Fluorine-containing pyrido[1,2-*a*]quinazolin-6-ones

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Reactions of 2-aminopyridine and 2-amino-5-methylpyridine with 2,3,4,5-tetrafluorobenzoyl chloride afforded *N*,*N*´-diaroylpyridinium salts, which were converted into 6*H*-pyrido[1,2-*a*]quinazolin-6-ones by refluxing in toluene in the presence of triethylamine. The angular structure of the tricyclic derivatives obtained was confirmed by ^{19}F and ^{13}C NMR spectroscopy and 2D heteronuclear HetCOR and HMBC experiments.

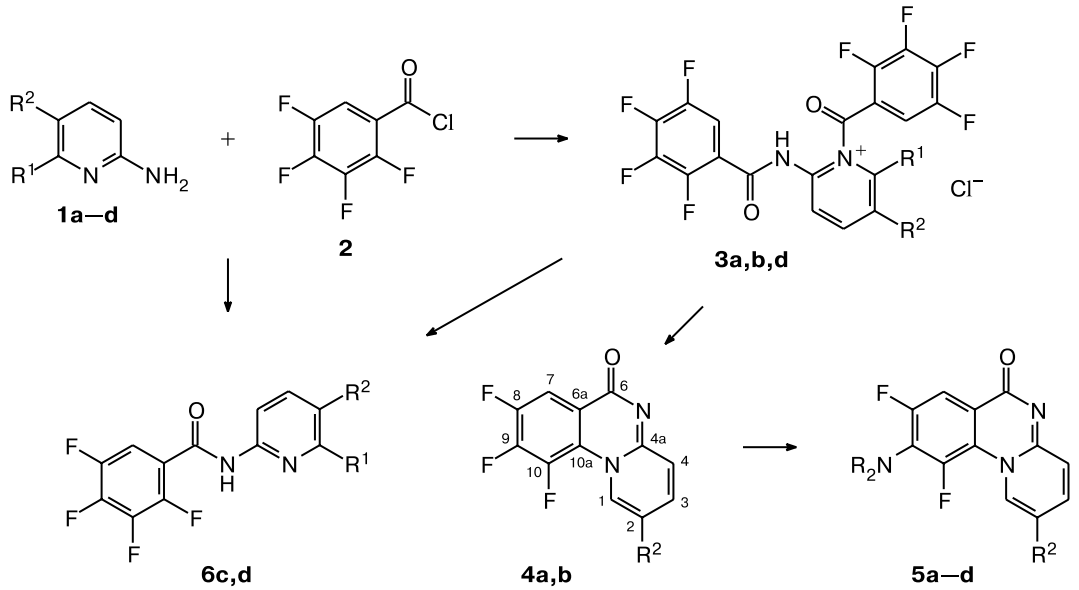
Key words: 2-aminopyridine, 2,3,4,5-tetrafluorobenzoyl chloride, pyrido[1,2-*a*]quinazolin-6-ones, aroylation, aminodefluorination.

Quinazolin-4-one derivatives have long attracted the attention of researchers because many of them exhibit a variety of biological (fungicidal, anticonvulsant, *etc.*) activity and are antagonists to some receptors.[1—4] Introduction of fluorine atoms into compounds is known[5—7] to impart them new biological properties. For instance, fluorine-containing pyrimido[*b*]quinazolinones were reported[8] to have antitumor activity.

In continuation of the studies[9—14] on the synthesis of fluorine-containing fused azaheterocycles, we obtained fluorine-containing pyrido[1,2-*a*]quinazolin-6-ones.

2-Aminopyridine (**1a**), 2-amino-5-methyl-, and 2-amino-6-methylpyridines (**1b,d**) were acylated with 2,3,4,5-tetrafluorobenzoyl chloride **2** in boiling toluene (2 h) at both (cyclic and exocyclic) nitrogen atoms to give diaroyl derivatives **3a,b,d** (Scheme 1). The ^1H NMR spec-

Scheme 1



1, 3, 4, 6: R^1 = H, R^2 = H (**a**), Me (**b**), NO_2 (**c**); R^1 = Me, R^2 = H (**d**)
5: NR_2 is pyrrolidin-1-yl, R^2 = H (**a**), Me (**c**); NR_2 is morpholin-4-yl, R^2 = H (**b**), Me (**d**)

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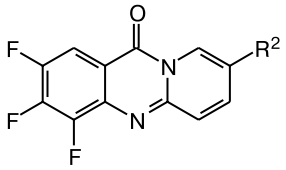
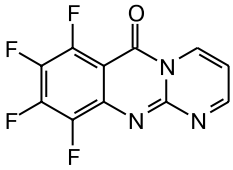
tra of salts **3** show a broadened singlet at δ 11.0 for NH of the amido group, two one-proton multiplets at δ 7.5—7.8 for the tetrafluorobenzoyl fragments, and signals for the protons of the pyridine ring (see Experimental). In the reaction of 2-amino-5-nitropyridine (**1c**) with acid chloride **2**, only the exocyclic amino group underwent acylation to give amide **6c**, probably because the pyridine N atom is less basic. The structure of compound **6c** was confirmed by ^{1}H NMR and MS data (see Experimental).

When boiled in toluene in the presence of triethylamine for 3 h, compounds **3a,b** yielded pyridoquinazolinone derivatives. The ^{1}H NMR spectra of the cyclization products show the signal for the proton of the tetrafluorobenzene fragment (δ 8.0—8.2, ddd) but no signals for the NH protons. The electronic system of the pyridine ring in the cyclization product **4a** changes in such a manner that the signal for the H(1) atom of the pyridine fragment is shifted downfield, while the signal for the H(4) atom is shifted upfield by 0.5 ppm compared to analogous signals for compound **3a** (Table 1). The mass spectra of the cyclization products **4a,b** agree with the fused structure. The ^{19}F NMR spectra of these compounds contain three signals for fluorine atoms (Table 2). Obviously, when heated, compounds **3a,b** undergo cyclization into angular pyridoquinazolinone derivatives **4a,b** since elimination of the aroyl fragment bound to the pyridine N atom is most probable. The conversion of diaroyl derivatives of benzoimidazole-2-thione and imidazolidine-2-thione into imidazobenzothiazinones was described earlier.[15]

Alternatively, the reactions of aminopyridines **1a,b** with tetrafluorobenzoyl chloride **2** could yield linear pyridoquinazolinones **7a,b**. [*b*]-Annelated quinazolinones **8** of this type have been obtained recently[8] under other cyclization conditions.



7a,b



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Evidence for angular structures **4a,b** is a characteristic signal for the F(10) atom in the ^{19}F NMR spectrum of compound **4a**. It was found that F(10) interacts not

Table 1. ^{1}H NMR data (DMSO-d_6) for compounds **4a,b** and **5a—d**

Compound	δ, *J*/Hz					
	H(1)	H(2)	H(3)	H(4)	H(7)	NR_2 (m, 4 H)
4a[a]	8.82 ddd, $^3J_{H(1),H(2)}$ = 7.3, $^4J_{H(1),H(3)}$ = 1.4, $^5J_{H(1),F(10)}$ = 6.9	6.99 dddd, $^3J_{H(2),H(1)}$ = 7.3, $^3J_{H(2),H(3)}$ = 6.7, $^4J_{H(2),H(4)}$ = 1.6, $^6J_{H(2),F(10)}$ = 1.7	7.68 ddd, $^3J_{H(3),H(4)}$ = 9.1, $^3J_{H(3),H(2)}$ = 6.7, $^4J_{H(3),H(1)}$ = 1.4	7.38 dd, $^3J_{H(4),H(3)}$ = 9.1, $^4J_{H(4),H(2)}$ = 1.6	8.16 ddd, $^3J_{H(7),F(8)}$ = 9.0, $^4J_{H(7),F(9)}$ = 8.0, $^5J_{H(7),F(10)}$ = 2.0	—
4b[a,b]	8.56 ddq, $^4J_{H(1),H(3)}$ = 1.9, $^4J_{H(1),CH_3}$ = 1.1, $^5J_{H(1),F(10)}$ = 5.2	—	7.54 dd, $^3J_{H(3),H(4)}$ = 9.2, $^4J_{H(3),H(1)}$ = 1.9	7.33 d, $^3J_{H(4),H(3)}$ = 9.2	8.17 ddd, $^3J_{H(7),F(8)}$ = 9.4, $^4J_{H(7),F(9)}$ = 8.1, $^5J_{H(7),F(10)}$ = 2.4	—
5a	8.68 ddd, $^3J_{H(1),H(2)}$ = 7.3, $^4J_{H(1),H(3)}$ = 1.6, $^5J_{H(1),F(10)}$ = 6.7	6.96 ddd, $^3J_{H(2),H(1)}$ = 7.3, $^3J_{H(2),H(3)}$ = 6.4, $^4J_{H(2),H(4)}$ = 1.2	7.62 ddd, $^3J_{H(3),H(4)}$ = 8.0, $^3J_{H(3),H(2)}$ = 6.4, $^4J_{H(3),H(1)}$ = 1.6	7.41 dd, $^3J_{H(4),H(3)}$ = 8.0, $^4J_{H(4),H(2)}$ = 1.2	7.57 dd, $^3J_{H(7),F(8)}$ = 13.9, $^5J_{H(7),F(10)}$ = 1.9	1.96 $(CH_2)_2$), 3.74 $(N(CH_2)_2)$
5b	8.72 ddd, $^3J_{H(1),H(2)}$ = 7.5, $^4J_{H(1),H(3)}$ = 1.1, $^5J_{H(1),F(10)}$ = 6.8	7.05 ddd, $^3J_{H(2),H(1)}$ = 7.5, $^3J_{H(2),H(3)}$ = 6.4, $^4J_{H(2),H(4)}$ = 1.0	7.67 ddd, $^3J_{H(3),H(4)}$ = 7.9, $^3J_{H(3),H(2)}$ = 6.4, $^4J_{H(3),H(1)}$ = 1.1	7.49 d, $^3J_{H(4),H(3)}$ = 7.9, $^4J_{H(4),H(2)}$ = 1.0	7.66 dd, $^3J_{H(7),F(8)}$ = 12.2, $^5J_{H(7),F(10)}$ = 1.7	3.36 $(N(CH_2)_2)$, 3.76 $(O(CH_2)_2)$
5c[b]	8.53 ddd, $^4J_{H(1),H(3)}$ = 1.9, $^4J_{H(1),CH_3}$ = 0.9, $^5J_{H(1),F(10)}$ = 6.6	—	7.58 dd, $^3J_{H(3),H(4)}$ = 9.3, $^4J_{H(3),H(1)}$ = 1.9	7.41 d, $^3J_{H(4),H(3)}$ = 9.3	7.62 dd, $^3J_{H(7),F(8)}$ = 14.2, $^5J_{H(7),F(10)}$ = 1.7	1.90 $((CH_2)_2)$, 3.69 $(N(CH_2)_2)$
5d[b]	8.59 ddd, $^4J_{H(1),H(3)}$ = 1.9, $^4J_{H(1),CH_3}$ = 1.0, $^5J_{H(1),F(10)}$ = 6.8	—	7.64 dd, $^3J_{H(3),H(4)}$ = 9.3, $^4J_{H(3),H(1)}$ = 1.9	7.50 d, $^3J_{H(4),H(3)}$ = 9.3	7.73 dd, $^3J_{H(7),F(8)}$ = 12.2, $^5J_{H(7),F(10)}$ = 1.6	3.34 $(N(CH_2)_2)$, 3.74 $(O(CH_2)_2)$

[a] In $CDCl_3$.

[b] The chemical shifts of the signals for the CH_3 protons, δ ($^4J_{CH_3,H(1)}$/Hz): **4b** 2.40 d (1.1), **5c** 2.31 d (0.9), **5d** 2.34 d (1.0).

Table 2. ^{19}F NMR (DMSO-d_6) and MS data for compounds **4a,b** and **5a—d**

Compound	δ_F, J/Hz			MS, m/z (I_{rel} (%))
	F(8)	F(9)	F(10)	
4a*	130.24 ddd, $^3J_{F(8),F(9)}$ = 21.8, $^3J_{F(8),H(7)}$ = 9.0, $^4J_{F(8),F(10)}$ = 8.6	149.42 ddd, $^3J_{F(9),F(8)}$ = 21.8, $^3J_{F(9),F(10)}$ = 17.4, $^4J_{F(9),H(7)}$ = 8.0	139.43 ddddd, $^3J_{F(10),F(9)}$ = 17.4, $^4J_{F(10),F(8)}$ = 8.6, $^5J_{F(10),H(1)}$ = 6.9, $^5J_{F(10),H(7)}$ = 2.0, $^6J_{F(10),H(2)}$ = 1.7	250 $[M]^+$ (70), 222 (100), 194 (10), 130 (14), 51 (10)
4b*	132.70 ddd, $^3J_{F(8),F(9)}$ = 23.2, $^3J_{F(8),H(7)}$ = 9.4, $^4J_{F(8),F(10)}$ = 7.5	152.12 ddd, $^3J_{F(9),F(8)}$ = 23.2, $^3J_{F(9),F(10)}$ = 18.9, $^4J_{F(9),H(7)}$ = 8.1	136.52 dddd, $^3J_{F(10),F(9)}$ = 18.9, $^4J_{F(10),F(8)}$ = 7.5, $^5J_{F(10),H(1)}$ = 5.2, $^5J_{F(10),H(7)}$ = 2.4	—
5a	121.91 m	—	141.23 m	302 $[M]^+$ (100), 301 (79), 245 (19), 231 (13), 78 (38)
5b	121.57 dd, $^3J_{F(8),H(7)}$ = 12.2, $^4J_{F(8),F(10)}$ = 8.2	—	135.46 m	318 $[M]^+$ (98), 260 (18), 259 (100), 231 (19), 203 (13), 130 (21), 129 (26), 78 (42)
5c	121.98 m	—	141.28 m	—
5d	121.73 dd, $^3J_{F(8),H(7)}$ = 12.2, $^4J_{F(8),F(10)}$ = 7.9	—	135.48 m	—

* In $CDCl_3$.

only with F(9), F(8), and H(7), but also with two protons of the pyridine fragment (J = 6.9 and 1.7 Hz; see Table 2).

The linear structure of the documented[8] pyrimido[2,3-*b*]quinazolinone derivative **8** was confirmed by the constant $^3J_{C,H}$ indicating the coupling between the carbonyl C atom and the proton of the pyrimidine ring (^{13}C NMR data). In connection with this, it was interesting to examine the ^{13}C NMR spectra of compounds **4a,b** (Table 3). It turned out that the C(6) atom interacts with H(7), F(8), F(9), and F(10) but does not interact with the protons of the pyridine fragment. The constant $^4J_{C(1),F(10)}$ = 29.0—29.5 Hz suggests the angular structures **4a,b**.

Structures **4a,b** were additionally confirmed by $^1H—^{13}C$ HMBC spectra (Fig. 1). Signals for the H(1)—H(4) protons in the ^1H NMR spectrum were assigned with a 2D correlation experiment (2D COSY). The signals for the protonated C atoms were unambiguously identified from the corresponding cross peaks in the 2D HetCOR spectrum. The bridgehead carbon atoms were assigned from the constants of their long-range spin-spin couplings with the fluorine atoms and the protons; the assignment was confirmed by $^2J_{H,C}$ and $^3J_{H,C}$ correlations in the 2D HMBC experiment.

Quaternary 2-methylpyridinium salt **3d** in boiling toluene in the presence of triethylamine afforded amide **6d** rather than cyclization product **4**; structure **6d** was confirmed by spectroscopic data (see Experimental). Apparently, the cyclization of salt **3d** is prevented by steric hindrances.

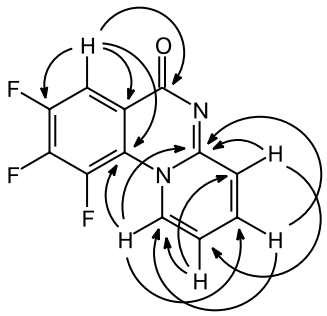

Fig. 1. Long-range $^1H—^{13}C$ couplings in the 2D HMBC spectrum of compound **4a**.

One of the fluorine atoms in fused compounds **4a,b** was replaced by amino groups. Heating of pyrido[1,2-*a*]quinazolin-6-ones **4a,b** with pyrrolidine or morpholine in DMF for 5 h yielded amino derivatives **5a—d** (^1H and ^{19}F NMR and MS data). The ^1H NMR spectra of compounds **5** contain a doublet of doublets for the H(7) proton. The ^{19}F NMR spectra of these derivatives show signals for two fluorine atoms (see Tables 1, 2). Note that the pyrido[1,2-*a*]quinazolinones obtained are inert toward N-nucleophiles; in contrast, the central ring in isomeric [*b*]-annelated derivatives easily undergoes opening.[8,16]

Hence, we proposed a route to fluorine-containing pyrido[1,2-*a*]quinazolinones.

Table 3. ^{13}C NMR data ($CDCl_3$) for compounds **4a,b**

Atom	δ_C, J/Hz					
	Compound **4a**			Compound **4b**		
	$^{13}C\{^1H\}$	$^nJ_{C,F}$	$^nJ_{C,H}$	$^{13}C\{^1H\}$	$^nJ_{C,F}$	$^nJ_{C,H}$
C(1)	131.78 (d)	$^4J_{C(1),F(10)} = 29.5$	$^1J_{C(1),H(1)} = 188.3$, $^2J_{C(1),H(2)} = 6.9$, $^3J_{C(1),H(3)} = 6.8$	128.95 (d)	$^4J_{C(1),F(10)} = 29.1$	$^1J_{C(1),H(1)} = 186.2$, $^3J_{C(1),CH_3} = 6.6$, $^3J_{C(1),H(3)} = 6.5$
C(2)	113.59 (dd)	$^5J_{C(2),F(10)} = 3.1$, $^6J_{C(2),F(9)} = 3.1$	$^1J_{C(2),H(2)} = 171.9$, $^2J_{C(2),H(4)} = 9.2$	123.45 (d)	$^5J_{C(2),F(10)} = 3.1$	$^2J_{C(2),H(1)} = 9.0$, $^2J_{C(2),CH_3} = 6.3$
C(3)	137.44 (dd)	$^6J_{C(3),F(10)} = 3.1$, $^7J_{C(3),F(9)} = 2.0$	$^1J_{C(3),H(3)} = 166.7$, $^2J_{C(3),H(1)} = 8.1$	140.35 (d)	$^6J_{C(3),F(10)} = 1.8$	$^1J_{C(3),H(3)} = 164.6$, $^2J_{C(3),H(4)} = 6.9$, $^3J_{C(3),CH_3} = 4.8$
C(4)	126.16 (s)	—	$^1J_{C(4),H(4)} = 172.9$, $^2J_{C(4),H(2)} = 7.1$	125.65 (s)	—	$^1J_{C(4),H(4)} = 173.7$
C(4a)	153.22 (s)	—	$^2J_{C(4a),H(1)} = 9.3$, $^3J_{C(4a),H(4)} = 5.2$, $^3J_{C(4a),H(3)} = 2.8$	152.23 (s)	—	$^2J_{C(4a),H(4)} = 9.8$, $^3J_{C(4a),H(3)} = 5.1$, $^3J_{C(4a),H(1)} = 2.4$
C(6)	163.90 (ddd)	$^4J_{C(6),F(8)} = 2.0$, $^5J_{C(6),F(9)} = 1.1$, $^6J_{C(6),F(10)} = 1.1$	$^3J_{C(6),H(7)} = 4.5$	164.04 (d)	$^4J_{C(6),F(8)} = 1.8$	$^3J_{C(6),H(7)} = 3.8$
C(6a)	118.65 (ddd)	$^3J_{C(6a),F(8)} = 5.9$, $^4J_{C(6a),F(9)} = 2.8$, $^5J_{C(6a),F(10)} = 2.2$	$^2J_{C(6a),H(7)} = 2.1$	118.66 (ddd)	$^3J_{C(6a),F(8)} = 5.8$, $^4J_{C(6a),F(9)} = 2.5$, $^5J_{C(6a),F(10)} = 2.4$	$^2J_{C(6a),H(7)} = 2.4$
C(7)	111.38 (dd)	$^2J_{C(7),F(8)} = 18.5$, $^3J_{C(7),F(9)} = 3.8$	$^1J_{C(7),H(7)} = 173.9$	111.39 (dd)	$^2J_{C(7),F(8)} = 18.4$, $^3J_{C(7),F(9)} = 3.7$	$^1J_{C(7),H(7)} = 173.9$
C(8)	150.46 (ddd)	$^1J_{C(8),F(8)} = 257.6$, $^2J_{C(8),F(9)} = 10.8$, $^3J_{C(8),F(10)} = 2.5$	$^2J_{C(8),H(7)} = 5.5$	150.34 (ddd)	$^1J_{C(8),F(8)} = 257.3$, $^2J_{C(8),F(9)} = 10.8$, $^3J_{C(8),F(10)} = 2.4$	$^2J_{C(8),H(7)} = 5.7$
C(9)	143.72 (ddd)	$^1J_{C(9),F(9)} = 259.5$, $^2J_{C(9),F(8)} = 16.8$, $^2J_{C(9),F(10)} = 16.8$	$^3J_{C(9),H(7)} = 9.5$	143.68 (ddd)	$^1J_{C(9),F(9)} = 259.2$, $^2J_{C(9),F(8)} = 16.8$, $^2J_{C(9),F(10)} = 16.8$	$^3J_{C(9),H(7)} = 9.5$
C(10)	142.85 (ddd)	$^1J_{C(10),F(10)} = 258.1$, $^2J_{C(10),F(9)} = 14.6$, $^3J_{C(10),F(8)} = 2.4$	$^4J_{C(10),H(7)} = 2.1$	142.78 (ddd)	$^1J_{C(10),F(10)} = 258.1$, $^2J_{C(10),F(9)} = 14.6$, $^3J_{C(10),F(8)} = 2.4$	$^4J_{C(10),H(7)} = 2.0$
C(10a)	123.83 (ddd)	$^2J_{C(10a),F(10)} = 3.3$, $^3J_{C(10a),F(9)} = 2.2$, $^4J_{C(10a),F(8)} = 1.1$	$^4J_{C(10a),H(7)} = 10.0$	123.83 (dd)	$^2J_{C(10a),F(10)} = 2.3$, $^3J_{C(10a),F(9)} = 2.3$	$^4J_{C(10a),H(7)} = 9.5$, $^3J_{C(10a),H(1)} = 1.1$
CH_3	—	—	—	18.27 (s)	—	$^1J_{C,H} = 128.7$, $^2J_{C,H(1)} = 3.7$, $^2J_{C,H(3)} = 3.7$

Experimental

^1H NMR spectra were recorded on Bruker WM-250 and Bruker DRX-400 spectrometers (250.14 and 400.13 MHz, respectively). ^{19}F NMR spectra were recorded on a Bruker DRX-400 spectrometer (376.45 MHz). Tetramethylsilane (^1H NMR) and hexafluorobenzene (^{19}F NMR) were used as the internal standards. ^{13}C NMR spectra were recorded on a Bruker DRX-400 spectrometer (100.61 MHz). Mass spectra were recorded on a Varian MAT 311A spectrometer (accelerating voltage 3 kV, cathode emission current 300 μA, ionizing voltage 70 eV, direct inlet probe).

1-(2,3,4,5-Tetrafluorobenzoyl)-2-(2,3,4,5-tetrafluorobenzoyl)amino-5-R^2-6-R^1-pyridinium chlorides (3a,b,d). Tetrafluorobenzoyl chloride **2** (2.7 mL, 25 mmol) was added to a suspension of 2-amino-5-methylpyridine **1b** (1.4 g, 13 mmol) in 18 mL of dry toluene. The reaction mixture was refluxed for 2 h and cooled. The precipitate was filtered off, the mother liquor was concentrated, and the residue was combined with the main precipitate. Product **3b** was recrystallized from ethanol. The yield of **3b** was 4.6 g (72%), m.p. 111—113 °C. Found (%): C, 48.21; H, 1.97; N, 5.52. $C_{20}H_9F_8N_2O_2Cl$. Calculated (%): C, 48.34; H, 1.81; N, 5.64. ^1H NMR (DMSO-d_6), δ: 2.29 (s, 3 H, CH_3); 7.69 (ddd, 1 H, H(4), ^3J = 8.4 Hz, ^4J = 2.4 Hz, ^4J = 0.6 Hz); 7.77 (m, 2 H, H(6′)); 8.03 (d, 1 H, H(3), ^3J = 8.4 Hz); 8.22 (dd, 1 H, H(6), ^4J = 2.4 Hz, ^5J = 0.7 Hz); 11.01 (br.s, 1 H, NH).

Compounds **3a,d** were obtained analogously.

Compound 3a, yield 70%, m.p. 102—104 °C. Found (%): C, 47.45; H, 1.49; N, 6.13. $C_{19}H_7F_8N_2O_2Cl$. Calculated (%): C, 47.27; H, 1.46; N, 5.80. ^1H NMR (DMSO-d_6), δ: 7.15 (ddd, 1 H, H(5), ^3J = 7.5 Hz, ^3J = 4.9 Hz, ^4J = 1.2 Hz); 7.50—7.70

(m, 2 H, H(6′)); 7.81 (ddd, 1 H, H(4), ^3J = 8.4 Hz, ^3J = 7.5 Hz, ^4J = 2.0 Hz); 8.16 (ddd, 1 H, H(3), ^3J = 8.5 Hz, ^4J = 1.2 Hz, ^3J = 0.9 Hz); 8.33 (ddd, 1 H, H(6), ^3J = 4.9 Hz, ^4J = 2.0 Hz, ^5J = 0.9 Hz); 10.93 (br.s, 1 H, NH).

Compound 3d, yield 59%, m.p. 106—108 °C. Found (%): C, 48.49; H, 2.13; N, 5.46. $C_{20}H_9F_8N_2O_2Cl$. Calculated (%): C, 48.38; H, 1.82; N, 5.64. ^{1}H NMR (DMSO-d_6), δ: 2.45 (s, 3 H, CH_3); 7.00 (d, 1 H, H(5), ^3J = 7.6 Hz); 7.50—7.70 (m, 2 H, H(6′)); 7.68 (dd, 1 H, H(4), ^3J = 8.4 Hz, ^3J = 7.6 Hz); 7.97 (d, 1 H, H(3), ^3J = 8.4 Hz); 10.90 (br.s, 1 H, NH).

8,9,10-Trifluoro-2-methyl-6*H*-pyrido[1,2-*a*]quinazolin-6-one (4b). Triethylamine (1.1 mL, 0.8 g, 18.6 mmol) was added to compound **3b** (4.6 g, 9.3 mmol) in 25 mL of dry toluene. The reaction mixture was refluxed for 3.5 h and cooled. The precipitate of compound **4b** was filtered off and recrystallized from ethanol. The yield of **4b** was 3.0 g (82%), m.p. 222—224 °C. Found (%): C, 58.95; H, 2.79; N, 10.52. $C_{13}H_7F_3N_2O$. Calculated (%): C, 59.09; H, 2.67; N, 10.60.

8,9,10-Trifluoro-6*H*-pyrido[1,2-*a*]quinazolin-6-one (4a) was obtained as described for compound **4b**. The yield of **4a** was 92%, m.p. 212—214 °C. Found (%): C, 57.67; H, 2.10; N, 11.44. $C_{12}H_5F_3N_2O$. Calculated (%): C, 57.60; H, 2.01; N, 11.19.

8,10-Difluoro-9-(pyrrolidin-1-yl)-6*H*-pyrido[1,2-*a*]quinazolin-6-one (5a). Pyrrolidine (0.75 mL, 10 mmol) was added to compound **4a** (0.6 g, 2.4 mmol) in 5 mL of DMF. The reaction mixture was refluxed for 5 h and cooled. The precipitate of derivative **5a** was filtered off and recrystallized from ethanol. The yield of **5a** was 0.45 g (63%), m.p. 140—142 °C. Found (%): C, 63.41; H, 4.16; N, 13.78. $C_{16}H_{13}F_2N_3O$. Calculated (%): C, 63.78; H, 4.34; N, 13.90.

Compounds **5b—d** were obtained analogously.

8,10-Difluoro-9-(morpholin-4-yl)-6*H*-pyrido[1,2-*a*]quinazolin-6-one (5b). Yield 71%, m.p. 150—152 °C. Found (%): C, 60.53; H, 4.03; N, 13.31. $C_{16}H_{13}F_2N_3O_2$. Calculated (%): C, 60.56; H, 4.12; N, 13.24.

8,10-Difluoro-2-methyl-9-(pyrrolidin-1-yl)-6*H*-pyrido[1,2-*a*]quinazolin-6-one (5c). Yield 73%, m.p. 148—150 °C. Found (%): C, 64.79; H, 4.71; N, 13.41. $C_{17}H_{15}F_2N_3O$. Calculated (%): C, 64.75; H, 4.79; N, 13.33.

8,10-Difluoro-2-methyl-9-(morpholin-4-yl)-6*H*-pyrido[1,2-*a*]quinazolin-6-one (5d). Yield 81%, m.p. 184—186 °C. Found (%): C, 61.58; H, 4.63; N, 12.62. $C_{17}H_{15}F_2N_3O_2$. Calculated (%): C, 61.63; H, 4.56; N, 12.68.

5-Nitro-2-(2,3,4,5-tetrafluorobenzoyl)aminopyridine (6c). Acid chloride **2** (1.3 mL, 8 mmol) was added to 2-amino-5-nitropyridine **1c** (0.5 g, 3.6 mmol) in 10 mL of dry toluene. The reaction mixture was refluxed for 3 h and cooled. The precipitate of compound **6c** was filtered off and recrystallized from DMSO. The yield of **6c** was 0.7 g (64%), m.p. 138—140 °C. Found (%): C, 45.46; H, 1.73; N, 13.44. $C_{12}H_5F_4N_3O_3$. Calculated (%): C, 45.72; H, 1.59; N, 13.33. ^{1}H NMR (DMSO-d_6), δ: 7.68 (m, 1 H, H(6′)); 8.39 (d, 1 H, H(3), ^3J = 9.2 Hz); 8.64 (dd, 1 H, H(4), ^3J = 9.3 Hz, ^4J = 2.8 Hz); 9.20 (d, 1 H, H(6), ^4J = 2.7 Hz); 11.78 (br.s, 1 H, NH). MS, m/z (I_{rel} (%)): 315 $[M]^+$ (20), 287 (10), 177 (100), 149 (27).

6-Methyl-2-(2,3,4,5-tetrafluorobenzoyl)aminopyridine (6d). Triethylamine (1.2 mL, 8 mmol) was added to compound **3d** (2.0 g, 4.0 mmol) in 15 mL of dry toluene. The reaction mixture was refluxed for 3 h and cooled. The precipitate of compound **6d** was filtered off, washed with water, and recrystallized from ethanol. The yield of **6d** was 0.9 g (82%), m.p. 76—78 °C. Found (%): C, 54.99; H, 3.10; N, 9.84. $C_{13}H_8F_4N_2O$. Calculated (%): C, 54.93; H, 2.83; N, 9.85. ^{1}H NMR (DMSO-d_6), δ: 2.45 (s, 3 H, CH_3); 6.99 (d, 1 H, H(5), ^3J = 7.6 Hz); 7.58 (m, 1 H, H(6′)); 7.68 (dd, 1 H, H(4), ^3J = 7.9 Hz, ^3J = 7.6 Hz); 7.97 (d, 1 H, H(3), ^3J = 7.9 Hz); 10.85 (br.s, 1 H, NH).

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