Supplemental Information

Synthesis and Insecticidal Activities of Tetrahydroimidazo[1,2-a]pyridinone: Further Exploration on *cis*-Neonicotinoids

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Experimental

Instrumentation and Chemicals. Melting points (mp) were recorded on Büchi B540 apparatus (Büchi Labortechnik AG, Flawil, Switzerland) and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AM-400 (400 MHz) spectrometer with DMSO-d_6 as the solvent and TMS as the internal standard. Chemical shifts are reported in δ (parts per million) values. High-resolution mass spectra were recorded under electron impact (70 eV) condition using a MicroMass GCT CA 055 instrument. Analytical thin-layer chromatography (TLC) was carried out on precoated plates (silica gel 60 F254), and spots were visualized with ultraviolet (UV) light.

Synthesis. Unless otherwise noted, reagents and solvents were used as received from commercial suppliers. Yields were not optimized. All reactions were carried out under a protective atmosphere of drying nitrogen or utilizing a calcium chloride tube.

General Synthetic Procedure for compound 10

A mixture of compound 6-Cl-PMNI (10 mmol), itaconic anhydride (10 mmol) and acetonitrile was refluxed until the reaction was completed, the product was precipitated. The precipitate was filtered, washed with acetonitrile and recrystalized from acetonitrile to give the corresponding product.

General Synthetic Procedure for compound *11a–d*.

A mixture of compound **10**（1.5mmol）and corresponding alcohol（12ml）was stirred at room temperature for 10 minutes,then $SOCl_2$ was dropped into and the reaction liquid was stirred at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction,the organic solvent was extracted thoroughly with CH_2Cl_2,washed with water,and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by flash chromatography eluting with dichloromethane/acetone (v/v 4:1) to afford target

products ***11a–d.***

General Synthetic Procedure for compound *12a–y*.

A mixture of compound **10** (1.5 mmol), corresponding anime (2.25 mmol), EDC·HCl (1.8 mmol) DMAP (0.15 mmol) and pyridine (10 ml) was stirred at room temperature for 10 minutes. Acetonitrile (20 ml) was added and the mixture was stirred at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure. The residue was purified by flash chromatography eluting with dichloromethane/acetone (v/v 10:1) to afford target products ***12a–y.***

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetic acid **10:** yield, 79%; yellow powder; mp = 225.0–225.7 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 12.35 (s, 1H), 8.41 (d, J = 2.4 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.98–3.66 (m, 4H), 3.25 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 2.95–2.98 (m, 1H), 2.73–2.60 (m, 2H), 2.55 (dd, J_1 = 7.2 Hz, J_2 = 15.6 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 173.0, 170.3, 153.3, 149.8, 149.7, 139.7, 131.7, 124.4, 104.6, 52.0, 50.7, 42.0, 38.0, 34.1, 28.3 ppm; HRMS (ES+) calcd for $C_{15}H_{15}N_4O_5{}^{35}Cl$ $(M+H)^+$, 366.0731; found, 366.0728. calcd for $C_{15}H_{15}N_4O_5{}^{37}Cl$ $(M+H)^+$, 368.0701; found, 368.0721.

Methyl

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetate **11a:** yield, 47%; yellow powder; mp = 171.9–172.4 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.40 (d, J = 2.4 Hz, 1H), 7.86 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.92–3.75 (m, 4H), 3.62 (s, 3H), 3.25 (dd, J_1 = 6.4 Hz, J_2

= 14.4 Hz, 1H), 3.07–2.99 (m, 1H), 2.76 (dd, J_1 = 5.6 Hz, J_2 = 16.8 Hz, 1H), 2.67–2.51 (m, 2H), ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 172.1, 170.1, 153.2, 149.8, 149.6, 139.7, 131.6, 124.4, 104.6, 55.3, 52.0, 50.7, 41.9, 37.9, 33.9, 28.3 ppm; HRMS (ES+) calcd for $C_{16}H_{17}N_4O_5{}^{35}Cl$ $(M+H)^+$, 380.0887; found, 380.0886. calcd for $C_{16}H_{17}N_4O_5{}^{37}Cl$ $(M+H)^+$, 382.0858; found, 382.0866.

ethyl

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetate **11b:** yield, 32%; yellow powder; mp = 136.2–136.6 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.41 (d, J = 2.0 Hz, 1H), 7.88 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 4.10 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 4.09 (d, J = 7.2 Hz, 2H), 3.93–3.76 (m, 4H), 3.26 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.05–3.01 (m, 1H), 2.74 (dd, J_1 = 5.2 Hz, J_2 = 16.4 Hz, 1H), 2.68–2.54 (m, 2H), 1.19 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 171.6, 170.1, 153.2, 149.8, 149.6, 139.6, 131.6, 124.4, 104.6, 60.61, 52.1, 50.7, 41.9, 37.9, 34.1, 28.3, 14.49 ppm; HRMS (ES+) calcd for $C_{17}H_{19}N_4O_5{}^{35}Cl$ $(M+H)^+$, 394.1004; found, 394.1011. calcd for $C_{17}H_{19}N_4O_5{}^{37}Cl$ $(M+H)^+$, 396.1014; found, 396.1018.

propyl

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetate **11c:** yield, 44%; yellow powder; mp = 111.0–111.3 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.40 (d, J = 1.6 Hz, 1H), 7.86 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 4.04–3.95 (m, 2H), 3.92–3.78 (m, 4H), 3.26 (dd, J_1 = 4.8 Hz, J_2 = 14.8 Hz, 1H), 3.06–2.98 (m, 1H), 2.75 (dd, J_1 = 5.6 Hz, J_2 = 16.4 Hz, 1H), 2.67–2.56 (m, 2H), 1.61–1.54 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 171.65, 170.11, 153.22, 149.80, 149.63, 139.66, 131.64, 124.41, 104.53, 66.08, 52.04, 50.74, 41.93, 37.91,

34.08, 28.26, 21.95, 10.71 ppm; HRMS (ES+) calcd for $C_{18}H_{21}N_4O_5{}^{35}Cl$ $(M+H)^+$, 408.1200; found, 408.1205. calcd for $C_{18}H_{21}N_4O_5{}^{37}Cl$ $(M+H)^+$, 410.1271; found, 401.1176

isopropyl

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetate **11d:** yield, 52%; yellow powder; mp = 138.1–140.1 °C; ^{1}H NMR (400 Mz, $CDCl_3$): δ 8.35 (d, J = 2.0 Hz, 1H), 7.79 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 5.08–5.00 (m, 1H), 4.97 (d, J = 15.2 Hz, 1H), 4.73 (d, J = 15.2 Hz, 1H), 4.10–4.03 (m, 1H), 3.93–3.86 (m, 1H), 3.81–3.74 (m, 1H), 3.69–3.62 (m, 1H), 3,44 (dd, J_1 = 6.8 Hz, J_2 = 15.2 Hz, 1H), 3.11–3.03 (m, 1H), 2.83–2.76 (m, 2H), 2.63 (dd, J_1 = 6.4 Hz, J_2 = 17.2 Hz, 1H), 1.26–1.24 (m, 6H) ppm; ^{13}C NMR (100 Mz, $CDCl_3$): δ 170.6, 169.8, 151.9, 151.6, 149.2, 138.9, 129.6, 124.7, 105.4, 68.6, 52.3, 50.0, 41.4, 37.9, 34.5, 28.3, 21.8, 21.8 ppm; HRMS (ES+) calcd for $C_{18}H_{21}N_4O_5{}^{35}Cl$ $(M+H)^+$, 408.1200; found, 408.1202. calcd for $C_{18}H_{21}N_4O_5{}^{37}Cl$ $(M+H)^+$, 410.1171; found, 401.1161.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N,N-diethylacetamide **12a:** yield, 63%; yellow powder; mp = 162.7–163.2 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 9.94 (s, 1H), 8.41 (s, 1H)), 7.87 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.93–3.75 (m, 4H), 3.27 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.10–3.05 (m, 1H), 2.85 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.67 (t, J = 8.0 Hz, 1H), 2.54 (dd, J_1 = 7.6 Hz, J_2 = 16.0 Hz, 1H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.9, 169.1, 153.4, 149.8, 149.6, 139.7, 131. 7, 124.4, 104.6, 52.0, 50.7, 41.9, 41.7, 40.1, 38.1, 32.6, 28.5, 14.55, 13.5 ppm; HRMS (EI+) calcd for $C_{19}H_{24}N_5O_4{}^{35}Cl$, 421.1489; found, 421.1495. calcd for $C_{19}H_{24}N_5O_4{}^{37}Cl$, 423.1460; found, 423.1476.

1-((6-chloropyridin-3-yl)methyl)-8-nitro-6-(2-oxo-2-(piperidin-1-yl)ethyl)-2,3,6,7-tetrahydroimida zo[1,2-a]pyridin-5(1H)-one **12b:** yield, 47%; yellow powder; mp = 98.2–99.0 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.41 (d, J = 2.0 Hz,1H)), 7.87 (dd, J_1 = 2.8 Hz, J_2 = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 4.88 (d, J = 16.0 Hz, 1H), 4.78 (d, J = 16.0 Hz, 1H), 3.95–3.75 (m, 4H), 3.48–3.39 (m, 4H), 3.19 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 3.05–2.97 (m, 1H), 2.80 (dd, J_1 = 3.6 Hz, J_2 = 16.4 Hz, 1H), 2.66–2.55 (m, 2H), 1.61–1.54 (m, 2H), 1.54–1.45 (m, 2H), 1.45–1.37 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.9, 168.3, 153,4, 149.8, 149.6, 139.7, 131.7, 124.4, 104.6, 52.0, 50.7, 46.3, 42.6, 41.9, 38.0, 32.7, 28.6, 26.4, 25.8, 24.5 ppm; HRMS (EI+) calcd for $C_{20}H_{24}N_5O_4{}^{35}Cl$, 433.1489; found, 433.1483. calcd for $C_{20}H_{24}N_5O_4{}^{37}Cl$, 435.1460; found, 435.1482.

N-butyl-2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]py ridin-6-yl)acetamide **12c:** yield, 68%; yellow powder; mp = 190.4–190.9 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.41 (d, J = 2.0 Hz, 1H)), 7.87 (dd, J_1 = 2.8 Hz, J_2 = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 4.88 (d, J = 16.0 Hz, 1H), 4.78 (d, J = 16.0 Hz, 1H), 3.95–3.75 (m, 4H), 3.48–3.39 (m, 4H), 3.19 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 3.05–2.97 (m, 1H), 2.80 (dd, J_1 = 3.6 Hz, J_2 = 16.4 Hz, 1H), 2.66–2.55 (m, 2H), 1.61–1.54 (m, 2H), 1.54–1.45 (m, 2H), 1.45–1.37 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 170.0, 153.3, 149.8, 149.6, 139.65, 131.7, 124.4, 104.6, 52.0, 50. 7, 41.9, 38.7, 38.2, 35.6, 31.7, 28.4, 20.0, 14.1 ppm; HRMS (EI+) calcd for $C_{19}H_{24}N_5O_4{}^{35}Cl$, 421.1489; found, 421.1482. calcd for $C_{19}H_{24}N_5O_4{}^{37}Cl$, 423.1460; found, 423.1466.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-phenylacetamide **12d:** yield, 88%; yellow powder; mp = 188.1–189.1 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.03 (s, 1H), 8.41 (d, J = 2.0 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.58 (d, J = 7.6 Hz, 2H), 7.53 (d, J = 8.4 Hz, 1H), 7.30 (t, J = 7.6 Hz, 2H), 7.04 (t, J = 7.2 Hz, 1H), 4.89 (d, J

= 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.97–3.73 (m, 4H), 3.29–3.25 (m, 1H), 3.13–3.06 (m, 1H), 2.87 (dd, J_1 = 4.8 Hz, J_2 = 15.6 Hz, 1H), 2.68 (dd, J_1 = 12.8 Hz, J_2 = 14.8 Hz, 1H), 2.55 (dd, J_1 = 7.6 Hz, J_2 = 16.0 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 169.4, 153.3, 149.8, 149.7, 139.7, 139.6, 131.7, 129.2, 124.4, 123.6, 119.6, 104.7, 52.0, 50.7, 42.0, 38.0, 36.5, 28.6 ppm; HRMS (EI+) calcd for $C_{21}H_{20}N_5O_4{}^{35}Cl$, 441.1204; found, 441.1233. calcd for $C_{21}H_{20}N_5O_4{}^{37}Cl$, 441.1204; found, 441.1233.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(4-fluorophenyl)acetamide **12e:** yield, 80%; yellow powder; mp = 149.5–150.4 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.1 (s, 1H), 8.42 (d, J = 2.4 Hz, 1H), 7.88 (dd, J_1 = 2.4 Hz, J_2 = 8.0 Hz, 1H), 7.60 (m, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 9.2 Hz, 2H), 4.90 (d, J = 16.0 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 3.95–3.77 (m, 4H), 3.29–3.25 (m, 1H), 3.28 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 3.14–3.06 (m, 1H), 2.86 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.68 (dd, J_1 = 12.4 Hz, J_2 = 14.4 Hz, 1H), 2.55 (dd, J_1 = 7.2 Hz, J_2 = 15.6 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 169.4, 158.9, 158.4 (d, $^{1'}J_{CF}$ = 238.2 Hz), 153.4, 149.7, 139.6, 136.0 (d, $^{4'}J_{CF}$ = 2.3 Hz), 131.6, 124.4, 121.3 (d, $^{3'}J_{CF}$ = 7.6 Hz), 115.6 (d, $^{2'}J_{CF}$ = 22.0 Hz), 104.6, 52.1, 50.7, 42.0, 38.1, 36.5, 28.6 ppm; HRMS (EI+) calcd for $C_{21}H_{19}N_5O_4F^{35}Cl$, 459.1110; found, 459.1116. calcd for $C_{21}H_{19}N_5O_4F^{37}Cl$, 461.1080; found, 461.1090.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(2-methyl-4-(perfluoropropan-2-yl)phenyl)acetamide **12f:** yield, 36 %; yellow powder; mp = 100.2–100.6 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 9.60 (s, 1H), 8.41 (d, J = 2.4 Hz, 1H) ,7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.58 (d, J = 7.6 Hz, 2H), 7.53 (d, J = 8.4 Hz, 1H), 7.30 (t, J = 7.6 Hz, 2H), 7.04 (t, J = 7.2 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.97–3.73 (m, 4H),

3.30–3.27 (m, 1H), 3.15–3.07 (m, 1H), 2.95 (dd, J_1 = 5.2 Hz, J_2 = 15.6 Hz, 1H), 2.74–2.62 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 169.9, 153.3, 149.8, 149.7, 140.0, 139.7, 132.6, 131.7, 127.5 (d, $^{3'}J_{CF}$ = 10.0 Hz), 125.4, 124.4, 123.7 (d, $^{3'}J_{CF}$ = 10.0 Hz), 122.3, 121.2, 104.6, 52.0, 50.7, 42.0, 38.2, 36.1, 31.1, 30.0, 28.6, 18.4 ppm; HRMS (EI+) calcd for $C_{25}H_{21}N_5O_4F_7{}^{35}Cl$, 623.1170; found, 623.1183. calcd for $C_{21}H_{19}N_5O_4F^{37}Cl$, 625.1141; found, 625.1132.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(2,3-difluorophenyl)acetamide **12g:** yield, 28%; yellow powder; mp = 162.8–163.3 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.1 (s, 1H), 8.41 (d, J = 2.4 Hz, 1H), 7.87 (dd, J_1 = 2.8 Hz, J_2 = 8.4 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.22–7.13 (m, 2H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.94–3.76 (m, 4H), 3.30–3.25 (m, 1H), 3.14–3.06 (m, 1H), 2.95 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.71–2.62 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.4, 170.0, 153.3, 150.5 (dd, $^{1'}J_{CF}$ = 250.0 Hz, $^{2''}J_{CF}$ = 11.0 Hz), 149.8, 149.7, 141.3, 139.7, 131.7, 128.4 (m, 1C), 124.3 (m, 1C), 124.4, 120.0, 113.0, 104.7, 52.0, 50.7, 42.0, 38.0, 36.5, 28.5 ppm; HRMS (ES+) calcd for $C_{21}H_{19}N_5O_4F_2{}^{35}Cl$ $(M+H)^+$, 478.1094; found, 478.1077. calcd for $C_{21}H_{19}N_5O_4F_2{}^{37}Cl$ $(M+H)^+$, 480.1064; found, 480.1054.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(2,4,5-trifluorophenyl)acetamide **12h:** yield, 25%; yellow powder; mp = 181.8–182.5 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.10 (s, 1H), 8.41 (d, J = 2.0 Hz, 1H), 8.06–7.98 (m, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.67–7.60 (m, 1H), 7.52 (d, J = 8.0 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.94–3.73 (m, 4H), 3.27 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.13–3.05 (m, 1H), 2.94 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.70–2.62 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.4, 170.3, 153.3, 149.8, 149.7, 146.7 (m, 1C), 144.4 (m, 1C), 139.7, 131.7, 124.4,

123.3 (m, 1C), 112.3 (m, 1C), 106.5, 106.3 (m, 1C), 104.6, 52.0, 50.7, 42.0, 38.0, 36.0, 28.5 ppm; HRMS (ES+) calcd for $C_{21}H_{17}N_5O_4F_3{}^{35}Cl$ $(M+H)^+$, 496.0999; found, 496.0988. calcd for $C_{21}H_{17}N_5O_4F_3{}^{37}Cl$ $(M+H)^+$, 498.0970; found, 498.0959.

N-(3-chloro-4-fluorophenyl)-2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetamide **12i:** yield, 37%; yellow powder; mp = 222.8–223.7 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.30 (s, 1H), 8.41 (d, J = 2.0 Hz, 1H) , 7.92 (dd, J_1 = 2.4 Hz, J_2 = 6.8 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.47–7.43 (m, 1H), 7.36 (t, J = 8.8 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 3.90–3.78 (m, 4H), 3.28 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.14–3.06 (m, 1H), 2.86 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.68 (dd, J_1 = 12.8 Hz, J_2 = 14.4 Hz, 1H), 2.60–2.58 (m, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 169.8, 153.5 (d, $^{1'}J_{CF}$ = 234.6 Hz), 153.3, 149.8, 149.7, 139.7, 136.8(d, $^{4'}J_{CF}$ = 3.0 Hz), 131.6, 124.4, 120.9, 119.7 (d, $^{3'}J_{CF}$ = 6.8 Hz), 119.5 (d, $^{2'}J_{CF}$ = 18.1 Hz), 117.3 (d, $^{2'}J_{CF}$ = 21.5 Hz), 104.6, 52.0, 50.7, 42.0, 38.0, 36.4, 28.5 ppm; HRMS (EI+) calcd for $C_{21}H_{18}N_5O_4F^{35}Cl_2$, 493.0720; found, 493.0723. calcd for $C_{21}H_{18}N_5O_4F^{35}Cl^{37}Cl$, 495.0690; found, 495.0712. calcd for $C_{21}H_{18}N_5O_4F^{35}Cl_2$, 497.0661; found, 497.0669.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(4-nitrophenyl)acetamide **12j:** yield, 21%; yellow powder; mp = 135.3–136.4 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.70 (s, 1H), 8.41 (d, J = 2.0 Hz, 1H) ,8.22 (d, J = 9.2 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.83 (d, J = 9.2 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 3.94–3.76 (m, 4H), 3.30 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 3.17–3.09 (m, 1H), 2.93 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.73–2.63 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 170.4, 153.3, 149.8, 149.7, 145.7, 142.6, 139.7, 131.6, 125.4, 124.4, 119.2,

104.6, 52.0, 50.7, 42.0, 37.9, 36.7, 28.6 ppm; HRMS (ES+) calcd for $C_{21}H_{20}N_6O_6F_2{}^{35}Cl$ $(M+H)^+$, 487.1133; found, 487.1134. calcd for $C_{21}H_{20}N_6O_6F_2{}^{37}Cl$ $(M+H)^+$, 489.1103; found, 489.1108.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(p-tolyl)acetamide **12k:** yield, 55%; yellow powder; mp = 188.2–189.9 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 9.94 (s, 1H), 8.41 (s, 1H)), 7.87 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.09(d, J = 8.0 Hz, 2H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.93–3.75 (m, 4H), 3.27 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.10–3.05(m, 1H), 2.85 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.67 (t, J = 8.0 Hz, 1H), 2.54 (dd, J_1 = 7.6 Hz, J_2 = 16.0 Hz, 1H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 169.1, 153.3, 149.8, 149.7, 139.7, 137.1, 132.5, 131.7, 129.5, 124.4, 119.6, 104.6, 52.0, 50.7, 42.0, 38.1, 36.5, 28.6, 20.9 ppm; HRMS (EI+) calcd for $C_{23}H_{22}N_5O_4{}^{35}Cl$, 455.1360; found, 455.1367. calcd for $C_{23}H_{22}N_5O_4{}^{37}Cl$, 457.1331; found, 457.1368.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(o-tolyl)acetamide **12l:** yield, 58%; yellow powder; mp = 114.6–115.4 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 9.38 (s, 1H), 8.41 (s, 1H), 7.87 (d, J = 8.4 Hz 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.46 (s, 3H)), 4.88 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.91–3.77 (m, 4H), 3.29 (dd, J_1 = 6.0 Hz, J_2 = 14.4 Hz, 1H), 3.10–3.07 (m, 1H), 2.88 (dd, J_1 = 4.4 Hz, J_2 = 15.6 Hz, 1H), 2.72–2.66 (m, 1H), 2.54 (dd, J_1 = 8.0 Hz, J_2 = 15.2 Hz, 1H), 2.16 (s, 6H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 169.0, 153.3, 149.8, 149.7, 139.7, 135.7, 135.6, 131.7, 128.0, 126.9, 124.4, 104.6, 52.0, 50.7, 42.0, 38.3, 35.5, 28.6, 18.6 ppm; HRMS (ES+) calcd for $C_{23}H_{24}N_4O_5{}^{35}Cl$ $(M+H)^+$, 469.1517; found, 469.1486. calcd for $C_{23}H_{24}N_4O_5{}^{37}Cl$ $(M+H)^+$, 471.1399; found, 471.1390.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(thiazol-2-yl)acetamide **12m:** yield, 51%; yellow powder; mp = 228.6–229.4 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 12.21 (s, 1H), 8.41 (d, J = 2.0 Hz, 1H)), 7.87 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 3.6 Hz, 1H), 7.21 (d, J = 3.6 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.93–3.75 (m, 4H), 3.48–3.39 (m, 4H), 3.26 (dd, J_1 = 6.8 Hz, J_2 = 14.4 Hz, 1H), 3.15–3.10 (m, 1H), 2.94 (dd, J_1 = 5.6 Hz, J_2 = 16.4Hz, 1H), 2.72–2.64 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.3, 169.6, 158.3, 153.3, 149.8, 149.65, 139. 7, 138.1, 131.6, 124.4, 113.8, 104.6, 52.1, 50.7, 42.0, 37.9, 35.2, 28.5 ppm; HRMS (EI+) calcd for $C_{18}H_{17}N_6O_4S^{35}Cl$, 448.0693; found, 448.0703. calcd for $C_{18}H_{17}N_6O_4S$ ^{37}Cl, 450.0664; found, 450.0641.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(pyridin-2-yl)acetamide **12n:** yield, 60%; yellow powder; mp = 225.8–226.0 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.60 (s, 1H), 8.41 (d, J = 2.4 Hz, 1H)), 8.31 (dd, J_1 = 1.2 Hz, J_2 = 4.8 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.79–7.75 (m, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.10 (dd, J_1 = 5.6 Hz, J_2 = 7.2 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.92–3.75 (m, 4H), 3.25 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 3.15–3.07 (m, 1H), 2.92 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.69–2.62 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 170.4, 153.3, 152.4, 149.8, 149.7, 148.8, 139.7, 138.6, 131.7, 124.4, 119.8, 114.0, 104.7, 52.0, 50.7, 42.0, 38.0, 36.3, 28.6 ppm; HRMS (EI+) calcd for $C_{20}H_{19}N_6O_5{}^{35}Cl$, 442.1129; found, 442.1106. calcd for $C_{20}H_{19}N_6O_5$ ^{37}Cl, 444.0970; found, 444.0948.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(4-methylpyridin-2-yl)acetamide **12o:** yield, 70%; yellow powder; mp = 101.1–102.9 °C; ^{1}H

NMR (400 Mz, DMSO-d_6): δ 10.60 (s, 1H), 8.40 (d, J = 2.0 Hz, 1H)), 8.16 (d, J = 5.2 Hz, 1H), 7.94 (s, 1H), 7.87 (dd, J_1 = 2.8 Hz, J_2 = 8.4 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 4.8 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.94–3.74 (m, 4H), 3.25 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.13–3.05 (m, 1H), 2.91 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.69–2.62 (m, 2H), 2.30 (s, 3H), ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 170.3, 153.3, 152.4, 149.8, 149.6, 149.3, 148.0, 139.7, 131.6, 124.4, 120.8, 114.4, 104.6, 52.0, 50.7, 41.9, 38.0, 36.4, 28.5, 21.3 ppm; HRMS (EI+) calcd for $C_{21}H_{21}N_6O_4{}^{35}Cl$, 456.1285; found, 456.1280. calcd for $C_{21}H_{21}N_6O_4{}^{37}Cl$, 458.1256; found, 458.1270.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(pyridin-3-yl)acetamide **12p:** yield, 77%; yellow powder; mp = 185.5–186.2 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.30 (s, 1H), 8.72 (d, J = 2.4 Hz, 1H)), 8.41 (d, J = 2.0 Hz, 1H)), 8.26 (dd, J_1 = 1.2 Hz, J_2 = 4.8 Hz, 1H), 8.05–8.02 (m, 1H), 7.87 (dd, J_1 = 2.8 Hz, J_2 = 8.4 Hz, 1H), 7.53 (d, J = 8.4Hz, 1H), 7.34 (dd, J_1 = 4.8 Hz, J_2 = 8.4 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.94–3.76 (m, 4H), 3.30–3.26 (m, 1H), 3.15–3.07 (m, 1H), 2.92 (dd, J_1 = 5.2 Hz, J_2 = 16.0 Hz, 1H), 2.69 (dd, J_1 =12.4 Hz, J_2 = 14.4 Hz, 1H), 2.60 (dd, J_1 = 7.2 Hz, J_2 = 16.0 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 170.1, 153.3, 149.8, 149.6, 144.5, 141.2, 139.6, 136.18, 131.6, 126.5, 124.4, 124.1, 104.7, 52.1, 50.7, 42.0, 38.0, 36.4, 28.6 ppm; HRMS (EI+) calcd for $C_{20}H_{19}N_6O_4{}^{35}Cl$, 442.1156; found, 442.1161;. calcd for $C_{20}H_{19}N_6O_4{}^{37}Cl$, 442.1147; found, 442.1141.

N-(5-chloropyridin-2-yl)-2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydro imidazo[1,2-a]pyridin-6-yl)acetamide ***12q:*** yield, 51%; yellow powder; mp = 218.1–218.3 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 10.78 (s, 1H), 8.41 (d, J = 2.4 Hz, 1H)), 8.37 (d, J = 2.4 Hz, 1H), 8.11

(d, J = 8.8 Hz, 1H), 7.91–7.86 (m, 2H), 7.53 (d, J = 8.0 Hz, 1H), 4.89(d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.93–3.75 (m, 4H), 3.25 (dd, J_1 = 8.0 Hz, J_2 = 14.8 Hz, 1H), 3.15–3.07 (m, 1H), 2.93 (dd, J_1 = 5.2 Hz, J_2 = 16.0 Hz, 1H), 2.69–2.63 (m, 2H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 170.4, 153.3, 151.0, 149.8, 149.7, 146.7, 139.7, 138.3, 131.6, 125.4, 124.4, 115.0, 104.6, 52.0, 50.7, 42.0, 37.9, 36.4, 28.5 ppm; HRMS (EI+) calcd for $C_{20}H_{18}N_6O_4{}^{35}Cl_2$, 476.0739; found, 476.0734. calcd for $C_{20}H_{18}N_6O_4{}^{35}Cl{}^{37}Cl$, 478.0710; found, 478.0718.

N-benzyl-2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetamide **12r:** yield, 90%; yellow powder; mp = 165.0–166.3 °C; ^{1}H NMR (400 Mz, $CDCl_3$): δ 8.34 (d, J = 1.6 Hz, 1H), 7.78 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H), 7.36–7.30 (m, 3H), 7.28–7.25 (m, 3H), 6.19 (s, 1H), 4.90 (d, J = 15.6 Hz, 1H), 4.73 (d, J = 15.6 Hz, 1H), 4.42 (d, J = 5.6 Hz, 2H), 4.06–3.99 (m, 1H), 3.93–3.86 (m, 1H), 3.76–3.69 (m, 1H), 3.66–3.59 (m, 1H), 3.40 (dd, J_1 = 6.8 Hz, J_2 = 15.2 Hz, 1H), 3.15–3.08 (m, 1H), 2.86 (dd, J_1 = 12.4 Hz, J_2 = 14.8 Hz, 1H), 2.69–2.60 (m, 2H) ppm; ^{13}C NMR (100 Mz, $CDCl_3$): δ 170.5, 169.9, 152.3, 151.5, 149.2, 138.9, 138.1, 129.6, 128.7, 127.7, 127.5, 124.6, 105.3, 52.4, 50.0, 43.7, 41.4, 38.1, 36.1, 28.4 ppm; HRMS (EI+) calcd for $C_{22}H_{22}N_5O_4{}^{35}Cl$, 455.1360; found, 455.1357. calcd for $C_{22}H_{22}N_5O_4{}^{37}Cl$, 457.1363; found, 547.1361.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(4-(trifluoromethyl)benzyl)acetamide **12s:** yield, 35%; yellow powder; mp = 183.5–184.7 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.60 (t, J = 6.0 Hz, 1H), 8.41 (d, J = 2.0 Hz, 1H), 7.87 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.51 (dd, J_1 = 8.8 Hz, J_2 = 10.8 Hz, 3H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 4.38 (d, J = 5.6 Hz, 2H), 3.94–3.76 (m, 4H), 3.22 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.08–3.00 (m, 1H), 2.73 (dd, J_1 = 4.4 Hz, J_2 = 15.2 Hz, 1H), 2.64 (dd, J_1

= 12.4 Hz, J_2 = 14.4 Hz, 1H), 2.40 (dd, J_1 = 8.0 Hz, J_2 = 15.6 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 170.9, 153.3, 149.8, 149.6, 144.9,139.7, 131.6, 128.2, 128.1, 127.8, 126.2, 125.6 (m, 1C), 124.4, 123.5, 104.6, 52.0, 50.7, 42.0, 38.2, 35.5, 29.5, 28.5 ppm; HRMS (EI+) calcd for $C_{23}H_{21}N_5O_4F_3{}^{35}Cl$, 523.1234; found, 523.1228. calcd for $C_{23}H_{21}N_5O_4F_3{}^{37}Cl$, 525.1205; found, 525.1254.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(3,4-difluorobenzyl)acetamide **12t:** yield, 66 %; yellow powder; mp = 105.0–106.9 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.53 (t, J = 5.6 Hz, 1H), 8.40 (s, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.37–7.29 (m, 2H), 7.12 (s, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 3.90–3.78 (m, 4H), 3.28 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.14–3.06 (m, 1H), 2.86 (dd, J_1 = 4.8 Hz, J_2 = 16.0 Hz, 1H), 2.68 (dd, J_1 = 12.8 Hz, J_2 = 14.4 Hz, 1H), 2.60–2.58 (m, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.1, 170.1, 152.8, 149.3, 149.2 (dd, $^{1'}J_{CF}$ = 244.0 Hz, $^{2''}J_{CF}$ = 12.0 Hz),149.1, 148.2 (dd, $^{1'}J_{CF}$ = 242.0 Hz, $^{2''}J_{CF}$ = 12.0 Hz), 139.1, 137.3 (m, 1C), 131.1, 123.9, 123.7 (dd, $^{3'}J_{CF}$ = 6.0 Hz, $^{4'}J_{CF}$ = 3.0 Hz), 117.1 (d, $^{2'}J_{CF}$ = 17.0 Hz), 116.0 (d, $^{2'}J_{CF}$ = 17.0 Hz), 104.1, 51.5, 50.2, 41.4, 41.0,37.6, 35.0, 28.0 ppm; HRMS (ES+) calcd for $C_{22}H_{20}N_5O_4F_2{}^{35}Cl$ $(M+H)^+$, 492.1250; found, 492.1233. calcd for $C_{22}H_{20}N_5O_4F_2{}^{37}Cl$ $(M+H)^+$, 494.1221; found, 494.1223.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(2,5-difluorobenzyl)acetamide **12u:** yield, 56%; yellow powder; mp = 174.5–175.6 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.53 (t, J = 6.0 Hz, 1H), 8.41 (d, J = 2.4 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.51 (d, J = 8 Hz, 1H), 7.25–7.10 (m, 3H), 7.12 (s, 1H), 4.88 (d, J = 15.6 Hz, 1H), 4.79 (d, J = 15.6 Hz, 1H), 4.31 (d, J = 4.8 Hz, 1H), 3.94–3.75 (m, 4H), 3.21 (dd, J_1 = 5.6 Hz, J_2 = 14.8 Hz, 1H), 3.07–3.00 (m, 1H), 2.71 (dd, J_1 = 4.8 Hz, J_2 = 15.6 Hz, 1H), 2.63 (dd, J_1 = 12.4 Hz, J_2

= 14.4 Hz, 1H), 2.41 (dd, J_1 = 7.2 Hz, J_2 = 15.2 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.2, 170.1, 152.7, 149.3, 149.1, 139.1, 131.1, 158.1 (dd, $^{1'}J_{CF}$ = 228.2 Hz, $^{4''}J_{CF}$ = 2.0 Hz), 155.9 (dd, $^{1'}J_{CF}$ = 238.7 Hz, $^{4''}J_{CF}$ = 2.0 Hz), 128.2 (dd, $^{2'}J_{CF}$ = 17.6 Hz, $^{3''}J_{CF}$ = 7.7 Hz), 116.4 (dd, $^{2'}J_{CF}$ = 24.3 Hz, $^{3''}J_{CF}$ = 8.9 Hz), 115.5 (dd, $^{1'}J_{CF}$ = 24.7 Hz, $^{3''}J_{CF}$ = 4.9 Hz), 114.9 (dd, $^{2'}J_{CF}$ = 24.0 Hz, $^{3''}J_{CF}$ = 8.6 Hz), 104.1, 51.5, 50.1, 41.4, 37.5, 35.8, 34.9, 28.0 ppm; HRMS (ES+) calcd for $C_{22}H_{20}N_5O_4F_2{}^{35}Cl$ $(M+H)^+$, 492.1250; found, 492.1238. calcd for $C_{22}H_{20}N_5O_4F_2{}^{37}Cl$ $(M+H)^+$, 494.1221; found, 494.1225.

N-(3-chloro-4-fluorobenzyl)-2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)acetamide **12v:** yield, 56%; yellow powder; mp = 105.1–105.8 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.54 (t, J = 5.6 Hz, 1H), 8.39 (d, J = 2.0 Hz ,1H), 7.86 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.48 (dd, J_1 = 1.6 Hz, J_2 = 7.2 Hz, 1H), 7.35 (t, J = 8.8 Hz, 1H), 7.29–7.25 (m, 1H), 4.88 (d, J = 15.6 Hz, 1H), 4.79 (d, J = 15.6 Hz, 1H), 4.32–4.22 (m, 2H), 3.96–3.73 (m, 4H), 3.20 (dd, J_1 = 6.4 Hz, J_2 = 14.8 Hz, 1H), 3.07–3.00 (m, 1H), 2.69 (dd, J_1 = 4.8 Hz, J_2 = 15.6 Hz, 1H), 2.63 (dd, J_1 = 12.4 Hz, J_2 = 14.4 Hz, 1H), 2.38(dd, J_1 = 7.6 Hz, J_2 = 15.2 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.0, 170.0，156.1 (d, $^{1'}J_{CF}$ = 243.8 Hz), 152.7, 149.2, 149.1, 139.1, 137.3 (d, $^{4'}J_{CF}$ = 3.6 Hz), 131.1, 129.1, 127.6 (d, $^{3'}J_{CF}$ = 7.3 Hz), 123.8, 119.2 (d, $^{2'}J_{CF}$ = 17.5 Hz), 116.6 (d, $^{2'}J_{CF}$ = 20.7 Hz), 104.0, 51.4, 50.1, 41.4, 41.0, 37.6, 35.0, 28.0 ppm; HRMS (EI+) calcd for $C_{22}H_{20}N_5O_4F{}^{35}Cl_2$, 507.0876; found, 507.0881. calcd for $C_{22}H_{20}N_5O_4F$ $^{35}Cl^{37}Cl$, 509.0869; found, 509.0874.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(2,3,6-trifluorobenzyl)acetamide **12w:** yield, 54%; yellow powder; mp = 190.6–191.8 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.47 (t, J = 4.8 Hz, 1H), 8.40 (d, J = 1.6 Hz, 1H), 7.86 (dd, J_1 = 2.4 Hz,

J_2 = 8.4 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.48–7.40 (m, 1H), 7.12 (t, J = 8.8 Hz, 1H), 4.87 (d, J = 16.0 Hz, 1H), 4.78 (d, J = 16.0 Hz, 1H), 4.39–4.30 (m, 2H), 3.94–3.72 (m, 4H), 3.16 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H), 3.00–2.93 (m, 1H), 2.64 (dd, J_1 = 4.4 Hz, J_2 = 19.6 Hz, 1H), 2.55 (t, J =12.8 Hz, 1H), 2.29 (dd, J_1 = 8.0 Hz, J_2 = 15.6 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.5, 170.2, 158.0 (m, 1C), 155.6 (m, 1C), 153.3, 149.8, 149.6, 148.1 (m, 1C), 145.7 (m, 1C), 139.6, 131.7, 124.5, 117.1 (m, 1C), 111.7 (m, 1C), 104.0, 52.0, 50.7, 41.9, 38.1, 35.2, 31.3, 28.4 ppm; HRMS (EI+) calcd for $C_{22}H_{19}N_5O_4F_3{}^{35}Cl$, 509.1078; found, 509.1069. calcd for $C_{22}H_{19}N_5O_4F_3{}^{37}Cl$, 511.1088; found, 511.1083.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(3-(trifluoromethyl)benzyl)acetamide **12x:** yield, 90%; yellow powder; mp = 86.3–86.5 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.59 (t, J = 6.0 Hz, 1H), 8.41 (d, J = 1.6 Hz, 1H), 7.87 (dd, J_1 = 2.4 Hz, J_2 = 8.0 Hz, 1H), 7.64 (s, 1H), 7.61–7.59 (m, 3H), 7.52 (d, J = 8.4 Hz, 1H), 4.88 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 4.38 (dd, J_1 = 2.4 Hz, J_2 = 5.2 Hz, 2H), 3.93–3.73 (m, 4H), 3.21 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.08–2.30 (m, 1H), 2.71 (dd, J_1 = 4.8 Hz, J_2 = 15.2 Hz, 1H), 2.67–2.60 (m, 1H), 2.40 (dd, J_1 = 7.6 Hz, J_2 = 15.6 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.7, 170.6, 153.3, 149.8, 149.7, 141.5, 139.7, 131.7 (m, 1C), 131.6, 129.6, 127.7 (d, $^{1'}J_{CF}$ = 328.7 Hz), 124.4, 124.1 (dd, $^{2'}J_{CF}$ = 20.3 Hz, $^{3''}J_{CF}$ = 3.8 Hz), 123.9 (d, $^{2'}J$ = 3.8 Hz), 123.4, 104.6, 52.0, 50.7, 42.2, 41.9, 38.2, 35.5, 28.5 ppm; HRMS (EI+) calcd for $C_{23}H_{21}N_5O_4F_3{}^{35}Cl$, 523.1234; found, 523.1236. calcd for $C_{23}H_{21}N_5O_4F_3{}^{37}Cl$, 525.1205; found, 525.1233.

2-(1-((6-chloropyridin-3-yl)methyl)-8-nitro-5-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-6-yl)-N-(4-methoxybenzyl)acetamide **12y:** yield, 60%; yellow powder; mp = 164.0–164.4 °C; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.59 (t, J = 6.0 Hz, 1H), 8.41 (d, J = 1.6 Hz, 1H), 7.87 (dd, J_1 = 2.4

Hz, J_2 = 8.0 Hz, 1H), 7.64 (s, 1H), 7.61–7.59 (m, 3H), 7.52 (d, J = 8.4 Hz, 1H), 4.88 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 4.38 (dd, J_1 = 2.4 Hz, J_2 = 5.2 Hz, 2H), 3.93–3.73 (m, 4H), 3.21 (dd, J_1 = 6.4 Hz, J_2 = 14.4 Hz, 1H), 3.08–2.30 (m, 1H), 2.71 (dd, J_1 = 4.8 Hz, J_2 = 15.2 Hz, 1H), 2.67–2.60 (m, 1H), 2.40 (dd, J_1 = 7.6 Hz, J_2 = 15.6 Hz, 1H) ppm; ^{13}C NMR (100 Mz, DMSO-d_6): δ 170.6, 170.2, 158.7, 153.3, 149.8, 149.7, 139.7, 131.8, 131.7, 129.0, 124.4, 114.1, 104.6, 55.5, 52.0, 50.7, 42.0, 41.9, 38.2, 35.5, 28.5 ppm; HRMS (EI+) calcd for $C_{23}H_{24}N_5O_5{}^{35}Cl$, 485.1466; found, 485.1465. calcd for $C_{23}H_{24}N_5O_5{}^{35}Cl$, 487.1436; found, 487.1433.

Biological Assay

All bioassays were performed on representative test organisms reared in the laboratory. The bioassay was repeated at 25 ± 1 °C according to statistical requirements. All compounds were dissolved in *N*, *N*-dimethylformamide (AP, Shanghai Chemical Reagent Co., Ltd., Shanghai, China) and diluted with distilled water containing Triton X-100 (0.1 mg L^{-1}) to obtain series concentrations of 500.0, 250.0, 125.0 mg L^{-1} and others for bioassays.

Insecticidal test for Cowpea aphids (Aphis craccivora). The activities of insecticidal compounds against cowpea aphids were tested by leaf-dip method according to our previously reported procedure.[1] The horsebean plant leaves with 40−60 apterous adults were dipped in diluted solutions of the chemicals containing Triton X-100 (0.1 mg L^{-1}) for 5 s and the excess dilution was sucked out with filter paper, and the burgeons were placed in the conditioned room (25 ± 1 °C, 50% RH). Water containing Triton X-100 (0.1 mg L^{-1}) was used as control. The mortality rates were evaluated 24 h after treatment. Each treatment had three repetitions and the data were adjusted and subjected to probit analysis as before.

Insecticidal test for Armyworm (Pseudaletia separate Walker). The activities of insecticidal compounds against armyworm were tested using previously reported procedures.[2] The insecticidal activity against armyworm was tested by foliar application. Individual corn (*Zea mays*) leaves were placed on moistened pieces of filter paper in Petri dishes. The leaves were then sprayed with the compounds solution and exposed to dry. The dishes were infested with 10 second-instar larvae and placed in the conditioned room. The mortality rates were evaluated 48 h after treatment. Each treatment had three repetitions and the data were adjusted and subjected to probit analysis as before.

Insecticidal test for brown planthopper (Nilaparvata lugens). The activities of insecticidal compounds against *Nilaparvata lugens* were tested using dipping method. Rice plants at tillering to booting stage were pulled out and the rice stems (about 10 cm lengths) with roots were cut and air dried to remove excess water. Three rice stems were dipped in appropriate solutions of tested compound for 30 s. After rice stems had been air dried, the rice roots was wrapped by moistened cotton. Then the rice stems were placed into a tumbler. Thirty *Nilaparvata lugens* were introduced into the tumbler and the treated insects were maintained at a temperature of 27 ± 1 °C. The distilled water only was used as control for each chemical. Each process was repeated for 3 times and the mortality rates were evaluated 48 h after treatment. The data were adjusted and subjected to probit analysis as before.

Insecticidal test for Tetranychus Cinnabarinus. Cut round sections from chemically untreated broad bean leaves. Leaves must be in good condition. Use a minimum of three replicates (leaf sections) per treatment. Place these sections, lower surface uppermost, on a small piece of cotton on moist cotton wool in open Petri dishes. Collect adult mites with the fine pointed brush onto each leaf section. The leaf disc with mites placed under the Potter spray tower (Quantitative volume 2.5mL),

sprayed with test liquids (pressure 5Ib/iW^2, settlement of 4.35 mg/cm^2). The test set with the highest concentrations of organic solvents Tween water as a blank control. The leaf discs with mite are air dried and placed at a room with temperature of 24–26 °C, photoperiod 14 h. Using a hand lens assess mortality after 48 h by checking each mite's ability to show co-ordinated movement in response to a touch with a small brush. Express results as percentage mortality and correct for untreated mortality using Abbott's formula. Each process was repeated for 3 times.

[1] Z. Z. Tian, X. S. Shao, Z. Li, X. H. Qian, J. Agric. Food Chem. **2007**, *55*, 2288.

[2] C. Li, Q. M. Wang, R. Q. Huang, C. H. Mao, J. Shang, F. C. Bi, J. Agric. Food Chem. **2005**, *49*, 38.