Pudovik reactions, it uses C-phosphorylated imines **III** as starting compounds (Scheme 1) [3, 6–8]. This approach extends the synthetic possibilities: in particular, phosphonyl group additionally activates the C=N bond allowing for the modification under milder conditions. Moreover, starting from one and the same imidoyl phosphonate **III** it is possible to obtain a variety of acyclic and heterocyclic derivatives bearing an aminophosphoryl fragment.

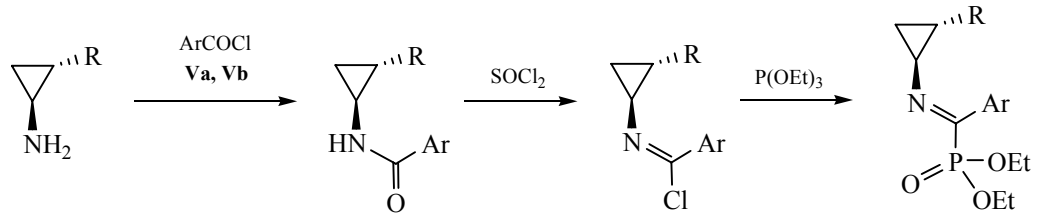
We have earlier elaborated methods to prepare NH-, *N*-alkyl-, *N*-acyl-, *N*-phosphoryl-, and *N*-sulfonylimidoyl phosphonates and demonstrated their application in synthesis of biologically important phosphorus analogs of amino acids [1, 2, 8, 9]. In this regard, the compounds containing cyclopropyl group are promising. The presence of rigid three-membered ring significantly limits the conformation lability of the molecule. The compounds modification via introduction of the strained cyclic fragments has been recognized among efficient approaches of modern medicinal chemistry [10]. We have recently prepared the first representatives of the *N*-cyclopropyltrifluoroacetimidoyl phosphonates family [11]. In this work we describe a synthetic approach to prepare fluoro-substituted benzimidoyl phosphonates containing cyclopropyl substituent at the nitrogen atom; electronic

Scheme 1.



II **I** **III**

Scheme 2.



IVa, IVb **VIa–VId** **VIIa–VIId** **VIIIa–VIIId**

IV: R = H (**a**), CF_3 (**b**); **V**: Ar = 4-FC_6H_4 (**a**), 3-FC_6H_4 (**b**); **VI–VIII**: R = H, Ar = 4-FC_6H_4 (**a**); R = CF_3, Ar = 4-FC_6H_4 (**b**); R = H, Ar = 3-FC_6H_4 (**c**); R = CF_3, Ar = 3-FC_6H_4 (**d**).

structure of the imidoyl phosphonate group was studied and some properties of the prepared phosphorylated imines were studied.

The most convenient route to the target imidoyl phosphonates is the reaction of the corresponding imidoyl chlorides with trialkyl phosphites. The first representatives of previously unknown benzimidoyl chlorides **VII** with cyclopropyl substituent at the nitrogen atom were prepared following Scheme 2.

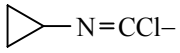
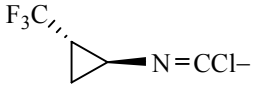
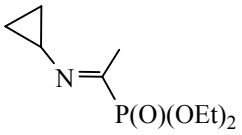
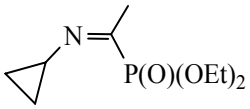
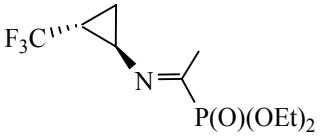
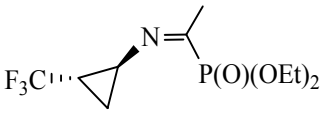
N-Cyclopropyl-substituted amides **VI** were prepared via acylation of the corresponding cyclopropylamines **IV** with fluorinated benzoic acids chlorides. Amides **IV** were converted into imidoyl chlorides **VII** with high yield upon heating with thionyl chloride; the products were liqiuds stable in anhydrous atmosphere that could be distilled in vacuum.

Heating of imidoyl chlorides **VII** with triethyl phosphite led to previously unknown benzimidoyl phosphonates **VIII** containing cyclopropyl fragment at the nitrogen atom. Imidoyl phosphonates **VIIIa**–**VIIId** were colorless or lightly colored liquids that could be distilled in high vacuum; they were stable in inert anhydrous atmosphere but were readily hydrolyzed with moisture. Spectral data of the C-phosphorylated imines confirmed their suggested structures. Signals of phosphorus nuclei at the imine carbon atom were found at 2.6–6.7 ppm, a region typical of benzimidoyl phosphonates [12, 13]. One of the most informative signals was that of imine carbon in the ^{13}C NMR spectrum (δ_C 162–163 ppm with high spin-spin coupling constant $^1J_{CP}$ 249–251 Hz) confirming the presence of the P–C=N fragment.

***Z*/*E*-Isomerism of *N*-cyclopropyl-substituted benzimidoyl phosphonates.** Earlier we have demonstrated that some imidoyl phosphonates exist in the form of *E*/*Z*-isomers at room temperature; furthermore, we have elucidated the NMR spectral features allowing for discrimination of the isomers [12, 14, 15]. In particular, NH-, *N*-alkyl-, and *N*-aryltrifluoroacetimidoyl phosphonates exist predominantly in the *Z*-form [*Z* : *E* ≈ (6–10) : 1] [14, 15], whereas the *E*-form is favorable in the case of the studied benzimidoyl phosphonates [12, 16, 17]. The investigations have revealed that ^{31}P NMR spectroscopy is the most convenient method of structure elucidation of the isomeric benzimidoyl phosphonates. The phosphorus nuclei chemical shift of *E*-isomers of imidoyl phosphonates **VIII** (δ_P 6.6–7.1 ppm) are shifted downfield as compared to these of the corresponding *Z*-isomers (δ_P 2.6–3.1 ppm). A notable difference of ^{13}C NMR spectra of the *E*- and *Z*-isomers is the value of spin-spin interaction constant of the cyclopropane ring carbon atom bound to the nitrogen atom with the phosphorus nuclei ($^3J_{C–N=C–P}$ 35–37 and 17–18 Hz for *E*- and *Z*-isomers, respectively), that is in accordance with the literature data [17]. We found that all the prepared imidoyl phosphonates **VIIIa**–**VIIId** existed predo-minantly in the *E*-configuration [(*E* : *Z* ≈ (8–10) : 1] at room temperature, the *N*-cyclopropyl group being *trans*-located with respect to more bulky phosphonyl group. Noteworthily, the recently synthesized *N*-cyclopropyl-substituted trifluoroacetimidoyl phos-phonates exist predominantly in the more hindered *Z*-configuration [11]. Likely, thermodynamic preference towards *E*- or *Z*-configuration is determined by both steric and electronic effects of the substituents.

Electronic structure of *N*-cyclopropyl-substituted imidoyl chloride and imidoyl phosphonate groups. Taking advantage of fluorine nuclei sensitivity to the electronic influence of substituents, we have estimated the electronic effects of *N*-cyclopropyl-

Chemical shifts of fluorine-substituted benzenes XC_6H_4F and σ-constants of N-substituted imidoyl chloride (nos. 1 and 2) and imidoyl phosphonate (nos. 3–6) series

Run no.	X	$\delta^F(XC_6H_4F)$		σ_I	σ_R	σ_p
		3-F	4-F			
1		0	3.92	0.09	0.13	0.22
2		0.46	4.84	0.15	0.15	0.30
3		1.35	1.60	0.275	0.008	0.28
4		–0.19	0.78	0.06	0.03	0.09
5		3.10	2.12	0.52	–0.03	0.49
6		2.39	0.24	0.42	–0.07	0.35

substituted imidoyl chloride and imidoyl phosphonyl groups for the first time. Having measured the chemical shifts of fluorine nuclei of imidoyl chlorides **VIIa**–**VIId** and imidoyl phosphonates **VIIIa**–**VIIId** in $CDCl_3$ relative to the fluorobenzene internal reference and using the Taft relations [(1) and (2)] [18], we determined inductive and resonance σ-constants of *N*-cyclopropyl-substituted imidoyl chloride and imidoyl phosphonyl moieties.

$$\sigma_I = (\delta_m^F + 0.6)/7.1, \quad (1)$$

$$\sigma_R = (\delta_p^F - \delta_m^F)/29.5. \quad (2)$$

Analysis of the results (see table) revealed that imidoyl chloride (nos. 1 and 2) as well as imidoyl phosphonate (nos. 3–6) groups with cyclopropyl substituent at the nitrogen atom possessed electron-accepting properties, the imidoylphosphonate groups being the stronger acceptors. Introduction of trifluoromethyl group at the cyclopropane ring significantly enhanced the accepting properties of the imidoyl group (cf. nos. 3 and 5; 4 and 6). Noteworthy, the σ-constant depended on the geometry configuration: the accepting properties of *E*-imidoyl phosphonate group (the major form for the imidoyl phosphonates **VIIIa**–**VIIId**) were significantly stronger than those of the corresponding *Z*-group (cf. nos. 3 and 4; 5 and 6). In accordance to the data shown in the table, imidoyl phosphonates **VIII** were less prone to addition of nucleophilic agents as compared to the similar *N*-aryl-, *N*-sulfonyl-, and *N*-phosphonylimidoyl phosphonates.

We have earlier demonstrated that the imidoyl phosphonates containing α-hydrogen in the *N*-alkyl substituent turned to undergo the 1,3-proton shift in the C=N–C triad to form alkylidenamino phosphonates [2, 19]. On the contrary, the imidoyl phosphonates containing cyclopropyl (**VIIIa**, **VIIIb**) or trifluoromethylcyclopropyl (**VIIIc**, **VIIId**) group at the nitrogen atom did not exhibit the prototropic isomerization even in the presence of nitrogen bases (Et_3N, 80°C or Et_3N–DBU, 80°C).

EXPRIMENTAL

^1H, ^{19}F, ^{31}P, and ^{13}C spectra were recorded using a Varian VXR-300 spectrometer at 299.95, 282.20, 121.42, and 75.429 MHz, respectively. The chemical

shifts are reported with respect to the internal [TMS (^{1}H and ^{13}C), $CFCl_3$ or PhF (^{19}F)] or external [85% H_3PO_4 (^{31}P)] references. All the reactions were performed in anhydrous media under argon atmosphere.

***N*-(Cyclopropyl)fluorobenzamides (VIa, VIc)**. A solution of 45.4 mmol of the corresponding fluorobenzoic acid chloride **Va** or **Vb** in 20 mL of anhydrous dichloromethane was added dropwise upon stirring to a solution of 45.4 mmol of cyclopropylamine **IVa** and 49.5 mmol of triethylamine in 100 mL of anhydrous dichloromethane at 0°C. The mixture was stirred during 12 h at room temperature, washed with aqueous $NaHCO_3$ (2 × 50 mL), water (3 × 50 mL), brine (50 mL), and dried over Na_2SO_4. After the solvent removal, the residue was crystallized from the ethyl acetate – hexane 10 : 1 mixture.

***N*-Cyclopropyl-4-fluorobenzamide (VIa).** Yield 67%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.62 m (2H, CH_2), 0.87 m (2H, CH_2), 2.88 m (1H, NCH), 6.37 br.s (1H, NH), 7.08 m (2H, Ar), 7.75 m (2H, Ar).

***N*-Cyclopropyl-3-fluorobenzamide (VIc).** Yield 67%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.63 m (2H, CH_2), 0.88 m (2H, CH_2), 2.90 m (1H, NCH), 6.29 br.s (1H, NH), 7.19 m (1H, Ar), 7.39 m (1H, Ar), 7.47 m (2H, Ar). ^{19}F NMR spectrum ($CDCl_3$): δ_F –112.32 ppm.

***N*-[(*trans*-2-Trifluoromethyl)cyclopropyl]fluorobenzamides (VIb, VId)**. A solution of the corresponding fluorobenzoic acid chloride (15.4 mmol) in 10 mL of anhydrous dichloromethane was added dropwise at 0°C upon stirring to a solution of *trans*-2-(trifluoromethyl)cyclopropylammonium chloride (15.4 mmol) and triethylamine (33.9 mmol) in 50 mL of anhydrous dichloromethane. The reaction mixture was stirred at room temperature overnight, washed with aqueous solution of $NaHCO_3$ (2 × 25 mL), water (3 × 25 mL), brine (25 mL), and dried over Na_2SO_4. After the solvent removal, the residue was crystallized from the ethyl acetate – hexane 10 : 1 mixture.

***N*-[(*trans*-2-Trifluoromethyl)cyclopropyl]-4-fluorobenzamide (VIb).** Yield 73%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.18 m (1H, C<u>H</u>H), 1.36 m (1H, CH<u>H</u>), 1.83 m (1H, $CHCF_3$), 3.21 m (1H, CHN), 6.45 br.s (1H, NH), 7.10 m (2H, Ar), 7.76 m (2H, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –66.82 d (3F, CF_3, $^3J_{FH}$ 6.0 Hz), –107.67 m (1F, ArF).

***N*-[(*trans*-2-Trifluoromethyl)cyclopropyl]-3-fluorobenzamide (VId)**. Yield 72%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19 m (1H, CH<u>H</u>), 1.37 m (1H, C<u>H</u>H), 1.84 m (1H, $CHCF_3$), 3.23 m (1H, CHN), 6.50 br.s (1H, NH), 7.21 m (1H, Ar), 7.39 m (1H, Ar), 7.48 m (2H, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –66.85 d (3F, CF_3, $^3J_{FH}$ 6.0 Hz), –111.93 m (1F, ArF).

***N*-(R-Cyclopropyl)benzimidoyl chlorides (VII)**. A mixture of the corresponding amide **VI** (30 mmol) and thionyl chloride (36 mmol) was heated at 100°C until the gas evolution ceased (≈2 h) and distilled in vacuum.

***N*-(Cyclopropyl)-4-fluorobenzimidoyl chloride (VIIa).** Yield 95.6%, bp 52–54°C (0.12 mmHg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.01 m (4H, CH_2), 3.47 m (1H, CHN), 7.05 m (2H, Ar), 7.92 m (2H, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 8.86 (CH_2), 35.31 (CHN), 114.84 d (C^3_{Ar}, C^5_{Ar}, $^2J_{CF}$ 22.0 Hz) 130.20 d (C^2_{Ar}, C^6_{Ar}, $^3J_{CF}$ 9.0 Hz), 131.68 d (C^1_{Ar}, $^4J_{CF}$ 3.0 Hz), 139.23 (C=N), 162.00 d (C^4_{Ar}, $^1J_{CF}$ 252.0 Hz). ^{19}F NMR spectrum ($CDCl_3$): δ_F –110.34 ppm.

***N*-[(*trans*-2-Trifluoromethyl)cyclopropyl]-4-fluorobenzimidoyl chloride (VIIb).** Yield 87%, bp 56°C (0.14 mmHg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 m (1H, C<u>H</u>H), 1.46 m (1H, CH<u>H</u>), 2.12 m (1H, $CHCF_3$), 3.80 m (1H, CHN), 7.08 m (2H, Ar), 7.95 m (2H, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 11.41 q (CH_2, $^3J_{CF}$ 2.0 Hz), 23.04 q (<u>C</u>HCF$_3$, $^2J_{CF}$ 37.0 Hz), 37.84 q (CHN, $^3J_{CF}$ 3.0 Hz), 115.02 d (C^3_{Ar}, C^5_{Ar}, $^2J_{CF}$ 22.0 Hz), 125.02 q (CF_3, $^1J_{CF}$ 271.0 Hz), 130.44 d (C^2_{Ar}, C^6_{Ar}, $^3J_{CF}$ 8.0 Hz), 131.10 d (C^1_{Ar}, $^4J_{CF}$ 3.0 Hz), 142.97 (C=N), 164.40 d (C^4_{Ar}, $^1J_{CF}$ 253.0 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –66.46 d (3F, CF_3, $^3J_{FH}$ 6.0 Hz), –108.76 m (1F, ArF). Found, %: C 49.50; H 3.09; Cl 13.43; N 5.31. $C_{11}H_8ClF_4N$. Calculated, %: C 49.74; H 3.04; Cl 13.35; N 5.27.

***N*-(Cyclopropyl)-3-fluorobenzimidoyl chloride (VIIc).** Yield 95%, bp 51–52°C (0.12 mmHg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.03 m (2H, CH_2), 1.04 m (2H, CH_2), 3.49 m (1H, CHN), 7.10 m (1H, Ar), 7.31 m (1H, Ar), 7.63 m (1H, Ar), 7.72 m (1H, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.11 (CH_2), 35.42 (=NCH), 115.00 d (C^2_{Ar}, $^2J_{CF}$ 24.0 Hz), 117.30 d (C^4_{Ar}, $^2J_{CF}$ 21.0 Hz), 123.74 d (C^6_{Ar}, $^4J_{CF}$ 3.0 Hz), 129.25 d (C^5_{Ar}, $^3J_{CF}$ 8.0 Hz), 137.76 d (C^1_{Ar}, $^2J_{CF}$ 8.0 Hz), 138.82 (C=N), 162.17 d (C^3_{Ar}, $^1J_{CF}$ 246.0 Hz). ^{19}F NMR spectrum ($CDCl_3$): δ_F 113.6 ppm. Found, %: C 60.53; H 4.61; Cl 18.28; N 7.21. $C_{10}H_9ClFN$. Calculated, %: C 60.77; H 4.59; Cl 17.94; N 7.09.

***N*-[(*trans*-2-Trifluoromethyl)cyclopropyl]-3-fluorobenzimidoyl chloride (VIId).** Yield 93%, bp 57°C (0.14 mmHg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm:

1.44 m (1H, CHH), 1.49 m (1H, CHH, cyclopropyl), 2.14 m (1H, $CHCF_3$), 3.82 m (1H, CHN), 7.17 m (1H, Ar), 7.37 m (1H, Ar), 7.65 m (1H, Ar), 7.74 m (1H, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 11.56 q (CH_2, $^3J_{CF}$ 2.0 Hz), 23.22 q ($CHCF_3$, $^2J_{CF}$ 37.0 Hz), 37.90 q (CHN, $^3J_{CF}$ 3.0 Hz), 115.18 d (C^2_{Ar}, $^2J_{CF}$ 24.0 Hz), 118.08 d (C^4_{Ar}, $^2J_{CF}$ 22.0 Hz), 124.98 q (CF_3, $^1J_{CF}$ 270.0 Hz), 123.96 d (C^6_{Ar}, $^4J_{CF}$ 3.0 Hz), 129.44 d (C^5_{Ar}, $^3J_{CF}$ 8.0 Hz), 137.06 d (C^1_{Ar}, $^3J_{CF}$ 8.0 Hz), 142.83 d (C=N, $^4J_{CF}$ 3.0 Hz), 162.16 d (C^3_{Ar}, $^1J_{CF}$ 247.0 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –66.48 d (3F, CF_3, $^3J_{FH}$ 6.0 Hz), –113.14 m (1F, ArF). Found, %: C 49.52; H 3.06; Cl 13.45; N 5.29. $C_{11}H_8ClF_4N$. Calculated, %: C 49.74; H 3.04; Cl 13.35; N 5.27.

***N*-(R-Cyclopropyl)benzimidoyl phosphonates (VIII)**. A mixture of the corresponding imidoyl chloride **VI** (25.3 mmol) and triethyl phosphite (30.4 mmol) was heated during 18 h at 135°C. The reaction course was monitored with ^{31}P and ^{19}F NMR spectroscopy. The target imidoyl phosphonates **VIIIa**–**VIIId** were isolated via vacuum distillation.

***O*,*O*-Diethyl-*N*-(cyclopropyl)-4-fluorobenzimidoyl phosphonate (VIIIa).** Yield 84.5%, bp 124°C (0.12 mmHg). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 m (2H, NCHCH), 1.12 m (2H, NCHCH), 1.27 t (6H, CH_3, $^3J_{HH}$ 7.1 Hz), 3.02 m (1H, CHN), 4.14 m (4H, OCH_2), 7.13 t (2H, $Ar^{3,5}$, $^3J_{HF}$ 8.5 Hz), 7.43 m (2H, $Ar^{2,6}$). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: *E*-isomer, 10.81 (NCHCH), 15.82 d (CH_3, $^3J_{CP}$ 6.0 Hz), 36.38 d (CHN, $^3J_{CP}$ 35.0 Hz), 62.72 d (OCH_2, $^2J_{CP}$ 7.0 Hz), 115.22 d ($C^{3,5}_{Ar}$, $^2J_{CF}$ 22.0 Hz), 129.54 d ($C^{2,6}_{Ar}$, $^3J_{CF}$ 8.0 Hz), 129.56 d (C^1_{Ar}, $^2J_{CP}$ 8.0 Hz), 162.50 d (C^1_{Ar}, $^1J_{CF}$ 250.0 Hz), 163.18 d (C=N, $^1J_{CP}$ 225.0 Hz); *Z*-isomer (selected signals), 11.42 s (NCHCH), 37.19 d (CHN, $^3J_{CP}$ 17.0 Hz), 61.96 d (OCH_2, $^2J_{CP}$ 6.0 Hz), 114.46 d ($C^{3,5}_{Ar}$, $^2J_{CF}$ 12.0 Hz), 129.70 d ($C^{2,6}_{Ar}$, $^3J_{CF}$ 4.0 Hz), 129.96 d (C^1_{Ar}, $^2J_{CP}$ 3.0 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –111.25 (*E*-isomer), –112.02 (*Z*-isomer, *E* : *Z* ≈ 9 : 1). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 8.09 quintet ($^3J_{PH}$ 8.0 Hz, *E*-isomer), 4.11 quintet ($^3J_{PH}$ 8 Hz, *Z*-isomer, *E* : *Z* ≈ 9 : 1). Found, %: C 55.98; H 6.35; N 4.55. $C_{14}H_{19}FNO_3P$. Calculated, %: C 56.19; H 6.40; N 4.68.

***O*,*O*-Diethyl-*N*-[(*trans*-2-тrifluoromethyl)cyclopropyl]-4-fluorobenzimidoyl phosphonate (VIIIb).** Yield 82.3%, bp 103–104°C (0.12 mmHg). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.27 m (6H, CH_3) 1.37 m (1H, NCHCHH), 1.54 m (1H, NCHCHH), 2.22 m (1H, $CHCF_3$), 3.30 m (1H, CHN), 4.14 m (4H, OCH_2), 7.17 m (2H, $Ar^{3,5}$), 7.40 m (2H, $Ar^{2,6}$). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 12.99 (NCHCH), 15.76 d (CH_3, $^3J_{CP}$ 6.0 Hz), 24.43 q ($CHCF_3$, $^2J_{CF}$ 37.0 Hz), 38.55 d.d (=NCH, $^3J_{CP}$ 36.0, $^3J_{CF}$ 2.0 Hz), 62.95 d (OCH_2, $^2J_{CP}$ 7.0 Hz), 63.02 d (OCH_2, $^2J_{CP}$ 6.0 Hz), 115.54 d ($C^{3,5}_{Ar}$, $^2J_{CF}$ 22.0 Hz), 124.86 q (CF_3, $^1J_{CF}$ 271.0 Hz), 129.40 d.d ($C^{2,6}_{Ar}$, $^3J_{CF}$ 8.0, $^3J_{CP}$ 4.0 Hz), 162.82 d (C^4_{Ar}, $^1J_{CF}$ 251.0 Hz), 167.32 d (C=N, $^1J_{CP}$ 223.0 Hz); *Z*-isomer (selected signals), 13.31 (NCHCH), 15.64 d (CH_3, $^3J_{CP}$ 6.0 Hz), 39.22 d.d (=NCH, $^3J_{CP}$ 18.0, $^3J_{CF}$ 2.0 Hz), 62.28 d (OCH_2, $^2J_{CP}$ 6.0 Hz), 62.38 d (OCH_2, $^2J_{CP}$ 6.0 Hz), 114.60 d ($C^{3,5}_{Ar}$, $^2J_{CF}$ 21.0 Hz), 125.14 q (CF_3, $^1J_{CF}$ 271.0 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –66.3 d (3F, CF_3, $^3J_{FH}$ 7.0 Hz), –110.50 m (1F, ArF, *E*-isomer); –65.94 d (3F, CF_3, $^3J_{FH}$ 4.0 Hz), –111.19 m (1F, ArF, *Z*-isomer, *E* : *Z* ≈ 8:1). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 6.62 (*E*-isomer), 2.68 (*Z*-isomer, *E* : *Z* ≈ 8 : 1). Found, %: C 48.98; H 4.89; N 3.73. $C_{15}H_{18}F_4NO_3P$. Calculated, %: C 49.05; H 4.94; N 3.81.

***O*,*O*-Diethyl-*N*-(cyclopropyl)-3-fluorobenzimidoyl phosphonate (VIIIc).** Yield 83%, bp 110–111°C (0.12 mmHg). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.97 m (2H, NCHCH), 1.14 m (2H, NCHCH), 1.28 t (6H, CH_3, $^3J_{HP}$ 7.2 Hz), 3.01 m (1H, =NCH), 4.14 m (4H, OCH_2), 7.12 m (2H, Ar), 7.19 m (1H, Ar), 7.42 m (1H, Ar). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –111.25 (*E*-isomer), –113.79 (*Z*-isomer, *E* : *Z* ≈ 10 : 1). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 7.75 (*E*-isomer), 3.72 (*Z*-isomer, *E* : *Z* ≈ 10 : 1). Found, %: C 56.12; H 6.38; N 4.63. $C_{14}H_{19}FNO_3P$. Calculated, %: C 56.19; H 6.40; N 4.68.

***O*,*O*-Diethyl-*N*-[(*trans*-2-trifluoromethyl)cyclopropyl]-3-fluorobenzimidoyl phosphonate (VIIId).** Yield 85%, bp 106°C (0.12 mmHg). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.28 t (6H, CH_3), 1.38 m (1H, NCHCHH), 1.54 m (1H, NCHCHH), 2.22 m (1H, $CHCF_3$), 3.28 m (1H, =NCH), 4.15 m (4H, OCH_2), 7.14 m (3H, Ar), 7.45 m (1H, Ar). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.12 (NCHCH), 15.84 d (CH_3, $^3J_{CP}$ 6.0 Hz), 24.61 q ($CHCF_3$, $^2J_{CF}$ 37.0 Hz), 38.73 d.q (=NCH, $^3J_{CP}$ 35.0, $^3J_{CF}$ 3.0 Hz), 63.12 d (OCH_2, $^2J_{CP}$ 6.0 Hz), 63.19 d (OCH_2, $^2J_{CP}$ 7.0 Hz), 114.40 d.d (C^2_{Ar}, $^2J_{CF}$ 23.0, $^3J_{CP}$ 3.0 Hz), 116.46 d (C^4_{Ar}, $^2J_{CF}$ 22.0 Hz), 122.96 d.d (C^6_{Ar}, $^3J_{CP}$ 4.0, $^4J_{CF}$ 1.8 Hz), 124.83 q (CF_3, $^1J_{CF}$ 271.0 Hz), 130.24 d (C^5_{Ar}, $^3J_{CF}$ 8.0 Hz), 134.98 d.d (C^1_{Ar}, $^2J_{CP}$ 30.0, $^3J_{CF}$ 7.0 Hz), 162.25 d (C^3_{Ar}, $^1J_{CF}$ 249.0 Hz), 166.92 d (C=N, $^1J_{CP}$ 223.0 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: –66.18 d (3F, CF_3, $^3J_{FH}$ 8.0 Hz), –114.44 m (1F, ArF, *E*-isomer); –65.98 d (3F, CF_3, $^3J_{FH}$ 6.0 Hz), –113.34 m (1F, ArF, *Z*-isomer, *E* : *Z* ≈

10 : 1). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: 6.66 (*E*-isomer), 2.64 (*Z*-isomer, $E : Z \approx 10 : 1$). Found, %: C 48.71; H 4.91; N 3.75. $C_{15}H_{18}F_4NO_3P$. Calculated, %: C 49.05; H 4.94; N 3.81.

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