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New 4*H*-thieno[3,2-*b*]pyrrole-5-carboxamides

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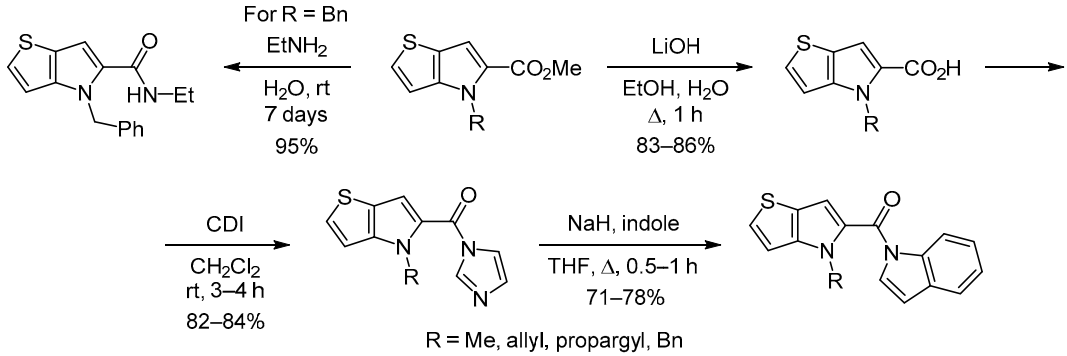


A series of *N*-substituted 4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acids and their imidazolyl derivatives was synthesized. 4-Methyl-, 4-allyl-, and 4-benzyl derivatives of (4*H*-thieno[3,2-*b*]pyrrol-5-yl)carboxylic acid or their imidazolides were used in reactions with $EtNH_2$ and indole sodium salt, providing the respective amides.

Keywords: acylimidazoles, ethylamine, indole, thieno[3,2-*b*]pyrrole-5-carboxamides, 4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acids.

Thieno[3,2-*b*]pyrrolecarboxamides have attracted significant attention over recent years due to the discovery of new types of activity for specific representatives in this series of compounds. Some of amides **1** have shown strong activity against hepatitis C virus (Fig. 1). These compounds include a new class of allosteric inhibitors for the RNA-dependent RNA polymerase of hepatitis C virus,[1] as well as inhibitors of CHIKV alphaviruses, flaviviruses,[2] and neurotropic arboviruses.[3]

An interesting discovery with relevance to medicinal chemistry research directed toward oncology targets is the ability of thienopyrrole **2** and similar compounds to inhibit the KDM1A and LSD1 demethylases, which regulate DNA methylation.[4,5] The balance of *N*-methylation extent in histones is one of the key factors in the regulation of gene transcription. Histones are methylated at lysine and arginine side chains by the action of methyltransferases. Demethylation of lysine is catalyzed by the lysine-specific demethylases KDM1 (LSD1). The activity of demethylases is elevated in many types of cancer cells and therefore KDM1 inhibitors[6] have been identified as new targets for anticancer therapy.

This work is devoted to the synthesis of new thienopyrroles **1** containing *N*-substituents in the bicyclic and carboxamide moieties. The starting materials for these syntheses were our previously prepared *N*-substituted thienopyrrolecarboxylate esters **3a**–**d**,[7,8] which were converted by alkaline hydrolysis to acids **4a**–**d** that were needed for the amidation reactions (Scheme 1). Two variants were explored for the synthesis of the target carboxamides. The first variant was based on the preparation of ethylamide **5d** by direct reaction between

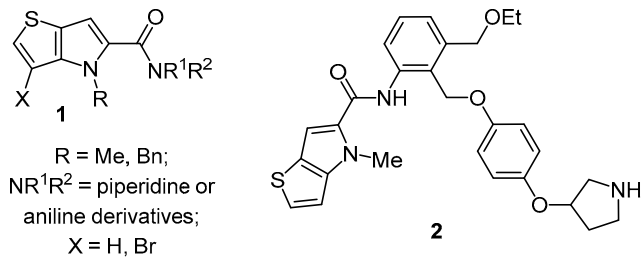
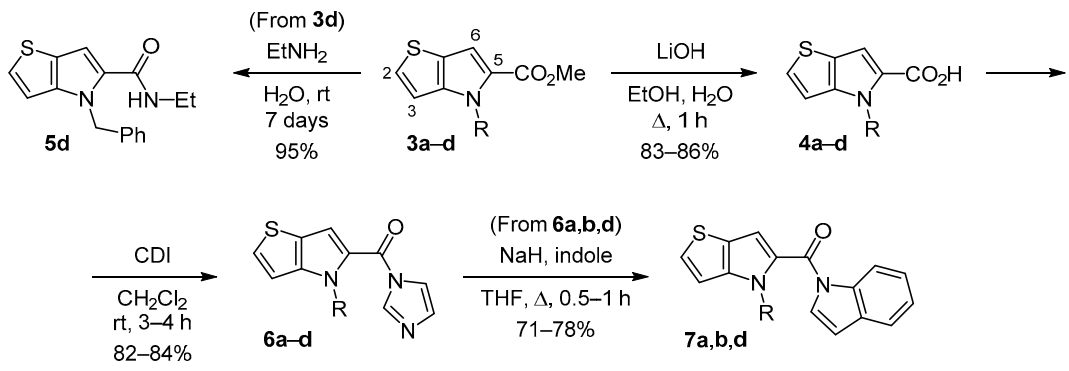


Figure 1. The structures of carboxamides **1** and compound **2**, which has been characterized as KDM1 inhibitor.

Scheme 1



a R = Me, **b** R = allyl, **c** R = propargyl, **d** R = Bn

ester **3d** and aqueous $EtNH_2$. However, this route was not suitable for the synthesis of amides with more complex structures.

The second variant requires preliminary activation of the carboxyl group by the transformation of carboxylic acids **4a**–**d** to acyl imidazoles **6a**–**d** (which rapidly darken and decompose upon exposure to air), followed by reactions of the acyl imidazoles with indole, which was demonstrated by the synthesis of products **7a**,**b**,**d** from imidazolides **6a**,**b**,**d**.

Thus, in the current work, we have developed synthetic approaches for the preparation of pharmaceutically relevant carboxamides from 4-alkyl derivatives of 4*H*-thieno[3,2-*b*]-pyrrole-5-carboxylic acids.

Experimental

IR spectra were recorded on a Shimadzu IR Prestige-21 spectrometer for samples prepared as thin films. ^1H and ^{13}C NMR spectra were acquired on Bruker AM-300 (300 MHz, ^1H NMR spectra of compounds **4c**, **7b**) and Bruker Avance-500 spectrometers (500 and 125 MHz, respectively, ^1H NMR spectra for the rest of the compounds and all ^{13}C NMR spectra), using $CDCl_3$ as solvent, internal standard was TMS. ^1H–^1H COSY, NOESY spectra (mixing time 0.5 s), ^1H–^{13}C HMBC, ^1H–^{13}C HSQC (for compounds **4**, **6 d**) were recorded on a Bruker Avance 500 spectrometer. Mass spectra (CI, water) were recorded on a Shimadzu LCMS-2010EV mass spectrometer (the sample solution in $CHCl_3$–MeCN was injected by syringe at 0.1 ml/min rate, the eluent was 95:5 MeCN–H_2O, positive ion mode using 4.5 kV potential on the ionizing needle electrode, interface capillary temperature 250°C, interface capillary voltage 5 V). Elemental analysis was performed on a EuroVector EA2000 CHNS-analyzer. The reaction progress was controlled by TLC on Sorbfil plates (Sorbpolymer, Russia), visualization with anisaldehyde solution and sulfuric acid in ethanol followed by heating at 120–150°C. The products were isolated by column chromatography using silica gel from Macherey-Nagel (30–60 g of sorbent for 1 g of compound).

N-Substituted methyl 4*H*-thieno[3,2-*b*]pyrrole-5-carboxylates **3a**–**d** were synthesized according to a published procedure,[7,8] while (4-methyl-4*H*-thieno[3,2-*b*]pyrrol-5-yl)-carboxylic acid (**4a**) was obtained by another previously described method.[9]

4-(Prop-2-en-1-yl)-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acid (4b). A solution of ester **3b** (40 mg, 0.18 mmol) in 3:1 EtOH–H_2O mixture (10 ml) was treated by adding LiOH (22 mg, 0.90 mmol). The reaction mixture was refluxed for 1 h (control by TLC). The mixture was cooled to room temperature, acidified with 2 M HCl solution to pH 2, and the precipitate was removed by filtration. Ethanol was evaporated, the product was extracted with CH_2Cl_2, the combined organic extracts were washed with distilled water, dried over anhydrous $MgSO_4$, solids were filtered off, and the filtrate was evaporated. Yield 33 mg (86%), white powder, mp 162–165°C. IR spectrum, ν, cm^{-1}: 3097, 3082, 2726, 2670, 1663, 1653, 1534, 1420, 1366, 1351, 1303, 1290, 1267, 1179, 926, 774, 721. ^1H NMR spectrum, δ, ppm (*J*, Hz): 5.01 (1H, d, *J* = 17.1) and 5.15 (1H, d, *J* = 10.2, $=CH_2$); 5.16 (2H, d, *J* = 4.4, NCH_2); 5.98–6.05 (1H, m, C<u>H</u>$=CH_2$); 6.93 (1H, d, *J* = 5.3, H-3); 7.37 (1H, s, H-6); 7.39 (1H, d, *J* = 5.3, H-2). ^{13}C NMR spectrum, δ, ppm: 49.5 (NCH_2); 110.5 (C-6); 111.5 (C-3); 116.5 ($=CH_2$); 122.5 (C-6a); 125.0 (C-5); 130.5 (C-2); 133.8 (–<u>C</u>H$=CH_2$); 146.1 (C-3a); 166.0 (CO_2H). Mass spectrum, *m*/*z* (I_{rel}, %): 208 $[M+H]^+$ (100), 164 $[M+H–CO_2]^+$ (54), 121 (53). Found, %: C 58.27; H 4.22; N 6.58; S 15.79. $C_{10}H_9NO_2S$. Calculated, %: C 57.95; H 4.38; N 6.76; S 15.47.

4-(Prop-2-yn-1-yl)-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acid (4c) was obtained analogously from ester **3c** (0.15 g, 0.68 mmol) and LiOH (93 mg, 3.90 mmol). Yield 0.14 g (87%), white powder, mp 204–206°C (decomp.). IR spectrum, ν, cm^{-1}: 3260, 1670, 1496, 1468, 1439, 1377, 1301, 1266, 724, 669. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.69 (1H, t, *J* = 2.4, ≡CH); 5.49 (2H, s, NCH_2); 7.15 (1H, d, *J* = 5.4, H-3); 7.21 (1H, s, H-6); 7.47 (1H, d, *J* = 5.4, H-2). ^{13}C NMR spectrum, δ, ppm: 35.3 (CH_2); 72.1 (≡CH); 78.5 (<u>C</u>≡CH); 109.8 (C-6); 110.3 (C-3); 122.5 (C-6a); 125.9 (C-5); 129.2 (C-2); 145.1 (C-3a); 163.0 (CO_2H). Mass spectrum, *m*/*z* (I_{rel}, %): 247 $[M+MeCN]^+$ (40), 206 $[M+H]^+$ (100). Found, %: C 58.76; H 3.32; N 6.57; S 15.96. $C_{10}H_7NO_2S$. Calculated, %: C 58.52; H 3.44; N 6.82; S 15.62.

4-Benzyl-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylic acid (4d) was obtained analogously from ester **3d** (0.16 g, 0.59 mmol) and LiOH (71 mg, 2.95 mmol). Yield 0.13 g (83%), colorless crystals, mp 180–182°C. IR spectrum, ν, cm^{-1}: 2870, 2726, 1673, 1668, 1491, 1367, 1311, 1298, 1269, 1177, 736, 722, 709. ^1H NMR spectrum, δ, ppm (*J*, Hz): 5.84 (2H, s, NCH_2); 7.13 (1H, d, *J* = 5.4, H-3);

7.16 (2H, d, *J* = 7.7, H Ph); 7.21–7.23 (1H, m, H Ph); 7.27–7.29 (2H, m, H Ph); 7.31 (1H, s, H-6); 7.49 (1H, d, *J* = 5.4, H-2). ^{13}C NMR spectrum, δ, ppm: 49.6 (CH_2); 109.6 (C-6); 111.0 (C-3); 122.2 (C-6a); 123.1 (C-5); 126.8 (C Ph); 127.2 (C Ph); 128.4 (C Ph); 129.4 (C-2); 131.7 (C Ph); 138.6 (C-3a); 161.9 (CO_2H). Mass spectrum, *m/z* (I_{rel}, %): 214 $[M+H–CO_2]^+$ (100). Found, %: C 65.72; H 4.42; N 5.58; S 12.69. $C_{14}H_{11}NO_2S$. Calculated, %: C 65.35; H 4.31; N 5.44; S 12.46.

4-Benzyl-*N*-ethyl-4*H*-thieno[3,2-*b*]pyrrolo-5-carboxamide (5d). Aqueous 70% ethylamine solution (3 ml) was added to compound **3d** (30 mg, 0.11 mmol). The mixture was stirred until complete disappearance of the starting ester (~7 days, control by TLC). Water was then partially evaporated, the product was extracted with CH_2Cl_2, the organic extracts were dried over anhydrous $MgSO_4$ and then evaporated, the residue was separated by silica gel column chromatography. Yield 30 mg (95%), pale-yellow viscous oil. IR spectrum, ν, cm^{-1}: 3508, 2956, 2833, 1753, 1737, 1723, 1464, 1380, 1228, 1198, 1067, 1045, 1012, 981, 925, 899, 783. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.19 (3H, t, *J* = 7.3, $NHCH_2C\underline{H}_3$); 3.42 (2H, qd, *J* = 13.1, *J* = 7.3, $NHC\underline{H}_2CH_3$); 5.76 (2H, s, $NC\underline{H}_2Ph$); 5.99 (1H, br. s, NH); 6.79 (1H, s, H-6); 6.84 (1H, d, *J* = 5.4, H-3); 7.16 (2H, d, *J* = 7.2, H Ph); 7.20 (1H, d, *J* = 5.4, H-2); 7.26 (3H, t, *J* = 7.2, H Ph). ^{13}C NMR spectrum, δ, ppm: 15.0 ($NHCH_2\underline{C}H_3$); 34.3 ($NH\underline{C}H_2CH_3$); 50.3 ($N\underline{C}H_2Ph$); 103.3 (C-6); 110.8 (C-3); 122.0 (C-6a); 126.9 (C Ph); 127.3 (C Ph, C-5); 128.5 (C Ph); 130.4 (C-2); 138.2 (C Ph); 141.5 (C-3a); 158.4 (CO). Mass spectrum, *m/z* (I_{rel}, %): 254 $[M–C_2H_6]^+$ (5), 222 (15), 191 (51), 173 (100), 111 (48). Found, %: C 67.96; H 5.86; N 9.68; S 11.54. $C_{16}H_{16}N_2OS$. Calculated, %: C 67.58; H 5.67; N 9.85; S 11.27.

(1*H*-Imidazol-1-yl)(4-methyl-4*H*-thieno[3,2-*b*]pyrrol-5-yl)-methanone (6a). *N*,*N*-carbonyldiimidazole (22 mg, 0.13 mmol) was added to a solution of acid **4a** (20 mg, 0.11 mmol) in anhydrous CH_2Cl_2 (10 ml) with stirring. The mixture was stirred at room temperature for 3–4 h until complete disappearance of the starting carboxylic acid (control by TLC). The solvent was then removed by evaporation and the product was purified by silica gel column chromatography (eluent 1:1 petroleum ether – EtOAc). Yield 22 mg (85%), colorless crystals, mp 65–66°C. IR spectrum, ν, cm^{-1}: 3298, 3061, 2925, 2852, 2375, 1672, 1664, 1437, 1375, 1275, 1234, 1187, 1097, 1062, 1022, 904, 748, 724. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.09 (2H, s, NCH_3); 7.01 (1H, d, *J* = 5.4, H-3); 7.09 (1H, s, H-6); 7.18 (1H, s, H-4 Im);* 7.51 (1H, d, *J* = 5.4, H-2); 7.62 (1H, s, H-5 Im); 8.25 (1H, s, H-2 Im). ^{13}C NMR spectrum, δ, ppm: 34.7 (NCH_3); 110.0 (C-6); 112.6 (C-3); 118.4 (C-4 Im); 122.8 (C-6a); 127.3 (C-5 Im); 130.5 (C-2 Im); 132.5 (C-2); 137.9 (C-5); 148.0 (C-3a); 157.8 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 273 $[M+H+MeCN]^+$ (50), 232 $[M+H]^+$ (100), 164 $[M–Im]^+$ (49). Found, %: C 57.46; H 4.08; N 18.35; S 14.13. $C_{11}H_7NO_2S$. Calculated, %: C 57.13; H 3.92; N 18.17; S 13.86.

(1*H*-Imidazol-1-yl)[4-(prop-2-en-1-yl)-4*H*-thieno[3,2-*b*]-pyrrol-5-yl]methanone (6b) was obtained analogously from carboxylic acid **4b** (30 mg, 0.15 mmol) and CDI (28 mg, 0.17 mmol). Yield 30 mg (84%), pale-yellow oil that rapidly darkens upon exposure to air. IR spectrum, ν, cm^{-1}: 1675, 1533, 1449, 1387, 1306, 1274, 1249, 1222, 1186, 910, 724. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.11 (1H, d, *J* = 17.1) and 5.22 (1H, dd, *J* = 10.4, *J* = 1.0, $=CH_2$); 5.14 (1H, d, *J* = 5.4, NCH_2); 6.07 (1H, ddd, *J* = 10.4, *J* = 6.7, *J* = 5.5, $C\underline{H}=CH_2$); 7.07 (1H, d, *J* = 5.3, H-3); 7.14 (1H, s, H-6); 7.20 (1H, s, H-4 Im); 7.53 (1H, d, *J* = 5.3, H-2); 7.74 (1H, s, H-5 Im); 8.27 (1H, s, H-2 Im). ^{13}C NMR spectrum, δ, ppm: 49.7 (NCH_2); 110.4 (C-6); 113.0 (C-3); 117.3 ($=CH_2$); 118.4 (C-4 Im); 123.2 (C-5 Im); 126.8 (C-6a); 130.4 (C-2 Im); 132.6 (C-2); 133.3 ($\underline{C}H=CH_2$); 137.9 (C-5); 147.4 (C-3a); 157.6 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 299 $[M+H+MeCN]^+$ (21), 258 $[M+H]^+$ (100), 190 $[M–Im]^+$ (61), 162 $[M–ImCO]^+$ (22). Found, %: C 60.99; H 4.39; N 16.58; S 12.79. $C_{13}H_{11}N_3OS$. Calculated, %: C 60.68; H 4.31; N 16.33; S 12.46.

1*H*-Imidazol-1-yl[4-(prop-2-yn-1-yl)-4*H*-thieno[3,2-*b*]-pyrrol-5-yl]methanone (6c) was obtained analogously from carboxylic acid **4c** (20 mg, 0.10 mmol) and CDI (19 mg, 0.12 mmol). Yield 21 mg (84%), light-yellow oil that rapidly darkens upon exposure to air. IR spectrum, ν, cm^{-1}: 3289, 3119, 2923, 2852, 2375, 1672, 1449, 1384, 1304, 1276, 1222, 1186, 1097, 1050, 1014, 898, 776, 723. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.37 (1H, t, *J* = 2.3, ≡CH); 5.33 (2H, d, *J* = 2.3, NCH_2); 7.14 (1H, s, H-6); 7.15 (1H, d, *J* = 5.3, H-3); 7.19 (1H, s, H-4 Im); 7.56 (1H, d, *J* = 5.3, H-2); 7.63 (1H, s, H-5 Im); 8.25 (1H, s, H-2 Im). ^{13}C NMR spectrum, δ, ppm: 36.6 (NCH_2); 73.4 (≡CH); 77.7 ($\underline{C}$≡CH); 110.6 (C-6); 113.8 (C-3); 118.4 (C-4 Im); 123.8 (C-5 Im); 126.5 (C-6a); 130.6 (C-2 Im); 133.1 (C-2); 137.9 (C-5); 147.2 (C-3a); 157.7 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 297 $[M+H+MeCN]^+$ (54), 256 $[M+H]^+$ (100), 188 $[M–Im]^+$ (77).

(4-Benzyl-4*H*-thieno[3,2-*b*]pyrrol-5-yl)(1*H*-imidazol-1-yl)-methanone (6d) was obtained analogously from carboxylic acid **4d** (30 mg, 0.12 mmol) and CDI (23 mg, 0.14 mmol). Yield 30 mg (82%), dark-yellow viscous oil. IR spectrum, ν, cm^{-1}: 2924, 1672, 1449, 1385, 1308, 1274, 1243, 1221, 1182, 1097, 1073, 908, 888, 745, 723. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.72 (2H, s, NCH_2); 6.91 (1H, d, *J* = 5.4, H-3); 7.15–7.16 (4H, m, H-6, H Ph); 7.26 (1H, s, H-4 Im); 7.27–7.31 (2H, m, H Ph); 7.47 (1H, d, *J* = 5.4, H-2); 7.59 (1H, s, H-5 Im); 8.21 (1H, s, H-2 Im). ^{13}C NMR spectrum, δ, ppm: 50.8 (NCH_2); 110.6 (C-6); 113.5 (C-3); 118.4 (C-4 Im); 123.4 (C-5 Im); 126.8 (C Ph); 127.1 (C-6a); 127.9 (C Ph); 128.8 (C Ph); 130.4 (C-2 Im); 132.8 (C-2); 137.1 (C Ph); 137.9 (C-5); 148.1 (C-3a); 157.8 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 349 $[M+MeCN]^+$ (39), 308 $[M+H]^+$ (94), 240 $[M–Im–H]^+$ (100). Found, %: C 66.76; H 4.34; N 13.93; S 10.77. $C_{17}H_{13}N_3OS$. Calculated, %: C 66.43; H 4.26; N 13.67; S 10.43.

(1*H*-Indol-1-yl)(4-methyl-4*H*-thieno[3,2-*b*]pyrrol-5-yl)-methanone (7a). Indole (42 mg, 0.36 mmol) in anhydrous THF (5 ml) was added with stirring to a suspension of NaH (11 mg, 0.45 mmol, washed with anhydrous hexane prior to use) in anhydrous THF (10 ml). The mixture was stirred for 15–20 min and then treated by crude carboxylic acid **6a**

* Here and further the imidazole proton and carbon signals in ^{1}H and ^{13}C NMR spectra, as well as the imidazole fragment ions in mass spectra are denoted as Im.

(70 mg, 0.30 mmol). The reaction mixture was refluxed until complete disappearance of compound **6a** (control by TLC, 30–40 min), then cooled to room temperature. The remaining NaH was decomposed by adding saturated NH_4Cl solution. THF was evaporated, the product was extracted with CH_2Cl_2 (3×4 ml), the combined extracts were dried over anhydrous $MgSO_4$. The solvent was evaporated, and the residue was purified by silica gel column chromatography (eluent 1:10 petroleum ether – EtOAc). Yield 60 mg (71%), beige powder, mp 134–136°C. IR spectrum, ν, cm^{-1}: 2925, 2852, 1664, 1449, 1437, 1382, 1368, 1319, 1294, 1231, 1207, 1183, 1122, 1059, 1017, 889, 873, 815, 766, 751, 719. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.09 (3H, s, NCH_3); 6.65 (1H, d, *J* = 3.6, H-3 Ind);* 6.96 (1H, s, H-6); 7.02 (1H, d, *J* = 5.3, H-3); 7.34 (1H, t, *J* = 7.5, H Ind); 7.43 (1H, t, *J* = 7.3, H Ind); 7.45 (1H, d, *J* = 5.3, H-2); 7.63 (1H, d, *J* = 7.7, H Ind); 7.75 (1H, d, *J* = 3.6, H-2 Ind); 8.38 (1H, d, *J* = 8.2, H Ind). ^{13}C NMR spectrum, δ, ppm: 34.4 (NCH_3); 107.6 (C-6); 110.1 (C-3 Ind); 110.8 (C-3); 115.8 (C-7 Ind); 120.9 (C-2 Ind); 122.2 (C-6a); 123.5 (C-5(4) Ind); 124.5 (C-4(5) Ind); 128.1 (C-6 Ind); 128.5 (C-5); 130.1 (C-2); 130.6 (C-3a Ind); 136.1 (C-7a Ind); 146.3 (C-3a); 160.8 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 281 $[M+H]^+$ (100), 164 $[M–Ind]^+$ (18). Found, %: C 68.92; H 4.45; N 10.13; S 11.68. $C_{16}H_{12}N_2OS$. Calculated, %: C 68.55; H 4.31; N 9.99; S 11.44.

(1*H*-Indol-1-yl)[4-(prop-2-en-1-yl)-4*H*-thieno[3,2-*b*]-pyrrol-5-yl]methanone (7b) was obtained analogously from compound **6b** (100 mg, 0.39 mmol) and indole (70 mg, 0.47 mmol). Yield 85 mg (71%), yellow viscous oil. IR spectrum, ν, cm^{-1}: 1712, 1665, 1532, 1472, 1446, 1387, 1348, 1324, 1295, 1207, 1123, 1073, 1016, 885, 868, 837, 768, 750, 721. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.13 (2H, d, *J* = 5.3, NCH_2); 5.14–5.15 (1H, m) and 5.19 (1H, d, *J* = 10.3, $=CH_2$); 6.09 (1H, ddd, *J* = 10.3, *J* = 7.0, *J* = 5.2, C<u>H</u>=CH_2); 6.62 (1H, d, *J* = 3.6, H-3 Ind); 6.97 (1H, s, H-6); 7.01 (1H, d, *J* = 5.3, H-3); 7.28–7.38 (2H, m, H Ind); 7.41 (1H, d, *J* = 5.3, H-2); 7.67 (1H, d, *J* = 7.8, H Ind); 7.73 (1H, d, *J* = 3.6, H-2 Ind); 8.39 (1H, d, *J* = 8.3, H Ind). ^{13}C NMR spectrum, δ, ppm: 49.6 (NCH_2); 107.7 (C-6); 110.6 (C-3 Ind); 111.2 (C-3); 114.9 (C-7 Ind); 117.1 ($=CH_2$); 120.9 (C-2 Ind); 122.7 (C-6a); 123.6 (C-5(4) Ind); 124.8 (C-4(5) Ind); 128.1 (C-6 Ind); 128.7 (C-5); 130.1 (C-2); 130.7 (C-3a Ind); 133.9 (<u>C</u>H=CH_2); 136.1 (C-7a Ind); 145.6 (C-3a); 160.7 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 348 $[M+H+MeCN]^+$ (24), 307 $[M+H]^+$ (100), 116 (35). Found, %: C 70.77; H 4.70; N 9.33; S 10.78. $C_{18}H_{14}N_2OS$. Calculated, %: C 70.56; H 4.61; N 9.14; S 10.47.

(4-Benzyl-4*H*-thieno[3,2-*b*]pyrrol-5-yl)(1*H*-indol-1-yl)-methanone (7d) was obtained analogously from compound **6d** (60 mg, 0.20 mol) and indole (25 mg, 0.43 mmol). Yield 54 mg (78%), white waxy solid, mp >180°C (decomp.). IR spectrum, ν, cm^{-1}: 2956, 2923, 2850, 1734, 1664, 1532, 1496, 1473, 1447, 1387, 1324, 1294, 1246, 1207, 1201, 1181, 1123, 1073, 886, 867, 839, 769, 750, 721, 698. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.33 (2H, s, NCH_2); 6.62 (1H, d, *J* = 3.6, H-3 Ind); 6.89 (1H, d, *J* = 5.4, H-3); 6.99 (1H, s, H-6); 7.19 (2H, d, *J* = 7.6, H Ph); 7.24 (1H, d, *J* = 7.6, H Ph); 7.26–7.30 (3H, m, H-2, H Ph); 7.34–7.36 (2H, m, H Ind); 7.62 (1H, d, *J* = 7.7, H Ind); 7.68 (1H, d, *J* = 3.6, H-2 Ind); 8.35 (1H, d, *J* = 8.3, H Ind). ^{13}C NMR spectrum, δ, ppm: 50.5 (NCH_2); 107.7 (C-3 Ind); 110.8 (C-6); 111.6 (C-3); 115.9 (C-Ar); 120.9 (C-2 Ind); 122.9 (C-6a); 123.5 (C Ar); 124.5 (C Ar); 127.0 (C Ar); 127.7 (C Ar); 128.0 (C Ar); 128.7 (C Ar); 129.0 (C-5); 130.2 (C-2); 130.7 (C Ar); 136.1 (C Ar); 137.5 (C Ar); 145.8 (C-3a); 160.8 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 357 $[M+H]^+$ (100). Found, %: C 73.92; H 4.41; N 7.99; S 9.28. $C_{22}H_{16}N_2OS$. Calculated, %: C 74.13; H 4.52; N 7.86; S 9.00.

* Here and further the indole proton and carbon signals in ^{1}H and ^{13}C NMR spectra, as well as the indole fragment ions in mass spectra are denoted as Ind.

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