Journal Pre-proof

One-pot approach to construct benzo[4,5]thieno[3,2-*b*]indoles, pyrido[3',2':4,5]thieno[3,2-*b*]indoles and pyrazino[2',3':4,5]thieno[3,2-*b*]indoles based on the Fischer indole synthesis

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PII: S0040-4020(20)30943-1

DOI: https://doi.org/10.1016/j.tet.2020.131723

Reference: TET 131723

To appear in: *Tetrahedron*

Received Date: 16 August 2020

Revised Date: 21 October 2020

Accepted Date: 23 October 2020

Please cite this article as: Irgashev RA, Steparuk AS, Rusinov GL, One-pot approach to construct benzo[4,5]thieno[3,2-*b*]indoles, pyrido[3',2':4,5]thieno[3,2-*b*]indoles and pyrazino[2',3':4,5]thieno[3,2-*b*]indoles based on the Fischer indole synthesis, *Tetrahedron*, https://doi.org/10.1016/j.tet.2020.131723.

Graphical abstract

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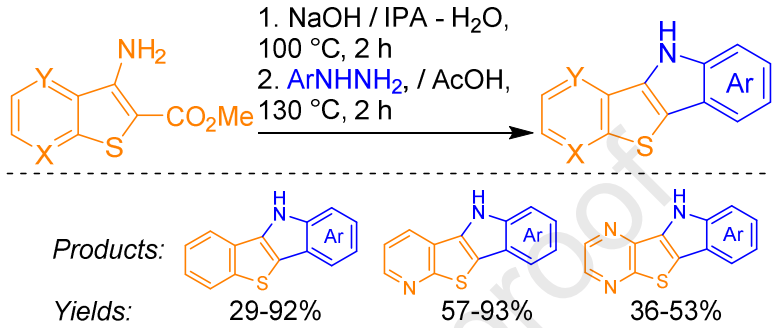

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One-pot approach to construct benzo[4,5]thieno[3,2-*b*]indoles, pyrido[3',2':4,5]thieno[3,2-*b*]indoles and pyrazino[2',3':4,5]thieno[3,2-*b*]indoles based on the Fischer indole synthesis

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Keywords: Benzo[4,5]thieno[3,2-*b*]indole; Aza-analogue; 3-Aminothiophene; the Fischer indole synthesis

ABSTRACT

During this study, series of benzo[4,5]thieno[3,2-*b*]indoles, pyrido[3',2':4,5]thieno[3,2-*b*]indoles and pyrazino[2',3':4,5]thieno[3,2-*b*]indoles were efficiently synthesized from benzo- and pyrido- or pyrazino-fused 3-aminothiophene-2-carboxylates, respectively, using one-pot two-step strategy based on the Fischer indolization reaction. The essence of this synthetic approach is acid-promoted reaction of the 3-aminothiophene intermediates, *in situ* generated from the corresponding ring-fused 3-aminothiophene-2-carboxylates, with arylhydrazines to give arylhydrazones of thiophen-3(2*H*)-ones, followed by their indolization to afford thieno[3,2-*b*]indole-cored molecules.

1. Introduction

Benzo[4,5]thieno[3,2-*b*]indole (BTI), also referred in the literature as [1]benzothieno[3,2-*b*]indole and thianaphtheno[3,2-*b*]indole, has been earlier used for the engineering of substances which are important both for materials science and medicinal chemistry. BTI framework has been utilized as electron-rich π-conjugated system in the design of organic semiconductors, such as 2,2-dicyanovinyl dyes which are shown solvatochromic properties [1], bipolar host materials [2], *e.g.* compound **mBTITrz** (Figure 1), and thermally activated delayed fluorescence emitters [3] for organic light-emitting diodes. In regard to application of BTI in medicinal chemistry, some of its derivatives have exhibited potential antihistaminic activity [4] and selective estrogen receptor modulator properties [5], *e.g.* compound **BTI-1** (Figure 1).

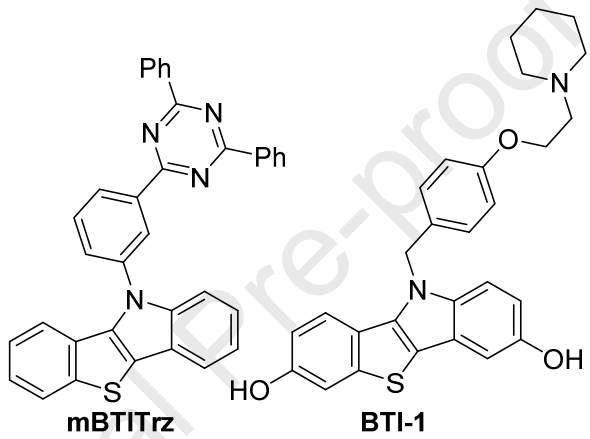
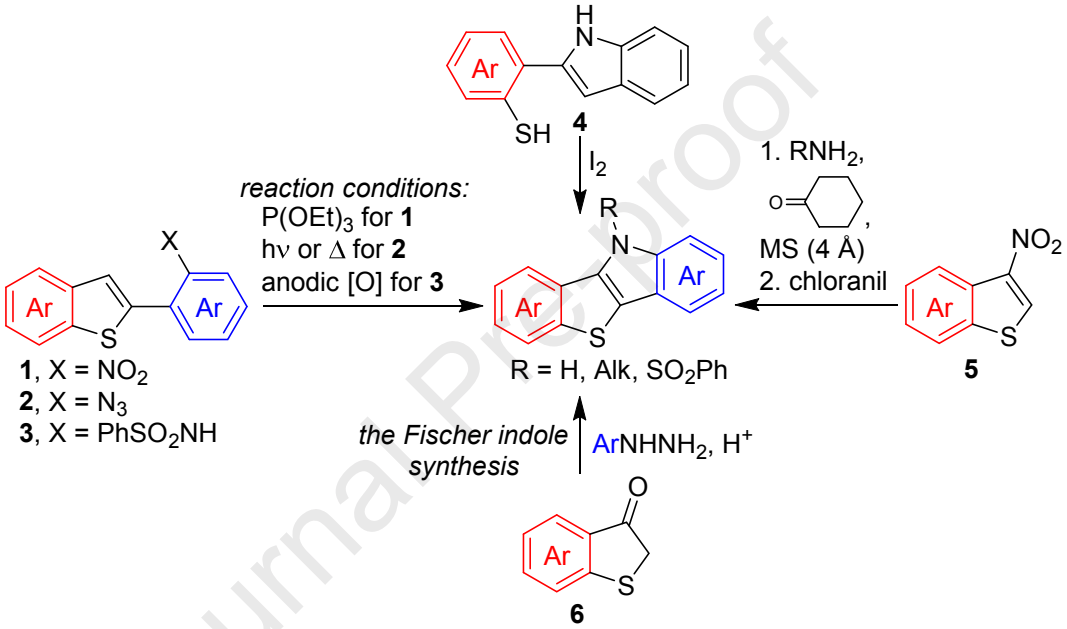


Figure 1. Benzo[4,5]thieno[3,2-*b*]indole-based functional compounds

Therefore, it is not surprising, that significant efforts of researchers have been focused on the elaboration of methods for the synthesis of BTI derivatives. Thus, the construction of BTI scaffolds has been successfully performed using different transition-metal-based strategies, including Pd- or Cu-catalyzed cyclization of aryl- or arylthio-linked indoles [6,7] as well as aryl- or arylamino-linked benzo[*b*]thiophenes [8–15], and Cu-catalyzed cascade double cyclization of N-protected 2-[(2-bromophenyl)ethynyl]anilines [16] or 2-[(2-halogenbenzyl)thio]benzonitriles [17]. Moreover, BTI derivatives have also been prepared in accordance with transition-metal-free methods, such as cyclization of 2-arylbenzo[*b*]thiophenes **1**-**3** under the Cadogan reaction conditions for **1** (X = NO_2) [1–3,18–21], thermal [18] or photochemical [22] conditions for **2** (X = N_3), electrochemical conditions for **3** (X = $NHSO_2Ph$) [23], oxidative cyclization of 2-(2-mercaptophenyl)indoles **4** with elemental iodine [24], three-component reaction of 3-nitrobenzo[*b*]thiophenes **5** with amines and cyclohexanones in the presence of 4 Å molecular sieves, followed by oxidation of the formed intermediates with chloranil [25], and reaction of benzo[*b*]thiophen-3(2*H*)-ones (thioindoxyls) **6** with arylhydrazines according to the Fischer

indole synthesis strategy [4,5,26–28] (Scheme 1). It should be noted, that the Fischer indole synthesis is very convenient method for the construction of thieno[3,2-*b*]indole-cored molecules, since, in general, the desired compounds can be directly formed by treatment of thiophen-3(2*H*)-one substrates with arylhydrazines in the glacial acetic acid solution without isolation of the intermediate arylhydrazones. Thus, we have previously described approaches towards 2-(hetero)arylthieno[3,2-*b*]indoles[29], and thieno[3,2-*b*]indole-cored heteroacenes [30–32] based on the Fischer indole synthesis. At the same time, thioindoxyls **6** have tendency to gradually oxidize with air oxygen, forming thioindigo derivatives[33,34], and their application as substrates for the synthesis of BTI derivatives can be limited taking into account this fact.



Scheme 1. Transition-metal-free protocols for the preparation of BTI derivatives

Recently, we have also described the Fischer indolization based approach for the preparation of 2-substituted thieno[3,2-*b*]indoles by reaction of 5-substituted 3-aminothiophenes, acted as synthetic equivalents of thiophen-3(2*H*)-ones, with arylhydrazines in glacial acetic acid [35]. In turn, 3-aminothiophene substrates were *in situ* generated from methyl 3-aminothiophene-2-carboxylates. In continuation of our research, we wish to report synthetic protocol for the preparation of BTI derivatives as well as BTI aza-analogues, namely pyrido[3',2':4,5]thieno[3,2-*b*]indole (PyrTI) and pyrazino[2',3':4,5]thieno[3,2-*b*]indole (PrzTI), illustrated in Figure 2, starting from benzo-, pyrido- or pyrazino-fused 3-aminothiophene-2-carboxylates, respectively, and arylhydrazines.

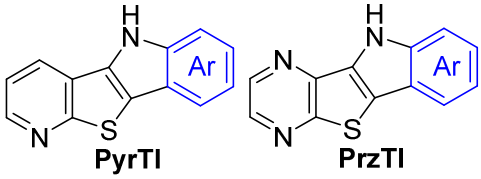
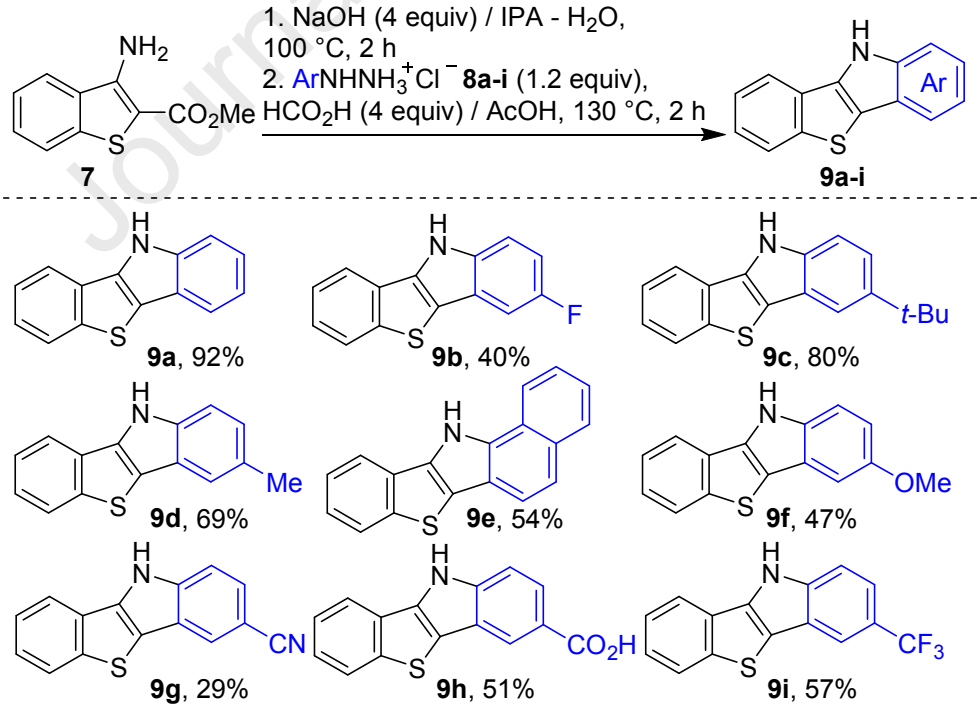


Figure 2. Structures of BTI aza-analogues

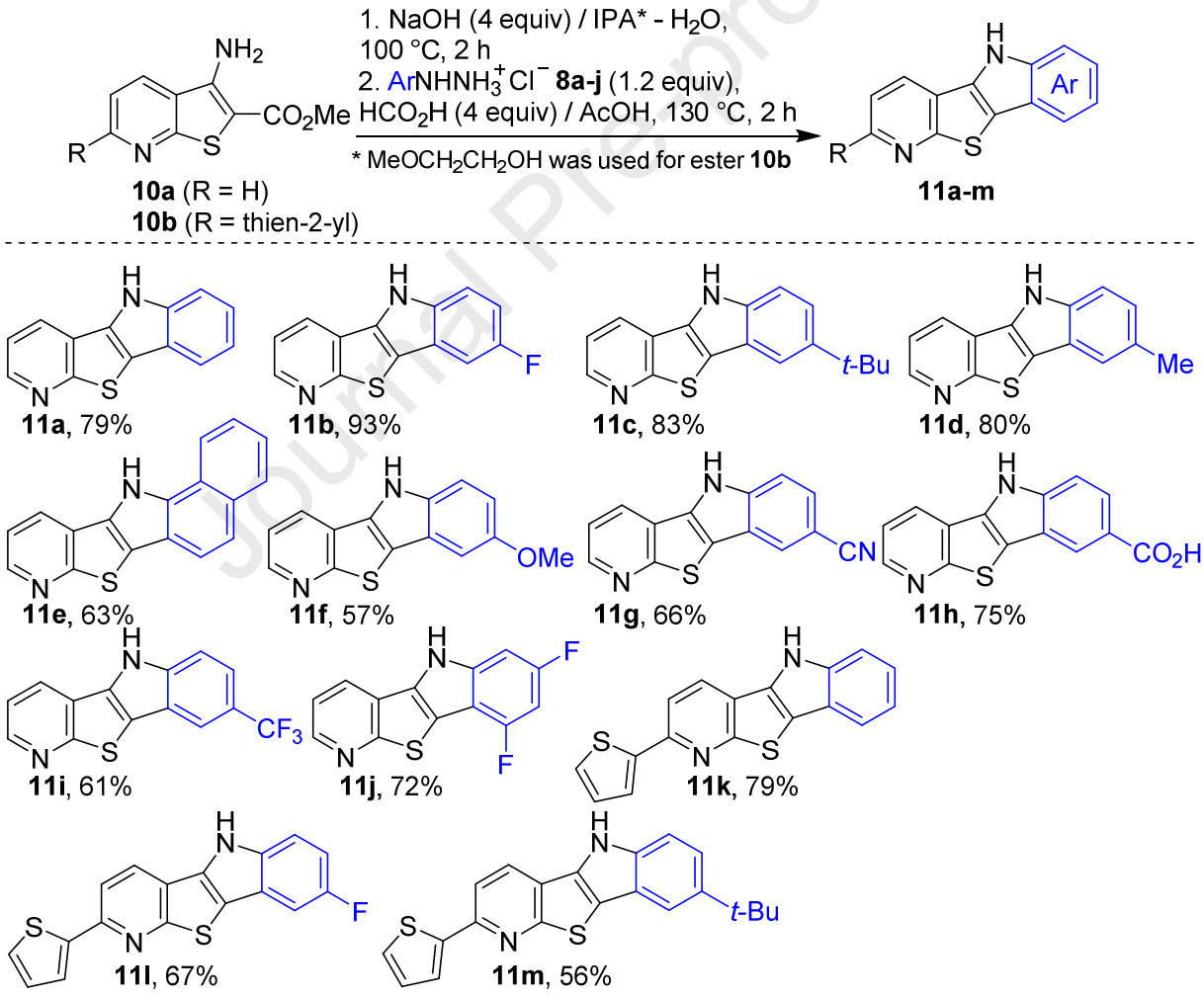
2. Results and discussion

To evaluate application of our synthetic strategy for the construction of BTI molecules, we selected methyl 3-aminobenzo[*b*]thiophene-2-carboxylate **7** as the key precursor. Substrate **7** was readily formed by reaction of 2-nitrobenzonitrile with methyl thioglycolate in the presence of KOH in accordance with the literature procedure [36]. Furthermore, alkyl 3-aminobenzo[*b*]thiophene-2-carboxylates can also be obtained by condensation of 2-fluoro- [37] or 2-chloro- [38] benzonitriles with alkyl thioglycolates in the presence of bases. Ester **7** was saponified with NaOH (4 equiv) in a solution of isopropanol – water (9:1, v/v) at reflux (100 °C) for 2 h, after that the reaction mixture was concentrated under reduced pressure to give crude sodium salt of amino acid. This salt was dissolved in glacial acetic acid with addition of formic acid (4 equiv) to speed up the salt dissolution, and treated with phenylhydrazine hidrochloride **8a** (1.2 equiv) at reflux (130 °C) for 2 h, thus affording compound **9a** in 92% yield (Scheme 2). To note, similar yield of product **9a** was obtained using phenylhydrazine free base instead of its hydrochloric salt. In the same manner, the use of arylhydrazines hydrochlorides **8b-j** (see Experimental) afforded products **9b-i** in 29-92% yields (Scheme 2). In the case of 3,5-difluorophenylhydrazine **8j**, we failed to prepare the desired BTI derivative, since complex mixture of compounds were obtained in this experiment.



Scheme 2. Synthesis of BTI compounds **9**, scope and yields of products

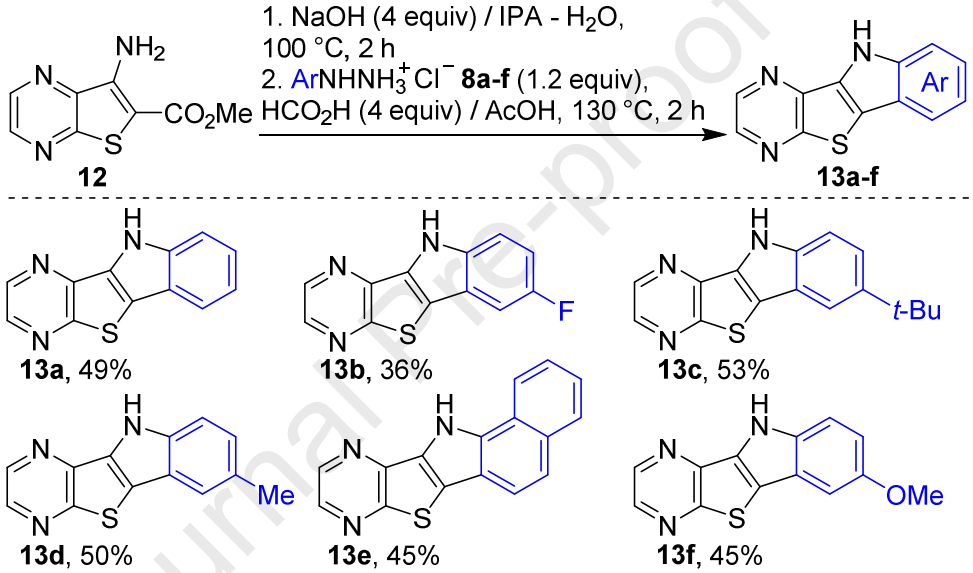
Next, we also utilized this synthetic strategy for the construction of BTI aza-analogues. To prepare PyrTI compounds, we used methyl 3-aminothieno[2,3-*b*]pyridine-2-carboxylates **10a,b** as the key precursors. These substrates were obtained by treatment of 2-chloronicotinonitrile with methyl thioglycolate in the presence of NaOMe, affording **10a** [39], and 6-(thien-2-yl)-substituted 3-cyanopyridine-2(1*H*)-thione with methyl bromoacetate in the presence of KOH, affording **10b** [40]. Saponification of ester **10a** was performed under the same reaction conditions as for ester **7**. Further treatment of the formed amino acid sodium salt with arylhydrazines hydrochlorides **8a-j** gave the desired products **11a-j** in 57-93% yields (Scheme 3). In the same manner, 2-(thien-2-yl)-substituted PyrTI derivatives **11k-m** were prepared in 56-79% yields starting from ester **10b** (Scheme 3). To note, we used 2-methoxyethanol as the solvent for saponification step of ester **10b**, since this compound was poorly soluble in isopropanol and the reaction proceeded extremely slow.



Scheme 3. Synthesis of PyrTI compounds **11**, scope and yields of products.

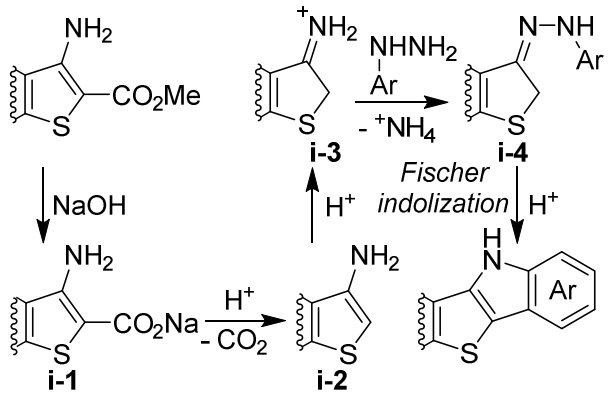
In turn, 7-aminothieno[2,3-*b*]pyrazine-6-carboxylate **12**, obtained by reaction of 3-chloropyrazine-2-carbonitrile with methyl thioglycolate in the presence of Et_3N [41], was used as

the key precursor to construct PrzTI molecules. Similar to esters **7** and **10a**, ester **12** was smoothly converted to the sodium salt of amino acid, and its further treatment with arylhydrazines hydrochlorides **8a-f** in glacial acetic acid solution afforded PrzTIs **13a-f** in 36-53% yields (Scheme 4). Unfortunately, the products **13** were not obtained when arylhydrazines **8g-i**, bearing CN, CO_2H or CF_3 groups at C-4 position, respectively, as well as 3,5-difluorophenylhydrazine **8j** were used for this reaction. It should be noted that compounds **13a-f** were also isolated only in moderate yields, which, for instance, were noticeably lower that the yields of PyrTIs **11a-f** (57-93%, Scheme 2). We assume that this peculiarity for PrzTI series can be associated with a more pronounced destruction of the intermediate thieno[2,3-*b*]pyrazine during the reaction as compared to the similar thieno[2,3-*b*]pyridine in the case of PyrTI series.



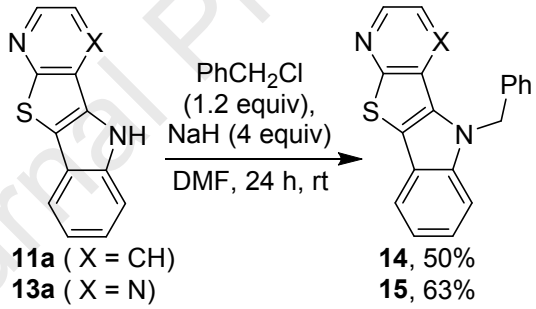
Scheme 4. Synthesis of PrzTI compounds **13**, scope and yields of products.

Taking into account that 3-aminothiophene-2-carboxylates are unusual substrates for the synthesis of thieno[3,2-*b*]indoles, we assume a possible mechanism of this reaction based on our findings (Scheme 5). Initially, sodium salt **i-1** converts to 3-aminothiophene **i-2** under acidic conditions by decarboxylation of the freed amino acid. Then, intermediate **i-2** protonated at C-2 position to give thiophen-3(2*H*)-iminium cation **i-3**, which reacts with arylhydrazine affording arylhydrazone of thiophen-3(2*H*)-one **i-4**. The latter one finally undergoes the Fischer indolization forming the desired thieno[3,2-*b*]indole product.



Scheme 5. Possible mechanism of thieno[3,2-*b*]indole core construction

We also studied alkylation of PyrTI and PrzTI compounds, since alkylation of pyrrole-containing ring-fused compounds in general is an important direction of their modification for different purposes. However, alkylation of PyrTIs and PrzTIs can be ambiguous since these molecules have nitrogen atoms of both pyrrole and pyridine types. Nevertheless, we were able to obtain N-benzyl derivatives **14** and **15** in 50% and 63% yields by treatment of compounds **11a** and **13a**, respectively, with benzyl chloride in the presence of NaH in DMF solution (Scheme 6).



Scheme 6. Alkylation of PyrTI and PrzTI compounds

3. Conclusion

In summary, we have developed a convenient approach to the synthesis of benzo[4,5]thieno[3,2-*b*]indole derivatives and their aza-analogues, such as pyridine and pyrazine annulated thieno[3,2-*b*]indoles PyrTIs and PrzTIs, from the ring-fused 3-aminothiophene-2-carboxylates by the one-pot procedure based on the Fischer indolization reaction. In turn, the starting substrates were readily obtained by reaction of (hetero)aryl nitriles, bearing a good leaving group in *ortho*-position to the cyano function, with methyl thioglycolate in the presence of bases. It should be noted, that PyrTI and PrzTI, similar in structure to the BTI, are potentially interesting scaffolds for the design of biologically active compounds and optoelectronic materials.

4. Experimental

Analytical studies were carried out using equipment of the Center for Joint Use "Spectroscopy and Analysis of Organic Compounds" at the Postovsky Institute of Organic Synthesis of the Russian Academy of Sciences (Ural Division). Melting points were determined on combined heating stages and are uncorrected. NMR measurements were performed on NMR spectrometers in DMSO-d_6 with tetramethylsilane as an internal standard for ^{1}H, ^{13}C spectra and perfluorobenzene for ^{19}F ones. Mass spectrometry was performed using a high resolution Q-TOF LC-MS/MS spectrometer. The literature procedures were used to prepare the key precursors **7** [36], **10a** [39], **10b** [40] and **12** [41]. Phenylhydrazine (**8a**), 4-fluorophenylhydrazine (**8b**), 4-(*tert*-butyl)phenylhydrazine (**8c**), 4-methylphenylhydrazine (**8d**), naphthalen-1-ylhydrazine (**8e**), 4-methoxyphenylhydrazine (**8f**), 4-cyanophenylhydrazine (**8g**), 4-hydrazinobenzoic acid (**8h**), 4-(trifluoromethyl)phenylhydrazine (**8i**) and 3,5-difluorophenylhydrazine (**8j**) (hydrochlorides) have been used in this study. Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification.

4.1 General procedure for the preparation of benzo[4,5]thieno[3,2-*b*]indoles (9a-i)

Methyl 3-aminobenzo[*b*]thiophene-2-carboxylate **7** (207 mg, 1 mmol) was immersed in IPA (9 ml) and suspended. Then, a solution of NaOH (160 mg, 4 mmol) in water (1 ml) was added in one portion, and the resulting mixture was stirred and heated at reflux (100 °C) for 2 h. The obtained solution was evaporated to dryness under reduced pressure, and the residue was dissolved in AcOH (7 ml) with addition of HCO_2H (0.15 ml, 4 mmol). An appropriate arylhydrazine hydrochloride **8a-i** (1.2 mmol) was added, and the reaction mixture was stirred and heated at reflux (130 °C) for 2 h. After that the obtained mixture was cooled to ambient temperature and diluted with MeOH (14 ml). The formed precipitate was filtered off, washed with a 50% aqueous MeOH (3 × 4 ml) and dried at 120 °C to afford product **9** in an analytically pure form.

4.1.1 10H-Benzo[4,5]thieno[3,2-b]indole (9a)

Light beige powder, yield 205 mg (92%), m.p. 255-256 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.12 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.32 – 7.25 (m, 1H), 7.15 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 142.0, 140.6, 137.5, 126.7, 124.5, 124.4, 124.3, 122.8, 121.5, 120.2, 119.4, 118.8, 113.8, 112.6. HRMS (APCI) calcd for $C_{14}H_{10}NS$ m/z 224.0528 $[M+H]^+$, found m/z 224.0528 $[M+H]^+$.

4.1.2 3-Fluoro-10H-benzo[4,5]thieno[3,2-b]indole (9b)

White powder, yield 96 mg (40%), m.p. 257-258 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.21 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.63 (dd, J = 9.7, 2.5 Hz, 1H), 7.59 (dd, J = 8.9, 4.5 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.43 – 7.38 (m, 1H), 7.12 (td, J = 9.2, 2.6 Hz, 1H); ^{19}F NMR (471 MHz, DMSO-d_6) δ 38.80 (td, J = 9.6, 4.6 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 156.8 (d, J_{CF} = 232.6 Hz), 142.3, 139.2, 137.2, 126.5, 124.7, 124.6, 124.4, 121.6 (d, J_{CF} = 11.0 Hz), 120.4, 113.7 (d, J_{CF} = 4.5 Hz), 113.5 (d, J_{CF} = 9.7 Hz), 110.8 (d, J_{CF} = 26.1 Hz), 104.0 (d, J_{CF} = 24.7 Hz). HRMS (APCI) calcd for $C_{14}H_8FNS$ m/z 241.0356 $[M]^+$, found m/z 241.0356 $[M]^+$.

4.1.3 3-(tert-Butyl)-10H-benzo[4,5]thieno[3,2-b]indole (9c)

Light beige crystals, yield 233 mg (80%), m.p. 217-218 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.03 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 1.5 Hz, 1H), 7.51 (d, J = 8.6 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.40 – 7.33 (m, 2H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 141.9, 138.7, 137.6, 126.8, 124.5, 124.4, 124.1, 121.3, 121.0, 120.0, 114.6, 113.9, 112.1, 34.4, 31.8. HRMS (APCI) calcd for $C_{18}H_{17}NS$ m/z 279.1076 $[M]^+$, found m/z 279.1080 $[M]^+$.

4.1.4 3-Methyl-10H-benzo[4,5]thieno[3,2-b]indole (9d)

Light beige crystals, yield 164 mg (69%), m.p. 263-264 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.97 (s, 1H), 8.04 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.55 (s, 1H), 7.51 – 7.45 (m, 2H), 7.41 – 7.33 (m, 1H), 7.10 (dd, J = 8.3, 0.9 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 141.9, 138.9, 137.6, 128.1, 126.8, 124.5, 124.40, 124.39, 124.2, 121.7, 120.1, 118.4, 113.4, 112.3, 21.1. HRMS (APCI) calcd for $C_{15}H_{11}NS$ m/z 237.0607 $[M]^+$, found m/z 237.0607 $[M]^+$.

4.1.5 12H-Benzo[g]benzo[4,5]thieno[3,2-b]indole (9e)

Pink powder, yield 147 mg (54%), m.p. 211-212 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.93 (s, 1H), 8.48 (d, J = 8.2 Hz, 1H), 8.16 (d, J = 7.8 Hz, 1H), 8.08 – 7.99 (m, 2H), 7.90 (d, J = 8.6 Hz, 1H), 7.68 – 7.58 (m, 2H), 7.56 – 7.49 (m, 2H), 7.42 – 7.35 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 141.7, 136.0, 135.3, 130.3, 128.7, 126.9, 125.8, 124.7, 124.48, 124.46, 124.0, 122.5, 120.9, 120.2, 119.8, 118.9, 117.1, 115.7. HRMS (APCI) calcd for $C_{18}H_{11}NS$ m/z 273.0607 $[M]^+$, found m/z 273.0606 $[M]^+$.

4.1.6 3-Methoxy-10H-benzo[4,5]thieno[3,2-b]indole (9f)

Orange powder, yield 119 mg (47%), m.p. 201-202 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.93 (s, 1H), 8.06 – 7.98 (m, 2H), 7.50 – 7.44 (m, 2H), 7.40 – 7.34 (m, 1H), 7.30 (d, *J* = 2.4 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.5, 141.9, 138.0, 135.5, 126.8, 124.5, 124.4, 124.2, 121.8, 120.0, 113.5, 113.3, 112.9, 100.7, 55.5. HRMS (APCI) calcd for $C_{15}H_{11}NOS$ m/z 253.0556 $[M]^+$, found m/z 253.0556 $[M]^+$.

4.1.7 10H-Benzo[4,5]thieno[3,2-b]indole-3-carbonitrile (9g)

Yellowish powder, yield 72 mg (29%), m.p. >350 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.76 (s, 1H), 8.45 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.63 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.49 – 7.41 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 142.7, 142.3, 139.3, 126, 125.4, 125.2, 124.8, 124.6, 124.5, 121.4, 120.6, 120.4, 114.4, 113.7, 101.3. HRMS (ESI) calcd for $C_{15}H_8N_2S$ m/z 248.0403 $[M]^+$, found m/z 248.0403 $[M]^+$.

4.1.8 10H-Benzo[4,5]thieno[3,2-b]indole-3-carboxylic acid (9h)

Light orange powder, yield 137 mg (51%), m.p. 344-345 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.61 (s, 1H), 12.53 (s, 1H), 8.47 – 8.43 (m, 1H), 8.12 – 8.03 (m, 2H), 7.89 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.66 (d, *J* = 8.6 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.45 – 7.40 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.0, 143.0, 142.3, 138.7, 126.4, 124.8, 124.7, 124.5, 124.0, 121.9, 121.3, 121.1, 120.3, 114.9, 112.3. HRMS (APCI) calcd for $C_{15}H_9NO_2S$ m/z 267.0349$[M]^+$, found m/z 267.0350 $[M]^+$.

4.1.9 3-(Trifluoromethyl)-10H-benzo[4,5]thieno[3,2-b]indole (9i)

Light beige powder, yield 166 mg (57%), m.p. 257-258 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.62 (s, 1H), 8.30 (s, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.57 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.41 (m, 1H); ^{19}F NMR (471 MHz, DMSO-d_6) δ 104.16; ^{13}C NMR (126 MHz, DMSO-d_6) δ 142.6, 142.0, 139.2, 126.2, 125.4 (q, *J* = 271.3 Hz), 125.0, 124.7, 124.5, 120.9, 120.5, 120.4 – 119.7 (m), 119.1 – 118.9 (m), 116.8 (q, *J* = 4.2 Hz), 114.6, 113.2. HRMS (ESI) calcd for $C_{15}H_8F_3NS$ m/z 291.0324 $[M]^+$, found m/z 291.0328 $[M]^+$.

4.2 General procedure for the preparation of pyrido[3',2':4,5]thieno[3,2-*b*]indoles (11a-m)

Methyl 3-aminothieno[2,3-*b*]pyridine-2-carboxylate **10a** (208 mg, 1 mmol) or methyl 3-amino-6-(thiophen-2-yl)thieno[2,3-*b*]pyridine-2-carboxylate **10b** (290 mg, 1 mmol) was immersed in IPA (9 ml) (for ester **10a**) or 2-methoxyethanol (9 ml) (for ester **10b**), and suspended. Then, a

solution of NaOH (160 mg, 4 mmol) in water (1 ml) was added in one portion to this suspension, and the resulting mixture was stirred and heated at reflux (100 °C) for 2 h. The obtained solution was evaporated to dryness under reduced pressure, and the residue was dissolved in AcOH (7 ml) with addition of HCO_2H (0.15 ml, 4 mmol). An appropriate arylhydrazine hydrochloride **8a-i** (1.2 mmol) was added, and the reaction mixture was stirred and heated at reflux (130 °C) for 2 h. After that the obtained mixture was cooled to ambient temperature and diluted with MeOH (14 ml). The formed precipitate was filtered off, washed with a 50% aqueous MeOH (3 × 4 ml) and dried at 120 °C to afford product **11** in an analytically pure form.

4.2.1 5H-Pyrido[3',2':4,5]thieno[3,2-b]indole (11a)

Orange powder, yield 177 mg (79%), m.p. 299-300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.25 (s, 1H), 8.54 (dd, J = 4.6, 1.3 Hz, 1H), 8.40 (dd, J = 7.9, 1.3 Hz, 1H), 7.84 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.54 (dd, J = 7.9, 4.7 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3, 145.6, 140.0, 133.8, 127.6, 123.5, 121.52, 121.47, 119.9, 119.7, 119.2, 112.7, 112.2. HRMS (APCI) calcd for $C_{13}H_9N_2S$ m/z 225.0481 $[M+H]^+$, found m/z 225.0485 $[M+H]^+$.

4.2.2 8-Fluoro-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11b)

Light beige powder, yield 225 mg (93%), m.p. 314-315 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.34 (s, 1H), 8.56 (dd, J = 4.6, 1.6 Hz, 1H), 8.41 (dd, J = 8.0, 1.6 Hz, 1H), 7.71 (dd, J = 9.7, 2.5 Hz, 1H), 7.64 (dd, J = 8.9, 4.5 Hz, 1H), 7.55 (dd, J = 7.9, 4.6 Hz, 1H), 7.17 (td, J = 9.2, 2.6 Hz, 1H); ^{19}F NMR (471 MHz, DMSO-d_6) δ 39.24 (td, J = 9.6, 4.6 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.4, 156.8 (d, J_{CF} = 233.1 Hz), 145.9, 136.6, 135.5, 127.9, 121.6 (d, J_{CF} = 11.0 Hz), 121.2, 119.8, 113.7 (d, J_{CF} = 9.6 Hz), 112.0 (d, J_{CF} = 4.7 Hz), 111.5 (d, J_{CF} = 26.1 Hz), 104.3 (d, J_{CF} = 24.8 Hz). HRMS (APCI) calcd for $C_{13}H_8FN_2S$ m/z 243.0387 $[M+H]^+$, found m/z 243.0390 $[M+H]^+$.

4.2.3 8-(tert-Butyl)-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11c)

White powder, yield 237 mg (83%), m.p. 272-273 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 8.52 (dd, J = 4.7, 1.6 Hz, 1H), 8.37 (dd, J = 8.0, 1.6 Hz, 1H), 7.79 (d, J = 1.7 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.41 (dd, J = 8.7, 1.9 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 145.3, 142.2, 138.2, 133.8, 127.4, 121.7, 121.6, 121.3, 119.8, 114.9, 112.4, 112.2, 34.4, 31.7. HRMS (APCI) calcd for $C_{17}H_{17}N_2S$ m/z 281.1107 $[M+H]^+$, found m/z 281.1102 $[M+H]^+$.

4.2.4 8-Methyl-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11d)

Beige powder, yield 190 mg (80%), m.p. 283-284 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 8.52 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.37 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.61 (s, 1H), 7.55 – 7.50 (m, 2H), 7.14 (dd, *J* = 8.4, 1.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 145.4, 138.3, 133.9, 128.5, 127.5, 125.1, 121.7, 121.6, 119.8, 118.7, 112.4, 111.7, 21.1. HRMS (APCI) calcd for $C_{14}H_{11}N_2S$ m/z 239.0637 $[M+H]^+$, found m/z 239.0641 $[M+H]^+$.

4.2.5 12H-Benzo[g]pyrido[3',2':4,5]thieno[3,2-b]indole (11e)

Yellow powder, yield 173 mg (63%), m.p. >350 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.17 (s, 1H), 8.54 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.50 – 8.45 (m, 2H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.72 – 7.62 (m, 2H), 7.60 – 7.50 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.9, 145.1, 135.0, 132.3, 130.5, 128.7, 127.3, 126.0, 124.8, 122.3, 121.7, 121.0, 120.6, 120.0, 119.0, 117.2, 114.0. HRMS (APCI) calcd for $C_{17}H_{11}N_2S$ m/z 275.0637 $[M+H]^+$, found m/z 275.0637 $[M+H]^+$.

4.2.6 8-Methoxy-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11f)

Deep orange powder, yield 145 mg (57%), m.p. 250-251 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.52 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.36 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.36 (d, *J* = 2.4 Hz, 1H), 6.95 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3, 153.7, 145.4, 134.9, 134.3, 127.5, 121.8, 121.6, 119.8, 113.8, 113.5, 111.9, 100.9, 55.5. HRMS (APCI) calcd for $C_{14}H_{11}N_2OS$ m/z 255.0587 $[M+H]^+$, found m/z 255.0590 $[M+H]^+$.

4.2.7 5H-Pyrido[3',2':4,5]thieno[3,2-b]indole-8-carbonitrile (11g)

Pink powder, yield 164 mg (66%), m.p. 328-329 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.85 (s, 1H), 8.60 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.50 (d, *J* = 0.7 Hz, 1H), 8.44 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.65 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.57 (dd, *J* = 8.0, 4.6 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 146.5, 141.6, 135.7, 128.3, 125.9, 125.0, 121.4, 120.8, 120.3, 120.1, 113.8, 112.7, 101.6. HRMS (APCI) calcd for $C_{14}H_8N_3S$ m/z 250.0433 $[M+H]^+$, found m/z 250.0434 $[M+H]^+$.

4.2.8 5H-Pyrido[3',2':4,5]thieno[3,2-b]indole-8-carboxylic acid (11h)

White powder, yield 201 mg (75%), m.p. >350 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.66 (s, 1H), 12.63 (s, 1H), 8.58 (dd, *J* = 4.6, 1.5 Hz, 1H), 8.51 (s, 1H), 8.43 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.92 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 7.56 (dd, *J* = 8.0, 4.6 Hz, 1H); ^{13}C NMR

(126 MHz, DMSO-d_6) δ 168.0, 163.5, 146.1, 142.4, 135.1, 128.0, 124.5, 122.2, 121.7, 121.20, 121.16, 120.0, 113.3, 112.5. HRMS (APCI) calcd for $C_{14}H_9N_2O_2S$ m/z 269.0379 $[M+H]^+$, found m/z 269.0377 $[M+H]^+$.

4.2.9 8-(Trifluoromethyl)-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11i)

Pink powder, yield 178 mg (61%), m.p. 292-293 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.73 (s, 1H), 8.60 (dd, J = 4.6, 1.6 Hz, 1H), 8.46 (dd, J = 8.0, 1.6 Hz, 1H), 8.38 (s, 1H), 7.83 (d, J = 8.6 Hz, 1H), 7.61 (dd, J = 8.7, 1.7 Hz, 1H), 7.58 (dd, J = 8.0, 4.7 Hz, 1H); ^{19}F NMR (471 MHz, DMSO-d_6) δ 104.04; ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 146.3, 141.4, 135.5, 128.1, 125.3 (q, J_{CF} = 271.5 Hz), 121.0, 121.0, 120.8 – 120.0 (m), 119.98, 119.7 – 119.4 (m), 117.2 (q, J_{CF} = 4.2 Hz), 113.3, 112.9. HRMS (ESI) calcd for $C_{14}H_8F_3N_2S$ m/z 293.0355 $[M+H]^+$, found m/z 293.0352 $[M+H]^+$

4.2.10 7,9-Difluoro-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11j)

Pink fleecy crystals, yield 187 mg (72%), m.p. >350 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.58 (dd, J = 4.7, 1.6 Hz, 1H), 8.44 (dd, J = 8.0, 1.6 Hz, 1H), 7.57 (dd, J = 8.0, 4.7 Hz, 1H), 7.39 (dd, J = 9.6, 2.0 Hz, 1H), 7.07 (td, J = 10.4, 2.0 Hz, 1H); ^{19}F NMR (376 MHz, DMSO-d_6) δ 46.95 (td, J = 9.9, 4.4 Hz), 43.58 (ddd, J = 10.5, 4.4, 2.3 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.1, 159.2 (dd, J_{CF} = 239.0, 12.1 Hz), 154.3 (dd, J_{CF} = 246.7, 15.9 Hz), 145.9, 141.2 (dd, J_{CF} = 15.0, 12.6 Hz), 134.2 (d, J_{CF} = 2.8 Hz), 128.0, 120.8, 120.1, 108.7, 107.7 (d, J_{CF} = 22.6 Hz), 95.8 (dd, J_{CF} = 26.5, 4.3 Hz), 95.2 (dd, J_{CF} = 29.7, 22.8 Hz). HRMS (APCI) calcd for $C_{13}H_7F_2N_2S$ m/z 261.0293 $[M+H]^+$, found m/z 261.0289 $[M+H]^+$.

4.2.11 2-(Thiophen-2-yl)-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11k)

Yellowish powder, yield 242 mg (79%), m.p. 290-291 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.22 (s, 1H), 8.39 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 3.6 Hz, 1H), 7.84 (d, J = 7.9 Hz, 1H), 7.69 (d, J = 5.0 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.24 – 7.15 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.1, 148.3, 144.2, 140.0, 134.0, 128.6, 128.5, 128.3, 125.7, 123.5, 121.6, 120.0, 119.8, 119.1, 115.4, 112.7, 112.2. HRMS (APCI) calcd for $C_{17}H_{11}N_2S_2$ m/z 307.0358 $[M+H]^+$, found m/z 307.0356 $[M+H]^+$.

4.2.12 8-Fluoro-2-(thiophen-2-yl)-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11l)

Yellowish powder, yield 217 mg (67%), m.p. 308-309 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.30 (s, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.89 (dd, J = 3.7, 0.9 Hz, 1H), 7.72 – 7.67 (m, 2H), 7.63 (dd, J = 8.9, 4.5 Hz, 1H), 7.21 (dd, J = 5.0, 3.7 Hz, 1H), 7.16 (td, J =

9.2, 2.6 Hz, 1H); ^{19}F NMR (471 MHz, DMSO-d_6) δ 39.32 (td, J = 9.5, 4.5 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3, 156.9 (d, J_{CF} = 233.2 Hz), 148.7, 144.0, 136.6, 135.7, 128.7, 128.6, 128.5, 125.8, 121.7 (d, J_{CF} = 11.1 Hz), 119.7, 115.4, 113.6 (d, J_{CF} = 9.6 Hz), 112.0 (d, J_{CF} = 4.6 Hz), 111.5 (d, J_{CF} = 26.1 Hz), 104.2 (d, J_{CF} = 24.8 Hz). HRMS (APCI) calcd for $C_{17}H_{10}FN_2S_2$ m/z 325.0264 $[M+H]^+$, found m/z 325.0259 $[M+H]^+$.

4.2.13 8-(tert-Butyl)-2-(thiophen-2-yl)-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (11m)

Beige powder, yield 203 mg (56%), m.p. 261-262 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.36 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 3.2 Hz, 1H), 7.79 (s, 1H), 7.68 (d, J = 5.0 Hz, 1H), 7.55 (d, J = 8.7 Hz, 1H), 7.40 (dd, J = 8.6, 1.5 Hz, 1H), 7.22 – 7.19 (m, 1H), 1.39 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.0, 148.1, 144.2, 142.3, 138.2, 134.0, 128.6, 128.4, 128.1, 125.6, 121.7, 121.4, 120.1, 115.4, 114.9, 112.4, 112.2, 34.5, 31.7. HRMS (APCI) calcd for $C_{21}H_{19}N_2S_2$ m/z 363.0984 $[M+H]^+$, found m/z 363.0979 $[M+H]^+$.

4.3 General procedure for the preparation of pyrazino[2',3':4,5]thieno[3,2-*b*]indoles (13a-f)

A solution of NaOH (160 mg, 4 mmol) in water (1 ml) was added to methyl 7-aminothieno[2,3-*b*]pyrazine-6-carboxylate **12** (209 mg, 1 mmol) dissolved in IPA (9 ml). The reaction mixture was stirred and heated at (100 °C) reflux for 2 h, and then evaporated to dryness under reduced pressure. The residue was dissolved in AcOH (7 ml) with addition of HCO_2H (0.15 ml, 4 mmol), and an appropriate arylhydrazine hydrochloride **8a-f** (1.2 mmol) was added. The reaction mixture was stirred and heated at reflux (130 °C) for 2 h, then it was cooled to ambient temperature and diluted with 50% aqueous MeOH (14 ml), and filtrated to remove a small amount of impurities. The main precipitate was formed at standing filtrate for 1 h at ambient temperature. The solid was filtrated, washed with a 50% aqueous MeOH (3 × 4 ml) and dried at 120 °C to give product **13** in an analytically pure form.

4.3.1 10H-Pyrazino[2',3':4,5]thieno[3,2-b]indole (13a)

Light beige powder, yield 110 mg (49%), m.p. 234-235 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.63 (s, 1H), 8.76 (d, J = 2.5 Hz, 1H), 8.57 (d, J = 2.5 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.3 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.26 – 7.19 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.9, 141.0, 140.9, 139.1, 138.5, 132.4, 124.9, 121.3, 120.1, 119.8, 116.6, 113.1. HRMS (APCI) calcd for $C_{12}H_8N_3S$ m/z 226.0433 $[M+H]^+$, found m/z 226.0435 $[M+H]^+$.

4.3.2 7-Fluoro-10H-pyrazino[2',3':4,5]thieno[3,2-b]indole (13b)

Light brown powder, yield 87 mg (36%), m.p. 301-302 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.71 (s, 1H), 8.77 (d, *J* = 2.5 Hz, 1H), 8.59 (d, *J* = 2.5 Hz, 1H), 7.82 (dd, *J* = 9.6, 2.4 Hz, 1H), 7.62 (dd, *J* = 8.9, 4.4 Hz, 1H), 7.25 (td, *J* = 9.2, 2.5 Hz, 1H); ^{19}F (471 MHz, DMSO-d_6) δ 39.81 (td, *J* = 9.4, 4.5 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 158.1, 156.9 (d, J_{CF} = 234.0 Hz), 141.1, 139.5, 138.3, 137.5, 134.1, 121.3 (d, J_{CF} = 11.2 Hz), 116.1 (d, J_{CF} = 4.8 Hz), 114.2 (d, J_{CF} = 9.6 Hz), 113.2 (d, J_{CF} = 26.3 Hz), 104.8 (d, J_{CF} = 24.8 Hz). HRMS (APCI) calcd for $C_{12}H_7FN_3S$ m/z 244.0339 $[M+H]^+$, found m/z 244.0340 $[M+H]^+$.

4.3.3 7-(tert-Butyl)-10H-pyrazino[2',3':4,5]thieno[3,2-b]indole (13c)

Light brown powder, yield 149 mg (53%), m.p. 211-212 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.47 (s, 1H), 8.74 (d, *J* = 2.5 Hz, 1H), 8.55 (d, *J* = 2.5 Hz, 1H), 7.90 (s, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.49 (dd, *J* = 8.7, 1.6 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.9, 142.7, 140.9, 139.1, 138.8, 138.6, 132.5, 123.3, 121.1, 116.7, 115.4, 112.7, 34.5, 31.7. HRMS (APCI) calcd for $C_{16}H_{16}N_3S$ m/z 282.1059 $[M+H]^+$, found m/z 282.1056 $[M+H]^+$.

4.3.4 7-Methyl-10H-pyrazino[2',3':4,5]thieno[3,2-b]indole (13d)

Light brown powder, yield 120 mg (50%), m.p. 249-250 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.74 (d, *J* = 2.5 Hz, 1H), 8.55 (d, *J* = 2.5 Hz, 1H), 7.71 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.22 (dd, *J* = 8.4, 1.4 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.9, 141.0, 139.3, 139.0, 138.6, 132.5, 129, 126.6, 121.4, 119.1, 116.0, 112.9, 21.1. HRMS (APCI) calcd for $C_{13}H_{10}N_3S$ m/z 240.0590 $[M+H]^+$, found m/z 240.0594 $[M+H]^+$.

4.3.5 12H-Benzo[g]pyrazino[2',3':4,5]thieno[3,2-b]indole (13e)

Light beige powder, yield 124 mg (45%), m.p. 297-298 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.58 (s, 1H), 8.78 (d, *J* = 2.5 Hz, 1H), 8.70 (d, *J* = 8.2 Hz, 1H), 8.56 (d, *J* = 2.5 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.59 – 7.54 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.8, 140.8, 138.7, 138.6, 136.5, 131.2, 130.9, 128.7, 126.2, 125.5, 122.5, 121.8, 121.2, 118.9, 118.2, 117.1. HRMS (APCI) calcd for $C_{16}H_{10}N_3S$ m/z 276.0590 $[M+H]^+$, found m/z 276.0591 $[M+H]^+$.

4.3.6 7-Methoxy-10H-pyrazino[2',3':4,5]thieno[3,2-b]indole (13f)

Brownish powder, yield 119 mg (45%), m.p. 275-276 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.44 (s, 1H), 8.73 (d, *J* = 2.5 Hz, 1H), 8.54 (d, *J* = 2.5 Hz, 1H), 7.51 (d, *J* = 8.9 Hz, 1H), 7.46 (d, *J* = 2.3 Hz, 1H), 7.03 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6)

δ 157.9, 153.9, 140.9, 138.9, 138.6, 135.9, 132.8, 121.5, 116.0, 115.6, 113.9, 100.9, 55.5. HRMS (APCI) calcd for $C_{13}H_{10}N_3OS$ m/z 256.0539 $[M+H]^+$, found m/z 256.0535 $[M+H]^+$.

4.4 General procedure for the preparation of compounds 14 and 15

PyrTI derivative **11a** (224 mg, 1 mmol) or PrzTI derivative **13a** (225 mg, 1 mmol) was dissolved in dry DMF (7 ml), then NaH (96 mg, 4 mmol) was added in one portion, and the obtained suspension was stirred for 30 min at ambient temperature under an argon atmosphere. Benzyl chloride (0.14 ml, 1.2 mmol) was added, and the resulted mixture was stirred at ambient temperature for 24 h. Then, the reaction mixture was diluted with H_2O (7 ml), and the formed precipitate was filtered off, washed with H_2O (2 × 10 ml) and dried on air. The crude product was crystallized from acetonitrile (5 ml) to afford N-benzyl derivative **14** or **15** in an analytically pure form.

4.4.1 5-Benzyl-5H-pyrido[3',2':4,5]thieno[3,2-b]indole (14)

Light beige powder (MeCN), yield 157 mg (50%), m.p. 184-185 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (dd, *J* = 4.5, 1.3 Hz, 1H), 8.42 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.46 (dd, *J* = 8.1, 4.6 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.28 – 7.18 (m, 4H), 7.11 (d, *J* = 7.3 Hz, 2H), 5.99 (s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 145.5, 140.9, 137.8, 133.8, 128.8, 128.0, 127.4, 126.2, 123.9, 121.12, 121.10, 120.2, 119.7, 119.6, 112.7, 111.1, 47.5. HRMS (ESI) calcd for $C_{20}H_{15}N_2S$ m/z 315.0950 $[M+H]^+$, found m/z 315.0956 $[M+H]^+$.

4.4.2 10-Benzyl-10H-pyrazino[2',3':4,5]thieno[3,2-b]indole (15)

Yellowish powder (MeCN), yield 200 mg (63%), m.p. 154-155 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.78 (d, *J* = 2.4 Hz, 1H), 8.60 (d, *J* = 2.4 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.32 – 7.11 (m, 6H), 6.05 (s, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 158.1, 141.0, 139.3, 138.7, 137.7, 132, 128.6, 127.5, 127, 125.1, 121.3, 120.5, 120.2, 116.3, 111.7, 47.5. HRMS (ESI) calcd for $C_{19}H_{14}N_3S$ m/z 316.0903 $[M+H]^+$, found m/z 316.0898 $[M+H]^+$

Conflicts of interest

There are no conflicts to declare.

Acknowledgments

This research study was supported by the Russian Foundation for Basic Research (research project No. 18-33-20083).

Appendix A. Supplementary data

Supplementary data to this article can be found online at

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HIGHLIGHTS

- Ring-annulated thieno[3,2-*b*]indoles were readily synthesized by one-pot procedure
- The synthesis was performed using easily accessible starting materials
- The Fischer indolization reaction is a key transformation of the current approach

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: