SUPPLEMENTARY MATERIAL

The analytical and spectral data of the synthesized compounds are available

**Synthesis and antimicrobial activity of new 3,5-diarylidene-4-piperidone derivatives**

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ANALYTICAL AND SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS

*3,5-Bis(4-fluorobenzylidene)piperidin-4-one hydrochloride (****3a****).*Yellow crystals; Yield: 94%; m.p. 236-238 °C; 1H-NMR (400 MHz, DMSO-*d*6, δ / ppm): 4.40 (4H, *s*, -NH-CH2), 7.35 (4H, *m*, aromatic), 7.59 (4H, *dd*, *J* = 8.8 Hz, 5.6 Hz, Ar), 7.84 (2H, *s*, Ar-CH=C), 9.64 (2H, *s*, NH.HCl); 13C-NMR (100 MHz, DMSO-*d6*, δ / ppm): 44.5 (NCH2), 116.4 (*d*, *J* = 21.6 Hz), 128.9, 130. 9, 133.4 (*d*, *J* = 8.6 Hz), 138.0, 162.0 (*d*, *J* = 247.8 Hz), 183.3 (CO); ESI-HRMS (*m/z*): Calcd. for C19H15F2NO: 311.1. Found: 312.2 (M+H).

*3,5-bis(Thiophen-2-ylmethylene)piperidin-4-one hydrochloride (****3b****).*Yellow crystals; Yield: 96%; m.p. 357-359 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.47 (4H, *s*, -NH-CH2), 7.31 (2H, *dd*, *J* = 5.0, 3.8 Hz, Ar), 7.69 (2H, *s*, Ar-CH=C), 8.02 (4H, *m*, Ar), 10.1 (2H, *s*, NH.HCl); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 44.0 (NCH2), 124.7, 129.3, 131.3, 133.4, 136.0, 137.4, 181.8 (CO); ESI-HRMS (*m/z*): Calcd. for C15H13NOS2:287.4. Found: 288.2 (M+H).

*3,5-bis(Benzo[d][1,3]dioxol-5-ylmethylene)piperidin-4-one (****3c****).*Yellow powder; Yield: 93%; m.p. 256-258 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 3.95 (4H, *s*, -NH-CH2), 5.75 (1H, *s*, NH), 6.09 (4H, *s*,OCH2O), 7.01 (4H, *m*, Ar), 7.05 (2H, *s*, Ar), 7.49 (2H, *s*, Ar-CH=C); 13C-NMR (100 MHz, DMSO-*d6 ,* δ / ppm): 48.1 (NCH2), 102.0 (OCH2O), 109.0, 110.5, 126.2, 129.6, 134.1, 134.9, 148.1, 148.5, 187.8 (CO); ESI-HRMS (*m/z*): Calcd. for C21H17NO5: 363.1. Found: 364.2 (M+H).

*3,5-bis(Thiophen-3-ylmethylene)piperidin-4-one hydrochloride (****3d****).* Yellow powder; Yield: 90%; m.p. 348-350 °C; 1H-NMR (400 MHz, DMSO-*d6 ,*δ / ppm): 4.49 (4H, *s*, -NH-CH2), 7.40 (2H, *d*, *J* = 5.2 Hz, Ar), 7.76 (2H, *m*, Ar), 7.85 (2H, *s*, Ar), 8.04 (2H, *s*, Ar-CH=C), 9.95 (2H,*s*, NH.HCl); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 44.3 (NCH2), 126.4, 128.2, 129.7, 132.0, 132.9, 136. 0, 182.8 (CO); ESI-HRMS (*m/z*): Calcd. for C15H13NOS2: 287. 0. Found: 287.7 (M).

*3,5-Dibenzylidenepiperidin-4-one (****3e****).*Yellow powder; Yield: 90%; m.p. 211-213 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.48 (4H, *s*, -NH-CH2), 7.52 (6H, *m*, Ar), 7.62 (4H, *m*, Ar), 7.68 (2H, *s*, Ar-CH=C), 9.81 (1H, *s*, NH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 44.6 (NCH2), 129.1, 131.1, 133.7, 138.2, 142.2, 144.7, 184.5 (CO); ESI-HRMS (*m/z*): Calcd. forC19H17NO:275.3. Found: 275.2 (M).

*3,5-bis(3-Chloro-4-hydroxybenzylidene)piperidin-4-one hydrochloride (****3f)****.* Yellow crystals; Yield: 95%; m.p. 320-322 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.46 (4H, *s*, -NH-CH2), 7.15 (2H, *d*, *J* = 8.4 Hz, Ar), 7.34 (2H, *m*, Ar), 7.57 (2H, *d*, *J* = 2.0 Hz, Ar), 7.74 (2H, *s*, Ar-CH=C), 9.76 (2H, *s*, NH.HCl), 11.12 (2H, *s*, OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 44.3 (NCH2), 117.4, 120. 8, 126.3, 126.4, 131.6, 132.9, 138.4, 155.6 (COH), 182.4 (CO); ESI-HRMS (*m/z*): Calcd. for C19H15Cl2NO3: 376.2. Found: 375.9 (M).

*3,5-bis(4-Fluorobenzylidene)-1-(3,5-dichloro-2-hydroxyphenylsulfonyl) piperidin-4-one (****5a****)*. Pale yellow solid; Yield: 92%; m.p. 221-223 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.73 (4H, *s*, -NCH2), 7.28 (1H, *d*, *J* = 2.8 Hz, -SO2-Aryl), 7.34 (4H, *t*, *J* = 8.8 Hz, aromatic), 7.52 (4H, *dd*, *J* = 8.4, 5.6 Hz, Ar), 7.57 (2H, *s*, ArCH=C), 7.82 (1H, *d*, *J* = 2.8 Hz, -SO2-Aryl), 11.06 (1H, *s*,-OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.8 (NCH2), 116.2 (*d*, *J*= 21.5 Hz), 124.7, 128.5, 128.8, 131.1, 131.5, 133.2 (*d*, *J* = 8.5 Hz), 134.3, 135.6, 151.7 (COH), 161.7 (*d*, *J* = 247.2 Hz), 185.4 (CO); ESI-HRMS (*m/z*): Calcd. for C25H17Cl2F2NO4S: 536.4. Found: 534.0 (M-2).

*1-(3,5-Dichloro-2-hydroxyphenylsulfonyl)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one (****5b****).* Pale yellow solid; Yield: 93.0%; m.p. 219-221°C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.77 (4H, *s*, -NCH2), 7.28 (2H, *dd*, *J* = 5.2, 3.6 Hz, Ar), 7.49 (1H, *d*, *J* = 2.4 Hz, Ar), 7.49 (2H, *d*, *J* = 3.6 Hz, Ar), 7.77 (2H, *s*, Ar-CH=C), 7.82 (1H,  *d*, *J* = 2.8 Hz, Ar), 7.98 (2H *, d*, *J* = 4.8 Hz, Ar), 11.16 (1H, *s*, OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.8 (NCH2), 123.4, 124.6, 127.5, 128.8, 129.0, 133.1, 133.9, 134.6, 135.3, 137.9, 138.3, 151.0 (COH), 184.3 (CO); ESI-HRMS (*m/z*): Calcd. for C21H15Cl2NO4S3: 510.9. Found: 509.82. (M-H).

*3,5-bis(Benzo[d][1,3]dioxol-5-ylmethylene)-1-(3,5-dichloro-2-hydroxyphenyl-sulfonyl)piperidin-4-one (****5c****).* Pale yellow solid; Yield: 95.0%; m.p. 242.5-243.4°C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.70 (4H, *s*, -NCH2), 6.1 (4H, *s*, OCH2O), 6.99 (6H, *m*, Ar), 7.34 (1H, *d*, *J* = 2.8 Hz, Ar), 7.57 (2H, *s*, Ar-CH=C), 7.82 (1H, *d*, *J* = 2.4 Hz, Ar), 11.04 (1H, *s*, OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.0 (NCH2), 102.2 (OCH2O), 109.2, 110.5, 126.5, 128.5, 128.7, 130.1, 131.1, 133.3, 133.5, 134.4, 136.7, 148.2, 149.0, 151.0 (COH), 185.1 (CO); ESI-HRMS (*m/z*): Calcd. for C27H19Cl2NO8S: 587.0. Found: 586.0 (M-2).

*1-(3,5-Dichloro-2-hydroxyphenylsulfonyl)-3,5-bis(thiophen-3-ylmethylene)piperidin-4-one (****5d****).*  Pale yellow solid; Yield: 92.0%; m.p. 217-219 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.73 (4H, *s*, -NCH2), 7.34 (2H, *d*, *J* = 4.4 Hz, Ar), 7.47 (1H, *d*, *J* = 5.6 Hz, Ar), 7.60 (2H, *s*, Ar), 7.72 (2H, *dd*, *J* = 5.2, 4.8 Hz, Ar), 7.84 (1H, *d*, *J* = 2.4 Hz, Ar), 7.92 (2H, *s*, Ar-CH=C); 11.08(1H, *s*, OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.3 (NCH2), 123.4, 124.3, 127.9, 128.7, 129.7, 130.0, 130.1, 131.0, 134.4, 136.3, 136.5, 150.8(COH), 185.2 (CO); ESI-HRMS (*m/z*): Calcd. for C21H15Cl2NO4S3: 510.9. Found: 511.9 (M+1).

*3,5-Dibenzylidene-1-(3,5-dichloro-2-hydroxyphenylsulfonyl)piperidin-4-one (****5e****).* Pale yellow solid; Yield: 98.0%; m.p. 191-193 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.75 (4H, *s*, -NCH2), 7.30 (1H, *d*, *J* = 2.4 Hz, SO2-aryl), 7.49 (10H,  *m*, Ar), 7.61 (2H, *s*, ArCH=C), 7.85 (1H, *d*, *J* = 2.4 Hz, -SO2-aryl), 11.07 (1H, *s*, OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.0 (NCH2), 123.3, 124.5, 128.5, 129.2, 129.3, 130.1, 130.9, 131.7, 134.5, 136.9, 150.8 (COH), 185.4 (CO); ESI-HRMS (*m/z*): Calcd. for C25H19Cl2NO4S: 499.0. Found: 498.0 (M-1).

*3,5-bis(3-Chloro-4-hydroxybenzylidene)-1-(3,5-dichloro-2-hydroxyphenylsulfonyl) piperidin-4-one (****5f****).* Yellow solid; Yield: 64.0%; m.p. 300-302°C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.69 (4H, *s*, -NCH2), 7.08 (2H, *d*, *J* = 8.4 Hz, Ar), 7.26 (2H, *dd*, *J* = 8.4, 2.0 Hz, Ar), 7.34 (1H, *d*, *J* = 2.4 Hz, SO2-aryl), 7.45 (4H, *m*, Ar and Ar-CH=C), 7.82 (1H, *d*, *J* = 2.4 Hz, SO2-aryl), 10.87 (2H, *s*, OH), 10.99 (1H, *s*, OH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.9, 117.3, 120.7, 123.4, 124.5, 126.8, 128.6, 129.1, 129.9, 131.2, 132.9, 134.4, 135.7, 150.8 (COH), 155.0 (COH), 184.9(CO); ESI-HRMS (*m/z*): Calcd. for C25H17Cl4NO6S: 598.9. Found: 599.8 (M+1).

*Methyl 2-(3,5-bis(4-fluorobenzylidene)-4-oxopiperidin-1-ylsulfonyl)benzoate* (**5g**). Pale yellow solid; Yield: 93.5%; m.p. 187-189 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 3.58 (3H, *s*, COOCH3), 4.66 (4H, *s*, -NCH2), 7.35 (4H, *t*, *J* = 8.8 Hz, Ar), 7.60 (5H, *m*, Ar), 7.78 (2H, *s*, Ar-CH=C), 7.99 (3H, *m*, Ar); 13C- NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.0 (NCH2), 53.2 (COOCH3), 116.3 (*d*, *J* = 28.5 Hz), 128.9, 129.3, 131.1, 131.4, 133.3, 133.5 (*d*, *J*= 8.5 Hz), 134.1, 134.8, 136.3, 161.9 (*d*, *J* = 247.6 Hz), 168.1 (COOCH3),184.8 (CO); ESI-HRMS (*m/z*): Calcd. for C27H21F2NO5S: 509.1. Found: 510.2 (M+H).

*3,5-bis(4-Fluorobenzylidene)-1-((E)-styrylsulfonyl)piperidin-4-one (****5h****).* Pale yellow solid; Yield: 92%; m.p. 204-206 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.64 (4H, *s*, -NCH2), 7.26 (6H, *m*, Ar), 7.48 (3H, *m*, Ar), 7.56 (4H,  *m*, Ar& styryl), 7.66 (2H, *m*, Ar& styryl), 7.72 (2H, *s*, ArCH=C); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.0 (NCH2), 116.3 (*d*, *J* = 21.5 Hz), 123.7, 129.2, 129.4, 131.1, 131.4, 133.0, 133.4 (*d*, *J* = 8.8 Hz), 136.3, 143.2, 161.9 (*d*, *J* = 247.6 Hz), 185.1 (CO); ESI-HRMS (*m/z*): Calcd. for C27H21F2NO3S: 477.1. Found: 476.0. (M-H).

*Methyl 2-(4-oxo-3,5-bis(thiophen-2-ylmethylene)piperidin-1-ylsulfonyl)benzoate (****5i****).* Pale yellow solid; Yield: 91.0%; m.p. 185-187 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 3.72 (3H, *s*, COOCH3), 4.70 (4H, *s*, -NCH2), 7.30 (2H, *m*, Ar), 7.63 (3H, *m*, Ar), 7.69 (3H, *m*, Ar), 7.76 (2H, *s*, ArCH=C), 8.01 (2H, *d*, *J* = 5.2 Hz, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.7(NCH2), 53.4 (COOCH3, 128.0, 129.1, 129.2, 129.3, 129.48, 131.4, 133.2, 133.3, 134.1, 135.0, 135.2, 137.8, 168.0 (COOCH3), 183.8 (CO); ESI-HRMS (*m/z*): Calcd. for C23H19NO5S3: 485.0. Found: 486.0 (M+H).

*1-(Styrylsulfonyl)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one (****5j)****.* Pale yellow solid; Yield: 93.0%; m.p. 200-202 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.69 (4H, *s*, -NCH2), 7.30 (2H, *m*, Ar), 7.35 (1H, *s*, Ar), 7.43 (4H, *m*, Ar& styryl), 7.63 (4H, *m*, Ar& styryl), 7.90 (2H, *s*, Ar-CH=C), 8.00 (2H, *d*, *J* = 4.8 Hz, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.7(NCH2), 123.6, 128.1, 129.2, 129.2, 129.4, 129.5, 131.5, 133.0, 133.1, 135.3, 137.8, 143.5, 184.0 (CO); ESI-HRMS (*m/z*): Calcd. for C23H19NO3S3:453.0. Found: 453.0 (M).

*Methyl 2-(3,5-bis(benzo[d][1,3]dioxol-5-ylmethylene)-4-oxopiperidin-1-ylsulfonyl) benzoate (****5k****).*Pale yellow solid; Yield: 95.0%; m.p. 191-193 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 3.64 (3H, *s*, -COOCH3), 4.63 (4H, *s*, -NCH2), 6.14 (4H, *s*,OCH2O), 7.08 (4H, *s*, Ar), 7.14 (2H, *s*, Ar), 7.59 (2H, *s*, Ar-CH=C), 7.61 (1H, *m*, Ar), 7.72 (3H, *m*, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.2 (NCH2), 53.5,102.0 (OCH2O), 109.0 (COOCH3), 109.5, 110.3, 110.8, 126.5, 127.1, 128.7, 129.6, 133.4, 134.0, 134.8, 137.3, 148.3, 149.2, 168,1 (COOCH3), 184.5 (CO); ESI-HRMS (*m/z*): Calcd. for C29H23NO9S: 561.1. Found: 562.2 (M+H).

*3,5-bis(Benzo[d][1,3]dioxol-5-ylmethylene)-1-((E)-styrylsulfonyl)piperidin-4-one (****5l****).* Pale yellow solid; Yield: 94.0%; m.p. 211-213 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.61 (4H, *s*, -NCH2), 6.13 (4H, *s*,OCH2O), 7.03 (6H, *m*, Ar), 7.28 (2H, *m*, Ar), 7.47 (3H, *m*, Ar and styryl), 7.64 (2H, *s*, Ar-CH=C), 7.68 (2H, *m*, Ar and styryl); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 47.2 (NCH2), 102.2 (OCH2O), 108.9, 110.2, 123.6, 127.0, 128.7, 129.2, 129.4, 129.9, 131.4, 133.1, 137.3, 143.07, 148.3, 149.2, 184.8 (CO); ESI-HRMS (*m/z*): Calcd. for C29H23NO7S: 529.1. Found: 529.9 (M+H).

*N-(4-Methyl-5-(4-oxo-3,5-bis(thiophen-2-ylmethylene)piperidin-1-ylsulfonyl)thiazol-2-yl)acetamide (****5m****).* Pale yellow solid; Yield: 93.0%; m.p. 231-233 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 2.18 (3H, *s*, CH3CO), 2.40 (3H, *s*, CH3), 4.71 (4H, *s*, -NCH2), 7.31 (2H, *m*, Ar), 7.65 (2H, *d*, *J* = 3.3 Hz, Ar), 7.88 (2H, *s*, Ar-CH=C), 8.03 (2H, *d*, *J* = 5.2 Hz, Ar), 12.65 (1H, *s*, NH); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 17.0 (CH3), 22.9 (COOCH3), 47.1 (NCH2), 119.0, 127.5, 129.2, 129.8, 133.4, 135.7, 137.6, 153.8, 160.4, 167.0 (COOCH3), 183.3 (CO); ESI-HRMS (*m/z*): Calcd. for C21H19N3O4S4: 505.0. Found: 504.0 (M-H).

*1-(1,2-Dimethyl-1H-imidazol-4-ylsulfonyl)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one (****5n****).* Pale yellow solid; Yield: 91.0%; m.p. 231-233 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 2.28 (3H, *s*, CH3), 3.58 (3H, *s*, NCH3), 4.57 (4H, *s*, -NCH2), 7.29 (2H, *m*, Ar), 7.60 (2H, *d*, *J* = 3.6 Hz, Ar), 7.74 (1H *s*, Ar), 7.82 (2H, *s*, Ar-CH=C), 7.98 (2H,  *d*, *J*= 5.2 Hz, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 12.9 (CH3), 33.5 (NCH3), 47.1 (NCH2), 127.0, 128.2, 128.9, 129.1, 132.9, 134.0, 135.1, 137. 9, 147.8, 184.0 (CO); ESI-HRMS (*m/z*): Calcd. for C20H19N3O3S3: 445.0. Found: 446.2 (M+H).

*1-(3,5-Dichlorophenylsulfonyl)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one (****5o****).* Yellow solid; Yield: 94.0%; m.p. 211-213 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.8 (4H, *s*, -NCH2), 7.3(2H, *m*, Ar), 7.51 (2H, *d*, *J* = 2.0 Hz, Ar), 7.64 (2H, *d*, *J* = 3.6 Hz, Ar), 7.76 (2H, *s*, ArCH=C), 7.99 (1H, *s*, Ar), 8.01 (2H, *m*, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.9 (NCH2), 126.1, 126.8, 129.3, 129.9, 133.4, 133.6, 135.7, 135.8, 137.5, 140.9, 183.1 (CO); ESI-HRMS (*m/z*): Calcd. for C21H15Cl2NO3S3: 494.9. Found: 496.8 (M+2).

*1-(6-Chloropyridin-3-ylsulfonyl)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one (****5p****).* Pale yellow solid; Yield: 91.0%; m.p. 234-235 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.72 (4H, *s*, -NCH2), 7.31 (2H, *m*, Ar), 7.67 (2H, *d*, *J* = 3.6 Hz, Ar), 7.77 (1H, *d*, *J* = 3.6 Hz, Ar), 7.79 (2H, *s*, ArCH=C), 8.03 (2H, *d*, *J* = 5.2 Hz, Ar), 8.12 (1H, *m*, Ar), 8.69 (1H, m, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 46.9 (NCH2), 125.9, 126.9, 129.3, 130.0, 133.5, 135.7, 137.6, 139.1, 143.2, 148.7, 155.3, 183.4 (CO); ESI-HRMS (*m/z*): Calcd. for C20H15ClN2O3S3: 462.0. Found: 462.0 (M).

*1-(3,5-Dimethylisoxazol-4-ylsulfonyl)-3,5-bis(thiophen-2-ylmethylene)-piperidin-4-one (****5q****).* Pale yellow solid; Yield: 92.0%; m.p. 232-233 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 2.21 (3H, *s*, CH3), 2.47 (3H, *s*, CH3), 4.76 (4H, *s*, -NCH2), 7.32 (2H, *m*, Ar), 7.70 (2H, *d*, *J* = 3.6 Hz, Ar), 7.92 (2H, *s*, ArCH=C), 8.03 (2H, *d*, *J* = 5.2 Hz, Ar); 13C-NMR (100 MHz, DMSO-*d6,* δ / ppm): 11.2 (CH3), 13.1 (CH3), 46.7 (NCH2), 114.8, 127.2, 129.3, 130.0, 133.7, 136.0, 137.5, 157.5, 174.4, 183.1 (CO); ESI-HRMS (*m/z*): Calcd. for C20H18N2O4S3: 446.0. Found: *m/z*446.0 (M).

*tert-Butyl 2-oxo-2-(4-oxo-3,5-bis(thiophen-2-ylmethylene)piperidin-1-yl)ethylcarbamate (****7a****).* Red crystals; Yield: 78.0%; m.p. 301-304 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 1.35 (9H,*s*,*t*-butyl), 3.87 (2H,*d*, *J* = 6.0 Hz, -COCH2NH), 4.82 (4H, *d*, *J* = 24.8 Hz, -NCH2), 6.81 (1H,*t*, *J* = 5.6 Hz, -NH), 7.30 (2H,*m*, Ar), 7.67 (2H,*d*, *J* = 8.8 Hz, Ar), 7.89 (2H, *s*, ArCH=C), 7.99 (2H, *d*, *J* = 5.2 Hz, Ar); 13C NMR (100 MHz, DMSO-*d6,* δ / ppm): 28.6 (-*C*(CH3)), 40.6 (-COCH2NH),47.0 (NCH2) 78.5 (-*C*(CH3)), 129.1, 133.0, 135.2, 138.0, 156.2 (-NCOO), 168.4 (-COCH2NH), 185.1 (CO); ESI-HRMS (*m/z*): Calcd. for C22H24N2O4S2: 444.1. Found: 345.2 (M-BOC)+

*tert-Butyl-(S)-3-methyl-1-oxo-1-(2-oxo-2-(4-oxo-3,5-bis(thiophen-2-ylmethylene)piperidin-1-yl)ethylamino)butan-2-ylcarbamate (****7b****).* Red crystals; 70% yield; m.p. 311-313 °C; 1H-NMR (400 MHz, CD3OD*,* δ / ppm): 1.27 (6H,*m*, -CH(CH3)2), 1.33 (9H, *s*, C(CH3)3), 2.07 (1H,*m*, -CH(CH3)2), 3.97 (1H, *d*, *J* = 6.0 Hz, -COCHNH), 4.13 (2H,*m*, -COCH2NH), 4.94 (4H,*d*, *J* = 25.2 Hz, -NCH2), 7.27 (2H,*m*, Ar), 7.28 (2H,*m*,Ar), 7.54 (2H, *d*, *J* = 3.2 Hz, Ar), 7.84 (2H, *m*, ArCH=C); 13C NMR (100 MHz, DMSO-*d6,* δ / ppm): 18.0 (CH(CH3)2), 28.8 (C(CH3)3), 31.4 (CH(CH3)2), 41.8(-COCH2NH), 46.6 (NCH2), 59.9(COCHNH), 79.1(C(CH3)3), 129.1, 129.4, 129.5, 133.0, 135. 6, 139.0, 154.1, 168.9 (-COCH2NH), 170.1 (COCHNH), 186.4 (CO); ESI-HRMS (*m/z*): Calcd. for C27H33N3O5S2: 543.2. Found: 444.2 (M-BOC)+

*1-(2-Aminoacetyl)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one trifluoroacetate (****8a****).*  Yellow powder; Yield: 93.0%; m.p. 333-335 °C; 1H-NMR (400 MHz, DMSO-*d6,* δ / ppm): 4.05 (2H, *d*, *J* = 5.2 Hz, -COCH2NH2), 4.78 (4H,*s*, -NCH2), 7.30 (2H, *m*, Ar), 7.68 (2H,*dd*, *J* = 9.6, 3.4 Hz, Ar), 7.90 (2H,*d*, *J* = 10.8 Hz, ArCH=C), 8.00 (2H, *m*, Ar); 13C NMR (100 MHz, DMSO-*d6,* δ / ppm): 42.6 (-COCH2NH2), 45.7 (NCH2), 128.9, 129.1, 129.2, 133.0, 135.0, 137.9, 165.8 (-COCH2NH2), 184.9 (CO); ESI-HRMS (*m/z*): Calcd. for C17H16N2O2S2: 344.1. Found: 345.0(M+1).

*(S)-2-Amino-3-methyl-N-(2-oxo-2-(4-oxo-3,5-bis(thiophen-2-ylmethylene)-piperidin-1-yl)ethyl)butanamide trifluoroacetate (****8b****).* Yellow powder; Yield: 94%; m.p. 341-343 °C; 1H-NMR (400 MHz, CD3OD*,* δ / ppm): 1.09 (6H, *m*, -CH(CH3)2), 2.17 (1H, *m*, -CH(CH3)2), 3.74 (1H,*d*, *J* = 5.6 Hz, -COCHNH), 4.25 (2H,*d*, *J* = 4.4 Hz, -COCH2NH), 4.95 (4H,*s*, -NCH2), 7.22 (2H, *s*, Ar), 7.46 (2H,*d*, *J* = 4.0 Hz, Ar), 7.79 (2H, *s*, ArCH=C), 7.90 (2H, *d*, *J* = 8.8 Hz, Ar); 13C NMR (100 MHz, DMSO-*d6,* δ / ppm): 31.0 (CH(CH3)2), 44.9 (-COCH2NH), 46.6 (NCH2), 59.9 (COCHNH2), 78.9, 129.1, 129.4, 131.1, 133.0, 135.6, 139.0, 168.8 (-COCH2NH), 170.0 (COCHNH2), 186.4 (CO); ESI-HRMS (*m/z*): Calcd. for C22H25N3O3S2: 443.13. Found: 444.2 (M+1).