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Fluoro-containing Heterocycles: V.* Cyclization of 3-Azolylamino-2-polyfluorobenzoylacrylates**

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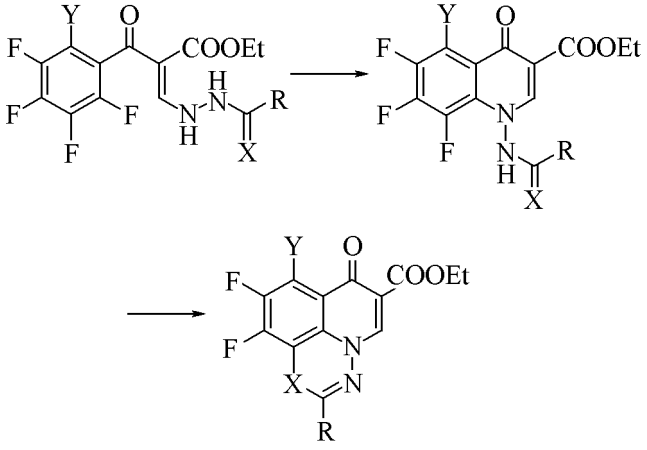
Abstract—The heating of ethyl 3-azolylamino-2-polyfluorobenzoylacrylates in acetonitrile in the presence of KF gave rise to derivatives of 1-azolyl-substituted quinolones or azolo[1,5-a]pyrimidines.

In our preceding studies we extensively used cyclization of 3-hydrazido derivatives of 2-polyflyoro-benzoylacrylic acids in the synthesis of [*i*,*j*]-annealed quinolonecarboxylic acids [2, 3] (Scheme 1). In these tricyclic systems the quinolone carcass is anneled with six-membered oxadiazine or thiadiazine rings, and they may be regarded as analogs of the known antibacterial agents, ofloxacin and marbofloxacin.

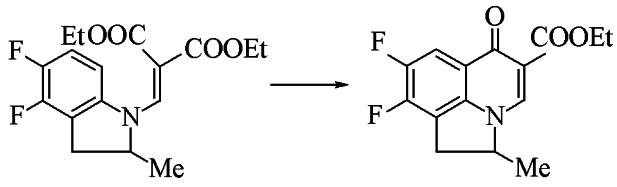
Scheme 1.



X = O, S; Y = H, F.

The other methods of synthesis of [*i*,*j*]-fused fluoroquinolones are also known [4]; however in the literature are hardly mentioned cases of a five-membered cycles annealed at facets [*i*,*j*] of a quinolone carcass. A single example concerns a preparation of derivatives of pyrrolo[3,2,1-*i*,*j*]quinoline-5-carboxylic acid by building up of a pyridone fragment (Scheme 2) [5].

Scheme 2.



Proceeding from the data of the previous research [2, 3, 6] we presumed that the reaction between 2-aminazoles **IIa, b** with ethyl 2-polyfluorobenzoyl-3-ethoxyacrylates (**Ia, b**) can provide derivatives of 1-azolylsubstituted quinolones **IV** capable of further cyclization into tetracyclic compounds **V**.

Actually we succeeded in carrying out the first part of the scheme. The reaction of compounds **Ia, b** and **IIa, b** in ethanol at 18–20°C gave rise to 3-azolylamino-2-polyfluorobenzoylacrylates (**IIIa–d**) (Scheme 3). The structure of these compounds was confirmed with ^{1}H NMR spectra. For instance, same as initial acrylate **Ia** compound **IIIa** in solution exists as two geometrical isomers with respect to the C^2–C^3 bond as shows the presence in the ^{1}H NMR spectrum of a double set of proton signals from the ester group, =CH–NH fragment, and from pyrazole and tetrafluorobenzoyl substituents.

Cyclization of acrylates **III** was carried out in boiling acetonitrile in the presence of KF within 2–4 h. We found that depending on the substituents X and Y the reaction occurs along different pathways. In cyclization of ethyl 2-pentafluorobenzoyl-3(pyrazol-3-yl)-aminoacrylate (**IIIb**) was obtained 1-substituted

* For communication IV, see [1].

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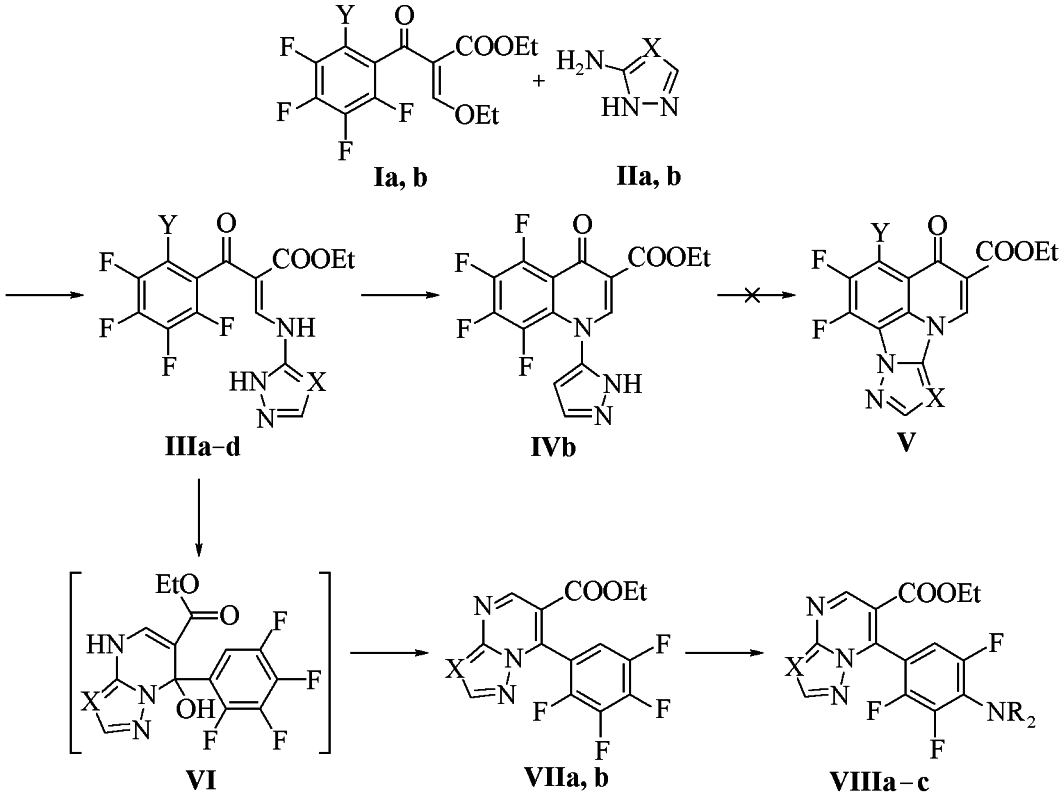
Scheme 3.



I, Y = H (**a**), F (**b**); **II, VI, VII**, X = CH (**a**), N (**b**); **III**, X = CH, Y = H (**a**), F (**b**); X = N, Y = H (**c**), F (**d**); **VIII**, NR_2 = pyrrolidin-1-yl, X = CH (**a**), N (**b**); NR_2 = morpholino, X = N (**c**).

quinolone **IVb**. In the mass spectrum of compound **IVb** is present a molecular peak with *m*/*z* 355 and also a strong peak (100%) corresponding to an ion $[M-COOC_2H_4]^+$. In the IR spectrum of compound **IVb** appear absorption bands at 1730 and 1640 cm^{-1} of the stretching vibrations from carbonyls in the ester group and quinolone fragment respectively. In the ^{19}F NMR spectrum are observed the signals from four fluorine atom; therewith the chemical shifts, multiplicity of signals, and coupling constants are similar to those in the ^{19}F NMR spectra of the other derivatives of 1,4-dihydro-4-oxo-5,6,7,8-tetrafluoroquinoline-3-carboxylic acid that we have prepared before [2]. The ^1H NMR spectrum is consistent with the structure **IVb**, and in distinction from the initial acrylate **IIIb** the doublet of NH group is lacking, and the signal of the CH= proton appears as a singlet.

The attempt to perform further cyclization of compound **IVb** with the use of a stronger agent for binding HF, diazabicycloundec-7-ene (DBU), failed. Note that in the mass spectrum of compound **IVb** the ion peak $[M-HF]^+$ is lacking; this peak usually is present among fragment peaks of compounds prone to further cyclization [2, 6]. The difficulty in performing the desired cyclization are probably due to the high strain in the fused system **V**.

It is interesting that the cyclization of tetrafluorobenzoyl analog **IIIa** occurs in dissimilar way: here forms not a quinolone structure of **IV** type but a derivative of pyrazolo[1,5-a]pyrimidine (**VIIa**). The structure of the latter was proved by ^1H and ^{19}F NMR spectra. In the mass spectrum of compound **VIIa** is present a peak of the molecular ion *m*/*z* 339, in the ^{19}F NMR spectrum appear signals from four fluorine atoms. In the IR spectrum of the compound in the C=O vibrations region is observed a single band from the ester group at 1725 cm^{-1}. Unlike the initial acrylate **IIIa**, compound **VIIa** in the ^1H NMR spectrum has no signals from two NH groups, and the characteristic multiplet belonging to the proton of the polyfluorobenzene fragment corresponds to the coupling thereof with four fluorine atoms of the ring. Thus all data indicate that in the concurrent reaction with the participation of a carbonyl group forms compound **VIIa**.

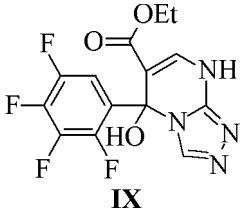
The cyclization of ethyl 2-tetrafluorobenzoyl-3-(1,2,4-triazol-3-yl)aminoacrylate (IIIc) takes a

Table 1. Yields, melting points, and elemental analyses of compounds synthesized

Compd. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIIa	82	140–142	50.61	3.24	11.61	$C_{15}H_{11}F_4N_3O_3$	50.43	3.10	11.76
IIIb	73	132–134	48.19	2.81	11.09	$C_{15}H_{10}F_5N_3O_3$	48.01	2.69	11.20
IIIc	76	146–148	41.10	2.91	15.52	$C_{14}H_{10}F_4N_4O_3$	40.93	2.79	15.64
IIId	71	178–180	44.81	2.58	14.70	$C_{14}H_9F_5N_4O_3$	44.69	2.41	14.89
IVb	70	244–246	50.49	2.58	12.01	$C_{15}H_9F_4N_4O_3$	50.71	2.55	11.83
VIIa	74	84–86	53.29	2.58	12.53	$C_{15}H_9F_4N_3O_2$	53.11	2.67	12.39
VIIb	60	102–104	49.10	2.32	16.35	$C_{14}H_8F_4N_4O_2$	49.41	2.35	16.47
VIIIa	56	85–87	55.90	2.31	10.41	$C_{19}H_{17}F_3N_3O_2$	55.75	2.16	10.27
VIIIb	61	118–120	55.50	4.31	18.02	$C_{18}H_{16}F_3N_5O_2$	55.24	4.12	17.90
VIIIc	60	104–106	53.40	4.11	17.42	$C_{18}H_{16}F_3N_5O_3$	53.07	3.96	17.19
XV	50	148–150	48.03	3.31	13.28	$C_{17}H_{13}F_3N_4O_6$	47.89	3.05	13.15

similar course, and arises only one of the two possible regioisomers, namely **VIIb**. This is evidenced by a single set of resonances in the ^{1}H and ^{19}F NMR spectra. In the ^{19}F NMR spectrum of compound **VIIb** appear signals of the four fluorine atoms as in the spectrum of initial acrylate **IIIb**. The most intensive peak in the mass spectra corresponds to the molecular ion with *m*/*z* 340. The main fragmentation paths of the molecular ion M^+ are as follows: fluorine atom elimination, decomposition of the ester moiety, cleavage of the tetrafluorophenyl fragment, and HCN elimination. This fragmentation pattern completely corresponds to structure **VIIb**. As in the IR spectrum of compound **VIIa**, in the spectrum of compound **VIIb** appears the ν(CO) absorption band of the ester group at 1720 cm^{-1} and no stretching vibrations of the carbonyl in quinolone fragment are observed. The ^{1}H NMR spectrum is also consistent with structure **VIIb** since there are no signals from NH groups, but appears a characteristic multiplet of an aromatic proton at 7.8 ppm. Two more singlets from aromatic protons are also observed at 8.8 and 9.4 ppm.

Since compounds **VII** originate from a nucleophilic attack of the carbonyl from the benzoyl moiety, triazolyl derivative **IIIc** may give rise to two alternative adducts **VIb** and **IX**.



IX

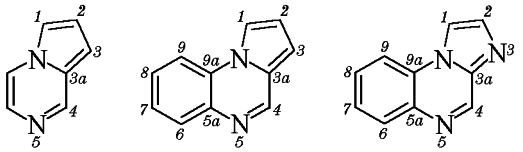
Thus the cyclization product of acrylate **IIIc** may have a structure of triazolo[1,5-a]pyrimidine or triazolo[4,3-a]pyrimidine. Basing on the literature data on the structure of 1,2,4-triazolopyrimidines obtained from 3-amino-1,2,4-triazole and β-diketones [7–10] we considered as more probable the structure of triazolo[1,5-a]pyrimidine (**VIIb**).

The structure of compound **VIIb** was supported experimentally by ^{13}C NMR spectra recorded without decoupling from protons and with usual wide-band decoupling (Table 2). The coupling ^{13}C–^{19}F allows unambiguous assignment of the carbon signals of the polyfluorophenyl substituent. The signal of the nodal carbon C^{3a} appears at 155.4 ppm as a doublet of doublets with the coupling constants 15.3 and 9.8 Hz. The assignment of the latter to $^3J(C^{3a}, H^5)$ and $^3J(C^{3a}, H^2)$ was carried out with the use of stationary selective decoupling from H^5 and H^2protons.

Decoupling from the proton signal at 9.4 ppm resulted in a change in multiplicity of carbonyl group carbon and of the doublet from C^6 (Table 2). Therefore the signal at 9.4 in the ^{1}H NMR spectrum was assigned to H^5 proton, and consequently the signal at 8.8 ppm belonged to H^2. In the ^{13}C NMR spectrum with selective decoupling from H^5 the C^{3a} signal is reduced to doublet with a coupling constant 9.8 Hz corresponding to coupling with H^2 atom. Thus the constant 15.3 Hz is due to the coupling of C^{3a} and H^5. Actually in the ^{13}C NMR spectrum with selective decoupling from H^2 the signal of C^{3a} appears as a doublet with a coupling constant $^3J(C^{3a}, H^5)$ of 15.3 Hz. In the literature [11, 12] were mentioned similar values of coupling constants: $^3J(C^{3a}, H^5)$

15.1 Hz for 5-methyltetrazolo[1,5-*a*]pyrimidine and $^3J(C^{3a}, H^2)$ 9.0 Hz for 1,2,4-triazolo[5,1-c][1,2,4]-triazine.

The 9,8 Hz value of the constant $^3J(C^{3a}, H^2)$ is an additional proof of the triazolo[1,5-a]pyrimidine structure of compound **VIIb** and not triazolo[4.3-a]-pyrimidine one. According to published data in the spectra of various azoloazines **X–XII** the coupling between atoms C^{3a} and H^1 via a nodal nitrogen atom is characterized by smaller values of constants than $^3J(C^{3a}, H^2)$ [13].



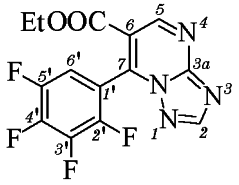
X **XI** **XII**

$^3J(C^{3a}, H^2)$ 7.7–8.0,
$^3J(C^{3a}, H^1)$ 5.3–5.8 Hz.

The fluoro-containing derivatives of azolopyrimidines (**VII**) may be potential biologically active compounds [9]. Therefore we studied substitution of fluorine atom with amine rests resulting in compounds **VIII**. The conclusion on replacement of the fluorine in *para*-position with respect to the heterocyclic substituent follows from the ^{1}H NMR spectra where the proton of the benzene ring appears as a doublet of doublets of doublets with the coupling constants 13.9–14.1, 6.0–6.1, and 2.1–2.4 Hz.

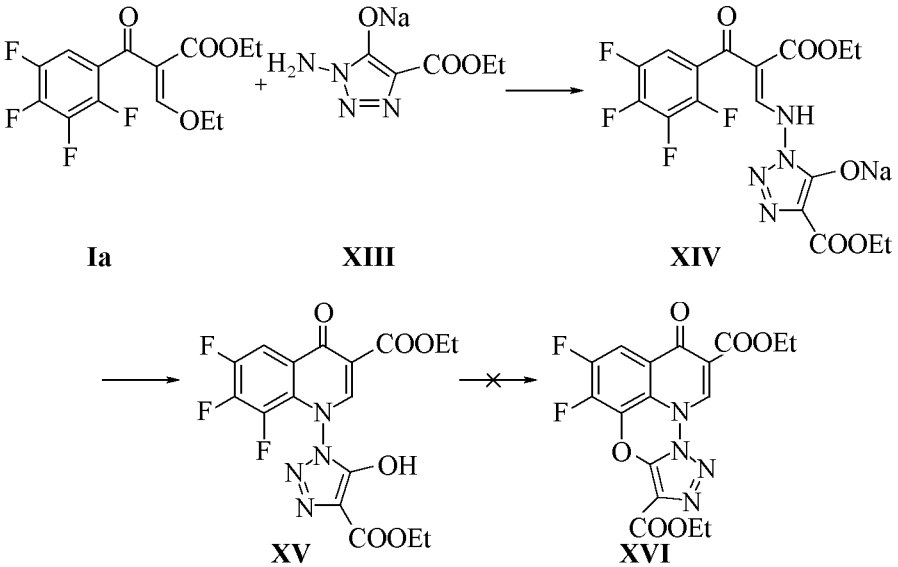
Ethyl 2-pentafluorobenzoyl-3-(1,2,4-triazol-3-yl)aminoacrylate (**IIId**) at heating in acetonitrile in the presence of KF (or DBU) failed to give cycliza-

Table 2. ^{13}C NMR spectrum of compound **VIIb**



Carbon atom	Chemical shifts, δ_C, ppm	$^nJ(^{13}C, ^1H)$ or $^nJ(^{13}C, ^{19}F)$
C=O	162.139	^3J(C, H) 3.0, ^3J(C, H^5) 1.7
OCH_2	61.964	^1J(C, H) 149.4, ^2J(C, H) 4.5
CH_3	13.423	^1J(C, H) 127.2, ^2J(C, H) 2.7
C^2	157.523 d	$^1J(C^2, H^2)$ 210.7
C^{3a}	155.437 d.d	$^3J(C^{3a}, H^5)$ 15.3, $^3J(C^{3a}, H^2)$ 9.8
C^5	155.706 d	$^1J_{(C^5}$, H^5) 191.8
C^6	114.593 d	$^2J(C^6, H^5)$ 7.8
C^7	141.599	–
$C^{1'}$	114.064	$^2J(C^{1'}, F^{2'})$ 14.0, $^3J(C^{1'}, F^{3'})$ 9.6, $^4J(C^{1'}, F^{4'})$ 3.9
$C^{2'}$	139.897	$^1J(C^{2'}, F^{2'})$ 251.45, $^2J(C^{2'}, F^{3'})$ 16.1, $^3J(C^{2'}, F^{4'})$ 12.5, $^4J(C^{2'}, F^{5'})$ 4.0
$C^{3'}$	144.687	$^1J(C^{3'}, F^{3'})$ 249.25, $^2J(C^{3'}, F^{4'})$ 12.6, $^3J(C^{3'}, F^{5'})$ 3.2
$C^{4'}$	146.216	$^1J(C^{4'}, F^{4'})$ 245.48, $^2J(C^{4'}, F^{3'})$ 10.6, $^3J(C^{4'}, F^{2'})$ 2.2
$C^{5'}$	141.294	$^1J(C^{5'}, F^{5'})$ 256.86, $^2J(C^{5'}, F^{4'})$ 17.0, $^3J(C^{5'}, F^{3'})$ 13.0, $^4J(C^{5'}, F^{2'})$ 3.8
$C^{6'}$	113.493	$^1J(C^{6'}, H^{6'})$ 174.5; $^2J(C^{6'}, F^{5'})$ 22.1, $^3J(C^{6'}, F^{4'})$ 3.5, $^4J(C^{6'}, F^{3'})$ 1.8

Scheme 4.



Ia **XIII** **XIV** **XV** **XVI**

tion products of type **IV** or **VII**. The lack of ability to form triazolopyrimidine in acrylate **IIId** in contrast to **IIIc** may be ascribed to more difficult cyclization of pentafluorobenzoyl derivatives than tetrafluorobenzoyl compounds [6]. Acrylate **IIId** also shows low capability of intramolecular substitution of fluorine atom. It should be noted that unlike acrylates **IIIa, b** in the mass spectrum of compound **IIId** the strongest peak (100%) corresponds to the molecular ion, and the peaks of ions $[M-HF]^+$ and $[M-H_2O]^+$ are lacking.

The reaction of acrylate **Ia** with 1-amino-1,2,3-triazole (**XIII**) in ethanol at 18–20°C in 2 h afforded a mixture of 3-(1,2,3-triazol-1-yl)aminoacrylate (**XIV**) and quinolone **XV**. The heating of the same mixture in benzene for 3 h yields exclusively quinolone **XV** (Scheme 4).

In this case no reaction with participation of the carbonyl group of compound **XIV** is observed. The structure of compound **XV** was established from ^1H and ^{19}F NMR and mass spectra. In the mass spectra is present the molecular ion peak *m*/*z* 426, in the ^{19}F NMR spectrum appear signals from three fluorine atoms. Each fluorine signal is a doublet of doublets of doublets, and the coupling constants are close in values to those in the spectra of derivatives of 1,4-dihydro-4-oxo-6,7,8-trifluoroquinoline-3-carboxylic acids we have described before [2]. In the ^1H NMR spectrum of compound **XV** the proton signal from benzene ring appears as a doublet of doublets of doublets with the coupling constants 10.3, 8.3, and 2.0 Hz. Also are present the signals from two ethyl groups, and singlets from CH= and OH groups.

The presence in the triazole moiety of compound **XV** a 5-hydroxy group suggested a possibility of further cyclization into a tetracyclic structure **XIII**. Regretfully this attempt failed either at heating quinolone **XII** in toluene in the presence of K_2CO_3 or in acetonitrile in DBU presence. Note that the mass spectrum of compound **XV** also does not contain a peak corresponding to ion $[M-HF]^+$.

EXPERIMENTAL

^1H NMR spectra were registered in DMSO-d_6 and $CDCl_3$ on spectrometer Bruker WP-250 at operating frequency 250.135 MHz, internal reference TMS. ^{19}F NMR spectra of solutions in DMSO-d_6 were recorded on spectrometer Bruker WP-80-SY at operating frequency 75.38 MHz, internal reference hexafluorobenzene. ^{13}C NMR spectra were recorded in DMSO-d_6 on spectrometer Bruker DRX-400 at operating frequency 100.61 MHz. Mass spectra were measured on spectrometer Varian MAT 311A under the following conditions: accelerating voltage 3kV, cathode emission current 300 μA, ionizing electrons energy 70eV, direct input of the sample into the source. IR spectra were registered on Specord 75IR instruments from KBr pellets. Yields, melting points, and elemental analyses of compounds **III, IV, VII, VIII, XII** are presented in Table 1.

Ethyl 3-(azol-3-yl)amino-2-[tetra(penta)fluorobenzoyl]acrylates IIIa–d. To a dispersion of 0.5 g (6.0 mmol) of 3-aminopyrazole (**IIa**) in 15 ml of ethanol was added 1.9 g (6.0 mmol) of ethyl 2-tetrafluorobenzoyl-3-ethoxyacrylate (**Ia**). The reaction mixture was stirred for 3 h at 18–20°C, the formed precipitate of compound **IIIa** was filtered off and recrystallized from benzene. Yield 1.8 g (82%). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.08 t (3H, CH_3, isomer 1), 0.99 t (3H, CH_3, isomer 2), 4.07 q (2H, OCH_2, isomer 1), 4.02 q (2H, OCH_2, isomer 2), 6.49 s (1H, $H^{4'}$, isomer 1), 6.42 s (1H, $H^{4'}$, isomer 2), 7.80 m (1H, $H^{6''}$, isomer 1), 7.50 m (1H, $H^{6''}$, isomer 2), 7.73 s (1H, $H^{5'}$, isomer 1), 7.36 s (1H, $H^{5'}$, isomer 2), 8.76 d (1H, H^3, $^3J_{HH}$ 13.2 Hz, isomer 1), 8.64 d (1H, H^3, $^3J_{HH}$ 13.1 Hz, isomer 2), 12.25 d (1H, NH, $^3J_{HH}$ 13.1 Hz, isomer 1), 11.07 d (1H, NH, $^3J_{HH}$ 13.1 Hz, isomer 2), 12.82 s (1H, NH, isomer 1), 12.74 s (1H, NH, isomer 2), ratio of isomers 1 and 2 is 2 : 1. Mass spectrum *m*/*z* (I_{rel}, %): 357 (60), M^+, 338 (16), 311 (56), 292 (56), 265 (100), 177 (64). IR spectrum (KBr), ν, cm^{-1}: 1670 (CO), 1640 (CO).

Similarly were prepared compounds **IIIb–d**; they were crystallized from ethanol.

Compound (IIIb). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.16 t (3H, CH_3), 4.08 q (2H, OCH_2), 6.40 s (1H, $H^{4'}$), 7.63 s (1H, $H^{5'}$), 8.81 d (1H, H^3, $^3J_{HH}$ 13.3 Hz), 12.41 br.d (1H, NH, $^3J_{HH}$ 13.1 Hz), 12.73 br.s (1H, NH). Mass spectrum, *m*/*z* ($I_{rel.}$, %): 375 (91) M^+, 355 (16), 329 (76), 310 (40), 283 (100), 258 (23), 195 (57). IR spectrum, KBr, ν, cm^{-1}: 1685 (CO), 1630 (CO).

Compound (IIIc). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.06 t (3H, CH_3), 4.03 q (2H, OCH_2), 7.66 m (1H, $H^{6''}$), 7.70 s (1H, $H^{5'}$), 7.89 s (1H, H^3), 11.56 br.s (1H, NH), 13.43 br.s (1H, NH). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 158.39 s, 157.37 s, 145.83 s, 141.96 s.

Compound (IIId). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.19 t (3H, CH_3), 4.11 q (2H, OCH_2), 8.42 s (1H, $H^{5'}$), 8.92 s (1H, H^3), 12.4 br.s (1H,

NH), 14.1 br.s (1H, NH). Mass spectrum, *m*/*z* ($I_{rel.}$, %): 376 (100) M^+, 357 (15), 330 (99), 302 (59), 284 (95), 195 (88), 163 (68). IR spectrum, KBr, ν, cm^{-1}: 1680 (CO), 1635 (CO).

Ethyl 4-oxo-1-(pyrazol-3-yl)-5,6,7,8-tetrafluoro-1,4-dihydroquinoline-3-carboxylate (IVb). To a dispersion of 0.6 g (1.6 mmol) of acrylate **IIIb** in 12 ml of anhydrous acetonitrile was added 0.2 g (3.2 mmol) of KF. The reaction mixture was boiled for 2 h. On cooling the precipitate was filtered off, washed with water, and recrystallized from DMSO. Yield 0.4 g (70%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.26 t (3H, CH_3), 4.22 q (2H, OCH_2), 6.59 s (1H, $H^{5'}$), 7.88 s (1H, $H^{4'}$), 8.27 s (1H, H^2), 13.7 s (1H, NH). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 162.10 d.d (1F, F^7, $^3J_{FF}$ 22.0, $^3J_{FF}$ 20.7 Hz), 150.57 t.d (1F, F^6, $^3J_{FF}$ 21.6, $^4J_{FF}$ 7.8 Hz), 147.32 d.d (1F, F^5, $^3J_{FF}$ 21.3, $^4J_{FF}$ 13.3 Hz), 143.78 d.d.d (1F, F^8, $^3J_{FF}$ 20.8, $^4J_{FF}$ 13.3, $^4J_{FF}$ 7.8 Hz). Mass spectrum, *m*/*z* ($I_{rel.}$, %): 355 (10) M^+, 311 (11), 310 (22), 283 (100), 263 (13), 258 (30). IR spectrum, KBr, ν, cm^{-1}: 1730 (CO), 1640 (CO).

7-Tetrafluorophenyl-6-ethoxycarbonylpyrazolo-[1,5-a]pyrimidine (VIIa). To 0.5 g (1.4 mmol) of acrylate **IIIa** in 10 ml of anhydrous acetonitrile was added 0.16 g (2.8 mmol) of KF, the reaction mixture was boiled for 2 h, cooled, and the precipitate was filtered off. The filtrate was evaporated, the residue was recrystallized from ethanol. Yield 0.35 g (74%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.29 t (3H, CH_3), 4.28 q (2H, OCH_2), 6.82 s (1H, H^3), 7.23 m (1H, $H^{6'}$), 7.38 s (1H, H^2), 9.16 s (1H, H^5). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 157.12 m, 153.67 m, 139.87 m, 138.31 m. Mass spectrum, *m*/*z* ($I_{rel.}$, %): 339 (85) M^+, 320 (87), 294 (29), 292 (100), 266 (21). IR spectrum, KBr, ν, cm^{-1}: 1725 (CO).

7-Tetrafluorophenyl-6-ethoxycarbonyl-1,2,4-triazolo[1,5-a]pyrimidine (VIIb). To 1.6 g (4.5 mmol) of acrylate IIIc in 10 ml of anhydrous acetonitrile was added 0.5 g (8.6 mmol) of KF, the reaction mixture was boiled for 2 h, cooled, and the precipitate was filtered off. The filtrate was evaporated, the residue was recrystallized from ethanol. Yield 0.9 g (60%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.15 t (3H, CH_3), 4.24 q (2H, OCH_2), 7.85 m (1H, $H^{6'}$), 8.80 s (1H, H^2), 9.40 s (1H, H^5). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 156.4 m, 151.9 m, 139.2 m, 137.5 m. Mass spectrum, *m*/*z* ($I_{rel.}$, %): 340 (100) M^+, 321 (32), 312 (29), 311 (16), 295 (92), 293 (91), 292 (51), 221 (15), 201 (14), 188 (13). IR spectrum, KBr, ν, cm^{-1}: 1720 (CO).

7-[4-(Pyrrolidin-1-yl)-2,3,5-trifluorophenyl]-6-ethoxycarbonylpyrazolo[1,5-a]pyrimidine (VIIIa). To a solution of 0.15 g (0.44 mmol) of compound **VIIa** in 6 ml of acetonitrile was added 0.2 g (2.8 mmol) of pyrrolidine. The reaction mixture was boiled for 3.5 h, and then evaporated. To the residue was added petroleum ether and ethanol, the separated precipitate was filtered off and recrystallized from ethanol. Yield 0.1 g (56%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.24 t (3H, CH_3), 1.86 m [4H, $(CH_2)_2$], 3.54 m [4H, $N(CH_2)_2$], 4.23 q (2H, OCH_2), 6.88 s (1H, H^3), 7.65 d.d.d (1H, $H^{6'}$, $^3J_{HF}$ 13.9, $^4J_{HF}$ 6.0, $^5J_{HF}$ 2.1 Hz), 7.73 s (1H, H^2), 8.16 s (1H, H^5).

7-[4-(Pyrrolidin-1-yl)-2,3,5-trifluorophenyl]-6-ethoxycarbonyl-1,2,4-triazolo[1,5-a]pyrimidine (VIIIb). To a solution of 0.55 g (1.6 mmol) of compound **VIIb** in 10 ml of acetonitrile was added 0.45 g (6.4 mmol) of pyrrolidine. The reaction mixture was boiled for 4 h, then cooled, the precipitate was filtered off and recrystallized from ethanol. Yield 0.4 g (61%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.31 t (3H, CH_3), 1.95 m [4H, $(CH_2)_2$], 3.73 m [4H, $N(CH_2)_2$], 4.35 q (2H, OCH_2), 7.13 d.d.d (1H, $H^{6'}$, $^3J_{HF}$ 14.1, $^4J_{HF}$ 6.1, $^5J_{HF}$ 2.3 Hz), 8.54 s (1H, H^2), 9.34 s (1H, H^5).

7-(4-Morpholino-2,3,5-trifluorophenyl)-6-ethoxycarbonyl-1,2,4-triazolo[1,5-a]pyrimidine (VIIIb). To a solution of 0.5 g (1.47 mmol) of compound **VIIb** in 8 ml of dimethylformamide was added 0.5 g (6.0 mmol) of morpholine. The reaction mixture was boiled for 4 h, cooled, diluted with water, the precipitate was filtered off and recrystallized from ethanol. Yield 0.38 g (60%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.29 t (3H, CH_3), 3.40 m [4H, $N(CH_2)_2$], 3.86 m [4H, $O(CH_2)_2$], 4.38 q (2H, OCH_2), 7.09 d.d.d (1H, $H^{6'}$, $^3J_{HF}$ 14.0, $^4J_{HF}$ 6.0, $^5J_{HF}$ 2.4 Hz), 8.55 s (1H, H^2), 9.40 s (1H, H^5).

Ethyl 1-(5-hydroxy-4-ethoxycarbonyl-1,2,3-triazol-1-yl)-4-oxo-6,7,8-trifluoro-1,4-dihydroquinoline-3-carboxylate (XV). To 0.55 g (2.83 mmol) of aminotriazole **XIII** in 15 ml of anhydrous ethanol was added 0.91 g (2.83 mmol) of ethyl 2-tetrafluorobenzoyl-3-ethoxyacrylate (**Ia**). The reaction mixture was stirred for 2 h at 18–20°C, then it was evaporated to 1/3 of its volume, and the separated precipitate was filtered off. We obtained 1.3 g of a mixture containing acrylate **XIV** and quinolone **XV**. To the precipitate was added 15 ml of anhydrous benzene, the reaction mixture was boiled for 3 h, then evaporated, and the residue was recrystallized from benzene. Yield 0.9 g (50%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.38 t (3H, CH_3), 1.40 t (3H, CH_3), 4.35 q

(2H, OCH_2), 4.43 q (2H, OCH_2), 8.09 d.d.d (1H, H^5, $^3J_{HF}$ *10.3*, $^4J_{HF}$ *8.3*, $^5J_{HF}$ 2.0 Hz), 8.30 s (1H, H^2), 10.63 s (1H, OH). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 151.61 d.d.d (1F, F^7, $^3J_{FF}$ 23.2, $^3J_{FF}$ 19.4, $^4J_{HF}$ 8.3 Hz), 148.04 d.d.d (1F, F^8, $^3J_{FF}$ 19.4, $^4J_{FF}$ 4.7, $^5J_{HF}$ 2.0 Hz), 136.48 d.d.d (F^6, $^3J_{FF}$ 23.1, $^3J_{HF}$ 10.3, $^4J_{FF}$ 4.7 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 426 (12) M^+, 381 (3), 354 (35), 334 (10), 283 (18), 271 (100), 226 (77), 197 (42), 169 (91).

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