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SUPPLEMENTARY MATERIAL TO

Thiazolidin-4-one, azetidin-2-one and 1,3,4-oxadiazole derivatives of isonicotinic acid hydrazide: synthesis and their biological evaluation

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ANALYTICAL AND SPECTRAL DATA OF THE NEWLY PREPARED COMPOUNDS

*(*E*)-*N*'-(2-Chlorobenzylidene)isonicotinohydrazide (**1a**)*. Yield: 90 %; m.p. 184–186 °C. Anal. Calcd. for $C_{13}H_{10}N_3OCl$ (*FW* 259.69): C, 60.12; H, 3.88; N, 16.18 %. Found: C, 60.10; H, 3.86; N, 16.16 %. IR (KBr, cm^{-1}): 3300 (N–H stretching), 1680 (C=O stretching of carbonyl), 1600 (–N=CH–Ar stretching of aromatic ring), 830 (C–Cl stretching of chlorine). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.9 (1H, *s*, –N=CH), 7.72, 8.63 (4H, *m*, Py), 7.12–7.15 (4H, *m*, *J* = 9 Hz, aromatic), 6.1 (1H, *s*, NH). MS (*m/z*): 259 $[M]^+$.

*(*E*)-*N*'-(4-Chlorobenzylidene)isonicotinohydrazide (**1b**)*. Yield: 90 %; m.p. 192–194 °C. Anal. Calcd. for $C_{13}H_{10}N_3OCl$ (*FW* 259.69): C, 60.12; H, 3.88; N, 16.18 %. Found: C, 60.11; H, 3.87; N, 16.17 %. IR (KBr, cm^{-1}): 3310 (N–H stretching), 1676 (C=O stretching of carbonyl), 1615 (–N=CH–Ar stretching of aromatic ring), 822 (C–Cl stretching of chlorine). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.72, 8.63 (4H, *m*, Py), 7.12–7.15 (4H, *m*, *J* = 9 Hz, aromatic,), 7.7 (1H, *s*, –N=CH), 6.4 (1H, *s*, NH). MS (*m/z*): 259 $[M]^+$.

*(*E*)-*N*'-(2-Hydroxybenzylidene)isonicotinohydrazide (**1c**)*. Yield: 80 %; m.p. 168–170 °C. Anal. Calcd. for $C_{13}H_{11}N_3O_2$ (*FW* 241.25): C, 64.72; H, 4.60; N, 17.42 %. Found: C, 64.70; H, 4.59; N, 17.40 %. IR (KBr, cm^{-1}): 3308 (N–H stretching), 1684 (C=O stretching of carbonyl), 1612 (–N=CH–Ar stretching of aromatic ring). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.40 (1H, *br*, OH), 7.8 (1H, *s*, –N=CH), 7.13–7.16 (4H, *m*, *J* = 9 Hz, aromatic), 7.70, 8.61 (4H, *m*, Py), 6.2 (1H, *s*, NH). MS (*m/z*): 241$[M]^+$.

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*(*E*)*-N'*-(3-Hydroxybenzylidene)isonicotinohydrazide (**1d**)*. Yield: 75 %; m.p. 186–188°C. Anal. Calcd. for $C_{13}H_{11}N_3O_2$ (FW 241.25): C, 64.72; H, 4.60; N, 17.42 %. Found: C, 64.70; H, 4.59; N, 17.40 %. IR (KBr, cm^{-1}): 3318 (N–H stretching), 1688 (C=O stretching of carbonyl), 1607 (–N=CH–Ar stretching of aromatic ring). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.40 (1H, *br*, OH), 7.7 (1H, *s*, –N=CH), 7.74, 8.62 (4H, *m*, Py), 7.11–7.14 (4H, *m*, *J* = 9 Hz, aromatic), 6.3 (1H, *s*, NH). MS (*m/z*): 241 $[M]^+$.

*(*E*)*-N'*-(4-Methoxybenzylidene)isonicotinohydrazide (**1e**)*. Yield: 80 %; m.p. 194–196 °C. Anal. Calcd. for $C_{14}H_{13}N_3O_2$ (*FW* 255.27): C, 65.87; H, 5.13; N, 16.46 %. Found: C, 65.85; H, 5.10; N, 16.44 %. IR (KBr, cm^{-1}): 3314 (N–H stretching), 1687 (C=O stretching of carbonyl), 1604 (–N=CH–Ar stretching of aromatic ring). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.73, 8.64 (4H, *m*, Py), 7.3 (1H, *s*, –N=CH), 7.13–7.16 (4H, *m*, *J* = 9 Hz, aromatic), 6.4 (1H, *s*, NH), 3.83 (3H, *s*, OCH_3). MS (*m/z*): 255 $[M]^+$.

*(*E*)*-N'*-(4-Fluorobenzylidene)isonicotinohydrazide (**1f**)*. Yield: 90 %; m.p. 182–184 °C. Anal. Calcd. for $C_{13}H_{10}FN_3O$ (*FW* 243.24): C, 64.19; H, 4.14; N, 17.28 %. Found: C, 64.16; H, 4.12; N, 17.26 %. IR (KBr, cm^{-1}): 3305 (N–H stretching), 1684 (C=O stretching of carbonyl), 1611 (–N=CH–Ar stretching of aromatic ring). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.70–8.61 (4H, *m*, Py), 7.6 (1H, *s*, –N=CH), 7.11–7.14 (4H, *m*, *J* = 9.0 Hz, aromatic), 6.3 (1H, *s*, NH). MS (*m/z*): 243 $[M]^+$.

*(*E*)*-N'*-(2-Nitrobenzylidene)isonicotinohydrazide* (**1g**). Yield: 85 %; m.p. 188–189 °C. Anal. Calcd. for $C_{13}H_{10}N_4O_3$ (*FW* 270.24): C, 57.78; H, 3.73; N, 20.73 %. Found: C, 57.76; H, 3.70; N, 20.71 %. IR (KBr, cm^{-1}): 3311 (N–H stretching), 1685 (C=O stretching of carbonyl), 1610 (–N=CH– Ar stretching of aromatic rings), 1366 (NO_2). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.8 (1H, *s*, –N=CH), 7.73, 8.61 (4H, *m*, Py), 7.10–7.13 (4H, *m*, *J* = 9.0 Hz, aromatic), 6.2 (1H, *s*, NH). MS (*m/z*): 270 $[M]^+$.

*(*E*)*-N'*-(4-(Dimethylamino)benzylidene)isonicotinohydrazide (**1h**)*. Yield: 85 %; m.p. 196–198 °C. Anal. Calcd. for $C_{15}H_{16}N_4O$ (*FW* 268.31): C, 67.15; H, 6.01; N, 20.88 %. Found: C, 67.12; H, 6.00; N, 20.86 %. IR (KBr, cm^{-1}): 3313 (N–H stretching), 1683(C=O stretching of carbonyl), 1613 (–N=CH–Ar stretching of aromatic rings). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.9 (1H, *s*, –N=CH), 7.72, 8.63 (4H, *m*, Py), 7.12–7.15 (4H, *m*, *J* = 9.0 Hz aromatic), 6.1 (1H, *s*, NH), 2.63 (6H, *s*, $N(CH_3)_2$). MS (*m/z*): 268 $[M]^+$.

N-*(2-(2-Chlorophenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2a**)*. Yield: 85 %; m.p. 198–200 °C. Anal. Calcd. for $C_{15}H_{12}ClN_3O_2S$ (*FW* 333.79): C, 53.97; H, 3.62; N, 12.59 %. Found: C, 53.94; H, 3.60; N, 12.57 %. IR (KBr, cm^{-1}): 3300 (N–H stretching), 1700 (C=O thiazolidinone), 1670 (C=O stretching of carbonyl), 1610 (C=N), 1574 (C=C stretching of chlorine), 830 (C–Cl stretching of chlorine), 700 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.8 (1H, *s*, CONH–),

7.74–8.64 (4H, *m*, Py), 7.20 (1H, *s*, N–CH–), 7.12–7.15 (4H, *m*, aromatic), 5.96 (1H, *s*, –S–CH–), 3.50 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 149.7, 140.8, 134.0, 130.1, 128.7, 128.5, 126.7, 121.7, 102.5, 59.2, 35.6. MS (*m/z*): 333 [M^+].

N-*(2-(4-Chlorophenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2b**)*. Yield: 85 %; m.p. 202–204 °C. Anal. Calcd. for $C_{15}H_{12}ClN_3O_2S$ (*FW* 333.79): C, 53.97; H, 3.62; N, 12.59 %. Found: C, 53.96; H, 3.61; N, 12.58 %. IR (KBr, cm^{-1}): 3310 (N–H stretching), 1706 (C=O thiazolidinone), 1666 (C=O stretching of carbonyl), 1612 (C=N), 1573 (C=C), 830 (C–Cl stretching of chlorine), 700 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.8 (1H, *s*, CONH–), 7.74, 8.64 (4H, *m*, Py), 7.2 (1H, *s*, N–CH–), 7.12–7.15 (4H, *m*, aromatic), 5.96 (1H, *s*, –S–CH–), 3.50 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 149.7, 140.8, 134.0, 130.1, 128.7, 128.5, 126.7, 121.7, 102.5, 59.2, 35.6. MS (*m/z*): 333 [M^+].

N-*(2-(2-Hydroxyphenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2c**)*. Yield: 70 %; m.p. 200–202 °C. Anal. Calcd. for $C_{15}H_{13}N_3O_3S$ (*FW* 315.07): C, 57.13; H, 4.16; N, 13.33 %. Found: C, 57.11; H, 4.14; N, 13.31 %. IR (KBr, cm^{-1}): 3318 (N–H stretching), 1716 (C=O thiazolidinone), 1674 (C=O stretching of carbonyl), 1626 (C=N), 1587 (C=C), 644 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.41 (1H, *br*, OH), 9.14 (1H, *s*, CONH–), 7.77–8.68 (4H, *m*, Py), 7.20 (1H, *s*, N–CH–), 7.17–7.20 (4H, *m*, Ar–H), 5.16 (1H, *s*, –S–CH–), 3.50 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 153.7,149.7, 140.8, 128.5, 128.0, 121.2, 121.7, 118.1,115.8, 58.1, 35.6. MS (*m/z*): 315 [M^+].

N-*(2-(3-Hydroxyphenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2d**)*. Yield: 70 %; m.p. 208–210 °C. Anal. Calcd. for $C_{15}H_{13}N_3O_3S$ (*FW* 315.07): C, 57.13; H, 4.16; N, 13.33 %. Found: C, 57.10; H, 4.13; N, 13.32 %. IR (KBr, cm^{-1}): 3317 (N–H stretching), 1717 (C=O thiazolidinone), 1672 (C=O stretching of carbonyl), 1624 (C=N), 1588 (C=C), 642 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / / ppm): 9.42 (1H, *br*, OH), 9.13 (1H, *s*, CONH–), 7.76–8.67 (4H, *m*, Py), 7.10 (1H, *s*, N–CH–), 7.17–7.20 (4H, *m*, aromatic), 5.16 (1H, *s*, –S–CH–), 3.50 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 153.7, 149.7, 140.8, 128.5, 128.0, 121.2, 121.7, 118.1, 115.8, 58.1, 35.6. MS (*m/z*): 315 [M^+].

N-*(2-(4-Methoxyphenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2e**)*. Yield: 75 %; m.p. 204–206 °C. Anal. Calcd. for $C_{16}H_{15}N_3O_3S$ (*FW* 329.37): C, 58.34; H, 4.59; N, 12.76 %. Found: C, 58.33; H, 4.58; N, 12.74 %. IR (KBr, cm^{-1}): 3302 (N–H stretching), 1760 (C=O thiazolidinone), 1632 (C=O stretching of carbonyl), 1667 (C=N), 1546 (C=C), 628 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / / ppm): 9.06 (1H, *s*, CONH–), 7.70, 8.64 (4H, *m*, Py), 7.40 (1H, *s*, N–CH–), 7.26––7.32 (4H, *m*, aromatic), 5.22 (1H, *s*, –S–CH–), 3.84 (3H, *s*, OCH_3), 3.80 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 159.0, 149.7, 121.7, 140.8, 131.5, 129.7, 121.7, 114.2, 64.3, 55.8, 35.6. MS (*m/z*): 329 [M^+].

N-*(2-(4-Fluorophenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2f**)*. Yield: 85 %; m.p. 196–200 °C. Anal. Calcd. for $C_{15}H_{12}FN_3O_2S$ (*FW* 317.34): C, 56.77; H, 3.81; N, 5.99 %. Found: C, 56.76; H, 3.80; N, 5.98 %. IR (KBr, cm^{-1}): 3316 (N–H stretching), 1769 (C=O thiazolidinone), 1661 (C=N), 1649 (C=O stretching of carbonyl), 1535 (C=C), 623 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.02 (1H, *s*, CONH–), 7.80 (1H, *s*, N–CH–), 7.75–8.60 (4H, *m*, Py), 7.30, 7.36 (4H, *m*, aromatic), 5.28 (1H, *s*, –S–CH–), 3.10 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 161.3, 149.7, 140.8, 134.8, 130.3, 121.7, 115.4, 64.3, 35.6. MS (*m/z*): 317 [M^+].

N-*(2-(2-Nitrophenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2g**)*. Yield: 80 %; m.p. 210–212 °C. Anal. Calcd. for $C_{15}H_{12}N_4O_4S$ (*FW* 344.35): C, 52.32; H, 3.51; N, 16.27 %. Found: C, 52.31; H, 3.50; N, 16.25 %. IR (KBr, cm^{-1}): 3328 (N–H stretching), 1774 (C=O thiazolidinone), 1660 (C=N), 1652 (C=O stretching of carbonyl), 1532 (C=C), 620 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.05 (1H, *s*, CONH–), 7.90 (1H, *s*, N–CH–), 7.78, 8.64 (4H, *m*, Py), 7.31–7.34 (4H, *m*, aromatic), 5.21 (1H, *s*, –S–CH–), 3.11 (2H, *s*, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 149.7, 149.0, 140.8, 134.7, 133.4, 129.6, 128.0, 124.8, 121.7, 59.7, 35.6. MS (*m/z*): 344 [M^+].

N-*(2-(4-(Dimethylamino)phenyl)-4-oxothiazolidin-3-yl)isonicotinamide (**2h**)*. Yield: 75 %; m.p. 204–206 °C. Anal. Calcd. for $C_{17}H_{18}N_4O_2S$ (*FW* 342.42): C, 59.63; H, 5.30; N, 16.36 %. Found: C, 59.61; H, 5.29; N, 16.34 %. IR (KBr, cm^{-1}): 3336 (N–H stretching), 1777 (C=O thiazolidinone), 1661 (C=N), 1635 (C=O stretching of carbonyl), 1539 (C=C), 625 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.03 (1H, *s*, CONH–), 7.71, 8.60 (4H, *m*, Py), 7.70 (1H, *s*, N–CH–), 7.28–7.32 (4H, *m*, aromatic), 5.20 (1H, *s*, –S–CH–), 3.09 (2H, *s*, CH_2), 2.65 (6H, *s*, $N(CH_3)_2$). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 163.7, 149.7, 149.5, 140.8, 128.7, 127.4, 121.7, 112.8, 64.3, 41.3, 35.6. MS (*m/z*): 342 [M^+].

*2-(2-(2-Chlorophenyl)-3-isonicotinamido-4-oxothiazolidin-5-yl)acetic acid (**3a**)*. Yield: 80 %; m.p. 210–212 °C. Anal. Calcd. for $C_{17}H_{14}ClN_3O_4S$ (*FW* 391.83): C, 52.11; H, 3.60; N, 10.72 %. Found: C, 52.10; H, 3.59; N, 10.70 %. IR (KBr, cm^{-1}): 3200 (N–H stretching), 1700 (C=O thiazolidinone), 1666 (C=O stretching of carbonyl), 1610 (C=N), 1572 (C=C), 700 (C–S–C), 830 (C–Cl stretching of chlorine). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 10.00 (1H, *s*, COOH), 9.40 (1H, *s*, CONH–), 7.71–8.60 (4H, *m*, Py), 7.20 (1H, *s*, N–CH–), 6.17—6.15 (4H, *m*, Ar–H), 5.95 (1H, *s*, –S–CH–Ar). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 149.7, 140.8, 134.0, 130.1, 121.7, 128.7, 128.5, 126.7, 102.5, 56.7, 47.5, 39.2. MS (*m/z*): 391 [M^+].

*2-(2-(4-Chlorophenyl)-3-isonicotinamido-4-oxothiazolidin-5-yl)acetic acid (**3b**)*. Yield: 85 %; m.p. 216–218 °C. Anal. Calcd. for $C_{17}H_{14}ClN_3O_4S$ (*FW* 391.83): Calcd: C, 52.11; H, 3.60; N, 10.72 %. Found: C, 52.09; H, 3.58; N, 10.71 %. IR (KBr, cm^{-1}): 3204 (N–H stretching), 1702 (C=O thiazolidinone),

1664 (C=O stretching of carbonyl), 1611 (C=N), 1572 (C=C), 701 (C–S–C), 832 (C–Cl stretching of chlorine). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 10.10 (1H, *s*, COOH), 9.50 (1H, *s*, CONH–), 7.72–8.61 (4H, *m*, Py), 7.10 (1H, *s*, N–CH–), 6.18–6.16 (4H, *m*, aromatic), 5.94 (1H, *s*, –S–CH–Ar). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 149.7, 140.8, 134.0, 130.1, 121.7, 128.7, 128.5, 126.7, 102.5, 56.7, 47.5, 39.2. MS (*m/z*): 391 [M^+].

*2-(2-(2-Hydroxyphenyl)-3-isonicotinamido-4-oxothiazolidin-5-yl)acetic acid (**3c**)*. Yield: 75 %; m.p. 222–224 °C. Anal. Calcd. for $C_{17}H_{15}N_3O_5S$ (*FW* 373.38): C, 54.68; H, 4.05; N, 11.25 %. Found: C, 54.67; H, 4.03; N, 10.23 %. IR (KBr, cm^{-1}): 3324 (N–H stretching), 1714 (C=O thiazolidinone), 1660 (C=O stretching of carbonyl), 1625 (C=N), 1579 (C=C), 710 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 10.02 (1H, *s*, COOH), 9.40 (1H, *s*, CONH–), 9.33 (1H, *br*, OH), 7.69––8.51 (4H, *m*, Py), 7.50 (1H, *s*, N–CH–), 6.20–6.17 (4H, *m*, aromatic), 5.90 (1H, *s*, –S–CH–Ar). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 153.7, 149.7, 140.8, 128.5, 128.0, 121.2, 118.1, 55.6, 47.5, 39.2. MS (*m/z*): 373 [M^+].

*2-(2-(3-Hydroxyphenyl)-3-isonicotinamido-4-oxothiazolidin-5-yl)acetic acid (**3d**)*. Yield: 60 %; m.p. 238–240 °C. Anal. Calcd. for $C_{17}H_{15}N_3O_5S$ (*FW* 373.38): C, 54.68; H, 4.05; N, 11.25 %. Found: C, 54.66; H, 4.04; N, 10.24 %. IR (KBr, cm^{-1}): 3325 (N–H stretching), 1713 (C=O thiazolidinone), 1662 (C=O stretching of carbonyl), 1624 (C=N), 1580 (C=C), 711 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 10.02 (1H, *s*, COOH), 9.40 (1H, *s*, CONH–), 9.32 (1H, *br*, OH), 7.68–8.52 (4H, *m*, Py), 7.50 (1H, *s*, N–CH–), 6.20–6.17 (4H, *m*, aromatic), 5.90 (1H, *s*, –S–CH–Ar). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 153.7, 149.7, 140.8, 128.5, 128.0, 121.2, 118.1, 55.6, 47.5, 39.2. MS (*m/z*): 373 [M^+].

*2-(3-Isonicotinamido-2-(4-methoxyphenyl)-4-oxothiazolidin-5-yl)acetic acid (**3e**)*. Yield: 65 %; m.p. 220–222 °C. Anal. Calcd. for $C_{18}H_{17}N_3O_5S$ (*FW* 387.41): C, 55.80; H, 4.42; N, 10.85 %. Found: C, 55.78; H, 4.41; N, 10.83 %. IR (KBr, cm^{-1}): 3330 (N–H stretching), 1720 (C=O thiazolidinone), 1669 (C=O stretching of carbonyl), 1629 (C=N), 1574 (C=C), 714 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 10.01 (1H, *s*, COOH), 9.60 (1H, *s*, CONH–), 7.70 (1H, *s*, N–CH–), 7.63, 8.55 (4H, *m*, Py), 6.22–6.18 (4H, *m*, Ar–H), 5.91 (1H, *s*, –S–CH–Ar), 3.80 (3H, *s*, $-OCH_3$). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 159.0, 149.7, 140.8, 131.5, 129.7, 121.7, 114.2, 61.8, 55.8, 47.5, 39.2. MS (*m/z*): 387 [M^+].

*2-(2-(4-Fluorophenyl)-3-isonicotinamido-4-oxothiazolidin-5-yl)acetic acid (**3f**)*. Yield: 75 %; m.p. 190–192 °C. Anal. Calcd. for $C_{17}H_{14}FN_3O_4S$ (*FW* 375.37): C, 54.39; H, 3.76; N, 11.19 %. Found: C, 54.38; H, 3.74; N, 11.18 %. IR (KBr, cm^{-1}): 3316 (N–H stretching), 1714 (C=O thiazolidinone), 1670 (C=O stretching of carbonyl), 1634 (C=N), 1578 (C=C), 720 (C–S–C). ^{1}H-NMR (300 MHz,

$CDCl_3$, δ / ppm): 10.04 (1H, *s*, COOH), 9.20 (1H, *s*, CONH–), 7.90 (1H, *s*, N–CH–), 7.66–8.58 (4H, *m*, Py), 6.20–6.17 (4H, *m*, aromatic), 5.93 (1H, *s*, –S–CH–Ar). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 161.3, 149.7, 140.8, 134.8, 130.3, 121.7, 115.4, 61.8, 47.5, 39.2. MS (*m/z*): 375 [M^+].

*2-(3-Isonicotinamido-2-(2-nitrophenyl)-4-oxothiazolidin-5-yl)acetic acid (**3g**)*. Yield: 80 %; m.p. 232–234 °C. Anal. Calcd. for $C_{17}H_{14}N_4O_6S$ (*FW* 402.38): C, 50.74; H, 3.51; N, 13.92 %. Found: C, 50.73; H, 3.50; N, 13.91 %. IR (KBr, cm^{-1}): 3310 (N–H stretching), 1704 (C=O thiazolidinone), 1660 (C=O stretching of carbonyl), 1632 (C=N), 1580 (C=C), 727 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / / ppm): 10.03 (1H, *s*, COOH), 9.40 (1H, *s*, CONH–), 7.63, 8.31 (4H, *m*, Py), 7.50 (1H, *s*, N–CH), 6.24–6.20 (4H, *m*, Ar–H), 5.90 (1H, *s*, –S–CH–Ar). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 149.0, 149.7, 140.8, 133.4, 134.7, 129.6, 128.0, 124.8, 121.7, 57.2, 47.5, 39.2. MS (*m/z*): 402 [M^+].

*2-(2-(4-(Dimethylamino)phenyl)-3-isonicotinamido-4-oxothiazolidin-5-yl)-acetic acid (**3h**)*. Yield: 70 %; m.p. 248–250 °C. Anal. Calcd. for $C_{19}H_{20}N_4O_4S$ (*FW* 400.45): C, 56.99; H, 5.03; N, 13.99 %. Found: C, 56.97; H, 5.01; N, 13.98 %. IR (KBr, cm^{-1}): 3315 (N–H stretching), 1710 (C=O thiazolidinone), 1666 (C=O stretching of carbonyl), 1632 (C=N), 1584 (C=C), 727 (C–S–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 10.06 (1H, *s*, COOH), 9.10 (1H, *s*, CONH–), 7.68––8.33 (4H, *m*, Py), 6.22–6.19 (4H, *m*, Ar–H), 7.10 (1H, *s*, N–CH–), 5.93 (1H, *s*, –S–CH–Ar), 2.72 (6H, *s*, $N(CH_3)_2$). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 175.3, 173.3, 163.7, 149.7, 149.5, 140.8, 128.7, 127.4, 121.7, 112.8, 57.2, 47.5, 39.2. MS (*m/z*): 400 [M^+].

N-*(3-Chloro-2-(2-chlorophenyl)-4-oxoazetidin-1-yl)isonicotinamide (**4a**)*. Yield: 75 %; m.p. 322–324 °C. Anal. Calcd. for $C_{15}H_{11}Cl_2N_3O_2$ (*FW* 336.17): C, 53.59; H, 3.30; N, 12.50 %. Found: C, 53.58; H, 3.29; N, 12.48 %. IR (KBr, cm^{-1}): 3250 (N–H stretching), 1745 (C=O β-lactam ring), 1616 (C=O stretching of carbonyl), 1600 (C=N), 1560 (C=C), 742 (C–Cl stretching of chlorine). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.40 (1H, *s*, CONH–), 7.70 (1H, *s*, N–CH–), 7.68––8.33 (4H, *m*, Py), 6.61–6.63 (4H, *m*, aromatic). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 163.7, 163.5, 149.7, 143.5, 140.8, 132.2, 128.6, 128.1, 126.6, 121.7. MS (*m/z*): 335 [M^+].

N-*(3-Chloro-2-(4-chlorophenyl)-4-oxoazetidin-1-yl)isonicotinamide (**4b**)*. Yield: 65 %; m.p. 328–330 °C. Anal. Calcd. for $C_{15}H_{11}Cl_2N_3O_2$ (*FW* 336.17): C, 53.59; H, 3.30; N, 12.50 %. Found: C, 53.57; H, 3.27; N, 12.46 %. IR (KBr, cm^{-1}): 3252 (N–H stretching), 1746 (C=O β-lactam ring), 1612 (C=O stretching of carbonyl), 1599 (C=N), 1562 (C=C), 741 (C–Cl stretching of chlorine). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.80 (1H, *s*, CONH–), 7.60 (1H, *s*, N–CH–), 7.67–8.32 (4H, *m*, Py), 6.62–6.64 (4H, *m*, Ar–H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 163.7, 163.5, 149.7, 143.5, 140.8, 132.2, 128.6, 128.1, 126.6, 121.7. MS (*m/z*): 335 [M^+].

N-*(3-Chloro-2-(2-hydroxyphenyl)-4-oxoazetidin-1-yl)isonicotinamide* (***4c***). Yield: 70 %; m.p. 346–348 °C. Anal. Calcd. for $C_{15}H_{12}ClN_3O_3$ (*FW* 317.73): C, 56.70; H, 3.81; N, 13.23 %. Found: C, 56.68; H, 3.80; N, 13.21 %. IR (KBr, cm^{-1}): 3256 (N–H stretching), 1749 (C=O *β*-lactam ring), 1614 (C=O stretching of carbonyl), 1602 (C=N), 1561 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$, *δ* / ppm): 9.20 (1H, *br*, OH), 9.90 (1H, *s*, CONH–), 7.64–8.31 (4H, *m*, Py), 7.40 (1H, *s*, N–CH–), 6.60–6.61 (4H, *m*, aromatic). ^{13}C-NMR (100 MHz, $CDCl_3$, *δ* / ppm): 163.7, 163.5, 154.0, 149.7, 140.8, 130.9, 128.1, 126.5, 121.7, 121.1, 115.7, 64.4, 61.2. MS (*m/z*): 317 [M^+].

N-*(3-Chloro-2-(3-hydroxyphenyl)-4-oxoazetidin-1-yl)isonicotinamide* (***4d***). Yield: 60 %; m.p. 330–332 °C. Anal. Calcd. for $C_{15}H_{12}ClN_3O_3$ (*FW* 317.73): C, 56.70; H, 3.81; N, 13.23 %. Found: C, 56.69; H, 3.80; N, 13.22 %. IR (KBr, cm^{-1}): 3259 (N–H stretching), 1752 (C=O *β*-lactam ring), 1672 (C=O stretching of carbonyl), 1605 (C=N), 1562 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$, *δ* / ppm): 9.30 (1H, *br*, OH), 9.80 (1H, *s*, CONH–), 7.64–8.31 (4H, *m*, Py), 7.40 (1H, *s*, N–CH–), 6.60–6.61 (4H, *m*, Ar–H). ^{13}C-NMR (100 MHz, $CDCl_3$, *δ* / ppm): 163.7, 163.5, 156.8, 149.7, 144.9, 140.8, 129.9, 121.7, 113.9, 112.6, 67.7, 64.1. MS (*m/z*): 317 [M^+].

N-*(3-Chloro-2-(4-methoxyphenyl)-4-oxoazetidin-1-yl)isonicotinamide* (***4e***). Yield: 55 %; m.p. 344–346 °C. Anal. Calcd. for $C_{16}H_{14}ClN_3O_3$ (*FW* 331.75): C, 57.93; H, 4.25; N, 12.67 %. Found: C, 57.91; H, 4.22; N, 12.65 %. IR (KBr, cm^{-1}): 3260 (N–H stretching), 1748 (C=O *β*-lactam ring), 1670 (C=O stretching of carbonyl), 1603 (C=N), 1558 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$, *δ* / ppm): 9.40 (1H, *s*, CONH–), 7.62, 8.31 (4H, *m*, Py), 7.20 (1H, *s*, N–CH–), 6.63–6.65 (4H, *m*, aromatic), 3.78 (3H, *s*, OCH_3). ^{13}C-NMR (100 MHz, $CDCl_3$, *δ* / ppm): 163.7, 163.5, 158.6, 149.7, 140.8, 135.8, 126.6, 121.7, 114.1, 67.4, 64.1. MS (*m/z*): 331 [M^+].

N-*(3-Chloro-2-(4-fluorophenyl)-4-oxoazetidin-1-yl)isonicotinamide* (***4f***). Yield: 75 %; m.p. 298–300 °C. Anal. Calcd. for $C_{15}H_{11}ClFN_3O_2$ (*FW* 319.72): C, 56.35; H, 3.47; N, 13.14 %. Found: C, 56.33; H, 3.46; N, 13.12 %. IR (KBr, cm^{-1}): 3264 (N–H stretching), 1747 (C=O *β*-lactam ring), 1672 (C=O stretching of carbonyl), 1613 (C=N), 1560 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$, *δ* / ppm): 9.60 (1H, *s*, CONH–), 7.60, 8.31 (4H, *m*, Py), 7.80 (1H, *s*, N–CH–), 6.62–6.67 (4H, *m*, Ar–H). ^{13}C-NMR (100 MHz, $CDCl_3$, *δ* / ppm): 163.7, 163.5, 160.9, 149.7, 140.8, 139.1, 128.5, 121.7, 115.3, 67.4, 64.1. MS (*m/z*): 319 [M^+].

N-*(3-Chloro-2-(2-nitrophenyl)-4-oxoazetidin-1-yl)isonicotinamide* (***4g***). Yield: 60 %; m.p. 294–296 °C. Anal. Calcd. for $C_{15}H_{11}ClN_4O_4$ (*FW* 346.73): C, 51.96; H, 3.20; N, 16.16 %. Found: C, 51.94; H, 3.19; N, 16.14 %. IR (KBr, cm^{-1}): 3268 (N–H stretching), 1740 (C=O *β*-lactam ring), 1662 (C=O stretching of carbonyl), 1614 (C=N), 1562 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$, *δ* / ppm): 9.40 (1H, *s*, CONH–), 7.63, 8.34 (4H, *m*, Py), 7.30 (1H, *s*, N–CH–), 6.64–6.66 (4H, *m*,

Ar–H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 163.7, 163.5, 149.7, 147.2, 140.8, 137.5, 134.6, 127.6, 124.7, 121.7, 63.1, 62.8. MS (*m/z*): 346 [M^+].

N-*(3-Chloro-2-(4-(dimethylamino)phenyl)-4-oxoazetidin-1-yl)isonicotinamide (**4h**)*. Yield: 65 %; m.p. 360–362 °C. Anal. Calcd. for $C_{17}H_{17}ClN_4O_2$ (*FW* 344.80): C, 59.22; H, 4.97; N, 16.25 %. Found: C, 59.21; H, 4.96; N, 16.23 %. IR (KBr, cm^{-1}): 3266 (N–H stretching), 1747 (C=O β-lactam ring), 1668 (C=O stretching of carbonyl), 1611 (C=N), 1565 (C=C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.10 (1H, *s*, CONH–), 7.90 (1H, *s*, N–CH–), 7.67, 8.32 (4H, *m*, Py), 6.65–6.69 (4H, *m*, Ar–H), 2.70 (6H, *s*, $N(CH_3)_2$. ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 163.7, 163.5, 149.7, 149.1, 140.8, 133.0, 129.2, 121.7, 112.7, 67.4, 64.1, 41.3. MS (*m/z*): 344 [M^+].

*1-(2-(2-Chlorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5a**)*. Yield: 65 %; m.p. 182–184 °C. Anal. Calcd. for $C_{15}H_{12}ClN_3O_2$ (*FW* 301.73): C, 59.71; H, 4.01; N, 13.93 %. Found: C, 59.70; H, 4.00; N, 13.91 %. IR (KBr, cm^{-1}): 1660 (acetyl C=O), 1614 (C=N), 1560 (C=C), 830 (C–Cl stretching of chlorine), 1500 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.72–8.64 (4H, *m*, Py), 7.12–7.14 (4H, *m*, aromatic), 7.19 (1H, *s*, CH– oxadiazole). ^{13}C--NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 149.4, 142.8, 138.4, 132.2, 128.6, 128.3, 128.1, 126.6, 124.1, 78.4, 23.4. MS (*m/z*): 301 [M^+].

*1-(2-(4-Chlorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5b**)*. Yield: 60 %; m.p. 186–188°C. Anal. Calcd. for $C_{15}H_{12}ClN_3O_2$ (*FW* 301.73): C, 59.22; H, 4.97; N, 16.25 %. Found: C, 59.21; H, 4.95; N, 16.23. IR (KBr, cm^{-1}): 1662 (acetyl C=O), 1616 (C=N), 1562 (C=C), 834 (C–Cl stretching of chlorine), 1504 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.73, 8.65 (4H, *m*, Py), 7.20 (1H, *s*, CH–oxadiazole), 7.13–7.15 (4H, *m*, aromatic). ^{13}C--NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 149.4, 138.4, 132.3, 128.6, 128.3, 124.1, 83.5, 23.4. MS (*m/z*): 301 [M^+].

*1-(2-(2-Hydroxyphenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5c**)*. Yield: 50 %; m.p. 198–200 °C. Anal. Calcd. for $C_{15}H_{13}N_3O_3$ (*FW* 283.28): C, 63.60; H, 4.63; N, 14.83 %. Found: C, 63.58; H, 4.61; N, 14.81 %. IR (KBr, cm^{-1}): 1664 (acetyl C=O), 1618 (C=N), 1563 (C=C), 1510 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.32 (1H, *br*, OH), 7.62, 8.34 (4H, *m*, Py), 7.20 (1H, *s*, CH–oxadiazole), 7.10–7.13 (4H, *m*, aromatic). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 149.4, 138.4, 129.6, 128.3, 128.1, 124.1, 121.1, 115.7, 77.3, 23.4. MS (*m/z*): 283 [M^+].

*1-(2-(3-Hydroxyphenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5d**)*. Yield: 65 %; m.p. 210–212 °C. Anal. Calcd. for $C_{15}H_{13}N_3O_3$ (*FW* 283.28): C, 63.60; H, 4.63; N, 14.83 %. Found: C, 63.59; H, 4.62; N, 14.82. IR (KBr, cm^{-1}): 1664 (acetyl C=O), 1618 (C=N), 1563 (C=C), 1510 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 9.32 (1H, *br*, OH), 7.62, 8.34 (4H, *m*, Py), 7.20 (1H, *s*, CH–oxadiazole), 7.10–7.13 (4H, *m*, aromatic). ^{13}C-NMR (100 MHz, $CDCl_3$, δ /

/ ppm): 168.8, 157.0, 156.8, 149.4, 141.7, 138.4, 129.9, 124.1, 113.9, 112.6, 83.8, 23.4. MS (*m/z*): 283 [M^+].

*1-(2-(4-Methoxyphenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5e**)*. Yield: 55 %; m.p. 202–204 °C. Anal. Calcd. for $C_{16}H_{15}N_3O_3$ (*FW* 297.31): C, 64.64; H, 5.09; N, 14.13 %. Found: C, 64.62; H, 5.07; N, 14.11 %. IR (KBr, cm^{-1}): 1667 (acetyl C=O), 1615 (C=N), 1561 (C=C), 1515 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.66, 8.38 (4H, *m*, Py), 7.22 (1H, *s*, CH–oxadiazole), 7.14–7.17 (4H, *m*, aromatic), 3.71 (3H, *s*, OCH_3). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 156.5, 149.4, 138.4, 127.9, 127.7, 124.1, 120.8, 112.1, 77.6, 23.4. MS (*m/z*): 297 [M^+].

*1-(2-(4-Fluorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5f**)*. Yield: 65 %; m.p. 206–208 °C. Anal. Calcd. for $C_{15}H_{12}FN_3O_2$ (*FW* 285.27): C, 63.15; H, 4.24; N, 14.73 %. Found: C, 63.14; H, 4.23; N, 14.71 %. IR (KBr, cm^{-1}): 1663 (acetyl C=O), 1620 (C=N), 1565 (C=C), 1518 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.69, 8.37 (4H, *m*, Py), 7.25 (1H, *s*, CH–oxadiazole), 7.13–7.18 (4H, *m*, aromatic). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 159.4, 149.4, 138.4, 129.4, 128.5, 128.3, 124.1, 76.7, 23.4. MS (*m/z*): 285 [M^+].

*1-(2-(2-Nitrophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**5g**)*. Yield: 70 %; m.p. 196–198 °C. Anal. Calcd. for $C_{15}H_{12}N_4O_4$ (*FW* 312.28): C, 57.69; H, 3.87; N, 17.94 %. Found: C, 57.67; H, 3.85; N, 17.93 %. IR (KBr, cm^{-1}): 1669 (acetyl C=O), 1619 (C=N), 1563 (C=C), 1517 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.67, 8.35 (4H, *m*, Py), 7.23 (1H, *s*, CH–oxadiazole), 7.12–7.15 (4H, *m*, aromatic). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 149.4, 148.2, 139.4, 138.4, 130.9, 129.4, 127.6, 124.7, 78.9, 23.4. MS (*m/z*): 312 [M^+].

*1-(2-(4-(Dimethylamino)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)-ethanone (**5h**)*. Yield: 75 %; m.p. 204–206 °C. Anal. Calcd. for $C_{17}H_{18}N_4O_2$ (*FW* 310.35): C, 65.79; H, 5.85; N, 18.05 %. Found: C, 65.78; H, 5.83; N, 18.03 %. IR (KBr, cm^{-1}): 1664 (acetyl C=O), 1624 (C=N), 1570 (C=C), 1511 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 7.65, 8.33 (4H, *m*, Py), 7.26 (1H, *s*, CH–oxadiazole), 7.14–7.18 (4H, *m*, aromatic), 2.73 (6H, *s*, $N(CH_3)_2$). ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 168.8, 157.0, 149.4, 149.1, 138.4, 129.8, 127.8, 124.1, 83.5, 41.3, 23.4. MS (*m/z*): 310 [M+].