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HETEROCYCLIC *ORTHO*-AMINOCARBONYL COMPOUNDS IN THE FRIEDLÄNDER REACTION PROMOTED BY CHLOROTRIMETHYLSILANE

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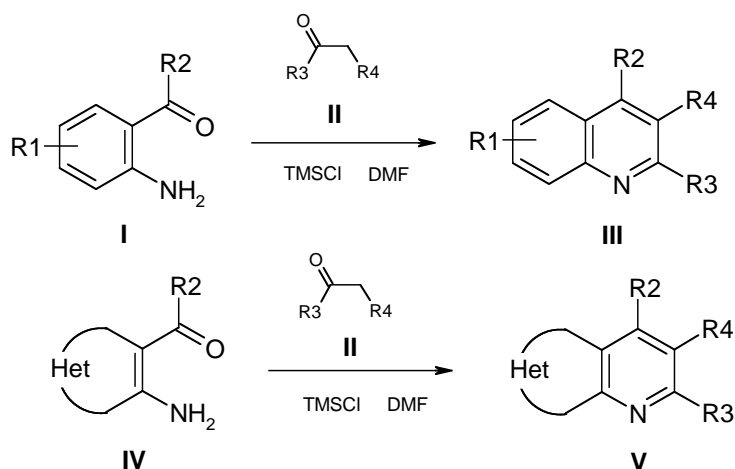
Abstract – A possibility of introduction of heterocyclic *ortho*-aminoketones into promoted by TMSCl Friedländer reaction with a wide set of α -methylene-carbonyl compounds was studied. A convenient synthetical method to obtain heterofused pyridine systems was elaborated; its scope and limitations were established as well. A set of derivatives of thieno[2,3-*b*]pyridines, [1]benzofuro[3,2-*b*]pyridines, 5*H*-chromeno[2,3-*b*]pyridin-5-ones, pyrido[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-diones was obtained in high preparative yields.

INTRODUCTION

The Friedländer reaction is a facile direct method to obtain the pyridine ring in the quinoline and other heterofused systems.¹ The diversity of α -methylene ketones available nowadays provides a possibility to vary easily the substituents in the formed compounds. In our previous work² we described a possibility to use TMSCl³ in DMF solution as a condensating agent for the synthesis of quinoline derivatives. That let extending the scope of the Friedländer reaction for different *ortho*-aminoketones **I** on α -methylene ketones **II**. During the investigation mentioned a range of diverse derivatives of quinoline **III** was synthesized, that demonstrated a possibility to introduce different substituents into the quinoline system.

In present paper we report the results of studying the subjection of heterocyclic aminoketones **IV** to the Friedländer reaction using TMSCl/DMF system (Scheme 1).

In present paper we report the results of studying the subjecting of heterocyclic aminoketones **IV** to the Friedländer reaction using TMSCl/DMF system (Scheme 1).



Scheme 1.

The corresponding aminoaldehydes and aminoketones depicted on the Figure 1 were chosen to be model objects for the investigation.

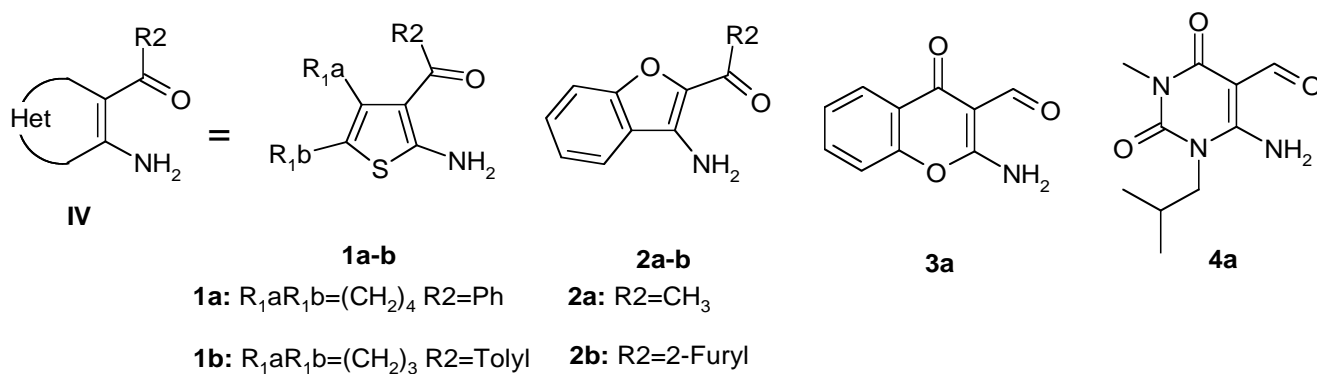


Figure 1.

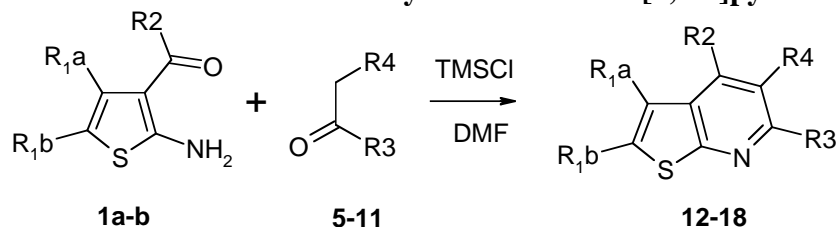
The heterofused systems (**V**) of thieno[2,3-*b*]pyridine, furo[3,2-*b*]pyridine, 5*H*-chromeno[2,3-*b*]pyridin-5-one, pyrido[2,3-*d*]pyridin-2,4(1*H*,3*H*)-dione, which are formed in the reaction of *ortho*-aminocarbonyl compounds with α -methylene ketones (**II**) are common among natural and synthetic chemical substances, and their derivatives exhibit a wide spectra of pharmacological activity. The thieno[2,3-*b*]pyridine derivatives are known as specific antagonists of LHRH receptors.⁴ Some derivatives of furo[3,2-*b*]pyridine reveal anticonvulsive action.⁵ Among the 5*H*-chromeno[2,3-*b*]pyridin-5-one derivatives there are many substances which have found an application as anti-allergic and anti-ulcer drugs.⁶ The derivatives of pyrido[2,3-*d*]pyridin-2,4(1*H*,3*H*)-dione exhibit antibacterial,^{7a} antitumor,^{7b} anticonvulsant^{7c} and other therapeutic activities.^{7d-h} Till the moment, there is a quite wide range of reagents, systems and conditions for subjecting heterocyclic *ortho*-aminocarbonyl compounds to the Friedländer reaction,^{5,8,9,10} however they are not sufficient to cover all the variety of α -methylene ketones which could

be used in this reaction. Therefore, the search for new preparative procedures for the Friedländer reaction and enlarging its scope and limitations by introducing more and more new substances remains still actually.


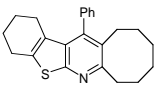
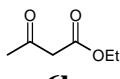
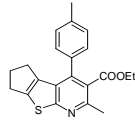
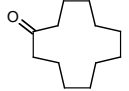
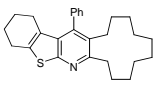
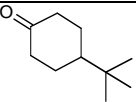
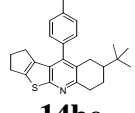
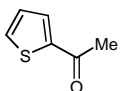
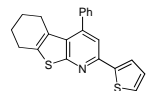
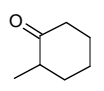
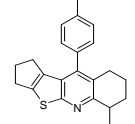
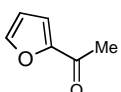
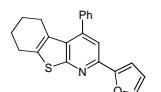
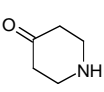
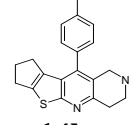
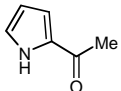
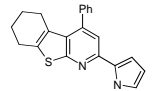
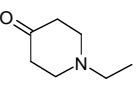
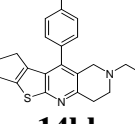
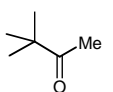
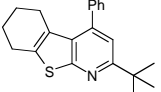
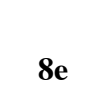
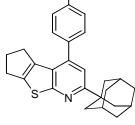
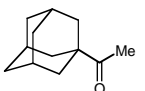
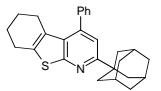
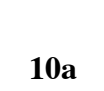
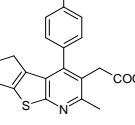
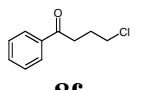
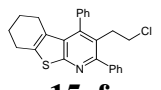
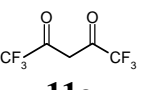
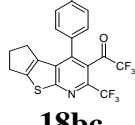
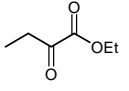
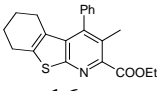
RESULTS AND DISCUSSION

Among the selected model compounds (**IV**), thiophene aminoketones (**1a-b**) are the closest analogues of the aromatic aminoketones (**I**). Therefore, for the elucidation of the possibility of using 2-aminothiophenes as substrates for the Friedländer reaction in TMSCl/DMF system, we used the conditions found to be the best for *o*-aminoacetophenone. Heating 1 equivalent of aminoketones (**1a-b**) with 1 equivalent of α -methylene ketone (**5-11**) and 4 equivalents of TMSCl at 100 °C led to the formation of a set of thieno[2,3-*b*]pyridines (Table 1).

Table 1. TMSCl Promoted Synthesis of thieno[2,3-*b*]pyridines^a



Entry	1	Carbonyl compound	Product	Time (h)	Yield ^a (%)	Entry	1	Carbonyl compound	Product	Time (h)	Yield ^b (%)
1	1a			10	94	15	1a			14	86
2	1a			10	89	16	1a			12	85
3	1a			10	93	17	1a			12	81
4	1a			12	96	18	1b	5a		10	92
5	1a			12	84	19	1b	5b		10	87

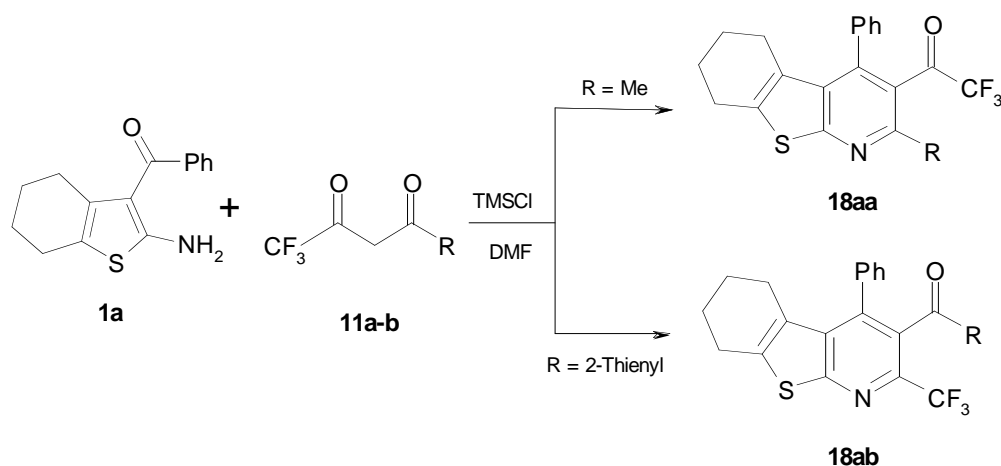
6	1a			12	87	20	1b			10	88
7	1a			12	88	21	1b			12	90
8	1a			14	79	22	1b			12	87
9	1a			14	81	23	1b			12	84
10	1a			14	77	24	1b			12	80
11	1a			14	86	25	1b			14	82
12	1a			14	83	26	1b			14	86
13	1a			14	82	27	1b			12	88
14	1a			14	87						

^aSatisfactory microanalysis obtained C ± 0.33; H ± 0.45; N ± 0.25
^bYields refer to pure isolated products

Analyzing the results obtained, it should be noted that, in general more drastical conditions are required for aminothiophenes **1a-b** in comparison with *o*-aminoacetophenone for the Friedländer reaction. Thus, even in the case of the most reactive α -methylene-carbonyl compounds such as β -ketonitriles (**5**), β -diketones (**6**, **11**) and cyclic ketones (**7**) which were subjected to the similar cyclizations before,⁸ the optimal heating time remains to be 10-12 hours. In the case of less active substrates such as acyclic methylketones (**8**),

dialkylketones with additional functional groups (**9-10**), even more prolonged heating time is required (14 hours).

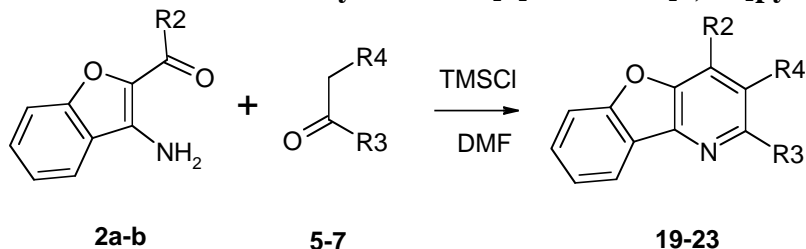
In the reaction of aminothiophene **1a** with unsymmetrical α -CF₃- β -diketones, either thienopyridine **18aa** or **18ab** are formed depending on the substituents, what is in agreement with previously obtained by us results concerning its behavior in the Friedländer reaction with *ortho*-aminobenzophenone² (Scheme 2).



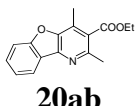
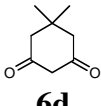
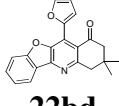
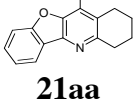
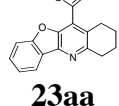
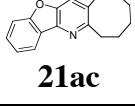
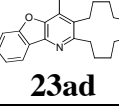
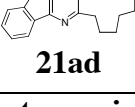
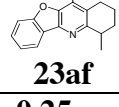
Changing from aminothiophenes to aminoketones of [1]benzofuran **2a-b** led to a significant narrowing the set of α -methylene carbonyl compounds which could be subjected to the reaction and more drastical reaction conditions.

We succeeded in reacting aminoketones **2a-b** with β -ketonitriles (**5**), β -diketones (**6**) and cyclic ketones (**7**) by heating their mixtures in the TMSCl/DMF system for 12-14 hours. An attempt to subject acyclic ketones **8-10** to the same conversion resulted in the formation of only trace amounts of products. All the [1]benzofuro[3,2-*b*]pyridines obtained are listed in Table 2.

Table 2. TMSCl Promoted Synthesis of [1]benzofuro[3,2-*b*]pyridines^a



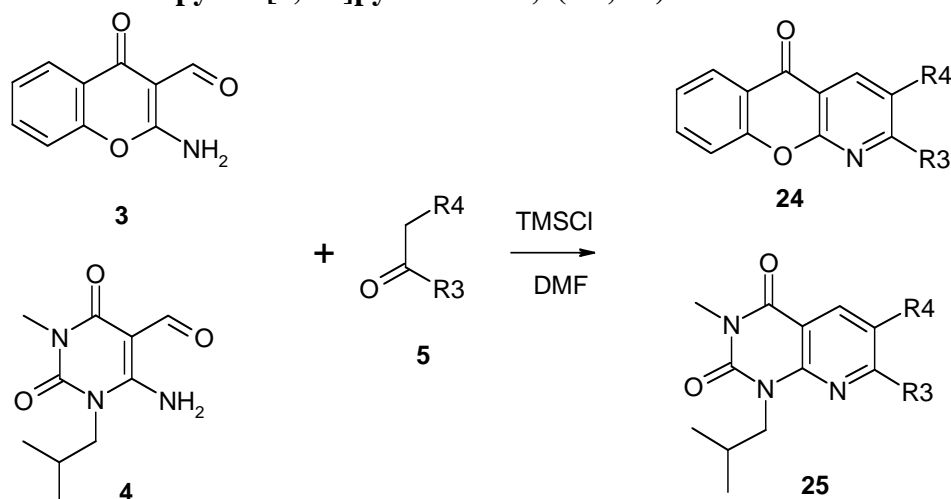
Entry	2	Carbonyl compound	Product	Time (h)	Yield ^a (%)	Entry	2	Carbonyl compound	Product	Time (h)	Yield (%) ^b
28	2a	5a		12	90	33	2b	6c		14	88

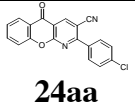
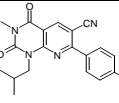
29	2a	6b	 20ab	14	87	34	2b	 6d	 22bd	14	92
30	2a	7a	 21aa	14	92	35	2b	7a	 23aa	14	90
31	2a	7c	 21ac	14	83	36	2b	7d	 23ad	14	83
32	2a	7d	 21ad	14	81	37	2b	7f	 23af	14	86
^a Satisfactory microanalysis obtained C ± 0.33; H ± 0.45; N ± 0.25 ^b Yields refer to pure isolated products											

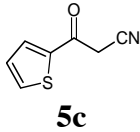
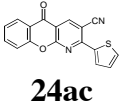
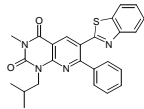
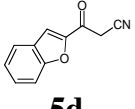
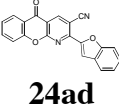
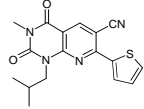
It should be noted that only ethyl acetoacetate was subjected to the Friedländer reaction with [1]benzofuro[3,2-*b*]pyridines before.⁵

The derivatives of 2-amino-3-uracil-carbaldehyde **3** and 2-amino-3-chromone-carbaldehyde **4** appeared to be even less active in the Friedländer reaction using our system in comparison with aminoketones of thiophene and furan. In this case we succeeded in reacting only α -methylene ketones **5** with aminoaldehydes **3** and **4** using more prolonged heating (Table 3).

Table 3. TMSCl Promoted Synthesis of 5*H*-chromeno[2,3-*b*]pyridin-5-ones, pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones.^a



Entry	3	Carbonyl compound	Product	Time (h)	Yield ^a (%)	Entry	4	Carbonyl compound	Product	Time (h)	Yield ^b (%)
38	3a	5a	 24aa	16	90	41	4a	5a	 25aa	16	89

39	3a			16	86	42	4a	5b		16	84
40	3a			16	83	43	4a	5c		16	81
^a Satisfactory microanalysis obtained C ± 0.33; H ± 0.45; N ± 0.25 ^b Yields refer to pure isolated products											

In conclusion, we described an efficient route for the synthesis of different heteroannulated pyridines using Me₃SiCl as a promoter and water scavenger *via* Friedländer annulation. The methodology is applicable to a wide variety of α-methylene ketones and delivers targeted products in good yields, excellent homogeneity and often in analytically pure form. The procedure is very simple and could be easily adapted to semi-automated solution-phase parallel synthesis of such libraries.

EXPERIMENTAL

General Data: All chemicals were obtained from commercially available sources (Aldrich, Fluka, Enamine Ltd.) and used without further purification. DMF was freshly distilled and dried by standard methods; monitoring of water concentration in solvents (the solvent contained < 0.05%, usually 0.02% of water) was performed using Mettler Toledo DL31 KF Titrator. All solvents for the crystallizations were used without additional purification.

Melting points were measured with a Buchi melting points apparatus and are uncorrected. The ¹H, ¹³C and ¹⁹F NMR spectra (500, 125 and 470 MHz, respectively) were recorded on a Bruker Avance drx 500 with DMSO-*d*₆ as a solvent, TMS (¹H and ¹³C) and CFC₃ (¹⁹F) were used as internal standards. LC/MS spectra were recorded using chromatography/mass spectrometric system that consists of high-performance liquid chromatograph "Agilent 1100 Series" equipped with diode-matrix and mass-selective detector "Agilent LC/MSD SL". According to HPLC MS data all the synthesized compounds have purity > 95%. BRANSON 2510E-MT ultrasonic bath and autoclave BERGHOF HR-500 were used.

General procedure for the preparation of thieno[2,3-*b*]pyridines, [1]benzofuro[3,2-*b*]pyridines, 5*H*-chromeno[2,3-*b*]pyridin-5-ones, pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones (12-25).

An appropriate aminocarbonyl compound **1-4** (1 mmol) and an appropriate carbonyl component **5-11** (1 mmol) were placed in 8 mL pressure tube and dissolved in DMF (2 mL). Chlorotrimethylsilane (4 mmol) was added dropwise to the solution. The tube was thoroughly sealed and heated on a water-bath for a particular time. (For the heating time see Tables 1-3.) After cooling the flask was opened (*caution!*

Excessive pressure inside); the reaction mixture was poured into water (5 mL) and allowed to stand at 20 °C in ultrasonic bath for 1h. The precipitate formed was filtered and washed with small amount of MeOH (or MeCN). Recrystallization from an appropriate solvent yielded the target compound.

2-(4-Chlorophenyl)-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine-3-carbonitrile (12aa)
mp 201 °C. ¹H NMR (DMSO-*d*₆) δ 1.53 (m, 2H), 1.75 (m, 2H), 1.85 (m, 2H), 2.87 (m, 2H), 7.49 (m, 2H), 7.56 (m, 3H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.92 (d, *J* = 7.7 Hz, 2H). [M+1]=402. Anal. Calcd for C₂₄H₁₇ClN₂S: C, 71.90; H, 4.27; N, 6.99. Found: C, 71.75; H, 4.30; N, 6.90.

3-(1,3-Benzothiazol-2-yl)-2,4-diphenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (12ab)
mp 178 °C. ¹H NMR (DMSO-*d*₆) δ 1.49 (m, 2H), 1.72 (m, 4H), 2.86 (m, 2H), 7.2 (m, 5H), 7.28 (m, 3H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.42 (m, 3H), 7.83 (t, *J* = 7.5 Hz, 2H). [M+1]=476. Anal. Calcd for C₃₀H₂₂N₂S₂: C, 75.92; H, 4.67; N, 5.90. Found: C, 75.86; H, 4.58; N, 6.06.

2-Methyl-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine-3-carboxamide (13aa)
mp 254 °C. ¹H NMR (DMSO-*d*₆) δ 1.45 (m, 2H), 1.69 (m, 4H), 2.57 (s, 3H), 2.77 (m, 2H), 7.29 (m, 3H), 7.39 (m, 3H), 7.67 (s, 1H) ¹³C NMR (DMSO-*d*₆) δ = 22.2, 22.5, 22.6, 25.9, 26.1, 127.7, 128.3, 128.6, 128.7, 129.8, 131.1, 136.4, 137.0, 141.7, 149.5, 158.4, 169.2. [M+1]=323. Anal. Calcd for C₁₉H₁₈N₂OS: C, 70.78; H, 5.63; N, 8.69. Found: C, 70.89; H, 5.52; N, 8.54.

11-Phenyl-1,2,3,4,7,8,9,10-octahydro[1]benzothieno[2,3-*b*]quinoline (14aa)
mp 190-191 °C. ¹H NMR (DMSO-*d*₆) δ 1.46 (m, 2H), 1.69 (m, 6H), 1.81 (m, 2H), 2.32 (t, *J* = 6.2 Hz, 2H), 2.74 (m, 2H), 2.94 (t, *J* = 6.2 Hz, 2H), 7.21 (m, 2H), 7.47 (m, 3H) . [M+1]=320. Anal. Calcd for C₂₁H₂₁NS: C, 78.95; H, 6.63; N, 4.38. Found: C, 78.77; H, 6.57; N, 4.32.

Methyl 12-phenyl-2,3,4,7,8,9,10,11-octahydro-1*H*-[1]benzothieno[2,3-*b*]cyclohepta[*e*]pyridine-7-carboxylate (14ab)
mp 121 °C. ¹H NMR (DMSO-*d*₆) δ 1.43 (m, 1H), 1.49 (m, 2H), 1.51 (m, 1H), 1.75 (m, 8H), 1.98 (m, 1H), 2.39 (m, 1H), 2.73 (m, 2H), 3.67 (s, 3H), 4.31 (m, 1H), 7.21 (m, 2H), 7.45 (m, 3H). [M+1]=393. Anal. Calcd for C₂₄H₂₅NO₂S: C, 73.62; H, 6.44; N, 3.58. Found: C, 73.90; H, 6.39; N, 3.68.

13-Phenyl-1,2,3,4,7,8,9,10,11,12-decahydro[1]benzothieno[2,3-*b*]cycloocta[*e*]pyridine (14ac)
mp 243 °C. ¹H NMR (DMSO-*d*₆) δ 1.29 (m, 2H), 1.38 (m, 6H), 1.66 (m, 4H), 1.82 (m, 2H), 2.61 (m, 2H), 2.81 (m, 2H), 3.24 (m, 2H), 7.32 (m, 2H), 7.51 (m, 3H) ¹³C NMR (DMSO-*d*₆) δ = 22.3, 22.4, 25.4, 25.6, 25.9, 26.2, 26.9, 30.9, 31.0, 33.3, 128.3, 128.4, 128.8, 129.1, 131.4, 131.7, 137.1, 137.9, 147.3, 153.2, 155.6. [M+1]=349. Anal. Calcd for C₂₃H₂₅NS: C, 79.49; H, 7.25; N, 4.03. Found: C, 79.37; H, 7.36; N, 4.11.

17-Phenyl-1,2,3,4,7,8,9,10,11,12,13,14,15,16-tetradecahydro[1]benzothieno[2,3-*b*]cyclododeca[*e*]pyridine (14ad)

mp 175-176 °C. ¹H NMR (DMSO-*d*₆) δ 1.24 (m, 2H), 1.51 (m, 14H), 1.68 (m, 2H), 1.78 (m, 2H), 1.96 (m, 2H), 2.46 (m, 2H), 2.82 (m, 2H), 2.88 (m, 2H), 7.21 (m, 2H), 7.46 (m, 3H) ¹³C NMR (DMSO-*d*₆) δ 22.7, 22.8, 23.3, 23.8, 26.1, 26.7, 26.9, 27.3, 27.5, 27.7, 29.3, 32.9, 128.1, 128.3, 129.7, 130.3, 136.1, 138.4, 144.8, 146.6, 155.4, 157.2, 181.9, 208.3, 212.9. [M+1]=405. Anal. Calcd for C₂₇H₃₃NS: C, 80.35; H, 8.24; N, 3.47. Found: C, 80.02; H, 8.53; N, 3.58.

4-Phenyl-2-thien-2-yl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (15aa)

mp 190 °C. ¹H NMR (DMSO-*d*₆) δ 1.52 (m, 2H), 1.74 (m, 2H), 1.92 (m, 2H), 2.81 (m, 2H), 7.13 (t, *J* = 3.4 Hz, 1H), 7.42 (m, 2H), 7.48 (m, 3H), 7.63 (d, *J* = 4.4 Hz 1H), 7.68 (s, 1H), 7.87 (d, *J* = 2.7 Hz, 1H). [M+1]=349. Anal. Calcd for C₂₁H₁₇NS₂: C, 72.58; H, 4.93; N, 4.03. Found: C, 72.44; H, 4.76; N, 4.19.

2-(2-Furyl)-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (15ab)

mp 199 °C. ¹H NMR (DMSO-*d*₆) δ 1.52 (m, 2H), 1.74 (m, 2H), 1.94 (m, 2H), 2.82 (m, 2H), 6.65 (m, 1H), 7.22 (d, *J* = 3 Hz, 1H), 7.42 (m, 2H), 7.48 (m, 4H), 7.82 (s, 1H). [M+1]=332. Anal. Calcd for C₂₁H₁₇NOS: C, 76.10; H, 5.17; N, 4.23. Found: C, 76.32; H, 5.05; N, 4.39.

4-Phenyl-2-(1*H*-pyrrol-2-yl)-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (15ac)

mp 215 °C. ¹H NMR (DMSO-*d*₆) δ 1.51 (m, 2H), 1.73 (m, 2H), 1.91 (m, 2H), 2.79 (m, 2H), 6.14 (s, 1H), 6.89 (s, 2H), 7.40 (s, 2H), 7.49 (s, 3H), 11.75 (s, 1H). [M+1]=331. Anal. Calcd for C₂₁H₁₈N₂S: C, 76.33; H, 5.49; N, 8.48. Found: C, 76.21; H, 5.63; N, 8.37.

2-*tert*-Butyl-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (15ad)

mp 120 °C. ¹H NMR (DMSO-*d*₆) δ 1.35 (s, 9H), 1.51 (m, 2H), 1.74 (m, 2H), 1.93 (m, 2H), 2.87 (m, 2H), 7.12 (s, 1H), 7.36 (m, 2H), 7.44 (m, 3H). [M+1]=322. Anal. Calcd for C₂₁H₂₃NS: C, 78.46; H, 7.21; N, 4.36. Found: C, 78.37; H, 7.30; N, 4.29.

2-(1-Adamantyl)-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (15ae)

mp 181 °C. ¹H NMR (DMSO-*d*₆) δ 1.50 (m, 2H), 1.72 (m, 8H), 1.97 (m, 8H), 2.03 (m, 3H), 2.49 (m, 2H), 7.04 (s, 1H), 7.33 (m, 2H), 7.43 (m, 3H). [M+1]=401. Anal. Calcd for C₂₇H₂₉NS: C, 81.16; H, 7.32; N, 3.51. Found: C, 81.05; H, 7.77; N, 3.41.

3-(2-Chloroethyl)-2,4-diphenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine (15af)

Mp 146-147 °C. ¹H NMR (DMSO-*d*₆) δ 1.48 (m, 2H), 1.71 (m, 4H), 2.79 (m, 2H), 2.88 (m, 2H), 3.22 (m, 2H), 7.41 (m, 2H), 7.52 (m, 8H). [M+1]=405. Anal. Calcd for C₂₅H₂₂ClNS: C, 74.33; H, 5.49; N, 3.47. Found: C, 74.45; H, 5.65; N, 3.32.

Ethyl 3-methyl-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridine-2-carboxylate (16aa)

mp 130 °C. ¹H NMR (DMSO-*d*₆) δ 0.84 (t, *J* = 7.2 Hz, 3H), 1.47 (m, 2H), 1.80 (m, 4H), 2.54 (s, 3H), 2.80 (m, 2H), 3.92 (q, *J* = 7.2 Hz, 2H), 7.24 (m, 2H), 7.45 (m, 3H). ¹³C NMR (DMSO-*d*₆) δ 13.8, 22.4, 22.5,

22.7, 25.9, 26.2, 61.3, 126.8, 128.0, 128.2, 128.3, 128.9, 129.4, 136.2, 137.7, 142.2, 149.8, 160.5, 168.1. [M+1]=352. Anal. Calcd for C₂₁H₂₁NO₂S: C, 71.77; H, 6.02; N, 3.99. Found: C, 71.58; H, 6.15; N, 4.13.

(2-Methyl-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridin-3-yl)acetic acid (17aa)

mp 276 °C. ¹H NMR (DMSO-*d*₆) δ 1.43 (m, 2H), 1.44 (m, 4H), 2.54 (s, 3H), 2.75 (m, 2H), 3.42 (s, 2H), 7.17 (m, 2H), 7.41 (m, 3H). [M+1]=338. Anal. Calcd for C₂₀H₁₉NO₂S: C, 71.19; H, 5.68; N, 4.15. Found: C, 71.35; H, 5.47; N, 4.26.

2,2,2-Trifluoro-1-(2-methyl-4-phenyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridin-3-yl)ethanone (18aa)

mp 111 °C. ¹H NMR (DMSO-*d*₆) δ 1.50 (m, 2H), 1.71 (m, 2H), 1.82 (m, 2H), 2.49 (s, 3H), 2.83 (m, 2H), 7.29 (m, 2H), 7.49 (m, 3H). ¹³C NMR (DMSO-*d*₆) δ 22.35, 22.44, 22.7, 26.0, 26.4, 114.9 (q, ¹J_{CF} = 292.7 Hz), 126.5, 128.2, 128.36, 128.40, 129.9, 130.3, 134.2, 139.0, 142.8, 149.0, 162.5, 189.9 (q, ²J_{CF} = 37.2 Hz). ¹⁹F NMR (DMSO-*d*₆) δ -76.3. [M+1]=376. Anal. Calcd for C₂₀H₁₆F₃NOS: C, 63.99; H, 4.30; N, 3.73. Found: C, 64.12; H, 4.24; N, 3.62.

4-Phenyl-2-(trifluoromethyl)-5,6,7,8-tetrahydro[1]benzothieno[2,3-*b*]pyridin-3-yl](thien-2-yl)methanone (18ab)

mp 210 °C. ¹H NMR (DMSO-*d*₆) δ 1.51 (m, 2H), 1.71 (m, 3H), 1.90 (m, 1H), 2.91 (m, 2H), 7.08 (m, 1H), 7.15 (m, 2H), 7.21 (m, 1H), 7.33 (m, 2H), 7.47 (d, *J* = 5.1 Hz, 1H), 7.97 (d, *J* = 5.1 Hz, 1H). ¹³C NMR (DMSO-*d*₆) δ 22.25, 22.28, 26.0, 26.4, 122.1 (q, ¹J_{CF} = 275.6 Hz), 127.5, 128.0, 128.9, 129.2, 129.3, 130.0, 130.3, 130.5, 133.3, 134.2, 137.5, 137.6, 143.8 (q, ²J_{CF} = 33.0 Hz), 144.6, 160.1, 185.9. ¹⁹F NMR (DMSO-*d*₆) δ -62.0. [M+1]=445. Anal. Calcd for C₂₃H₁₆F₃NOS₂: C, 62.29; H, 3.64; N, 3.16. Found: C, 62.43; H, 3.57; N, 3.26.

2-(4-Chlorophenyl)-4-(4-methylphenyl)-6,7-dihydro-5*H*-cyclopenta[4,5]thieno[2,3-*b*]pyridine-3-carbonitrile (12ba)

mp 216 °C. ¹H NMR (DMSO-*d*₆) δ 2.18 (m, 2H), 2.24 (m, 2H), 2.42 (s, 3H), 3.01 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H). [M+1]=402. Anal. Calcd for C₂₄H₁₇ClN₂S: C, 71.90; H, 4.27; N, 6.99. Found: C, 71.76; H, 4.15; N, 6.85.

3-(1,3-Benzothiazol-2-yl)-4-(4-methylphenyl)-2-phenyl-6,7-dihydro-5*H*-cyclopenta[4,5]thieno[2,3-*b*]pyridine (12bb)

mp 250 °C. ¹H NMR (DMSO-*d*₆) δ 2.06 (m, 2H), 2.22 (m, 5H), 2.99 (m, 2H), 7.06 (d, *J* = 7.3 Hz, 2H), 7.17 (m, 5H), 7.32 (t, *J* = 8 Hz, 1H), 7.41 (m, 3H), 7.86 (t, *J* = 8 Hz, 2H). [M+1]=476. Anal. Calcd for C₃₀H₂₂N₂S₂: C, 75.92; H, 4.67; N, 5.90. Found: C, 76.06; H, 4.53; N, 5.82.

Ethyl 2-methyl-4-(4-methylphenyl)-6,7-dihydro-5*H*-cyclopenta[4,5]thieno[2,3-*b*]pyridine-3-carbo-

xylate (13bb)

mp 99 °C. ¹H NMR (DMSO-*d*₆) δ 0.96 (t, *J* = 7.2 Hz, 3H), 2.18 (m, 2H), 2.29 (m, 2H), 2.46 (s, 3H), 2.61 (s, 3H), 3.01 (m, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H)

¹³C NMR (DMSO-*d*₆) δ 13.9, 21.3, 22.8, 27.1, 29.8, 29.9, 61.4, 125.9, 126.2, 128.7, 129.2, 133.0, 137.4, 138.2, 141.9, 142.8, 150.0, 165.8, 168.2. [M+1]=352. Anal. Calcd for C₂₁H₂₁NO₂S: C, 71.77; H, 6.02; N, 3.99. Found: C, 71.64; H, 6.18; N, 4.09.

8-tert-Butyl-10-(4-methylphenyl)-2,3,6,7,8,9-hexahydro-1H-cyclopenta[4,5]thieno[2,3-*b*]quinoline (14be)

mp 193 °C. ¹H NMR (DMSO-*d*₆) δ 0.85 (s, 9H), 1.44 (m, 2H), 1.97 (m, 1H), 2.05 (m, 2H), 2.21 (m, 3H), 2.49 (s, 3H), 2.51 (m, 1H), 2.92 (m, 3H), 3.07 (m, 1H), 7.06 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 2H). ¹³C NMR (DMSO-*d*₆) 21.3, 24.2, 27.0, 27.4, 28.2, 29.4, 29.9, 32.6, 33.8, 44.5, 126.6, 126.8, 126.9, 128.9, 129.0, 134.2, 137.2, 137.4, 140.7, 143.7, 163.0. [M+1]=377. Anal. Calcd for C₂₅H₂₉NS: C, 79.95; H, 7.78; N, 3.73. Found: C, 80.05 H, 7.63; N, 3.65.

6-Methyl-10-(4-methylphenyl)-2,3,6,7,8,9-hexahydro-1H-cyclopenta[4,5]thieno[2,3-*b*]quinoline (14bf)

mp 179 °C. ¹H NMR (DMSO-*d*₆) δ 1.36 (d, *J* = 4.7 Hz, 3H), 1.60 (m, 2H), 1.72 (m, 1H), 1.95 (m, 3H), 2.14 (m, 2H), 2.37 (s, 3H), 2.45 (m, 2H), 2.87 (m, 2H), 3.06 (m, 1H), 7.11 (m, 2H), 7.27 (m, 2H). ¹³C NMR (DMSO-*d*₆) 20.4, 21.3, 21.8, 27.0, 27.6, 29.3, 29.9, 31.0, 35.9, 126.5, 127.0, 129.01, 129.05, 129.1, 134.2, 137.1, 137.5, 141.4, 157.0, 169.5. [M+1]=335. Anal. Calcd for C₂₂H₂₃NS: C, 79.23; H, 6.95; N, 4.20. Found: C, 79.17 H, 7.04; N, 4.33.

10-(4-Methylphenyl)-2,3,4,7,8,9-hexahydro-1H-cyclopenta[4,5]thieno[2,3-*b*]-1,6-naphthyridine (14bg)

mp 258-259 °C. ¹H NMR (DMSO-*d*₆) δ 2.02 (m, 2H), 2.17 (m, 2H), 2.40 (s, 3H) 2.92 (m, 2H), 3.25 (m, 2H), 3.46 (m, 2H), 3.99 (m, 2H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.35 (d, *J* = 7.3 Hz, 2H). [M+1]=321. Anal. Calcd for C₂₀H₂₀N₂S: C, 74.96; H, 6.29; N, 8.74. Found: C, 75.15 H, 6.34; N, 8.56.

2-Ethyl-10-(4-methylphenyl)-2,3,4,7,8,9-hexahydro-1H-cyclopenta[4,5]thieno[2,3-*b*]-1,6-naphthyridine (14bh)

mp 239-240 °C. ¹H NMR (DMSO-*d*₆) δ 1.21 (m, 3H), 2.03 (m, 2H), 2.17 (m, 2H), 2.40 (s, 3H), 2.91 (m, 2H), 3.02 (m, 2H), 3.23 (m, 4H), 4.09 (m, 2H), 7.53 (m, 2H), 7.35 (m, 2H), 8.94 (br s, 1H), 11.69 (br s, 1H). [M+1]=350. Anal. Calcd for C₂₂H₂₄N₂S: C, 75.82; H, 6.94; N, 8.04. Found: C, 75.87 H, 6.81; N, 7.80.

2-(1-Adamantyl)-4-(4-methylphenyl)-6,7-dihydro-5H-cyclopenta[4,5]thieno[2,3-*b*]pyridine (15be)

mp 195 °C. ¹H NMR (DMSO-*d*₆) δ 1.71 (m, 6H), 2.03 (m, 11H), 2.21 (m, 2H), 2.38 (s, 3H) 2.94 (m, 2H),

7.17 (d, $J = 7.3$ Hz, 2H), 7.31 (d, $J = 7.3$ Hz, 2H). $[M+1]=401$. Anal. Calcd for $C_{27}H_{29}NS$: C, 81.16; H, 7.32; N, 3.51. Found: C, 80.98; H, 7.51; N, 3.42.

[2-Methyl-4-(4-methylphenyl)-6,7-dihydro-5H-cyclopenta[4,5]thieno[2,3-b]pyridin-3-yl]acetic acid (17ba)

mp 141 °C. 1H NMR (DMSO- d_6) δ 1.92 (m, 2H), 2.05 (m, 2H), 2.38 (s, 3H), 2.52 (s, 3H), 2.87 (m, 2H), 3.44 (s, 2H), 7.06 (d, $J = 7.0$ Hz, 2H), 7.28 (d, $J = 7.0$ Hz, 2H), 12.30 (br s, 1H). $[M+1]=338$. Anal. Calcd for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.68; N, 4.15. Found: C, 71.28; H, 5.53; N, 4.28.

2,2,2-Trifluoro-1-[4-(4-methylphenyl)-2-(trifluoromethyl)-6,7-dihydro-5H-cyclopenta[4,5]thieno[2,3-b]pyridin-3-yl]ethanone (18bc)

mp 147 °C. 1H NMR (DMSO- d_6) δ 2.18 (m, 2H), 2.24 (m, 2H), 2.39 (s, 3H), 3.07 (m, 2H), 7.25 (d, $J = 8.0$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (DMSO- d_6) δ 21.4, 27.2, 29.5, 30.6, 114.7 (q, $^1J_{CF} = 292.8$ Hz), 118.7, 121.6 (q, $^1J_{CF} = 274.6$ Hz), 129.2, 129.6, 129.8, 130.4, 138.0, 140.1, 143.3 (q, $^2J_{CF} = 32.6$ Hz), 143.5, 150.8, 166.7, 186.6 (q, $^2J_{CF} = 38.9$ Hz). ^{19}F NMR (DMSO- d_6) δ -76.3, -62.3. $[M+1]=430$. Anal. Calcd for $C_{20}H_{13}F_6NOS$: C, 55.95; H, 3.05; N, 3.26. Found: C, 56.16; H, 3.23; N, 3.16.

2-(4-Chlorophenyl)-4-methyl[1]benzofuro[3,2-b]pyridine-3-carbonitrile (19aa)

mp 220-221 °C. 1H NMR (DMSO- d_6) δ 2.73 (s, 3H), 7.55 (t, $J = 7.3$ Hz, 1H), 7.68 (d, $J = 8.5$ Hz, 2H), 7.78 (t, $J = 7.3$ Hz, 1H), 7.91 (m, 3H), 8.23 (d, $J = 7.3$ Hz, 1H). $[M+1]=320$. Anal. Calcd for $C_{19}H_{11}ClN_2O$: C, 71.59; H, 3.48; N, 8.79. Found: C, 71.45; H, 3.58; N, 8.65.

Ethyl 2,4-dimethyl[1]benzofuro[3,2-b]pyridine-3-carboxylate (20ab)

mp 167 °C. 1H NMR (DMSO- d_6) δ 1.35 (t, $J = 7.3$ Hz, 3H), 2.54 (s, 3H), 3.63 (s, 3H), 4.45 (q, $J = 7.3$ Hz, 2H), 7.49 (t, $J = 7.5$ Hz, 1H), 7.67 (t, $J = 7.5$ Hz, 1H), 7.82 (d, $J = 7.5$ Hz, 1H), 8.21 (d, $J = 7.5$ Hz, 1H). $[M+1]=270$. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.25; H, 5.50; N, 5.15.

11-Methyl-1,2,3,4-tetrahydro[1]benzofuro[3,2-b]quinoline (21aa)

mp 284 °C. 1H NMR (DMSO- d_6) δ 1.86 (m, 4H), 2.87 (s, 3H), 2.87 (m, 2H), 3.19 (m, 2H), 7.56 (t, 1H, $J = 7.2$ Hz), 7.75 (t, 1H, $J = 7.2$ Hz), 7.88 (d, 1H, $J = 7.2$ Hz), 8.53 (m, 1H). $[M+1]=238$. Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.06; H, 6.52; N, 5.98.

6-Methyl-7,8,9,10,11,12-hexahydro[1]benzofuro[3,2-b]cycloocta[e]pyridine (21ac)

mp 268 °C. 1H NMR (DMSO- d_6) δ 1.29 (m, 2H), 1.41 (m, 2H), 1.71 (m, 2H), 1.83 (m, 2H), 2.69 (s, 3H), 3.32 (m, 2H), 3.33 (m, 2H), 7.57 (t, 1H, $J = 7.3$ Hz), 7.76 (t, 1H, $J = 7.3$ Hz), 7.91 (d, 1H, $J = 7.3$ Hz), 8.60 (m, 1H). $[M+1]=266$. Anal. Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.59; H, 7.10; N, 5.35.

6-Methyl-7,8,9,10,11,12,13,14,15,16-decahydro[1]benzofuro[3,2-b]cyclododeca[e]pyridine (21ad)

mp 265 °C. ¹H NMR (DMSO-*d*₆) δ 1.7 (m, 6H), 1.53 (m, 8H), 1.84 (m, 2H), 2.79 (s, 3H), 2.96 (m, 2H), 2.97 (m, 2H), 7.45 (t, 1H, *J* = 7.5 Hz), 7.65 (t, 1H, *J* = 7.5 Hz), 7.79 (d, 1H, *J* = 7.5 Hz), 8.50 (br s, 1H). [M+1]=322. Anal. Calcd for C₂₂H₂₇NO: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.06; H, 8.31; N, 4.24.

1-[4-(2-Furyl)-2-methyl[1]benzofuro[3,2-*b*]pyridin-3-yl]ethanone (22bc)

mp 245 °C. ¹H NMR (DMSO-*d*₆) δ 2.51 (s, 3H), 2.59 (s, 3H), 6.87 (s, 1H), 7.52 (t, *J* = 8.2 Hz, 1H), 7.58 (s, 1H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 8.04 (s, 1H), 8.26 (d, *J* = 7.4 Hz, 1H). [M+1]=292. Anal. Calcd for C₁₈H₁₃NO₃: C, 74.22; H, 4.50; N, 4.81. Found: C, 74.11; H, 4.45; N, 4.93.

11-(2-Furyl)-3,3-dimethyl-3,4-dihydro[1]benzofuro[3,2-*b*]quinolin-1(2*H*)-one (22bd)

mp 220 °C. ¹H NMR (DMSO-*d*₆) δ 1.07 (s, 6H), 2.19 (s, 2H), 2.56 (s, 2H), 6.86 (m, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.91 (m, 1H), 8.17 (m, 1H). [M+1]=332. Anal. Calcd for C₂₁H₁₇NO₃: C, 76.12; H, 5.17; N, 4.23. Found: C, 76.28; H, 5.04; N, 4.38.

11-(2-Furyl)-1,2,3,4-tetrahydro[1]benzofuro[3,2-*b*]quinoline (23aa)

mp 266 °C. ¹H NMR (DMSO-*d*₆) δ 1.84 (m, 4H), 3.08 (m, 2H), 3.17 (m, 2H), 6.87 (m, 1H), 7.49 (m, 2H), 7.68 (m, 1H), 7.78 (m, 1H), 8.13 (m, 1H), 8.45 (m, 1H), 8.96 (br s, 1H). [M+1]=290. Anal. Calcd for C₁₉H₁₅NO₂: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.77; H, 5.15; N, 4.94.

6-(2-Furyl)-7,8,9,10,11,12,13,14,15,16-decahydro[1]benzofuro[3,2-*b*]cyclododeca[*e*]pyridine (23ad)

mp 160 °C. ¹H NMR (DMSO-*d*₆) δ 1.35 (m, 6H), 1.50 (m, 8H), 1.86 (m, 2H), 2.94 (m, 2H), 3.00 (m, 2H), 6.78 (m, 1H), 7.19 (d, *J* = 3.0 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.76 (d, *J* = 7.3 Hz, 1H), 8.00 (s, 1H), 8.11 (d, *J* = 7.3 Hz, 1H). [M+1]=375. Anal. Calcd for C₂₅H₂₇NO₂: C, 80.40; H, 7.29; N, 3.75. Found: C, 80.52; H, 7.18; N, 3.62.

11-(2-Furyl)-4-methyl-1,2,3,4-tetrahydro[1]benzofuro[3,2-*b*]quinoline (23af)

mp 252 °C. ¹H NMR (DMSO-*d*₆) δ 1.50 (d, *J* = 6.5 Hz, 3H), 1.71 (m, 1H), 1.87 (m, 2H), 2.02 (m, 1H), 3.04 (m, 1H), 3.16 (m, 1H), 3.47 (m, 1H), 6.87 (s, 1H), 7.51 (s, 2H), 7.70 (t, *J* = 7.2 Hz, 1H), 7.81 (d, *J* = 7.2 Hz, 1H), 8.13 (s, 1H), 8.59 (s, 1H). [M+1]=304. Anal. Calcd for C₂₀H₁₇NO₂: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.01; H, 5.56; N, 4.74.

2-(4-Chlorophenyl)-5-oxo-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (24aa)

mp 266 °C. ¹H NMR (DMSO-*d*₆) δ 7.24 (m, 3H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.83 (d, *J* = 6.0 Hz, 2H), 8.33 (d, *J* = 7.2 Hz, 1H), 9.05 (s, 1H). [M+1]=334. Anal. Calcd for C₁₉H₉ClN₂O₂: C, 68.58; H, 2.73; N, 8.42. Found: C, 68.43; H, 2.80; N, 8.39.

5-Oxo-2-thien-2-yl-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (24ac)

mp 260 °C. ¹H NMR (DMSO-*d*₆) δ 7.33 (m, 1H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.91 (t, *J* = 7.3 Hz, 1H), 8.00 (m, 1H), 8.15 (d, *J* = 7.3 Hz, 1H), 8.34 (m, 1H), 8.94 (s, 1H). [M+1]=305. Anal. Calcd for C₁₇H₈N₂O₂S: C, 67.09; H, 2.65; N, 9.20. Found: C, 67.21; H, 2.79; N, 9.15.

2-(1-Benzofuran-2-yl)-5-oxo-5H-chromeno[2,3-*b*]pyridine-3-carbonitrile (24ad)

mp 295 °C. ¹H NMR (DMSO-*d*₆) δ 7.38 (d, *J* = 7.2 Hz, 1H), 7.54 (m, 2H), 7.72 (m, 2H), 7.86 (m, 1H), 7.93 (m, 1H), 8.05 (m, 1H), 8.19 (d, *J* = 7.2 Hz, 1H), 9.00 (s, 1H). [M+1]=339. Anal. Calcd for C₂₁H₁₀N₂O₃: C, 74.55; H, 2.98; N, 8.28. Found: C, 74.43; H, 2.77; N, 8.17.

7-(4-Chlorophenyl)-1-isobutyl-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (25aa)

mp 222 °C. ¹H NMR (DMSO-*d*₆) δ 0.90 (d, *J* = 9.6 Hz, 6H), 2.25 (m, 1H), 3.32 (s, 3H), 4.11 (m, 2H), 7.71 (m, 2H), 7.98 (d, *J* = 6.9 Hz, 2H), 8.85 (s, 1H). [M+1]=370. Anal. Calcd for C₁₉H₁₇ClN₄O₂: C, 61.88; H, 4.65; N, 15.19. Found: C, 61.76; H, 4.73; N, 15.26.

6-(1,3-Benzothiazol-2-yl)-1-isobutyl-3-methyl-7-phenylpyrido[2,3-*d*]pyrimidine-2,4(1H,3H)-dione (25ab)

mp 220 °C. ¹H NMR (DMSO-*d*₆) δ 0.92 (d, *J* = 9.6 Hz, 6H), 2.07 (m, 1H), 3.35 (s, 3H), 4.13 (d, *J* = 10.0 Hz, 2H), 7.52 (m, 7H), 7.99 (m, 2H), 8.83 (s, 1H). [M+1]=444. Anal. Calcd for C₂₅H₂₂N₄O₂S: C, 67.85; H, 5.01; N, 12.66. Found: C, 67.73; H, 4.92; N, 12.78.

1-iso-Butyl-3-methyl-2,4-dioxo-7-thien-2-yl-1,2,3,4-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (25ac)

mp 200 °C. ¹H NMR (DMSO-*d*₆) δ 0.95 (d, *J* = 6.3 Hz, 6H), 2.15 (m, 1H), 3.31 (s, 3H), 4.07 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 4.1 Hz, 1H), 8.29 (d, *J* = 4.1 Hz, 1H), 8.04 (d, *J* = 4.1 Hz, 1H), 8.70 (s, 1H). [M+1]=341. Anal. Calcd for C₁₇H₁₆N₄O₂S: C, 59.98; H, 4.74; N, 16.46. Found: C, 59.86; H, 4.84; N, 16.53.

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REFERENCES

- (a) P. Friedländer, *Ber.*, 1882, **15**, 2572. (b) C. C. Cheng and S.-J. Yan, *Org. React.*, 1982, **28**, 37. (c) S. Gladiali, G. Chelucci, M. S. Mudadu, M.-A. Gastaut, and R. P. Thummel, *J. Org. Chem.*, 2001, **66**, 400.
- S. V. Ryabukhin, D. M. Volochnyuk, A. S. Plaskon', V. S. Naumchik, and A. A. Tolmachev, *Synthesis*, 2007, 1214.

3. For using Me_3SiCl as condensation agent see: (a) S. V. Ryabukhin, A. S. Plaskon, A. V. Tverdokhlebov, and A. A. Tolmachev, *Synth. Commun.*, 2004, **34**, 1483. (b) S. V. Ryabukhin, A. S. Plaskon, D. M. Volochnyuk, and A. A. Tolmachev, *Synlett*, 2004, 2287. (c) H. Heaney, G. Papageorgeogu, and R. F. Wilkins, *Tetrahedron*, 1997, **53**, 2941. For using Me_3SiI as condensation agent see: (d) G. Sabitha, G. S. K. K. Reddy, K. B. Reddy, and J. S. Yadav, *Synthesis*, 2004, 263. (e) G. Sabitha, G. S. K. K. Reddy, C. S. Reddy, and J. S. Yadav, *Synlett*, 2003, 858. (f) G. Sabitha, G. S. K. K. Reddy, C. S. Reddy, and J. S. Yadav, *Tetrahedron Lett.*, 2003, **44**, 4129. (g) S. V. Ryabukhin, A. S. Plaskon, D. M. Volochnyuk, and A. A. Tolmachev, *Synthesis*, 2006, 3715. (h) S. V. Ryabukhin, A. S. Plaskon, E. N. Ostapchuk, D. M. Volochnyuk, and A. A. Tolmachev, *Synthesis*, 2007, 417.
4. N. Cho, M. Harada, T. Imaeda, T. Imada, H. Matsumoto, Y. Hayase, S. Sasaki, S. Furuya, N. Suzuki, S. Okubo, K. Ogi, S. Endo, H. Onda, and M. Fujino, *J. Med. Chem.*, 1998, **41**, 4190.
5. E. G. Paronikyan, A. Kh. Oganisyan, A. S. Noravyan, R. G. Paronikyan, and I. A. Dzhagatspanyan, *Khim. Farm. Zh.*, RU, 2002, **36**, 17.
6. (a) Y. Isoda, H. Fujiwara, and T. Hosogami, *Chem. Abstr.*, 1991, 115, 183264z. (b) A. Nohara, T. Ishiguro, K. Ukawa, H. Sugihara, Y. Maki, and Y. Sanno, *J. Med. Chem.*, 1985, **28**, 559. (c) A. Nohara, H. Kuriki, T. Sajio, H. Sugihara, M. Kanno, and Y. Sanno, *J. Med. Chem.*, 1977, **20**, 141. (d) A. Nohara, H. Sugihara, and K. Ukawa, *Chem. Abstr.*, 1981, 94, 192310m. (e) K. Ukawa, T. Ishiguro, H. Kuriki, and A. Nohara, *Chem. Pharm. Bull.*, 1985, **33**, 4432. (f) G. Singh, R. Singh, N. K. Girdhar, and M. P. S. Ishar, *Tetrahedron*, 2002, **58**, 2471. (g) P. Langer and B. Apple, *Tetrahedron Lett.*, 2003, **44**, 5133.
7. (a) N. Suzuki, *Chem. Pharm. Bull.*, 1980, **28**, 761. (b) E. M. Grivsky, S. Lee, C. W. Sigel, D. S. Duch, and C. A. Nichol, *J. Med. Chem.*, 1980, **23**, 327. (c) E. Kretzchmar, *Farmazie*, 1980, **35**, 253. (d) R. K. Robins and G. H. Hitchings, *J. Am. Chem. Soc.*, 1958, **80**, 3449. (e) D. A. Vanden Berghe and A. J. Vlietinck, *J. Heterocycl. Chem.*, 1988, **25**, 217. (f) W. I. Irwin and D. G. Webberley, *Adv. Heterocycl. Chem.*, 1969, **10**, 146. (g) S. Minamis, *Chem. Pharm. Bull.*, 1971, **19**, 1426. (h) A. D. Broom, J. L. Shim, and G. L. Anderson, *J. Org. Chem.*, 1976, **41**, 1095.
8. S. Schefer, K. Gewald, and H. Hartman, *J. Prakt. Chem.*, 1974, **316**, 169.
9. A-R. H. Abdel-Rahman, M. M. Girges, A-A. S. El-Ahl, and L. M. Sallam, *Heteroatom Chem.*, 2006, **17**, 2.
10. (a) P. Matyus, P. Sohar, and H. Wamhoff, *Liebigs Ann. Chem.*, 1984, **10** 1653. (b) A. Sivaprasad, J. S. Sandhu, and J. N. Baruah, *Indian J. Chem. Sect. B*, 1985, **24**, 305.