SUPPORTING INFORMATION

Chloroacetylthiophenes. General procedure. The corresponding thiophene was added to a stirred mixture of chloroacetyl chloride (ClAc-Cl) and anhydrous aluminium chloride ($AlCl_3$) in dry carbon disulfide (CS_2). Then, the mixture was stirred at room temperature overnight, refluxed for 1 h and cooled in an ice bath. Under vigorous stirring, HCl 1N was cautiously added to this cooled mixture, the present solid disappeared and the reaction mixture separated in two layers. The organic layer was separated, washed with water (50 ml), dried ($MgSO_4$) and evaporated. The compounds were purified by column chromatography or recrystallization.

2-Chloro-1-[4-(2-chloro-acetyl)-thiophen-2-yl]-ethanone (24). ClAc-Cl (5.18 gr, 0.046 moles), anhydrous $AlCl_3$ (6.12 gr, 0.046 moles); thiophene (1.68 gr, 0.020 moles) in dry CS_2 (50 mL). Two products were isolated by column chromatography (hexane:ethyl acetate 4:1). Compound **24**: yield 68%, m.p.: 154-155 ºC (water/methanol), ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.4 (s, 1H, H_5), 8.2 (s, 1H, H_3), 4.6 (s, 2H, CH_2), 4.5 (s, 2H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 189.0 (CO), 188.2 (CO), 145.9 (C-CO), 144.3 (CH), 143.3 (C-CO), 135.9(CH), 49.7 (CH_2), 49.1 (CH_2); M/z (EI): 240, 238, 236 (M^+, 1, 2, 8 %), 189, 187 (M-CH_2Cl, 39, 100 %); HPLC: Delta Pak Column C18, 5 µm, 300 Å, (150 X 3.9 mm), Purity: 96 %, r.t.= 3.21 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N)]50/50. Anal. Calcd. for $C_8H_6Cl_2O_2S$: C, 40.52; H, 2.55; Cl, 29.90; S, 13.52. Found : C, 40.27; H, 2.50; Cl, 29.67; S, 13.65.The second isolated compound was **22**: 0.22 gr (13%).

2-Chloro-1-[4-(2-chloro-acetyl)-5-methyl-thiophen-2-yl]-ethanone (26) and 2-Chloro-1-(5-methyl-thiophen-2-yl)-ethanone (25). ClAc-Cl (5.18 gr, 0.046 moles), anhydrous $AlCl_3$ (6.12 gr, 0.046 moles); thiophene (1.68 gr, 0.020 moles) in dry CS_2 (50 mL). Two products were isolated by column chromatography (hexane:ethyl acetate 6:1). Compound **26**: 3.66 gr (73%), yellowish solid, m.p.: 110-111 ºC (hexane), ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.0 (s, 1H, Ar), 4.54 (s, 2H, CH_2), 4.52 (s, 2H, CH_2), 2.8 (s , 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 190.3 (CO), 187.7 (CO), 164.6 (C-CH_3), 140.3 (C-CO), 137.4 (C-CO), 137.1 (CH), 51.2 (CH_2), 48.9 (CH_2), 21.1 (CH_3); M/z (EI): 254, 252, 250 (M^+, 2, 11, 15 %), 203, 201 (M-CH_2Cl, 52, 100 %); HPLC: Delta Pak Column C18, 5 µm, 300 Å, (150 X 3.9 mm), Purity 94 %, r.t.= 3.89 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_9H_8Cl_2O_2S$: C, 43.04; H, 3.21; Cl, 28.23; S, 12.77. Found : C, 43.16; H, 3.15; S, 13.02. The second compound was **25**: 0.22 gr (8%), colorless solid, m.p.: 50-51 ºC (hexane), ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.60 (d, *J*= 3.8 Hz, 1H, Ar), 6.83 (dc, *J*= 3.8 Hz, 1H, Ar), 4.53 (s, 2H, CH_2), 2.55 (s , 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 187.7 (CO), 155.4 (C-CH_3), 142.5 (C-CO), 137.7 (CH), 131.1 (CH), 49.2 (CH_2), 20.0 (CH_3); M/z (EI): 176, 174 (M^+, 3, 8 %), 125 (M-CH_2Cl, 100 %); HPLC: Delta Pak Column C18, 5 µm, 300 Å, (150 X 3.9 mm), Purity 94 %, r.t.= 3.38 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for C_7H_7ClOS: C, 48.14; H, 4.04; Cl, 20.30; S, 18.36. Found: C, 48.31; H, 4.11; S, 18.60.

2-Chloro-1-(2,5-dimethyl-thiophen-3-yl)-ethanone (27). ClAc-Cl (1.30 gr, 0.012 moles), anhydrous $AlCl_3$ (1.53 gr, 0.012 moles) and 2,5-dimethylthiophene (1.12 gr, 0.010 moles) in dry CS_2 (50 mL). After purification by column chromatography (hexane:ethyl acetate 8:1), 1.51 gr (80%), brownish solid, m.p.: 54-55 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 6.9 (s, 1H, H_4), 4.5 (s, 2H, CH_2), 2.7 (s, 3H, CH_3), 2.4 (s, 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 188.9 (CO), 152.7 (C-CH_3), 138.5 (C-CO), 134.8 (C-CH_3), 127.6 (CH), 50.6 (CH_2), 18.6 (CH_3), 17.5 (CH_3); M/z (EI): 190, 188 (M^+, 13, 34 %), 139 (M-CH_2Cl, 100 %); HPLC: Delta Pak Column C18, 5 µm, 300 Å, (150 X 3.9 mm), Purity 98 %, r.t.= 4.52 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N)]50/50. Anal. Calcd. for $C_8H_6Cl_2O_2S$: C, 50.93; H, 4.81; S, 17.00. Found : C, 50.84; H, 4.81; S, 16.95.

2-Chloro-1-[5-(2-chloro-acetyl)-4-methyl-thiophen-3-yl]-ethanone (30) 2-chloro-1-(4-methyl-thiophen-2-yl)-ethanone (29) and 2-chloro-1-(3-methyl-thiophen-2-yl)-ethanone (28). According to the general method, 3-methylthiophene (3.92 gr, 0.020 moles) was added dropwise to a stirred solution of ClAc-Cl (5.18 gr, 0.046 moles) and anhydrous $AlCl_3$ (6.12 gr, 0.046 moles) in dry carbon disulfide (50 ml). Three products were isolated by column chromatography (hexane:ethyl acetate 3:1). Compound **30**: 3.46 gr (69 %), colorless solid, m.p.: 155-156 ºC , ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.2 (s, 1H, Ar), 4.54 (s, 2H, CH_2), 4.52 (s, 2H, CH_2), 2.8 (s , 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 187.2 (CO), 185.1 (CO), 148.2 (C-CO), 139.1 (C-CO), 137.9 (CH), 48.1 (CH_2), 47.3 (CH_2), 16.0 (CH_3); M/z (EI): 254, 252, 250 (M^+, 1, 6, 9 %), 203, 201 (M-CH_2Cl, 47, 100 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 99 %, r.t.= 4.73min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_9H_8Cl_2O_2S$: C, 43.04; H, 3.21; S, 12.77. Found : C, 42.98; H, 3.18; S, 12.68. Compound **29**: 0.27 gr (8 %), colorless solid, m.p.: 76-77 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.6 (s, 1H, Ar), 7.1 (s, 1H, Ar), 4.55 (s, 2H, CH_2), 2.3 (s , 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 188.1 (CO), 144.2 (C-CO), 143.2 (C-CH_3), 138.9 (CH), 134.9 (CH), 49.4 (CH_2), 19.5 (CH_3); M/z (EI): 176, 174 (M^+, 9, 23 %), 125 (M-CH_2Cl, 100 %); HPLC: Column µ Bondapack C18, 10 µm, 125Å, (300 X 3.9 mm), Purity 98 %, r.t.= 4.56 min, Conditions Acetonitrile / H_2O [(0.05 % H_3PO_4 + 0.04 % Et_3N)] 50/50. Anal. Calcd. for C_7H_7ClOS: C, 48.14; H, 4.04; S, 18.36. Found : C, 48.04; H, 3.99; S, 18.19. Finally, compound **28**: 0.17 gr, (5 %), colorless solid, m.p.: 35-36 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.44 (d, *J*= 4.9 Hz, 1H, Ar), 7.0 (d, *J*= 4.9 Hz, 1H, Ar), 4.55 (s, 2H, CH_2), 2.3 (s ,3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 188.2 (CO), 151.3 (C-CH_3), 136.8 (CH), 136.2 (C-CO), 135.0 (CH), 51.5 (CH_2), 20.9 (CH_3); M/z (EI): 176, 174 (M^+, 6, 16 %), 125 (M-CH_2Cl, 100 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 99 %, r.t.= 3.65 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for C_7H_7ClOS: C, 48.14; H, 4.04; S, 18.36. Found : C, 48,24; H, 4.14; S, 18.22.

2-Chloro-1-(5-chloro-thiophen-2-yl)-ethanone (31). ClAc-Cl (2.59 gr, 0.023 moles), anhydrous $AlCl_3$ (3.06 gr, 0.023 moles); 2-chlorothiophene (2.37 gr, 0.020 moles) and dry CS_2 (50 mL). Purified by column chromatography (hexane:ethyl acetate 5:1), 3.20 gr (80%), colorless solid, m.p.: 80-81 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.58 (d, *J*= 3.8 Hz, 1H, Ar), 7.0 (s, *J*= 3.8 Hz, 1H, Ar), 4.51 (s, 2H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 184.1 (CO), 154.2 (C-CO), 139.5 (C-Cl), 132.5 (CH), 128.0 (CH), 45.3 (CH_2); M/z (EI): 198, 196, 194 (M^+, 2, 12, 18 %), 147, 145 (M-CH_2Cl, 54, 100 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 98 %, r.t = 3.80 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_6H_4Cl_2OS$: C, 36.94; H, 2.07; S, 16.44. Found : C, 37.04; H, 2.10; S, 16.25.

1-(5-Bromo-thiophen-2-yl)-2-chloro-ethanone (32). ClAc-Cl (2.59 gr, 0.023 moles), anhydrous $AlCl_3$ (3.06 gr, 0.023 moles), 2-bromothiophene (3.26 gr, 0.020 moles) and dry CS_2 (50 mL). Purified by column chromatography (hexane:ethyl acetate 5:1), 3.91 gr (82%), colorless solid, m.p.: 95-96 ºC (heptane), ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.53 (d, *J*= 4.02 Hz, 1H, Ar), 7.14 (s, *J*= 4.02 Hz, 1H, Ar), 4.51 (s, 2H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 183.7 (CO), 142.1 (C-CO), 133.8 (CH), 131.9 (CH), 124.1 (C-CBr), 42.5 (CH_2); M/z (EI): 242, 240, 238 (M^+, 4, 13, 10 %), 191, 189 (M-CH_2Cl, 100, 100 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 96 %, r.t = 4.47 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_6H_4BrClOS$: C, 30.09; H, 1.68; S, 13.39. Found : C, 30.06; H, 1.67; S, 13.21.

2-Chloro-1-(3,4-dibromo-thiophen-2-yl)-ethanone (33). ClAc-Cl (0.54 gr, 4.75 mmoles), anhydrous AlCl3 (0.63 gr, 4.75 mmoles), 3,4-dibromothiophene (1.0 gr, 4.13 mmoles) and dry CS_2 (50 mL). Column chromatography (hexane:ethyl acetate 8:1), 1.27 gr (97%), reddish solid, m.p.: 86-87 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.71 (s, 1H, Ar), 4.85 (s, 2H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 185.4 (CO), 140.0 (C-CO), 133.7 (CH), 120.8 (C-Br), 119.6 (C-Br), 50.1 (CH_2); M/z (EI): 322, 320, 318, 316 (M^+, 3, 11, 15, 7 %), 271, 269, 267 (M-CH_2Cl, 56, 100, 56 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 97 %, r.t

= 3.83 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_6H_3Br_2ClOS$: C, 22.63; H, 0.95; S, 10.07. Found : C, 22.48; H, 0.85; S, 10.04.

2-Chloro-1-(4,5-dibromo-thiophen-2-yl)-ethanone (34). ClAc-Cl (0.54 gr, 4.75 mmoles); anhydrous $AlCl_3$ (0.63 gr, 4.75 mmoles), 2,3-dibromothiophene (1.0 gr, 4.13 mmoles) and dry CS_2 (50 mL). Column chromatography (hexane:ethyl acetate 8:1), 1.19 gr (91%), reddish solid, m.p.: 90-91 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.58 (s, 1H, Ar), 4.48 (s, 2H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 182.9 (CO), 141.0 (C-CO), 135.1 (CH), 123.3 (C-Br), 115.6 (C-Br), 44.9 (CH_2); M/z (EI): 322, 320, 318, 316 (M^+, 3, 11, 15, 7 %), 271, 269, 267 (M-CH_2Cl, 56, 100, 56 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 95 %, r.t = 7.62 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_6H_3Br_2ClOS$: C, 22.63; H, 0.95; S, 10.07. Found : C, 22.54; H, 0.82; S, 10.78.

2-Chloro-1-(2,5-dichloro-thiophen-3-yl)-ethanone (35). ClAc-Cl (2.59 gr, 0.023 moles), anhydrous $AlCl_3$ (3.06 gr, 0.023 moles), 2,5-dichlorothiophene (3.06 gr, 0.02 moles) and dry CS_2 (50 mL). Column chromatography (hexane:ethyl acetate 12:1), 4.17 gr (91%), brownish solid, m.p.: 43-44 ºC (ethanol), ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.1 (s, 1H, Ar), 4.6 (s, 2H, CH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) : 186.6 (CO), 136.9 (C-Cl), 136.0 (C-CO), 130.2 (C-Cl), 129.4 (CH-Ar), 50.6 (CH_2); M/z (EI): 234, 232, 230, 228 (M^+, 1, 6, 16, 16 %), 183, 181, 179 (M-CH_2Cl, 18, 79, 100 %), 155, 153, 151 (M-$COCH_2Cl$, 3, 13, 19 %), 118, 116 (M-$COCH_2Cl_2$, 5, 13 %); HPLC: Delta Pak Column C18, 5 µm, 300 Å, (150 X 3.9 mm), Purity 99 %, r.t.= 6.16 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_6H_3Cl_3OS$: C, 31.40; H, 1.32; S, 13.97. Found : C, 31.35; H, 1.27; S, 13.94.

1-(5-Acetyl-thiophen-2-yl)-2-chloro-ethanone (36). ClAc-Cl (2.59 gr, 0.023 moles), anhydrous $AlCl_3$ (3.06 gr, 0.023 moles), 2-acetylthiophene (2.52 gr, 0.02 moles) and dry CS_2 (50 mL). Column chromatography (hexane:ethyl acetate 3:1), 1.0 gr (25%), colorles solid, m.p.: 94-95 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.3 (d, *J* = 4.2 Hz, 1H, Ar), 8.1 (d, *J*=4.2 Hz, 1H, Ar), 4.55 (s, 2H, CH_2), 2.6 (s, 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 193.0 (CO), 187.8 (CO), 148.3 (C-CO), 142.0 (CH), 141.7 (C-CO), 133.7 (CH), 48.3 (CH_2), 29.2 (CH_3); M/z (EI): 204, 202 (M^+, 4, 10 %), 153 (M-CH_2Cl, 100 %); HPLC: Column µ Bondapack C18, 10 µm, 125 Å, (300 X 3.9 mm), Purity 98 %, r.t.= 3.50 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_8H_7ClO_2S$: C, 47.41; H, 3.48; S, 15.82. Found : C, 47.35; H, 3.38; S, 15.71.

1-(4-Acetyl-thiophen-2-yl)-2-chloro-ethanone (37). ClAc-Cl (1.02 gr, 9.10 mmoles); anhydrous $AlCl_3$ (1.21 gr, 9.10 mmoles); 3-acetylthiophen (1.0 gr, 7.92 mmoles) and CS_2 (50 mL). Column chromatography (hexane:ethyl acetate 2:1), 0.65 gr (41%), colorless solid, m.p.: 118-119 ºC, ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.3 (s, 1H, Ar), 8.1 (s, 1H, Ar), 4.60 (s, 2H, CH_2), 2.56 (s, 3H, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 191.6 (CO), 184.5 (CO), 143.3 (C-CO), 141.7 (C-CO), 139.7 (CH), 132.0 (CH), 45.4 (CH_2), 27.4 (CH_3); M/z (EI): 204, 202 (M^+, 6, 17 %), 153 (M-CH_2Cl, 100 %); HPLC: Delta Pak Column C18, 5 µm, 300 Å, (150 X 3.9 mm), Purity 94 %, r.t.= 2.70 min, acetonitrile / H_2O (0.05 % H_3PO_4 + 0.04 % Et_3N) 50/50. Anal. Calcd. for $C_8H_7ClO_2S$: C, 47.41; H, 3.48; S, 15.82. Found : C, 47.38; H, 3.40; S, 15.77.

Inhibition of GSK-3β. GSK-3β enzyme (Sigma) was incubated with 15 µM of ATP, 0,2 µCi of [γ-^{32}P] ATP, GS-1 substrate[14], and different concentration of test compound. GSK-3β activity was assayed in 50 mM tris, pH 7,5, 10 mM $MgCl_2$, 1 mM EGTA, and 1 mM EDTA buffer, at 37 ºC, in the presence of 15 µM GS-1 (substrate), 15 µM ATP and 0,2 µCi of [γ-^{32}P] ATP in a final volume of 12 µl. After 20 min incubation at 37 ºC, 4 µl alicuots of the supernatant were spotted onto 2x2 cm pieces of whatman P81 phosphocellulose paper, and the filter were washed four times (for at least 10 min each time) in 1% phosphoric acid. The dried filters were transferred into scintillation vials, and the radioactivity was measured in a liquid scintillation counter. Blank values were subtrated, and the GSK-3β activity was expressed in percentage of maximal activity. The IC50 is defined as the concentration of each compound that reduces a 50% the enzimatic activity with respect to that without inhibitors.