Synthesis and transformations of 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridines

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Reactions of 2,5-dimethoxytetrahydrofuran with 3-aminothieno[2,3-*b*]pyridines afford a number of substituted 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridines. The possibility of the reaction and the yield of the product are determined by the character of a substituent in position 2 of thieno[2,3-*b*]pyridine. The Curtius rearrangement of 2-acylazido-3(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridines yields 4,5-dihydropyrido[3′,2′:4,5]thieno[2,3-*e*]pyrrolo[1,2-*a*]pyrazin-4-ones. The molecular and crystal structures of ethyl 4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxylate were determined by X-ray diffraction analysis.

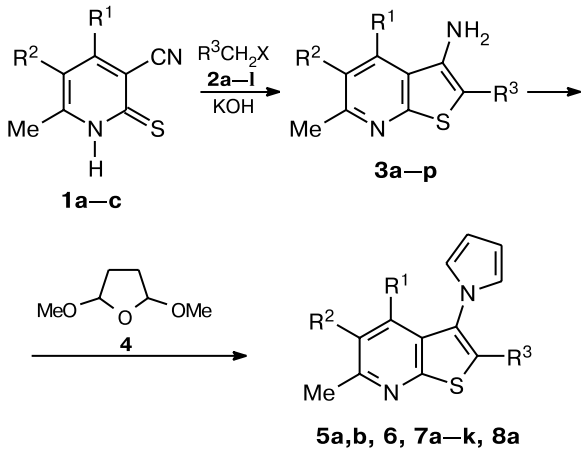
Key words: 3-aminothieno[2,3-*b*]pyridines, 2,5-dimethoxytetrahydrofuran, 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridines, 4,5-dihydropyrido[3′,2′:4,5]thieno[2,3-*e*]pyrrolo[1,2-*a*]pyrazin-4-ones, IR spectroscopy, UV spectroscopy, ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, X-ray diffraction analysis.

In recent years, the potentialities of the synthesis of conjugated and fused compounds containing a thieno[2,3-*b*]pyridine fragment have been under extensive investigations.[1—3] Earlier,[4] we obtained systems simultaneously containing pyrrole, thiophene, and pyridine rings. The present work was devoted to the directed synthesis, properties, and transformations of 3(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine derivatives.

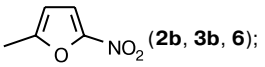
Alkylation of 3-cyanopyridine-2(1*H*)-thiones **1a—c** with halides **2a—l** in the presence of KOH followed by the Thorpe—Ziegler cyclization of alkyl derivatives gave a number of 3-aminothieno[2,3-*b*]pyridines **3a—p** (Scheme 1). Compounds **3a—c,f—k,n** were reported earlier,[3,5—8] while products **3d,e,l,m,o,p** were obtained for the first time.

Pyrrolylthienopyridines were synthesized by reactions of 3-aminothieno[2,3-*b*]pyridines **3** with 2,5-dimethoxytetrahydrofuran in boiling conc. AcOH; the molar ratio of the reagents was 1 : 1.2 (see Scheme 1). When their equimolar ratio is used, the reaction time extends approximately two times, while the yield of the product decreases by 5 to 7%. The starting reagents are well soluble in acetic acid, which ensures the necessary reaction temperature as well. As the result, 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridines containing aryl (compounds **5a,b**), hetaryl (5-nitro-2-furyl, **6**), ester (**7a—k**), and tertiary amide fragments (**8a**) in position 2 of the thiophene ring were obtained in good yields (Table 1).

Scheme 1



R^1 = CH_2OMe, R^2 = H (**1a**, **3a—k**, **5a**, **6**, **7b**,**e**,**k**, **8a**);
R^1 = Me, R^2 = H (**1c**, **3n**, **7c**), Cl (**1b**, **3l,m,o,p**, **5b**, **7a**,**d**,**f**);

R^3 = *p*-$NO_2C_6H_4$ (**2a**, **3a**,**l**, **5a,b**);  (**2b**, **3b**, **6**);

COOMe (**2c**, **3m**, **7a**); COOEt (**2d**, **3c**,**n**,**o, 7b,c,d**);
COOPh (**2e**, **3d**,**p**, **7e**,**f**); $COOC_6H_4Cl$-*p* (**2f**, **3e**, **7k**);
$CONPh_2$ (**2g**, **3f**, **8a**); CONHPh (**2h**, **3g**); $CONH_2$ (**2i**, **3h**);
COOH (**2j**, **3i**); CN (**2k**, **3j**); COPh (**2l**, **3k**);
X = Br (**2a—d**,**l**), Cl (**2e—h**,**k**), (**2i**,**j**)

A substituent in position 2 of thieno[2,3-*b*]pyridine was found to significantly affect the possibility of its reac-

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Table 1. Physicochemical characteristics and yields of compounds **3d,e,l—p** and **5—8**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%)			Molecular formula
			C	H	N	
3d	85	123—124	62.16	4.90	8.51	$C_{17}H_{16}N_2O_3S$
			62.18	4.91	8.53	
3e	87	121—122	56.26	4.17	7.70	$C_{17}H_{15}ClN_2O_3S$
			56.28	4.17	7.72	
3l	92	>300	53.95	3.61	12.57	$C_{15}H_{12}ClN_3O_2S$
			53.98	3.62	12.59	
3m	80	205—206	48.78	4.10	10.33	$C_{11}H_{11}ClN_2O_2S$
			48.80	4.10	10.35	
3n	75	159—160	57.56	5.65	11.16	$C_{12}H_{14}N_2O_2S$
			57.58	5.54	11.19	
3o	83	194—195	50.60	4.59	9.81	$C_{12}H_{13}ClN_2O_2S$
			50.62	4.60	9.84	
3p	84	238—239	57.72	3.93	8.40	$C_{16}H_{13}ClN_2O_2S$
			57.74	3.94	8.42	
5a	86	203—204	63.29	4.51	11.05	$C_{20}H_{17}N_3O_3S$
			63.31	4.52	11.07	
5b	84	239—240	59.44	3.68	10.93	$C_{19}H_{14}CIN_3O_2S$
			59.45	3.68	10.95	
6	86	200—201	58.51	4.07	11.36	$C_{18}H_{15}N_3O_4S$
			58.53	4.09	11.38	
7a	86	202—203	56.16	4.06	8.71	$C_{15}H_{13}ClN_2O_2S$
			56.16	4.08	8.73	
7b	93	111—112	61.78	5.48	8.45	$C_{17}H_{18}N_2O_3S$
			61.80	5.49	8.48	
7c	90	148—149	63.96	5.36	9.32	$C_{16}H_{16}N_2O_2S$
			63.98	5.37	9.33	
7d	92	140—141	57.38	4.50	8.36	$C_{16}H_{15}ClN_2O_2S$
			57.40	4.52	8.37	
7e	94	124—125	66.63	4.78	7.38	$C_{21}H_{18}N_2O_3S$
			66.65	4.79	7.40	
7f	93	148—149	62.73	3.95	7.30	$C_{20}H_{15}ClN_2O_2S$
			62.74	3.95	7.32	
7k	91	162—163	61.07	4.14	6.76	$C_{21}H_{17}ClN_2O_3S$
			61.09	4.15	6.78	
8a	88	149—150	71.48	5.10	9.24	$C_{27}H_{23}N_3O_2S$
			71.50	5.11	9.26	
8b	84	168—169	63.82	6.48	11.73	$C_{19}H_{23}N_3O_2S$
			63.84	6.48	11.75	
8c	88	145—146	65.75	6.56	10.94	$C_{21}H_{25}N_3O_2S$
			65.77	6.57	10.96	
8d	84	150—151	67.48	5.40	10.71	$C_{22}H_{21}N_3O_2S$
			67.50	5.41	10.73	

tion with dimethoxytetrahydrofuran and the yield of the product. On attempted involvement of thieno[2,3-*b*]pyridines containing carboxy, cyano, and phenacyl groups in position 2 (compounds **3i—k**) in this reaction, the starting reagents were recovered. Primary and secondary amides (in contrast to tertiary ones, which smoothly react with dimethoxytetrahydrofuran) give complex mixtures of products difficult to separate.

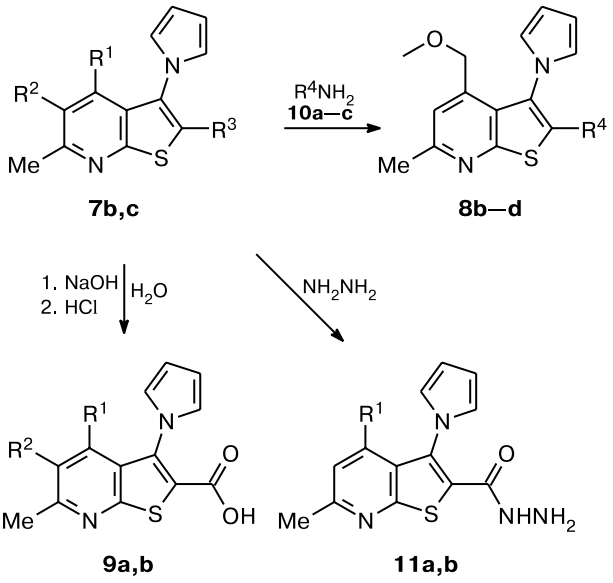
By alkaline hydrolysis of esters **7b**,**d** (Scheme 2, Table 2), carboxylic acids **9a**,**b** were obtained. Amination of ester **7b** with butyl-, benzyl-, and cyclohexylamines **10a—c** easily gives secondary 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxamides **8b—d** (see Scheme 2). The reactions of esters **7b**,**c** with hydrazine hydrate in ethanol afforded the corresponding hydrazides **11a,b** (see Table 2).

Unlike the corresponding starting thieno[2,3-*b*]pyridines **3a,c—p**, which are colored substances, 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridines **5**, **7—9**, and **11** form colorless crystals. The exception is 2-(5-nitro-2-furyl) de-

Table 2. Physicochemical characteristics and yields of compounds **9**, **11**, and **12**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%)			Molecular formula
			C	H	N	
9a	96	233—234	59.56	4.66	9.24	$C_{15}H_{14}N_2O_3S$
			59.59	4.67	9.27	
9b	96	256—257	54.80	3.60	9.11	$C_{14}H_{11}ClN_2O_2S$
			54.82	3.61	9.13	
11a	85	174—175	56.93	5.09	17.69	$C_{15}H_{16}N_4O_2S$
			56.95	5.10	17.71	
11b	81	219—220	58.74	4.91	19.55	$C_{14}H_{14}N_4OS$
			58.72	4.93	19.57	
12a	68	280—281 (decomp.)	60.17	4.38	14.02	$C_{15}H_{13}N_3O_2S$
			60.19	4.38	14.04	
12b	72	>300	62.43	4.11	15.58	$C_{14}H_{11}N_3OS$
			62.44	4.12	15.60	

Scheme 2



$R^1 = CH_2OMe$, $R^2 = H$ (**9a**), $R^1 = Me$, $R^2 = Cl$ (**9b**);
$R^1 = CH_2OMe$ (**11a**), Me (**11b**)
$R^4 = CONHBu$ (**8b**), $CONHBn$ (**8c**), $CONHC_6H_{11}$ (**8d**);
$R^4 = Bu$ (**10a**), Bn (**10b**), C_6H_{11} (**10c**)

rivative **6**. Apparently, the decolorization is due to steric hindrances arising when the pyrrole ring is formed. The pyrrole ring cannot be coplanar with the thieno[2,3-*b*]pyridine system already bearing bulky substituents in positions 2 and 4 and thus is approximately perpendicular to it, which breaks the conjugation between the pyrrole and thiophene rings. This is indicated by the anomalous upfield shift (δ 5.47) of the signal for the $H(3)_{Fur}$ proton in the ^1H NMR spectrum of nitrofuryl derivative **6** (Table 3), which can be associated with the position of this proton within the "shielding cone" of the perpendicular pyrrole ring.

To verify the assumption that the pyrrole and the thienopyridine fragments are mutually perpendicular in compounds **5**—**9** and **11**, X-ray diffraction analysis of ethyl 4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxylate (**7b**) was carried out. The projection of the 3D model of compound **7b** is shown in Fig. 1. Interatomic distances and bond and torsion angles are given in Tables 4—6.

As can be seen from the presented data, the interatomic distances and bond angles in structure **7b** have standard values. The thienopyridine fragment is planar with an average deviation of 0.0117 Å (plane *1*). The pyrrole ring is also planar to within 0.0017 Å (plane *2*). The angle between planes *1* and *2* is 85.1°; *i.e.*, there is no efficient conjugation between the aromatic thienopyridine and pyrrole fragments (which is confirmed by the elec-

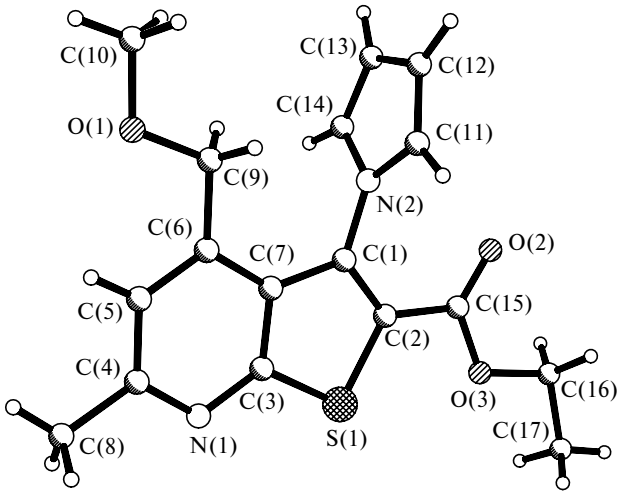


Fig. 1. Projection of the molecular model of compound **7a**.

Table 3. UV, IR, and ^{1}H NMR spectra of compounds **5—9**, **11**, and **12**

Compound	UV, λ_{max}/nm (logε)	IR, ν/cm^{-1}	^{1}H NMR, δ (J/Hz)
5a	217 (3.69), 241 (3.63), 343 (3.65)	1560 (C=C); 1315 (N—O); 1150 (C—O—C)	2.67 (s, 3 H, 6-Me); 3.23 (s, 3 H, OMe); 4.02 (s, 2 H, CH_2O); 6.35 (m, 2 H, H_β pyrrole); 6.73 (m, 2 H, H_α pyrrole); 7.27 (d, 2 H, H(2) and H(6) arom., J = 8.5); 7.37 (s, 1 H, H_{Py}); 8.13 (d, 2 H, H(3) and H(5) arom., J = 8.5)
5b	208 (3.82), 244 (3.77), 340 (3.72)	1580 (C=C); 1310 (N—O)	1.97, 2.73 (both s, 3 H each, 4-Me, 6-Me); 6.34 (m, 2 H, H_β pyrrole); 6.78 (m, 2 H, H_α pyrrole); 7.33 (d, 2 H, H(2) and H(6) arom., J = 8.6); 8.13 (d, 2 H, H(3) and H(5) arom., J = 8.6)
6	312 (4.14), 389 (3.72)	3100 (C—H); 1580 (C=C); 1360 (N—O); 1150 (C—O—C)	2.67 (s, 3 H, 6-Me); 3.22 (s, 3 H, OMe); 4.02 (s, 2 H, CH_2O); 5.47 (d, 1 H, $H(3)_{Fur}$, J = 5.2); 6.47 (m, 2 H, H_β pyrrole); 6.83 (m, 2 H, H_α pyrrole); 7.37 (s, 1 H, H_{Py}); 7.47 (d, 1 H, $H(4)_{Fur}$, J = 5.2)
7a	212 (3.93), 246 (3.84), 298 (3.62)	1710 (C=O); 1530 (C=C); 1230 (C—O—C)	1.87, 2.73 (both s, 3 H each, 4-Me, 6-Me); 3.75 (s, 3 H, COOMe); 6.27 (m, 2 H, H_β pyrrole); 6.73 (m, 2 H, H_α pyrrole)
7b	222 (3.77), 238 (3.71), 298 (3.69)	1700 (C=O); 1530 (C=C); 1230 (C—O—C); 1100 (C—O—C)	1.16 (t, 3 H, $COOCH_2\underline{Me}$); 2.63 (s, 3 H, 6-Me); 3.23 (s, 3 H, OMe); 3.93 (s, 2 H, CH_2O); 4.17 (q, 2 H, $COC\underline{H}_2Me$); 6.27 (m, 2 H, H_β pyrrole); 6.73 (m, 2 H, H_α pyrrole); 7.32 (s, 1 H, H_{Py})
7c	228(3.76), 241(3.72), 298 (3.65)	1690 (C=O); 1570 (C=C); 1250 (C—O—C)	1.17 (t, 3 H, $COOCH_2\underline{Me}$); 1.91, 2.59 (both s, 3 H each, 4-Me, 6-Me); 4.17 (q, 2 H, $OC\underline{H}_2Me$, J = 7.2); 6.23 (m, 2 H, H_β pyrrole); 6.72 (m, 2 H, H_α pyrrole); 7.03 (s, 1 H, H_{Py})
7d	212 (3.95), 246 (3.85), 298 (3.64)	1705 (C=O); 1530 (C=C); 1245 (C—O—C)	1.17 (t, 3 H, $OCH_2\underline{Me}$, J = 7.2); 1.87, 2.73 (both s, 3 H each, 4-Me, 6-Me); 4.17 (q, 2 H, $OC\underline{H}_2Me$ J = 7.2); 6.27 (m, 2 H, H_β pyrrole); 6.73 (m, 2 H, H_α pyrrole)
7e	208 (3.94), 227(3.78), 305 (3.78)	1690 (C=O); 1525 (C=C); 1245 (C—O—C); 1105 (C—O—C)	2.67 (s, 3 H, 6-Me); 3.23 (s, 3 H, OMe); 3.97 (s, 2 H, CH_2O); 6.31 (m, 2 H, H_β pyrrole); 6.85 (m, 2 H, H_α pyrrole); 7.05—7.50 (m, 5 H, Ph); 7.43 (s, 1 H, H_{Py})
7f	211 (3.75), 248 (3.58), 302 (3.45)	1690 (C=O); 1530 (C=C); 1245 (C—O—C)	1.93, 2.78 (both s, 3 H each, 4-Me, 6-Me); 6.28 (m, 2 H, H_β pyrrole); 6.71 (m, 2 H, H_α pyrrole); 7.01—7.21 (m, 5 H, Ph)
7k	211 (3.79), 245 (3.64), 299 (3.55)	1700 (C=O); 1545 (C=C); 1260 (C—O—C); 1100 (C—O—C)	2.67 (s, 3 H, 6-Me); 3.24 (s, 3 H, OMe); 3.97 (s, 2 H, CH_2O); 6.32 (m, 2 H, H_β pyrrole); 6.84 (m, 2 H, H_α pyrrole); 7.07 (d, 2 H, H(2) and H(6) arom., J = 8.7); 7.33 (d, 2 H, H(3) and H(5) arom., J = 8.7); 7.43 (s, 1 H, H_{Py})
8a	207 (4.12), 233 (3.97), 308 (3.62)	1640 (C=O); 1580 (C=C)	2.57 (s, 3 H, 6-Me); 3.15 (s, 3 H, OMe); 3.83 (s, 2 H, CH_2O); 6.27 (m, 2 H, H_β pyrrole); 6.53 (s, 2 H, H_α pyrrole); 7.05—7.28 (m, 10 H, 2 Ph); 7.06 (s, 1 H, H_{Py})
8b	208 (3.79), 303 (3.69),	3410 (N—H); 3100 (C—H); 1640 (C=O); 1580 (C=C)	0.86 (t, 3 H, Me, J = 6.9); 1.23 (m, 4 H, CH_2CH_2); 3.11 (t, 2 H, NCH_2, J = 6.9); 2.63 (s, 3 H, 6-Me); 3.23 (s, 3 H, OMe); 3.93 (s, 2 H, CH_2O); 5.67 (br.s, 1 H, NH); 6.42 (m, 2 H, H_β pyrrole); 6.93 (m, 2 H, H_α pyrrole); 7.01 (s, 1 H, H_{Py})
8c	208 (3.81), 237 (3.71), 300 (3.59)	3395 (N—H); 1620 (C=O); 1580 (C=C)	2.64 (s, 3 H, 6-Me); 3.19 (s, 3 H, OMe); 3.91 (s, 2 H, CH_2O); 4.32 (d, 2 H, NCH_2, J = 7.2); 6.33 (m, 2 H, H_β pyrrole); 6.43 (s, 1 H, NH); 6.93 (m, 2 H, H_α pyrrole); 7.03—7.27 (m, 5 H, Ph); 7.33 (s, 1 H, H_{Py})
8d	227 (3.63), 300 (3.58)	3410 (N—H); 1610 (C=O); 1550 (C=C); 1100 (C—O—C)	0.93 (m, 2 H, H_{ax}(3) and H_{ax}(5)); 1.15 (m, 1 H, H_{ax}(4)); 1.31 (m, 2 H, H_{ax}(2) and H_{ax}(6)); 1.56 (m, 3 H, H_{eq}(3), H_{eq}(4), H_{eq}(5)); 1.70 (m, 2 H, H_{eq}(2), H_{eq}(6)); 2.65 (s, 3 H, 6-Me); 3.23 (s, 3 H, OMe); 3.63 (m, 1 H, CHN); 3.93 (s, 2 H, CH_2O); 5.46 (d, 1 H, NH); 6.43 (m, 2 H, H_β pyrrole); 6.93 (m, 2 H, H_α pyrrole); 7.33 (s, 1 H, H_{Py})
9a	212 (3.89), 239 (3.89), 298 (3.57)	1670 (C=O); 1570 (C=C); 1220 (C—O—C)	2.63 (s, 3 H, 6-Me); 3.20 (s, 3 H, OMe); 3.87 (s, 2 H, CH_2O); 6.26 (m, 2 H, H_β pyrrole); 6.73 (m, 2 H, H_α pyrrole); 7.33 (s, 1 H, H_{Py}); 12.97 (br.s, 1 H, OH)

(*to be continued*)

Table 3 (*continued*)

Compound	UV, λ_{max}/nm (log ε)	IR, ν/cm^{-1}	^{1}H NMR, δ (*J*/Hz)
9b	211 (3.86), 248 (3.83), 298 (3.28)	1695 (C=O); 1560 (C=C)	1.85, 2.71 (both s, 3 H each, C(4)Me, C(6)Me); 6.23 (m, 2 H, H_β pyrrole); 6.73 (m, 2 H, H_α pyrrole); 12.97 (br.s, 1 H, OH)
11a	208(3.44), 233 (3.49), 307 (3.47)	3399, 3315 (N—H); 1615 (C=O); 1585 (C=C); 1090 (C—O—C)	2.63 (s, 3 H, 6-Me); 3.20 (s, 3 H, OMe); 3.87 (s, 2 H, CH_2O); 4.23 (br.s, 2 H, NH_2); 6.37 (m, 2 H, H_β pyrrole); 6.90 (m, 2 H, H_α pyrrole); 7.33 (s, 1 H, H_{Py}); 7.47 (br.s, 1 H, NH)
11b	301(3.38),	3390, 3310 (N—H); 1620 (C=O); 1590 (C=C)	1.87, 2.57 (both s, 3 H each, 4-Me, 6-Me); 4.23 (br.s, 2 H, NH_2); 6.37 (m, 2 H, H_β pyrrole); 6.93 (m, 2 H, H_α pyrrole); 7.03 (s, 1 H, H_{Py}); 7.43 (br.s, 1 H, NH)
12a	263 (4.00), 337 (3.81)	1640 (C=O); 1590 (C=C); 1090 (C—O—C)	2.59 (s, 3 H, 10-Me); 3.48 (s, 3 H, OMe); 4.76 (s, 2 H, CH_2O); 6.57 (m, 1 H, H(2) pyrrole); 7.07 (m, 1 H, H(3) pyrrole); 7.29 (s, 1 H, H_{Py}); 8.13 (m, 1 H, H(1) pyrrole); 11.82 (br.s, 1 H, NH)
12b	262 (3.82), 349 (3.87)	1620 (C=O); 1580 (C=C)	2.49, 2.86 (both s, 3 H each, 10-Me, 8-Me); 6.63 (m, 1 H, H(2) pyrrole); 7.11 (m, 1 H, H(3) pyrrole); 7.19 (s, 1 H, H_{Py}); 8.09 (m, 1 H, H(1) pyrrole); 11.92 (br.s, 1 H, NH)

Table 4. Selected bond lengths (*d*) in ethyl 4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxylate **7b**

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(3)	1.7270(19)	C(1)—C(7)	1.435(3)
S(1)—C(2)	1.7338(19)	C(2)—C(15)	1.476(3)
O(1)—C(9)	1.383(3)	C(3)—C(7)	1.399(2)
O(1)—C(10)	1.420(3)	C(4)—C(5)	1.402(3)
O(2)—C(15)	1.193(2)	C(4)—C(8)	1.494(3)
O(3)—C(15)	1.330(2)	C(5)—C(6)	1.377(3)
O(3)—C(16)	1.451(3)	C(6)—C(7)	1.415(3)
N(1)—C(4)	1.332(3)	C(6)—C(9)	1.502(3)
N(1)—C(3)	1.342(2)	C(11)—C(12)	1.352(3)
N(2)—C(11)	1.369(2)	C(12)—C(13)	1.402(3)
N(2)—C(14)	1.372(2)	C(13)—C(14)	1.347(3)
N(2)—C(1)	1.416(2)	C(16)—C(17)	1.477(4)
C(1)—C(2)	1.362(3)		

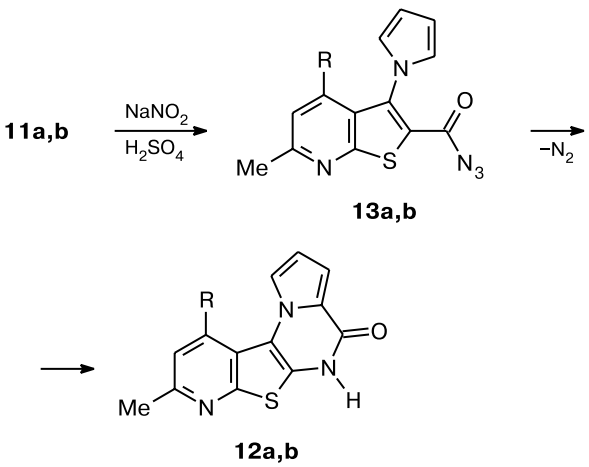
tronic absorption spectra of compounds **5**—**9** and **11**). The carboxylate fragment is also planar (all the five atoms of the ethoxycarbonyl group are coplanar); the average deviation of the atoms from the plane is 0.0084 Å (plane *3*). The planar ethoxycarbonyl group is rotated about plane *1* through an angle of 7° along the C(2)—C(15) bond; *i.e.*, there is an efficient conjugation (π,π-interaction) between the aromatic thienopyridine fragment and the ethoxycarbonyl group.

The presence of the pyrrole ring in structures **5**—**9** and **11** was confirmed by ^{1}H NMR data. Their spectra contain multiplet signals for the protons at δ 6.23—6.47 (β-protons) and δ 6.59—6.93 (α-protons), with spin-spin coupling constants characteristic of an *N*-substituted pyrrole.

In the IR spectra, the absorption band of CO stretching vibrations is shifted to the higher-frequency region by 20 to 55 (for esters **7a**—**k**), 70 (for amide **8a**), and ~20 cm^{-1} (for acid **9a**) compared to the spectra of the corresponding 3-aminothieno[2,3-*b*]pyridines **3a**—**e**,**f**,**i**,**n** [7] (see Tables 2, 3 and Experimental).

Diazotization of 3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carbohydrazides **11a,b** (Scheme 3) gave acyl azides **13a,b**, which are colorless crystals growing dark in air.

Scheme 3



R = CH_2OMe (**a**), Me (**b**)

Structure **13** was confirmed by IR spectroscopic data. In the IR spectra of compounds **13**, an intense absorption band for the stretching vibrations of the azido group ap-

Table 5. Selected bond angles (ω) in ethyl 4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxylate **7b**

Bond angle	ω/deg
C(3)—S(1)—C(2)	90.70(9)
C(9)—O(1)—C(10)	111.8(2)
C(15)—O(3)—C(16)	117.11(18)
C(4)—N(1)—C(3)	115.46(16)
C(11)—N(2)—C(14)	108.67(17)
C(11)—N(2)—C(1)	126.70(16)
C(14)—N(2)—C(1)	124.42(16)
C(2)—C(1)—N(2)	123.53(17)
C(2)—C(1)—C(7)	113.18(16)
N(2)—C(1)—C(7)	123.28(15)
C(1)—C(2)—C(15)	127.59(17)
C(1)—C(2)—S(1)	112.72(14)
C(15)—C(2)—S(1)	119.69(14)
N(1)—C(3)—C(7)	126.65(17)
N(1)—C(3)—S(1)	120.46(14)
C(7)—C(3)—S(1)	112.88(13)
N(1)—C(4)—C(5)	122.59(18)
N(1)—C(4)—C(8)	116.45(19)
C(5)—C(4)—C(8)	121.0(2)
C(6)—C(5)—C(4)	121.80(19)
C(5)—C(6)—C(7)	116.64(17)
C(5)—C(6)—C(9)	121.66(18)
C(7)—C(6)—C(9)	121.69(17)
C(3)—C(7)—C(6)	116.84(16)
O(3)—C(15)—C(2)	110.02(17)
O(3)—C(16)—C(17)	106.7(2)
C(3)—C(7)—C(1)	110.51(15)
C(6)—C(7)—C(1)	132.64(16)
O(1)—C(9)—C(6)	111.51(18)
C(12)—C(11)—N(2)	107.68(19)
C(11)—C(12)—C(13)	107.9(2)
C(14)—C(13)—C(12)	107.69(19)
C(13)—C(14)—N(2)	108.01(19)
O(2)—C(15)—O(3)	124.37(19)
O(2)—C(15)—C(2)	125.60(18)

Table 6. Selected torsion angles (θ) in ethyl 4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxylate **7b**

Torsion angle	θ/deg
C(5)—C(6)—C(9)—O(1)	−9.6
C(6)—C(9)—O(1)—C(10)	−174.6
C(2)—C(1)—N(2)—C(11)	−88.6
S(1)—C(2)—C(15)—O(2)	175.9
C(2)—C(15)—O(3)—C(16)	−176.2
C(15)—O(3)—C(16)—C(17)	178.1

pears at 2150—2130 cm^{-1} and the bands of C=O stretching vibrations are shifted to the higher-frequency region by 50 to 65 cm^{-1} compared to those for the starting hydrazides **11**.

Thermal decomposition of acyl azides **13a,b** affords tetracyclic products **12a,b** containing an amide CO group (see Table 3, IR spectra). The ^1H NMR spectra of compounds **12a,b** show three signals of equal intensity for the protons of the 1,2-disubstituted pyrrole ring (see Table 3). The $^1H—^1H$ NOESY 2D homonuclear spectrum of compound **12b** contains no cross peak corresponding to the spin-spin coupling between the N(5)H and C(3)H protons. This suggests that these protons are very distant from each other, thus confirming structure **12**.

Experimental

^1H NMR spectra were recorded on a Bruker WM-250 instrument (250.13 MHz) in DMSO-d_6—CCl_4 (1 : 3). $^1H—^1H$ NOESY 2D homonuclear spectra and ^{13}C NMR spectra with complete proton decoupling were recorded on a DRX-500 spectrometer in DMSO-d_6. IR spectra were recorded on a Specord IR75 instrument (NaCl prisms, suspensions of KBr in Vaseline oil). UV spectra were recorded on a Specord UV-VIS instrument in EtOH.

The physicochemical characteristics of the compounds obtained are given in Tables 1—3.

3-Amino-4-methoxymethyl-6-methylthieno[2,3-*b*]pyridines (3d,e,l,m,o,p). Solutions of a corresponding 3-cyanopyridine-2(1*H*)-thione (10 mmol) in 20—25 mL of DMF, 10% KOH (5.6 mL), and alkyl halide (10 mmol) were mixed. The reaction mixture was kept for 15 min and 10% KOH (5.6 mL) was added. The mixture was stirred at ~20 °C for 2.5—3 h and then diluted with water (10 mL). The precipitate was filtered off, washed with water, and dried. Compounds **3d,e**,**l**,**m**,**p** were recrystallized from DMF, while compound **3o** was recrystallized from EtOH.

IR, ν/cm^{-1}: **3d**, 3400, 3310, 1660, 1595, 1100; **3e**, 3410, 3320, 1680, 1595, 1080; **3l**, 3480, 3405, 1580, 1518, 1230; **3m**, 3420, 3320, 1660, 1595; **3o**, 3480, 3340, 1650, 1590; **3p**, 3510, 3370, 1660, 1580.

^1H NMR, δ: **3d**, 2.63 (s, 3 H, Me), 3.47 (s, 3 H, OMe), 4.83 (s, 2 H, CH_2), 7.03 (br.s, 2 H, NH_2), 7.17 (s, 1 H, H_{Py}), 7.19—7.45 (m, 5 H, Ph); **3e**, 2.61 (s, 3 H, Me), 3.37 (s, 3 H, OMe), 4.70 (s, 2 H, CH_2), 6.85—7.28 (m, 7 H, ΣNH_2, H_{Py}, H arom.); **3m**, 2.60, 2.73 (both s, 3 H each, Me(6), Me(4)), 3.75 (s, 3 H, COOMe), 6.02 (br.s, 2 H, NH_2); **3o**, 1.32 (t, 3 H, Me, J = 7.1 Hz), 2.63, 2.85 (both s, 3 H each, Me(6), Me(4)), 4.27 (q, 2 H, CH_2, J = 7.1 Hz), 6.77 (br.s, 2 H, NH_2); **3p**, 2.63, 2.78 (both s, 3 H each, Me(6), Me(4)), 6.17 (br.s, 2 H, NH_2), 7.15—7.39 (m, 5 H, Ph).

UV, λ_{max}/nm (logε): **3d**, 293 (5.52), 378 (4.78); **3e**, 208 (4.01), 219 (3.93), 292 (3.69), 382 (3.39); **3l**, 288 (3.65), 379 (3.16); **3m**, 289 (4.00), 373 (3.26); **3o**, 289 (4.11), 372 (3.29); **3p**, 292 (3.99), 427 (3.52).

Ethyl 4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxylate (7b). 2,5-Dimethoxytetrahydrofuran (0.46 mL, 3.5 mmol) was added to a stirred boiling solution of compound **3c** (0.84 g, 3 mmol) in 4 mL of glacial AcOH. The reaction mixture was refluxed for 3 h, cooled, and diluted with ice water (15 mL). The precipitate that formed was filtered off, washed with water to a neutral reaction, dried, and recrystallized from EtOH—DMF (5 : 1). The yield of compound **7b** was 0.92 g (93%). Compounds **5**, **6**, **7a,c—k**, and **8a**

were obtained analogously. The completion of each reaction was determined by TLC in hexane—acetone (2 : 1). The reaction was prolonged until the spot of the starting 3-aminothieno[2,3-*b*]pyridine disappeared. Compounds **5**, **6**, **7a**,**c**—**k**, and **8a** were recrystallized from aqueous DMF.

Crystals for X-ray diffraction analysis were obtained by repeated crystallization of compound **7b** from acetone. Colorless crystals are monoclinic, $C_{17}H_{18}N_2O_3S$, a = 8.490(2) Å, b = 20.497(4) Å, c = 9.975(2) Å; α = 90.0(3)°, β = 103.80(3)°, γ = 90.00(3)°, V = 1685.7(6) Å^3, d_{calc} = 1.302 g cm^{-3}, space group $P2(1)/c$, Z = 4. The X-ray diffraction analysis was carried out at 293(2) K on a CAD4 automatic diffractometer (Mo-$K\alpha$ radiation, graphite monochromator, θ/2θ scan mode from 2.33° to $2\theta_{max}$ = 24.98°). The crystal size is 0.48×0.35×0.28 mm. The number of reflections with $I > 3\sigma$ was 2206. The structure was solved by the direct method with the SHELXTL program package[9] and refined in the anisotropic (isotropic for H atoms) approximation to R_1 = 0.0315 and wR_2 = 0.0869. Atomic coordinates have been deposited with the Cambridge Crystallographic Database.

***N*-Butyl-4-methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carboxamide (8b).** A solution of compound **7b** (0.99 g, 3 mmol) in butylamine (4 mL, 41 mmol) was refluxed for 6.5 h. The reaction mixture was diluted with water (20 mL). The precipitate that formed was filtered off, washed with water, dried, and recrystallized from aqueous DMF (DMF—water, 3 : 1). The yield of carboxamide **8b** was 0.92 g (86%). Compounds **8c**,**d** were obtained analogously.

4-Methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridinecarboxylic acid (9a). To a suspension of ester **7b** (0.99 g, 3 mmol) in 10 mL of EtOH 30% KOH (4.54 mmol, 0.19 mL) was added. The reaction mixture was heated until it was completely homogeneous. On cooling, the mixture was acidified with 10% HCl to pH ≈3. The precipitate that formed was filtered off, washed with water, dried, and recrystallized from dioxane. The yield of acid **9a** was 0.87 g (96%). Compound **9b** was obtained analogously.

4-Methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carbohydrazide (11a). Aqueous 85% hydrazine (0.85 mL, 27 mmol) was added to a suspension of ester **7b** (0.99 g, 3 mmol) in 20 mL of EtOH. The reaction mixture was refluxed for 5 h, concentrated to 1/3 of the initial volume, and then diluted with water. Crystals of compound **11a** were filtered off, washed with water, dried, and recrystallized from DMF. The yield of carbohydrazide **11a** was 0.82 g (85%). Compound **11b** was obtained analogously.

4-Methoxymethyl-6-methyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carbonyl azide (13a). Conc. H_2SO_4 (0.23 mL) was added to a solution of compound **11a** (1 g, 3.02 mmol) in 7 mL of glacial AcOH. The reaction mixture was cooled to +5 °C and then $NaNO_2$ (0.29 g, 4.23 mmol) in 1 mL of water was added for 10 min. The reaction mixture was warmed to ~20 °C, stirred for 1.5 h, and poured into water with finely crushed ice. The precipitate that formed was filtered off, washed with cold water to a neutral reaction, and dried in a desiccator over P_2O_5. The yield of azide **13a** was 0.65 g (65%), m.p. 112—113 °C (decomp.). IR, ν/cm^{-1}: 2130, 1680, 1580, 1095.

4,6-Dimethyl-3-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyridine-2-carbonyl azide (13b) was obtained by analogy with compound **13a**. The yield of azide **13b** was 63%, m.p. 108—109 °C (decomp.). IR, ν/cm^{-1}: 2150, 1670, 1580.

10-Methoxymethyl-8-methyl-4,5-dihydropyrido[3′,2′:4,5]thieno[2,3-*e*]pyrrolo[1,2-*a*]pyrazin-4-one (12a). A suspension of compound **13a** (1 g, 3.05 mmol) in 20 mL of anhydrous toluene was refluxed for 40 min. On cooling, crystals were filtered off, dried, and recrystallized from DMF. The yield of compound **12a** was 0.62 g (68%).

8,10-Dimethyl-4,5-dihydropyrido[3,′2′:4,5]thieno[2,3-*e*]pyrrolo[1,2-*a*]pyridin-4-one (12b) was obtained analogously. ^{13}C NMR, δ: 22.98 (C(8)$\underline{C}H_3$); 24.35 (C(10)$\underline{C}H_3$); 110.89 (C(2)H); 111.05 (C(3)); 111.45 (C(5a)); 120.75 (C(10b)); 122.11 (C(1)); 123.06 (C(9)); 123.88 (C(10a)); 126.79 (C(3a)); 138.38 (C(10)); 152.89 (C=O); 152.95 (C(8)) 154.09 (C(6a)).

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