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2-(2-THIENYL)- AND 2-PHENYLTHIENO[2,3-*b*][1,4]THIAZINES: SYNTHESIS *VIA* SUZUKI REACTION OF THE DIPHENYLPHOSPHATES[1]

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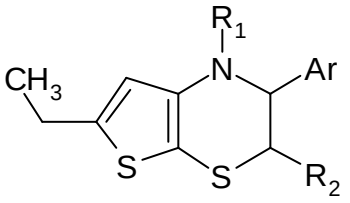
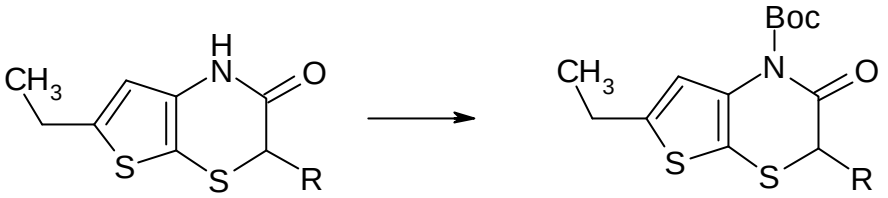
Abstract - Thienothiazinones can be coupled with arylboronic acids using diphenyl phosphates as intermediates and $Pd(PPh_3)_4$ as catalyst.

The current interest in 2-arylthieno[2,3-*b*][1,4]thiazines is based on their potential usefulness as therapeutic agents for the treatment of various diseases. Thieno[2,3-*b*][1,4]thiazine derivatives have been studied as smooth muscle relaxants,[2] NO synthase inhibitors,[3] potassium channel opening agents[4] and benzodiazepin receptor partial agonists .[3] The conventional synthesis of 2-arylthieno[2,3-*b*][1,4]thiazines does not allow an immediate access to various structural analogues so interest was roused in developing a new synthetic pathway to prepare substances of the following type:



R_1 = Boc, CH_3; R_2 = H, Ph
Ar = Ph, thiophene

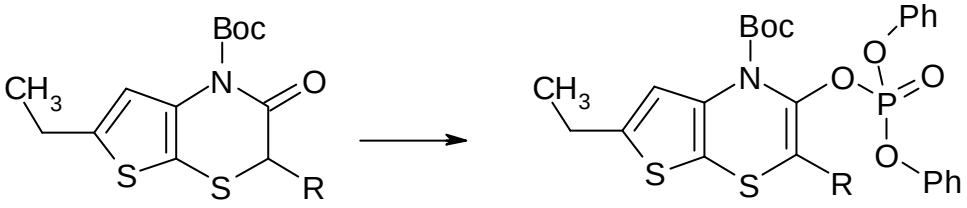
Recently Coudert *et al*.[5] described the synthesis of 3-substituted 4*H*-1,4-benzoxazines *via* palladium-catalysed coupling reactions. As we expected 2-substituted thieno[2,3-*b*]thiazines could be obtained in a similar way from 6-ethyl-1*H*-thieno[2,3-*b*][1,4]thiazin-2(3*H*)-one (**1**)[6] which is readily accessible. The N-Boc derivative (**3**) was first prepared from the lactam (**1**). This was accomplished by treatment with di-*tert*-butyl dicarbonate in dry tetrahydrofuran at room temperature in the presence of dimethylaminopyridine.



1 R = H
2 R = Ph

3 R = H
4 R = Ph

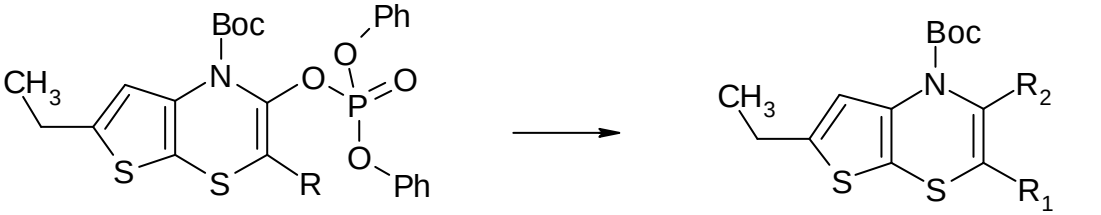
For introduction of an adequate leaving group we prepared the diphenyl phosphate (**5**) from compound (**3**) *via* its lithium enolate. The intermediate (**5**) proved to be stable enough to be purified by columne chromatography on silica gel.



3 R = H
4 R = Ph

5 R = H
6 R = Ph

The palladium-catalysed Suzuki-coupling of this intermediate with boronic acids was accomplished by use of the procedure previously described by Snieckus:[7] to a suspension of $Pd(PPh_3)_4$ in anhydrous dimethoxyethane compound (**5**) was added and the mixture was strirred for 10 min at room temperature. The corresponding boronic acid - benzolboronic acid or thiopheneboronic acid - solved in a minimum of ethanol and aqueous sodium carbonate - was then added. After 2 h the reaction was completed and the products (**7**) and (**9**) could be purified by preparative layer chromatography.

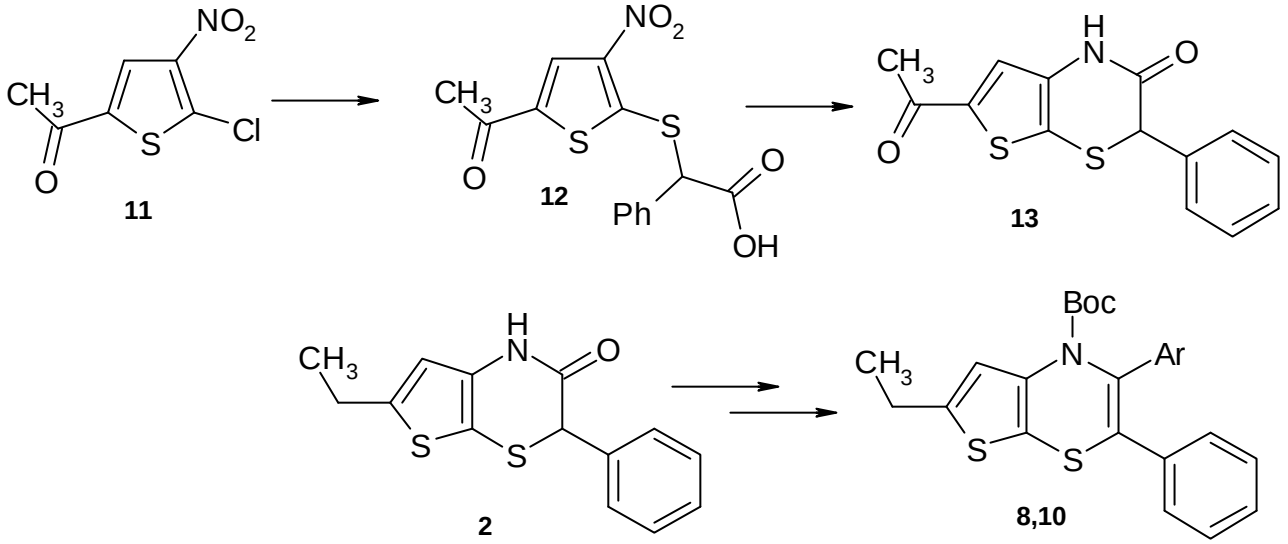


5 R = H
6 R = Ph

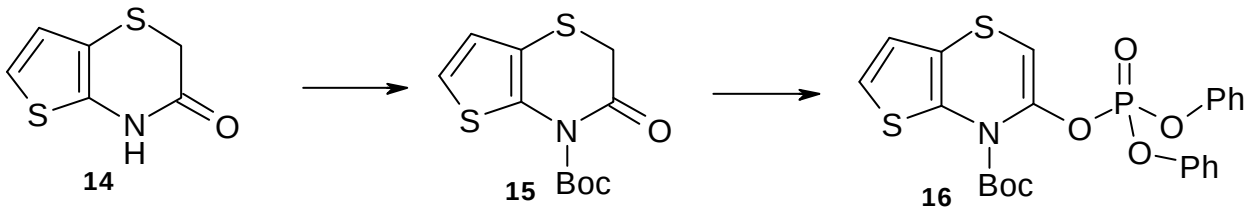
7 R_1 = H, R_2 = Ph
8 R_1 = Ph, R_2 = Ph
9 R_1 = H, R_2 = thiophene
10 R_1 = Ph, R_2 = thiophene

Postulating that a phenyl group in position 3 would be favorable we also prepared 6-ethyl-3-phenyl-1*H*-thieno[2,3-*b*][1,4]thiazin-2(3*H*)-one (**2**). We started from 5-acetyl-2-chloro-3-nitrothiophene (**11**), which

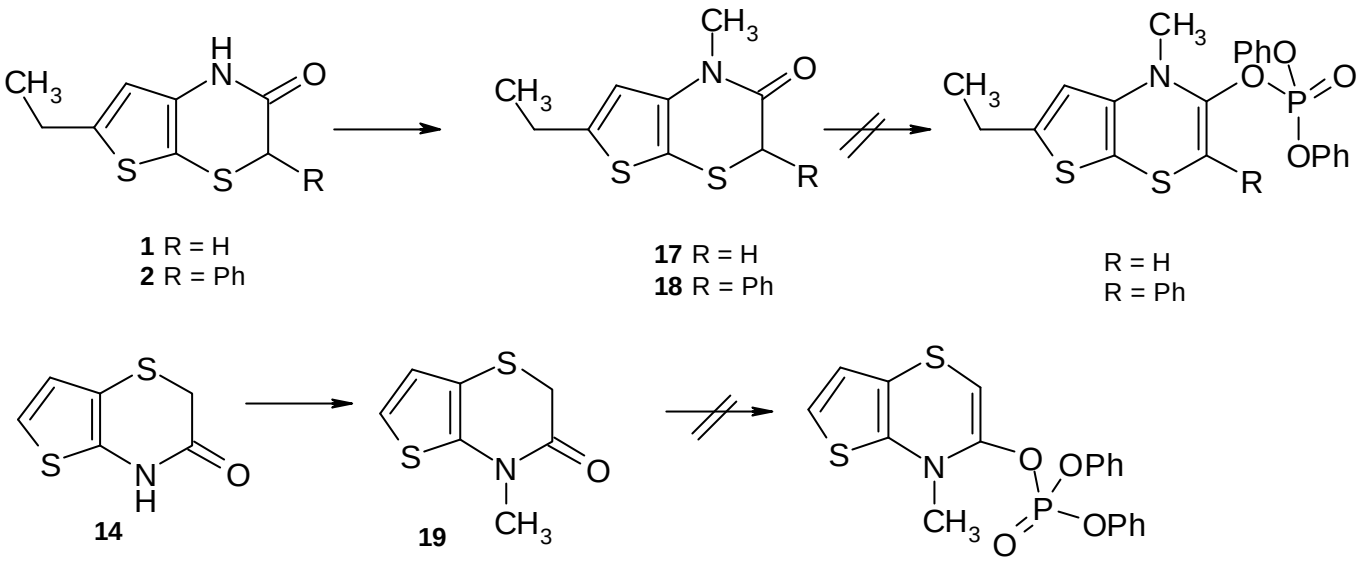
reacted with α-bromophenylacetic acid in the presence of sodium sulfide to compound (**12**). Cyclisation to bicycle (**13**) could be accomplished by using iron powder/ acetic acid. Triflouracetic acid / triethylsilane reduced selectively the carbonyl group. Lactam (**2**) was subject to the above mentioned procedure. In the first step compound (**2**) was treated with di-*tert*-butyl dicarbonate to give the heterocycle (**4**). Subsequent reaction with lithium diisopropylamide and diphenyl chlorophosphate afforded compound (**6**). After Suzuki reaction with the appropriate boronic acids the thieno[2,3-*b*][1,4]thiazine derivates (**8**) and (**10**) could be isolated.



To prove the applicability of our procedure to other thienothiazinones we decided to try it on thieno[3,2-*b*][1,4]thiazinone (**14**) .[8] In this case the last step (Suzuki reaction) could not be accomplished because of the instability of compound (**16**).



Futhermore the use of the *N*-methyl- instead of the *N*-Boc-derivatives seemed to be interesting. The compounds (**1**), (**2**) and (**14**) gave with methyl iodide in a phase transfer reaction in presence of water and potassium hydroxide with benzyltriethylammonium chloride as catalyst the bicycles (**17**), (**18**) and (**19**). But these intermediates were inert or decomposed during the treatment with lithium diisopropylamide. As a consequence non of the desired products could be synthetized.



EXPERIMENTAL

Melting ranges were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Avance DPX 200 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.

6-Ethyl-3-phenyl-1*H*-thieno[2,3-*b*][1,4]thiazin-2(3*H*)-on (2)

Compound (**13**) (289 mg, 1 mmol) was dissolved in trifluoracetic acid (1.2 mL, 15.6 mmol) under argon atmosphere and triethylsilane (0.8 mL, 0.5 mmol) was added dropwise. After 14 h the mixture was cooled with ice and neutralized with saturated sodium hydrogen carbonat solution. The precipitate was collected, dried and crystalized in ethanol to yield **2** (88 mg, 32%); mp: 209-211°C; MS: m/z (rel. int.) 275(M^+, 10), 246 (1), 118 (100), 90 (50); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 9.73 (s, 1H, NH), 7.46-7.20 (m, 5H, Ph-H), 6.42 (s, 1H, thiophene-H), 4.70 (s, 1H, SCH), 2.70 (q, 2H, *J* = 7.5 Hz, CH_2), 1.25 (t, 3H, *J* = 7.5 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 166.5, 146.1, 135.8 , 135.2, 129.1, 128.6, 128.4, 115.9, 106.4, 48.3, 24.1, 15.9. Anal. Calcd for $C_{14}H_{13}NOS_2$: C, 61.06; H, 4.76; N, 5.09. Found: C, 61.00; H, 4.62; N, 5.05

General procedure for the synthesis of compouds (3, 4, 15)

To a solution of the lactam (2.5 mmol) (**1**), (**2**) or (**14**) in 1,2-dichlorethane (5 mL) were added triethylamine (253 mg, 2.5 mmol) , di-*tert*-butyl dicarbonate (1.09 g, 5 mmol) and dimethylaminopyridine (0.31 g, 2.5 mmol). The solution was stirred at rt under argon atmosphere for 3 h. The solvent was evaporated and the residue was purified by preparative layer chromatography.

***tert*-Butyl 6-ethyl-2-oxo-2,3-dihydro-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (3)**

Prepared from **1** (533 mg, 2.5 mmol). Eluent: toluene-ethyl acetate (6:4). After crystallization from ethanol **3** (384 mg, 48 %) was obtained as jellow needles; mp 91-93°C; MS: m/z (rel. int.) 299 (M^+, 4), 199 (M^+-Boc, 64), 184 (42); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 6.61 (s, 1H), 3.43 (s, 2H, CH_2), 2.74 (q, 2H, *J* = 6.2 Hz, CH_2), 1.57 (s, 9H, CH_3), 1.26 (t, 3H, *J* = 6.2 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): δ 164.1, 151.3, 146.0, 136.5, 118.9, 112.9, 85.5, 35.8, 28.2, 24.4, 15.9. Anal. Calcd for $C_{13}H_{17}NO_3S_2$: C, 52.15; H, 5.72; N, 4.68. Found: C, 52.38; H, 5.65; N, 4.62.

***tert*-Butyl 6-ethyl-2-oxo-3-phenyl-2,3-dihydro-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (4)**

Prepared from **2** (688 mg, 2.5 mmol) to give **4** (258 mg, 28 %); mp 147-150°C; MS: m/z (rel. int.) 375 (M^+, 1), 275 (M^+-Boc, 15), 118 (98), 57 (100); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.39-7.26 (m, 5H, Ph-H), 6.56 (s, 1H, thiophene-H), 4.66 (s, 1H,), 2.75 (q, 2H, *J* = 8.0 Hz, CH_2), 1.62 (s, 9H, CH_3), 1.26 (t, 3H, *J* = 8.0 Hz, CH_3). Anal. Calcd for $C_{19}H_{21}NO_3S_2$: C, 60.77; H, 5.64; N, 3.73. Found: C, 60.47; H, 5.52; N, 3.53.

General procedure for the synthesis of compouds (5), (6), (18)

Tetrahydrofuran (2 mL) and diisopropylamine (243 mg, 2.4 mmol) were cooled to -78°C under argon atmosphere and butyllithium (1.6 molar solution in hexane, 1.5 mL, 2.4 mmol) was added. After stirring for 30 min at 0°C the solution was again cooled to -78°C and **2** (2 mmol solved in tetrahydrofuran, 4 mL) was added and stirred for 1 h. Diphenyl chlorophosphate (537 mg, 2 mmol) was added slowly. After 30 min stirring at -78°C the mixture was warmed to rt. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were dried and the solvent was evaporated.

***tert*-Butyl 2-[(diphenoxyphosphoryl)oxy]-6-ethyl-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (5)**

Compound (**5**) was prepared from **3** (599 mg, 2 mmol). The residue was purified *via* column chromatography on silica gel (eluent: toluene- ethyl acetate (9:1)) as eluent to give **5** (250 mg, 24%) as an oil; MS: m/z (rel. int.) 531 (M^+, 0.4), 431 (M^+-Boc, 74), 326 (61), 57 (100); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.40- 7.14 (m, 10H, Ph-H), 6.71 (s, 1H, thiophene-H), 6.19 (s, 1H, CH), 2.75 (q, 2H, *J* = 7.4 Hz, CH_2), 1.49 (s, 9H, CH_3), 1.28 (t, 3H, *J* = 7.4 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 151.3, 150.5, 148.4, 139.4, 139.1, 137.5, 130.2, 126.0, 120.8, 120.3, 103.3, 83.5, 28.4, 24.8, 15.8. Anal. Calcd for $C_{25}H_{26}NO_6PS_2$: C, 56.49; H, 4.93; N, 2.63. Found: C, 56.38; H, 5.12; N, 2.68.

***tert*-Butyl 2-[(diphenoxyphosphoryl)oxy]-6-ethyl-3-phenyl-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (6)**

Comound (**6**) was prepared from **4** (751 mg, 2 mmol) to give **6 (**157 mg, 17 %) as an oil; MS: m/z (rel. int.) 607 (M^+, 0.05), 507 (M^+-Boc, 13), 274 (14), 57 (100); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.55- 6.86 (m, 16H, Ph-H, CH), 6.74 (s, 1H, thiophene-H), 2.79 (q, 2H, *J* = 8.2 Hz, CH_2), 1.55 (s, 9H, CH_3), 1.30 (t, 3H, *J* = 8.2 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 151.3, 150.2, 148.3, 145.9, 138.5, 132.6, 129.8, 128.8, 125.5, 125.2, 120.3, 120.1, 119.6, 83.0, 28.0, 24.2, 15.6. Anal. Calcd for $C_{31}H_{30}NO_6PS_2$x0.3 toluene: C, 62.58; H, 5.14; N, 2.20. Found: C, 62.47; H, 4.85; N, 2.04.

General procedure for the synthesis of compouds (7-10)

To a suspension of $Pd(PPh_3)_4$ (0.058 g, 0.05 mmol) in dry 1,2-dimethoxyethane (10 mL) **5** or **6** (1 mmol) was added under argon atmosphere at rt. The mixture was stirred for 10 min and benzeneboronic acid (183 mg, 1.5 mmol) or thiophene-2-boronic acid (192 mg, 1.5 mmol) dissolved in a small amount of ethanol and a 2M Na_2CO_3-solution (1mL) were added. The progress of the reaction was controlled by TLC. The mixture was distributed between dichlormethane and brine. The organic layer was dried and evaporated.

***tert*-Butyl 6-ethyl-2-phenyl-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (7)**

Compound (**7**) was prepared from **5** (531 mg, 1 mmol) to give **7** (290 mg, 40 %) as an oil; MS: m/z (rel. int.) 359 (M^+, 0.5), 259 (M^+-Boc, 3), 154 (100); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.44- 7.22 (m, 5H, Ph-

H), 7.04 (s, 1H, thiophene-H), 6.28 (s, 1H, CH), 2.79 (q, 2H, *J* = 7.3 Hz, CH_2), 1.33 (t, 3H, *J* = 7.3 Hz, CH_3), 1.18 (s, 9H, CH_3); ^{13}C- NMR ($CDCl_3$): δ 151.7, 147.8, 142.1, 138.4, 137.2, 128.7, 128.1, 125.7, 120.9, 113.5, 82.3, 28.0, 24.6, 15.9. Anal. Calcd for $C_{19}H_{21}NO_2S_2$: C, 63.48; H, 5.89; N, 3.90. Found: C, 63.50; H, 6.10; N, 3.61.

***tert*-Butyl 6-ethyl-2,3-diphenyl-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (8)**

Compound (**8**) was prepared from **6** (607 mg, 1 mmol). The reaction time was 40 h. Purification by preparativ layer chromatography (eluent: toluene-ethyl acetate (9+1)) gave **8 (**3 mg, 1 %), mp: 42°C; HRMS: Calcd for $C_{25}H_{25}NO_2S_2$: 435.1327; Found: 435.1319; MS: m/z (rel. int.) 435 (M^+, 2), 379 (M^+-*t*-butyl, 14), 334 (M^+-Boc, 100), 57 (70); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.20- 6.91 (m, 11H, thiophene-H, Ph-H), 2.77 (q, 2H, *J* = 7.5 Hz, CH_2), 1.25 (t, 3H, *J* = 7.5 Hz, CH_3), 1.06 (s, 9H, CH_3); ^{13}C- NMR ($CDCl_3$): δ 151.7, 147.7, 137.8, 137.7, 137.5, 137.3, 128.9, 128.7, 128.6, 128.4, 127.6, 127.5, 127.3, 121.8, 120.1, 81.9, 27.7, 24.3, 15.4.

***tert*-Butyl 6-ethyl-2-(2-thienyl)-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (9)**

Compound (**9**) was prepared from **5** (531 mg, 1 mmol). Purification by preparative layer chromatografy (eluent: toluene-ethyl acetate (9+1)) gave **9** (90 mg, 25 %) as an oil; MS: m/z (rel. int.) 365 (M^+, 2), 309 (M^+-*t*-butyl, 3), 265 (M^+-Boc, 5), 166 (100); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.28- 6.94 (m, 4H, thiophene-H), 6.44 (s, 1H, CH), 2.63 (q, 2H, *J* = 6.6 Hz, CH_2), 1.32 (s, 9H, CH_3), 1.31 (t, 3H, *J* = 6.6 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 152.0, 147.8, 141.3, 137.1, 136.0, 127.4, 124.6, 124.3, 121.3, 121.1, 113.8, 82.5, 28.2, 24.5, 15.9. Anal. Calcd for $C_{17}H_{19}NO_2S_3$x0.1 toluene: C, 56.73; H, 5.33; N, 3.74. Found: C, 56.87; H, 5.33; N, 3.63.

***tert*-Butyl 6-ethyl-3-phenyl-2-(2-thienyl)-1*H*-thieno[2,3-*b*][1,4]thiazine-1-carboxylate (10)**

Compound (**10**) was prepared from **6** (150 mg, 0.25 mmol). The reaction time was 50 h. Purification by preparative layer chromatography (eluent: toluene-ethyl acetate (9+1)) gave **10** (40 mg, 37%); mp 38-40°C; MS: m/z (rel. int.) 441 (M^+, 1), 385 (M^+-*t*-butyl-, 2), 340 (M^+-Boc, 11), 149 (27), 57 (100); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 7.30- 7.21 (m, 5H, Ph-H), 6.97 (m, 1H, thiophene-H), 6.87 (s, 1H, thiophene-H), 6.71- 6.63 (m, 2H, thiophene-H), 2.75 (q, 2H, *J* = 9.1 Hz, CH_2), 1.28 (s, 9H, CH_3), 1.28- 1.22 (t, 3H, *J* = 9.1 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 152.3, 147.6, 140.3, 137.4, 136.4, 129.8, 129.6, 128.8, 128.7,

126.7, 126.1, 124.9, 122.7, 120.1, 81.9 , 68.1, 27.9, 24.2, 15.4. Anal. Calcd for $C_{23}H_{23}NO_2S_3$: C, 62.55; H, 5.25; N, 3.17. Found: C, 62.41; H, 5.52; N, 3.19.

a **-(5-Acetyl-3-nitro-2-thienylthio)phenylacetic acid (12)**

Pulverized $Na_2S.9H_2O$ (480 mg, 2 mmol) in ethanol (10 mL) was stirred for 30 min under argon atmosphere. 5-Acetyl-2-chlor-3-nitrothiophene (410 mg, 2 mmol) was added in small portions and the mixture was stirred for 1 h. After adding α-bromphenylacetic acid (860 mg, 4 mmol) the reaction was stirred for 14 h. The mixture was poured on iced water and the precipitate was collected and dried. The product (**12**) (500 mg, 79 %) could be characterized without further purification; mp 203-205°C; MS: m/z (rel. int.) 337 (M^+, 1), 187 (13), 135 (100), 79 (100); ^{1}H- NMR (DMSO-d_6, 200 MHz): δ 13.89 (br, 1H, OH), 8.47 (s, 1H, thiophene-H), 7.68-7.36 (m, 5H, Ph-H), 5.61 (s, 1H, PhCH), 2.55 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): δ 190.2, 170.0, 153.9, 141.8, 139.0, 134.5, 129.4, 128.9, 56.5, 26.0. Anal. Calcd for $C_{14}H_{11}NO_5S_2$: C, 49.84; H, 3.29; N, 4.15. Found: C, 49.70; H, 3.24; N, 4.11.

6-Acetyl-3-phenyl-1*H*-thieno[2,3-*b*][1,4]thiazine-2(3*H*)-one (13)

Compound (**12)** (321 mg, 1 mmol) and acetic acid (4 mL, 99%) were heated to 80°C. Iron powder (0.4 g, 7.2 mmol) was added in small portions. The mixture was stirred at 110°C for 30 min. Then the iron powder and -salts were filtered off and washed with hot water. The filtrate was cooled with ice and the precipitate was collected and dried to yield **13 (**90 mg, 32%), mp183-185°C; MS: m/z (rel. int.) 289 (M^+, 21), 118 (67), 90 (87), 43 (100); ^{1}H- NMR (DMSO-d_6, 200 MHz): δ 11.14 (s, 1H, NH), 7.41 (s, 1H, thiophene-H), 7.36-7.22 (m, 5H, Ph-H), 5.13 (s, 1H, SCH), 2.45 (s, 3H, CH_3); ^{13}C- NMR (DMSO-d_6): δ 189.8, 164.1, 141.2, 138.1, 135.9, 129.1, 128.5, 128.1, 124.0, 119.7, 46.3, 26.5. Anal. Calcd for $C_{14}H_{11}NO_2S_2$: C, 58.11; H, 3.83; N, 4.84. Found: C, 58.37; H, 3.83; N, 4.72.

***tert*-Butyl 3-oxo-3,4-dihydro-2*H*-thieno[3,2-*b*][1,4]thiazine-4-carboxylate (15)**

Prepared from **14** (428 mg, 2.5 mmol) to give **17** (70 mg, 10 %), as an oil; MS: m/z (rel. int.) 271 (M^+, 8), 215 (22), 171 (M^+-Boc, 86), 57 (100); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 6.99 (d, 1H, *J* = 6.3 Hz, thiophene-H.), 6.76 (d, 1H, *J* = 6.3 Hz, thiophene-H), 3.46 (s, 2H, CH_2), 1.60 (s, 9H, CH_3); ^{13}C- NMR ($CDCl_3$): δ 164.9, 150.6, 135.0, 124.7 119.9, 115.9, 86.4, 34.3, 28.2. Anal. Calcd for $C_{11}H_{13}NO_3S_2$x0.1 toluene: C, 50.09; H, 4.96; N, 4.99. Found: C, 50.12; H, 5.29; N, 5.28.

tert-Butyl 3-[(diphenoxyphosphoryl)oxy]-4*H*-thieno[3,2-*b*][1,4]thiazine-4-carboxylate (16)

Compound (**16**) was prepared from **15** (542 mg, 2 mmol) to give **16 (**46 mg 46%) as an oil; MS: m/z (rel. int.) 502 (M^+, 0.05), 445 (1), 403 (M^+-Boc, 0.04); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.47- 7.07 (m, 13H, Ar-H, CH), 1.67-1.29 (m, 9H, CH_3).

General procedure for the synthesis of compouds (17-19)

A solution of **1**, **2** or **16** (1 mmol) and methyl iodide (156 mg, 1.1 mmol) in tetrahydrofuran (10 mL) was added slowly to a solution of benzyltriethylammonium chloride (54 mg, 0.237 mmol) and of potassium hydroxide (67 mg, 1.2 mmol) in tetrahydrofuran (10 mL). The addition of 1 drop of water accelerated the reaction rate considerably. The mixture was stirred at rt until consumption of the starting material was completed. The solvent was evaporated and the residue was distributed between water and dichloromethane. The organic layers were collected and after drying the solvent was evaporated. Purification was accomplished by preparartive layer chromatography and/ or crystallisation.

6-Ethyl-1-methyl-1*H*-thieno[2,3-*b*][1,4]thiazin-2(3*H*)-one (17)

Prepared from **1** (213 mg, 1mmol). Purification by crystallization from ethanol gave **17** (110 mg, 48%); mp 70-72°C; MS: m/z (rel. int.) 213 (M^+, 100), 198 (71), 184 (10), 170 (31), 156 (18); ^{1}H- NMR ($CDCl_3$, 200 MHz); δ 6.56 (s, 1H, thiophene-H), 3.48 (s, 2H, CH_2), 3.35 (s, 3H, NCH_3), 2.86 - 2.70 (q, 2H, J =7.3 Hz, CH_2), 1.30 (t, 3H, J = 7.3 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 163.4, 146.1, 139.9, 115.9, 109.0, 33.1, 32.3, 24.4, 16.0. Anal. Calcd for $C_9H_{11}NOS_2$: C, 50.67; H, 5.20; N, 6.57. Found: C, 50.73; H, 5.25; N, 6.45.

6-Ethyl-1-methyl-3-phenyl-2,3-dihydro-1*H*-thieno[2,3-*b*][1,4]thiazin-2-one (18)

Prepared from **2** (275 mg, 1 mmol). Purified by crystallization from ethanol gave **18** (180 mg, 62 %); mp 82-84°C; MS: m/z (rel. int.) 289 (M^+, 100), 274 (6), 256 (28), 246 (2), 224 (32), 118 (42); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 7.37- 724 (m, 5H, Ar-H), 6.56 (s, 1H, thiophene-H), 4.71 (s, 1H, CH), 3.43 (s, 3H, NCH_3), 2.77 (q, 2H, J = 6.7 Hz, CH_2), 1.28 (t, 3H, J = 6.7 Hz, CH_3); ^{13}C- NMR ($CDCl_3$): δ 164.6, 146.5, 139.6, 135.6, 115.9, 128.9, 128.4, 128.3, 115.7, 107.9, 49.1, 33.0, 24.2, 15.9. Anal. Calcd for $C_{15}H_{15}NOS_2.3H_2O$: C, 61.11; H, 5.33; N, 4.75. Found: C, 61.25; H, 5.27; N, 4.64.

4-Methyl-2*H*-thieno[3,2-*b*][1,4]thiazin-3(4*H*)-one (19)

Compound (**19**) was prepared from **16** (171 mg, 1 mmol). Purification by preparative layer chromatography (eluent: toluene- ethyl acetate (8+2)) gave **19** (100 mg, 54 %) as an oil; MS: m/z (rel. int.) 185 (M^+, 100), 170 (1), 156 (39), 142 (53), 128 (15), 102 (27); ^{1}H- NMR ($CDCl_3$, 200 MHz): δ 6.93 (d, 1H, *J* = 5.3 Hz, thiophene-H), 6.78 (d, 1H, *J* = 5.3 Hz, thiophene-H), 3.50 (s, 2H, CH_2), 3.43 (s, 3H, NCH_3); ^{13}C- NMR ($CDCl_3$): δ 163.5 140.6, 125.8, 116.5, 112.3, 34.6, 31.8. Anal. Calcd for $C_7H_7NOS_2$: C, 45.38; H, 3.81; N, 7.56. Found: C, 45.28; H, 3.87; N, 7.32.

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