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PREPARATION OF THIENO[2,3-*b*]PYRAZINES AS BIOISOSTERES FOR QUINOXALINE DERIVATIVES WITH REVERSE TRANSCRIPTASE INHIBITION[1]

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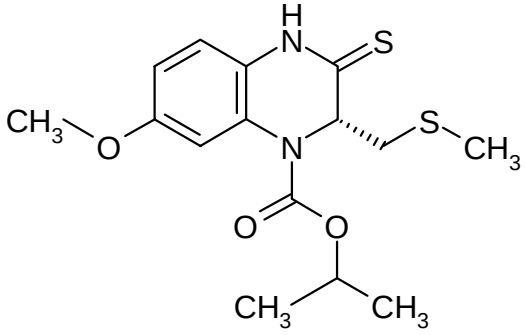
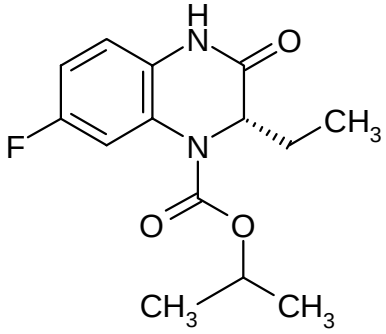
Abstract – Replacement of the fused aromatic moiety in GW-420867X, a HIV-1 specific nonnucleoside reverse transcriptase inhibitor, with thiophene provided 2-oxo-1,2,3,4-tetrahydrothieno[2,3-*b*]pyrazine derivatives. The synthesis starts with the reaction of 5-acyl-2-chloro-3-nitrothiophene and different amino acid derivatives. The resulting substitution products are reduced, cyclized and *N*-acylated to give the desired compounds (**27** – **33**).

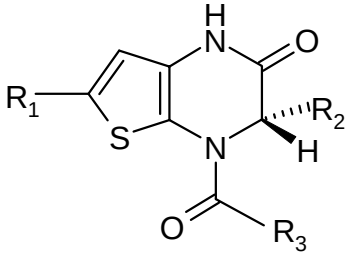
Remarkable effort has been focused over the past fifteen years on the development of the HIV-1 specific nonnucleoside reverse transcriptase inhibitors due to their desirable safety, selectivity, and antiviral profiles, for the treatment of humanimmunodeficiency viruses infection. A number of different structural classes of nonnucleoside analogues i.e. quinoxaline derivatives, have been identified as potent and highly specific inhibitors of HIV-1 replication. Moreover, long-term treatment with all of these agents has led to drug-resistent HIV strains, and primary infections can occur with AZT-resistant HIV strains. The need for new candidates with improved selectivity and activity for anti-HIV therapy is therefore evident. GW-420867X,[2] a follow-up to the known compound HBY-097,[3] is a new member of the quinoxaline class



HBY-097



GW-420867X



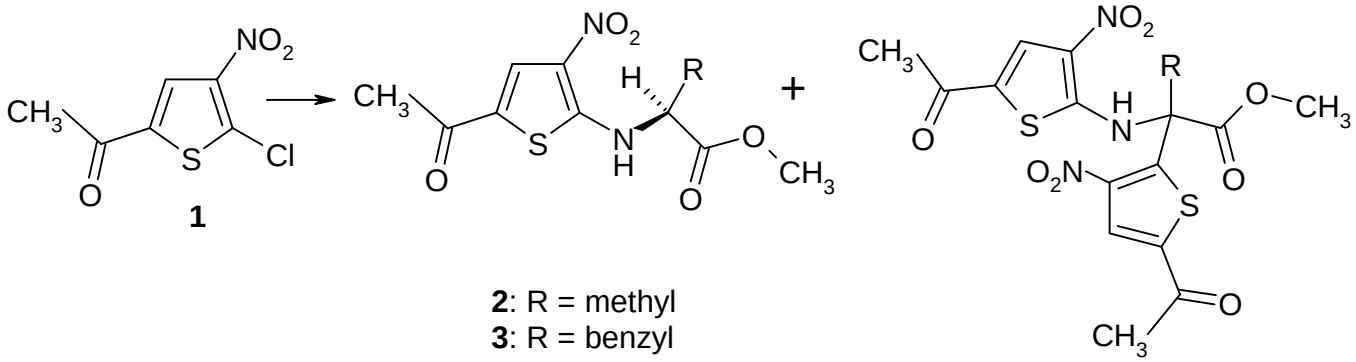
of nonnucleoside reverse transcriptase inhibitors with potent antiviral activity (IC_{50} = 33.5 nM) *in vitro* in the presence of human serum.[4]

A replacement of the benzene nucleus by a thiophene ring might result in a different biochemical profile and/ or a further elimination of side effects. This research was to prepare the shown thienoanalogous derivatives.

To realize this project, nucleophilic subtituion reactions with thiophene derivatives had to be studied in order to select the best reaction conditions.

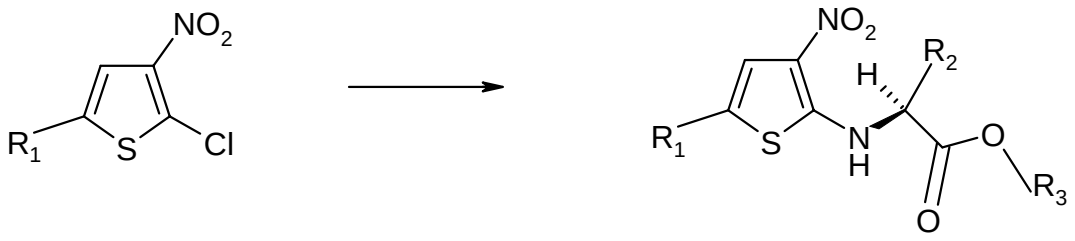
5-Acetyl-2-chloro-3-nitrothiophene[5] (**1**) was chosen for an initial trial since the acetyl group (another electron withdrawing substituent) was supposed to support the nucleophilic attack at the aromatic ring. Furthermore alkyl groups at the 6-position of the bicycle, as observed in various cases,[6] should intensify any biological activity.

1 were stirred with L-alanine methyl ester hydrochloride or L-phenylalanine methyl ester hydrochloride at room temperature using *N*,*N*-dimethylformamide (dried over molecular sieves) as a solvent, until TLC analysis indicated that all of the starting material was consumed. Beside the desired substitution products (**2** and **3;** 15 % and 41% yield) two compounds (**4** and **5**) in small amounts could also be isolated.



In order to increase the yields of **2** and **3** and to avoid the formation of by-products (**4** and **5**) other solvents and reaction temperatures were tried out. The best results (71% and 75%) were achieved by means of potassium carbonate in dry acetonitrile at 40^0C. Under these reaction conditiones no traces of compound (**4**) or (**5**) could be dedected.

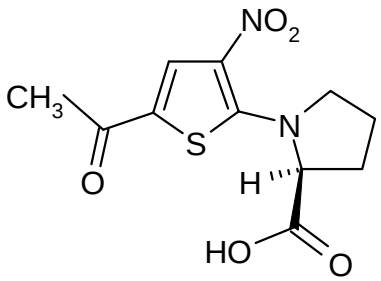
The surprisingly good results that were reached by a nucleophilic substitution of the chloro atom on the π-excessive heterocycle were also observed by using other amino acid derivatives. Thus reaction of the thiophene derivatives (**1** and **6**[7]) with L-phenylalanine ethyl ester hydrochloride, L-phenylalanine, L-methionine methyl ester hydrochloride, S-methyl-L-cysteine or glycine ethyl ester hydrochloride gave compounds (**7** – **14**).



1: R_1 = acetyl
6: R_1 = benzoyl

7 (93 %):	R_1 = acetyl	R_2 = benzyl	R_3 = ethyl
8 (81 %):	R_1 = acetyl	R_2 = benzyl	R_3 = H
9 (96 %):	R_1 = acetyl	R_2 = -CH_2-CH_2-SCH_3	R_3 = methyl
10 (86 %):	R_1 = acetyl	R_2 = -CH_2-SCH_3	R_3 = H
11 (71 %):	R_1 = acetyl	R_2 = H	R_3 = ethyl
12 (59 %):	R_1 = benzoyl	R_2 = H	R_3 = ethyl
13 (29 %):	R_1 = benzoyl	R_2 = methyl	R_3 = methyl
14 (57 %):	R_1 = benzoyl	R_2 = benzyl	R_3 = methyl

5- Acetyl-2-chloro-3-nitrothiophene (**1**) reacted with L-proline in a similar way to give the substitution product (**15**) too. Treatment of **1** with L-cystine dimethyl ester dihydrochloride gave not the expected condensation product but the symmetrical compound (**16**).



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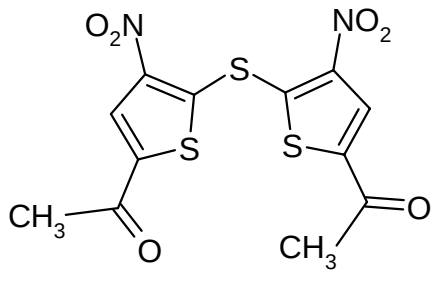

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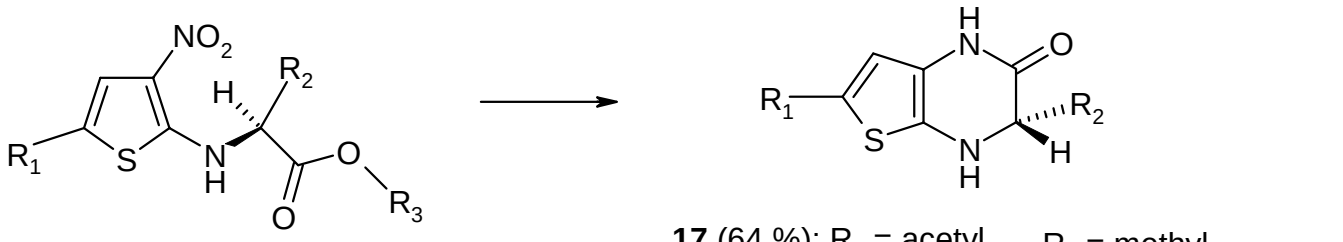
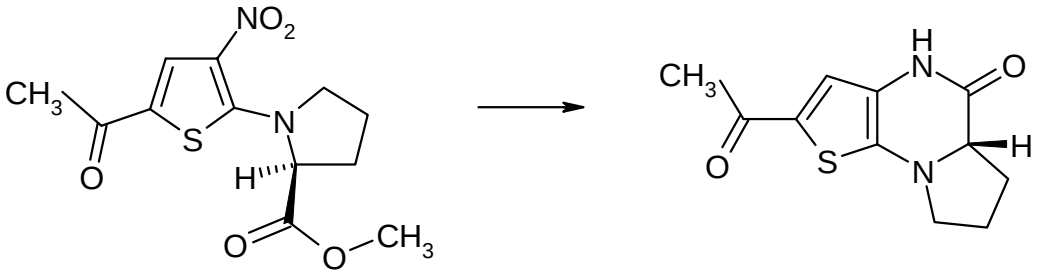
To accomplish the necessary lactam linkage the nitro group of substances (**2**, **3** and **9 – 15**) were reduced by treatment with iron powder in glacial acetic acid/ water at 70°C. After working up the bicycles (**17 - 24**) could be isolated. This approach provides a possibility to synthesize till now unknown thieno[2,3-*b*]pyrazine-2(1*H*)-ones.



7 - 14

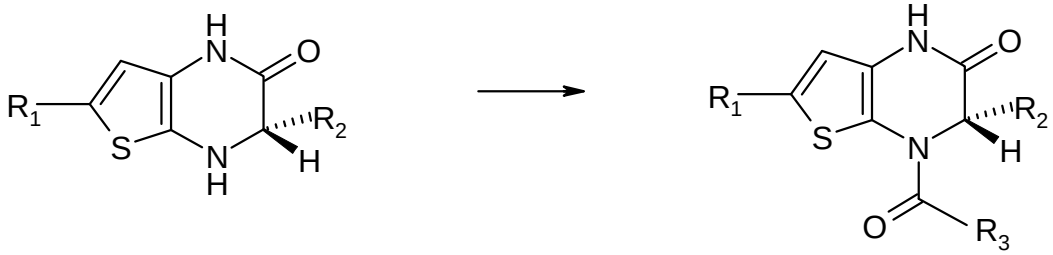
17 (64 %): R_1 = acetyl R_2 = methyl
18 (81 %): R_1 = acetyl R_2 = benzyl
19 (56 %): R_1 = acetyl R_2 = $-CH_2-CH_2-SCH_3$
20 (39 %): R_1 = acetyl R_2 = $-CH_2-SCH_3$
21 (50 %): R_1 = acetyl R_2 = H
22 (65 %): R_1 = benzoyl R_2 = H
23 (51 %): R_1 = benzoyl R_2 = methyl
24 (65 %): R_1 = benzoyl R_2 = benzyl

Compound (**15**) had to be esterified to substance (**25**). After this reduction and cyclisation led to **26**.



25 **26**

The *N*-acylation of the bicycles (**17** – **21** and **23**, **24**) was initially carried out with acyl chlorides in THF in the presence of triethylamine. However, higher yields were obtained when the reactions were conducted without any bases in dry dioxane at 40^0C.



17 - **20** and **22** - **24**

27 (46 %): R_1 = acetyl R_2 = methyl R_3 = $-OCH=CH_2$
28 (61 %): R_1 = acetyl R_2 = benzyl R_3 = $-OCH=CH_2$
29 (38 %): R_1 = acetyl R_2 = $-CH_2-CH_2-SCH_3$ R_3 = $-OCH=CH_2$
30 (13 %): R_1 = acetyl R_2 = $-CH_2-SCH_3$ R_3 = -O-isopropyl
31 (38 %): R_1 = acetyl R_2 = H R_3 = -cyclopropyl
32 (72 %): R_1 = benzoyl R_2 = methyl R_3 = $-OCH=CH_2$
33 (58 %): R_1 = benzoyl R_2 = benzyl R_3 = $-OCH=CH_2$

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian Unity*Plus* 300 spectrometer (using TMS as internal reference, δ values in ppm). MS spectra were obtained by a Shimadzu QP 5000 or a Hewlett Packard 5970 spectrometer. Analytical TLC was performed on silica gel F254 plates, psc on silica gel F254s plates. Column chromatography was done on Merck silica gel 60, 0.063- 0.200 mm. Evaporation refers to evaporation under reduced pressure, and drying of solutions refers to the use of anhydrous sodium sulfate. Optical rotations were measured on Perkin-Elmer 241 polarimeter at 20^{0}C.

General procedure for the synthesis of compounds (2 - 5 and 7 - 15)

To a suspension of the amino acid derivative (8 mmol) and potassium carbonate (2.208 g, 16 mmol) in absolute acetonitrile (15 mL) 5- acetyl-2-chloro-3-nitrothiophene (0.512 g, 2.5 mmol) was added and the mixture was stirred under argon atmosphere at rt. After the reaction was completed (TLC analysis) the organic solvent was removed under reduced pressure. Then the residue was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 the solvent was evaporated.

(2*S*)-Methyl 2-[(5-acetyl-3-nitro-2-thienyl)amino]propionate (2)

The mixture of **1** (0.512 g, 2.5 mmol) and L-alanine methyl ester hydrochloride (1.117 g, 8 mmol) was stirred at 40^{0}C for 16 h. After crystallization from methanol **2** (483 mg, 71 %) was obtained; mp 79-80^{0}C; $[\alpha]_D$ +2.5 ^{0} (c 1.0, toluene); MS: m/z (rel. int.) 272 (M^+, 42), 213 (100), 169 (53), 153 (30); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.87 (br d, 1H, *J* = 7.2 Hz, NH), 7.94 (s, 1H, thiophene-H), 4.19 (quint, 1H, *J* = 7.2 Hz, CH), 3.84 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 1.67 (d, 3H, *J* = 7.2 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): δ 210.3, 189.6, 170.6, 162.0, 128.4, 125.6, 55.7, 53.2, 24.9, 17.7; Anal. Calcd for $C_{10}H_{12}N_2O_5S$: C, 44.11; H, 4.44; N, 10.29. Found: C, 44.37; H, 4.26; N, 10.21.

(2*S*)-Methyl 2-[(5-acetyl-3-nitro-2-thienyl)amino]-3-phenylpropionate (3)

The mixture of **1** (0.512 g, 2.5 mmol) and L-phenylalanine methyl ester hydrochloride (1.725 g, 8 mmol) was stirred at 40^{0}C for 45 h. After crystallization from methanol **3** (653 mg, 75 %) was obtained; mp 130^{0}C; $[\alpha]_D$ –28.8 ^{0} (c 1.0, toluene); MS: m/z (rel. int.) 348 (M^+, 51), 289 (23), 257 (46), 91 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.86–8.77 (m, 1H, NH), 7.89 (s, 1H, thiophene-H), 7.37–7.24 (m, 3H, phenyl-H), 7.21–7.12 (m, phenyl-H, 2H), 4.40-4.30 (m, 1H, CH), 3.79 (s, 3H, CH_3), 3.30 (AB-system,

1H, J_{AB} = 6.0 Hz, benzyl-CH_2), 3.24 (AB-system, 1H, J_{AB} = 6.0 Hz, benzyl-CH_2), 2.46 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 189.6, 169.3, 162.4, 134.2, 129.1, 129.0, 128.3, 127.8, 124.7, 61.5, 53.0, 37.8, 24.9; Anal. Calcd for $C_{16}H_{16}N_2O_5S$: C, 55.16; H, 4.63; N, 8.04. Found: C, 55.01; H, 4.52; N, 7.91.

Methyl 2-(5-acetyl-3-nitro-2-thienyl)-2-[(5-acetyl-3-nitro-2-thienyl)amino]propionate (4)

The mixture of **1** (0.512 g, 2.5 mmol) and L-alanine methyl ester hydrochloride (1.117 g, 8 mmol) was stirred in dry DMF (5 mL) at rt for 16 h. After purification on a silica gel column eluting with toluene/ ethyl acetate (8 + 2) **4** (66 mg, 6 %) was obtained; mp 230-232^{0}C (ethanol); MS: m/z (rel. int.) 441 (M^+, 31), 382 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.28 (s, 1H, NH), 8.12 (s, 1H, thiophene-H), 7.88 (s, 1H, thiophene-H), 3.88 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.26 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 189.6, 189.1, 169.3, 157.2, 148.0, 144.1, 142.3, 128.4, 128.3, 128.0, 125.2, 62.2, 54.7, 26.2, 25.1, 23.4; Anal. Calcd for $C_{16}H_{15}N_3O_8S_2$: C, 43.53; H, 3.43; N, 9.52. Found: C, 43.59; H, 3.41; N, 9.30.

Methyl 2-(5-acetyl-3-nitro-2-thienyl)-2-[(5-acetyl-3-nitro-2-thienyl)amino]-2-phenylpropionate (5)

The mixture of **1** (0.512 g, 2.5 mmol) and L-phenylalanine methyl ester hydrochloride (1.726 g, 8 mmol) was stirred in dry DMF (5 mL) at rt for 24 h. After purification on a silica gel column eluting with toluene/ ethyl acetate (8 + 2) **5** (78 mg, 6 %) was obtained; mp 229^{0}C (ethanol); MS: m/z (rel. int.) 518 (M^+, 4), 427 (98), 198 (100), 91 (68); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 9.97 (br s, 1H, NH), 8.12 (s, 1H, thiophene-H), 7.96 (s, 1H, thiophene-H), 7.34-7.23 (m, 3H, phenyl-H), 6.95-6.87 (m, 2H, phenyl-H), 4.21 (AB-system, 1H, J_{AB} = 13.1 Hz, benzyl-CH_2), 3.72 (AB-system, 1H, J_{AB} = 13.1 Hz, benzyl-CH_2), 3.78 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 2.46 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 189.6, 189.1, 166.9, 157.1, 147.0, 144.7, 142.7, 131.8, 129.6, 128.9, 128.7, 128.3, 128.2, 128.1, 125.6, 66.8, 54.2, 40.8, 26.3, 25.2; Anal. Calcd for $C_{22}H_{19}N_3O_8S_2$: C, 51.06; H, 3.70; N, 8.12. Found: C, 50.86; H, 3.74; N, 7.91.

(2*S*)-Ethyl 2-[(5-acetyl-3-nitro-2-thienyl)amino]-3-phenylpropionate (7)

The mixture of **1** (0.512 g, 2.5 mmol) and L-phenylalanine ethyl ester hydrochloride (1.837 g, 8 mmol) was stirred at 40^{0}C for 48 h. After crystallization from ethanol **6** (842 mg, 93 %) was obtained; mp 93^{0}C; $[\alpha]_D$ –46.0 ^{0} (c 1.0, toluene); MS: m/z (rel. int.) 362 (M^+, 45), 289 (31), 271 (42), 91 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.85 (d, 1H, J = 7.9 Hz, NH), 7.89 (s, 1H, thiophene-H), 7.38–7.11 (m, 5H, phenyl-H), 4.38-4.29 (m, 1H, CH), 4.24 (q, 2H, J = 6.2 Hz, CH_3), 3.35 (AB-system, 1H, J_{AB} = 6.2 Hz, benzyl-CH_2), 3.24 (AB-system, 1H, J_{AB} = 6.2 Hz, benzyl-CH_2), 2.45 (s, 3H, CH_3), 1.26 (t, 3H, J = 7.1 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): δ 189.5, 168.8, 162.3, 134.2, 129.1, 128.9, 127.7, 126.8, 124.5, 62.4, 61.5, 37.8, 24.9, 13.9; Anal. Calcd for $C_{17}H_{18}N_2O_5S$: C, 56.34; H, 5.01; N, 7.73. Found: C, 56.21; H, 5.00; N, 7.65.

(2*S*)-2-[(5-Acetyl-3-nitro-2-thienyl)amino]-3-phenylpropionic acid (8)

The mixture of **1** (0.512 g, 2.5 mmol) and L-phenylalanine (1.322 g, 8 mmol) was stirred at rt for 5 d. After crystallization from ethanol **8** (676 mg, 81 %) was obtained; mp 233^{0}C; $[\alpha]_D$ –48.6 ^{0} (c 1.0, methanol); MS: m/z (rel. int.) 334 (M^+, 31), 289 (18), 288 (49), 241 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.85 (d, 1H, *J* = 7.9 Hz, NH), 8.75 (s, 1H, OH), 7.89 (s, 1H, thiophene-H), 7.42–7.07 (m, 5H, phenyl-H), 4.45-4.31 (m, 1H, CH), 3.49-3.34 (m, 1H, benzyl-CH_2), 3.32-3.20 (m, 1H, benzyl-CH_2), 2.44 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 190.5, 172.6, 162.7, 134.1, 129.2, 129.0, 128.8, 127.8, 127.0, 124.3, 61.3, 37.5, 24.9; Anal. Calcd for $C_{15}H_{14}N_2O_5S$: C, 53.89; H, 4.22; N, 8.38. Found: C, 53.73; H, 4.11; N, 8.15.

(2*S*)-Methyl (5-acetyl-3-nitro-2-thienyl)aminomethylsulfanylethylacetate (9)

The mixture of **1** (0. 512g, 2.5 mmol) and L-methionine methyl ester hydrochloride (1.598 g, 8 mmol) was stirred at rt for 4 d. After purification on a silica gel column eluting with toluene/ ethyl acetate (8 + 2) **9** (797 mg, 96 %) was obtained as an oil; $[\alpha]_D$ –41.7 ^{0} (c 0.8, acetone); MS: m/z (rel. int.) 332 (M^+, 16), 273 (33), 170 (59), 62 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.90 (d, 1H, *J* = 8.3 Hz, NH), 7.94 (s, 1H, thiophene-H), 4.44-4.34 (m, 1H, CH), 3.84 (s, 3H, CH_3), 2.72-2.53 (m, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.44-2.17 (m, 2H, CH_2), 2.12 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 189.6, 169.9, 162.6, 128.3, 127.0, 124.8, 59.1, 53.2, 30.8, 29.7, 24.9, 15.4; Anal. Calcd for $C_{12}H_{16}N_2O_5S$: C, 43.36; H, 4.85; N, 8.43. Found: C, 43.58; H, 4.70; N, 8.28.

(2S)-2-[(5-Acetyl-3-nitro-2-thienyl)amino]-3-(methylsulfanyl)propionic acid (10)

The mixture of **1** (0.512 g, 2.5 mmol) and S-methyl-L-cysteine (1.082 g, 8 mmol) was stirred at 40^{0}C for 4 d. After purification on a silica gel column eluting with methanol/ ethyl acetate (3 + 7) **10** (654 mg, 86 %) was obtained; mp 150^{0}C (diluted ethanol); $[\alpha]_D$ –13.3 ^{0} (c 0.8, methanol); MS: m/z (rel. int.) 304 (M^+, 100), 181 (100); ^{1}H-NMR (DMSO-d_6/ $CDCl_3$, 300 MHz): δ 9.51 (d, 1H, *J* = 6.9 Hz, NH), 7.97 (s, 1H, thiophene-H), 4.11-4.07 (m, 1H, CH), 3.89 (br s, 1H, OH), 3.18 (m, 2H, CH_2), 2.45 (s, 3H, CH_3), 2.02 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 188.1, 170.4, 161.2, 127.5, 124.8, 121.8, 61.1, 34.6, 23.6, 15.0; Anal. Calcd for $C_{10}H_{12}N_2O_5S_2$: C, 39.47; H, 3.97; N, 9.20. Found: C, 39.15; H, 3.93; N, 8.88.

Ethyl (5-acetyl-3-nitro-2-thienyl)aminoacetate (11)

The mixture of **1** (0.512 g, 2.5 mmol) and glycine ethyl ester hydrochloride (1.117 g, 8 mmol) was stirred at 40^{0}C for 18 h. After crystallization from ethanol **11** (483 mg, 71 %) was obtained; mp 165^{0}C; MS: m/z (rel. int.) 272 (M^+, 1), 227 (11), 44 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.86 (br s, 1H, NH), 7.95 (s, 1H, thiophene-H), 4.33 (q, 2H, *J* = 7.1 Hz, CH_2), 4.14 (d, 2H, *J* = 5.3 Hz, CH_2), 2.49 (s, 3H, CH_3), 1.35 (t,

3H, J = 7.1 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): δ 189.7, 166.9, 162.8, 128.4, 126.7, 124.7, 62.5, 48.1, 24.9, 14.0; Anal. Calcd for $C_{10}H_{12}N_2O_5S$: C, 44.11; H, 4.44; N, 10.29. Found: C, 44.35; H, 4.20; N, 10.22.

Ethyl (5-benzoyl-3-nitro-2-thienyl)aminoacetate (12)

The mixture of **1** (0.512 g, 2.5 mmol) and glycine ethyl ester hydrochloride (1.117 g, 8 mmol) was stirred at 40^{0}C for 4 h. After crystallization from ethanol **12** (493 mg, 59 %) was obtained; mp 127^{0}C; MS: m/z (rel. int.) 334 (M^+, 20), 261 (15), 105 (49), 69 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.92 (br s, 1H, NH), 7.89 (s, 1H, thiophene-H), 7.83-7.75 (m, 2H, phenyl-H), 7.66-7.47 (m, 3H, phenyl-H), 4.34 (q, 2H, J = 7.1 Hz, CH_2), 4.19 (d, 2H, J = 5.3 Hz, CH_2), 1.35 (t, 3H, J = 7.1 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): δ 186.9, 166.9, 162.9, 136.4, 132.5, 130.7, 128.7, 127.1, 124.3, 62.6, 48.2, 14.1; Anal. Calcd for $C_{15}H_{14}N_2O_5S$: C, 53.89; H, 4.22; N, 8.38. Found: C, 53.73; H, 4.20; N, 8.38.

(2*S*)-Methyl 2-[(5-benzoyl-3-nitro-2-thienyl)amino]propionate (13)

The mixture of **1** (0.512 g, 2.5 mmol) and L-alanine methyl ester hydrochloride (1.117 g, 8 mmol) was stirred at 40^{0}C for 6 h. After purification on a silica gel column eluting with toluene/ ethyl acetate (8 + 2) **13** (242 mg, 29 %) as an oil was obtained; $[\alpha]_D$ –8.0 ^{0} (c 0.6, methanol); MS: m/z (rel. int.) 334 (M^+, 100), 275 (65), 105 (3); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.94 (d, 1H, J = 7.7 Hz, NH), 7.88 (s, 1H, thiophene-H), 7.83-7.76 (m, 2H, phenyl-H), 7.66-7.46 (m, 3H, phenyl-H), 4.27 (quint, 1H, J = 7.1 Hz, CH), 3.86 (s, 3H, CH_3), 1.70 (d, 3H, J = 7.1 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): δ 186.8, 170.6, 163.1, 136.5, 132.5, 130.7, 128.7, 128.6, 127.2, 124.1, 55.8, 53.2, 17.8; Anal. Calcd for $C_{15}H_{14}N_2O_5S$: C, 53.89; H, 4.22; N, 8.38. Found: C, 53.70; H, 4.12; N, 8.32.

(2*S*)-Methyl 2-[(5-benzoyl-3-nitro-2-thienyl)amino]-3-phenylpropionate (14)

The mixture of **1** (0.512 g, 2.5 mmol) and L-phenylalanine methyl ester hydrochloride (1.726 g, 8 mmol) was stirred at 40^{0}C for 46 h. After crystallization from methanol **14** (584 mg, 57 %) was obtained; mp 116-117^{0}C; $[\alpha]_D$ –35.0 ^{0} (c 0.55, toluene); MS: m/z (rel. int.) 410 (M^+, 3), 231 (8), 105 (81), 77 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.96-8.81 (m, 1H, NH), 7.83 (s, 1H, thiophene-H), 7.80-7.73 (m, 2H, phenyl-H), 7.64-7.44 (m, 3H, phenyl-H), 7.39-7.25 (m, 3H, phenyl-H), 7.23-7.19 (m, 2H, phenyl-H), 4.49-4.36 (m, 1H, CH), 3.80 (s, 3H, CH_3), 3.39 (AB-system, 1H, J_{AB} = 14 Hz, benzyl-CH_2), 3.28 (AB-system, 1H, J_{AB} = 14 Hz, benzyl-CH_2); ^{13}C-NMR ($CDCl_3$): δ 186.8, 169.3, 162.4, 136.4, 134.2, 132.5, 130.6, 129.1, 129.0, 128.7, 128.6, 127.8, 127.3, 124.1, 61.6, 53.0, 37.8; Anal. Calcd for $C_{21}H_{18}N_2O_5S$: C, 61.45; H, 4.42; N, 6.83. Found: C, 61.34; H, 4.32; N, 6.92.

(2*S*)-1-(5-Acetyl-3-nitro-2-thienyl)-2-pyrrolidinecarboxylic acid (15)

The mixture of **1** (0.512 g, 2.5 mmol) and L-proline (920 mg, 8 mmol) was stirred at rt for 20 h. After crystallization from diluted ethanol **15** (554 mg, 78 %) was obtained; mp 100^{0}C; $[\alpha]_D$ –427.5 ^{0} (c 1.0, methanol); MS: m/z (rel. int.) 284 (M^+, 31), 239 (100); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 13.17 (br s, 1H, OH), 8.26 (s, 1H, thiophene-H), 4.89-4.80 (m, 1H, proline-CH), 3.79-3.66 (m, 1H, proline-CH_2), 3.64-3.53 (m, 1H, proline-CH_2), 2.52 (s, 3H, CH_3), 2.19-2.02 (m, 4H, proline-CH_2); ^{13}C-NMR ($CDCl_3$): δ 189.3, 171.8, 160.3, 130.9, 128.0, 123.9, 65.4, 55.9, 31.3, 24.6, 23.8; Anal. Calcd for $C_{12}H_{16}N_2O_5S$ x 1 H_2O: C, 43.70; H, 4.67; N, 9.27. Found: C, 43.73; H, 4.43; N, 9.12.

1,1' -[Thiobis(3-nitro-2,5-thiophendiyl)]bis-(1-ethanone) (16)

To a suspension of L-cystine dimethyl ester dihydrochloride (2.730 g, 8 mmol) and potassium carbonate (2.208 g, 16 mmol) in absolute acetonitrile (15 mL) 5- acetyl-2-chloro-3-nitrothiophene (0.512 g, 2.5 mmol) was added and the mixtuture was stirred under argon atmosphere. After the reaction was completed (TLC analysis) the organic solvent was removed under reduced pressure. Then the residue was diluted with water and extracted with ethyl acetate. The combined organic layers were dried and the solvent was evaporated. After crystallization from methanol **16** (177 mg, 38 %) was obtained; mp 190^{0}C; MS: m/z (rel. int.) 372 (M^+, 74), 186 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.18 (s, 1H, thiophene-H), 2.61 (s, 3H, CH_3); Anal. Calcd for $C_{12}H_8N_2O_6S_3$: C, 38.71; H, 2.17; N, 7.52. Found: C, 38.61; H, 2.04; N, 7.22.

General procedure for the synthesis of compounds (17 – 24 and 26)

Iron powder (1.562 g) was added in small portions to a suspension of the amino acid derivative (4 mmol) in glacial acetic acid (14 mL) and water (1.5 mL). Then the reaction mixture was heated at 70^{0}C for 1.5 h, filtered in hot, washed with water and allowed to cool. The resulting precipitate was filtered off and recrystallized.

(3*S*)-6-Acetyl-3-methyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (17)

After crystallization from methanol **17** (537 mg, 64 %) was obtained; mp 240^{0}C (decomp); $[\alpha]_D$ –56.9 ^{0} (c 0.5, DMSO); MS: m/z (rel. int.) 210 (M^+, 15), 195 (99), 167 (100); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.37 (br s, 1H, NH), 7.64 (br s, 1H, NH), 7.19 (s, 1H, thiophene-H), 4.08 (dq, 1H, *J* = 1.5 Hz, *J* = 6.6 Hz, CH), 2.37 (s, 3H, CH_3), 1.36 (d, 3H, *J* = 6.6 Hz, CH_3); ^{13}C-NMR ($CDCl_3$/ DMSO-d_6): δ 185.9, 164.6, 142.3, 122.6, 121.2, 119.1, 51.2, 23.6, 16.8; Anal. Calcd for $C_9H_{10}N_2O_2S$: C, 51.41; H, 4.79; N, 13.32. Found: C, 51.55; H, 4.68; N, 13.19.

(3*S*)-6-Acetyl-3-benzyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (18)

After crystallization from methanol **18** (927 mg, 81 %) was obtained; mp 210^{0}C; $[\alpha]_D$ +199.4 ^{0} (c 1.0, DMSO); MS: m/z (rel. int.) 286 (M^+, 15), 195 (100), 91 (18); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.42 (br s, 1H, NH), 7.62 (br s, 1H, NH), 7.41-7.19 (m, 5H, phenyl-H), 7.17 (s, 1H, thiophene-H), 4.36 (br s, 1H, CH), 3.04 (s, 2H, CH_2), 2.33 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ 186.9, 164.3, 143.0, 136.6, 129.6, 128.1, 126.4, 123.5, 122.3, 119.6, 57.7, 38.0, 24.9; Anal. Calcd for $C_{15}H_{14}N_2O_2S$ x 0.25 methanol: C, 62.23; H, 5.14; N, 9.52. Found: C, 62.06; H, 4.85; N, 9.61.

(3*S*)-6-Acetyl-3-[(2-methylsulfanyl)ethyl]-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (19)

After crystallization from methanol **19** (605 mg, 56 %) was obtained; mp 150-152^{0}C; $[\alpha]_D$ +98.6 ^{0} (c 0.5, DMSO); MS: m/z (rel. int.) 270 (M^+, 100), 222 (63), 195 (97); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.44 (br s, 1H, NH), 7.70 (br s, 1H, NH), 7.17 (s, 1H, thiophene-H), 4.17-4.07 (m, 1H, CH), 2.69-2.54 (m, 2H, CH_2), 2.35 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.02-1.89 (m, 2H, CH_2); ^{13}C-NMR (DMSO-d_6): δ 187.2, 164.6. 142.7, 123.7, 122.5, 119.8, 55.3, 31.3, 28.7, 25.0, 14.4; Anal. Calcd for $C_{11}H_{14}N_2O_2S_2$: C, 48.87; H, 5.22; N, 10.36. Found: C, 48.66; H, 5.06; N, 10.09.

(3*S*)-6-Acetyl-3-[(methylsulfanyl)methyl]-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (20)

After crystallization from methanol **20** (399 mg, 39 %) was obtained; mp 183^{0}C; $[\alpha]_D$ +83.2 ^{0} (c 0.5, DMSO); MS: m/z (rel. int.) 256 (M^+, 28), 195 (100); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.53 (br s, 1H, NH), 7.83 (br s, 1H, NH), 7.16 (s, 1H, thiophene-H), 4.40-4.29 (m, 1H, CH), 3.01-2.82 (m, 2H, CH_2), 2.36 (s, 3H, CH_3), 2.17 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ 187.0, 163.8, 142.9, 123.4, 122.5, 119.5, 56.4, 37.0, 25.0, 15.9; Anal. Calcd for $C_{10}H_{12}N_2O_2S_2$: C, 46.86; H, 4.72; N, 10.93. Found: C, 46.93; H, 4.57 N, 10.66.

6-Acetyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (21)

After crystallization from methanol **21** (392 mg, 50 %) was obtained; mp 240 ^{0}C (decomp); MS: m/z (rel. int.) 196 (M^+, 11), 179 (6), 69 (10), 44 (100); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.37 (br s, 1H, NH), 7.53 (br s, 1H, NH), 7.15 (s, 1H, thiophene-H), 3.97 (m, 2H, CH_2), 2.33 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ 186.9, 163.1, 143.9, 123.2, 122.6, 120.1, 46.6, 25.9; Anal. Calcd for $C_8H_8N_2O_2S$: C, 48.97; H, 4.11; N, 14.28. Found: C, 46.14; H, 3.99; N, 14.21.

6-Benzoyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (22)

After crystallization from ethanol **22** (671 mg, 65 %) was obtained; mp 215 ^{0}C; MS: m/z (rel. int.) 258

(M^+, 57), 256 (44), 105 (100), 77 (99); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.31 (br s, 1H, NH), 7.90 (br s, 1H, NH), 7.80-7.45 (m, 5H, phenyl-H), 7.00 (s, 1H, thiophene-H), 4.07 (s, 2H, CH_2); ^{13}C-NMR (DMSO-d_6): δ 184.1, 162.7, 145.6, 138.8, 130.9, 128.4, 127.9, 124.5, 121.8, 120.7, 46.5; Anal. Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85. Found: C, 60.19; H, 3.95; N, 10.56.

(3*S*)-6-Benzoyl-3-methyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (23)

After crystallization from ethanol **23** (555 mg, 51 %) was obtained; mp 240 ^{0}C (decomp); $[\alpha]_D$ -60.0 ^{0} (c 0.5, DMSO); MS: m/z (rel. int.) 272 (M^+, 10), 229 (21), 105 (58), 77 (100); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.29 (br s, 1H, NH), 7.98 (br s, 1H, NH), 7.83-7.50 (m, 5H, phenyl-H), 7.02 (s, 1H, thiophene-H), 4.17 (d, 1H, *J* = 6.4 Hz, CH), 1.40 (d, 2H, *J* = 6.4 Hz, CH_3); ^{13}C-NMR (DMSO-d_6): δ 184.3, 165.3, 144.9, 138.7, 130.9, 128.4, 127.9, 124.5, 122.4, 120.9, 52.1, 18.2; Anal. Calcd for $C_{14}H_{12}N_2O_2S$: C, 61.75; H, 4.44; N, 10.29. Found: C, 61.53; H, 4.57; N, 10.14.

(3*S*)-6-Benzoyl-3-benzyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1*H*)-one (24)

After crystallization from diluted ethanol **24** (905 mg, 65 %) was obtained; mp 190 ^{0}C; $[\alpha]_D$ -46.0 ^{0} (c 0.5, DMSO); MS: m/z (rel. int.) 348 (M^+, 8), 257 (100), 105 (65), 91 (29); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.31 (br s, 1H, NH), 7.95 (br s, 1H, NH), 7.77-7.50 (m, 5H, phenyl-H), 7.46-7.19 (m, 5H, phenyl-H), 6.89 (s, 1H, thiophene-H), 4.46 (s, 1H, CH), 3.07 (s, 2H, CH_2); ^{13}C-NMR (DMSO-d_6): δ 184.1, 164.0, 144.9, 138.8, 136.4, 130.9, 129.7, 128.3, 128.1, 127.9, 126.5, 124.2, 122.1, 120.3, 57.7, 38.3; Anal. Calcd for $C_{20}H_{16}N_2O_2S$: C, 68.95; H, 4.63; N, 8.04. Found: C, 68.69; H, 4.66; N, 8.07.

(2*S*)-Methyl 1-(5-acetyl-3-nitro-2-thienyl)-2-pyrrolidinecarboxylate (25)

A solution of compound (**15**) (1.136 g, 4 mmol) in methanol (10 mL) and 2 drops of concentrated sulfuric acid was refluxed for 20 h. After the reaction was completed (TLC analysis) the organic solvent was removed under reduced pressure. Then the residue was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated. After crystallization from methanol **25** (858 mg, 72 %) was obtained; mp 97-98^{0}C; $[\alpha]_D$ –420.1 ^{0} (c 1.0, acetone); MS: m/z (rel. int.) 298 (M^+, 20), 239 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.97 (s, 1H, thiophene-H), 4.99-4.92 (m, 1H, proline-CH), 3.73 (s, 3H, CH_3), 3.82-3.71 (m, 1H, proline-H), 3.61-3.51 (m, 1H, proline-H), 2.52 (s, 3H, CH_3), 2.56-2.41 (m, 1H, proline-H); 2.28-2.06 (m, 3H, proline-H); ^{13}C-NMR ($CDCl_3$): δ 189.5, 170.9, 160.4, 131.0, 128.3, 124.7, 65.4, 56.0, 52.7, 31.5, 24.9, 23.9; Anal. Calcd for $C_{121}H_{14}N_2O_5S$: C, 48.32; H, 4.73; N, 9.39. Found: C, 48.17; H, 4.58; N, 9.24.

(5a*S*)-2-Acetyl-5a, 6, 7, 8-tetrahydropyrrolo[1,2-*a*]thieno[3,2-*e*]pyrazin-5(4*H*)-one (26)

After crystallization from diluted ethanol **26** (642 mg, 68 %) was obtained; mp 205-210 ^{0}C (decomp); $[\alpha]_D$ -486.6 ^{0} (c 0.5, DMSO); MS: m/z (rel. int.) 236 (M^+, 100), 193 (12), 165 (66); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.34 (br s, 1H, NH), 7.14 (s, 1H, thiophene-H), 4.10-4.01 (m, 1H, CH), 3.53-3.38 (m, 2H, CH_2), 2.39-2.29 (m, 1H, CH), 2.35 (s, 3H, CH_3), 2.17-1.99 (m, 3H, CH/ CH_2); ^{13}C-NMR (DMSO-d_6): δ 186.1, 162.3, 143.0, 123.7, 121.2, 119.6, 60.0, 49.2, 27.3, 23.9, 22.1; Anal. Calcd for $C_{11}H_{12}N_2O_2S$: C, 55.92; H, 5.12; N, 11.86. Found: C, 55.55; H, 5.00; N, 11.65.

General procedure for the synthesis of compounds (27 – 33)

To a solution of the corresponding lactam (**17** – **21** and **23**, **24**) (4 mmol) in dry 1,4-dioxane (15 mL) the acyl chloride derivative (8 mmol) was added. Then the reaction mixture was heated at 40^{0}C for 24 h. After the reaction was completed (TLC analysis) the organic solvent was removed under reduced pressure. Then the residue was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated.

(3*S*)-Vinyl 6-acetyl-3-methyl-2-oxo-1, 2, 3, 4-tetrahydrothieno[2,3-*b*]pyrazine-4-carboxylate (27)

After crystallization from methanol **27** (515 mg, 46 %) was obtained; mp 162^{0}C; $[\alpha]_D$ +184.1 ^{0} (c 1.0, acetone); MS: m/z (rel. int.) 280 (M^+, 100), 209 (36), 71 (33); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.34-10.12 (m, 1H, NH), 7.36-7.15 (m, 2H, thiophene-H/ vinyl-H), 5.21-4.95 (m, 2H, vinyl-CH_2), 4.73 (dd, 1H, *J* = 12.2 Hz, *J* = 6.2 Hz, CH), 2.51 (s, 3H, CH_3), 1.59-1.38 (m, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 190.3, 167.6, 149.5, 141.3, 135.1, 127.8, 123.9, 120.0, 98.8, 54.9, 26.1, 17.6; Anal. Calcd for $C_{12}H_{12}N_2O_4S$: C, 51.42; H, 4.32; N, 9.99. Found: C, 51.45; H, 4.35; N, 9.93.

(3*S*)-Vinyl 6-acetyl-3-benzyl-2-oxo-1, 2, 3, 4-tetrahydrothieno[2,3-*b*]pyrazine-4-carboxylate (28)

After crystallization from acetone / water **28** (870 mg, 61 %) was obtained; mp 80^{0}C; $[\alpha]_D$ +125.9 ^{0} (c 1.0, toluene); MS: m/z (rel. int.) 356 (M^+, 34), 265 (34), 195 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 9.86-9.68 (m, 1H, NH), 7.31-7.05 (m, 6H, thiophene-H/ phenyl-H), 6.74 (dd, 1H, *J* = 6.2 Hz, *J* = 13.7 Hz, CH), 5.24-5.17 (m, 1H, CH), 4.66 (dd, 1H, *J* = 2.3 Hz, *J* = 13.7 Hz, CH), 4.46 (dd, 1H, *J* = 2.3 Hz, *J* = 6.2 Hz, CH), 3.20-3.12 (m, 1H, benzyl-CH_2), 3.00-2.91 (m, 1H, benzyl-CH_2), 2.52 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 190.2, 166.6, 149.8, 140.8, 135.6, 134.2, 129.3, 128.6, 127.5, 124.4, 119.9, 98.2, 60.2, 37.4, 26.2; Anal. Calcd for $C_{18}H_{16}N_2O_4S$: C, 60.66; H, 4.53; N, 7.86. Found: C, 60.58; H, 4.43; N, 7.60.

(3*S*)-Vinyl 6-acetyl-3-[2-methylsulfanyl)ethyl]-2-oxo-1, 2, 3, 4-tetrahydrothieno[2,3-*b*]pyrazine-4-carboxylate (29)

After purification on a silica gel column eluting with toluene/ ethyl acetate (2 + 8) **29** (517 mg, 38 %) was obtained as an oil; $[\alpha]_D$ +220.2 ^{0} (c 1.0, toluene); MS: m/z (rel. int.) 340 (M^+, 75), 266 (61), 221 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.20-9.97 (m, 1H, NH), 7.33-7.16 (m, 2H, thiophene-H/ vinyl-H), 5.25-4.99 (m, 2H, CH_2), 4.76-4.71 (m, 1H, CH), 2.62-2.47 (m, 5H, CH_3/ CH_2), 2.09 (s, 5H, CH_3/ CH_2); ^{13}C-NMR ($CDCl_3$): δ 190.2, 166.4, 149.7, 141.2, 135.6, 128.0, 124.4, 119.9, 98.7, 57.8, 31.2, 29.5, 26.1, 15.4; Anal. Calcd for $C_{14}H_{16}N_2O_4S_2$: C, 49.40; H, 4.74; N, 8.23. Found: C, 49.29; H, 4.66; N, 8.02.

(3*S*)-Isopropyl 6-acetyl-3-[2-methylsulfanyl)methyl]-2-oxo-1, 2, 3, 4-tetrahydrothieno[2,3-*b*]pyrazine-4-carboxylate (30)

After purification on a silica gel column eluting with toluene/ ethyl acetate (2 + 8) **30** (172 mg, 13 %) was obtained as an oil; MS: m/z (rel. int.) 342 (M^+, 32), 195 (100), 61 (64); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.18-9.99 (m, 1H, NH), 7.34-7.19 (m, 2H, thiophene-H), 5.28-5.00 (m, 2H, 2 CH), 2.89-2.68 (m, 2H, CH_2), 2.50 (s, 3H, CH_3), 2.12 (m, 3H, CH_3), 1.52-1.23 (m, 6H, 2 CH_3); ^{13}C-NMR ($CDCl_3$): δ 190.2, 166.7, 152.1, 134.5, 129.4, 123.4, 119.8, 72.3, 57.4, 36.1, 26.1, 21.8, 16.6; Anal. Calcd for $C_{14}H_{18}N_2O_4S_2$: C, 49.11; H, 5.30; N, 8.18. Found: C, 49.21; H, 5.17; N, 8.07.

6-Acetyl-4-cyclopropylcarbonyl-3, 4-dihydrothieno[2,3-*b*]pyrazin-2(1H)-one (31)

After crystallization from diluted ethanol **31** (402 mg, 38 %) was obtained; mp 260^{0}C (decomp); MS: m/z (rel. int.) 264 (M^+, 5), 196 (23), 69 (100); ^{1}H-NMR (DMSO-d_6, 300 MHz): δ 10.91 (m, 1H, NH), 7.32 (s, 1H, thiophene-H), 4.91 (s, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.29-2.17 (m, 1H, CH), 1.08-0.97 (m, 4H, 2 CH_2); ^{13}C-NMR (DMSO-d_6): δ 190.3, 171.4, 162.9, 132.2, 127.3, 124.1, 120.3, 48.5, 26.0, 11.4, 8.9; Anal. Calcd for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60. Found: C, 54.53; H, 4.55; N, 10.34.

(3*S*)-Vinyl 6-benzoyl-3-methyl-2-oxo-1, 2, 3, 4-tetrahydrothieno[2,3-*b*]pyrazine-4-carboxylate (32)

After purification on a silica gel column eluting with toluene/ ethyl acetate (6 + 4) **30** (986 mg, 72 %) was obtained as an oil; $[\alpha]_D$ +233.7 ^{0} (c 0.4, toluene); MS: m/z (rel. int.) 342 (M^+, 9), 271 (12), 105 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 9.91 (s, 1H, NH), 7.81 (s, 1H, thiophene-H), 7.90-7.71 (m, 1H, vinyl-CH), 7.64-7.41 (m, 3H, phenyl-H), 7.33-7.11 (m, 2H, phenyl-H), 5.19-4.94 (m, 2H, vinyl-CH_2), 4.73-4.67 (m, 1H, CH), 1.59 (m, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): δ 187.7, 167.4, 149.6, 141.4, 137.7, 134.3, 132.2, 128.8, 128.5, 123.9, 122.3, 98.7, 55.1, 17.8; Anal. Calcd for $C_{17}H_{14}N_2O_4S$: C, 59.64; H, 4.12; N, 8.18. Found: C, 59.45; H, 4.35; N, 8.03.

(3S)-Vinyl 6-benzoyl-3-benzyl-2-oxo-1, 2, 3, 4-tetrahydrothieno[2,3-*b*]pyrazine-4-carboxylate (33)

After purification on a silica gel column eluting with toluene/ ethyl acetate (6 + 4) **30** (971 mg, 58 %) was

obtained as an oil; $[\alpha]_D$ +105.2 ^{0} (c 1.0, toluene); MS: m/z (rel. int.) 418 (M^+, 6), 179 (1), 105 (100); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 10.08-9.92 (m, 1H, NH), 7.80 (s, 1H, thiophene-H), 7.90-7.68 (m, 1H, vinyl-H), 7.63-7.42 (m, 4H, phenyl-H), 7.29-7.04 (m, 6H, phenyl-H), 5.32-5.03 (m, 1H, CH), 4.72-4.40 (m, 2H, CH_2), 3.20-2.90 (m, 2H, CH_2); ^{13}C-NMR ($CDCl_3$): δ 187.7, 166.4, 149.8, 140.8, 137.7, 134.7, 134.3, 132.1, 129.3, 128.9, 128.8, 128.6, 128.5, 127.4, 124.5, 98.3, 60.2, 37.6; Anal. Calcd for $C_{23}H_{18}N_2O_4S$: C, 66.02; H, 4.34; N, 6.69. Found: C, 66.29; H, 4.47; N, 6.55.

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