Regioselective acylation of methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate

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The influence of catalysts, acid chlorides, and solvents on the acylation of methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate was studied. The use of $AlCl_3$ allows the regioselective introduction of the acyl group into position 3 to be performed, whereas the acyl group is regioselectively introduced into position 6 of thienopyrrole when $SnCl_4$ is used.

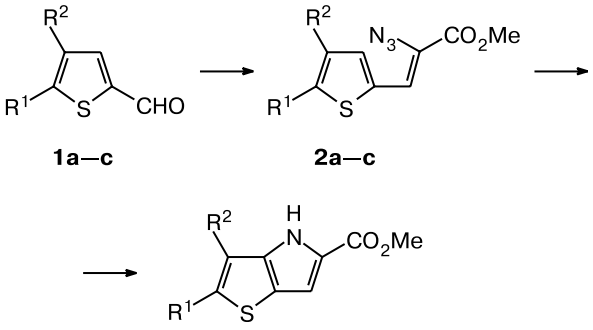
Key words: thienopyrroles, regioselective acylation, ionic liquid.

Thienopyrroles are thio analogs of indoles and, hence, are of great interest for syntheses of various biologically active compounds. Considerable attention is presently given to the synthesis of physiologically active compounds from esters of 4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acid.[1—3]

Taking into account the electron-excessive nature of thienopyrroles, they are modified, as a rule, using electrophilic processes. However, regioselective reactions with thienopyrroles bearing free positions in both the thiophene and pyrrole cycles are a serious and yet poorly studied problem.

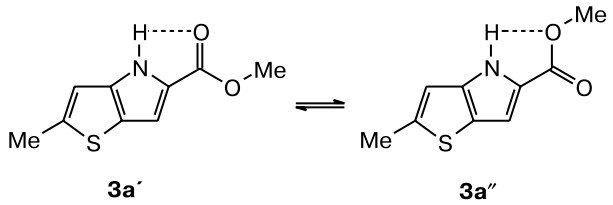
In this work, using a described method,[4] we carried out condensations of thiophenecarbaldehydes **1** with methyl azidoacetate to form esters of 2-azido-3-(2-thienyl)acrylic acids, which produced thienopyrrolecarboxylates **3** (Scheme 1) and studied the regioselectivity of acylation of methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (**3a**) (Scheme 2). Compounds **3b,c** were synthesized for unambiguous interpretation of NMR spectra of the isomers formed upon acylation of ester **3a**.

Scheme 1



R^1 = Me, R^2 = H (**a**), Br (**b**); $R^1 = R^2$ = H (**c**)

Thienopyrrole **3a** can exist as two rotamers (**3a′** and **3a″**) stabilized by the intramolecular hydrogen bond.



The IR spectrum of thienopyrrole **3a** exhibits one band with the frequency ν(NH) = 3466 cm^{-1}. Since the IR spectrum of ethyl 1*H*-pyrrole-2-carboxylate is known to have two absorption bands with the frequencies ν(NH) = 3465 and 3482 cm^{-1}, which are assigned to rotamers with the intramolecular hydrogen bond of the pyrrole nitrogen atom with the keto or ester group, respectively,[5] we can conclude that thienopyrrole **3a** exists in the form of **3a′**.* Also note that, according to the X-ray diffraction data, the pyrrole nitrogen atom in ethyl 4*H*-furan[3,2-*b*]pyrrole-5-carboxylate is bound to the carbonyl group of the ester fragment.[6]

Since a molecule of thienopyrrole **3a** has several reaction centers, we studied the influence of the nature of catalysts, reactants, and solvents on the acylation process.

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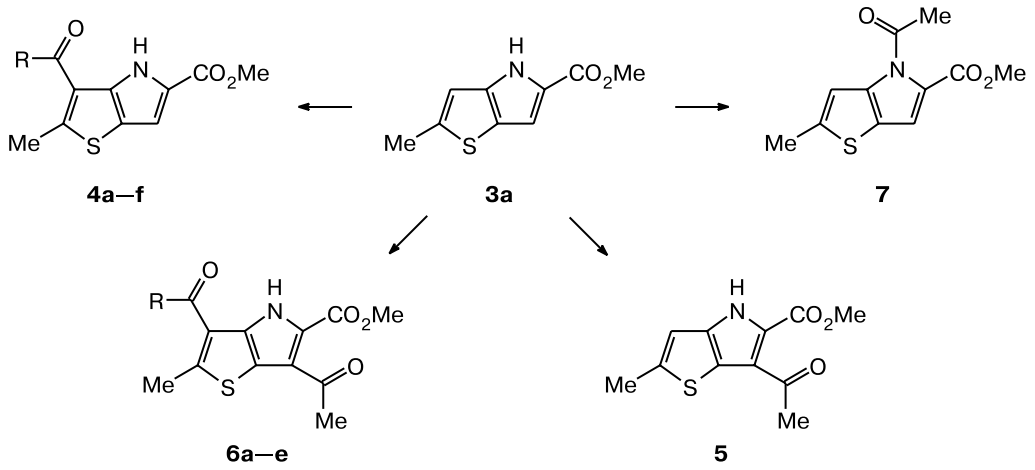
Scheme 2



R = Me (**a**), Et (**b**), $ClCH_2$ (**c**), Cl_2CH (**d**), Cl_3C (**e**), Pr^i (**f**)

The results of acylation in dichloroethane, nitromethane, and ionic liquid, *viz.*, 1-butyl-3-methylimidazolium heptachloroaluminate(III) [bmim][Al_2Cl_7], at different ratios of acyl halide, $AlCl_3$, $SnCl_4$, and thienopyrrole **3a** are presented in Table 1.

It is seen from the data in Table 1 that acylation in dichloroethane is regioselective to the thiophene cycle when two or three equivalents of $AlCl_3$ and acyl halide are used (entries *1*—*7*). The $AlCl_3$ complexes formed at the ester and acyl groups prevent, most likely, the interaction of acid chloride with the pyrrole ring of the initial ester **3a** and acylation products **4a—f**.

When equimolar amounts of the reactants are used in both nitromethane and dichloroethane, the formation of

Table 1. Acylation of thienopyrrole **3a**

Entry	Acyl halide	Molar ratio[a]	Solvent	Composition of acylation products (%) **4a—f** : **6a** : **5**
1	MeCOCl	1 : 1 : 2.1 [b]	$Cl(CH_2)_2Cl$	100 (**4a**) : 0 : 0
2	MeCOCl	2.1 : 1 : 3.1 [b]	$Cl(CH_2)_2Cl$	100 (**4a**) : 0 : 0
3	EtCOCl	1 : 1 : 2.1 [b]	$Cl(CH_2)_2Cl$	100 (**4b**) : 0 : 0
4	$ClCH_2COCl$	1 : 1 : 2.1 [b]	$Cl(CH_2)_2Cl$	100 (**4c**) : 0 : 0
5	$Cl_2CHCOCl$	1 : 1 : 2.1 [b]	$Cl(CH_2)_2Cl$	100 (**4d**) : 0 : 0
6	Cl_3CCOCl	1 : 1 : 2.1 [b]	$Cl(CH_2)_2Cl$	100 (**4e**) : 0 : 0
7	Pr^iCOCl	1 : 1 : 2.1 [b]	$Cl(CH_2)_2Cl$	100 (**4f**) : 0 : 0
8	MeCOCl	1 : 1 : 1.1 [b]	$Cl(CH_2)_2Cl$	25 (**4a**) : 0 : 75
9	MeCOCl	1 : 1 : 1.1 [b]	$MeNO_2$	10 (**4a**) : 0 : 90
10	MeCOCl	3.1 : 1 : 5 [b]	$Cl(CH_2)_2Cl$	40 (**4a**) : 60 : 0
11	MeCOCl	1.1 : 1 : 1.1 [c]	$Cl(CH_2)_2Cl$	35 (**4a**) : 0 : 60
12	MeCOCl	1.1 : 1 : 2 [b,d]	[bmim][Al_2Cl_7]	100 (**4a**) : 0 : 0
13	$ClCH_2COCl$	1.1 : 1 : 2 [b,d]	[bmim][Al_2Cl_7]	100 (**4c**) : 0 : 0
14	MeCOCl	1.1 : 1 : 1.1 [e]	$Cl(CH_2)_2Cl$	35 (**4a**) : 0 : 65
15	MeCOCl	2.1 : 1 : 2.1 [e]	$Cl(CH_2)_2Cl$	0 (**4a**) : 20 : 80
16	MeCOCl	2.1 : 1 : 4.1 [e]	$Cl(CH_2)_2Cl$	0 (**4a**) : 100 : 0
17	MeCOCl	1 : 1 : 2.1 [e]	$Cl(CH_2)_2Cl$	0 (**4a**) : 0 : 100

[a] Acyl halide : thienopyrrole **3a** : Lewis acid.
[b] Lewis acid is $AlCl_3$.
[c] Lewis acid is $AlBr_3$.
[d] No $AlCl_3$ was added in excess of the amount contained in the Al_2Cl_7 anion.
[e] Lewis acid is $SnCl_4$.

product **5** becomes predominant because thienopyrrole, which is not bound to the catalyst, enters into the reaction under these conditions (entries *8* and *9*). It is of interest that the use of a significant excess of $AlCl_3$ and acetyl chloride also results in the acylation of the pyrrole cycle to form diacylation product **6a** (entry *10*). This is possibly reasoned by the formation of the $AlCl_3$ complex at the thiophene cycle, which also decreases the relative reactivity of the latter. Diketone **6a** is not formed by the acetylation of 3-acetylthienopyrrole-5-carboxylate **4a** in the presence of $AlCl_3$ but can be synthesized from keto ester **5**. This indicates that the reaction leading to the diacetyl-substituted compound **6a** begins from the introduction of the acetyl group into the pyrrole cycle.

The use of a stronger Lewis acid ($AlBr_3$) in equimolar amounts with acetyl chloride and thienopyrrole decreases the formation of the product of acylation at the pyrrole cycle compared to that formed when $AlCl_3$ is used. This is likely related to an increase in the volume of the acylating complex and an enhancement of its reactivity (entry *11*). The acylation of thienopyrrole **3a** with acyl halides in 1-butyl-3-methylimidazolium heptachlorodialuminate(III) affords in high yields only products of substitution at the thiophene cycle (entries *12* and *13*). When 1 equiv. of $SnCl_4$, which is a weaker Lewis acid than $AlCl_3$, and 1 equiv. of acetyl chloride in dichloroethane are used, a smaller amount of keto ester **5** and, correspondingly, more keto ester **4a** (entry *14*) are formed than in experiments with $AlCl_3$. The use of 2 equiv. of $SnCl_4$ and 2 equiv. of acetyl chloride makes it possible to increase the yield of keto ester **5** with the additional formation, however, of diacylation product **6a** (entry *15*). Only diacetyl-substituted ester **6a** forms in the presence of 4 equiv. and more of $SnCl_4$ and 2 equiv. of acetyl chloride (entry *16*). We succeeded to selectively synthesize monoketo ester **5** when using 2 equiv. of $SnCl_4$ and 1 equiv. of acetyl chloride (entry *17*).

Thus, the use of $SnCl_4$ allows the regioselective acetylation of the pyrrole cycle to be performed with the formation of diacetyl-substituted ester **6a** in one step.

The target synthesis of various mixed diacyl-substituted derivatives **6b—e** was performed by the successive regioselective introduction of one acyl group into the thiophene cycle of thienopyrrole **3a** in the presence of $AlCl_3$ in dichloroethane (products **4b—e**) and then another introduction into the pyrrole ring in the presence of $SnCl_4$ in nitromethane. The latter reaction does not occur in dichloroethane, which poorly dissolve complexes of compounds **4b—e** with the catalyst.

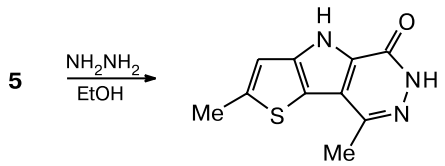
Acetylation at the pyrrole nitrogen atom of thienopyrrole **3a** was successful in the presence of potassium *tert*-butoxide (product **7**).

The structures of the synthesized compounds were proved by the data of ^1H and ^{13}C spectroscopy, elemental analysis, and chemical transformations.

The ratios of ketones resulting from acylation were determined from the ratio of intensities of signals from the pyrrole, thiophene, and ester protons. The ^1H NMR spectrum of thienopyrrole **7** acylated at the nitrogen atom contains signals from both rings of the diheterocycle, and the signal of the proton at the nitrogen atom is absent.

The signals in the ^{13}C NMR spectrum of thienopyrrole **3c** were completely assigned from their multiplicity in the gated regime. This assignment exactly coincided with the data of the {^1H and ^{13}C} correlation spectrum by far-range spin-spin coupling constants. The signals in compounds **3a**, **4a**, and **5** were assigned based on the data for ester **3c** using the additive scheme taking into account the influence of substituents on the chemical shifts of ^{13}C in thiophenes[7] and pyrroles[8] (Table 2).

The structure of keto ester **5** was chemically confirmed by its transformation into pyridazinone **8** under the action of hydrazine.



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Thus, we developed the methods for regioselective introduction of acyl groups into different positions of thienopyrrole **3a**. It was shown that the position of acyl groups in the reaction products can unambiguously be determined from the NMR spectroscopic data.

Table 2. ^{13}C NMR spectra (δ) of thienopyrroles **3a,c**, **4a**, and **5**

Compound	C(2)	C(3)	C(5)	C(6)	C(7)	C(8)	C(O)O	OMe	2-Me	3-MeC(O)		6-MeC(O)	
										Me	C(O)	Me	C(O)
3a	143.8	110.3	124.7	107.4	121.9	142.1	161.4	51.2	16.6	—	—	—	—
3c	129.7	111.8	126.2	107.2	123.3	142.4	161.3	51.4	—	—	—	—	—
4a	153.2	126.0	123.5	107.5	119.3	140.1	160.9	51.5	17.6	30.8	192.7	—	—
5	145.6	109.7	124.8	123.4	121.4	138.7	160.3	51.3	16.4	—	—	30.2	193.2

Experimental

^{1}H NMR spectra were recorded on Bruker WM-200 (200 MHz) and Bruker WM-250 (250 MHz) instruments in DMSO-d_6 and $CDCl_3$ relatively to HMDS. {^{1}H and ^{13}C} correlation spectra by long-range spin-spin coupling constants were obtained on a Bruker DRX-500 instrument. Mass spectra were recorded on a Varian MAT CH-6 instrument with direct injection of a sample into the ion source, an ionization energy of 70 eV, and an accelerating voltage of 1.75 kV. Melting points were measured on a Boetius heating stage and were not corrected. Reaction mixtures were analyzed and purity of isolated products was monitored by TLC on Silufol UV-254 plates using an AcOEt—hexane (1 : 3, vol/vol) mixture as eluent.

IR spectra were recorded on a Specord M-80 instrument in the 3600—3000 and 1800—1600 cm^{-1} frequency regions (c = 0.01 mol L^{-1} in dichloroethane) in cells with windows of fluorite CaF_2 and d = 0.165 and 3.10 cm, respectively.

In order to synthesize complexes, anhydrous $AlCl_3$ ($SnCl_4$) was weighted guarding against air moisture and added by required amounts of thienopyrrole and anhydrous dichloroethane with slight heating until a suspension formed. The resulting complexes were rapidly transferred into cells.

Anhydrous dichloroethane was prepared by distillation above P_2O_5. Commercially available 2-thiophenecarbaldehyde and 5-methyl-2-thiophenecarbaldehyde were used as initial substances in the syntheses of compounds **2a—c**. 4-Bromo-5-methylthiophene-2-carbaldehyde and methyl azidoacetate were synthesized using described procedures.[9,10] 1-Butyl-3-methylimidazolium heptachlorodialuminate(III) was synthesized according to a known procedure.[11]

Methyl 2-azido-3-(2-thienyl)acrylates (2a—c) (general procedure). A mixture of sodium methoxide, prepared from Na (1.8 g, 78.3 mmol) and dehydrated MeOH (30 mL), and methyl azidoacetate (22.8 g, 0.2 mol) was added by the corresponding thiophenecarbaldehyde (25—45 mmol) with stirring at −5—0 °C. The mixture was stirred for 30 min at 0 °C and for 2 h at ~20 °C. An aqueous solution of saturated NH_4Cl was added, and the resulting mixture was stirred for 10 min. The precipitated that formed was filtered off and dried.

Methyl 2-azido-3-(5-methyl-2-thienyl)acrylate (2a). The yield was 76%, m.p. 51 °C (with decomp.). MS, *m/z*: 223 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 2.55 (s, 3 H, Me); 3.80 (s, 3 H, MeO); 6.74 (s, 1 H, CH); 7.10 (s, 1 H, CH_{arom}); 7.15 (s, 1 H, CH_{arom}). IR (KBr), ν/cm^{-1}: 2120 v.s (N_3). Found (%): C, 48.52; H, 4.20; N, 19.02; S, 14.81. $C_9H_9N_3O_2S$. Calculated (%): C, 48.42; H, 4.06; N, 18.82; S, 14.36.

Methyl 2-azido-3-(4-bromo-5-methyl-2-thienyl)acrylate (2b). The yield was 52%, m.p. 91 °C (with decomp.). MS, *m/z*: 301 and 303 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 2.45 (s, 3 H, Me); 3.90 (s, 3 H, MeO); 6.98 (s, 1 H, CH); 7.14 (s, 1 H, CH_{arom}). IR (KBr), ν/cm^{-1}: 2128 v.s (N_3). Found (%): C, 36.00; H, 2.79; Br, 26.52; N, 14.05; S, 10.81. $C_9H_8BrN_3O_2S$. Calculated (%): C, 35.78; H, 2.67; Br, 26.45; N, 13.91; S, 10.61.

Methyl 2-azido-3-(2-thienyl)acrylate (2c). The yield was 49%, m.p. 43 °C (with decomp.). MS, *m/z*: 209 $[M]^+$. Found (%): C, 46.12; H, 3.36; N, 19.02; S, 15.41. $C_8H_7N_3O_2S$. Calculated (%): C, 45.92; H, 3.37; N, 19.11; S, 15.33.

Methyl 4*H*-thieno[3,2-*b*]pyrrole-5-carboxylates (3a—c) (general procedure). A solution of methyl 2-azido-3-(2-thienyl)acrylate **2a—c** (30 mmol) in toluene (10—15 mL) was refluxed for 3 h. A precipitate that formed was filtered off, and the mother liquor was concentrated *in vacuo* and recrystallized from toluene. The residues were combined.

Methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (3a). The yield was 95%, m.p. 189—190 °C (from toluene). MS, *m/z*: 195 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 2.54 (s, 3 H, Me); 3.82 (s, 3 H, MeO); 6.65 (s, 1 H, CH_{arom}); 7.06 (s, 1 H, CH_{arom}); 9.25 (br.s, 1 H, NH). Found (%): C, 55.40; H, 4.65; N, 7.23; S, 16.53. $C_9H_9NO_2S$. Calculated (%): C, 55.37; H, 4.65; N, 7.17; S, 16.42.

Methyl 3-bromo-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (3b). The yield was 93%, m.p. 163—165 °C (from toluene). MS, *m/z*: 195 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 2.54 (s, 3 H, Me); 3.82 (s, 3 H, MeO); 6.65 (s, 1 H, CH_{arom}); 7.06 (s, 1 H, CH_{arom}); 9.25 (br.s, 1 H, NH). Found (%): C, 39.53; H, 2.93; Br, 29.15; N, 5.19; S, 11.82. $C_9H_8BrNO_2S$. Calculated (%): C, 39.43; H, 2.94; Br, 29.15; N, 5.11; S, 11.70.

Methyl 4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (3c). The yield was 93%, m.p. 143—145 °C (from toluene). MS, *m/z*: 181 $[M]^+$. ^{1}H NMR (DMSO-d_6), δ: 3.81 (s, 3 H, MeO); 6.99 (dd, 1 H, CH_{arom}, ^3J = 5.3 Hz, ^4J = 0.73 Hz); 7.11 (s, 1 H, CH_{arom}); 7.52 (d, 1 H, CH_{arom}, ^3J = 5.3 Hz); 12.09 (br.s, 1 H, NH). Found (%): C, 53.12; H, 3.90; N, 7.82; S, 17.68. $C_8H_7NO_2S$. Calculated (%): C, 53.02; H, 3.89; N, 7.73; S, 17.70.

3-Acyl derivatives of methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4a—f) (general procedure). Acyl chloride (0.52 mmol) was added with stirring to a suspension of methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (0.1 g, 0.51 mmol) and $AlCl_3$ (0.14 g, 1.02 mmol) in dichloroethane (5 mL). The mixture was stirred for 5 h (TLC monitoring), poured into water, extracted with AcOEt, washed with water and a saturated aqueous solution of NaCl, and dried with $MgSO_4$. The solvent was distilled off *in vacuo*. The product was recrystallized from EtOH.

Methyl 3-acetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4a). The yield was 95%, m.p. 168—170 °C (from EtOH). MS, *m/z*: 237 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 2.58 (s, 3 H, Me); 2.82 (s, 3 H, MeC(O)); 3.90 (s, 3 H, MeO); 7.02 (s, 1 H, CH); 9.84 (br.s, 1 H, NH). Found (%): C, 55.72; H, 4.65; N, 6.05; S, 13.71. $C_{13}H_{13}NO_4S$. Calculated (%): C, 55.68; H, 4.67; N, 5.90; S, 13.51.

Methyl 2-methyl-3-propionyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4b). The yield was 67%, m.p. 134—136 °C (from EtOH). MS, *m/z*: 251 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 1.10 (t, 3 H, Me, J = 7 Hz); 2.72 (s, 3 H, Me); 3.05 (q, 2 H, CH_2, J = 7 Hz); 3.83 (s, 3 H, MeO); 7.12 (s, 1 H, CH); 11.17 (br.s, 1 H, NH). Found (%): C, 57.55; H, 5.19; N, 5.77; S, 12.87. $C_{12}H_{13}NO_3S$. Calculated (%): C, 57.35; H, 5.21; N, 5.57; S, 12.76.

Methyl 3-chloroacetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4c). The yield was 77%, m.p. 158—160 °C (from EtOH). MS, *m/z*: 271 $[M]^+$. ^{1}H NMR (DMSO-d_6), δ: 2.74 (s, 3 H, Me); 3.84 (s, 3 H, MeO); 5.16 (s, $CH_2C(O)$); 7.14 (s, 1 H, CH); 11.44 (s, 1 H, NH). Found (%): C, 48.72; H, 3.70; Cl, 13.10; N, 5.23; S, 11.92. $C_{11}H_{10}ClNO_3S$. Calculated (%): C, 48.62; H, 3.71; Cl, 13.05; N, 5.15; S, 11.80.

Methyl 3-dichloroacetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4d). The yield was 67%, m.p. 163—165 °C (from

EtOH). MS, *m/z*: 306 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 2.74 (s, 3 H, Me); 3.84 (s, 3 H, MeO); 7.20 (s, 1 H, CH); 7.88 (s, 1 H, Cl_2CH); 11.98 (s, 1 H, NH). Found (%): C, 43.22; H, 2.95; Cl, 23.24; N, 4.64; S, 10.62. $C_{11}H_9Cl_2NO_3S$. Calculated (%): C, 43.15; H, 2.96; Cl, 23.16; N, 4.57; S, 10.47.

Methyl 2-methyl-3-trichloroacetyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4e). The yield was 66%, m.p. 147—149 °C (from EtOH). MS, *m/z*: 341 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 2.62 (s, 3 H, Me); 3.72 (s, 3 H, MeO); 7.14 (s, 1 H, CH); 11.54 (s, 1 H, NH). Found (%): C, 38.92; H, 2.37; Cl, 31.28; N, 4.20; S, 9.61. $C_{11}H_8Cl_3NO_3S$. Calculated (%): C, 38.79; H, 2.37; Cl, 31.23; N, 4.11; S, 9.41.

Methyl 3-isobutyryl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (4f). The yield was 63%, m.p. 107—109 °C (from EtOH). MS, *m/z*: 265 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 1.08 (s, 3 H, Me); 1.11 (s, 3 H, Me); 2.66 (s, 3 H, Me); 3.55 (t, 1 H, CH, J = 6.68 Hz); 3.83 (s, 3 H, MeO); 7.13 (s, 3 H, CH_{arom}); 11.51 (s, 1 H, NH). Found (%): C, 58.90; H, 5.71; N, 5.31; S, 12.14. $C_{13}H_{15}NO_3S$. Calculated (%): C, 58.85; H, 5.70; N, 5.28; S, 12.09.

The influence of the amount of reactants and nature of the catalyst and solvent on the direction of acylation of thienopyrrole **3a** was studied under similar conditions.

Acylation of thienopyrrole 3a in the ionic liquid, 1-butyl-3-methylimidazolium heptachlorodialuminate(III). 1-Butyl-3-methylimidazolium heptachlorodialuminate(III) (0.132 g, 0.75 mmol) was added by $AlCl_3$ (0.202 g, 1.52 mmol) with gentle stirring in an argon atmosphere until a homogeneous mixture formed (the mixture warmed). Acyl chloride (0.77 mmol) was added to the resulting ionic liquid with stirring under argon. The mixture was stirred for 15 min, and thienopyrrole **3a** (0.146 g, 0.75 mmol) was added. The mixture was stirred for 2 h, poured into water, and filtered off. Keto esters **4a** and **4b** were obtained in 92 and 90% yields, respectively.

Methyl 6-acetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (5). Ester **3a** (0.1 g, 0.51 mmol) was added to $SnCl_4$ (0.063 mL, 0.54 mmol) and acetyl chloride (0.04 mL, 0.57 mmol) in dichloroethane (5 mL). The mixture was stirred for 3 h (TLC monitoring). The reaction mixture was poured into water, extracted with AcOEt, washed with water and a saturated aqueous solution of NaCl, and dried with $MgSO_4$. The solvent was distilled off *in vacuo*. The yield was 93%, m.p. 139—141 °C (from EtOH). MS, *m/z*: 237 $[M]^+$. ^1H NMR ($CDCl_3$), δ: 2.58 (s, 3 H, Me); 2.82 (s, 3 H, MeC(O)); 3.90 (s, 3 H, MeO); 7.02 (s, 1 H, CH); 9.84 (br.s, 1 H, NH). Found (%): C, 55.73; H, 4.65; N, 5.95; S, 13.62. $C_{11}H_{11}NO_3S$. Calculated (%): C, 55.68; H, 4.67; N, 5.90; S, 13.51.

Methyl 3,6-diacetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (6a). Acetyl chloride (0.23 mL, 3.23 mmol) was added to methyl 2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (0.3 g, 1.54 mmol) and $SnCl_4$ (0.74 mL, 6.31 mmol) in dichloroethane (10 mL). The mixture was stirred for 3 h (TLC monitoring). The reaction mixture was poured into water, extracted with AcOEt, and dried with $MgSO_4$. The solvent was distilled off *in vacuo*. The residue was recrystallized from EtOH. The yield was 78%, m.p. 141—144 °C (from EtOH). MS, *m/z*: 279 $[M]^+$. ^1H NMR ($CDCl_3$), δ: 2.60 (s, 3 H, Me); 2.82 (s, 3 H, MeC(O)); 2.86 (s, 3 H, MeC(O)); 4.00 (s, 3 H, MeO); 10.12 (br.s, 1 H, NH). Found (%): C, 56.12; H, 4.75; N, 5.12; S, 11.68. $C_{13}H_{13}NO_4S$. Calculated (%): C, 55.90; H, 4.69; N, 5.01; S, 11.48.

Methyl 3,6-diacetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylates (6b—e) (general procedure). Methyl 3-acyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate **4b—e** (0.3 mmol) and $SnCl_4$ (0.14 mL, 1.23 mmol) in nitromethane (2 mL) were added by the corresponding acyl halide (0.35 mmol). The mixture was stirred for 3 h (TLC monitoring). The reaction mixture was poured into water and extracted with AcOEt. The extract was washed with water and a saturated aqueous solution of NaCl and dried with $MgSO_4$. The solvent was distilled off.

Methyl 6-acetyl-2-methyl-3-propionyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (6b). The yield was 62%, m.p. 123—125 °C (from EtOH). MS, *m/z*: 293 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 1.10 (t, 3 H, Me, J = 6.86 Hz); 2.61 (s, 3 H, Me); 2.74 (s, 3 H, MeC(O)); 3.01 (q, 2 H, CH_2, J = 6.82 Hz); 3.92 (s, 3 H, MeO); 11.66 (br.s, 1 H, NH). Found (%): C, 57.41; H, 5.14; N, 4.88; S, 11.05. $C_{14}H_{15}NO_4S$. Calculated (%): C, 57.32; H, 5.15; N, 4.77; S, 10.93.

Methyl 6-acetyl-3-chloroacetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (6c). The yield was 62%, m.p. 145—147 °C (from EtOH). MS, *m/z*: 382 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, Me); 2.75 (s, 3 H, MeC(O)); 3.94 (s, 3 H, MeO); 5.13 (s, 2 H, $ClCH_2$); 11.90 (s, 1 H, NH). Found (%): C, 49.80; H, 3.86; Cl, 11.32; N, 4.51; S, 10.34. $C_{13}H_{12}ClNO_4S$. Calculated (%): C, 49.76; H, 3.85; Cl, 11.30; N, 4.46; S, 10.22.

Methyl 6-acetyl-3-dichloroacetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (6d). The yield was 65%, m.p. 143—145 °C (from EtOH). MS, *m/z*: 348 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 2.62 (s, 3 H, Me); 2.72 (s, 3 H, MeC(O)); 3.95 (s, 3 H, MeO); 7.74 (s, 1 H, Cl_2CH); 12.28 (s, 1 H, NH). Found (%): C, 44.93; H, 3.17; Cl, 20.40; N, 4.12; S, 9.41. $C_{13}H_{11}Cl_2NO_4S$. Calculated (%): C, 44.84; H, 3.18; Cl, 20.36; N, 4.02; S, 9.21.

Methyl 6-acetyl-2-methyl-3-trichloroacetyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (6e). The yield was 69%, m.p. 166—168 °C (from EtOH). MS, *m/z*: 382 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, Me); 2.75 (s, 3 H, MeC(O)); 3.93 (s, 3 H, MeO); 11.68 (s, 1 H, NH). Found (%): C, 44.92; H, 3.18; Cl, 20.40; N, 4.15; S, 9.30. $C_{13}H_{10}Cl_3NO_4S$. Calculated (%): C, 44.84; H, 3.18; Cl, 20.36; N, 4.02; S, 9.21.

Methyl 4-acetyl-2-methyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate (7). Thienopyrrole **3a** (0.5 g, 2.56 mmol) in anhydrous dioxane (7 mL) was added by Bu^tOK (0.345 g, 3.07 mmol), and the mixture was stirred for 15 min. Then AcCl (0.22 mL, 3.11 mmol) was added. The reaction mixture was stirred for 2 h (TLC monitoring), poured into water, extracted with AcOEt, washed with a saturated aqueous solution of NaCl, and dried with $MgSO_4$. The solvent was distilled off *in vacuo*. The yield was 89%, m.p. 94—96 °C (from EtOH). MS, *m/z*: 237 $[M]^+$. ^1H NMR (DMSO-d_6), δ: 2.55 (s, 3 H, Me); 2.62 (s, 3 H, Me); 3.82 (s, 3 H, MeO); 7.14 (s, 3 H, CH_{arom}); 7.33 (s, 1 H, CH_{arom}). Found (%): C, 55.72; H, 4.67; N, 5.95; S, 13.59. $C_{11}H_{11}NO_3S$. Calculated (%): C, 55.68; H, 4.67; N, 5.90; S, 13.51.

2,8-Dimethyl-4,6-dihydro-5*H*-thieno[2′,3′:4,5]pyrrole[2,3-*d*]pyridazin-5-one (8). Thienopyrrole **4a** (0.1 g, 0.42 mmol) in EtOH (10 mL) was added by 85% hydrazine hydrate (0.1 g, 1.7 mmol). The reaction mixture was heated with stirring until the precipitate dissolved and stored for 48 h (TLC monitoring). The resulting mixture was poured into water, and the precipitate was filtered off and washed with water. The yield was 69%, m.p. >250 °C (from EtOH). MS, *m/z*: 219 $[M]^+$.

^{1}H NMR (DMSO-d_6), δ: 2.48 (s, 3 H, Me); 2.61 (s, 3 H, Me); 6.98 (s, 1 H, CH_{arom}); 12.18 (s, 1 H, NH); 12.61 (br.s, 1 H, NH). Found (%): C, 54.83; H, 4.15; N, 19.24; S, 14.70. $C_{10}H_9N_3OS$. Calculated (%): C, 54.78; H, 4.14; N, 19.16; S, 14.62.

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