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J. Serb. Chem. Soc. 81 (8) S232–S243 (2016) *Supplementary material*

SUPPLEMENTARY MATERIAL TO

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

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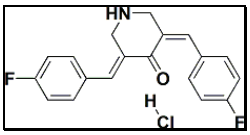
J. Serb. Chem. Soc. 81 (8) (2016) 859–870

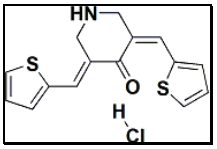
SPECTRAL DATA FOR COMPOUNDS **3A**–**F**

*3,5-Bis(4-fluorobenzylidene)piperidin-4-one hydrochloride (**3a**)*



Yield: 94 %; yellow crystals; m.p.: 236–238 °C; IR (KBr, cm^{-1}): 3157 (N–H), 2814 (C–H), 1663 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.40 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.35–7.40 (4H, *m*, Ar-H), 7.59 (4H, *dd*, J = 8.8 Hz & 5.6 Hz, Ar-H), 7.84 (2H, *s*, Ar-CH=C), 9.64 (2H, *s*, N**H**·**H**Cl); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 44.5 (NCH_2), 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 $C_{19}H_{15}F_2NO$ $[M+H]^+$: 312.3262. Found: 312.3241.

*3,5-Bis(2-thienylmethylene)piperidin-4-one hydrochloride (**3b**)*



Yield: 96 %; yellow crystals; m.p. 357–359 °C; IR (KBr, cm^{-1}): 3051 (N–H), 2789 (C–H), 1668 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.47 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.31 (2H, *dd*, J = 5.0, 3.8 Hz, Ar), 7.69 (2H, *s*,

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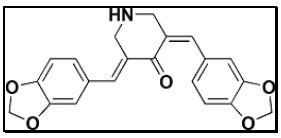
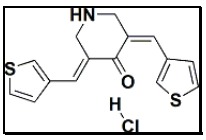
Ar-CH=C), 8.02–8.06 (4H, *m*, Ar-H), 10.1 (2H, *s*, N**H**·**H**Cl); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 44.0 (NCH_2), 124.7, 129.3, 131.3, 133.4, 136.0, 137.4, 181.8 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{15}H_{13}NOS_2$ $[M+H]^+$: 288.4006. Found: 288.4001.

*3,5-Bis(1,3-benzodioxol-5-ylmethylene)piperidin-4-one (**3c**)*



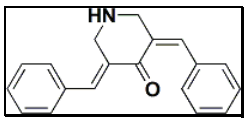
Yield: 93 %; yellow powder; m.p.: 256–258 °C; IR (KBr, cm^{-1}): 3122 (N–H), 2811 (C–H), 1669 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 3.95 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 5.75 (1H, *s*, NH), 6.09 (4H, *s*, OCH_2O), 7.01–7.05 (6H, *m*, Ar-H), 7.49 (2H, *s*, Ar-CH=C); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 48.1 (NCH_2), 102.0 (OCH_2O), 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 $C_{21}H_{17}NO_5$ $[M+H]^+$: 363.3644. Found: 364.3647.

*3,5-Bis(2-thienylmethylene)piperidin-4-one hydrochloride (**3d**)*



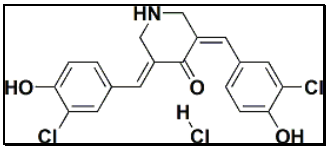
Yield: 90 %; yellow powder; m.p.: 348–350 °C; IR (KBr, cm^{-1}): 3108 (N–H), 2784 (C–H), 1667 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.49 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.40 (2H, *d*, *J* = 5.2 Hz, Ar-H), 7.76–7.77 (2H, *m*, Ar-H), 7.85 (2H, *s*, Ar-H), 8.04 (2H, *s*, Ar-CH=C), 9.95 (2H, *s*, N**H**·**H**Cl); ^{13}C--NMR (100 MHz, DMSO-d_6, δ / ppm): 44.3 (NCH_2), 126.4, 128.2, 129.7, 132.0, 132.9, 136. 0, 182.8 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{15}H_{13}NOS_2$ $[M^+]$: 287.7606. Found: 287.7646.

*3,5-Dibenzylidenepiperidin-4-one (**3e**)*



Yield: 90 %; yellow powder; m.p.: 211–213 °C; IR (KBr, cm^{-1}): 3128 (N–H), 2815 (C–H), 1668 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.48 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.52–7.60 (6H, *m*, Ar-H), 7.62–7.64 (4H, *m*, Ar-H), 7.68 (2H, *s*, Ar-CH=C), 9.81 (1H, *s*, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 44.6 (NCH_2), 129.1, 131.1, 133.7, 138.2, 142.2, 144.7, 184.5 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{19}H_{17}NO$ $[M^+]$: 275.2954. Found: 275.2954.

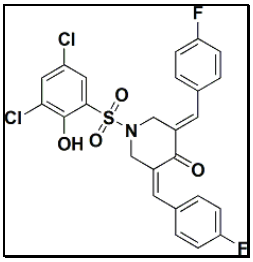
*3,5-Bis(3-chloro-4-hydroxybenzylidene)piperidin-4-one hydrochloride (**3f**)*



Yield: 95 %; yellow crystals; m.p.: 320–322 °C; IR (KBr, cm^{-1}): 3188 (N–H), 2810 (C–H), 1663 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.46 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.15 (2H, *d*, *J* = 8.4 Hz, Ar-H), 7.34–7.37 (2H, *m*, Ar-H), 7.57 (2H, *d*, *J* = 2.0 Hz, Ar-H), 7.74 (2H, *s*, Ar-CH=C), 9.76 (2H, *s*, N**H**·**H**Cl), 11.12 (2H, *s*, OH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 44.3 (NCH_2), 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 $C_{19}H_{15}Cl_2NO_3$ [M^+]: 375.9442. Found: 375.9401.

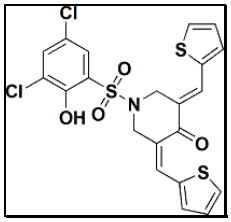
SPECTRAL DATA OF COMPOUNDS **5a**–**q**

*1-[(3,5-Dichloro-2-hydroxyphenyl)sulfonyl]-3,5-Bis(4-fluorobenzylidene)piperidin-4-one (**5a**)*



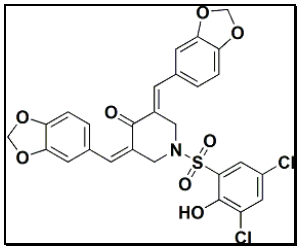
Yield: 92 %; pale yellow solid; m.p.: 221–223 °C; IR (KBr, cm^{-1}): 2856 (C–H), 1663 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.73 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.28 (1H, *d*, *J* = 2.8 Hz, SO_2-aryl), 7.34 (4H, *t*, *J* = 8.8 Hz, Ar-H), 7.52 (4H, *dd*, *J* = 8.4, 5.6 Hz, Ar-H), 7.57 (2H, *s*, Ar-CH=C), 7.82 (1H, *d*, *J* = 2.8 Hz, SO_2-aryl), 11.06 (1H, *s*, OH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 46.8 (NCH_2), 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 $C_{25}H_{17}Cl_2F_2NO_4S$ [M^+–2]: 534.0356. Found: 534.0356.

*1-(3,5-Dichloro-2-hydroxyphenylsulfonyl)-3,5-bis(2-thienylmethylene)piperidin--4-one (**5b**)*



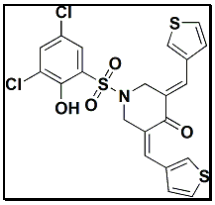
Yield: 93.0 %; pale yellow solid; m.p.: 219–221 °C; IR (KBr, cm^{-1}): 2891 (C–H), 1661 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.77 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.28 (2H, *dd*, *J* = 5.2, 3.6 Hz, Ar-H), 7.49 (1H, *d*, *J* = 2.4 Hz, Ar-H), 7.59 (2H, *d*, *J* = 3.6 Hz, Ar-H), 7.77 (2H, *s*, Ar-CH=C), 7.82 (1H, *d*, *J* = = 2.8 Hz, Ar-H), 7.98 (2H , *d*, *J* = 4.8 Hz, Ar-H), 11.16 (1H, *s*, OH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 46.8 (NCH_2), 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 $C_{21}H_{15}Cl_2NO_4S_3$ [M^+–2]: 509.8200. Found: 509.8210.

*3,5-Bis(1,3-benzodioxol-5-ylmethylene)-1-[(3,5-dichloro-2-hydroxyphenyl)sul-fonyl]piperidin-4-one (**5c**)*



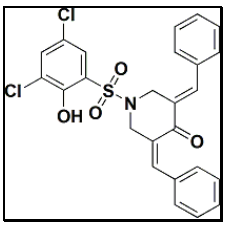
Yield: 95.0 %; pale yellow solid; m.p.: 242.5–243.4 °C; IR (KBr, cm^{-1}): 2946 (C–H), 1669 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.70 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 6.1 (4H, *s*, OCH_2O), 6.99 (6H, *m*, Ar-H), 7.34 (1H, *d*, *J* = 2.8 Hz, Ar-H), 7.50 (2H, *s*, Ar-CH=C), 7.82 (1H, *d*, *J* = 2.4 Hz, Ar-H), 11.04 (1H, *s*, OH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 47.0 (NCH_2), 102.2 (OCH_2O), 109.2, 110.5, 126.5, 128.5, 128.7, 130.1, 134.4, 136.7, 148.2, 149.0, 151.0 (COH), 185.1 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{27}H_{19}Cl_2NO_8S$ [M^+–2]: 586.4138. Found: 586.4142.

*1-[(3,5-Dichloro-2-hydroxyphenyl)sulfonyl]-3,5-bis(3-thienylmethylene)piperidin-4-one (**5d**)*



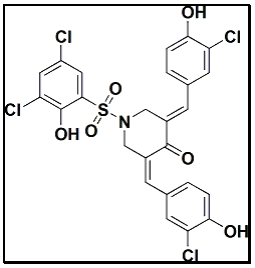
Yield: 92.0 %; pale yellow solid; m.p.: 217–219 °C; IR (KBr, cm^{-1}): 2818 (C–H), 1667 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.73 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.34 (2H, *d*, *J* = 4.4 Hz, Ar-H), 7.47 (1H, *d*, *J* = 5.6 Hz, Ar-H), 7.60 (2H, *s*, Ar-H), 7.72 (2H, *dd*, *J* = 5.2, 4.8 Hz, Ar-H), 7.84 (1H, *d*, *J* = 2.4 Hz, Ar-H), 7.92 (2H, *s*, Ar-CH=C); 11.08(1H, *s*, OH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 47.3 (NCH_2), 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 $C_{21}H_{15}Cl_2NO_4S_3$ [M^+–2]: 511.9000. Found: 511.9017.

*3,5-Dibenzylidene-1-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]piperidin-4-one (**5e**)*



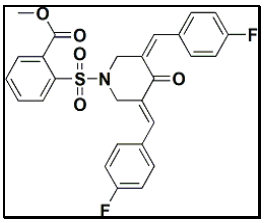
Yield: 98.0 %; pale yellow solid; m.p.: 191–193 °C; IR (KBr, cm^{-1}): 2896 (C–H), 1659 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.75 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.30 (1H, *d*, *J* = 2.4 Hz, SO_2-aryl), 7.49–7.54 (10H, *m*, Ar-H), 7.61 (2H, *s*, Ar-CH=C), 7.85 (1H, *d*, *J* = 2.4 Hz, SO_2-aryl), 11.07 (1H, *s*, OH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 47.0 (NCH_2), 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 $C_{25}H_{19}Cl_2NO_4S$ [M^+–2]: 498.1048. Found: 498.1091.

*3,5-Bis(3-chloro-4-hydroxybenzylidene)-1-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]piperidin-4-one (**5f**)*



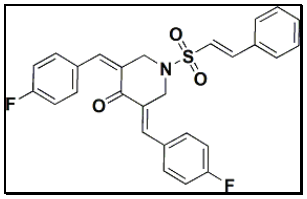
Yield: 64.0 %; yellow solid; m.p.: 300–302 °C; IR (KBr, cm^{-1}): 2916 (C–H), 1661 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.69 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.08 (2H, *d*, *J* = 8.4 Hz, Ar-H), 7.26 (2H, *dd*, *J* = 8.4 & 2.0 Hz, Ar-H), 7.34 (1H, *d*, *J* = 2.4 Hz, SO_2-aryl), 7.45–7.47 (4H, *m*, Ar-H & Ar-CH=C), 7.82 (1H, *d*, *J* = 2.4 Hz, SO_2-aryl), 10.87 (2H, *s*, OH), 10.99 (1H, *s*, OH); ^{13}C--NMR (100 MHz, DMSO-d_6, 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 $C_{25}H_{17}Cl_4NO_6S$ [M^+–1]: 599.7236. Found: 599.7242.

*Methyl 2-{[3,5-bis(4-fluorobenzylidene)-4-oxopiperidin-1-yl]sulfonyl}benzoate (**5g**)*



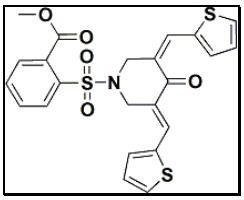
Yield: 93.5 %; pale yellow solid; m.p.: 187–189 °C; IR (KBr, cm^{-1}): 2916 (C–H), 1647 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 3.58 (3H, *s*, $COOCH_3$), 4.66 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.35 (4H, *t*, *J* = 8.8 Hz, Ar-H), 7.60––7.76 (5H, *m*, Ar-H), 7.78 (2H, *s*, Ar-CH=C), 7.79–7.80 (3H, *m*, Ar-H); ^{13}C- NMR (100 MHz, DMSO-d_6, δ / ppm): 47.0 (NCH_2), 53.2 ($COO\mathbf{C}H_3$), 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 (**C**$OOCH_3$),184.8 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{27}H_{21}F_2NO_5S$ [M+1]$^+$: 510.2624. Found: 510.2614.

*3,5-Bis(4-fluorobenzylidene)-1-((*E*)-styrylsulfonyl)piperidin-4-one (**5h**)*



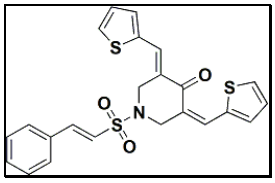
Yield: 92 %; pale yellow solid; m.p.: 204–206 °C; IR (KBr, cm^{-1}): 2891 (C–H), 1659 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.64 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.26–7.47 (6H, *m*, Ar-H), 7.48–7.49 (3H, *m*, Ar-H), 7.56–7.59 (4H, *m*, Ar-H & styryl), 7.66–7.68 (2H, *m*, Ar-H & styryl), 7.72 (2H, *s*, Ar-CH=C); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 47.0 (NCH_2), 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 $C_{27}H_{21}F_2NO_3S$ [M^+–1]: 476.0436. Found: 476.0439.

*Methyl 2-{[4-oxo-3,5-bis(2-thienylmethylene)piperidin-1-yl]sulfonyl}benzoate (**5i**)*



Yield: 91.0 %; pale yellow solid; m.p.: 185–187 °C; IR (KBr, cm^{-1}): 2891 (C–H), 1661 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 3.72 (3H, *s*, $COOCH_3$), 4.70 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 6.96–6.97 (1H, *m*, Ar-H), 7.00–7.03 (2H, *m*, Ar-H), 7.07–7.09 (5H, *m*, Ar-H), 7.21–2.24 (1H, *m*, Ar-CH=C), 7.42–7.47 (3H, *m*, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 46.7 (NCH_2), 53.4 (COO**C**H_3, 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 (**C**$OOCH_3$), 183.8 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{23}H_{19}NO_5S_3$ [M+1]$^+$: 486.0768. Found: 486.0792.

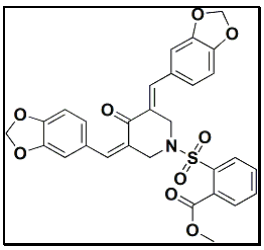
*1-(Styrylsulfonyl)-3,5-bis(2-thienylmethylene)piperidin-4-one (**5j**)*



Yield: 93.0 %; pale yellow solid; m.p.: 200–202 °C; IR (KBr, cm^{-1}): 2816 (C–H), 1667 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.69 (4H, *s*,

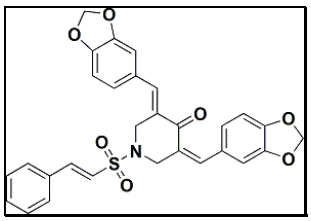
C**H**$_2$–NH–C**H**$_2$), 7.30–7.32 (2H, *m*, Ar-H), 7.35 (1H, *s*, Ar-H), 7.43–7.46 (4H, *m*, Ar-H & styryl), 7.63–7.69 (4H, *m*, Ar-H & styryl), 7.90 (2H, *s*, Ar-CH=C), 8.00 (2H, *d*, *J* = 4.8 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 46.7(NCH$_2$), 123.6, 128.1, 129.2, 129.2, 129.4, 129.5, 131.5, 133.0, 133.1, 135.3, 137.8, 143.5, 184.0 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{23}H_{19}NO_3S_3$ [M$^+$]: 453.0480. Found: 453.0472.

*Methyl 2-{[3,5-bis(1,3-benzodioxol-5-ylmethylene)-4-oxopiperidin-1-yl]sulfonyl}benzoate (**5k**)*



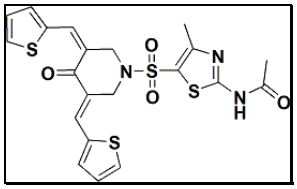
Yield: 95.0 %; pale yellow solid; m.p.: 191–193 °C; IR (KBr, cm^{-1}): 2816 (C–H), 1669 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 3.64 (3H, *s*, COOCH$_3$), 4.63 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 6.14 (4H, *s*, OCH$_2$O), 7.08 (4H, *s*, Ar-H), 7.14 (2H, *s*, Ar-H), 7.59 (2H, *s*, Ar-CH=C), 7.61–7.63 (1H, *m*, Ar-H), 7.72–7.80 (3H, *m*, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 47.2 (NCH$_2$), 53.5,102.0 (OCH$_2$O), 109.0 (COO**C**H3), 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 (**C**OOCH3), 184.5 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{29}H_{23}NO_9S$ [M+1]$^+$: 562.2406. Found: 562.2470.

*3,5-Bis(1,3-benzodioxol-5-ylmethylene)-1-((*E*)-styrylsulfonyl)piperidin-4-one (**5l**)*



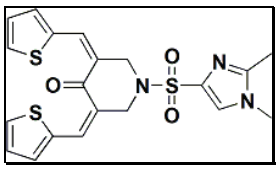
Yield: 94.0 %; pale yellow solid; m.p.: 211–213 °C; IR (KBr, cm^{-1}): 2819 (C–H), 1654 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.61 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 6.13 (4H, *s*, OCH$_2$O), 7.03–7.09 (6H, *m*, Ar-H), 7.28–7.39 (2H, *m*, Ar-H), 7.47–7.49 (3H, *m*, Ar-H & styryl), 7.64 (2H, *s*, Ar-CH=C), 7.68–7.70 (2H, *m*, Ar-H & styryl); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 47.2 (NCH$_2$), 102.2 (OCH$_2$O), 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 $C_{29}H_{23}NO_7S$ [M$^+$]: 529.8618. Found: 529.8614.

N-*{4-Methyl-5-[(4-oxo-3,5-bis(2-thienylmethylene)piperidin-1-yl)sulfonyl]thiazol-2-yl}acetamide (**5m**)*



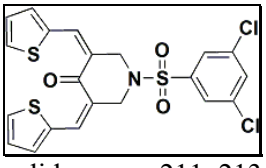
Yield: 93.0 %; pale yellow solid; m.p.: 231–233 °C; IR (KBr, cm^{-1}): 2812 (C–H), 1661 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 2.18 (3H, *s*, CH_3CO), 2.40 (3H, *s*, CH_3), 4.71 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.31–7.33 (2H, *m*, Ar-H), 7.65 (2H, *d*, *J* = 3.3 Hz, Ar-H), 7.88 (2H, *s*, Ar-CH=C), 8.03 (2H, *d*, *J* = = 5.2 Hz, Ar-H), 12.65 (1H, *s*, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 17.0 (CH_3), 22.9 (COO**C**H_3), 47.1 (NCH_2), 119.0, 127.5, 129.2, 129.8, 133.4, 135.7, 137.6, 153.8, 160.4, 170.0 (**C**OOCH_3), 183.3 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{21}H_{19}N_3O_4S_4$ [M^+–1]: 504.6444. Found: 504.6416.

*1-[(1,2-Dimethyl-1*H*-imidazol-4-yl)sulfonyl]-3,5-bis(2-thienylmethylene)piperidin-4-one (**5n**)*



Pale yellow solid; Yield: 91.0 %; m.p.: 231–233 °C; IR (KBr, cm^{-1}): 2861 (C–H), 1657 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 2.28 (3H, *s*, CH_3), 3.58 (3H, *s*, NCH_3), 4.57 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.28–7.30 (2H, *m*, Ar-H), 7.60 (2H, *d*, *J* = 3.6 Hz, Ar-H), 7.74 (1H *s*, Ar-H), 7.82 (2H, *s*, Ar-CH=C), 7.98 (2H, *d*, *J*= 5.2 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 12.9 (CH_3), 33.5 (NCH_3), 47.1 (NCH_2), 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 $C_{20}H_{19}N_3O_3S_3$ [M+1]$^+$: 446.5793. Found: 446.5723.

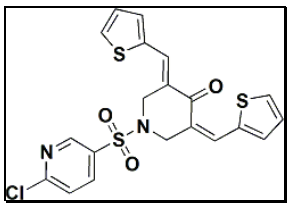
*1-[(3,5-Dichlorophenyl)sulfonyl]-3,5-bis(2-thienylmethylene)piperidin-4-one (**5o**)*



Yield: 94.0 %; yellow solid; m.p.: 211–213 °C; IR (KBr, cm^{-1}): 2856 (C–H), 1681 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.8 (4H, *s*, C**H**$_2$– –NH–C**H**$_2$), 7.31–7.33 (2H, *m*, Ar-H), 7.51 (2H, *d*, *J* = 2.0 Hz, Ar-H), 7.64 (2H,

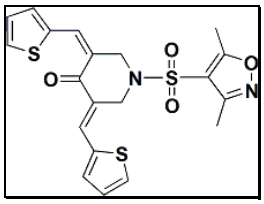
d, *J* = 3.6 Hz, Ar-H), 7.76 (2H, *s*, Ar-CH=C), 7.99 (1H, *s*, Ar-H), 8.00–8.04 (2H, *m*, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 46.9 (NCH_2), 126.1, 126.8, 129.3, 129.9, 133.4, 133.6, 135.7, 135.8, 137.5, 140.9, 183.1 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{21}H_{15}Cl_2NO_3S_3$ [M^+]: 496.4606. Found: 496.4610.

*1-[(6-Chloropyridin-3-yl)sulfonyl]-3,5-bis(2-thienylmethylene)piperidin-4-one (**5p**)*



Yield: 91.0 %; pale yellow solid; m.p.: 234–235 °C; IR (KBr, cm^{-1}): 2891 (C–H), 1659 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.72 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.31–7.33 (2H, *m*, Ar-H), 7.67 (2H, *d*, *J* = 3.6 Hz, Ar-H), 7.77 (1H, *d*, *J* = 3.6 Hz, Ar-H), 7.79 (2H, *s*, Ar-CH=C), 8.03 (2H, *d*, *J* = 5.2 Hz, Ar-H), 8.12–8.31 (1H, *m*, Ar-H), 8.69–8.70 (1H, *m*, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 46.9 (NCH_2), 125.9, 126.9, 129.3, 130.0, 133.5, 135.7, 137.6, 139.1, 148.7, 155.3, 183.4 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{20}H_{15}ClN_2O_3S_3$ [M^+]: 462.9936. Found: 462.9937.

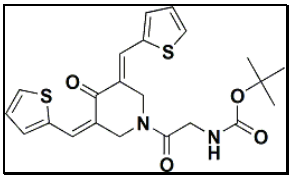
*1-[(3,5-Dimethylisoxazol-4-yl)sulfonyl]-3,5-bis(2-thienylmethylene)-piperidin-4--one (**5q**)*



Yield: 92.0 %; pale yellow solid; m.p.: 232–233 °C; IR (KBr, cm^{-1}): 2892 (C–H), 1659 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 2.21 (3H, *s*, CH_3), 2.47 (3H, *s*, CH_3), 4.76 (4H, *s*, C**H**$_2$–NH–C**H**$_2$), 7.32–7.33 (2H, *m*, Ar-H), 7.70 (2H, *d*, *J* = 3.6 Hz, Ar-H), 7.92 (2H, *s*, Ar-CH=C), 8.03 (2H, *d*, *J* = 5.2 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 11.2 (CH_3), 13.1 (CH_3), 46.7 (NCH_2), 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 $C_{20}H_{18}N_2O_4S_3$ [M^+]: 446.5640. Found: 446.5671.

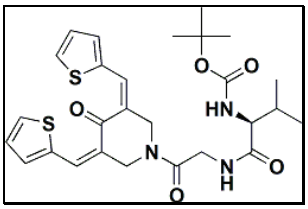
SPECTRAL DATA FOR COMPOUNDS **7a** AND **b**

tert-*Butyl {2-oxo-2-[4-oxo-3,5-bis(2-thienylmethylene)piperidin-1-yl]ethyl}carbamate (7**a**)*



Yield: 78.0 %; red crystals; m.p.: 301–304 °C; IR (KBr, cm^{-1}): 3340 (N–H), 2892 (C–H), 1710, 1663, 1595; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.35 (9H, *s* ,*t*-butyl), 3.87 (2H, *d*, *J* = 6.0 Hz, COC**H**$_2$NH), 4.82 (4H, *d*, *J* = 24.8 Hz, C**H**$_2$–NH–C**H**$_2$), 6.81 (1H, *t*, *J* = 5.6 Hz, NH), 7.30–7.32 (2H, *m*, Ar-H), 7.67 (2H, *d*, *J* = 8.8 Hz, Ar-H), 7.89 (2H, *s*, Ar-CH=C), 7.99 (2H, *d*, *J* = 5.2 Hz, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6, δ / ppm): 28.6 (C(**C**H$_3$)$_3$), 40.6 (CO**C**H$_2$NH), 47.0 (NCH$_2$) 78.5 (**C**(CH$_3$)), 129.1, 133.0, 135.2, 138.0, 156.2 (N**C**OO), 168.4 (**C**OCH$_2$NH), 185.1 (**C**O); ESI-HRMS (*m*/*z*): Calcd. for $C_{22}H_{24}N_2O_4S_2$ [M+1–BOC]$^+$: 345.2684. Found: 345.2637.

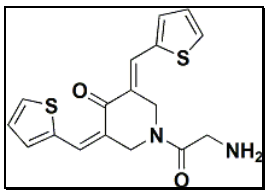
tert-*Butyl {(*S*)-2-methyl-1-[((2-oxo-2-(4-oxo-3,5-bis(2-thienylmethylene)piperidin-1-yl)ethyl)amino)carbonyl]propyl}carbamate (7**b**)*



Yield 70 %; red crystals; m.p.: 311–313 °C; IR (KBr, cm^{-1}): 3310, 3216, 2892, 1719, 1671, 1616, 1595; ^{1}H-NMR (400 MHz, CD_3OD, δ / ppm): 1.27 (6H, *m*, CH(C**H**$_3$)$_2$), 1.33 (9H, *s*, C(C**H**$_3$)$_3$), 2.07 (1H, *m*, C**H**(CH$_3$)$_2$), 3.97 (1H, *d*, *J* = = 6.0 Hz, COC**H**NH), 4.13 (2H, *m*, COC**H**$_2$NH), 4.94 (4H, *d*, *J* = 25.2 Hz, NCH$_2$), 7.26–7.28 (2H, *m*, Ar-H), 7.54–7.55 (2H, *m*, Ar-H), 7.84 (2H, *d*, *J* = 3.2 Hz, Ar-H), 7.84–7.91 (2H, *m*, Ar-CH=C); ^{13}C NMR (100 MHz, DMSO-d_6, δ / ppm): 18.0 (CH(**C**H$_3$)$_2$), 28.8 (C(**C**H$_3$)$_3$), 31.4 (**C**H(CH$_3$)$_2$), 41.8 (CO**C**H$_2$NH), 46.6 (NCH$_2$), 59.9 (CO**C**HNH), 79.1 (**C**(CH$_3$)$_3$), 129.1, 129.4, 129.5, 133.0, 135.6, 139.0, 154.1 (NCOO), 168.9 (**C**OCH$_2$NH), 170.1 (**C**OCHNH), 186.4 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{27}H_{33}N_3O_5S_2$ [M+1–BOC]$^+$: 444.7000. Found: 444.7124.

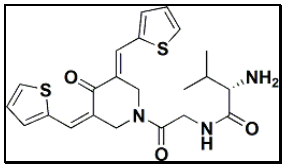
SPECTRAL DATA FOR COMPOUNDS **8a** AND **b**

*1-(2-Aminoacetyl)-3,5-bis(2-thienylmethylene)piperidin-4-one (**8a**)*



Yield: 93.0 %; yellow powder; m.p.: 333–335 °C; IR (KBr, cm^{-1}): 3378, 2812, 1696, 1671; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 4.05 (2H, *d*, *J* = 5.2 Hz, COC**H**$_2$NH$_2$), 4.78 (2H, *s*, NCH$_2$), 4.96 (2H, *s*, NCH$_2$), 7.30 (2H, *m*, Ar-H), 7.68 (2H, *dd*, *J* = 9.6, 3.4 Hz, Ar-H), 7.90 (2H, *d*, *J* = 10.8 Hz, Ar-CH=C), 8.00-8.05 (2H, *m*, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 42.6 (CO**C**H$_2$NH$_2$), 45.7 (N**C**H$_2$), 128.9, 129.1, 129.2, 133.0, 135.0, 137.9, 165.8 (**C**OCH$_2$NH$_2$), 184.9 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{17}H_{16}N_2O_2S_2$ $[M+1]^+$: 345.4521. Found: 345.4513.

*(*S*)-2-Amino-3-methyl-*N*-{2-oxo-2-[4-oxo-3,5-bis(thiophen-2-ylmethylene)-piperidin-1-yl]ethyl}butanamide (**8b**)*



Yield: 94 %; yellow powder; m.p.: 341–343 °C; IR (KBr, cm^{-1}): 3321, 2822, 1696, 1671, 1604; ^{1}H-NMR (400 MHz, CD$_3$OD, δ / ppm): 1.09–1.10 (6H, *m*, CH(C**H**$_3$)$_2$), 2.17–2.25 (1H, *m*, C**H**(CH$_3$)$_2$), 3.74 (1H, *d*, *J* = 5.6 Hz, COC**H**NH), 4.25 (2H, *d*, *J* = 4.4 Hz, COC**H**$_2$NH), 4.95 (4H, *s*, NCH$_2$), 7.22 (2H, *s*, Ar-H), 7.46 (2H, *d*, *J* = 4.0 Hz, Ar-H), 7.79 (2H, *s*, Ar-CH=C), 7.90 (2H, *d*, *J* = = 8.8 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 31.0 (CH(**C**H$_3$)$_2$), 41.8 (**C**H(CH$_3$)$_2$), 44.9 (CO**C**H$_2$NH), 46.6 (NCH$_2$), 59.9 (CO**C**HNH$_2$), 129.1, 129.4, 131.1, 133.0, 135.6, 139.0, 168.8 (**C**OCH$_2$NH), 170.0 (**C**OCHNH$_2$), 186.4 (CO); ESI-HRMS (*m*/*z*): Calcd. for $C_{22}H_{25}N_3O_3S_2$ $[M+1]^+$: 444.5837. Found: 444.5819.