Trifluoromethyl-substituted 1,6-naphthyridines and pyrido[4,3-*d*]pyrimidines

L. S. Vasil´ev, F. E. Surzhikov, S. V. Baranin, and V. A. Dorokhov*†

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5328. E-mail: svbar@ioc.ac.ru

A convenient method for the synthesis of 1-alkyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-ones was elaborated based on the reaction of 4-alkylamino-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron chelates with dimethylformamide dimethyl acetal. 3-Acetyl-4-amino-2-trifluoromethylpyridine was used to obtain 5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one and its 2-methoxycarbonyl derivative, as well as 4-methyl-5-trifluoromethylpyrido-[4,3-*d*]pyrimidine.

Key words: 1-alkyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one, 5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one, dimethylformamide dimethyl acetal, ethyl orthoformate, dimethyl oxalate, 2-methoxycarbonyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one, 4-methyl-5-trifluoromethylpyrido[4,3-*d*]pyrimidine.

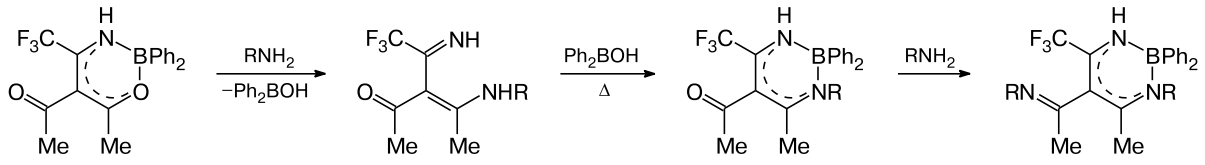
In the last years, 1,6-naphthyridine and pyrido[4,3-*d*]-pyrimidine derivatives attract much attention of researches, because these compounds were found to possess a wide range of biological activity (see Refs 1 and 2 and references cited therein). At the same time, the interest to organofluorine compound have sharply grown, especially, because of their use in medicine and agrochemistry. Thus, if in 1970 only 2% of new produced drugs contained fluorine atoms, in 2002 this index increased to 18% worldwide, and to 29% in the USA (see Ref. 3). In this connection, the interest to 1,6-naphthyridines and pyrido[4,3-*d*]-pyrimidines is explainable, in particular, to those containing a CF_3 group directly bonded to the heterocycle, which were not described in the literature before our works.

In the present work, we suggest a method for the synthesis of these compounds with the use of available boron diiminates.

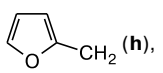
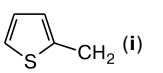
Recently, we have found[4] that the reaction of 3-acetyl-4-amino-5,5,5-trifluoro-3-penten-2-one diphenylboron chelate (**1**) with ammonia or primary amines led to 4-amino- or 4-alkylamino-3-trifluoroacetimidoyl-3-penten-2-ones (**2**), which under the reaction conditions were converted to boron diiminates (**3**) (Scheme 1, Table 1). This process is slow at room temperature and considerably accelerates upon reflux in benzene. For the reaction of **1** with ammonia, $MeNH_2$, and $EtNH_2$ to proceed, solutions of the corresponding amine in THF should be used and the reaction of mixture should be kept at ~20 °C for ~24 h.

The complexation activated (with respect to amines) not only the carbonyl group of the chelate ring, but also the free acetyl group, which resulted in the formation of compound **4** as the side product. The reaction of complex **1** with $PrNH_2$ was studied in detail as a model example. It was shown that when the ratio **1** : $PrNH_2$ = 1 : 1.5,* the

Scheme 1



1 **2** **3a—i** **4**

R = H (**a**), Me (**b**), Et (**c**), Pr (**d**), All (**e**), $MeO(CH_2)_3$ (**f**), 4-$FC_6H_4CH_2$ (**g**),  (**h**),  (**i**)

† Deceased.

* When the ratio was 1 : 1, the starting compound **1** was not completely used-up and was difficult to separate from the reaction products.

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Table 1. Yields, melting points, elemental analysis and ^{1}H NMR spectroscopic data for compounds **3a—i**, **4**, and **10**

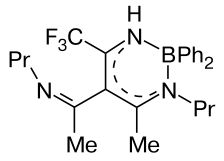
Compound	Yield (%)	M.p./°C	Found / Calculated (%)			Molecular formula	^{1}H NMR ($CDCl_3$, δ, *J*/Hz)
			C	H	N		
3a	65	184—185	64.01 63.68	5.34 5.06	7.91 7.81	$C_{19}H_{18}BF_3N_2O$	2.28 (s, 3 H, MeCO); 2.36 (s, 3 H, MeCN); 6.51, 6.88 (2 H, 2 NH); 7.22—7.42 (m, 10 H, 2 Ph)
3b	81	113—114	64.35 64.54	5.57 5.42	7.38 7.52	$C_{20}H_{20}BF_3N_2O$	2.25 (s, 3 H, MeCO); 2.30 (s, 3 H, MeCN); 2.97 (s, 3 H, MeN); 6.07 (s, 1 H, NH); 7.29—7.38 (m, 10 H, 2 Ph)
3c	74	142—143	65.24 65.30	5.46 5.74	7.31 7.25	$C_{21}H_{22}BF_3N_2O$	0.78 (t, 3 H, MeCH_2, *J* = 7.0); 2.18 (s, 3 H, MeCO); 2.38 (s, 3 H, MeCN); 3.42 (q, 2 H, CH_2N, *J* = 7.0); 6.20 (s, 1 H, NH); 7.08—7.62 (m, 10 H, 2 Ph)
3d	70	144—145	66.12 66.01	6.28 6.04	6.98 7.00	$C_{22}H_{24}BF_3N_2O$	0.50 (t, 3 H, MeCH_2, *J* = 7.0); 1.05—1.20 (m, 2 H, MeCH_2); 2.20 (s, 3 H, MeCO); 2.36 (s, 3 H, MeCN); 3.25 (t, 2 H, CH_2N, *J* = 6.5); 6.20 (s, 1 H, NH); 7.18—7.48 (m, 10 H, 2 Ph)
3e	63	137—138	66.33 66.33	5.74 5.52	7.20 7.03	$C_{22}H_{22}BF_3N_2O$	2.20 (s, 3 H, MeCO); 2.34 (s, 3 H, MeCN); 4.06 (d, 2 H, CH_2N, *J* = 6.0); 4.87 (d, 1 H, CH_2=CH, *J* = 17.0); 5.01 (d, 1 H, CH_2=CH, *J* = 10.0); 5.25 (m, 1 H, CH_2=CH); 6.27 (s, 1 H, NH); 7.27—7.35 (m, 10 H, 2 Ph)
3f	76	85—86	64.01 64.20	6.12 6.09	6.63 6.51	$C_{23}H_{26}BF_3N_2O_2$	1.28 (m, 2 H, CH_2); 2.21 (s, 3 H, MeCO); 2.38 (s, 3 H, MeCN); 2.92 (t, 2 H, CH_2O, *J* = 6.0); 3.12 (s, 3 H, MeOCH_2); 3.45 (t, 3 H, CH_2N, *J* = 6.0); 6.21 (s, 1 H, NH); 7.20—7.40 (m, 10 H, 2 Ph)
3g	80	128—129	68.17 68.44	5.12 5.08	6.08 6.14	$C_{26}H_{23}BF_4N_2O$	2.18 (s, 3 H, MeCO); 2.22 (s, 3 H, MeCN); 4.70 (s, 2 H, CH_2N); 6.41 (s, 1 H, NH); 6.70 (m, 2 H, C_6H_4); 6.85 (t, 2 H, C_6H_4, *J* = 7.5)
3h	82	135—137	65.69 65.77	5.30 5.06	6.38 6.39	$C_{24}H_{22}BF_3N_2O_2$	2.17 (s, 3 H, MeCO); 2.52 (s, 3 H, MeCN); 4.55 (s, 2 H, CH_2N); 5.36 (d, 1 H, H(3´), *J* = 6.0); 6.14 (t, 1 H, H(4´), *J* = 6.0, *J* = 2.0); 6.36 (s, 1 H, NH); 7.21—7.27 (m, 11 H, 2 Ph + H(5´))
3i	86	119—121	63.62 63.46	4.92 4.88	6.12 6.17	$C_{24}H_{22}BF_3N_2OS$	2.16 (s, 3 H, MeCO); 2.38 (s, 3 H, MeCN); 4.83 (s, 2 H, CH_2N); 6.40 (d, 1 H, H(3´), *J* = 3.0); 6.44 (s, 1 H, NH); 6.79 (t, 1 H, H(4´); *J* = 6.0, *J* = 3.0); 7.10 (d, 1 H, H(5´), *J* = 6.0); 7.24—7.28 (m, 10 H, 2 Ph)
4		112—113	68.06 68.03	7.37 7.08	9.53 9.52	$C_{25}H_{31}BF_3N_3$	0.48, 1.02 (both t, 2 H, 2 MeCH_2, *J* = 7.0, *E*-isomer)*; 0.52, 1.06 (both t, 2 H, 2 MeCH_2, *J* = 7.0, *Z*-isomer); 1.05—1.80 (m, 4 H, 2 CH_2, *E*+*Z*-isomers); 1.88, 2.20 (both s, 2 H, 2 Me, *E*-isomer); 2.14, 2.24 (both s, 4 H, 2 Me, *Z*-isomer); 2.85—3.34 (m, 4 H, 2 CH_2N, *E*+*Z*-isomers); 5.75 (br.s, 0.33 H, NH, *E*-isomer); 5.85 (br.s, 0.67 H, NH, *Z*-isomer); 7.24—7.42 (m, 10 H, 2 Ph)
10	43	214—215	65.07 65.24	5.28 5.00	9.87 9.92	$C_{23}H_{21}BF_3N_3O$	3.27 (br.s, 6 H, Me_2N)**; 6.03 (d, 1 H, C(4)H, *J* = 9.5); 7.12—7.28 (m, 10 H, 2 Ph); 7.50 (d, 1 H, C(5)H, *J* = 9.5); 7.80 (s, 1 H, C(3)=NH); 8.20 (s, 1 H, Me_2NCH=); 9.46 (s, 1 H, C(10)NH)

* The spectrum was recorded on a Bruker Avance 600 spectrometer.
** The spectrum was recorded in DMSO-d_6.

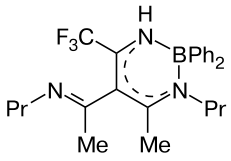
yield of **3** and chelate **4** (R = Pr) was 72% and 18%, respectively. For the ratio complex **1** : $PrNH_2$ = 1 : 5.3, the yield of diiminate **3d** decreased to 34%, whereas the yield of **4** increased to 61%. In other cases, the side products similar to compound **4** were also isolated, however, they were not studied.

Boron diiminates **3a—i** and **4** are yellow crystalline compounds, well soluble in acetone, ethanol, $CHCl_3$, and DMSO, have limited solubility in benzene, and poorly soluble in light petroleum. In the mass spectra, strong peaks of the $[M - Ph]^+$ ions are observed. The structure of compounds **3a—i** and **4** was also confirmed by elemental analysis and NMR spectroscopy. In the ^{1}H NMR spectrum of compound **4**, a double set of signals is observed, that indicates the presence of *E*- and *Z*-isomers.

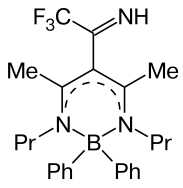
Besides, a possibility of the formation of an alternative structure **5** was not excluded either (a similar structure



4 (*Z*)



4 (*E*)



5

was initially obtained when 3-acetyl-4-amino-5,5,5-trichloro-3-penten-2-one was treated with Ph_2BOBu[5]). In this case, the 2D $^1H/^{15}N$ HMBC NMR spectrum should exhibit a correlation of the signal for the NH proton with the low-field signal for the nitrogen atom. However, a correlation of the signal for the proton of the NH group with the signal for the high-field nitrogen atom is actually observed in the spectra of both isomers, that confirms the formation of the structure **4**. The ^{19}F NMR spectrum of compound **4** also exhibits two signals (the signal of *Z*-isomer is observed more upfield), with the ratio *Z*- and *E*-isomers in $CDCl_3$ being 2 : 1, whereas in DMSO-d_6 it is 4 : 1.

Diiminates **3c—i** in refluxing toluene or xylene react with two equivalents of dimethylformamide dimethyl acetal (DMF DMA) with the formation of 5-trifluoromethyl-1,6-naphthyridine-4(1*H*)-ones (**6**) in 40—87% yields (see preliminary communication[6]). The following scheme can be suggested for the process: initially DMF DMA undergoes condensation at the two methyl groups with the formation of chelate **7** (Scheme 2), which reacts with methanol liberated in the process (apparently, this reaction is reversible) with the formation of ligand **8**, isomerizing to **9**. The latter cyclizes to 1,6-naphthyridinone **6**, thus shifting the equilibrium reaction of chelate **7** with methanol to the side of the formation of ligand **8**, that finally leads to naphthyridinones **6**.

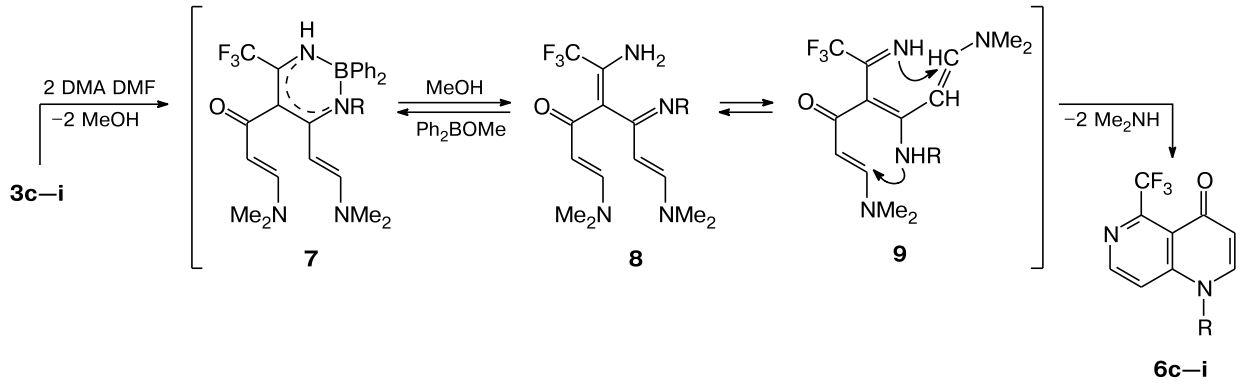
The structure of naphthyridinones **6c—i** was confirmed by elemental analysis and spectroscopic data, which are given in Table 2.

Quite unexpected pattern was observed in the reaction of compound **3a** with two equivalents of DMF DMA. Instead of expected naphthyridine **6a**, a resin-like substance was obtained, which after multiple column chromatography on SiO_2 yielded boron chelate **10**. Such a different behavior of complex **3a** and chelates **3c—i** can be probably explained by the smaller steric hindrance and, hence, the higher stability of the intermediately formed chelate **7** to methanolysis, which causes the cyclization with elimination of Me_2NH to follow an alternative scheme (Scheme 3).

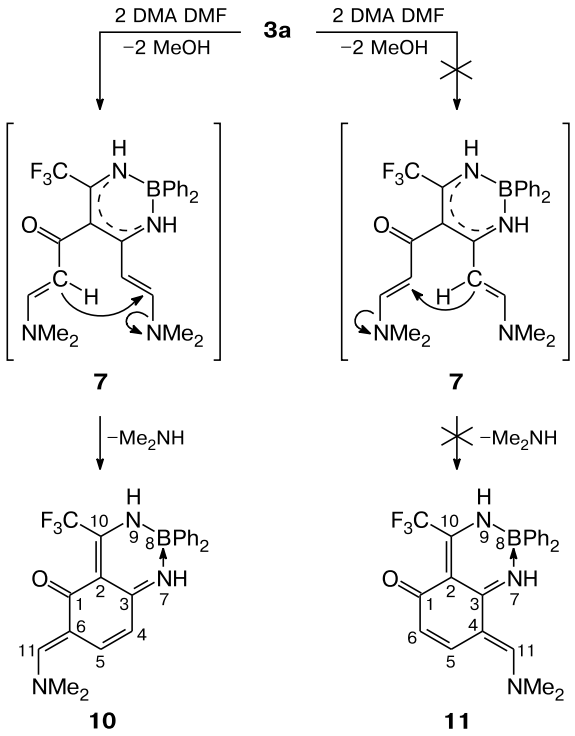
The ^1H NMR spectrum of compound **10** in DMSO-d_6 exhibited signals for the protons of the Me_2N group (δ 3.27), two doublets for the protons of the CH= fragment (δ 6.03 and 7.50), two signals for the protons of the NH groups (δ 7.80 and 9.46), a singlet for the proton of the N—CH= fragment (δ 8.20), as well as signals for the protons of two Ph groups. The structure of compound **10** was established using 2D COSY and ROESY spectra. The ROESY spectrum exhibited the following correlation peaks: MeN/H(11), MeN/H(5), and H(4)/NH(7), that unambiguously confirmed the formation of structure **10**, rather than **11**. The mass spectrum of compound **10** exhibited a peak of the ion $[M - Ph]^+$ (364) characteristic of diphenylboron chelates. A signal at δ −2.1 observed in the ^{11}B NMR spectrum of this compound indicates the presence of a four-coordinated boron atom.

This approach failed to yield compound **6a**, therefore, we used an alternative method for its synthesis. Earlier,[7] based on chelate **3a** we obtained 3-acetyl-4-amino-2-trifluoromethylpyridine (**12**), which was treated with DMF DMA to afford amidine **13**. The latter reacted with MeONa to be converted to **6a** according to the procedure described earlier.[8,9] (Scheme 4).

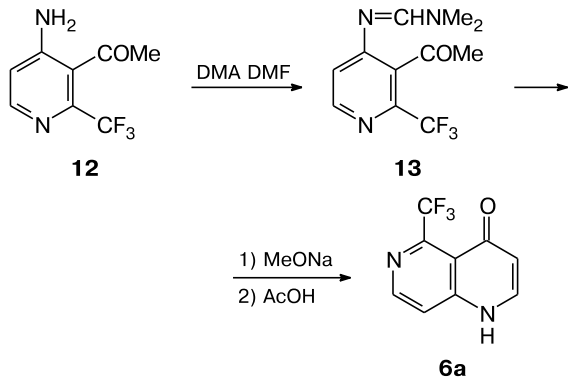
Scheme 2



Scheme 3



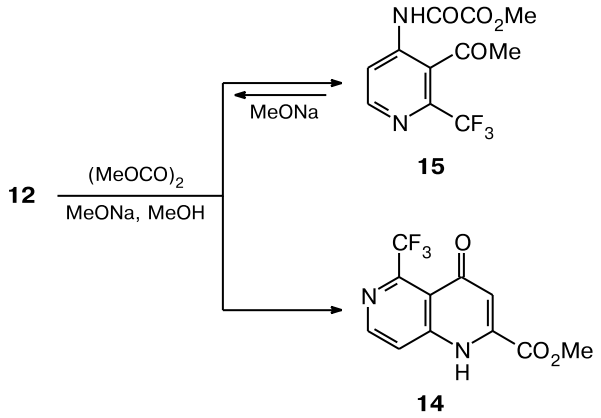
Scheme 4



The reaction of pyridine **12** with an excess of dimethyl oxalate in the presence of MeONa in methanol (following the method suggested in Refs. 10 and 11) led to 2-methoxycarbonylnaphthyridinone **14**. Apparently, this reaction follows two alternative directions, since, besides product **14**, amide **15** was also isolated. The latter under the reaction conditions undergoes hydrolysis back to pyridine **12**, which in the large excess of dimethyl oxalate is gradually converted to naphthyridinone **14**. And in fact, the isolated amide **15** reacts with MeONa in methanol to give pyridine **12**, whereas in the presence of dimethyl oxalate and MeONa, it is converted to naphthyridinone **14** (Scheme 5).

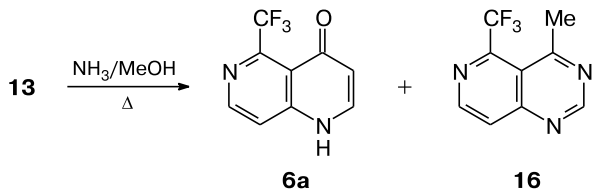
Recently,[12] we reacted 5-acetyl-4-dimethylaminovinyl-6-trifluoromethylpyrimidine with the methanolic

Scheme 5



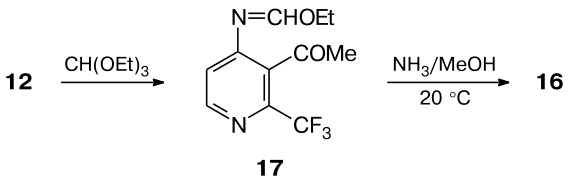
solution of NH_3 to obtain 5-methyl-4-trifluoromethylpyrido[4,3-*d*]pyrimidine. We expected that this approach would be a convenient method for the synthesis of 4-methyl-5-trifluoromethylpyrido[4,3-*d*]pyrimidine (**16**) from amidine **13**. However, it appeared that the yield of compound **16** was only 21% after heating of **13** with the methanolic solution of NH_3 in a sealed tube. This reaction gave naphthyridinone **6a** as the major product. It is obvious, that in this case ammonia played the role of a base, too (Scheme 6).

Scheme 6



An alternative approach to the synthesis of pyridopyrimidine **16** has proved more successful. The reaction of pyridine **12** with ethyl orthoformate gave imine **17**, which reacted with NH_3 in methanol at room temperature to be converted to **16** in 96% yield (Scheme 7).

Scheme 7



The isomer of compound **16**, *viz.*, 5-methyl-4-trifluoromethylpyrido[4,3-*d*]pyrimidine, synthesized by us earlier can add alcohols, water, and amines[12,13] to give the corresponding 1,4-dihydropyrido[4,3-*d*]pyrimidines. However, this property is not characteristic of pyridopyri-

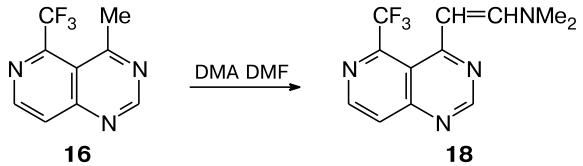
Table 2. Yields, melting points, elemental analysis and ^{1}H NMR spectroscopic data for compounds **6a**,**c**—**i** and **13**—**18**

Compound	Yield (%)	M.p./°C	Found / Calculated (%)			Molecular formula	^{1}H NMR ($CDCl_3$, δ, *J*/Hz)				
							H(2) (d, 1 H, *J* = 8)	H(3) (d, 1 H, *J* = 8)	H(7) (d, 1 H, *J* = 6)	H(8) (d, 1 H, *J* = 6)	Other signals
			C	H	N						
6a	72	>350	50.45 50.47	2.66 2.35	12.91 13.08	$C_9H_5F_3N_2O$	7.98	6.20	8.61	7.71	12.0 (s, 1 H, NH)
6c	67	203—204	54.81 54.55	3.72 3.74	11.15 11.36	$C_{11}H_9F_3N_2O$	7.51	6.39	8.70	7.48	1.51 (t, 3 H, Me, *J* = 7); 4.18 (q, 2 H, CH_2N, *J* = 7)
6d	76	182—183	56.13 56.25	4.56 4.32	11.01 10.93	$C_{12}H_{11}F_3N_2O$	7.50	6.36	8.68	7.74	1.03 (t, 3 H, Me, *J* = 7); 1.88 (m, 2 H, CH_2); 4.06 (t, 2 H, CH_2N, *J* = 7)
6e	63	186—187	56.60 56.69	3.59 3.54	10.81 11.02	$C_{12}H_9F_3N_2O$	7.50	6.39	8.65	7.39	4.52 (d, 2 H, CH_2N, *J* = 7); 5.15 (d, 1 H, CH_2=CH, *J* = 17); 5.40 (d, 1 H, CH_2=CH, *J* = 10); 5.98 (m, 1 H, CH=)
6f	69	154—155	54.37 54.55	4.62 4.58	9.65 9.78	$C_{13}H_{13}F_3N_2O_2$	7.52	6.34	8.67	7.48	2.05 (m, 2 H, CH_2); 3.35 (m, 5 H, CH_2O + MeO); 4.23 (t, 2 H, CH_2N, *J* = 7)
6g	78	187—188	59.49 59.63	3.08 3.13	8.75 8.69	$C_{16}H_{10}F_4N_2O$	7.58	6.40	8.58	7.32	5.27 (s, 2 H, CH_2N); 7.06—7.15 (m, 4 H, C_6H_4F)
6h	76	164—165	57.08 57.15	3.11 3.08	9.47 9.52	$C_{14}H_9F_3N_2O_2$	7.59		8.66	7.62	5.21 (s, 2 H, CH_2N); 6.33—6.46 (m, 3 H, H(3), H(3′), H(4′)); 7.41 (d, 1 H, H(5′), *J* = 2)
6i	72	182—183	54.05 54.19	2.87 2.92	8.97 9.03	$C_{14}H_9F_3N_2OS$	8.27	6.34	8.72	8.08	5.75 (s, 2 H, CH_2N); 7.01 (t, 1 H, H(4′), $J_{4',5'}$ = 5, $J_{3',4'}$ = 3); 7.22 (d, 1 H, H(3′), *J* = 3); 7.50 (d, 1 H, H(5′), *J* = 3)
13	95	112—113	50.80 50.96	4.78 4.66	16.68 16.47	$C_{11}H_{12}F_3N_3O$	—	—	—	—	2.55 (s, 3 H, Me); 3.00, 3.08 (both s, 6 H, NMe_2); 6.90 (d, 1 H, C(5)H, *J* = 6); 8.39 (d, 1 H, C(6)H, *J* = 6); 8.42 (s, 1 H, CH=N)
14	90	>300	48.38 48.58	2.71 2.60	10.15 10.29	$C_{11}H_7F_3N_2O_3$	—	6.75 (s)	8.68	8.08	3.98 (s, 3 H, Me); 12.45 (br.s, 1 H, NH)
15	46	136—138	45.40 45.52	3.20 3.13	9.52 9.66	$C_{11}H_9F_3N_2O_4$	—	—	—	—	2.62 (s, 3 H, MeCO); 4.00 (s, 3 H, MeO), 8.50 (d, 1 H, H(5), *J* = 6); 8.75 (d, 1 H, H(6), *J* = 6); 9.90 (s, 1 H, NH)
16	96	102—103	50.65 50.62	2.84 2.95	19.79 19.64	$C_9H_6F_3N_3$	9.32 (s)	—	8.92 (*J* = 5.5)	8.08 (*J* = 5.5)	3.16 (q, 3 H, Me, J_{Me,CF_3} = 6)
17	93	71—72	50.67 50.77	4.31 4.26	10.72 10.77	$C_{11}H_{11}F_3N_2O_2$	—	—	—	—	1.37 (t, 3 H, $MeCH_2$, *J* = 7); 2.25 (s, 3 H, Me); 4.31 (q, 2 H, CH_2O, *J* = 7); 6.99 (d, 1 H, C(5)H, *J* = 6); 7.73 (s, 1 H, EtOCH=); 8.58 (d, 1 H, C(6)H, *J* = 6)
18	97	130—131	53.67 53.54	4.13 4.25	20.97 20.89	$C_{12}H_{11}F_3N_4$	8.67 (s)	—	8.65	7.64	3.03, 3.26 (both br.s, 6 H, NMe_2); 5.87 (d, 1 H, CH=, *J* = 12); 8.42 (d, 1 H, Me_2NCH=, *J* = 12)

midine **16**, that indicates that the reactivity of substituted pyrido[4,3-*d*]pyrimidines is considerably affected by the location of CF_3 group.

Pyridopyrimidine **16** readily reacted with DMF DMA in refluxing benzene to be converted to dimethylaminovinyl compound **18** (Scheme 8), which can be used for the synthesis of new nitrogen-containing heterocycles.

Scheme 8



16 **18**

Experimental

^{1}H NMR spectra were recorded on a Bruker WM-250 spectrometer (250.13 MHz), ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (75.47 MHz). Chemical shifts in the ^{1}H NMR spectra were calculated using residual signals of deuterated solvents as references (δ 7.27 for $CDCl_3$ and δ 2.50 for DMSO-d_6), in ^{13}C NMR spectra the reference was the multiplet signals of the deuterated solvents (δ 39.50 for DMSO-d_6 and δ 77.00 for $CDCl_3$). 2D ^{1}H/^{13}C and ^{1}H/^{15}N HMBC NMR spectra were recorded on a Bruker Avance 600 spectrometer (600 MHz, 150 MHz, and 60.8 MHz for ^{1}H, ^{13}C, and ^{15}N, respectively). The signals in the ^{1}H and ^{13}C NMR spectra of were assigned based on the 2D ^{1}H/^{13}C HMBC NMR spectra. Chemical shifts for ^{15}N were measured relative to $MeNO_2$ as an external standard (the upfield chemical shifts are given as negative values) based on the analysis of 2D ^{1}H/^{15}N HMBC NMR spectra. The ^{1}H NMR spectrum of compound **10** was interpreted using a 2D procedure COSY and ROESY, the signals of the protonated carbon atoms were assigned based on the analysis of the 2D ^{1}H/^{13}C HSQC heteronuclear spectrum. IR spectra were recorded on a Specord-M82 spectrometer, mass spectra were obtained on a Kratos MS-30 instrument (EI, 70 eV, temperature of the ionizing chamber 250 °C, direct injection of the compounds). High resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF II instrument using electrospray ionization (ESI). The measurements were performed for the positive ions (capillary voltage 4500 V). The scanning range of masses *m/z* 50—3000 Da, an external and an internal calibration (Electrospray Calibrant Solution, Fluka). Solutions of samples in CH_3CN were injected with a syringe, the flow rate 3 μL min^{-1}. Sprayer gas nitrogen (4 L min^{-1}), the interface temperature 180 °C. 3-Acetyl-4-amino-5,5,5-trifluoro-3-penten-2-one diphenylboron complex[5] and 3-acetyl-4-amino-2-trifluoromethylpyridine[6] were synthesized according to the procedures described earlier. Amines and dimethylformamide dimethyl acetal were purchased from Acros. Merk-60 silica gel (0.063—0.200 nm) was used for column chromatography. The yields, melting points, elemental analysis data, and ^{1}H NMR spectra of compounds **3a**—**i**, **4**, and **10** are given in Table 1, those for naphthyridinones **6a**,**c**—**i**, as well as for compounds **13**—**18** — in Table 2.

4-Amino-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (3a). Compound **1** (5.44 g, 15 mmol) was dissolved in 0.6 *M* solution of NH_3 in THF NMR (60 mL) and kept for 24 h at ~20 °C. The solvent was evaporated, the residue recrystallized from a mixture of benzene (20 mL) and light petroleum (15 mL) to obtain compound **3a** (2.21 g). The filtrate was concentrated, the residue was subjected to column chromatography on SiO_2 (eluent: first benzene, then benzene—chloroform) to additionally obtain compound **3a** (1.31 g). The total yield was 3.52 g. MS, *m/z*: 281 $[M - Ph]^+$. IR (KBr), ν/cm^{-1}: 3385 (NH), 1675 (C=O). ^{19}F NMR ($CDCl_3$), δ: –67.0. ^{13}C NMR ($CDCl_3$), δ: 24.7 (q, MeCN, J = 129 Hz); 32.5 (q, MeCO, J = 129 Hz); 106.0 (s, C—COMe); 120.0 (q, CF_3, $^1J_{C,F}$ = 280 Hz); 126.8, 127.6, 132.2, 149.00 (2 Ph); 151.0 (q, CF_3—C, $^2J_{C,F}$ = 34 Hz); 167.6 (s, NC—Me); 197.9 (q, C=O, J = 6 Hz).

4-Methylamino-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (3b) was obtained similarly to **3a**, but the reaction mixture was subjected to column chromatography on SiO_2 (eluent: first a mixture of benzene—light petroleum, then benzene) immediately after evaporation of the solvent.

4-Ethylamino-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (3c) was obtained similarly to complex **3b**.

4-*n*-Propylamino-3-trifluoroacetimidoyl-3-penten-2-one (3d) and 4-*n*-propylamino-2-*n*-propylimino-3-trifluoroacetimidoylpent-3-ene diphenylboron complexes (4). A mixture of chelate **1** (1.0 g, 2.6 mmol) and $PrNH_2$ (0.34 mL, 4.1 mmol) in benzene (5 mL) was refluxed for 3 h. Benzene and excess of amine were evaporated, the residue was subjected to column chromatography on SiO_2 (eluent: first a mixture of benzene—light petroleum (2 : 1), then benzene, and finally a mixture of benzene—acetone (4 : 1)). The isolation gave product **3d** (0.85 g) and compound **4** (0.22 g). ^{15}N NMR of chelate **4** ($CDCl_3$), δ, *Z*-isomer/*E*-isomer): –261.8/–263.5 (NH, correlation with proton NH); –204/–206 (NB, correlation with protons MeCNB); –42.5/–39.7 (C=N, correlation with protons MeC=N). ^{19}F NMR ($CDCl_3$), δ: –68.6 (*Z*-isomer), –66.8 (*E*-isomer) (the ratio $Z : E$ = 2 : 1). ^{19}F NMR (DMSO-d_6), δ: –66.2 (*Z*-isomer), –64.6 (*E*-isomer) (the ratio $Z : E$ = 4 : 1).

The following compounds were obtained similarly to **3d**: 4-allylamino-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (**3e**), 4-(3-methoxypropylamino)-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (**3f**), 4-(4-fluorobenzylamino)-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (**3g**), 4-(2-furfurylamino)-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (**3h**), 4-(2-thienylmethylamino)-3-trifluoroacetimidoyl-3-penten-2-one diphenylboron complex (**3i**).

2-(1´-Amino-2´,2´,2´-trifluoroethylidene)-6-dimethylaminomethylene-3-iminocyclohex-4-en-1-one diphenylboron complex (10). A mixture of chelate **3a** (1.6 g, 4.47 mmol) and DMF DMA (2.6 g, 22.35 mmol) in toluene (15 mL) was refluxed for 9 h. The solvent was evaporated, the residue was subjected to column chromatography on SiO_2 (eluent: a mixture of benzene—acetone, first 10 : 1, then 4 : 1) to sequentially isolate 4-amino-6-dimethylamino-3-trifluoroacetimidoylhexa-3,5-dien-2-one diphenylboron complex (0.35 g, 19%), whose m.p. and spectroscopic data completely agreed with those of this compound obtained earlier,[6] and compound **10** (0.82 g). MS, *m/z*: 346 $[M - Ph]^+$. IR (KBr), ν/cm^{-1}: 3395 (NH), 1640 (C=O). ^{13}C NMR (DMSO-d_6), δ: 41.2, 48.1 (Me_2N); 105.8 (C(4)); 115.3 (C(6)); 118.4 (C(2)); 120.2 (CF_3); 125.5 (*p*-C_{Ph}); 126.8 (*m*-C_{Ph}); 128.5 (C_{Ph}-B); 132.5 (*o*-C_{Ph}); 136.7 (C(5)); 152.1 (C(3)); 152.8 (C(10)); 178.0 (C=O). ^{11}B NMR ($CDCl_3$), δ: –2.1.

1-*n*-Propyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (6d). A mixture of complex **3d** (1.47 g, 3.7 mmol) and DMF DMA (1.5 mL, 11 mmol) in *o*-xylene (25 mL) was refluxed for 4 h. The solvent was evaporated, the residue was subjected to column chromatography on SiO_2 (eluent: first benzene, then a mixture of benzene—acetone (first 10 : 1, then 4 : 1) to obtain naphthyridinone **6d** (0.72 g). MS, *m/z*: 256 $[M]^+$. IR (KBr), ν/cm^{-1}: 1635 (C=O). ^{13}C NMR ($CDCl_3$), δ: 10.9 (Me); 21.8 (CH_2); 54.9 (CH_2N); 113.3 (C(8)); 115.0 (C(3)); 120.2 (C(4a)); 121.3 (CF_3); 143.3 (C(2)); 146.9 (C(8a)); 147.7 (C(7)); 148.1 (C(5)); 175.3 (C=O).

The following compounds were obtained similarly to **6d**: 1-ethyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (**6c**), 1-allyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (**6e**), 1-(3-methoxypropyl)-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (**6f**), 1-(4-fluorobenzyl)-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (**6g**), 1-(2-furfuryl)-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (**6h**), 1-(2-thienylmethyl)-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (**6i**).

3-Acetyl-4-(dimethylaminomethyleneamino)-2-trifluoromethylpyridine (13). A mixture of pyridine **12** (0.37 g, 1.8 mmol) and

DMF DMA (0.5 mL) in benzene (15 mL) was refluxed for 2 h. Benzene was evaporated, the residue was triturated with light petroleum (10 mL). A precipitate formed was washed with light petroleum to obtain amidine **13** (0.45 g). MS, *m/z*: 259 $[M]^+$. IR (KBr), ν/cm^{-1}: 1700 (C=O); 1635, 1570 (the region of multiple bonds); 1260—1140 (C—F).

5-Trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (6a). ***A.*** A solution of amidine **13** (0.05 g, 0.19 mmol) and 1 *N* methanolic solution of MeONa (0.19 mL) in methanol (5 mL) was refluxed for 3 h, followed by the addition of a threefold excess of acetic acid. The solvents were evaporated, the residue was washed with water, and dried to obtain compound **6a** (0.03 g). MS, *m/z*: 214 $[M]^+$. IR (KBr), ν/cm^{-1}: 3258 (NH), 1645 (C=O). ^{13}C NMR (DMSO-d_6), δ: 113.9 (C(8)); 117.0 (C(3)); 118.5 (C(4a)); 121.6 (CF_3); 140.0 (C(2)); 145.7 (C(5)); 147.0 (C(7)); 147.4 (C(8a)); 174.6 (C=O). ^{19}F NMR ($CDCl_3$), δ: −61.8.

B. A solution of amidine **13** (0.12 g, 0.46 mmol) in 4.5 *N* methanolic solution of NH_3 (10 mL) was heated in a sealed tube for 10 h at 80—90 °C. The solvent was evaporated, the residue was subjected to column chromatography on SiO_2 (eluent: a mixture of benzene—acetone, first 20 : 1, then 5 : 1, further 1 : 1, and finally 1 : 3) to sequentially isolate pyrido[4,3-*d*]pyrimidine **16** (0.021 g, 21%) and naphthyridine **6a** (0.059 g, 60%).

3-Acetyl-4-(methyloxalylamino)-2-trifluoromethylpyridine (15). Dimethyl oxalate (0.95 g) and a 1.17 *M* solution of MeONa in methanol (7 mL) were sequentially added to a solution of pyridine **12** (0.4 g, 1.96 mmol) in methanol (10 mL). After 3 h, acetic acid (0.6 mL) was added. The solvents were evaporated, the residue was diluted with water (30 mL). A precipitate formed was filtered off, washed with water (3×15 mL), dried, and subjected to column chromatography on SiO_2 (eluent: a mixture of benzene—acetone, first 20 : 1, then 2 : 1) to sequentially isolate amide **15** (0.264 g) and naphthyridine **14** (0.08 g).

2-Methoxycarbonyl-5-trifluoromethyl-1,6-naphthyridin-4(1*H*)-one (14). ***A.*** Dimethyl oxalate (0.1 g, 0.85 mmol) was added to a solution of compound **15** (0.08 g, 0.28 mmol) in methanol, then after 20 min a 1.1 *M* solution of MeONa in methanol (0.8 mL) was also added, and the mixture was allowed to stand for 18 h at ~20 °C. Then, dimethyl oxalate (0.075 g) and a 1.1 *M* solution of MeONa in methanol (0.6 mL) were added to the reaction mixture once more and it was allowed to stand for another 18 h. The latter procedure was repeated one more time, then a solution of acetic acid (0.25 mL) in water (75 mL) was added. A precipitate formed was filtered off, washed with water (2×15 mL), dried, and finally washed with benzene (25 mL) to obtain naphthyridine **14** (0.068 g).

B. A 1.17 *M* solution of MeONa in methanol (2.3 mL) was added to a solution of compound **12** (0.18 g, 0.88 mmol) and dimethyl oxalate (0.312 g) in methanol (10 mL), and the mixture was allowed to stand for 5 h at ~20 °C. Then another portion of dimethyl oxalate (0.21 g) was added, and after standing for 18 h, a 1.17 *M* solution of MeONa in methanol (1.55 mL) was added. After 24 h, a solution of acetic acid (0.5 mL) in water (15 mL) was added to the mixture. A precipitate formed was filtered off, washed with water (2×15 mL), and dried to obtain naphthyridine **14** (0.182 g). ^{19}F NMR (DMSO-d_6), δ: −63.6. HRMS: found, *m/z*: 273.0483 $[M + H]^+$, 295.097 $[M + Na]^+$. $C_{11}H_7F_3N_2O_3$. Calculated: 273.0482 $[M + H]^+$, 295.0301 $[M + Na]^+$.

3-Acetyl-2-trifluoromethyl-4-ethoxymethyleneaminopyridine (17). A mixture of pyridine **12** (0.21 g, 0.1 mmol) and ethyl orthoformate (3 mL) (3 mL) was refluxed for 2 h, then ethanol and an excess of ethyl orthoformate were slowly evaporated. The procedure was repeated three more times. The residue was extracted with warm light petroleum (4×10 mL), then light petroleum was evaporated to obtain crude compound **17** (0.25 g, 93%). Pure product **17** (0.173 g, 65%) was obtained after crystallization from light petroleum (7 mL). HRMS: found, *m/z*: 261.052 $[M + H]^+$. $C_{11}H_{11}F_3N_2O_2$. Calculated: 261.0845 $[M + H]^+$.

4-Methyl-5-trifluoromethylpyrido[4,3-*d*]pyrimidine (16). A mixture of compound **17** (0.69 g, 2.6 mmol) and a 1.7 *M* solution of NH_3 in methanol (25 mL) was stirred for 1.5 h, the solvent was evaporated, the residue was sublimed *in vacuo* (1—2 Torr) at 65—90 °C using a water bath to obtain compound **16** as a white powder (0.542 g). ^{19}F NMR ($CDCl_3$), δ: −60.3. HRMS: found, *m/z*: 214.0592 $[M + H]^+$. $C_9H_6F_3N_3$. Calculated: 214.0587 $[M + H]^+$.

4-Dimethylaminovinyl-5-trifluoromethylpyrido[4,3-*d*]pyrimidine (18). A mixture of pyridopyrimidine **16** (0.1 g, 0.47 mmol) (0.1 g, 0.47 mmol) and DMF DMA (0.2 mL) in benzene (2 mL) was refluxed for 5 h. The solvent was evaporated, the residue was subjected to column chromatography on SiO_2 (eluent: first benzene, then a mixture of benzene—acetone (5 : 1)) to obtain compound **18** (0.122 g).

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