Supplementary Information

Novel isoniazid-amidoether derivatives: Synthesis, characterization and their antimycobacterial activity evaluation

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Experimental Protocols

All the chemicals were purchased from Sigma-Aldrich. Solvents used for the chemical synthesis were acquired from commercial sources, were of analytical grade and used without further purification. Thin layer chromatography (Merck Kiesel 60 F254, 0.2 mm thickness) was used to monitor the progress of the reactions and the compounds were purified by silica gel (60-120 mesh) column chromatography. Melting points were recorded on EZ-Melt automated melting point apparatus, Stanford Research Systems and are uncorrected. IR spectra were recorded on Perkin-elmer FT-IR spectrophotometer using KBr pellets or as film in chloroform and the values were expressed in cm^{-1}. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Jeol ECX spectrospin instrument using $CDCl_3$ or DMSO-d_6 as solvent and TMS as internal reference. The chemical shift values were expressed on δ scale and the coupling constant (*J*) in Hz. Mass data were recorded in Jeol-Accu TOF JMS-T100LC mass spectrometer.

Typical procedure for the syntheses of 2-chloro-*N*-phenylacetamide (1a) and related compounds (1b-1v): To a well stirred solution of aniline (500 mg, 0.0053 mol) and K_2CO_3 (2.61 g, 0.019 mol) in dry CH_2Cl_2 (20 mL), chloroacetyl chloride (712 mg, 0.0063 mol) was added dropwise at 0 ^oC. The mixture was stirred for 4-6 h at room temperature. After completion of the reaction, excess DCM was evaporated in rotary evaporator. The solid formed was washed with excess of water and crystallised by using hexane/ethyl acetate.

Typical procedure for the synthesis of 2-(4-formylphenoxy)-*N*-phenylacetamide (2a) and related compounds (2b-2v): The 2-chloro-*N*-phenylacetamide (**1a**, 500 mg, 2.9 mmol)

and 4-hydroxy benzaldehyde (354 mg, 2.9 mmol) were dissolved in 30 mL of acetone. To this, K_2CO_3 (1.2 g, 8.7 mmol) and KI (100 mg, 0.5 mmol) was added and the reaction mixture was stirred for 10-12 h at room temperature. After completion of the reaction, acetone was evaporated and the product was extracted with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4. Excess solvent was removed under vacuum and the crude product was purified by column chromatography to get pure compound **2a**.

2-(4-Formylphenoxy)-*N*-phenylacetamide (2a): Yield 80%; IR (film, cm^{-1}): 2913, 2825, 2738, 1682, 1600, 1578, 1533, 1508, 1428, 1304, 1260, 1162, 1064, 831; ^1H NMR (400 MHz, $CDCl_3$): δ 4.69 (s, 2H, O*CH*$_2$), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.15-7.19 (m, 1H, Ar*H*), 7.34-7.38 (m, 2H, Ar*H*), 7.57-7.60 (m, 2H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.20 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{13}NO_3$: 255.08, found: 256.11 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-*p*-tolylacetamide (2b): Yield 70%; IR (film, cm^{-1}): 2921, 2852, 1689, 1600, 1532, 1508, 1407, 1312, 1250, 1162, 1059, 817; ^1H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H, *CH*$_3$), 4.68 (s, 2H, O*CH*$_2$), 7.11 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.16 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.46 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.90 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.15 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{16}H_{15}NO_3$: 269.10, found: 270.09 $(M + H)^+$.

***N*-(4-Ethylphenyl)-2-(4-formylphenoxy)acetamide (2c):** Yield 68%; IR (film, cm^{-1}): 2961, 2922, 2850, 1686, 1678, 1606, 1582, 1535, 1508, 1413, 1253, 1212, 1160, 1065, 828; ^1H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, *J* = 8.0 Hz, 3H, CH_2*CH*$_3$), 2.63 (q, *J* = 8.0 Hz, 2H, *CH*$_2$$CH_3$), 4.69 (s, 2H, O*CH*$_2$), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.19 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.48 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.12 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{17}H_{17}NO_3$: 283.12, found: 284.16 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(4-*iso*-propylphenyl)acetamide (2d): Yield 65%; IR (film, cm^{-1}): 2960, 2923, 2852, 1686, 1600, 1534, 1508, 1417, 1311, 1250, 1162, 1056, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 1.23 (d, *J* = 7.3 Hz, 6H, CH(*CH*$_3$)$_2$), 2.89 (septet, *J* = 7.3 Hz, 1H, *CH*(CH_3)$_2$), 4.69 (s, 2H, O*CH*$_2$), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.22 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.48 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.12 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{18}H_{19}NO_3$: 297.13, found: 298.14 $(M + H)^+$.

***N*-(2-Fluorophenyl)-2-(4-formylphenoxy)acetamide (2e):** Yield 65%; IR (film, cm^{-1}): 2924, 2853, 2740, 1690, 1598, 1541, 1508, 1458, 1311, 1260, 1160, 1103, 1063, 828; ^1H NMR (400 MHz, $CDCl_3$): δ 4.73 (s, 2H, O*CH*$_2$), 7.11-7.18 (m, 5H, Ar*H*), 7.91 (d, *J* = 8.7 Hz,

2H, Ar*H*), 8.33-8.37 (m, 1H, Ar*H*), 8.52 (brs, 1H, CO*NH*), 9.94 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}FNO_3$: 273.08, found: 273.12 $(M + H)^+$.

***N*-(3-Fluorophenyl)-2-(4-formylphenoxy)acetamide (2f):** Yield 65%; IR (film, cm^{-1}): 2920, 2850, 1686, 1601, 1542, 1508, 1492, 1447, 1312, 1249, 1216, 1162, 1060, 862, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 4.69 (s, 2H, O*CH*$_2$), 6.85-6.89 (m, 1H, Ar*H*), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.22-7.26 (m, 1H, Ar*H*), 7.28-7.33 (m, 1H, Ar*H*), 7.55-7.58 (m, 1H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.28 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}FNO_3$: 273.08, found: 273.10 $(M + H)^+$.

***N*-(4-Fluorophenyl)-2-(4-formylphenoxy)acetamide (2g):** Yield 70%; ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 2H, O*CH*$_2$), 7.04-7.08 (m, 2H, Ar*H*), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.54-7.57 (m, 2H, Ar*H*), 7.91 (d, *J* = 8.0 Hz, 2H, Ar*H*), 8.20 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}FNO_3$: 273.08, found: 273.14 $(M + H)^+$.

***N*-(2-Chlorophenyl)-2-(4-formylphenoxy)acetamide (2h):** Yield 70%; IR (film, cm^{-1}): 2922, 2852, 1701, 1601, 1533, 1508, 1440, 1307, 1249, 1219, 1161, 1057, 830; ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 2H, O*CH*$_2$), 7.10-7.16 (m, 3H, Ar*H*), 7.26-7.31 (m, 1H, Ar*H*), 7.44-7.46 (m, 1H, Ar*H*), 7.71-7.72 (m, 1H, Ar*H*), 7.89-7.92 (m, 2H, Ar*H*), 8.24 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}ClNO_3$: 289.05, found: 290.08 $(M + H)^+$, 292.12 $(M + 2)^+$.

***N*-(3-Chlorophenyl)-2-(4-formylphenoxy)acetamide (2i):** Yield 70%; IR (film, cm^{-1}): 2924, 2851, 1686, 1596, 1534, 1508, 1426, 1307, 1250, 1162, 1060, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 2H, O*CH*$_2$), 7.10-7.16 (m, 3H, Ar*H*), 7.26-7.31 (m, 1H, Ar*H*), 7.44-7.46 (m, 1H, Ar*H*), 7.71-7.72 (m, 1H, Ar*H*), 7.89-7.92 (m, 2H, Ar*H*), 8.24 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}ClNO_3$: 289.05, found: 290.07 $(M + H)^+$, 292.11 $(M + 2)^+$.

***N*-(4-Chlorophenyl)-2-(4-formylphenoxy)acetamide (2j):** Yield 80%; IR (film, cm^{-1}): 2923, 2853, 1686, 1596, 1508, 1401, 1306, 1249, 1162, 1059, 828; ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 2H, O*CH*$_2$), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.33 (d, *J* = 9.5 Hz, 2H, Ar*H*), 7.55 (d, *J* = 9.5 Hz, 2H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.21 (brs, 1H, CO*NH*), 9.94 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}ClNO_3$: 289.05, found: 290.10 $(M + H)^+$, 292.08 $(M + 2)^+$.

***N*-(2-Bromophenyl)-2-(4-formylphenoxy)acetamide (2k):** Yield 75%; IR (film, cm^{-1}): 2921, 2853, 1675, 1597, 1508, 1438, 1300, 1243, 1157, 1055, 866, 824; ^1H NMR (400 MHz,

$CDCl_3$): δ 4.74 (s, 2H, O*CH*$_2$), 7.01-7.05 (m, 1H, Ar*H*), 7.14 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.34-7.38 (m, 1H, Ar*H*), 7.57 (dd, *J* = 1.4, 8.0 Hz, 1H, Ar*H*), 7.92 (t, *J* = 8.7 Hz, 2H, Ar*H*), 8.44 (dd, *J* = 1.4, 8.0 Hz, 1H, Ar*H*), 8.96 (brs, 1H, CO*NH*), 9.94 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}BrNO_3$: 333.0, found: 334.03 $(M + H)^+$, 336.05 $(M + 2)^+$.

***N*-(3-Bromophenyl)-2-(4-formylphenoxy)acetamide (2l):** Yield 75%; IR (film, cm^{-1}): 2923, 2852, 1686, 1591, 1528, 1508, 1478, 1422, 1304, 1247, 1161, 1061, 831; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 2H, O*CH*$_2$), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.23 (t, *J* = 8.0 Hz, 1H, Ar*H*), 7.31 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.52 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.84 (t, *J* = 2.2 Hz, 1H, Ar*H*), 7.92 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.93 (brs, 1H, CO*NH*), 9.94 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}BrNO_3$: 333.0, found: 334.07 $(M + H)^+$, 336.10 $(M + 2)^+$.

***N*-(4-Bromophenyl)-2-(4-formylphenoxy)acetamide (2m):** Yield 85%; IR (film, cm^{-1}): 2924, 2851, 1688, 1593, 1509, 1433, 1309, 1245, 1159, 1063, 837; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.69 (s, 2H, O*CH*$_2$), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.48-7.49 (m, 4H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.19 (brs, 1H, CO*NH*), 9.94 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}BrNO_3$: 333.0, found: 334.10 $(M + H)^+$, 336.14 $(M + 2)^+$.

2-(4-Formylphenoxy)-*N*-(4-methoxyphenyl)acetamide (2n): Yield 65%; IR (film, cm^{-1}): 2919, 2850, 2734, 1685, 1605, 1580, 1539, 1509, 1427, 1302, 1240, 1163, 1109, 1060, 1031, 823; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H, O*CH*$_3$), 4.69 (s, 2H, O*CH*$_2$), 6.89 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.12 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.81 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.11 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{16}H_{15}NO_4$: 285.10, found: 286.16 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(4-nitrophenyl)acetamide (2o): Yield 75%; IR (film, cm^{-1}): 2923, 2893, 1686, 1597, 1542, 1508, 1410, 1341, 1302, 1253, 1164, 1111, 853, 831; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.75 (s, 2H, O*CH*$_2$), 7.14 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.81-7.83 (m, 2H, Ar*H*), 7.93 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.25-8.27 (m, 2H, Ar*H*), 8.53 (brs, 1H, CO*NH*), 9.95 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{15}H_{12}N_2O_5$: 300.07, found: 301.12 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(pyridin-2-yl)acetamide (2p): Yield 60%; IR (film, cm^{-1}): 2923, 2850, 1689, 1600, 1578, 1527, 1508, 1435, 1303, 1251, 1162, 1055, 832; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.72 (s, 2H, O*CH*$_2$), 7.10-7.14 (m, 3H, Ar*H*), 7.74-7.78 (m, 1H, Ar*H*), 7.89-7.92 (m, 2H, Ar*H*), 8.27 (d, *J* = 8.7 Hz, 1H, Ar*H*), 8.32-8.33 (m, 1H, Ar*H*), 8.88 (brs, 1H, CO*NH*), 9.93 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{14}H_{12}N_2O_3$: 256.08, found: 257.14 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(pyridin-4-yl)acetamide (2q): Yield 60%; IR (film, cm^{-1}): 2922, 2851, 1686, 1598, 1531, 1459, 1253, 1162, 1051, 837; ^1H NMR (400 MHz, $CDCl_3$): δ 4.72 (s, 2H, O*CH*$_2$), 7.09-7.11 (m, 2H, Ar*H*), 7.59-7.60 (m, 2H, Ar*H*), 7.88-7.91 (m, 2H, Ar*H*), 8.53-8.54 (m, 2H, Ar*H*), 8.73 (brs, 1H, CO*NH*), 9.92 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{14}H_{12}N_2O_3$: 256.08, found: 257.16 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(4-methylbenzyl)acetamide (2r): Yield 70%; IR (film, cm^{-1}): 2922, 2853, 1692, 1659, 1602, 1580, 1542, 1421, 1355, 1252, 1213, 1162, 1057, 840, 817; ^1H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H, *CH*$_3$), 4.51 (d, *J* = 5.8 Hz, 2H, *CH*$_2$Ph), 4.61 (s, 2H, O*CH*$_2$), 6.86 (brs, 1H, CO*NH*), 7.02 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.14 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.18 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.85 (d, *J* = 8.7 Hz, 2H, Ar*H*), 9.90 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{17}H_{17}NO_3$: 283.12, found: 284.18 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(4-methoxybenzyl)acetamide (2s): Yield 65%; IR (film, cm^{-1}): 2928, 2853, 1676, 1600, 1510, 1303, 1249, 1219, 1162, 1031, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H, O*CH*$_3$), 4.48 (d, *J* = 5.8 Hz, 2H, *CH*$_2$Ph), 4.61 (s, 2H, O*CH*$_2$), 6.78 (brs, 1H, CO*NH*), 6.87 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.02 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.22 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.86 (d, *J* = 8.7 Hz, 2H, Ar*H*), 9.91 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{17}H_{17}NO_4$: 299.11, found: 300.08 $(M + H)^+$.

***N*-Benzyl-2-(4-formylphenoxy)acetamide (2t):** Yield 75%; IR (film, cm^{-1}): 2924, 2851, 1673, 1600, 1548, 1310, 1251, 1162, 1055, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 4.57 (d, *J* = 5.8 Hz, 2H, *CH*$_2$Ph), 4.62 (s, 2H, O*CH*$_2$), 6.86 (brs, 1H, CO*NH*), 7.03 (dd, *J* = 2.2, 6.5 Hz, 2H, Ar*H*), 7.26-7.30 (m, 2H, Ar*H*), 7.31-7.37 (m, 3H, Ar*H*), 7.86 (dd, *J* = 2.2, 6.5 Hz, 2H, Ar*H*), 9.90 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{16}H_{15}NO_3$: 269.10, found: 270.19 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-phenethylacetamide (2u): Yield 75%; IR (film, cm^{-1}): 2922, 2851, 1686, 1600, 1580, 1542, 1508, 1440, 1309, 1252, 1218, 1162, 1053, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 2.85 (t, *J* = 6.5 Hz, 2H, *CH*$_2$Ph), 3.62 (q, *J* = 6.5 Hz, 2H, NH*CH*$_2$), 4.54 (s, 2H, O*CH*$_2$), 6.54 (brs, 1H, CO*NH*), 6.96 (dd, *J* = 2.2, 6.5 Hz, 2H, Ar*H*), 7.14-7.16 (m, 2H, Ar*H*), 7.23-7.25 (m, 1H, Ar*H*), 7.26-7.31 (m, 2H, Ar*H*), 7.86 (dd, *J* = 2.2, 6.5 Hz, 2H, Ar*H*), 9.91 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{17}H_{17}NO_3$: 283.12, found: 284.22 $(M + H)^+$.

2-(4-Formylphenoxy)-*N*-(naphthalen-1-yl)acetamide (2v): Yield 70%; IR (film, cm^{-1}): 2924, 2951, 1686, 1603, 1581, 1507, 1305, 1249, 1218, 1164, 1066, 862; ^1H NMR (400 MHz, $CDCl_3$): δ 4.84 (s, 2H, O*CH*$_2$), 7.19 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.49-7.55 (m, 3H, Ar*H*),

7.75 (d, *J* = 7.3 Hz, 2H, Ar*H*), 7.88-7.91 (m, 1H, Ar*H*), 7.94 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.02 (d, *J* = 7.3 Hz, 1H, Ar*H*), 8.70 (brs, 1H, CO*NH*), 9.95 (s, 1H, *CHO*); ESI-MS (*m/z*) calculated for $C_{19}H_{15}NO_3$: 305.10, found: 305.15 $(M + H)^+$.

Typical procedure for the synthesis of (*E*)-2-(4-((2-isonicotinoylhydrazono)methyl) phenoxy)-*N*-phenylacetamide (3a) and related compounds (3b-3v): A mixture of isoniazid (200 mg, 1.45 mmol) and 2-(4-formylphenoxy)-*N*-phenylacetamide (**2a**, 335 mg, 1.31 mmol) in EtOH/H_2O was stirred at room temperature for 4-6 h. After completion of the reaction, separated solid was filtered and washed with cold EtOH to get the pure compound **3a**.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-phenylacetamide (3a): Yield 85%; mp 229-230 ^oC; IR (KBr, cm^{-1}): 3305, 3245, 3061, 2925, 1676, 1648, 1600, 1547, 1533, 1514, 1445, 1373, 1315, 1300, 1259, 1170, 1060, 966, 825; ^1H NMR (400 MHz, DMSO-d_6): δ 4.77 (s, 2H, O*CH*$_2$), 7.07-7.10 (m, 3H, Ar*H*), 7.29-7.33 (m, 2H, Ar*H*), 7.63 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (dd, *J* = 1.4, 4.4 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.77 (dd, *J* = 1.4, 4.4 Hz, 2H, Ar*H*), 10.12 (s, 1H, CO*NH*), 11.95 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 67.10, 115.14, 119.79, 121.59, 123.80, 127.24, 128.80, 128.96, 138.40, 140.61, 148.85, 150.34, 159.66, 161.54, 166.30; ESI-HRMS (*m/z*) calculated for $C_{21}H_{18}N_4O_3$: 374.1379, found: 375.1686 $(M + H)^+$, 397.1495 $(M + Na)^+$; Anal. calcd. for $C_{21}H_{18}N_4O_3$: C, 67.37; H, 4.85; N, 14.96; O, 12.82, found: C, 67.31; H, 4.79; N, 14.87; O, 12.93.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-*p*-tolylacetamide (3b): Yield 85%; mp 239-241 ^oC; IR (KBr, cm^{-1}): 3376, 3301, 3125, 3057, 1680, 1652, 1556, 1532, 1511, 1449, 1410, 1364, 1284, 1249, 1172, 1054, 958, 818; ^1H NMR (400 MHz, DMSO-d_6): δ 2.24 (s, 3H, *CH*$_3$), 4.75 (s, 2H, O*CH*$_2$), 7.08-7.13 (m, 4H, Ar*H*), 7.51 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.81 (d, *J* = 5.8 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=C*H*), 8.77 (d, *J* = 5.8 Hz, 2H, Ar*H*), 10.02 (s, 1H, CO*NH*), 11.95 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.45, 67.12, 115.13, 119.76, 121.51, 127.18, 128.89, 129.12, 132.71, 135.81, 140.59, 148.78, 150.31, 159.63, 161.44, 165.97; ESI-HRMS (*m/z*) calculated for $C_{22}H_{20}N_4O_3$: 388.1535, found: 389.1840 $(M + H)^+$, 411.2082 $(M + Na)^+$; Anal. calcd. for $C_{22}H_{20}N_4O_3$: C, 68.03; H, 5.19; N, 14.42; O, 12.36, found: C, 68.19; H, 5.33; N, 14.67; O, 12.23.

(*E*)-*N*-(4-Ethylphenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3c): Yield 82%; mp 231-234 ^oC; IR (KBr, cm^{-1}): 3323, 3036, 2962, 2870, 1655, 1609, 1542, 1515, 1420, 1367, 1308, 1254, 1177, 1066, 833, 753; ^1H NMR (400 MHz, DMSO-d_6): δ 1.13 (t,

J = 7.3 Hz, 3H, CH_2CH_3), 2.53 (q, *J* = 7.3 Hz, 2H, CH_2CH_3), 4.75 (s, 2H, OCH_2), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.14 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.53 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.70 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (d, *J* = 5.8 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.76 (d, *J* = 5.8 Hz, 2H, Ar*H*), 10.05 (s, 1H, CO*NH*), 11.96 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.73, 27.67, 67.17, 115.16, 119.93, 121.58, 127.24, 127.97, 128.96, 136.04, 139.26, 140.62, 148.88, 150.33, 159.68, 161.56, 166.06; ESI-HRMS (*m/z*) calculated for $C_{23}H_{22}N_4O_3$: 402.1692, found: 403.1426 $(M + H)^+$, 425.1743 $(M + Na)^+$; Anal. calcd. for $C_{23}H_{22}N_4O_3$: C, 68.64; H, 5.51; N, 13.92; O, 11.93, found: C, 68.73; H, 5.48; N, 13.87; O, 12.01.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(4-isopropylphenyl) acetamide (3d): Yield 85%; mp 209-211 °C; IR (KBr, cm^{-1}): 3431, 3197, 3035, 2956, 1636, 1609, 1546, 1514, 1420, 1307, 1254, 1177, 1089, 1065, 955, 831; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.15 (d, *J* = 7.3 Hz, 6H, $CH(CH_3)_2$), 2.81 (septet, *J* = 6.5 Hz, 1H, $CH(CH_3)_2$), 4.75 (s, 2H, OCH_2), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.17 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.54 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.71 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.81 (d, *J* = 5.1 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.76 (d, *J* = 5.1 Hz, 2H, Ar*H*), 10.06 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ESI-HRMS (*m/z*) calculated for $C_{24}H_{24}N_4O_3$: 416.1848, found: 417.1917 $(M + H)^+$, 418.2331 $(M + Na)^+$; Anal. calcd. for $C_{24}H_{24}N_4O_3$: C, 69.21; H, 5.81; N, 13.45; O, 11.52, found: C, 69.34; H, 5.95; N, 13.33; O, 11.80.

(*E*)-*N*-(2-Fluorophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3e): Yield 72%; mp 245-248 °C; IR (KBr, cm^{-1}): 3413, 3263, 3045, 2907, 1692, 1653, 1607, 1548, 1515, 1483, 1458, 1366, 1297, 1253, 1176, 1064, 968, 838; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.84 (s, 2H, OCH_2), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.17-7.20 (m, 2H, Ar*H*), 7.25-7.30 (m, 1H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.79-7.81 (m, 3H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.76-8.78 (m, 2H, Ar*H*), 9.96 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); Anal. calcd. for $C_{21}H_{17}FN_4O_3$: C, 64.28; H, 4.37; F, 4.84; N, 14.28; O, 12.23, found: C, 64.36; H, 4.46; F, 4.91; N, 14.37; O, 12.33.

(*E*)-*N*-(3-Fluorophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3f): Yield 70%; mp 215-217 °C; IR (KBr, cm^{-1}): 3435, 3214, 3039, 1683, 1654, 1610, 1572, 1549, 1515, 1304, 1256, 1178, 1143, 1066, 956, 864; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.78 (s, 2H, OCH_2), 7.90-7.92 (m, 1H, Ar*H*), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.34-7.39 (m, 2H, Ar*H*), 7.59-7.62 (m, 1H, Ar*H*), 7.70 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.79-7.81 (m, 2H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.76 (dd, *J* = 1.4, 4.4 Hz, 2H, Ar*H*), 10.34 (s, 1H, CO*NH*), 11.96 (s, 1H, CO*NH*);

Anal. calcd. for $C_{21}H_{17}FN_4O_3$: C, 64.28; H, 4.37; F, 4.84; N, 14.28; O, 12.23, found: C, 64.39; H, 4.41; F, 4.88; N, 14.36; O, 12.36.

(*E*)-*N*-(4-Fluorophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3g): Yield 75%; mp 231-234 ^oC; IR (KBr, cm^{-1}): 3456, 3213, 3063, 1696, 1648, 1576, 1507, 1441, 1411, 1386, 1318, 1273, 1259, 1212, 1175, 1071, 968, 839; ^1H NMR (400 MHz, DMSO-d_6): δ 4.77 (s, 2H, OCH_2), 7.09 (d, J = 8.7 Hz, 2H, Ar*H*), 7.14-7.18 (m, 2H, Ar*H*), 7.64-7.67 (m, 2H, Ar*H*), 7.71 (d, J = 8.7 Hz, 2H, Ar*H*), 7.81 (d, J = 5.8 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=C*H*), 8.77 (d, J = 5.8 Hz, 2H, Ar*H*), 10.20 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ESI-HRMS (*m/z*) calculated for $C_{21}H_{17}FN_4O_3$: 392.1285, found: 393.1458 $(M + H)^+$, 415.1294 $(M + Na)^+$; Anal. calcd. for $C_{21}H_{17}FN_4O_3$: C, 64.28; H, 4.37; F, 4.84; N, 14.28; O, 12.23, found: C, 64.34; H, 4.40; F, 4.92; N, 14.41; O, 12.19.

(*E*)-*N*-(2-Chlorophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3h): Yield 75%; mp 242-244 ^oC; IR (KBr, cm^{-1}): 3382, 3212, 3050, 1700, 1668, 1595, 1539, 1511, 1441, 1300, 1253, 1172, 1059, 829, 754; ^1H NMR (400 MHz, DMSO-d_6): δ 4.85 (s, 2H, OCH_2), 7.12 (d, J = 8.7 Hz, 2H, Ar*H*), 7.19-7.23 (m, 1H, Ar*H*), 7.32-7.36 (m, 1H, Ar*H*), 7.50-7.52 (m, 1H, Ar*H*), 7.72 (d, J = 8.7 Hz, 2H, Ar*H*), 7.79-7.81 (m, 3H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.76-8.77 (m, 2H, Ar*H*), 9.71 (s, 1H, CO*NH*), 11.98 (s, 1H, CO*NH*); Anal. calcd. for $C_{21}H_{17}ClN_4O_3$: C, 61.69; H, 4.19; Cl, 8.67; N, 13.70; O, 11.74, found: C, 61.80; H, 4.27; Cl, 8.77; N, 13.93; O, 11.84.

(*E*)-*N*-(3-Chlorophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3i): Yield 85%; mp 160-162 ^oC; IR (KBr, cm^{-1}): 3449, 3370, 3230, 3050, 2926, 1702, 1655, 1598, 1534, 1511, 1424, 1295, 1252, 1174, 1079, 835, 807; ^1H NMR (400 MHz, DMSO-d_6): δ 4.79 (s, 2H, OCH_2), 7.09 (d, J = 8.7 Hz, 2H, Ar*H*), 7.13-7.15 (m, 1H, Ar*H*), 7.35 (t, J = 8.0 Hz, 1H, Ar*H*), 7.52-7.54 (m, 1H, Ar*H*), 7.71 (d, J = 8.7 Hz, 2H, Ar*H*), 7.80 (d, J = 6.5 Hz, 2H, Ar*H*), 7.83-7.84 (m, 1H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.77 (dd, J = 1.4, 4.0 Hz, 2H, Ar*H*), 10.33 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 67.04, 115.16, 118.12, 119.21, 121.56, 123.49, 127.29, 128.94, 130.49, 133.11, 139.82, 140.60, 148.79, 150.33, 159.54, 161.50, 166.73; Anal. calcd. for $C_{21}H_{17}ClN_4O_3$: C, 61.69; H, 4.19; Cl, 8.67; N, 13.70; O, 11.74, found: C, 61.82; H, 4.24; Cl, 8.81; N, 13.89; O, 11.77.

(*E*)-*N*-(4-Chlorophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3j): Yield 90%; mp 244-246 ^oC; IR (KBr, cm^{-1}): 3463, 3200, 2994, 2849, 1674, 1592, 1511, 1527, 1493, 1443, 1401, 1306, 1240, 1173, 1067, 825; ^1H NMR (400 MHz, DMSO-d_6): δ

4.78 (s, 2H, O*CH*$_2$), 7.09 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.38 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.68 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.81 (d, *J* = 6.5 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.77 (dd, *J* = 1.4, 4.4 Hz, 2H, Ar*H*), 10.28 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ESI-HRMS (*m/z*) calculated for $C_{21}H_{17}ClN_4O_3$: 408.0989, found: 409.1182 $(M + H)^+$, 411.1345 $(M + 2)^+$, 431.1845 $(M + Na)^+$; Anal. calcd. for $C_{21}H_{17}ClN_4O_3$: C, 61.69; H, 4.19; Cl, 8.67; N, 13.70; O, 11.74, found: C, 61.85; H, 4.20; Cl, 8.72; N, 13.88; O, 11.96.

(*E*)-*N*-(2-Bromophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3k): Yield 75%; mp 231-234 ^oC; IR (KBr, cm^{-1}): 3470, 3363, 3211, 3048, 1700, 1669, 1595, 1578, 1536, 1511, 1438, 1366, 1300, 1249, 1171, 1059, 968, 830; ^1H NMR (400 MHz, DMSO-d_6): δ 4.84 (s, 2H, O*CH*$_2$), 7.13-7.15 (m, 3H, Ar*H*), 7.37-7.41 (m, 1H, Ar*H*), 7.65-7.69 (m, 1H, Ar*H*), 7.67 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.73 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80-7.82 (m, 3H, Ar*H*), 8.41 (s, 1H, N=*CH*), 8.76-8.78 (m, 2H, Ar*H*), 9.65 (s, 1H, CO*NH*), 11.99 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.97, 115.27, 117.26, 121.53, 123.17, 125.74, 127.14, 127.48, 128.28, 128.95, 132.69, 135.37, 140.58, 148.70, 149.54, 150.32, 159.17, 161.48, 166.51; ESI-HRMS (*m/z*) calculated for $C_{21}H_{17}BrN_4O_3$: 452.0484, found: 453.0821 $(M + H)^+$, 455.1809 $(M + 2)^+$; Anal. calcd. for $C_{21}H_{17}BrN_4O_3$: C, 55.64; H, 3.78; Br, 17.63; N, 12.36; O, 10.59, found: C, 55.81; H, 3.85; Br, 17.77; N, 12.42; O, 10.66.

(*E*)-*N*-(3-Bromophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3l): Yield 85%; mp 166-168 ^oC; IR (KBr, cm^{-1}): 3448, 3369, 3228, 3054, 2900, 1705, 1607, 1553, 1531, 1511, 1423, 1295, 1249, 1173, 1082, 995, 835, 806; ^1H NMR (400 MHz, DMSO-d_6): δ 4.79 (s, 2H, O*CH*$_2$), 7.09 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.26-7.29 (m, 2H, Ar*H*), 7.56-7.59 (m, 1H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (d, *J* = 6.5 Hz, 2H, Ar*H*), 7.98 (s, 1H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.77 (dd, *J* = 1.4, 4.3 Hz, 2H, Ar*H*), 10.31 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 67.06, 115.16, 118.53, 121.58, 122.12, 126.41, 127.31, 128.96, 130.77, 139.95, 140.60, 148.84, 150.32, 159.54, 161.54, 166.72; Anal. calcd. for $C_{21}H_{17}BrN_4O_3$: C, 55.64; H, 3.78; Br, 17.63; N, 12.36; O, 10.59, found: C, 55.71; H, 3.91; Br, 17.86; N, 12.50; O, 10.74.

(*E*)-*N*-(4-Bromophenyl)-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3m): Yield 88%; mp 246-249 ^oC; IR (KBr, cm^{-1}): 3459, 3324, 3199, 2995, 2849, 1671, 1598, 1525, 1511, 1489, 1443, 1397, 1305, 1241, 1173, 1067, 1008, 821; ^1H NMR (400 MHz, DMSO-d_6): δ 4.77 (s, 2H, O*CH*$_2$), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.50 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.62 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.70 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (d, *J* = 5.8 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=C*H*), 8.76 (d, *J* = 5.8 Hz, 2H, Ar*H*), 10.28 (s, 1H, CO*NH*), 11.97 (s, 1H,

CO*NH*); ESI-HRMS (*m/z*) calculated for $C_{21}H_{17}BrN_4O_3$: 452.0484, found: 453.0583 $(M + H)^+$, 455.1146 $(M + 2)^+$; Anal. calcd. for $C_{21}H_{17}BrN_4O_3$: C, 55.64; H, 3.78; Br, 17.63; N, 12.36; O, 10.59, found: C, 55.75; H, 3.93; Br, 17.82; N, 12.55; O, 10.70.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(4-methoxyphenyl)acetamide (3n): Yield 80%; mp 243-245 ^oC; IR (KBr, cm^{-1}): 3438, 3388, 3236, 3055, 2924, 1662, 1596, 1546, 1511, 1448, 1369, 1239, 1175, 1060, 1021, 830; ^1H NMR (400 MHz, DMSO-d_6): δ 3.71 (s, 3H, O*CH*$_3$), 4.73 (s, 2H, O*CH*$_2$), 6.89 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.09 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.53 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (d, *J* = 5.8 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.77 (d, *J* = 5.8 Hz, 2H, Ar*H*), 10.00 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 55.22, 67.13, 113.90, 115.19, 121.44, 121.59, 127.21, 128.96, 131.42, 140.63, 148.82, 150.37, 155.61, 159.67, 161.51, 165.81; ESI-HRMS (*m/z*) calculated for $C_{22}H_{20}N_4O_4$: 404.1485, found: 405.1537 $(M + H)^+$, 427.1346 $(M + Na)^+$; Anal. calcd. for $C_{22}H_{20}N_4O_4$: C, 65.34; H, 4.98; N, 13.85; O, 15.82, found: C, 65.52; H, 5.14; N, 13.77; O, 16.02.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(4-nitrophenyl)acetamide (3o): Yield 85%; mp 255-258 ^oC; IR (KBr, cm^{-1}): 3447, 3195, 2920, 2834, 1690, 1660, 1597, 1537, 1512, 1440, 1408, 1332, 1302, 1236, 1173, 1111, 1065, 855, 836, 751; ^1H NMR (400 MHz, DMSO-d_6): δ 4.86 (s, 2H, O*CH*$_2$), 7.09 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.71 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (d, *J* = 5.8 Hz, 2H, Ar*H*), 7.90 (d, *J* = 9.5 Hz, 2H, Ar*H*), 8.23 (d, *J* = 9.5 Hz, 2H, Ar*H*), 8.40 (s, 1H, N=C*H*), 8.76 (d, *J* = 5.8 Hz, 2H, Ar*H*), 10.75 (s, 1H, CO*NH*), 11.97 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 67.03, 115.13, 119.34, 121.56, 124.97, 127.34, 128.95, 140.58, 142.55, 144.59, 148.78, 150.32, 159.52, 161.51, 167.33; Anal. calcd. for $C_{21}H_{17}N_5O_5$: C, 60.14; H, 4.09; N, 16.70; O, 19.07, found: C, 60.29; H, 4.34; N, 16.88; O, 19.27.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(pyridin-2-yl)acetamide (3p): Yield 85%; mp 215-217 ^oC; IR (KBr, cm^{-1}): 3385, 3207, 3051, 2945, 1690, 1657, 1604, 1577, 1529, 1433, 1407, 1300, 1254, 1173, 1063, 995, 832; ^1H NMR (400 MHz, DMSO-d_6): δ 4.87 (s, 2H, O*CH*$_2$), 7.05 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.10-7.13 (m, 1H, Ar*H*), 7.69 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.76-7.78 (m, 1H, Ar*H*), 7.79-7.81 (m, 2H, Ar*H*), 8.04 (d, *J* = 7.3 Hz, 1H, Ar*H*), 8.32-8.33 (m, 1H, Ar*H*), 8.40 (s, 1H, N=*CH*), 8.75-8.77(m, 2H, Ar*H*), 10.57 (s, 1H, CO*NH*), 11.95 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.70, 113.73, 115.05, 119.90, 121.63, 123.28, 127.22, 129.02, 138.44, 140.65, 148.17, 148.89, 149.61, 150.37, 151.41, 159.72, 161.58, 167.08; ESI-HRMS (*m/z*) calculated for $C_{20}H_{17}N_5O_3$: 375.1331,

found: 376.1203 $(M + H)^+$, 398.1660 $(M + Na)^+$; Anal. calcd. for $C_{20}H_{17}N_5O_3$: C, 63.99; H, 4.56; N, 18.66; O, 12.79, found: C, 64.11; H, 4.72; N, 18.78; O, 12.85.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(pyridin-4-yl)acetamide (3q): Yield 80%; mp 189-192 ^oC; IR (KBr, cm^{-1}): 3402, 3259, 3187, 3099, 3045, 1718, 1654, 1594, 1549, 1528, 1511, 1421, 1297, 1256, 1203, 1170, 1079, 838, 750; ^1H NMR (400 MHz, DMSO-d_6): δ 4.83 (s, 2H, OCH_2), 6.62 (d, J = 6.5 Hz, 2H, ArH), 7.07 (d, J = 8.7 Hz, 2H, ArH), 7.70 (d, J = 8.7 Hz, 2H, ArH), 7.80 (d, J = 5.8 Hz, 2H, ArH), 8.40 (s, 1H, N=CH), 8.44 (d, J = 5.8 Hz, 2H, ArH), 8.76 (d, J = 6.5 Hz, 2H, ArH), 10.53 (s, 1H, CONH), 11.97 (s, 1H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.99, 113.58, 115.12, 121.53, 127.31, 128.93, 140.59, 145.06, 148.77, 150.32, 150.45, 159.51, 161.49, 167.56; Anal. calcd. for $C_{20}H_{17}N_5O_3$: C, 63.99; H, 4.56; N, 18.66; O, 12.79, found: C, 64.15; H, 4.74; N, 18.80; O, 12.67.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(4-methylbenzyl)acetamide (3r): Yield 85%; mp 216-218 ^oC; IR (KBr, cm^{-1}): 3268, 2922, 1656, 1605, 1542, 1510, 1287, 1257, 1172, 1059, 838, 790; ^1H NMR (400 MHz, DMSO-d_6): δ 2.25 (s, 3H, CH_3), 4.29 (d, J = 5.86 Hz, 2H, CH_2Ph), 4.61 (s, 2H, OCH_2), 7.05 (d, J = 8.7 Hz, 2H, ArH), 7.10 (d, J = 8.0 Hz, 2H, ArH), 7.13 (d, J = 8.0 Hz, 2H, ArH), 7.70 (d, J = 8.7 Hz, 2H, ArH), 7.81 (dd, J = 1.4, 4.4 Hz, 2H, ArH), 8.40 (s, 1H, N=CH), 8.66 (t, J = 5.8 Hz, 1H, CO$NH$$CH_2$), 8.76-8.78 (m, 2H, Ar$H$), 11.95 (s, 1H, CO$NH$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.65, 41.58, 66.96, 115.18, 121.51, 127.23, 128.78, 128.84, 135.83, 136.20, 140.58, 148.76, 150.31, 159.49, 161.44, 167.37; ESI-HRMS (*m/z*) calculated for $C_{23}H_{22}N_4O_3$: 402.1692, found: 403.1410 $(M + H)^+$, 425.1716 $(M + Na)^+$; Anal. calcd. for $C_{23}H_{22}N_4O_3$: C, 68.64; H, 5.51; N, 13.92; O, 11.93, found: C, 68.81; H, 5.64; N, 13.81; O, 12.03.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(4-methoxybenzyl)acetamide (3s): Yield 70%; mp 201-203 ^oC; IR (KBr, cm^{-1}): 3368, 3260, 2933, 1654, 1530, 1298, 1241, 1177, 1112, 1066, 808; ^1H NMR (400 MHz, DMSO-d_6): δ 3.71 (s, 3H, OCH_3), 4.27 (d, J = 5.8 Hz, 2H, CH_2Ph), 4.60 (s, 2H, OCH_2), 6.85 (d, J = 8.7 Hz, 2H, ArH), 7.05 (d, J = 8.7 Hz, 2H, ArH), 7.17 (d, J = 8.7 Hz, 2H, ArH), 7.70 (d, J = 8.7 Hz, 2H, ArH), 7.80-7.81 (m, 2H, ArH), 8.40 (s, 1H, N=CH), 8.63 (t, J = 5.8 Hz, 1H, CO$NH$$CH_2$), 8.76-8.78 (m, 2H, Ar$H$), 11.97 (s, 1H, CO$NH$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 41.30, 55.05, 66.96, 113.64, 115.19, 121.52, 127.19, 128.63, 128.85, 131.21, 140.59, 148.75, 150.32, 158.22, 159.49, 161.44, 167.30; ESI-HRMS (*m/z*) calculated for $C_{23}H_{22}N_4O_4$: 418.1641, found: 419.1514 $(M + H)^+$, 441.1928 $(M + Na)^+$; Anal. calcd. for $C_{23}H_{22}N_4O_4$: C, 66.02; H, 5.30; N, 13.39; O, 15.29, found: C, 66.21; H, 5.16; N, 13.45; O, 15.36.

(*E*)-*N*-Benzyl-2-(4-((2-isonicotinoylhydrazono)methyl)phenoxy)acetamide (3t): Yield 80%; mp 225-228 ^{o}C; IR (KBr, cm^{-1}): 3235, 3201, 3034, 2933, 2861, 1651, 1596, 1569, 1507, 1444, 1368, 1313, 1252, 1225, 1170, 1081, 994, 828; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.35 (d, *J* = 5.8 Hz, 2H, *CH*$_2$Ph), 4.63 (s, 2H, O*CH*$_2$), 7.07 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.20-7.31 (m, 5H, Ar*H*), 7.70 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.82 (dd, *J* = 1.4, 4.4 Hz, 2H, Ar*H*), 8.41 (s, 1H, N=*CH*), 8.71 (t, *J* = 5.8 Hz, 1H, CON*H*CH$_2$), 8.78 (dd, *J* = 1.4, 4.4 Hz, 2H, Ar*H*), 11.97 (s, 1H, CO*NH*); Anal. calcd. for $C_{22}H_{20}N_4O_3$: C, 68.03; H, 5.19; N, 14.42; O, 12.36, found: C, 68.15; H, 5.22; N, 14.36; O, 12.52.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-phenethylacetamide (3u): Yield 75%; mp 196-198 ^{o}C; IR (KBr, cm^{-1}): 3474, 3236, 3069, 3046, 2906, 1646, 1603, 1552, 1513, 1434, 1369, 1300, 1258, 1171, 1072, 920, 836; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.74 (t, *J* = 7.3 Hz, 2H, NHCH$_2$*CH*$_2$Ph), 3.37 (t, *J* = 7.3 Hz, 2H, NH*CH*$_2$CH$_2$Ph), 4.52 (s, 2H, O*CH*$_2$), 7.01 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.15-7.20 (m, 3H, Ar*H*), 7.26 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.69 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.80 (d, *J* = 6.5 Hz, 2H, Ar*H*), 8.20 (t, *J* = 5.8 Hz, 1H, CO*NH*CH$_2$), 8.40 (s, 1H, N=*CH*), 8.76 (d, *J* = 6.5 Hz, 2H, Ar*H*), 11.95 (s, 1H, CO*NH*); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.10, 40.11, 66.96, 115.15, 121.52, 126.13, 127.19, 128.35, 128.63, 128.87, 139.28, 140.59, 148.76, 150.32, 159.49, 161.45, 167.26; ESI-HRMS (*m/z*) calculated for $C_{23}H_{22}N_4O_3$: 402.1692, found: 403.1733 $(M + H)^+$, 425.2031 $(M + Na)^+$; Anal. calcd. for $C_{23}H_{22}N_4O_3$: C, 68.64; H, 5.51; N, 13.92; O, 11.93, found: C, 68.71; H, 5.47; N, 13.96; O, 12.07.

(*E*)-2-(4-((2-Isonicotinoylhydrazono)methyl)phenoxy)-*N*-(naphthalen-1-yl)acetamide (3v): Yield 75%; mp 250-252 ^{o}C; IR (KBr, cm^{-1}): 3431, 3255, 3046, 2928, 1670, 1605, 1550, 1513, 1277, 1241, 1213, 1175, 1065, 962, 833, 799, 774; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.95 (s, 2H, O*CH*$_2$), 7.18 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.51-7.55 (m, 3H, Ar*H*), 7.65-7.67 (m, 1H, Ar*H*), 7.76 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.79-7.83 (m, 3H, Ar*H*), 7.93-7.96 (m, 1H, Ar*H*), 7.98-8.01 (m, 1H, Ar*H*), 8.43 (s, 1H, N=C*H*), 8.77-8.79 (m, 2H, Ar*H*), 10.21 (s, 1H, CO*NH*), 11.98 (s, 1H, CO*NH*); Anal. calcd. for $C_{25}H_{20}N_4O_3$: C, 70.74; H, 4.75; N, 13.20; O, 11.31, found: C, 70.88; H, 4.69; N, 13.27; O, 11.43.