Amide acetals in the synthesis of pyridothienopyrimidines

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Methyl 3-amino-4-arylaminothieno[2,3-*b*]pyridine-2-carboxylates containing various substituents in the benzene ring were synthesized by the Thorpe-Ziegler reaction of 4-arylamino-2-chloropyridine-3-carbonitriles with methyl thioglycolates. The influence of the substituent in the benzene ring, acetal structure, the solvent and the process temperature on the reactions of obtained compounds with amide acetals was studied. It was established that reactions with dimethylacetamide dimethylacetal in toluene smoothly results in amidine derivatives, *viz.*, methyl 4-arylamino-3-[1-(dimethylamino)ethylidene]aminothieno[2,3-*b*]pyridine-2-carboxylates, regardless of the substituent in the benzene ring. Analogous reaction of *p*-fluoroderivative with dimethylacetamide dimethylacetal in refluxing anhydrous ethanol leads to intramolecular cyclocondensation to produce substituted pyridothienopyrimidines, *viz.*, 5*H*-1-thia-3,5,8-triazaacenaphthenes, in good yields. Amidine derivatives were the major products in the case of the coupling of aminothienopyridines with dimethylformamide dimethylacetal under the same conditions. A new approach to the synthesis of substituted pyridothienopyrimidines, *viz.*, 3*H*-1-thia-3,5,8-triazaacenaphthylenes, based on the prolonged heating of methyl 4-arylamino-3-[1-(dimethylamino)ethylidene]aminothieno[2,3-*b*]pyridine-2-carboxylates in the excess of acetic anhydride was elaborated. Putative mechanisms of the processes concerned are given.

Key words: 4-arylamino-2-chloropyridine-3-carbonitriles, methyl 3-amino-4-arylaminothieno[2,3-*b*]pyridine-2-carboxylates, amide acetals, methyl 4-arylamino-3-[1-(dimethylamino)ethylidene]aminothieno[2,3-*b*]pyridine-2-carboxylates, pyridothienopyrimidines, 5*H*-1-thia-3,5,8-triazaacenaphthenes, 3*H*-1-thia-3,5,8-triazaacenaphthylenes, the Thorpe-Ziegler reaction, X-ray diffraction.

Numerous compounds with marked biological activity were found among thieno[2,3-*b*]pyridines.[1—3] In particular, recently,[4] thieno[2,3-*b*]pyridine derivatives fused to the pyrimidine ring have been shown to be potent antagonists of glutamate receptors.

3-Aminothieno[2,3-*b*]pyridines are convenient starting compounds for the synthesis of polyheterocyclic systems. Earlier,[5,6] aminothieno[2,3-*b*]pyridines have been obtained by S-alkylation of 3-cyanopyridine-2-thiones and subsequent intramolecular Thorpe-Ziegler cyclization. Moreover, such thieno[2,3-*b*]pyridines and polyheterocyclic systems synthesized therefrom can be obtained based on 2-chloro-3-cyanopyridines.[7—9] The most versatile procedure for the synthesis of 3-aminopyrroles and 3-aminothiophenes and various heterocyclic systems is the Thorpe-Ziegler reaction.[10,11]

In the present work, synthesis and some reactions of thienopyridines containing mono- and dihalogenoaniline substituents in the position 4 were studied. This choice of the starting compounds is not fortuitous. Firstly, it was of interest to examine the influence of halogen atoms in the benzene ring located at a considerable distance from the reaction centers on the reactivity of compounds under study. Secondly, and it is not the least of the factors, the present work envisages subsequent study of the biological activity of compounds synthesized and modification of their derivatives. We take into account the fact that the presence of halogens as the substituents usually apprecia-

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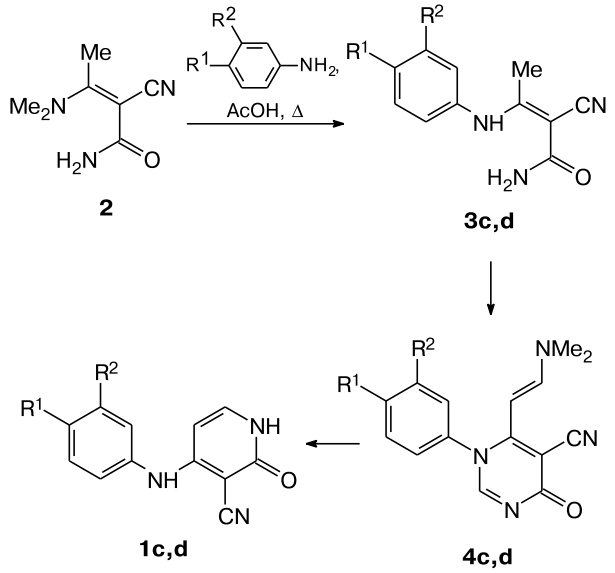
bly increases penetration through the lipophilic biological membranes. This fact, in turn, often causes an increase in the biological effect.

Earlier,[12] we have synthesized 4-arylamino-2-oxo-1,2-dihydropyridine-3-carbonitriles **1a,b**. Pyridones **1c,d** were prepared from 2-cyano-3-dimethylaminocrotonamide (**2**) according to the known procedure[13] *via* intermediate enaminoamides **3c,d** and pyrimidinones **4c,d** (Scheme 1).

Scheme 1



R^1 = H, R^2 = F (**c**); R^1 = R^2 = F (**d**)

The corresponding 2-chloropyridines **5a—d** were obtained in high yields by refluxing compounds **1a—d** in the excess of phosphoryl chloride in the presence of triethylamine hydrochloride (Scheme 2).

Methyl 3-amino-4-arylaminothieno[2,3-*b*]pyridine-2-carboxylates **6a—e** were obtained (without isolation of intermediate mercapto derivatives) in 77—94% yield by refluxing 2-chloropyridines **5a—e** with methyl thioglycolate in the presence of sodium methoxide in methanol (see Scheme 2). The putative mechanism of the reaction **5**→**6** is shown in Scheme 3.

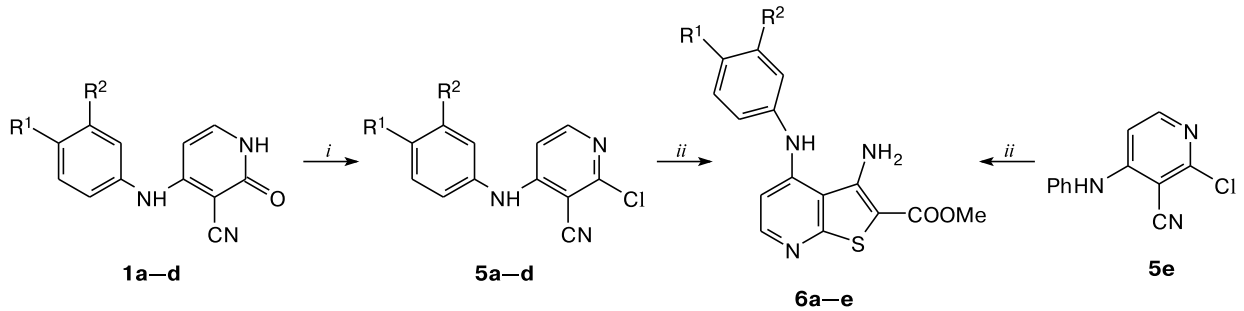
We further investigated the reaction of obtained aminothiophene derivatives **6a—e** with amide acetals **7a**,**b**. Stirring of amines **6b—e** with dimethylacetamide dimethylacetal (**7a**) at 80 °C in anhydrous toluene leads unambiguously to the corresponding amidines **8b—e** in 74—93% yields (Scheme 4). In the reaction of **6a** with **7a**, a mixture of amidine **8a** and pyrimidine **9a** in 96 : 4 ratio (based on ^{1}H NMR spectroscopy) was obtained.

If these reactions are carried out in refluxing toluene, resinification took place and it was possible to isolate analytically pure amidines **8a—e** in considerably smaller yields.

The reaction of dimethylacetamide dimethylacetal (**7a**) with aminothiophenes **6a—e** in anhydrous ethanol is complicated by transesterification and, in addition to methoxycarbonyl compounds, ethoxycarbonyl homologs formed (**8´** and **9´**, respectively) (see Scheme 4). It should be noted that sharp difference was observed for the reactions of *p*-F- and *p*-Cl-substituted derivatives in anhydrous ethanol, other reaction conditions (the ratio of the reactants, the reaction time, the work-up of the reaction mixture and isolation of the products being the same). Reaction of *p*-chloroanilinothienopyridine **6a** with acetal **7a** proceeds as expected to give a mixture of amidines **8a** and **8´a**. In the case of *p*-fluoroanilinothienopyridine **6b**, the reaction was not stopped at the step of formation of amidine **8b** and subsequent cyclization to pyrimidine took place and tricyclic compound **9b** was isolated in 74% yield (crude product, the yield of recrystallized product was 51%). The mother liquor after isolation of the major reaction products contained only the intramolecular condensation products (**9b** and **9´b**) (^{1}H NMR data).

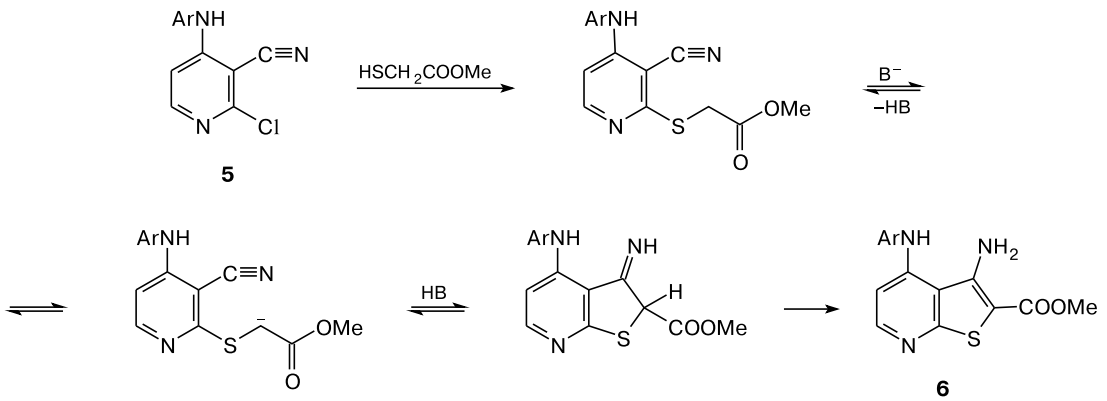
Analogous reaction of *p*-fluoroanilinothienopyridine **6b** with dimethylacetamide dimethylacetal (**7a**) in methanol was carried out to prevent transesterification of the product with ethanol. In this case, based on the ^{1}H NMR

Scheme 2



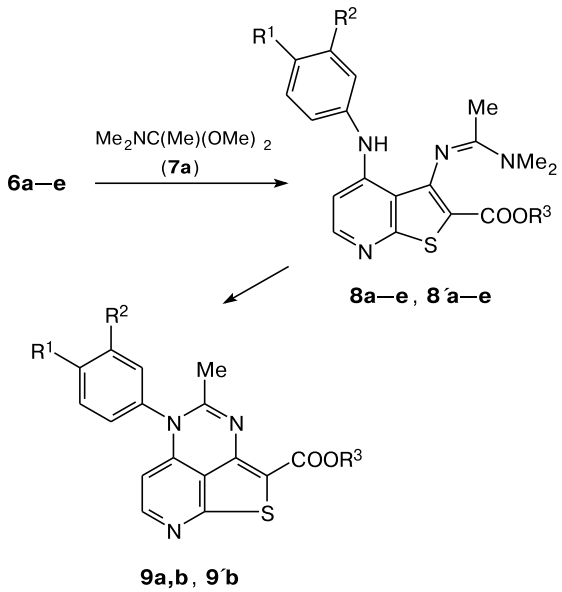
R^1 = Cl, R^2 = H (**a**); R^1 = F, R^2 = H (**b**); R^1 = H, R^2 = F (**c**); R^1 = R^2 = F (**d**); R^1 = R^2 = H (**e**)
i. $POCl_3$, $Et_3N \cdot HCl$, reflux; *ii*. $HSCH_2COOMe$, MeONa, MeOH, reflux.

Scheme 3



B = MeO^-, $MeOC(O)CH_2S^-$

Scheme 4



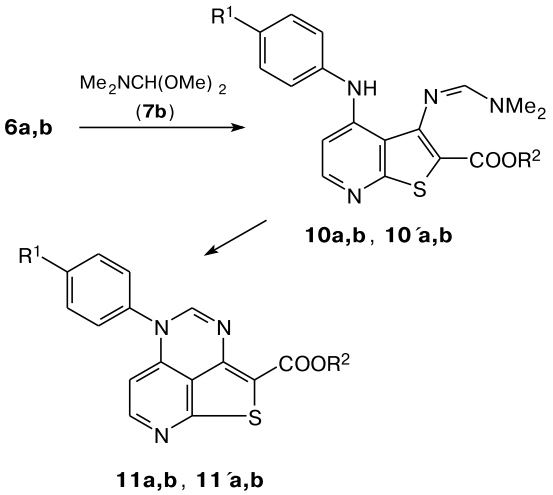
6, **8**, **8´**, **9**, **9´**: R^1 = Cl, R^2 = H (**a**); R^1 = F, R^2 = H (**b**); R^1 = H, R^2 = F (**c**); R^1 = R^2 = F (**d**); R^1 = R^2 = H (**e**)
8, **9**: R^3 = Me
8´, **9´**: R^3 = Et

data, a mixture of amidine **8b** and pyrimidine derivative **9b** in the ratio 1 : 1 formed. Hence, higher temperature is required for the quantitative transformation, which can be achieved on refluxing in ethanol.

Investigation of the influence of acetal structure on the course of this process showed that crystalline products obtained upon the reaction of compounds **6a**,**b** with dimethylformamide dimethylacetal (**7b**) in dry toluene (80 °C, 4 h) represent mixtures of the corresponding amidines **10** and pyrimidines **11** in 89 : 11 ratio in the case of *p*-F-substituted and in 84 : 16 ratio in the case of *p*-Cl-substituted derivatives (^{1}H NMR data) (Scheme 5).

The following ratios of the reaction products were determined when carrying out analogous reactions in refluxing anhydrous ethanol: the ratio of total amount of amidines **10** and **10´** to the total amount of pyrimidines **11** and **11´** in the case of *p*-F-substituted derivative (**10b** + **10´b**) : (**11b** + **11´b**) was 80 : 20, and in the case of *p*-Cl-substituted derivative (**10a** + **10´a**) : (**11a** + **11´a**) was 90 : 10. It also confirms the fact that cyclocondensation of *p*-fluorophenyl-substituted aminothienopyridine with formation of pyrimidine derivatives in refluxing anhydrous ethanol occurs two times faster than that of *p*-chlorophenyl analog (the results obtained with dimethylformamide and dimethylacetamide dimethylacetals (**7a**) and (**7b**) coincided qualitatively).

Scheme 5



R^1 = Cl (**a**), F (**b**); R^2 = Me (**10a,b**, **11a,b**); R^2 = Et (**10´a,b**, **11´a,b**)

Thus, the extent of transformation of fluorosubstituted derivative (**10b**) into fused pyrimidines **11b** and **11´b** is

20% in refluxing ethanol and of chloro-substituted derivative **10a** into pyrimidines **11a** and **11´a** is 10%, whereas in toluene the pattern was slightly different and *p*-chlorophenyl derivative undergoes cyclization in a somewhat greater extent then *p*-fluorophenyl-substituted amidine. This was in contrast to the results obtained with acetal **7a**. We will adduce the putative interpretation of these contradictions after discussion of the presumable mechanisms of intramolecular cyclizations observed.

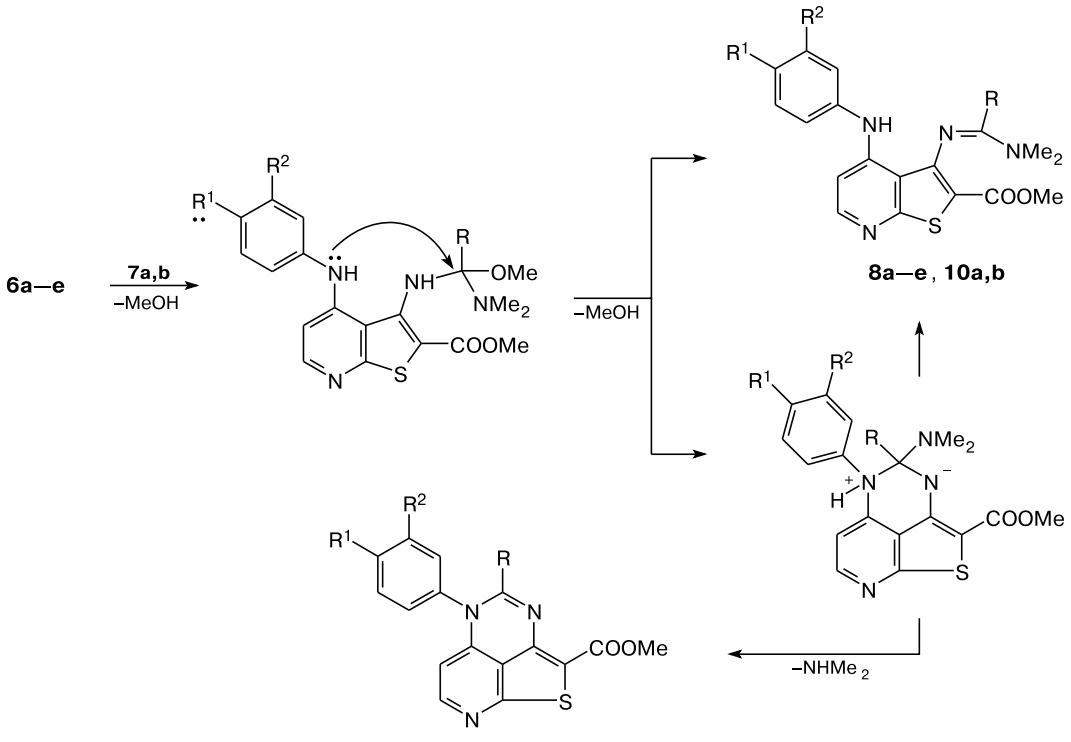
We succeed in isolation of tricyclic compounds **11a**,**b** in good yields under long-term refluxing (~20 h) of amines **6a**,**b** with dimethylformamide dimethylacetal (**7b**) in toluene.

For the explanation of the reasons for different courses of the reaction and elucidation of its presumable mechanism, we synthesized *m*-fluoro- and 3,4-difluoroanilinothienopyridine derivatives (**6c,d**). In both cases, the reactions of these compounds with dimethylacetamide dimethylacetal (**7a**) in refluxing anhydrous ethanol leads to amidines virtually exclusively (see Scheme 4). Traces of pyrimidine derivatives were observed only in the mother liquors obtained after isolation of the major products (^{1}H NMR data).

The results obtained allow us to suggest a putative mechanism of the reaction of amines **6a**—**e** with acetals **7a**,**b** (Scheme 6).

Halogens exert the negative inductive effect (–*I*) and positive mesomeric effect (+*M*). The differences in the behavior of *p*-Cl- and *p*-F-substituted derivatives is interpreted from comparison of σ constants of these substituents. Despite the plurality of these constants (for example see Ref. 14) based on them it is possible to obtain quite distinct qualitative pattern of the influence of the substituents on the reaction. Thus σ-constant for the *p*-F-substituent in the benzene ring is +0.062 and for the *p*-Cl-substituent it is +0.227 (electrophylic σ^+-constants are –0.073 and +0.114, respectively), *i.e.*, the fluorine atom is either a weak electron-withdrawing or a weak electron-donor group, but the chlorine atom is a strong electron-withdrawing group. The fluorine atom in the *para*-position of the benzene ring increases the electron density on the reaction center, which is the NH group in this case, and facilitates the intramolecular cyclocondensation with formation of a substituted pyrimidine. If the florine atom is in the *meta*-position of the benzene ring or the *m*-F-atom is in addition to the *p*-F-atom, the cyclization to pyrimidines under the conditions used becomes virtually impos-

Scheme 6



6, **8—11**: R^1 = Cl, R^2 = H (**a**); R^1 = F, R^2 = H (**b**); R^1 = H, R^2 = F (**c**); R^1 = R^2 = F (**d**); R^1 = R^2 = H (**e**)
8, **9**: R = Me
10, **11**: R = H

sible due to significant negative inductive effect. Trace amounts of the corresponding pyrimidine derivatives **9** were observed only in the mother liquors (reactions of aminothiophene derivatives **6c,d** with acetal **7a** in ethanol) (^{1}H NMR data). These compounds could be identified based on the fact that amidine derivatives (compounds **8**) and pyrimidine derivatives (compounds **9**) can distinctly be differentiated by the location of the signals for protons of the pyridine ring in the ^{1}H NMR spectra: in the case of amidine derivatives, the proton H(5) is observed at δ 6.89—7.02, and the proton H(6) of pyrimidine derivatives is observed at δ 5.78—5.83. The difference in chemical shifts of other signals is also evident: protons H(6) of amidines are observed at δ 8.14—8.24 and analogous protons H(7) of pyrimidine derivatives are observed at δ 8.22—8.26. A broadened singlet for the aniline NH proton and a singlet for the dimethylamino group are also observed in the ^{1}H NMR spectra of amidine derivatives **8**. Analogously, amidines **10** can be distinguished from pyrimidine derivatives **11**.

It should be noted that besides the presumable mechanism of cyclization (see Scheme 6), it is necessary to consider yet another mechanism, which is possible for the reaction in nonpolar aprotic solvent (for example, in toluene) (Scheme 7). Probably, in this case, ionization is the dominant process due to the presence of the NH group at the pyridine ring. The process of ionization is realized to a small extent (NH acidity of the substituted anilines is very low), but in long-term reactions with amide acetals different behavior of *p*-fluoro- and *p*-chloro-substituted derivatives was observed: for the latter cyclization to pyrimidines proceeds faster. Obviously, the presence of electron-withdrawing substituent (*p*-chloroanilino group instead of electron-donating *p*-fluoroanilino group) stabilizes anion **A** (see Scheme 7), which accounts for the contradictions observed in studies of the reactions of aminothiophene derivatives **6a,b** with amide acetals **7a** and **7b**.

Thus, the following factors influence the course of the reaction of aminothiophene derivatives **6** with amide acetals **7**:

1) the electronic effect of the substituents in the benzene ring: in the case of electron-donating group (*p*-F, the overall $-I$ and $+M$ effect), cyclocondensation of amidines into pyrimidine tricyclic compounds is observed with acetal **7a**, but in the case of electron-withdrawing group (*p*-Cl) the process is stopped mainly in the step of amidine formation;

2) the influence of the solvent: in the case of a nonpolar aprotic solvent (toluene), amidines are formed in all reactions with amide acetal **7a** regardless of the electron effect of the substituent in the benzene ring; in a polar protic solvent (ethanol), cyclization to pyrimidine is the dominant process in the case of *p*-F-substituted derivative in contrast to *p*-Cl one;

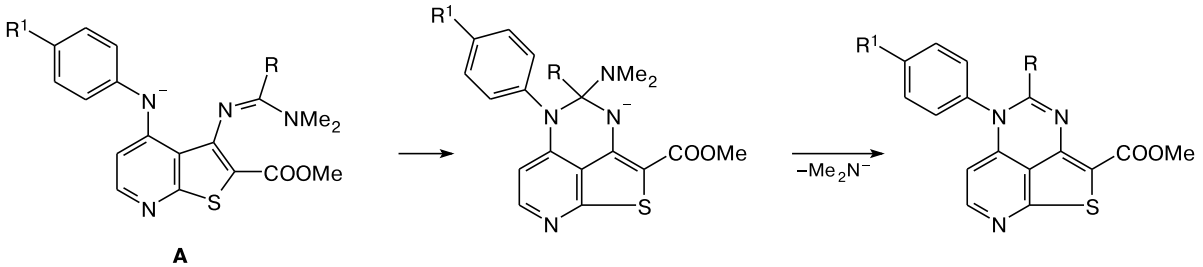
3) the reaction temperature: the reaction of *p*-F-substituted aminothienopyridine derivative **6b** with dimethylacetamide dimethylacetal (**7a**) in refluxing methanol (lower temperature), other conditions being the same (the reaction time is 4 h) leads to amidine **8b** and pyrimidine **9b** in the ratio 1 : 1 (^{1}H NMR data);

4) the influence of the acetal: the presumable mechanism of the reaction of aminothienopyridine derivatives **6a—e** with amide acetals (**7a** or **7b**) (see Scheme 6) points to the formation of trisaminomethane derivatives. In the case of acetal **7a**, this system is more sterically hindered and transforms into pyrimidine derivative **9** preferably with elimination of the bulky dimethylamino group with acquirement of aromaticity and gain in energy.

Virtually no cyclocondensation into pyrimidine derivative is observed in the reaction of phenyl-substituted compound **6e** with acetal **7a** in toluene or ethanol as in the cases of 4-chloro, 3-fluoro and 3,4-difluoro derivatives.

It should be noted that we succeded in obtaining *p*-chlorophenyl-substituted pyrimidine **9a** in 35% yield only by heating amidine **8a** in diphenyl oxide at 200 °C in the presence of catalytic amounts of *p*-toluenesulfonic acid (Scheme 8). All other attempts to carry out intramolecular cyclocondensation of compound **8a** were unsuccessful: fusion with *p*-toluenesulfonic acid or refluxing in DMF in the presence of *p*-toluenesulfonic acid lead only to resinification of the reaction mixtures. Earlier,[15] tricyclic pyrimidine derivatives (of the type **9**) have been obtained by heating of the corresponding amidines in 70% aqueous

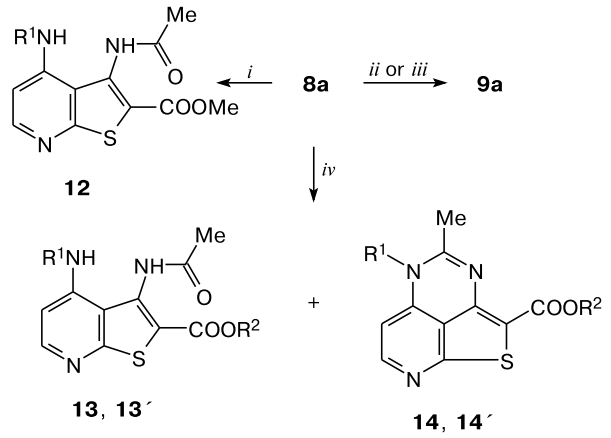
Scheme 7



R = Me, H; R^1 = Cl, F

acetic acid for 30 min. An attempt to carry out such a reaction with compound **8a** lead only to hydrolysis of the amidine fragment of the molecule and compound **12** was isolated in 75% yield as a result of refluxing for 14 h.

Scheme 8



i. 70% aqueous AcOH, reflux; *ii*. *p*-TsOH, H_2O, 200 °C; *iii*. AcOH, reflux; *iv*. 1) Bu^tONa, Bu^tOH. 2) AcOH, H_2O.
R^1 = 4-ClC_6H_4, R^2 = H (**13**, **14**), Bu^t (**13´**, **14´**)

Compound **13** was isolated in 84% yield as the main product upon attempted intramolecular cyclocondensation **8a**→**9a** under the action of a strong base (1.5 equiv. Bu^tONa) in refluxing *tert*-butyl alcohol for 3 h and subsequent treatment of reaction mixture with water and glacial acetic acid. The reaction proceeds towards the formation of substituted pyrimidine **14**, which was confirmed by the presence of the signal for the proton H(6) of the pyridine ring at δ 5.57 in the ^{1}H NMR spectrum. The mass spectrum shows a peak of the molecular ion of compound **14**.

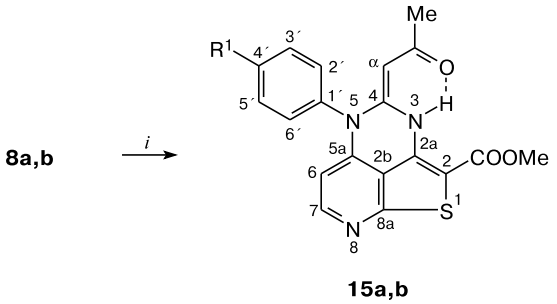
Thus, cyclocondensation of *p*-chloro-substituted amidine **8a** into substituted pyrimidine **9a** under the action of 70% aqueous AcOH, base or mere refluxing in a solvent either does not proceed at all or proceeds very slowly and the yield is small. The formation of pyrimidine derivative **9a** smoothly occurs under long-term refluxing (18 h) of amidine **8a** in glacial acetic acid (see Scheme 8).

Amidines **8a**—**e** are interesting and promising syntons for the synthesis of polyheterocyclic systems. The presence of various functional groups in compounds **8a**—**e**, such as the amidine fragment, an ester group, and the aniline group, assumes various directions of heterocyclization.

We developed a new procedure for the synthesis of pyridothienopyrimidines (3*H*-1-thia-3,5,8-triazaacenaphthylenes) **15a**,**b** from amidines **8a**,**b** (Scheme 9).

Compounds **15a,b** were isolated in good yields upon prolonged refluxing of amidines **8a,b** in acetic anhydride. Their structures were established based on data from ^{1}H and ^{13}C NMR and IR spectroscopy, mass spectrometry, and elemental analysis. A characteristic feature of the ^{1}H NMR spectra of these compounds is the presence of singlets at δ 14.5. Therefore, one can suppose that an intramolecular hydrogen bond exists in the structures **15a**,**b**. It is stabilized by strong interaction of the proton at the nitrogen atom N(3) with the acetyl group, which results in formation of a six-membered ring (see Scheme 9). The ^{13}C NMR spectrum of compound **15b** without ^{1}H-^{13}C spin-spin decoupling shows a signal at δ 196.8 as a quartet due to the interaction with the protons of the adjacent methyl group. The chemical shift and coupling constant of this signal suggest that compound **15b** exists in the keto form. An analogous set of signals is observed in the ^{13}C NMR spectrum of compound **15a**.

Scheme 9



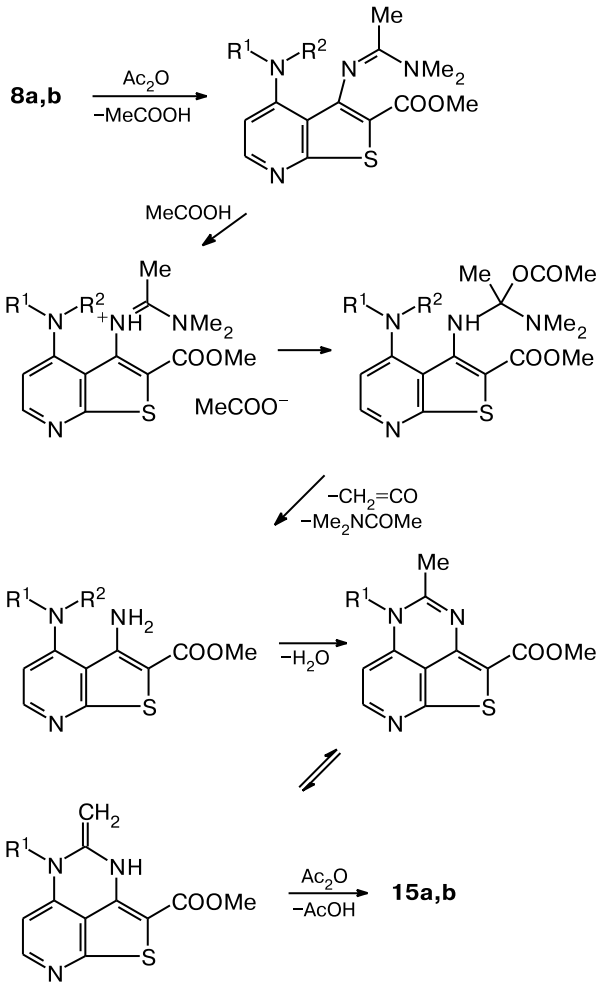
i. Ac_2O, reflux.
R^1 = Cl (**a**), F (**b**)

It should be noted that the mechanism of formation of compounds **15a,b** is quite not that simple and it is hardly possible to designate the intermediates of this process without additional experiments. Heating in acetic anhydride lasts for a long time (34 h), *i.e.*, the reactions rate under these rather drastic conditions is low. This fact, in particular, can imply the presence of many intermediates, which rather slowly transform into the final products. However, the yields of tricycles obtained are quite satisfactory (61% for **15a** and 76% for **15b**).

We suggest here one of the variants of the mechanism according to which these cyclizations can proceed (Scheme 10).

Powder X-ray diffraction analysis (see Ref. 16) of compounds **15a,b** was carried out to prove their structures. All geometrical characteristics of the molecules in the crystal structures of **15a** and **15b** (Fig. 1) have values similar to those found in the Cambridge Crystallographic Database (CCDC).[17] In both molecules, the benzene ring C(13)—C(18) is almost perpendicular to the plane of the tricycle, being turned relative the latter by 87.3(5)° and 88.1(4)° in **15a** and **15b**, respectively. The crystal packings in both compounds are very similar and characterized first of all by the presence of centrosymmetrical dimers where

Scheme 10



R^1 = 4-ClC_6H_4, 4-FC_6H_4; R^2 = COMe

the aromatic rings C(2)N(3)C(4)C(5)C(6)C(12) of two molecules, which form the dimer, are related by π—π interaction with short distances between their centers,

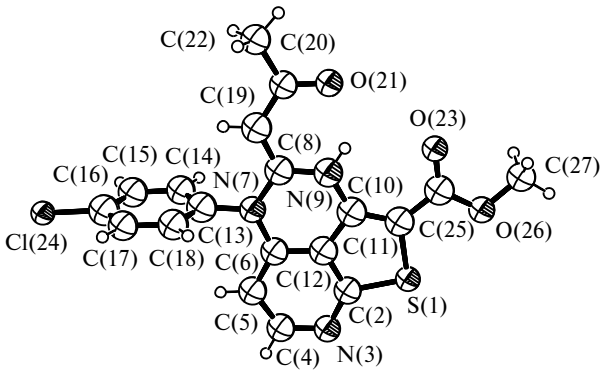


Fig. 1. Molecular structure and atomic numbering of compound **15a**. Spheres of atom displacements are presented with 50% probability for nonhydrogen atoms.

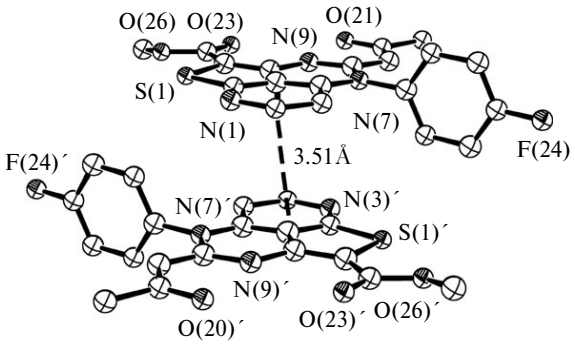


Fig. 2. Centrosymmetrical dimer in the crystal structure of **15b**, π—π interaction is indicated by dashed lines. Code of symmetry: (i) $1-x$, $1-y$, $1-z$.

3.599(12) Å in **15a** and 3.506(9) Å in **15b**. The dimer in the molecular packing of **15b** is shown in Fig. 2. The amine proton is involved in the intramolecular hydrogen bonding N—H...O, so weak intermolecular interactions C—H...O, C—H...Cl (in **15a**) and C—H...F (in **15b**) play the dominant role in the formation of three-dimensional packings (Table 1).

Experimental

The IR-spectra were recorded on an FSM-1201 instrument in Nujol mulls and on a Specord-M82 instrument in KBr pellets. Mass spectra (EI, 70 eV, temperature of the ionization chamber is 250 °C) were obtained on a Kratos MS-30 mass spectrometer using a direct inlet system and on a Waters ZQ-2000 mass spectrometer using the electrospray ionization technique with

Table 1. Characteristics of hydrogen bonds in compounds **15a** and **15b**

Compound	D—H...A	D—H	H...A	D...A	D—H...A /deg
		Å			
15a	N(9)—H(9)...O(21)	0.86	1.90	2.576(18)	134
	N(9)—H(9)...O(23)	0.86	2.52	3.050(19)	121
	C(17)—H(17)...O(23)^{i}	0.93	2.54	3.09(2)	119
	C(18)—H(18)...O(21)^{i}	0.93	2.59	3.490(18)	163
	C(15)—H(15)...O(26)^{ii}	0.93	2.57	3.466(19)	163
	C(4)—H(4)...O(23)^{iii}	0.93	2.34	3.17(2)	148
	C(19)—H(19)...C(l24)^{iv}	0.93	2.72	3.569(16)	152
15b	N(9)—H(9)...O(21)	0.86	1.89	2.569(14)	135
	N(9)—H(9)...O(23)	0.86	2.53	3.051(16)	120
	C(15)—H(15)...O(26)^{ii}	0.93	2.60	3.450(15)	153
	C(4)—H(4)...O(23)^{iii}	0.93	2.45	3.256(16)	146
	C(18)—H(18)...O(21)^{v}	0.93	2.51	3.404(13)	160
	C(19)—H(19)...F(24)^{vi}	0.93	2.41	3.288(13)	157
	C(27)—H(27)B...F(24)^{vii}	0.96	2.47	3.367(14)	156

Code of symmetry: (i) $1-x$, $1-y$, $1-z$; (ii) x, $1+y$, z; (iii) $1+x$, y, z; (iv) $1-x$, $2-y$, $1-z$; (v) $-x$, $1-y$, $-z$; (vi) $-x$, $2-y$, $-z$; (vii) x, $y-1$, $1+z$.

the inlet omitting a chromatographic column. The ^{1}H NMR spectra were recorded on Bruker AC-300, Bruker AM-300, and Varian Unity+400 spectrometers in DMSO-d_6, $CDCl_3$, DMSO-d_6—CD_3OD (10 : 1). The ^{13}C NMR spectra were recorded on a Varian Unity+400 (operating frequency 100 MHz) in $CDCl_3$—F_3CCOOH without ^{1}H-^{13}C spin-spin decoupling. The course of the reactions was monitored and the purity of the compounds was checked by TLC on Merck Silica gel 60 F_{254} plates (chloroform, ethyl acetate, ethyl acetate—ethanol (10 : 1 and 1 : 1)). The melting points were determined on an Electrotermal 9100 instrument (UK). Elemental analysis was performed at the Laboratory for Microanalysis of the N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences.

The following reagents (Lancaster) were used: *N,N*-dimethylacetamide dimethylacetal (**7a**) (purity 90%), *N,N*-dimethylformamide dimethylacetal (**7b**) (purity 95%), *m*-fluoroaniline (purity 98%), 3,4-difluoroaniline (purity 99%). 2-Chloro-4-phenylpyridine-3-carbonitrile (**5e**) was prepared according to a known procedure.[13]

4-(3-Fluoroanilino)-2-oxo-1,2-dihydropyridine-3-carbonitrile (1c). A mixture of enaminoamide **3c** (6.00 g, 27.4 mmol) and acetal **7b** (38.6 mL, 0.274 mmol) in anh. ethanol (150 mL) was refluxed for 5 h. The reaction mixture was cooled to 20 °C and kept for 3 days. The yellow precipitate that formed was filtered off, washed with ethanol, and dried. Pyrimidinone **4c** obtained in a yield of 5.59 g was refluxed for 1 h without purification in 4% aqueous NaOH (75 mL). The reaction mixture was cooled to 20 °C, diluted with 3 volumes of water, insoluble products were filtered off through a paper filter. Clear solution obtained was neutralized with concentrated HCl. The white precipitate that formed was filtered off, washed with water to pH 7, and dried. Compound **1c** was obtained in a yield of 3.26 g (52%). The mother liquor obtained after separation of pyrimidinone **4c** was concentrated *in vacuo* almost to dryness, 4% aqueous NaOH (75 mL) was added to red oily residue obtained and the mixture was processed as described above. Compound **1c** was aditionally obtained in a yield of 2.70 g (43%). The total yield was 95%, m.p. 272—274 °C (Pr^iOH). IR (KBr), ν/cm^{-1}: 3236 (NH); 2224 (CN); 1652 (CONH). ^{1}H NMR (DMSO-d_6), δ: 5.90 (d, 1 H, H(5), J_o = 7.55 Hz); 7.02—7.16 (m, 3 H, Ar); 7.39 (d, 1 H, H(6), J_o = 7.55 Hz); 7.41—7.47 (m, 1 H, Ar); 9.44 (br.s, 1 H, NHC(4)); 11.43 (br.s, 1 H, N(1)H). Found (%): C, 62.78; H, 3.62; N, 18.47. $C_{12}H_8FN_3O$. Calculated (%): C, 62.88; H, 3.52; N, 18.33.

4-(3,4-Difluoroanilino)-2-oxo-1,2-dihydropyridine-3-carbonitrile (1d). A mixture of enaminoamide **3d** (7.50 g, 31.6 mmol) and acetal **7b** (44.6 mL, 0.310 mol) in anh. ethanol (150 mL) was refluxed for 13 h. The reaction mixture was cooled to 20 °C, the solvent and excess of acetal were evaporated *in vacuo*, 4% aqueous NaOH (150 mL) was added to red oily residue and then the reaction mixture was processed as described for the preparation of carbonitrile **1c**. Compound **1d** was obtained in a yield of 5.43 g (70%), m.p. 293 °C (Pr^iOH). ^{1}H NMR (DMSO-d_6), δ: 5.82 (d, 1 H, H(5), J_o = 7.60 Hz); 7.10—7.14 (m, 1 H, Ar); 7.38 (d, 1 H, H(6), J_o = 7.60 Hz); 7.40—7.51 (m, 2 H, Ar); 9.40 (br.s, 1 H, NHC(4)); 11.42 (br.s, 1 H, N(1)H). Found (%): C, 58.58; H, 2.98; N, 16.90. $C_{12}H_7F_2N_3O$. Calculated (%): C, 58.30; H, 2.85; N, 17.00.

2-Cyano-3-(3-fluoroanilino)crotonamide (3c). A mixture of 2-cyano-3-dimethylaminocrotonamide **2** (10.00 g, 65.4 mmol) and *m*-fluoroaniline (8.89 g, 80 mmol) in glacial acetic acid (120 mL) was refluxed for 6 h. The reaction mixture was kept at 20 °C for 16 h and concentrated *in vacuo* almost to dryness. Ethyl acetate (10 mL) was added to semicrystalline residue obtained, then it was triturated, the white precipitate that formed was filtered off and washed with ethyl acetate. The crude product was obtained in a yield of 7.00 g (49%), recrystallization from anh. ethanol afforded pure compound **3c** in a yield of 6.39 g (45%), m.p. 184—185 °C (EtOH). IR (KBr), ν/cm^{-1}: 3392, 3264 (NH, NH_2); 2196 (CN); 1644 ($CONH_2$). ^{1}H NMR (DMSO-d_6), δ: 2.24 (s, 3 H, CH_3); 6.90—7.36 (m, 5 H, Ar, $CONH_2$); 7.40—7.50 (m, 1 H, Ar); 12.76 (br.s, 1 H, NH). Found (%): C, 60.14; H, 4.68; N, 19.13. $C_{11}H_{10}FN_3O$. Calculated (%): C, 60.27; H, 4.60; N, 19.17.

2-Cyano-3-(3,4-difluoroanilino)crotonamide (3d) was prepared analogously to **3c** from compound **2** and 3,4-difluoroaniline, the reaction time was 11 h. The yield was 49%, m.p. 215—217 °C (toluene). ^{1}H NMR (DMSO-d_6), δ: 2.19 (s, 3 H, CH_3); 6.86—7.39 (m, 3 H, Ar, $CONH_2$); 7.38—7.66 (m, 2 H, Ar); 12.63 (br.s, 1 H, NH). Found (%): N, 17.68. $C_{11}H_9F_2N_3O$. Calculated (%): N, 17.71.

6-[2-(Dimethylamino)vinyl]-1-(3-fluorophenyl)-4-oxo-1,4-dihydropyrimidine-5-carbonitrile (4c). A mixture of enaminoamide **3c** (0.20 g, 0.913 mmol) and acetal **7b** (1.29 mL, 9.13 mmol) in anh. ethanol (3 mL) was refluxed for 5.5 h. The reaction mixture was kept at 20 °C for 48 h, the yellow precipitate that formed was filtered off, washed with anh. ethanol, and dried. Compound **4c** was obtained in a yield of 0.17 g (66%), m.p. 242 °C (Pr^iOH). IR (KBr), ν/cm^{-1}: 2204 (CN); 1624 (CO). ^{1}H NMR (DMSO-d_6), δ: 2.64, 3.14 (both br.s, 3 H each, NMe_2); 4.06 (d, 1 H, H(α), J_{trans} = 13.00 Hz); 7.32—7.39 (m, 2 H, Ar); 7.43—7.46 (m, 1 H, Ar); 7.60—7.65 (m, 1 H, Ar); 7.95 (d, 1 H, H(β), J_{trans} = 13.00 Hz); 8.07 (s, 1 H, H(2)). Found (%): C, 63.42; H, 4.82; N, 19.93. $C_{15}H_{13}FN_4O$. Calculated (%): C, 63.37; H, 4.61; N, 19.71.

1-(3,4-Difluorophenyl)-6-[2-(dimethylamino)vinyl]-4-oxo-1,4-dihydropyrimidine-5-carbonitrile (4d) was prepared analogously from compound **3d**, the reaction time was 8 h. The yield was 43%, m.p. 243 °C (Pr^iOH). ^{1}H NMR (DMSO-d_6), δ: 2.61, 3.09 (both br.s, 3 H each, NMe_2); 4.03 (d, 1 H, H(α), J_{trans} = = 12.60 Hz); 7.44—7.45 (m, 1 H, Ar); 7.66—7.73 (m, 1 H, Ar); 7.83—7.88 (m, 1 H, Ar); 7.94 (d, 1 H, H(β), J_{trans} = 12.60 Hz); 8.20 (s, 1 H, H(2)). Found (%): C, 59.83; H, 4.29; N, 18.53. $C_{15}H_{12}F_2N_4O$. Calculated (%): C, 59.60; H, 4.00; N, 18.53.

2-Chloro-4-(4-chloroanilino)pyridine-3-carbonitrile (5a). A mixture of compound **1a** (5.15 g, 20.98 mmol), triethylamine hydrochloride (3.09 g, 22.31 mmol), and phosphoryl chloride (100 mL) was refluxed for 7 h. The reaction mixture was cooled to 20 °C, concentrated *in vacuo* to dryness, dry residue was triturated with toluene, and concentrated *in vacuo* to dryness again. An excess of ice was added to the residue obtained, and a white precipitate formed. The suspension obtained was refluxed for 1 h and cooled. The white precipitate was filtered off and washed with water to pH 7. The crude product **5a** was obtained in a yield of 5.40 g, which was recrystallized from dry toluene (50 mL). The yield was 4.77 g (86%), m.p. 215 °C (EtOH), 213—214 °C (toluene) (*cf.* Ref. 13: m.p. 221—222 °C (EtOH)). IR (Nujol mulls), ν/cm^{-1}: 3289 (NH); 2224 (CN). MS (ES), *m/z*: 266 $[M + H]^{+\cdot}$, 228 $[M - Cl]^{+\cdot}$, 531 $[2\ M + H]^{+\cdot}$. ^{1}H NMR (DMSO-d_6), δ: 6.85 (d, 1 H, H(5), J_o = 6.30 Hz); 7.30, 7.43 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 8.05 (d, 1 H, H(6), J_o = 6.30 Hz); 9.50 (s, 1 H, NH).

2-Chloro-4-(4-fluoroanilino)pyridine-3-carbonitrile (5b) was prepared analogously from compound **1b**, the reaction time was

5.5 h. The yield was 80%, m.p. 181.6—182.2 °C (toluene). IR (Nujol mulls), ν/cm^{-1}: 3312 (NH); 2224 (CN). MS (ES), *m/z*: 248 $[M + H]^{+\cdot}$, 212 $[M + H - Cl]^{+\cdot}$. ^{1}H NMR (DMSO-d_6), δ: 6.71 (d, 1 H, H(5), J_o = 6.11 Hz); 7.18, 7.28 (both m, 4 H, Ar); 7.99 (d, 1 H, H(6), J_o = 6.11 Hz); 9.38 (s, 1 H, NH). Found (%): C, 58.27; H, 2.90; N, 16.99. $C_{12}H_7ClFN_3$. Calculated (%): C, 58.20; H, 2.85; N, 16.97.

2-Chloro-4-(3-fluoroanilino)pyridine-3-carbonitrile (5c) was prepared analogously to **5a** from compound **1c**, the reaction time was 7.5 h. The yield was 77%, m.p. 165 °C (hexane). IR (KBr), ν/cm^{-1}: 3296 (NH); 2228 (CN). ^{1}H NMR (DMSO-d_6), δ: 6.97 (d, 1 H, H(5), J_o = 6.10 Hz); 7.03—7.12 (m, 1 H, Ar); 7.18 (m, 2 H, Ar); 7.35—7.53 (m, 1 H, Ar); 8.12 (d, 1 H, H(6), J_o = 6.10 Hz); 9.63 (s, 1 H, NH). Found (%): C, 58.03; H, 3.04; N, 16.78. $C_{12}H_7ClFN_3$. Calculated (%): C, 58.20; H, 2.85; N, 16.97.

2-Chloro-4-(3,4-difluoroanilino)pyridine-3-carbonitrile (5d) was prepared analogously to **5a** from compound **1d**, the reaction time was 6 h. The yield was 58%, m.p. 197 °C (toluene). ^{1}H NMR (DMSO-d_6), δ: 6.88 (d, 1 H, H(5), J_o = 6.20 Hz); 7.15—7.20 (m, 1 H, Ar); 7.43—7.54 (m, 2 H, Ar); 8.10 (d, 1 H, H(6), J_o = = 6.20 Hz); 9.59 (s, 1 H, NH). Found (%): C, 54.46; H, 2.31; N, 15.89. $C_{12}H_6ClF_2N_3$. Calculated (%): C, 54.26; H, 2.28; N, 15.82.

Methyl 3-amino-4-(4-chloroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (6a). Methyl thioglycolate (2.34 mL, 25.62 mmol) was added to a solution of sodium methoxide (1.06 g, 19.6 mmol, prepared from sodium (0.45 g)). The solution obtained was stirred at 20 °C for 30 min, and compound **5a** (4.51 g, 17.08 mmol) was added. The reaction mixture was refluxed for 6 h and kept at 10 °C for 12 h. The yellow precipitate was filtered off, washed with methanol, and dried. Analytically pure compound **6a** was obtained in a yield of 4.52 g (79%), m.p. 223—225 °C (DMF). IR (Nujol mulls), ν/cm^{-1}: 3329, 3367 (NH_2, NH); 1668 ($COOCH_3$). MS (ES), *m/z*: 334 $[M + H]^{+\cdot}$, 667 $[2M + H]^{+\cdot}$, 1000 $[3M + H]^{+\cdot}$, 302 $[M - OCH_3]^{+\cdot}$, 274 $[M - COOCH_3]^{+\cdot}$, 241 $[M - H - COOCH_3 - S]^{+\cdot}$. ^{1}H NMR (DMSO-$d_6$), δ: 3.78 (s, 3 H, $COOCH_3$); 6.83 (d, 1 H, H(5), J_o = 5.30 Hz); 7.03 (br.s, 2 H, NH_2); 7.27, 7.42 (A_2B_2, 4 H, Ar, J_o = 8.60 Hz); 8.22 (d, 1 H, H(6), J_o = 5.30 Hz); 8.58 (br.s, 1 H, NH). Found (%): C, 53.72; H, 3.88; N, 12.61; S, 9.47. $C_{15}H_{12}ClN_3O_2S$. Calculated (%): C, 53.97; H, 3.62; N, 12.59; S, 9.61.

Methyl 3-amino-4-(4-fluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (6b) was prepared analogously from compound **5b**, the reaction time was 5 h. The yield was 92%, m.p. 257 °C (DMF). IR (Nujol mulls), ν/cm^{-1}: 3374 (NH, NH_2); 1668 ($COOCH_3$). MS (ES), *m/z*: 318 $[M + H]^{+\cdot}$, 286 $[M + H - S]^{+\cdot}$, 258 $[M - COOCH_3]^{+\cdot}$, 635 $[2M + H]^{+\cdot}$. ^{1}H NMR (DMSO-d_6), δ: 3.80 (s, 3 H, $COOCH_3$); 6.65 (d, 1 H, H(5), J_o = 5.60 Hz); 7.03 (br.s, 2 H, NH_2); 7.21—7.34 (m, 4 H, Ar); 8.18 (d, 1 H, H(6), J_o = 5.56 Hz); 8.41 (br.s, 1 H, NH). Found (%): C, 56.68; H, 3.95; N, 13.24; S, 10.55. $C_{15}H_{12}FN_3O_2S$. Calculated (%): C, 56.77; H, 3.81; N, 13.24; S, 10.10.

Methyl 3-amino-4-(3-fluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (6c) was prepared analogously from compound **5c**, the reaction time was 7 h. The yield was 94%, m.p. 256 °C (toluene). IR (KBr), ν/cm^{-1}: 3176, 3344 (NH, NH_2); 1680 ($COOCH_3$). ^{1}H NMR (DMSO-d_6), δ: 3.80 (s, 3 H, $COOCH_3$); 6.91 (t, 1 H, Ar, J_o = 8.30 Hz); 6.98 (d, 1 H, H(5), J_o = 5.50 Hz); 7.04 (br.s, 2 H, NH_2); 7.09 (m, 2 H, Ar); 7.47—7.31 (m, 1 H, Ar); 8.29 (d, 1 H, H(6), J_o = 5.50 Hz); 8.71 (br.s, 1 H, NH). Found (%): C, 56.83; H, 3.85; N, 13.26. $C_{15}H_{12}FN_3O_2S$. Calculated (%): C, 56.77; H, 3.81; N, 13.24.

Methyl 3-amino-4-(3,4-difluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (6d) was prepared analogously from compound **5d**, the reaction time was 9 h. The yield was 86%, m.p. 271 °C (toluene). ^{1}H NMR (DMSO-d_6), δ: 3.79 (s, 3 H, $COOCH_3$); 6.85 (d, 1 H, H(5), J_o = 4.70 Hz); 6.95—7.19 (m, 3 H, Ar, NH_2); 7.27—7.40 (m, 1 H, Ar); 7.45 (m, 1 H, Ar); 8.25 (d, 1 H, H(6), J_o = 4.70 Hz); 8.63 (br.s, 1 H, NH). Found (%): C, 53.70; H, 3.44; N, 12.65. $C_{15}H_{11}F_2N_3O_2S$. Calculated (%): C, 53.73; H, 3.31; N, 12.53.

Methyl 3-amino-4-anilinothieno[2,3-*b*]pyridine-2-carboxylate (6e) was prepared analogously from compound **5e**, the reaction time was 12.5 h. The yield was 77%, m.p. 232—233 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 3.79 (s, 3 H, $COOCH_3$); 6.81 (d, 1 H, H(5), J_o = 5.60 Hz); 6.99—7.22 (m, 3 H, Ar, NH_2); 7.23—7.54 (m, 4 H, Ar); 8.22 (d, 1 H, H(6), J_o = 5.60 Hz); 8.53 (br.s, 1 H, NH). Found (%): C, 60.17; H, 4.65; N, 14.04. $C_{15}H_{13}N_3O_2S$. Calculated (%): C, 60.19; H, 4.38; N, 14.04.

Methyl 3-[1-(dimethylamino)ethylidene]amino-4-(4-chloroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8a). ***A.*** Acetal **7a** (9.73 mL, 59.9 mmol) was added to a suspension of compound **6a** (2.50 g, 7.49 mmol) in anh. toluene (6 mL). The yellow solution obtained was stirred at 78—80 °C for 6 h. The reaction mixture was cooled to 20 °C, the solvent and excess of acetal was evaporated *in vacuo*, the crystalline residue obtained was triturated with methanol, the yellow precipitate that formed was filtered off, washed with methanol, and dried. Analytically pure compound **8a** was obtained in a yield of 2.81 g (93%), m.p. 179—180 °C (MeOH). IR (KBr), ν/cm^{-1}: 3450, 3228 (NH); 1696 ($COOCH_3$). MS (EI), *m/z*, (I_{rel} (%)): 402 $[M]^{+\cdot}$ (91), 357 $[M - NHMe_2]^{+\cdot}$ (100), 326 $[M - NHMe_2 - OCH_3]^{+\cdot}$ (17). ^{1}H NMR (DMSO-d_6), δ: 1.98 (s, 3 H, $NCC\underline{H}_3N(CH_3)_2$); 3.12 (s, 6 H, $N(CH_3)_2$); 3.71 (s, 3 H, $COOCH_3$); 6.89 (d, 1 H, H(5), J_o = 5.70 Hz); 7.32, 7.44 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 8.19 (d, 1 H, H(6), J_o = 5.70 Hz); 9.99 (br.s, 1 H, NH). Found (%): C, 56.57; H, 4.81; N, 13.87. $C_{19}H_{19}ClN_4O_2S$. Calculated (%): C, 56.64; H, 4.75; N, 13.91.

B. Acetal **7a** (0.273 mL, 1.677 mol) was added to a suspension of compound **6a** (0.070 g, 0.210 mmol) in dry toluene (3 mL). The mixture was refluxed for 11 h and cooled to 20 °C. The solvent and excess of acetal was evaporated *in vacuo*, semicrystalline brown residue was triturated with methanol, the yellow precipitate that formed was filtered off and washed with methanol. Compound **8a** was obtained in a yield of 0.020 g (24%), its physicochemical properties were identical to those of the sample prepared by method ***A***.

Methyl 3-[1-(dimethylamino)ethylidene]amino-4-(4-fluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8b) was prepared analogously to **8a** (method ***A***), the reaction time was 5.5 h. The yield was 93%, m.p. 179—180 °C (MeOH). MS (EI), *m/z*, (I_{rel} (%)): 386 $[M]^{+\cdot}$ (35), 341 $[M - NHMe_2]^{+\cdot}$ (100), 310 $[M - NHMe_2 - OCH_3]^{+\cdot}$ (72), 283 $[M - NHMe_2 - OCH_3 - HCN]^{+\cdot}$ (49). ^{1}H NMR (DMSO-d_6), δ: 1.98 (s, 3 H, $NCC\underline{H}_3N(CH_3)_2$); 3.11 (s, 6 H, $N(CH_3)_2$); 3.70 (s, 3 H, $COOCH_3$); 6.76 (d, 1 H, H(5), J_o = 5.70 Hz); 7.05—7.44 (m, 4 H, Ar); 8.14 (d, 1 H, H(6), J_o = 5.70 Hz); 9.84 (br.s, 1 H, NH). Found (%): C, 58.92; H, 5.11; N, 14.58. $C_{19}H_{19}FN_4O_2S$. Calculated (%): C, 59.05; H, 4.96; N, 14.50.

Methyl 3-[1-(dimethylamino)ethylidene]amino-4-(3-fluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8c) was prepared

analogously to **8a** (method *A*), the reaction time was 6 h. The yield was 74%, m.p. 181 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 2.00 (s, 3 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.16 (s, 6 H, N$(CH_3)_2$); 3.73 (s, 3 H, COOCH_3); 6.97—7.02 (m, 2 H, Ar, H(5)); 7.14—7.23 (m, 2 H, Ar); 7.42—7.46 (m, 1 H, Ar); 8.24 (d, 1 H, H(6), J_o = 6.00 Hz); 10.03 (br.s, 1 H, NH). Found (%): C, 59.16; H, 5.02; N, 14.51. $C_{19}H_{19}FN_4O_2S$. Calculated (%): C, 59.05; H, 4.96; N, 14.50.

Methyl 3-[1-(dimethylamino)ethylidene]amino-4-(3,4-difluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8d) was prepared analogously to **8a** (method *A*), the reaction time was 4 h. The yield was 83%, m.p. 157 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 1.99 (s, 3 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.14 (s, 6 H, N$(CH_3)_2$); 3.73 (s, 3 H, COOCH_3); 6.90 (d, 1 H, H(5), J_o = 5.70 Hz); 7.07—7.26 (m, 1 H, Ar); 7.35—7.61 (m, 2 H, Ar); 8.21 (d, 1 H, H(6), J_o = = 5.70 Hz); 9.96 (br.s, 1 H, NH). Found (%): C, 56.32; H, 4.67; N, 13.74. $C_{19}H_{18}F_2N_4O_2S$. Calculated (%): C, 56.43; H, 4.49; N, 13.85.

Methyl 3-[1-(dimethylamino)ethylidene]amino-4-anilinothieno[2,3-*b*]pyridine-2-carboxylate (8e) was prepared analogously to **8a** (method *A*), the reaction time was 4 h. The yield was 85%, m.p. 158 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 2.00 (s, 3 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.15 (s, 6 H, N$(CH_3)_2$); 3.73 (s, 3 H, COOCH_3); 6.93 (d, 1 H, H(5), J_o = 5.70 Hz); 7.08—7.26 (m, 1 H, Ar); 7.32 (d, 2 H, Ar, J_o = 7.80 Hz); 7.43 (t, 2 H, Ar, J_o = 7.80 Hz); 8.19 (d, 1 H, H(6), J_o = 5.70 Hz); 9.98 (br.s, 1 H, NH). Found (%): C, 61.92; H, 5.49; N, 15.01. $C_{19}H_{20}N_4O_2S$. Calculated (%): C, 61.94; H, 5.47; N, 15.21.

A mixture of methyl and ethyl 3-[1-(dimethylamino)ethylidene]amino-4-(4-chloroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8a and 8´a). Acetal **7a** (1.56 mL, 9.587 mmol) was added to a suspension of compound **6a** (0.40 g, 1.2 mmol) in anh. ethanol (2 mL), the mixture was refluxed for 4 h, and cooled to 20 °C. The solvent and excess of acetal were evaporated *in vacuo*, the yellow precipitate was obtained, which represents a mixture of compounds **8a** and **8´a** in 1 : 2 ratio based on the ^{1}H NMR and mass spectra, m.p. 165 °C. ^{1}H NMR spectrum of compound **8´a** (DMSO-d_6), δ: 1.22 (t, 3 H, COOCH_2C$\underline{H}_3$, J = 7.10 Hz); 1.98 (s, 6 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.12 (s, 3 H, N$(CH_3)_2$); 4.16 (q, 2 H, COOC$\underline{H}_2$CH_3, J = 7.10 Hz); 6.89 (d, 1 H, H(5), J_o = 5.70 Hz); 7.32, 7.44 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 8.19 (d, 1 H, H(6), J_o = 5.70 Hz); 9.95 (br.s, 1 H, NH). MS (EI), m/z, (I_{rel} (%)): 371 $[M_{\mathbf{8´a}} - NHMe_2]^{+\cdot}$ (65).

A mixture of methyl and ethyl 3-[1-(dimethylamino)ethylidene]amino-4-(3-fluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8c and 8´c) was prepared analogously in a ratio 1 : 2. ^{1}H NMR spectrum of compound **8´c** (DMSO-d_6), δ: 1.23 (t, 3 H, COOCH_2C$\underline{H}_3$, J = 7.10 Hz); 1.98 (s, 3 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.14 (s, 6 H, N$(CH_3)_2$); 4.17 (q, 2 H, COOC$\underline{H}_2$CH_3, J = 7.10 Hz); 6.97—7.02 (m, 2 H, Ar, H(5)); 7.14—7.23 (m, 2 H, Ar); 7.42—7.46 (m, 1 H, Ar); 8.24 (d, 1 H, H(6), J_o = 6.00 Hz); 10.00 (br.s, 1 H, NH).

A mixture of methyl and ethyl 3-[1-(dimethylamino)ethylidene]amino-4-(3,4-difluoroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (8d and 8´d) was prepared analogously in a ratio 1 : 2. ^{1}H NMR spectrum of compound **8´d** (DMSO-d_6), δ: 1.24 (t, 3 H, COOCH_2C$\underline{H}_3$, J = 7.10 Hz); 1.99 (s, 3 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.14 (s, 6 H, N$(CH_3)_2$); 4.18 (q, 2 H, COOC$\underline{H}_2$CH_3, J = 7.10 Hz); 6.90 (d, 1 H, H(5), J_o = 5.85 Hz); 7.07—7.26 (m, 1 H, Ar); 7.35—7.61 (m, 2 H, Ar); 8.24 (d, 1 H, H(6), J_o = 5.85 Hz); 9.92 (br.s, 1 H, NH).

A mixture of methyl and ethyl 3-[1-(dimethylamino)ethylidene]amino-4-anilinothieno[2,3-*b*]pyridine-2-carboxylate (8e and 8´e) was prepared analogously in a ratio 1.5 : 1. ^{1}H NMR spectrum of compound **8´e** (DMSO-d_6), δ: 1.22 (t, 3 H, COOCH_2C$\underline{H}_3$, J = 7.10 Hz); 2.00 (s, 3 H, NCC$\underline{H}_3$N$(CH_3)_2$); 3.15 (s, 6 H, N$(CH_3)_2$); 4.19 (q, 2 H, COOC$\underline{H}_2$CH_3, J = 7.10 Hz); 6.93 (d, 1 H, H(5), J_o = 5.70 Hz); 7.08—7.26 (m, 1 H, Ar); 7.32 (d, 2 H, Ar, J_o = 7.80 Hz); 7.43 (t, 2 H, Ar, J_o = 7.80 Hz); 8.19 (d, 1 H, H(6), J_o = 5.70 Hz); 9.95 (br.s, 1 H, NH).

Methyl 5-(4-chlorophenyl)-4-methyl-5*H*-1-thia-3,5,8-triazaacenaphthene-2-carboxylate (9a). ***A.*** Diphenyl oxide (2.00 g) was heated up to 200 °C, compound **8a** (0.10 g) and *p*-toluenesulfonic acid (catalytic amount) were added to the liquid obtained. The reaction mixture was stirred at 215 °C for 8 h, then cooled to 30 °C, and poured into cold hexane. The brown precipitate that formed was filtered off and washed with cold hexane. Crude compound **9a** was obtained in a yield of 0.03 g (35%), m.p. 264 °C. MS (EI), m/z, (I_{rel} (%)): 357 $[M]^{+\cdot}$ (100), 343 $[M - CH_3 + H]^{+\cdot}$ (16), 326 $[M - OCH_3]^{+\cdot}$ (17). ^{1}H NMR (DMSO-d_6), δ: 2.01 (s, 3 H, C(4)C$\underline{H}_3$); 3.78 (s, 3 H, COOCH_3); 5.83 (d, 1 H, H(6), J_o = 5.45 Hz); 7.63, 7.74 (A_2B_2, 4 H, Ar, J_o = 8.60 Hz); 8.26 (d, 1 H, H(7), J_o = 5.45 Hz).

B. Compound **8a** (0.05 g, 0.124 mmol) was dissolved in glacial acetic acid (2 mL), the yellow solution obtained was refluxed for 18 ч. The reaction mixture was concentrated *in vacuo*. The residue was triturated with ethyl acetate and concentrated. Compound **9a** was obtained in a yield of 0.04 g (90%), m.p. 267 °C (MeCN). Found (%): C, 56.85; H, 3.48; N, 11.75. $C_{17}H_{12}ClN_3O_2S$. Calculated (%): C, 57.07; H, 3.38; N, 11.74.

Methyl 5-(4-fluorophenyl)-4-methyl-5*H*-1-thia-3,5,8-triazaacenaphthene-2-carboxylate (9b). Acetal **7a** (2.33 mL, 0.014 mol) was added to a suspension of compound **6b** (0.57 g, 1.79 mmol) in anh. ethanol (2 mL). The mixture was refluxed under argon for 3 h and then kept at 10 °C for 24 h. The yellow precipitate that formed was filtered off, washed with anh. ethanol, and dried. Crude compound **9b** was obtained in a yield of 0.45 g (74%), recrystallization from MeCN afforded the analytically pure compound **9b** in a yield of 0.31 g (51%), m.p. 228—230 °C (MeCN). IR (Nujol mulls), ν/cm^{-1}: 1690 (COOCH_3). MS (ES), m/z: 342 $[M + H]^{+\cdot}$, 364 $[M + Na]^{+\cdot}$, 683 $[2M + H]^{+\cdot}$, 705 $[2M + Na]^{+\cdot}$, 310 $[M - OMe]^{+\cdot}$. ^{1}H NMR (DMSO-d_6), δ: 2.06 (s, 3 H, CH_3); 3.83 (s, 3 H, COOCH_3); 5.78 (d, 1 H, H(6), J_o = 5.40 Hz); 7.44 (t, 2 H, Ar, J = 5.60 Hz); 7.63 (m, 2 H, Ar); 8.22 (d, 1 H, H(7), J_o = 5.40 Hz). Found (%): C, 59.81; H, 3.63; N, 12.20. $C_{17}H_{12}FN_3O_2S$. Calculated (%): C, 59.82; H, 3.54; N, 12.31.

A mixture of methyl and ethyl 4-methyl-5-(4-fluorophenyl)-5*H*-1-thia-3,5,8-triazaacenaphthene-2-carboxylate (9b and 9´b). ***A.*** Acetal **7a** (0.41 mL, 2.52 mmol) was added to a suspension of compound **6b** (0.10 g, 0.32 mmol) in anh. ethanol (2 mL), the mixture was refluxed for 4 h. The reaction mixture was cooled to 10 °C and kept for 12 h. The yellow precipitate that formed was filtered off, washed with anh. ethanol, and dried. The precipitate represented a mixture of compounds **9b** and **9´b** in 1 : 4 ratio based on the ^{1}H NMR and mass spectra, yield 0.10 g, m.p. 225 °C. ^{1}H NMR spectrum of compound **9´b** (DMSO-d_6), δ: 1.28 (t, 3 H, COOCH_2C$\underline{H}_3$, J = 7.10 Hz); 2.06 (s, 3 H, CH_3); 4.23 (q, 2 H, COOC$\underline{H}_2$CH_3, J = 7.10 Hz); 5.80 (d, 1 H, H(6), J_o = 5.50 Hz); 7.51 (t, 2 H, J = 5.60 Hz, Ar); 7.66 (d.d, 2 H, Ar, J = 8.80 Hz, J = 5.00 Hz); 8.25 (d, 1 H, H(7), J_o = 5.50 Hz). MS (EI), m/z, (I_{rel} (%)): 283 $[M_{\mathbf{6a}} - COOCH_3, M_{\mathbf{6´a}} - COOEt]^{+\cdot}$

(100), 355 $[M_{6'a}]^{+\cdot}$ (65), 341 $[M_{6a}]^{+\cdot}$ (22), 310 [M_{6a} – OMe, $M_{6'a}$ – OEt]$^{+\cdot}$ (17).

B. A mixture of compounds **9b** and **9´b** was prepared analogously to a mixture of compounds **8a** and **8´a**. **9b** : **9´b** ratio was 1 : 4.

Methyl 5-(4-chlorophenyl)-5*H*-1-thia-3,5,8-triazaacenaphthene-2-carboxylate (11a). Acetal **7b** (0.64 mL, 4.80 mmol) was added to a suspension of compound **6a** (0.20 g, 0.60 mmol) in anh. toluene (5 mL). The mixture obtained was refluxed for 20 h. The reaction mixture was cooled to 20 °C, the yellow precipitate that formed was filtered off, washed with anh. toluene, and dried. Compound **11a** was obtained in a yield of 0.15 g (72%), m.p. 253 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 3.80 (s, 3 H, $COOCH_3$); 6.28 (d, 1 H, H(6), J_o = 5.50 Hz); 7.66, 7.71 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 7.96 (s, 1 H, H(4)); 8.33 (d, 1 H, H(7), J_o = 5.50 Hz). Found (%): C, 55.96; H, 2.94; N, 12.12. $C_{16}H_{10}ClN_3O_2S$. Calculated (%): C, 55.90; H, 2.93; N, 12.22.

Methyl 5-(4-fluorophenyl)-5*H*-1-thia-3,5,8-triazaacenaphthene-2-carboxylate (11b) was prepared analogously from compound **6b**, the reaction time was 19 h. The yield was 74%, m.p. 253 °C (MeOH). ^{1}H NMR (DMSO-d_6), δ: 3.81 (s, 3 H, $COOCH_3$); 6.25 (d, 1 H, H(6), J_o = 5.50 Hz); 7.52 (m, 2 H, Ar); 7.72 (m, 2 H, Ar); 7.99 (s, 1 H, H(4)); 8.35 (d, 1 H, H(7), J_o = 5.50 Hz). Found (%): C, 58.64; H, 3.23; N, 12.89. $C_{16}H_{10}FN_3O_2S$. Calculated (%): C, 58.71; H, 3.08; N, 12.84.

Reaction of compound 6a with acetal 7b. ***A.*** Acetal **7b** (0.34 mL, 2.40 mmol) was added to a suspension of compound **6a** (0.10 g, 0.30 mmol) in anh. ethanol (3 mL). The mixture was refluxed for 4 h. The solvent and excess of acetal were evaporated *in vacuo*, the yellow precipitate was obtained, which contains compounds **10a** and **11a**, and also small amount of compound **10´a** (^{1}H NMR), (**10a** + **10´a**) : **11a** ratio was 9 : 1. ^{1}H NMR spectrum of compound **10a** (DMSO-d_6), δ: 3.08, 3.12 (both s, 3 H each, $N(CH_3)_2$); 3.75 (s, 3 H, $COOCH_3$); 6.94 (d, 1 H, H(5), J_o = = 5.70 Hz); 7.38, 7.47 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 8.06 (s, 1 H, NC<u>H</u>NMe_2); 8.21 (d, 1 H, H(6), J_o = 5.70 Hz); 10.53 (br.s, 1 H, NH). ^{1}H NMR spectrum of compound **10´a** (DMSO-d_6), δ: 1.25 (t, 3 H, $COOCH_2C\underline{H}_3$, J = 7.10 Hz); 3.08, 3.12 (both s, 3 H each, $N(CH_3)_2$); 4.21 (q, 2 H, $COOC\underline{H}_2CH_3$, J = 7.10 Hz); 6.94 (d, 1 H, H(5), J_o = 5.70 Hz); 7.38, 7.47 (A_2B_2, 4 H, Ar, J_o = = 8.70 Hz); 8.03 (s, 1 H, H(4)); 8.21 (d, 1 H, H(6), J_o = 5.70 Hz); 10.50 (br.s, 1 H, NH).

B. Acetal **7b** (0.34 mL, 2.40 mmol) was added to a suspension of compound **6a** (0.10 g, 0.30 mmol) in anh. toluene (3 mL), the mixture was refluxed for 4 h. The solvent and excess of acetal were evaporated *in vacuo*, the yellow precipitate was obtained, which represents a mixture of compounds **10a** and **11a** in 5.3 : 1 ratio (^{1}H NMR).

Reaction of compound 6b with acetal 7b. ***A.*** Acetal **7b** (0.36 mL, 2.52 mmol) was added to a suspension of compound **6b** (0.10 g, 0.32 mmol) in anh. ethanol (3 mL), the mixture was refluxed for 4 h. The solvent and excess of acetal were evaporated *in vacuo*, the yellow precipitate was obtained, which contained compounds **10b** and **11b**, and also small amount of compounds **10´b** and **11´b** (^{1}H NMR), (**10b** + **10´b**) : (**11b** + **11´b**) ratio was 4 : 1. ^{1}H NMR spectrum of compound **10b** (DMSO-d_6), δ: 3.07, 3.12 (both s, 3 H each, $N(CH_3)_2$); 3.75 (s, 3 H, $COOCH_3$); 6.80 (d, 1 H, H(5), J_o = 5.70 Hz); 7.30—7.19 (m, 2 H, Ar); 7.34—7.44 (m, 2 H, Ar); 8.06 (s, 1 H, NC<u>H</u>NMe_2); 8.17 (d, 1 H, H(6), J_o = 5.70 Hz); 10.37 (br.s, 1 H, NH). ^{1}H NMR spectrum of compound **10´b** (DMSO-d_6), δ: 1.26 (t, 3 H, $COOCH_2C\underline{H}_3$, J = 7.10 Hz); 3.07, 3.12 (both s, 3 H each, $N(CH_3)_2$); 4.21 (q, 2 H, $COOC\underline{H}_2CH_3$, J = 7.10 Hz); 6.80 (d, 1 H, H(5), J_o = = 5.70 Hz); 7.30—7.19 (m, 2 H, Ar); 7.34—7.44 (m, 2 H, Ar); 8.03 (s, 1 H, NC<u>H</u>NMe_2); 8.17 (d, 1 H, H(6), J_o = 5.70 Hz); 10.37 (br.s, 1 H, NH). ^{1}H NMR spectrum of compound **11´b** (DMSO-d_6), δ: 1.30 (t, 3 H, $COOCH_2C\underline{H}_3$, J = 7.10 Hz); 4.30 (q, 2 H, $COOC\underline{H}_2CH_3$, J = 7.10 Hz); 6.25 (d, 1 H, H(6), J_o = 5.50 Hz); 7.52 (t, 2 H, Ar, J = 8.70 Hz); 7.72 (d.d, 2 H, Ar, J = 8.90 Hz, J = 4.90 Hz); 7.99 (s, 1 H, H(4)); 8.35 (d, 1 H, H(7), J_o = 5.50 Hz).

B. Acetal **7b** (0.36 mL, 2.52 mmol) was added to a suspension of compound **6b** (0.10 g, 0.32 mmol) in anh. toluene (3 mL), the mixture was refluxed for 4 h. The solvent and excess of acetal were evaporated *in vacuo*, the yellow precipitate was obtained, which represents a mixture of compounds **10b** and **11b** in 8 : 1 ratio (^{1}H NMR).

Methyl 3-acetamido-4-(4-chloroanilino)thieno[2,3-*b*]pyridine-2-carboxylate (12). An aqueous solution of acetic acid (70%, 3 mL) was added to compound **8a** (0.10 g, 0.25 mmol), the yellow solution was refluxed for 14 h. The reaction mixture was cooled to 20 °C and concentrated *in vacuo* almost to dryness. The brown semicrystalline residue obtained was triturated with methanol, the white precipitate that formed was filtered off, washed with methanol, and dried. Compound **12** was obtained in a yield of 0.07 g (75%), m.p. 210 °C (MeCN). MS (EI), *m/z*, (I_{rel} (%)): 375 $[M]^{+\cdot}$ (41), 357 $[M - H_2O]^{+\cdot}$ (48), 344 $[M - OCH_3]^{+\cdot}$ (33), 333 $[M - CH_2CO]^{+\cdot}$ (48), 326 $[M - H_2O - OCH_3]^{+\cdot}$ (53), 301 $[M - COOCH_3 - CH_3]^{+\cdot}$ (80), 274 $[M - COOCH_3 - CO + H]^{+\cdot}$ (57), 265 $[M - H_2O - OCH_3 - Cl - CN]^{+\cdot}$ (96), 238 $[M - COOCH_3 - CO - Cl + H]^{+\cdot}$ (100), 229 $[M - H_2O - OCH_3 - Cl - CH_3 - NH - S]^{+\cdot}$ (68). ^{1}H NMR (DMSO-d_6), δ: 2.08 (s, 3 H, $COCH_3$); 3.82 (s, 3 H, $COOCH_3$); 6.89 (d, 1 H, H(5), J_o = 5.60 Hz); 7.29, 7.45 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 8.27 (d, 1 H, H(6), J_o = 5.60 Hz); 8.37 (br.s, 1 H, N<u>H</u>$COCH_3$); 9.90 (br.s, 1 H, NHC(4)). ^{1}H NMR (DMSO-d_6—CD_3OD), δ: 2.08 (s, 3 H, $COCH_3$); 3.83 (s, 3 H, $COOCH_3$); 6.89 (d, 1 H, H(5), J_o = 5.60 Hz); 7.28, 7.42 (A_2B_2, 4 H, Ar, J_o = 8.70 Hz); 8.25 (d, 1 H, H(6), J_o = 5.60 Hz). Found (%): C, 54.02; H, 3.67; N, 11.19. $C_{17}H_{14}ClN_3SO_3$. Calculated (%): C, 54.33; H, 3.75; N, 11.18.

3-Acetamido-4-(4-chloroanilino)thieno[2,3-*b*]pyridine-2-carboxylic acid (13). Compound **8a** (0.24 g, 0.60 mmol) was added at 30 °C to a solution of sodium *tert*-butoxide (0.08 g, 0.87 mmol prepared from sodium (0.02 g)) in *tert*-butyl alcohol (12.42 g) and the red solution obtained was refluxed for 3 h. The reaction mixture was cooled to 20 °C, concentrated *in vacuo*, anh. ethanol was added to the red oily residue obtained, and it was concentrated *in vacuo* again. Cold water (200 mL) was added to the semicrystalline residue and the suspension obtained was stirred for 30 min. The red precipitate that has not been dissolved was filtered off and washed with water to pH 7. The precipitate was obtained in a yield of 0.05 g, which represented a mixture of four products: compound **14** was the main product and **13**, **13´**, **14´** were the minor ones. Glacial acetic acid was added dropwise to weakly alkaline mother liquor until acid reaction. The white precipitate that formed was filtered off and washed with water to pH 7. Compound **13** was obtained in a yield of 0.18 g (84%), m.p. 206 °C (H_2O). MS (EI), *m/z*, (I_{rel} (%)): 361 $[M]^{+\cdot}$ (32), 343 $[M - H_2O]^{+\cdot}$ (100), 299 $[343 - CO_2]^{+\cdot}$ (42). ^{1}H NMR spectrum of compound **13** (DMSO-d_6), δ: 2.08 (s, 3 H, $COCH_3$); 6.92 (d, 1 H, H(5), J_o = 5.60 Hz); 7.29, 7.46

(A_2B_2, 4 H, Ar, J_o = 8.75 Hz); 8.26 (d, 1 H, H(6), J_o = 5.60 Hz); 8.42 (br.s, 1 H, N<u>H</u>COCH$_3$); 10.08 (br.s, 1 H, NHC(4)). Found (%): C, 53.69; H, 3.61; N, 11.64. $C_{16}H_{12}ClN_3O_3S$. Calculated (%): C, 53.12; H, 3.34; N, 11.61.

Methyl (4*E*)-4-(2-oxopropylidene)-5-(4-chlorophenyl)-4,5-dihydro-3*H*-1-thia-3,5,8-triazaacenaphthylene-2-carboxylate (15a). A suspension of amidine **8a** (0.90 g) in acetic anhydride (20 mL) was refluxed for 34 h. The reaction mixture was cooled to 20 °C, the yellow precipitate was filtered off, washed with methanol, and dried. Analytically pure compound **15a** was obtained in a yield of 0.55 g (61%), m.p. 315 °C (decomp.). IR (KBr), ν/cm^{-1}: 3400, 3092 br.s. (NH); 1696, 1632 (COCH$_3$, COOCH$_3$). MS (EI), *m*/*z*, (I_{rel} (%)): 399 $[M]^{+\cdot}$ (79), 368 $[M - OMe]^{+\cdot}$ (18), 352 $[M - MeOH - NH]^{+\cdot}$ (87), 339 $[M - CH_3COOH]^{+\cdot}$ (31), 325 $[M - COOCH_3 - CH_3]^{+\cdot}$ (100), 297 $[325 - CO]^{+\cdot}$ (12). ^{1}H NMR (DMSO-d$_6$), δ: 1.91 (s, 3 H, COCH$_3$); 3.89 (s, 3 H, COOCH$_3$); 4.44 (s, 1 H, C(4)=CH); 5.94 (d, 1 H, H(6), J_o = 5.50 Hz); 7.58, 7.77 (A_2B_2, 4 H, Ar, J_o = = 8.60 Hz); 8.32 (d, 1 H, H(7), J_o = 5.50 Hz); 14.56 (s, 1 H, NH). ^{1}H NMR ($CDCl_3$), δ: 1.99 (s, 3 H, COCH$_3$); 3.99 (s, 3 H, COOCH$_3$); 4.42 (s, 1 H, C(4)=CH); 5.82 (d, 1 H, H(6), J_o = 5.50 Hz); 7.29, 7.63 (A_2B_2, 4 H, Ar, J_o = 8.60 Hz); 8.26 (d, 1 H, H(7), J_o = 5.50 Hz); 14.56 (s, 1 H, NH). Found (%): C, 56.84; H, 3.78; N, 10.60. $C_{19}H_{14}ClN_3O_3S$. Calculated (%): C, 57.07; H, 3.53; N, 10.51.

Methyl (4*E*)-4-(2-oxopropylidene)-5-(4-fluorophenyl)-4,5-dihydro-3*H*-1-thia-3,5,8-triazaacenaphthylene-2-carboxylate (15b) was prepared analogously from compound **8b**. The yield was 76%, m.p. 310 °C (decomp.). IR (KBr), ν/cm^{-1}: 3400, 3116 br.s. (NH); 1696, 1632 (COCH$_3$, COOCH$_3$). MS (EI), *m*/*z*, (I_{rel} (%)): 383 $[M]^{+\cdot}$ (72), 353 $[M - OMe]^{+\cdot}$ (7), 336 $[M - MeOH - NH]^{+\cdot}$ (65), 323 $[M - CH_3COOH]^{+\cdot}$ (24), 309 $[M - COOCH_3 - CH_3]^{+\cdot}$ (100), 281 $[325 - CO]^{+\cdot}$ (37). ^{1}H NMR (DMSO-d$_6$), δ: 1.91 (s, 3 H, COCH$_3$); 3.89 (s, 3 H, COOCH$_3$); 4.42 (s, 1 H, C(4)=CH); 5.92 (d, 1 H, H(6), J_o = 5.50 Hz); 7.45—7.67 (m, 4 H, Ar); 8.33 (d, 1 H, H(7), J_o = 5.50 Hz); 14.56 (s, 1 H, NH). ^{1}H NMR ($CDCl_3$), δ: 1.99 (s, 3 H, COCH$_3$); 4.00 (s, 3 H, COOCH$_3$); 4.42 (s, 1 H, C(4)=CH); 5.82 (d, 1 H, H(6), J_o = 5.50 Hz); 7.28—7.38 (m, 4 H, Ar); 8.27 (d, 1 H, H(7), J_o = = 5.50 Hz); 14.59 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$—F_3CCOOH), δ: 29.3 (q, <u>C</u>H$_3$CO, $^1J_{CH}$ = 128 Hz); 52.7 (q, COO<u>C</u>H$_3$, $^1J_{CH}$ = = 148 Hz); 87.0 (d, C(α), $^1J_{CH}$ = 175 Hz); 102.8 (d.d, C(6), $^1J_{CH}$ = 173 Hz, $^2J_{CH(7)}$ = 8.0 Hz); 117.2 (t, C(2b), $^3J_{CH(6)} = {}^3J_{CH(3)}$ = = 5.1 Hz); 118.9 (d.d.d, C(2′), C(6′), $^1J_{CH}$ = 168 Hz, $^3J_{CF}$ = = 23 Hz, $^3J_{C(2')H(6')}$ = 4 Hz, $^3J_{C(6')H(2')}$ = 4 Hz); 129.8 (m, C(1′)); 130.3 (d.d.d, C(3′), C(5′), $^1J_{CH}$ = 166 Hz, $^3J_{CF}$ = 8.9 Hz, $^3J_{C(3')H(5')}$ = 5.6 Hz; $^3J_{C(5')H(3')}$ = 5.6 Hz); 131.2; 151.8; 152.4 (C(2), C(2a), C(4), C(8a)); 147.3 (d.d, C(5a), $J_{CH(7)}$ = 8.8 Hz, $J_{CH(6)}$ = 3 Hz); 148.2 (d.d, C(7), $^1J_{CH}$ = 187 Hz, $^2J_{CH(6)}$ = 3.4 Hz); 161.8 (q, <u>C</u>OOCH$_3$, $^3J_{CO,CH3}$ = 4.1 Hz); 163.6 (d.m, C(4′), $^1J_{CF}$ = 254 Hz); 196.8 (q, <u>C</u>OCH$_3$, ^2J = 4.0 Hz). Found (%): C, 59.20; H, 3.72; N, 11.00. $C_{19}H_{14}FN_3O_3S$. Calculated (%): C, 59.52; H, 3.68; N, 10.96.

X-Ray diffraction analysis of compounds 15a,b. The structures of compounds **15a,b** were established by powder X-ray diffraction.[16] Powder diagram was measured in the Guinier camera Huber G670 containing bent germanium monochromator. The positions of first 30 peaks were refined on the powder diagram. Using these positions, indicating in the triclinic cell was carried out with the TREOR90 program.[18] The crystal structures of compounds **15a** and **15b** were solved by the method of systematic search[19] in the centrosymmetrical *P*-1 group. Rigid three-dimensional molecule model obtained as a result of the optimization by the density functional method using the PRIRODA program[20] was used. Then the solution obtained was refined by the Rietveld method using the MRIA program,[21] peak profiles were described by the modified Voight function.[22] In the refinement, restriction to the permissible deflections of the interatomic distances in the molecule and to the planarity of the rings were applied. Parameters of thermal fluctuations of nonhydrogen atoms were refined in an isotropic approximation. Hydrogen atoms were placed at the calculated positions and were not refined. The principal crystallographic characteristics and experimental parameters of compounds **15a** and **15b** are given in Table 2. The experimental powder diagram and the difference curve as a result of refinement using the Rietveld method are shown in Fig. 3. All structural data were deposited with the Cambridge Crystallographic Database (CCDC 773568 and CCDC 773569).

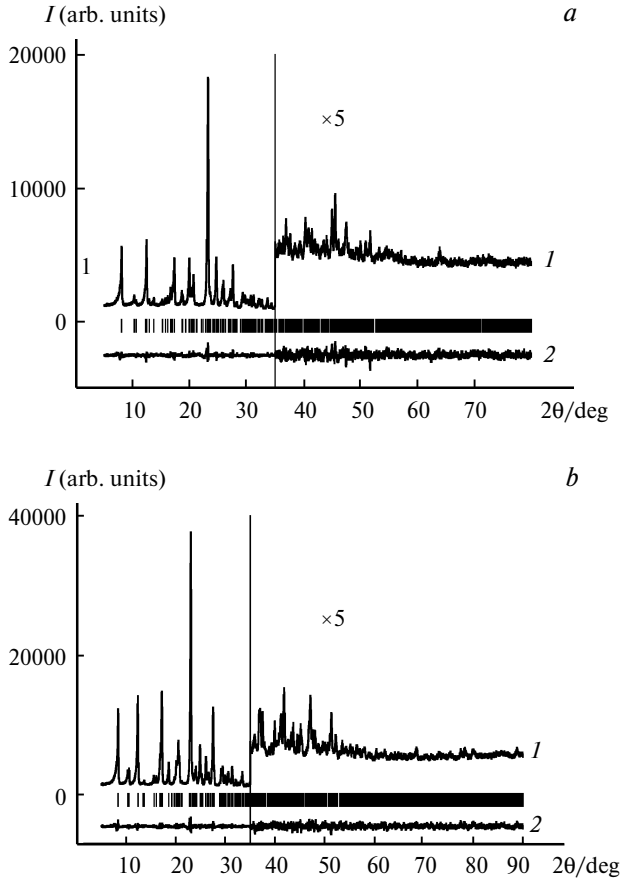


Fig. 3. The result of elucidation of crystal structure of compounds **15a** (*a*) and **15b** (*b*) by the Rietveld method: experimental curve (*1*), the difference between the experimental and calculated curves as a result of refinement (*2*); high-angle area (2θ > 40°) is presented on a large scale. The calculated positions of reflexes are indicated as vertical segments.

Table 2. Crystallographic characteristics of compounds **15a** and **15b**

Compound	**15a**	**15b**
Molecular formula	$C_{19}H_{14}ClN_3O_3S$	$C_{19}H_{14}FN_3O_3$
Crystal system	Triclinic	Triclinic
Space group	*P*-1	*P*-1
a/Å	9.7539(11)	9.7922(9)
b/Å	11.938(2)	11.4999(17)
c/Å	8.8749(8)	8.8545(7)
α/deg	100.58(2)	98.749(17)
β/deg	109.65(2)	109.52(2)
γ/deg	66.950(18)	66.270(15)
V/Å^3	894.0(2)	860.15(16)
M_{20}*	27	32
F_{30}*	35 (0.011, 57)	44 (0.009, 54)
Z	2	2
D_x (g cm^{-3})	1.485	1.480
Radiation (wave-length (Å))	Cu-Kα$_1$ (1.5406)	Cu-Kα$_1$ (1.5406)
Powder diagram: $2\theta_{min}$—$2\theta_{max}$/deg	4.00—80.00	4.00—90.00
Step of measurement/deg	0.01	0.01
R_p*	0.0280	0.0300
R_{wp}*	0.0358	0.0391
R_{exp}*	0.0274	0.0232
χ^{2}*	1.703	2.829

* Indicators of indication quality M_{20} (see Ref. 23) and F_{30} (see Ref. 24) were determined previously, R_p, R_{wp}, R_{exp} and χ^2 — see Ref. 25.

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