

1 *Supporting information for:*
2 **Synthesis and Insecticidal Activities of Novel Anthranilic Diamides Containing**
3 **Modified *N*-pyridylpyrazoles**

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1 **Ethyl 5-(2-(methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-**
2 **2-yl)-1H-pyrazole-3-carboxylate 8a.** Yield 55.8%, white solid, mp 226-227 °C; ¹H NMR (400
3 MHz, CDCl₃): δ 10.20 (s, 1H, CONHAr), 8.45 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H), 7.84 (d, 1H, ³J_{HH}
4 =8.0 Hz, Ar-H), 7.76 (s, 1H, Ar-H), 7.38 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.16 (s, 1H,
5 Ar-H), 7.15 (s, 1H, Ar-H), 6.29 (d, 1H, ³J_{HH}=4.8 Hz, NHCH₃), 4.46 (q, 2H, ³J_{HH}=7.2 Hz,
6 CH₂CH₃), 2.92 (d, 1H, ³J_{HH}=4.8 Hz, NHCH₃), 2.14 (s, 3H, Ar-CH₃), 1.42 (t, 3H, ³J_{HH}=7.2 Hz,
7 CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 168.5, 161.4, 157.1, 149.5, 146.8, 145.0, 138.8, 138.7,
8 138.2, 133.2, 132.7, 132.3, 131.2, 129.2, 125.9, 124.5, 110.4, 61.6, 26.9, 18.7, 14.4. HRMS calcd
9 for C₂₁H₁₉³⁵Cl₂N₅O₄Na ([M+Na]⁺): 498.0699, found: 498.0706; calcd for
10 C₂₁H₁₉³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 500.0666, found: 500.0679; calcd for C₂₁H₁₉³⁷Cl₂N₅O₄Na
11 ([M+Na]⁺): 502.0651, found: 502.0655.

12 **Ethyl 5-(2-(isopropylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-**
13 **chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8b.** Yield 57.0%, white solid, mp 138-140 °C;
14 ¹H NMR (400 MHz, CDCl₃): δ 10.22 (s, 1H, CONHAr), 8.47 (dd, 1H, ⁴J_{HH}=1.4 Hz, ³J_{HH}=4.4 Hz
15 , Ar-H), 7.84 (dd, 1H, ⁴J_{HH}=1.2 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.71 (s, 1H, Ar-H), 7.39 (dd, 1H, ³J_{HH}
16 =4.6 Hz, ³J_{HH}=8.2 Hz, Ar-H), 7.20 (d, 1H, ⁴J_{HH}=1.6 Hz, Ar-H), 7.17 (d, 1H, ⁴J_{HH}=2.4 Hz, Ar-H),
17 5.99 (d, 1H, ³J_{HH}=7.6 Hz, NHCH), 4.47 (q, 2H, ³J_{HH}=7.2 Hz, CH₂CH₃), 4.22-4.14 (m, 1H,
18 NHCH), 2.16 (s, 3H, Ar-CH₃), 1.41 (t, 3H, ³J_{HH}=7.2 Hz, CH₂CH₃), 1.18 (d, 6H, ³J_{HH}=6.8 Hz,
19 CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 167.2, 161.4, 157.9, 149.7, 146.7, 145.0, 139.0,
20 138.6, 138.0, 135.4, 132.7, 132.0, 130.3, 129.2, 125.9, 124.6, 110.5, 61.5, 42.5, 22.2, 18.3, 14.4.
21 HRMS calcd for C₂₃H₂₃³⁵Cl₂N₅O₄Na ([M+Na]⁺): 526.1019, found: 526.1019; calcd for
22 C₂₃H₂₃³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 528.0992, found: 528.0992; calcd for C₂₃H₂₃³⁷Cl₂N₅O₄Na
23 ([M+Na]⁺): 530.0988, found: 530.0971.

24 **Ethyl 5-(2-(tert-butylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-**
25 **chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8c.** Yield 53.2%, white solid, mp 254-256 °C;
26 ¹H NMR (400 MHz, CDCl₃): δ 10.53 (s, 1H, CONHAr), 8.44 (d, 1H, ³J_{HH}=4.8 Hz, Ar-H), 8.09 (s,
27 1H, Ar-H), 7.83 (d, 1H, ³J_{HH}=7.6 Hz, Ar-H), 7.37 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H),
28 7.06 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 6.08 (s, 1H, CONHC), 4.46 (q, 2H, ³J_{HH}=7.2 Hz,
29 CH₂CH₃), 2.09 (s, 3H, Ar-CH₃), 1.41 (t, 3H, ³J_{HH}=7.2 Hz, CH₂CH₃), 1.34 (s, 9H, C(CH₃)₃). ¹³C
30 NMR (100 MHz, CDCl₃): δ 167.5, 161.4, 158.2, 149.8, 146.6, 145.1, 139.3, 138.6, 137.9, 136.9,
31 133.0, 131.8, 129.9, 129.2, 125.8, 124.3, 110.5, 61.4, 52.5, 28.4, 18.2, 14.4. HRMS calcd for
32 C₂₄H₂₅³⁵Cl₂N₅O₄Na ([M+Na]⁺): 540.1171, found: 540.1176; calcd for C₂₄H₂₅³⁵Cl³⁷ClN₅O₄Na
33 ([M+Na]⁺): 542.1142, found: 542.1149; calcd for C₂₄H₂₅³⁷Cl₂N₅O₄Na ([M+Na]⁺): 544.1156,
34 found: 544.1128.

35 **Ethyl 5-(2-(cyclopropylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-**
36 **chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8d.** Yield 60.2%, white solid, mp 232-234 °C;
37 ¹H NMR (400 MHz, CDCl₃): δ 10.17 (s, 1H, CONHAr), 8.47 (dd, 1H, ⁴J_{HH}=1.2 Hz, ³J_{HH}=4.4 Hz,
38 Ar-H), 7.85 (dd, 1H, ⁴J_{HH}=1.4 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.71 (s, 1H, Ar-H), 7.39 (dd, 1H,
39 ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.22 (d, 1H, ⁴J_{HH}=2.0 Hz, Ar-H), 7.15 (d, 1H, ⁴J_{HH}=2.0 Hz,
40 Ar-H), 6.30 (d, 1H, ³J_{HH}=1.6 Hz, CONHCH), 4.47 (q, 2H, ³J_{HH}=7.2 Hz, CH₂CH₃), 2.84-2.80 (m,
41 1H, NHCH), 2.17 (s, 3H, Ar-CH₃), 1.42 (t, 3H, ³J_{HH}=7.2 Hz, CH₂CH₃), 0.90-0.85 (m, 2H,
42 cyclopropyl), 0.57-0.53 (m, 2H, cyclopropyl). ¹³C NMR (100 MHz, CDCl₃): δ 169.4, 161.4,
43 157.4, 149.5, 146.8, 145.0, 138.8, 138.7, 138.1, 133.6, 132.5, 132.4, 130.9, 129.2, 125.9, 124.6,
44 110.5, 61.5, 23.2, 18.5, 14.4, 6.6. HRMS calcd for C₂₃H₂₁³⁵Cl₂N₅O₄Na ([M+Na]⁺): 524.0856,

found: 524.0863; calcd for $C_{23}H_{21}^{35}Cl^{37}ClN_5O_4Na$ ($[M+Na]^+$): 526.0823, found: 526.0836; calcd for $C_{23}H_{21}^{37}Cl_2N_5O_4Na$ ($[M+Na]^+$): 528.0810, found: 528.0814.

Ethyl 5-(2-(methoxycarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8e. Yield 65.5%, white solid, mp 122-124 °C; 1H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H, CONHAr), 8.94 (s, 1H, CONHO), 8.45 (d, 1H, $^3J_{HH}=4.8$ Hz, Ar-H), 7.84 (d, 1H, $^3J_{HH}=8.0$ Hz, Ar-H), 7.62 (s, 1H, Ar-H), 7.39 (dd, 1H, $^3J_{HH}=4.8$ Hz, $^3J_{HH}=8.0$ Hz, Ar-H), 7.26 (s, 1H, Ar-H), 7.19 (s, 1H, Ar-H), 4.46 (q, 2H, $^3J_{HH}=7.2$ Hz, CH_2CH_3), 3.78 (s, 3H, OCH_3), 2.17 (s, 3H, Ar- CH_3), 1.42 (t, 3H, $^3J_{HH}=7.2$, CH_2CH_3). ^{13}C NMR (100 MHz, DMSO- d_6): δ 160.8, 156.0, 148.8, 147.1, 143.6, 139.2, 139.0, 138.5, 133.7, 133.6, 131.8, 131.7, 131.0, 127.8, 126.8, 125.5, 110.2, 63.0, 61.0, 17.5, 14.1. HRMS calcd for $C_{21}H_{19}^{35}Cl_2N_5O_5Na$ ($[M+Na]^+$): 514.0650, found: 514.0655; calcd for $C_{21}H_{19}^{35}Cl^{37}ClN_5O_5Na$ ($[M+Na]^+$): 516.0618, found: 516.0628; calcd for $C_{21}H_{19}^{37}Cl_2N_5O_5Na$ ($[M+Na]^+$): 518.0620, found: 518.0606.

Ethyl 5-(2-(benzylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8f. Yield 50.4%, white solid, mp 178-180 °C; 1H NMR (400 MHz, $CDCl_3$): δ 10.15 (s, 1H, CONHAr), 8.44 (dd, 1H, $^4J_{HH}=0.8$ Hz, $^3J_{HH}=4.8$ Hz, Ar-H), 7.82 (d, 1H, $^3J_{HH}=8.0$ Hz, Ar-H), 7.64 (s, 1H, Ar-H), 7.37 (dd, 1H, $^3J_{HH}=4.8$ Hz, $^3J_{HH}=8.0$ Hz, Ar-H), 7.33-7.26 (m, 5H, Ar-H), 7.21 (s, 2H, Ar-H), 6.50 (t, 1H, $^3J_{HH}=6.4$ Hz, $NHCH_2$), 4.53 (d, 2H, $^3J_{HH}=6.4$ Hz, $NHCH_2$), 4.46 (q, 2H, $^3J_{HH}=7.2$ Hz, CH_2CH_3), 2.16 (s, 3H, Ar- CH_3), 1.41 (t, 3H, $^3J_{HH}=7.2$ Hz, CH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 161.4, 157.4, 149.5, 146.7, 144.9, 138.8, 138.7, 138.0, 137.1, 133.9, 133.8, 132.5, 130.9, 129.1, 128.8, 127.8, 127.7, 125.9, 124.7, 110.5, 61.5, 44.2, 18.5, 14.4. HRMS calcd for $C_{27}H_{23}^{35}Cl_2N_5O_4Na$ ($[M+Na]^+$): 574.1017, found: 574.1019; calcd for $C_{27}H_{23}^{35}Cl^{37}ClN_5O_4Na$ ($[M+Na]^+$): 576.0991, found: 574.0993; calcd for $C_{27}H_{23}^{37}Cl_2N_5O_4Na$ ($[M+Na]^+$): 578.1007, found: 578.0975.

Ethyl 5-(2-(isopropylcarbamoyl)-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8g. Yield 60.7%, white solid, mp 172-174 °C; 1H NMR (400 MHz, $CDCl_3$): δ 10.39 (s, 1H, CONHAr), 8.46 (d, 1H, $^3J_{HH}=4.4$ Hz, Ar-H), 7.83 (d, 1H, $^3J_{HH}=8.0$ Hz, Ar-H), 7.71 (s, 1H, Ar-H), 7.39-7.36 (m, 1H, Ar-H), 7.25-7.19 (m, 2H, Ar-H), 7.13-7.09 (m, 1H, Ar-H), 6.04 (d, $^3J_{HH}=7.6$ Hz, $CONHCH$), 4.47 (q, 2H, $^3J_{HH}=7.2$ Hz, CH_2CH_3), 4.20-4.12 (m, 1H, $CONHCH$), 2.18 (s, 3H, Ar- CH_3), 1.43 (t, 3H, $^3J_{HH}=7.2$ Hz, CH_2CH_3), 1.14 (d, 6H, $^3J_{HH}=6.4$ Hz, $CH(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 161.4, 156.8, 149.6, 146.7, 145.0, 138.7 (2C), 136.6, 133.2, 133.0, 131.6, 129.2, 126.6, 125.8, 124.5, 110.1, 61.4, 42.2, 22.4, 18.8, 14.4. HRMS calcd for $C_{23}H_{24}^{35}ClN_5O_4Na$ ($[M+Na]^+$): 492.1404, found: 492.1409; calcd for $C_{23}H_{24}^{37}ClN_5O_4Na$ ($[M+Na]^+$): 494.1384, found: 494.1394.

Ethyl 5-(2-(propylcarbamoyl)-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 8h. Yield 65.2%, white solid, mp 162-164 °C; 1H NMR (400 MHz, $CDCl_3$): δ 10.34 (s, 1H, CONHAr), 8.47 (d, 1H, $^3J_{HH}=4.8$ Hz, Ar-H), 7.84 (d, 1H, $^3J_{HH}=8.0$ Hz, Ar-H), 7.59 (s, 1H, Ar-H), 7.38 (dd, 1H, $^3J_{HH}=4.8$ Hz, $^3J_{HH}=7.6$, Ar-H), 7.28-7.23 (m, 2H, Ar-H), 7.16-7.12 (m, 1H, Ar-H), 6.19 (br s, 1H, $CONHCH_2$), 4.47 (q, 2H, $^3J_{HH}=7.2$ Hz, CH_2CH_3), 3.33 (q, 2H, $^3J_{HH}=6.8$ Hz, $NHCH_2$), 2.20 (s, 3H, Ar- CH_3), 1.59-1.51 (m, 2H, $CH_2CH_2CH_3$), 1.43 (t, 3H, $^3J_{HH}=7.2$ Hz, CH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 161.4, 156.6, 149.6, 146.7, 145.0, 138.7 (2C), 136.5, 133.5, 133.2, 130.8, 129.3, 126.6, 125.8, 124.5, 110.1, 61.5, 41.7, 22.6, 19.0, 14.4, 11.4. HRMS calcd for $C_{23}H_{24}^{35}ClN_5O_4Na$ ($[M+Na]^+$): 492.1412, found: 492.1409; calcd for $C_{23}H_{24}^{37}ClN_5O_4Na$ ($[M+Na]^+$): 494.1379, found: 494.1385.

Butyl 5-(2-(methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 11a. Yield 22.5%, white solid, mp 123-125 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.14 (s, 1H, CONHAr), 8.46 (dd, 1H, ⁴J_{HH}=1.2 Hz, ³J_{HH}=4.8 Hz, Ar-H), 7.84 (dd, 1H, ⁴J_{HH}=1.2 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.67 (s, 1H, Ar-H), 7.39 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.21 (s, 1H, Ar-H), 7.19 (s, 1H, Ar-H), 6.21 (d, 1H, ³J_{HH}=4.8 Hz, NHCH₃), 4.40 (q, 2H, ³J_{HH}=7.0 Hz, CH₂CH₂), 2.94 (d, 1H, ³J_{HH}=4.8 Hz, NHCH₃), 2.16 (s, 3H, Ar-CH₃), 1.82-1.75 (m, 2H, CH₂CH₂CH₂), 1.51-1.42 (m, 2H, CH₂CH₂CH₃), 0.97 (t, 3H, ³J_{HH}=7.4 Hz, CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 168.5, 161.5, 157.3, 149.5, 146.7, 145.0, 138.8, 138.6, 138.1, 133.7, 132.5, 132.4, 131.0, 129.2, 125.9, 124.6, 110.5, 65.4, 30.7, 26.9, 19.1, 18.6, 13.7. HRMS calcd for C₂₃H₂₃³⁵Cl₂N₅O₄Na ([M+Na]⁺): 526.1027, found: 526.1019; calcd for C₂₃H₂₃³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 528.0999, found: 528.0992; calcd for C₂₃H₂₃³⁷Cl₂N₅O₄Na ([M+Na]⁺): 530.0989, found: 530.0971.

Isopropyl 5-(2-(methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 11b. Yield 24.0%, white solid, mp 152-154 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.08 (s, 1H, CONHAr), 8.47 (dd, 1H, ⁴J_{HH}=1.6, ³J_{HH}=4.8 Hz, Ar-H), 7.84 (dd, 1H, ⁴J_{HH}=1.6 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.61 (s, 1H, Ar-H), 7.39 (dd, 1H, ³J_{HH}=4.6 Hz, ³J_{HH}=7.8 Hz, Ar-H), 7.25 (d, 1H, ⁴J_{HH}=2.0 Hz, Ar-H), 7.22 (s, 1H, ⁴J_{HH}=2.4 Hz, Ar-H), 6.15 (d, 1H, ³J_{HH}=4.8 Hz, NHCH₃), 5.39-5.33 (m, 1H, OCH), 2.95 (d, 1H, ³J_{HH}=5.2 Hz, NHCH₃), 2.18 (s, 3H, Ar-CH₃), 1.41 (d, 6H, ³J_{HH}=7.4 Hz, CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 168.5, 161.0, 157.2, 149.6, 146.8, 145.4, 138.7, 138.6, 138.1, 133.4, 132.6, 132.3, 131.2, 129.3, 125.9, 124.5, 110.5, 69.2, 26.9, 21.0, 18.6. HRMS calcd for C₂₂H₂₁³⁵Cl₂N₅O₄Na ([M+Na]⁺): 512.0859, found: 512.0863; calcd for C₂₂H₂₁³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 514.0836, found: 514.0835; calcd for C₂₂H₂₁³⁷Cl₂N₅O₄Na ([M+Na]⁺): 516.0796, found: 516.0813.

Benzyl 5-(2-(methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 11c. Yield 25.0%, white solid, mp 118-120 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.11 (s, 1H, CONHAr), 8.46 (s, 1H, Ar-H), 7.85 (d, 1H, ³J_{HH}=7.6 Hz, Ar-H), 7.62 (s, 1H, Ar-H), 7.49 (s, 1H, Ar-H), 7.47 (s, 1H, Ar-H), 7.38-7.34 (m, 4H, Ar-H), 7.24 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 6.12 (br s, 1H, CONHCH₃), 5.44 (s, 2H, COOCH₂), 2.90 (s, 3H, CONHCH₃), 2.16 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 168.5, 161.2, 157.4, 149.5, 146.7, 145.8, 144.6, 138.7, 138.6, 138.2, 135.5, 134.1, 132.4, 132.3, 130.8, 129.2, 128.7, 128.6, 128.4, 125.9, 124.6, 123.5, 110.7, 67.1, 26.8, 18.5. HRMS calcd for C₂₆H₂₁³⁵Cl₂N₅O₄Na ([M+Na]⁺): 560.0867, found: 560.0863; calcd for C₂₆H₂₁³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 562.0842, found: 562.0837; calcd for C₂₆H₂₁³⁷Cl₂N₅O₄Na ([M+Na]⁺): 564.0835, found: 564.0818.

Cyclohexyl 5-(2-(methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-3-carboxylate 11d. Yield 20.4%, white solid, mp 146-148 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.09 (s, 1H, CONHAr), 8.46 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H), 7.84 (dd, 1H, ⁴J_{HH}=1.6 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.65 (s, 1H, Ar-H), 7.38 (dd, 1H, ³J_{HH}=4.4 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.21 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 6.21 (d, 1H, ³J_{HH}=4.4 Hz, CONHCH₃), 5.11-5.05 (m, 1H, COOCH), 2.94 (d, 3H, ³J_{HH}=4.8 Hz, CONHCH₃), 2.05-2.01 (m, 2H, cyclohexyl), 1.84-1.80 (m, 2H, cyclohexyl), 1.63-1.58 (m, 4H, cyclohexyl), 1.46-1.41 (m, 2H, cyclohexyl). ¹³C NMR (100 MHz, CDCl₃): δ 168.5, 160.9, 157.3, 149.6, 146.8, 145.4, 138.7 (2C), 138.1, 133.4, 132.6, 132.3, 131.2, 129.2, 125.9, 124.5, 110.4, 74.3, 31.7, 26.9, 25.3, 24.1, 18.6. HRMS calcd for C₂₅H₂₅³⁵Cl₂N₅O₄Na ([M+Na]⁺): 552.1174, found: 552.1176; calcd for C₂₅H₂₅³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 554.1139, found: 554.1149; calcd for C₂₅H₂₅³⁷Cl₂N₅O₄Na

1 ([M+Na]⁺): 556.1113, found: 556.1129.

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3 ***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-methyl-1*H***
4 **-pyrazole-3, 5-dicarboxamide 13a.** Yield 24.0%, white solid, mp 183-185 °C; ¹H NMR (400
5 MHz, CDCl₃): δ 10.13 (s, 1H, CONHAr), 8.49 (d, 1H, ³*J*_{HH} = 4.4 Hz, Ar-H), 7.88 (d, 1H, ³*J*_{HH}
6 = 8.0 Hz, Ar-H), 7.67 (s, 1H, Ar-H), 7.42 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.26-7.25
7 (m, 2H, Ar-H), 6.97 (d, 1H, ³*J*_{HH} = 5.2 Hz, *NHCH*₃), 6.20 (d, 1H, ³*J*_{HH} = 4.4 Hz, *NHCH*₃), 2.97 (d,
8 3H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.92 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.20 (s, 3H, Ar-CH₃). ¹³C NMR
9 (100 MHz, CDCl₃): δ 168.0, 161.6, 157.7, 149.5, 147.7, 146.8, 138.9, 138.8, 138.7, 134.6, 132.6,
10 132.4, 130.9, 129.1, 125.9, 125.2, 108.8, 26.8, 25.9, 18.6. HRMS calcd for C₂₀H₁₈³⁵Cl₂N₆O₃Na
11 ([M+Na]⁺): 483.0711, found: 483.0710; calcd for C₂₀H₁₈³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 485.0678,
12 found: 485.0682; calcd for C₂₀H₁₈³⁷Cl₂N₆O₃Na ([M+Na]⁺): 487.0656, found: 487.0657.

13 ***N*⁵-(2-(isopropylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-methy**
14 ***l*-1*H*-pyrazole-3, 5-dicarboxamide 13b.** Yield 26.0%, white solid, mp 251-253 °C; ¹H NMR
15 (400 MHz, CDCl₃): δ 10.24 (s, 1H, CONHAr), 8.49 (dd, 1H, ⁴*J*_{HH} = 1.4 Hz, ³*J*_{HH} = 4.6 Hz, Ar-H),
16 7.88 (dd, 1H, ⁴*J*_{HH} = 1.4 Hz, ³*J*_{HH} = 8.2 Hz, Ar-H), 7.74 (s, 1H, Ar-H), 7.41 (dd, 1H, ³*J*_{HH} = 4.8 Hz,
17 ³*J*_{HH} = 8.0 Hz, Ar-H), 7.23 (s, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 6.97 (d, 1H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃),
18 6.01 (d, 1H, ³*J*_{HH} = 8.0 Hz, *NHCH*₃), 4.20-4.11 (m, 1H, *NHCH*), 2.95 (d, H, ³*J*_{HH} = 4.8 Hz,
19 *NHCH*₃), 2.19 (s, 3H, Ar-CH₃), 1.15 (d, 6H, ³*J*_{HH} = 6.8 Hz, CH(*CH*₃)₂). ¹³C NMR (100 MHz,
20 CDCl₃): δ 166.6, 161.5, 157.4, 149.5, 147.9, 146.9, 138.9, 138.8, 138.7, 134.2, 132.5, 131.2,
21 129.1, 125.8, 125.0, 124.8, 108.5, 42.3, 25.9, 22.4, 18.7. HRMS calcd for C₂₂H₂₂³⁵Cl₂N₆O₃Na
22 ([M+Na]⁺): 511.1018, found: 511.1023; calcd for C₂₂H₂₂³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 513.0990,
23 found: 513.0995; calcd for C₂₂H₂₂³⁷Cl₂N₆O₃Na ([M+Na]⁺): 515.0978, found: 515.0972.

24 ***N*⁵-(2-(*tert*-butylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-methy**
25 ***l*-1*H*-pyrazole-3,5-dicarboxamide 13c.** Yield 24.5%, white solid, mp 153-155 °C; ¹H NMR
26 (400 MHz, CDCl₃): δ 10.47 (s, 1H, CONHAr), 8.45 (d, 1H, ³*J*_{HH} = 4.8 Hz, Ar-H), 8.01 (s, 1H,
27 Ar-H), 7.85 (d, 1H, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.39 (dd, 1H, ³*J*_{HH} = 4.6 Hz, ³*J*_{HH} = 7.8 Hz, Ar-H), 7.10
28 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 6.98 (d, 1H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 6.07 (s, 1H, *NHC*), 2.94
29 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.12 (s, 3H, Ar-CH₃), 1.31 (s, 9H, C(*CH*₃)₃). ¹³C NMR (100 MHz,
30 CDCl₃): 167.2, 161.5, 158.3, 149.7, 147.9, 146.7, 139.2, 138.8, 138.4, 137.3, 133.0, 131.6, 129.8,
31 129.2, 125.9, 124.7, 108.8, 52.4, 28.4, 25.9, 18.2. HRMS calcd for C₂₃H₂₄³⁵Cl₂N₆O₃Na ([M+Na]
32 ⁺): 525.1180, found: 525.1179; calcd for C₂₃H₂₄³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 527.1148, found:
33 527.1152; calcd for C₂₃H₂₄³⁷Cl₂N₆O₃Na ([M+Na]⁺): 529.1121, found: 529.1130.

34 ***N*⁵-(2-(cyclopropylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-**
35 **methyl-1*H*-pyrazole-3, 5-dicarboxamide 13d.** Yield 23.8%, white solid, mp 254-256 °C; ¹H
36 NMR (400 MHz, CDCl₃): δ 10.09 (s, 1H, CONHAr), 8.50 (dd, 1H, ⁴*J*_{HH} = 1.0 Hz, ³*J*_{HH} = 4.6 Hz,
37 Ar-H), 7.88 (dd, 1H, ⁴*J*_{HH} = 1.6 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.65 (s, 1H, Ar-H), 7.42 (dd, 1H, ³*J*_{HH}
38 = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.26 (s, 1H, Ar-H), 7.20 (d, 1H, ⁴*J*_{HH} = 2.4 Hz, Ar-H), 6.96 (d, 1H,
39 ³*J*_{HH} = 5.2 Hz, *NHCH*₃), 6.22 (s, 1H, *NHCH*), 2.98 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.84-2.79 (m,
40 1H, *NHCH*), 2.20 (s, 3H, Ar-CH₃), 0.86 (q, 2H, ³*J*_{HH} = 6.8 Hz, cyclopropyl), 0.55 (q, 2H, ³*J*_{HH}
41 = 6.4 Hz, cyclopropyl). ¹³C NMR (100 MHz, CDCl₃): 166.8, 160.7, 156.2, 149.0, 147.5, 147.0,
42 139.0, 138.7, 138.5, 136.2, 131.5, 131.0, 130.8, 128.1, 126.6, 125.4, 108.1, 25.7, 22.7, 17.6, 5.6.
43 HRMS calcd for C₂₂H₂₀³⁵Cl₂N₆O₃Na ([M+Na]⁺): 509.0869, found: 509.0866; calcd for
44 C₂₂H₂₀³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 511.0834, found: 511.0839; calcd for C₂₂H₂₀³⁷Cl₂N₆O₃Na

1 ([M+Na]⁺): 513.0839, found: 513.0816.

2 ***N*⁵-(2-(methoxycarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-**
3 **methyl-1*H*-pyrazole-3, 5-dicarboxamide 13e.** Yield 24.0%, white solid, mp 206-208 °C; ¹H
4 NMR (400 MHz, CDCl₃): δ 10.08 (s, 1H, CONHAr), 9.64 (s, 1H, NHO), 8.45 (d, 1H, ³*J*_{HH} = 4.4
5 Hz, Ar-H), 7.87-7.85 (m, 2H, Ar-H), 7.39 (dd, 1H, ³*J*_{HH} = 4.6 Hz, ³*J*_{HH} = 7.8 Hz, Ar-H), 7.28 (s,
6 2H, Ar-H), 7.09 (d, 1H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 3.69 (s, 1H, OCH₃), 2.84 (d, H, ³*J*_{HH} = 4.4 Hz,
7 *NHCH*₃), 2.23 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 162.6, 160.7, 156.2, 149.0,
8 147.4, 147.0, 139.1, 139.0, 138.4, 133.7, 131.9, 131.6, 130.9, 128.1, 126.6, 125.4, 108.2, 63.0,
9 25.7, 17.6. HRMS calcd for C₂₀H₁₈³⁵Cl₂N₆O₄Na ([M+Na]⁺): 499.0664, found: 499.0659; calcd
10 for C₂₀H₁₈³⁵Cl³⁷ClN₆O₄Na ([M+Na]⁺): 501.0635, found: 501.0631; calcd for C₂₀H₁₈³⁷Cl₂N₆O₄Na
11 ([M+Na]⁺): 503.0655, found: 503.0608.

12 ***N*⁵-(2-(benzylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-methyl-1*H*-**
13 **pyrazole-3,5-dicarboxamide 13f.** Yield 27.1%, white solid, mp 217-219 °C; ¹H NMR (400 MHz,
14 CDCl₃): δ 10.11 (s, 1H, CONHAr), 8.47 (d, 1H, ³*J*_{HH} = 4.4 Hz, Ar-H), 7.85 (d, 1H, ³*J*_{HH} = 7.6
15 Hz, Ar-H), 7.62 (s, 1H, Ar-H), 7.40 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.30-7.26 (m,
16 7H, Ar-H), 6.98 (d, 1H, ³*J*_{HH} = 4.4 Hz, *NHCH*₃), 6.48 (t, 1H, ³*J*_{HH} = 5.6 Hz, *NHCH*₂), 4.51 (d, 2H,
17 ³*J*_{HH} = 5.6 Hz, *NHCH*₂), 2.96 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.21 (s, 3H, Ar-CH₃). ¹³C NMR (100
18 MHz, CDCl₃): 167.1, 161.6, 157.6, 149.5, 147.7, 146.8, 138.9, 138.8, 138.7, 137.5, 134.4, 132.8,
19 132.6, 129.1, 128.8, 128.7, 127.8, 127.6, 125.9, 125.4, 108.7, 44.1, 29.7, 19.3. HRMS calcd for
20 C₂₆H₂₂³⁵Cl₂N₆O₃Na ([M+Na]⁺): 559.1018, found: 559.1023; calcd for C₂₆H₂₂³⁵Cl³⁷ClN₆O₃Na
21 ([M+Na]⁺): 561.0985, found: 561.0996; calcd for C₂₆H₂₂³⁷Cl₂N₆O₃Na ([M+Na]⁺): 563.0988,
22 found: 563.0977.

23 ***N*⁵-(2-(butylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-methyl-1*H*-p**
24 **yrazole-3, 5-dicarboxamide 13g.** Yield 28.0%, white solid, mp 231-232 °C; ¹H NMR (400 MHz,
25 CDCl₃): δ 10.28 (s, 1H, CONHAr), 8.48 (d, 1H, ³*J*_{HH} = 4.4 Hz, Ar-H), 7.87 (d, 1H, ³*J*_{HH} = 8.0 Hz,
26 Ar-H), 7.82 (s, 1H, Ar-H), 7.41 (dd, 1H, ³*J*_{HH} = 4.4 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.23 (s, 2H, Ar-H),
27 7.02 (d, 1H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 6.38 (t, 1H, ³*J*_{HH} = 5.2 Hz, *NHCH*₃), 3.31 (q, 2H, ³*J*_{HH} = 6.8
28 Hz, *NHCH*₂), 2.91 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.20 (s, 3H, Ar-CH₃), 1.47-1.40 (m, 2H,
29 CH₂CH₂CH₂), 1.32-1.26 (m, 2H, CH₂CH₂CH₃), 0.86 (t, 3H, ³*J*_{HH} = 7.2 Hz, CH₂CH₂CH₃). ¹³C
30 NMR (100 MHz, CDCl₃): 167.3, 161.6, 157.9, 149.5, 147.7, 146.8, 138.9, 138.8, 138.6, 135.4,
31 132.8, 132.2, 130.6, 129.1, 125.8, 125.4, 108.8, 39.9, 31.6, 25.9, 20.1, 18.5, 13.7. HRMS calcd
32 for C₂₃H₂₄³⁵Cl₂N₆O₃Na ([M+Na]⁺): 525.1182, found: 525.1179; calcd for C₂₃H₂₄³⁵Cl³⁷ClN₆O₃Na
33 ([M+Na]⁺): 527.1154, found: 527.1152; calcd for C₂₃H₂₄³⁷Cl₂N₆O₃Na ([M+Na]⁺): 529.1122,
34 found: 529.1130.

35 ***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-benzyl-1**
36 ***H*-pyrazole-3, 5-dicarboxamide 13h.** Yield 32.1%, white solid, mp 234-236 °C; ¹H NMR (400
37 MHz, CDCl₃): δ 10.19 (s, 1H, CONHAr), 8.47 (d, 1H, ³*J*_{HH} = 4.8 Hz, Ar-H), 7.32- (d, 1H, ³*J*_{HH}
38 = 8.0 Hz, Ar-H), 7.80 (s, 1H, Ar-H), 7.39 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.32-7.28
39 (m, 6H, Ar-H, *NHCH*₂), 7.21 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 6.32 (s, 1H, *NHCH*₃), 4.58 (d, 2H,
40 ³*J*_{HH} = 5.6 Hz, *NHCH*₂), 2.89 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.16 (s, 3H, Ar-CH₃). ¹³C NMR (100
41 MHz, CDCl₃): 168.0, 160.9, 157.7, 149.5, 147.6, 146.8, 138.9, 138.7, 137.6 (2C), 134.8, 132.6,
42 132.3, 130.8, 129.1, 128.7, 127.7, 127.5, 125.9, 125.2, 109.0, 43.3, 26.9, 18.5. HRMS calcd for
43 C₂₆H₂₂³⁵Cl₂N₆O₃Na ([M+Na]⁺): 559.1021, found: 559.1023; calcd for C₂₆H₂₂³⁵Cl³⁷ClN₆O₃Na
44 ([M+Na]⁺): 561.0988, found: 561.0996; calcd for C₂₆H₂₂³⁷Cl₂N₆O₃Na ([M+Na]⁺): 563.0992,

found: 563.0977.

***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-isopropyl-1*H*-pyrazole-3, 5-dicarboxamide 13i.** Yield 35.9%, white solid, mp 212-214 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.30 (s, 1H, CONHAr), 8.49 (d, 1H, ³*J*_{HH} = 4.8 Hz, Ar-H), 7.88-7.86 (m, 2H, Ar-H), 7.41 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.23 (s, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 6.83 (d, 1H, ³*J*_{HH} = 8.0 Hz, *NHCH*), 6.45 (d, 1H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 4.16-4.08 (m, 1H, *NHCH*), 2.86 (d, H, ³*J*_{HH} = 4.4 Hz, *NHCH*₃), 2.20 (s, 3H, Ar-CH₃), 1.17 (d, 6H, ³*J*_{HH} = 6.8 Hz, CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 168.0, 160.1, 157.7, 149.6, 148.1, 146.8, 138.9, 138.8, 138.7, 134.9, 132.7, 132.3, 131.0, 129.3, 125.8, 125.3, 108.9, 41.5, 30.3, 22.6, 18.5. HRMS calcd for C₂₂H₂₂³⁵Cl₂N₆O₃Na ([M+Na]⁺): 511.1023, found: 511.1023; calcd for C₂₂H₂₂³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 513.0994, found: 513.0995; calcd for C₂₂H₂₂³⁷Cl₂N₆O₃Na ([M+Na]⁺): 515.1000, found: 515.0972.

***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-*tert*-butyl-1*H*-pyrazole-3, 5-dicarboxamide 13j.** Yield 37.0%, white solid, mp 116-118 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.15 (s, 1H, CONHAr), 8.50 (d, 1H, ³*J*_{HH} = 4.4 Hz, Ar-H), 7.87 (d, 1H, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.60 (s, 1H, Ar-H), 7.41 (dd, 1H, ³*J*_{HH} = 4.6 Hz, ³*J*_{HH} = 7.8 Hz, Ar-H), 7.24 (s, 1H, Ar-H), 7.23 (s, 1H, Ar-H), 6.84 (s, 1H, *NHC*), 6.23 (d, 1H, ³*J*_{HH} = 3.6 Hz, *NHCH*₃), 2.90 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.20 (s, 3H, Ar-CH₃), 1.46 (s, 9H, C(CH₃)₃). ¹³C NMR (100 MHz, CDCl₃): δ 168.1, 160.2, 157.6, 149.5, 148.8, 146.8, 138.8, 138.7, 138.6, 134.2, 132.4, 131.2, 129.2, 125.8, 125.1, 108.5, 51.5, 30.3, 28.8, 26.8, 18.6. HRMS calcd for C₂₃H₂₄³⁵Cl₂N₆O₃Na ([M+Na]⁺): 525.1176, found: 525.1179; calcd for C₂₃H₂₄³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 527.1151, found: 527.1152; calcd for C₂₃H₂₄³⁷Cl₂N₆O₃Na ([M+Na]⁺): 529.1136, found: 529.1130.

***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-phenyl-1*H*-pyrazole-3, 5-dicarboxamide 13k.** Yield 36.3%, white solid, mp 238-240 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.15 (s, 1H, CONHAr), 8.72 (s, 1H, CONH-phenyl), 8.53 (dd, 1H, ⁴*J*_{HH} = 1.4 Hz, ³*J*_{HH} = 4.4, Ar-H), 7.91 (dd, 1H, ⁴*J*_{HH} = 1.6 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.69-7.67 (m, 3H, Ar-H), 7.45 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.36 (t, 2H, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.28- 7.25 (m, 2H, Ar-H), 7.14 (t, 1H, ³*J*_{HH} = 7.4 Hz, Ar-H), 6.10 (d, 1H, ³*J*_{HH} = 4.4 Hz, *NHCH*₃), 2.95 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.21 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 166.1, 159.0, 156.1, 148.9, 147.5, 147.0, 139.1, 138.9, 138.8, 138.4, 136.1, 131.6, 131.1, 130.9, 128.5, 128.2, 126.7, 125.3, 123.8, 120.6, 108.9, 26.1, 17.7. HRMS calcd for C₂₅H₂₀³⁵Cl₂N₆O₃Na ([M+Na]⁺): 545.0858, found: 545.0866; calcd for C₂₅H₂₀³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 547.0827, found: 547.0839; calcd for C₂₅H₂₀³⁷Cl₂N₆O₃Na ([M+Na]⁺): 549.0820, found: 549.0819.

***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-cyclohexyl-1*H*-pyrazole-3, 5-dicarboxamide 13l.** Yield 35.0%, white solid, mp 238-240 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.09 (s, 1H, CONHAr), 8.51 (d, 1H, ³*J*_{HH} = 4.4 Hz, Ar-H), 7.87 (d, 1H, ³*J*_{HH} = 7.6 Hz, Ar-H), 7.70 (s, 1H, Ar-H), 7.42 (dd, 1H, ³*J*_{HH} = 4.4 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.26 (s, 2H, Ar-H), 6.84 (d, 1H, ³*J*_{HH} = 8.4 Hz, *NHCH*), 6.21 (d, 1H, ³*J*_{HH} = 3.2 Hz, *NHCH*₃), 3.92-3.82 (m, 1H, *NHCH*), 2.92 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.21 (s, 3H, Ar-CH₃), 1.99-1.96 (m, 2H, cyclohexyl), 1.74-1.71 (m, 2H, cyclohexyl), 1.64-1.56 (m, 1H, cyclohexyl), 1.38-1.29 (m, 2H, cyclohexyl), 1.26-1.13 (m, 3H, cyclohexyl). ¹³C NMR (100 MHz, DMSO-*d*₆): 166.1, 159.3, 156.2, 150.0, 147.7, 147.0, 139.0, 138.8, 138.5, 136.1, 131.7, 131.1, 130.8, 128.1, 126.6, 125.3, 108.4, 47.9, 32.1, 26.1, 25.1, 25.0, 17.7. HRMS calcd for C₂₅H₂₆³⁵Cl₂N₆O₃Na ([M+Na]⁺): 551.1330, found: 551.1336; calcd for C₂₅H₂₆³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 553.1300, found: 553.1309; calcd

for $C_{25}H_{26}^{37}Cl_2N_6O_3Na$ ($[M+Na]^+$): 555.1291, found: 555.1289.

***N*⁵-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-1-(3-chloropyridin-2-yl)-*N*³-butyl-1*H*-pyrazole-3, 5-dicarboxamide 13m.** Yield 34.0%, white solid, mp 180-182 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.24 (s, 1H, CONHAr), 8.49 (d, 1H, ³*J*_{HH} = 4.4 Hz, Ar-H), 7.87 (d, 1H, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.83 (s, 1H, Ar-H), 7.41 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.25 (s, 1H, Ar-H), 7.23 (s, 1H, Ar-H), 6.98 (t, 1H, ³*J*_{HH} = 5.8 Hz, *NHCH*₂), 6.39 (s, 1H, *NHCH*₃), 3.32 (q, 2H, ³*J*_{HH} = 6.8 Hz, *NHCH*₂), 2.88 (d, 3H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.20 (s, 3H, Ar-CH₃), 1.55-1.47 (m, 2H, CH₂CH₂CH₂), 1.37-1.28 (m, 2H, CH₂CH₂CH₃), 0.91 (t, 3H, ³*J*_{HH} = 7.4 Hz, CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 167.6, 160.7, 159.9, 148.9, 147.9, 147.1, 139.5, 138.4, 138.2, 134.9, 133.0, 132.2, 131.0, 128.8, 125.3, 123.7, 109.8, 61.6, 39.4, 31.2, 20.1, 14.1, 13.7. HRMS calcd for $C_{23}H_{24}^{35}Cl_2N_6O_3Na$ ($[M+Na]^+$): 525.1183, found: 525.1179; calcd for $C_{23}H_{24}^{35}Cl^{37}ClN_6O_3Na$ ($[M+Na]^+$): 527.1155, found: 527.1152; calcd for $C_{23}H_{24}^{37}Cl_2N_6O_3Na$ ($[M+Na]^+$): 529.1139, found: 529.1139.

(5-(2-(methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazol-3-yl)methyl acetate 16a. Yield 35.0%, white solid, mp 108-109 °C; ¹H NMR (400 MHz, CDCl₃): δ 9.94 (s, 1H, CONHAr), 8.47 (dd, 1H, ⁴*J*_{HH} = 1.4 Hz, ³*J*_{HH} = 4.6 Hz, Ar-H), 7.84 (dd, 1H, ⁴*J*_{HH} = 1.2 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.37 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.23 (s, 1H, Ar-H), 7.23 (s, 1H, Ar-H), 7.11 (s, 1H, Ar-H), 6.15 (d, 1H, ³*J*_{HH} = 4.4 Hz, *NHCH*₃), 5.25 (s, 2H, Ar-CH₂), 2.95 (d, H, ³*J*_{HH} = 4.8 Hz, *NHCH*₃), 2.20 (s, 3H, Ar-CH₃), 2.16 (s, 3H, CH₃CO). ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 168.5, 157.8, 149.7, 149.2, 146.8, 138.8, 138.4, 138.0, 133.6, 132.3, 132.1, 131.1, 129.0, 125.5, 124.7, 108.5, 59.8, 26.8, 20.9, 18.5. HRMS calcd for $C_{21}H_{19}^{35}Cl_2N_5O_4Na$ ($[M+Na]^+$): 498.0706, found: 498.0706; calcd for $C_{21}H_{19}^{35}Cl^{37}ClN_5O_4Na$ ($[M+Na]^+$): 500.0672, found: 500.0679; calcd for $C_{21}H_{19}^{37}Cl_2N_5O_4Na$ ($[M+Na]^+$): 502.0661, found: 500.0655.

(5-(2-(Isopropylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazol-3-yl)methyl acetate 16b. Yield 37.8%, white solid, mp 180-182 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.02 (s, 1H, CONHAr), 8.48 (dd, 1H, ⁴*J*_{HH} = 1.4 Hz, ³*J*_{HH} = 4.6 Hz, Ar-H), 7.83 (dd, 1H, ⁴*J*_{HH} = 1.6 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.36 (dd, 1H, ³*J*_{HH} = 4.8 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.24 (d, 1H, ⁴*J*_{HH} = 2.4 Hz, Ar-H), 7.20 (d, 1H, ³*J*_{HH} = 2.0 Hz, Ar-H), 7.13 (s, 1H, Ar-H), 6.15 (d, 1H, ³*J*_{HH} = 4.4 Hz, *NHCH*₃), 5.24 (s, 2H, Ar-CH₂), 4.22-4.11 (m, 1H, *NHCH*), 2.19 (s, 3H, Ar-CH₃), 2.15 (s, 3H, COCH₃). ¹³C NMR (100 MHz, CDCl₃): δ 170.7, 167.1, 157.8, 149.8, 149.2, 146.8, 138.9, 138.7, 138.0, 134.0, 132.4, 132.3, 131.2, 129.1, 125.5, 124.5, 108.2, 59.8, 42.4, 22.3, 20.9, 18.6. HRMS calcd for $C_{23}H_{23}^{35}Cl_2N_5O_4Na$ ($[M+Na]^+$): 502.1058, found: 502.1054; calcd for $C_{23}H_{23}^{35}Cl^{37}ClN_5O_4Na$ ($[M+Na]^+$): 504.1034, found: 504.1027; calcd for $C_{23}H_{23}^{37}Cl_2N_5O_4Na$ ($[M+Na]^+$): 506.0983, found: 506.1005.

(5-(2-(*tert*-Butylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazol-3-yl)methyl acetate 16c. Yield 36.5%, white solid, mp 91-93 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.23 (s, 1H, CONHAr), 8.45 (dd, 1H, ⁴*J*_{HH} = 1.2 Hz, ³*J*_{HH} = 4.8 Hz, Ar-H), 7.83 (dd, 1H, ⁴*J*_{HH} = 1.2 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.47 (s, 1H, Ar-H), 7.35 (dd, 1H, ³*J*_{HH} = 4.4 Hz, ³*J*_{HH} = 8.0 Hz, Ar-H), 7.08 (s, 2H, Ar-H), 7.13 (s, 1H, Ar-H), 6.07 (s, 1H, *NHCH*₃), 5.25 (s, 2H, Ar-CH₂), 4.22-4.11 (m, 1H, *NHCH*), 2.13 (s, 6H, Ar-CH₃, COCH₃), 1.32 (s, 9H, C(CH₃)₃). ¹³C NMR (100 MHz, CDCl₃): δ 170.6, 167.7, 158.6, 150.0, 149.1, 146.7, 139.3, 138.6, 137.8, 136.8, 132.8, 131.7, 130.0, 129.2, 125.5, 124.3, 108.3, 59.9, 52.3, 28.4, 20.9, 18.3. HRMS calcd for $C_{24}H_{25}^{35}Cl_2N_5O_4Na$ ($[M+Na]^+$): 540.1180, found: 540.1176; calcd for $C_{24}H_{25}^{35}Cl^{37}ClN_5O_4Na$

1 ([M+Na]⁺): 542.1150, found: 542.1149; calcd for C₂₄H₂₅³⁷Cl₂N₅O₄Na ([M+Na]⁺): 544.1112,
2 found: 544.1128.

3 **(5-(2-(Cyclopropylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16d.** Yield 37.0%, white solid, mp 191-193 °C; ¹H NMR
4 (400 MHz, CDCl₃): δ 9.95 (s, 1H, CONHAr), 8.47 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H), 7.84 (d, 1H, ³J_{HH}
5 =8.0 Hz, Ar-H), 7.37 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.25 (s, 1H, Ar-H), 7.17 (s, 1H,
6 Ar-H), 7.15 (s, 1H, Ar-H), 6.28 (s, 1H, NHCH), 5.25 (s, 2H, Ar-CH₂), 2.84-2.79 (m, 1H, NHCH),
7 2.18 (s, 3H, Ar-CH₃), 2.15 (s, 3H, COCH₃), 0.86 (q, 2H, ³J_{HH}=6.2 Hz, cyclopropyl), 0.56 (q, 2H,
8 ³J_{HH}=6.6 Hz, cyclopropyl). ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 169.4, 157.6, 149.7, 149.2,
9 146.8, 138.8, 138.7, 138.0, 133.0, 132.6, 132.2, 131.3, 129.0, 125.5, 124.7, 108.4, 59.7, 23.1,
10 20.9, 18.7, 6.5. HRMS calcd for C₂₃H₂₁³⁵Cl₂N₅O₄Na ([M+Na]⁺): 524.0867, found: 524.0863;
11 calcd for C₂₃H₂₁³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 526.0838, found: 526.0836; calcd for
12 C₂₃H₂₁³⁷Cl₂N₅O₄Na ([M+Na]⁺): 528.0805, found: 528.0814.

13 **(5-(2-(Methoxycarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16e.** Yield 35.0%, white solid, mp 100-102 °C; ¹H NMR (400
14 MHz, CDCl₃): δ 9.50 (s, 1H, CONHAr), 8.88 (s, 1H, CONHO), 8.46 (dd, 1H, ⁴J_{HH}=1.4, ³J_{HH}
15 =4.6 Hz, Ar-H), 7.84 (dd, 1H, ⁴J_{HH}=1.6 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.37 (dd, 1H, ³J_{HH}=4.8 Hz,
16 ³J_{HH}=8.0 Hz, Ar-H), 7.29 (d, 1H, ⁴J_{HH}=2.4 Hz, Ar-H), 7.21 (s, 1H, Ar-H), 7.10 (s, 1H, Ar-H),
17 5.23 (s, 2H, Ar-CH₂), 3.79 (s, 1H, NHCH), 2.19 (s, 3H, Ar-CH₃), 2.15 (s, 3H, COCH₃). ¹³C NMR
18 (100 MHz, DMSO-*d*₆): 170.1, 162.7, 156.5, 149.2, 148.2, 147.2, 146.8, 139.0, 138.2, 133.7,
19 132.1, 131.6, 130.8, 127.9, 126.1, 125.4, 108.1, 63.0, 59.2, 20.6, 17.6. HRMS calcd for
20 C₂₁H₁₉³⁵Cl₂N₅O₅Na ([M+Na]⁺): 514.0660, found: 514.0655; calcd for C₂₁H₁₉³⁵Cl³⁷ClN₅O₅Na
21 ([M+Na]⁺): 516.0627, found: 516.0628; calcd for C₂₁H₁₉³⁷Cl₂N₅O₅Na ([M+Na]⁺): 518.0604,
22 found: 518.0606.

23 **(5-(2-(Benzylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16f.** Yield 39.0%, white solid, mp 79-81 °C; ¹H NMR (400
24 MHz, CDCl₃): δ 9.95 (s, 1H, CONHAr), 8.46 (d, 1H, ³J_{HH}=4.8 Hz, Ar-H), 7.84 (d, 1H, ³J_{HH}=8.4
25 Hz, Ar-H), 7.37-7.24 (m, 8H, Ar-H), 7.09 (s, 1H, Ar-H), 6.44 (t, 1H, ³J_{HH}=1.2 Hz, NHCH₂), 5.24
26 (s, 2H, Ar-CH₂), 4.55 (d, 1H, ³J_{HH}=5.6 Hz, NHCH₂), 2.20 (s, 3H, Ar-CH₃), 2.13 (s, 3H, COCH₃).
27 ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 167.9, 157.6, 149.7, 149.1, 146.8, 138.8 (2C), 138.0,
28 137.2, 133.1, 132.7, 132.2, 131.4, 129.0, 128.8, 127.8, 127.7, 125.5, 124.6, 108.4, 59.8, 44.1,
29 20.9, 18.7. HRMS calcd for C₂₇H₂₃³⁵Cl₂N₅O₄Na ([M+Na]⁺): 574.1025, found: 574.1019; calcd
30 for C₂₇H₂₃³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 576.0995, found: 576.0993; calcd for C₂₇H₂₃³⁷Cl₂N₅O₄Na
31 ([M+Na]⁺): 578.0967, found: 578.0975.

32 **(5-(2-(Methylcarbamoyl)-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16g.** Yield 41.3%, white solid, mp 196-198 °C; ¹H NMR (400 MHz,
33 CDCl₃): δ 10.08 (s, 1H, CONHAr), 8.47 (dd, 1H, ³J_{HH}=4.8 Hz, Ar-H), 7.84 (dd, 1H, ⁴J_{HH}=1.2 Hz,
34 ³J_{HH}=8.0 Hz, Ar-H), 7.36 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.31-7.24 (m, 2H, Ar-H),
35 7.15 (t, 1H, ³J_{HH}=7.8 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 6.12 (d, 1H, ³J_{HH}=4.4, NHCH₃), 5.25 (s, 2H,
36 Ar-CH₂), 2.95 (d, 3H, ³J_{HH}=4.8 Hz, NHCH₃), 2.23 (s, 3H, Ar-CH₃), 2.16 (s, 3H, COCH₃). ¹³C
37 NMR (100 MHz, CDCl₃): δ 170.8, 169.5, 157.1, 149.7, 149.1, 146.8, 138.8, 138.5, 136.3, 133.4,
38 130.2, 129.1, 126.4, 125.5, 124.6, 124.5, 108.1, 59.8, 26.7, 20.9, 19.0. HRMS calcd for
39 C₂₁H₂₀³⁵ClN₅O₄Na ([M+Na]⁺): 464.1092, found: 464.1096; calcd for C₂₁H₂₀³⁷ClN₅O₄Na
40 ([M+Na]⁺): 466.1064, found: 466.1070.

(5-(2-(Isopropylcarbamoyl)-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16h. Yield 43.0%, white solid, mp 138-140 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.14 (s, 1H, CONHAr), 8.47 (dd, 1H, ⁴J_{HH}=1.4 Hz, ³J_{HH}=4.6 Hz, Ar-H), 7.83 (dd, 1H, ⁴J_{HH}=1.2 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.36 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.29-7.24 (m, 2H, Ar-H), 7.15 (t, 1H, ³J_{HH}=7.6 Hz, Ar-H), 7.07 (s, 1H, Ar-H), 5.92 (d, 1H, ³J_{HH}=7.6 Hz, NHCH), 5.24 (s, 2H, Ar-CH₂), 4.23-4.15 (m, 1H, NHCH), 2.22 (s, 3H, Ar-CH₃), 2.16 (s, 3H, COCH₃), 1.22 (d, 6H, ³J_{HH}=6.4 Hz, CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 168.9, 157.3, 149.7, 149.1, 146.8, 138.8, 138.5, 136.6, 133.2, 132.8, 129.1, 126.3, 125.4, 125.3, 124.5, 108.1, 59.8, 22.4, 20.9, 18.8, 18.5. HRMS calcd for C₂₃H₂₄³⁵ClN₅O₄Na ([M+Na]⁺): 492.1414, found: 492.1409; calcd for C₂₃H₂₄³⁷ClN₅O₄Na ([M+Na]⁺): 494.1395, found: 494.1384.

(5-(2-(Cyclopropylcarbamoyl)-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16i. Yield 42.5%, white solid, mp 186-188 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.18 (s, 1H, CONHAr), 8.47 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H), 7.84 (d, 1H, ³J_{HH}=8.0 Hz, Ar-H), 7.36 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=8.0 Hz, Ar-H), 7.27-7.25 (m, 1H, Ar-H), 7.12-7.07 (m, 3H, Ar-H), 7.07 (s, 1H, Ar-H), 6.42 (s, 1H, NHCH), 5.25 (s, 2H, Ar-CH₂), 2.77-2.73 (m, 1H, NHCH), 2.21 (s, 3H, Ar-CH₃), 2.16 (s, 3H, COCH₃), 0.82 (q, 2H, ³J_{HH}=6.4, cyclopropyl), 0.52 (q, 2H, ³J_{HH}=6.8, cyclopropyl). ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 170.4, 157.1, 149.8, 149.1, 146.8, 138.7, 138.3, 136.3, 133.4, 133.3, 129.8, 129.2, 126.3, 125.5, 124.9, 108.1, 59.8, 22.8, 20.9, 18.9, 6.4. HRMS calcd for C₂₃H₂₂³⁵ClN₅O₄Na ([M+Na]⁺): 490.1247, found: 490.1253; calcd for C₂₃H₂₂³⁷ClN₅O₄Na ([M+Na]⁺): 492.1210, found: 492.1227.

(5-(2-(Propylcarbamoyl)-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl acetate 16j. Yield 38.0%, white solid, mp 159-161 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.12 (s, 1H, CONHAr), 8.47 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H), 7.83 (d, 1H, ³J_{HH}=8.0 Hz, Ar-H), 7.35 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=7.6 Hz, Ar-H), 7.31-7.26 (m, 2H, Ar-H), 7.16 (t, 1H, ³J_{HH}=7.4 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 6.11 (br s, 1H, NHCH₂), 5.24 (s, 2H, Ar-CH₂), 3.35 (q, 2H, ³J_{HH}=7.0 Hz, NHCH₂CH₂), 2.23 (s, 3H, Ar-CH₃), 2.16 (s, 3H, COCH₃), 1.62-1.57 (m, 2H, CH₂CH₂CH₃), 0.96 (t, 3H, ³J_{HH}=7.4 Hz, CH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 169.0, 157.1, 149.7, 149.1, 146.8, 138.8, 138.5, 136.4, 133.4, 133.3, 130.8, 129.1, 126.4, 125.4, 124.6, 108.1, 59.8, 41.7, 22.6, 20.9, 18.9, 11.4. HRMS calcd for C₂₃H₂₄³⁵ClN₅O₄Na ([M+Na]⁺): 492.1408, found: 492.1409; calcd for C₂₃H₂₄³⁷ClN₅O₄Na ([M+Na]⁺): 494.1382, found: 494.1384.

(5-(2-(Methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl methanesulfonate 16k. Yield 86.0%, white solid, mp 160-162 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.15 (s, 1H, CONHAr), 8.46 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H), 7.86 (d, 1H, ³J_{HH}=8.0 Hz, Ar-H), 7.39 (dd, 1H, ³J_{HH}=4.8 Hz, ³J_{HH}=7.6 Hz, Ar-H), 7.34 (s, 1H, Ar-H), 7.15 (s, 1H, Ar-H), 7.14 (s, 1H, Ar-H), 6.27 (s, 1H, NHCH₃), 5.39 (s, 2H, Ar-CH₂), 3.06 (s, 3H, SO₂CH₃), 2.91 (d, 3H, ³J_{HH}=4.0 Hz, NHCH₃), 2.13 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 168.6, 157.5, 149.6, 147.1, 146.9, 138.8, 138.5, 137.6, 133.8, 131.9, 130.8, 130.5, 128.9, 125.7, 124.8, 109.0, 64.9, 38.1, 26.9, 18.2. HRMS calcd for C₂₀H₁₉³⁵Cl₂N₅O₅Na ([M+Na]⁺): 534.0374, found: 534.0376; calcd for C₂₀H₁₉³⁵Cl³⁷ClN₅O₅Na ([M+Na]⁺): 536.0345, found: 536.0348; calcd for C₂₀H₁₉³⁷Cl₂N₅O₅Na ([M+Na]⁺): 538.0308, found: 538.0322.

(5-(2-(Methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)methyl 4-methylbenzenesulfonate 16l. Yield 80.0%, white solid, mp 170-172 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.09 (s, 1H, CONHAr), 8.42 (d, 1H, ³J_{HH}=4.4 Hz, Ar-H),

1 7.85-7.81 (m, 3H, Ar-H), 7.35-7.28 (m, 3H, Ar-H), 7.13 (s, 2H, Ar-H), 6.38 (d, 1H, $^3J_{\text{HH}}=4.4$ Hz,
2 NHCH_3), 5.19 (s, 2H, Ar-CH₂), 2.89 (d, 3H, $^3J_{\text{HH}}=4.4$ Hz, NHCH_3), 2.43 (s, 3H, Ar-CH₃), 2.12 (s,
3 3H, Ar-CH₃). ^{13}C NMR (100 MHz, CDCl_3): δ 168.5, 157.5, 149.5, 147.0, 146.8, 145.1, 138.8,
4 138.5, 138.4, 132.8, 132.3, 132.2, 131.1, 130.0, 129.9, 129.0, 128.2, 125.6, 124.6, 108.6, 65.2,
5 26.9, 21.7, 18.5. HRMS calcd for $\text{C}_{26}\text{H}_{23}^{35}\text{Cl}_2\text{N}_5\text{O}_5\text{SNa}$ ($[\text{M}+\text{Na}]^+$): 610.0690, found: 610.0689;
6 calcd for $\text{C}_{26}\text{H}_{23}^{35}\text{Cl}^{37}\text{ClN}_5\text{O}_5\text{SNa}$ ($[\text{M}+\text{Na}]^+$): 612.0669, found: 612.0663; calcd for
7 $\text{C}_{26}\text{H}_{23}^{37}\text{Cl}_2\text{N}_5\text{O}_5\text{SNa}$ ($[\text{M}+\text{Na}]^+$): 614.0666, found: 614.0641.

8 **(5-(2-(Methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1**
9 **H-pyrazol-3-yl)methyl 2,2,2-trifluoroacetate 16m.** Yield 90.2%, white solid, mp 213-215 °C; ^1H
10 NMR (400 MHz, CDCl_3): δ 10.15 (s, 1H, CONHAr), 8.45 (d, 1H, $^3J_{\text{HH}}=4.0$ Hz, Ar-H), 7.85
11 (d, 1H, $^3J_{\text{HH}}=8.0$ Hz, Ar-H), 7.38 (dd, 1H, $^3J_{\text{HH}}=4.8$ Hz, $^3J_{\text{HH}}=8.0$ Hz, Ar-H), 7.32 (s, 1H, Ar-H),
12 7.13 (s, 1H, Ar-H), 7.11 (s, 1H, Ar-H), 6.30 (s, 1H, NHCH_3), 5.50 (s, 2H, Ar-CH₂), 2.89 (d, 3H,
13 $^3J_{\text{HH}}=4.4$ Hz, NHCH_3), 2.12 (s, 3H, Ar-CH₃). ^{13}C NMR (100 MHz, CDCl_3): δ 169.0, 158.3,
14 158.0, 154.6, 149.5, 146.5, 139.0, 137.6, 136.9, 133.7, 131.9, 131.6, 130.0, 129.3, 125.7, 125.2,
15 112.2, 108.2, 58.2, 27.0, 17.8. HRMS calcd for $\text{C}_{21}\text{H}_{16}^{35}\text{Cl}_2\text{F}_3\text{N}_5\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$): 552.0416,
16 found: 552.0424; calcd for $\text{C}_{21}\text{H}_{16}^{35}\text{Cl}^{37}\text{ClF}_3\text{N}_5\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$): 554.0383, found: 554.0396;
17 calcd for $\text{C}_{21}\text{H}_{16}^{37}\text{Cl}_2\text{F}_3\text{N}_5\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$): 556.0347, found: 556.0374.

18 **(5-(2-(Methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1**
19 **H-pyrazol-3-yl)methyl 4-chlorobutanoate 16n.** Yield 84.0%, white solid, mp 72-74 °C; ^1H
20 NMR (400 MHz, CDCl_3): δ 9.91 (s, 1H, CONHAr), 8.47 (d, 1H, $^3J_{\text{HH}}=4.4$ Hz, Ar-H), 7.85 (d,
21 1H, $^3J_{\text{HH}}=7.6$ Hz, Ar-H), 7.37 (dd, 1H, $^3J_{\text{HH}}=4.8$ Hz, $^3J_{\text{HH}}=7.8$ Hz, Ar-H), 7.29 (s, 1H, Ar-H),
22 7.25 (s, 1H, Ar-H), 7.07 (s, 1H, Ar-H), 6.10 (d, 1H, $^3J_{\text{HH}}=5.2$ Hz, NHCH_3), 5.27 (s, 2H, Ar-CH₂),
23 3.63 (t, 2H, $^3J_{\text{HH}}=6.4$ Hz, CH_2Cl), 2.95 (d, 3H, $^3J_{\text{HH}}=4.8$ Hz, NHCH_3), 2.61 (t, 2H, $^3J_{\text{HH}}=7.2$ Hz,
24 COCH_2), 2.21 (s, 3H, Ar-CH₃), 2.19-2.13 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2$). ^{13}C NMR (100 MHz, CDCl_3): δ
25 172.4, 168.6, 157.7, 149.7, 149.0, 146.9, 138.9, 138.6, 138.1, 133.5, 132.5, 132.2, 131.2, 129.0,
26 125.6, 124.7, 108.5, 59.9, 44.1, 31.2, 27.6, 27.0, 18.7. HRMS calcd for $\text{C}_{23}\text{H}_{22}^{35}\text{Cl}_3\text{N}_5\text{O}_4\text{Na}$
27 ($[\text{M}+\text{Na}]^+$): 560.0626, found: 560.0629; calcd for $\text{C}_{23}\text{H}_{22}^{35}\text{Cl}_2^{37}\text{ClN}_5\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$): 562.0625,
28 found: 562.0602; calcd for $\text{C}_{23}\text{H}_{22}^{35}\text{Cl}^{37}\text{Cl}_2\text{N}_5\text{O}_4\text{Na}$ ($[\text{M}+\text{Na}]^+$): 564.0569, found: 564.0576.

29 **(5-(4-Chloro-2-methyl-6-(methylcarbamoyl)phenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1**
30 **H-pyrazol-3-yl)methyl 2-acetoxyacetate 16o.** Yield 83.6%, white solid, mp 89-91 °C; ^1H NMR
31 (400 MHz, CDCl_3): δ 10.00 (s, 1H, CONHAr), 8.46 (d, 1H, $^3J_{\text{HH}}=4.4$ Hz, Ar-H), 7.84 (d, 1H,
32 $^3J_{\text{HH}}=8.0$ Hz, Ar-H), 7.36 (dd, 1H, $^3J_{\text{HH}}=4.4$ Hz, $^3J_{\text{HH}}=8.0$ Hz, Ar-H), 7.21 (s, 1H, Ar-H), 7.19 (s,
33 1H, Ar-H), 7.18 (s, 1H, Ar-H), 6.26 (s, 1H, $^3J_{\text{HH}}=4.4$ Hz, NHCH_3), 5.34 (s, 2H, Ar-CH₂), 4.70 (s,
34 2H, CH_2O), 2.92 (d, 3H, $^3J_{\text{HH}}=4.4$ Hz, NHCH_3), 2.18 (s, 3H, Ar-CH₃), 2.17 (s, 3H, COCH_3). ^{13}C
35 NMR (100 MHz, CDCl_3): δ 170.3, 168.5, 167.7, 157.5, 149.6, 148.4, 146.8, 138.8, 138.6, 138.2,
36 133.3, 132.6, 132.2, 131.3, 129.0, 125.6, 124.6, 108.5, 60.7, 60.4, 26.9, 20.5, 18.6. HRMS calcd
37 for $\text{C}_{23}\text{H}_{21}^{35}\text{Cl}_2\text{N}_5\text{O}_6\text{Na}$ ($[\text{M}+\text{Na}]^+$): 556.0767, found: 556.0761; calcd for $\text{C}_{23}\text{H}_{21}^{35}\text{Cl}^{37}\text{ClN}_5\text{O}_6\text{Na}$
38 ($[\text{M}+\text{Na}]^+$): 558.0748, found: 558.0735; calcd for $\text{C}_{23}\text{H}_{21}^{37}\text{Cl}_2\text{N}_5\text{O}_6\text{Na}$ ($[\text{M}+\text{Na}]^+$): 560.0723,
39 found: 560.0714.

40 **(5-(2-(Methylcarbamoyl)-4-chloro-6-methylphenylcarbamoyl)-1-(3-chloropyridin-2-yl)-1H**
41 **-pyrazol-3-yl)methyl benzoate 16p.** Yield 87.5%, white solid, mp 204-206 °C; ^1H NMR (400
42 MHz, CDCl_3): δ 10.02 (s, 1H, CONHAr), 8.45 (d, 1H, $^3J_{\text{HH}}=4.4$ Hz, Ar-H), 8.11 (d, 1H, $^3J_{\text{HH}}=8.0$
43 Hz, Ar-H), 7.83 (s, 1H, $^3J_{\text{HH}}=8.0$ Hz, Ar-H), 7.57 (t, 1H, $^3J_{\text{HH}}=7.4$ Hz, Ar-H), 7.44 (t, 1H, $^3J_{\text{HH}}$
44 $=7.6$ Hz, Ar-H), 7.35 (dd, 1H, $^3J_{\text{HH}}=4.8$ Hz, $^3J_{\text{HH}}=8.0$ Hz, Ar-H), 7.32 (s, 1H, Ar-H), 7.16 (s, 1H,

Ar-H), 7.13 (s, 1H, Ar-H), 6.29 (s, 1H, *NHCH*₃), 5.50 (s, 2H, Ar-CH₂), 2.83 (d, 3H, ³*J*_{HH}=4.0, *NHCH*₃), 2.15 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 168.4, 166.3, 157.7, 149.7, 149.3, 146.8, 138.8, 138.7, 138.2, 133.3, 133.2, 132.6, 132.2, 131.4, 129.9, 129.8, 129.0, 128.4, 125.5, 124.5, 108.5, 60.2, 26.8, 18.7. HRMS calcd for C₂₆H₂₁³⁵Cl₂N₅O₄Na ([M+Na]⁺): 560.0860, found: 560.0863; calcd for C₂₆H₂₁³⁵Cl³⁷ClN₅O₄Na ([M+Na]⁺): 562.0843, found: 562.0837; calcd for C₂₆H₂₁³⁷Cl₂N₅O₄Na ([M+Na]⁺): 564.0843, found: 564.0818.

***N*-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-3-(acetamidomethyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamide 21a.** Yield 91.0%, white solid, mp 232-234 °C; ¹H NMR (400 MHz, CDCl₃): δ 9.90 (s, 1H, CONHAr), 8.48 (d, 1H, ³*J*_{HH}=6.0 Hz, Ar-H), 7.84 (d, 1H, ³*J*_{HH}=8.0 Hz, Ar-H), 7.37 (dd, 1H, ³*J*_{HH}=4.8 Hz, ³*J*_{HH}=8.0 Hz, Ar-H), 7.26 (s, 1H, Ar-H), 7.24 (s, 1H, Ar-H), 6.99 (s, 1H, Ar-H), 6.19 (br s, 1H, CONH), 6.13 (br s, 1H, CONH), 4.60 (d, 2H, ³*J*_{HH}=5.2 Hz, CH₂*NH*), 2.94 (d, 2H, ³*J*_{HH}=4.8 Hz, *NHCH*₃), 2.19 (s, 3H, COCH₃), 2.05 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 169.3, 166.3, 156.7, 151.4, 149.4, 146.8, 139.0, 138.8, 138.1, 135.9, 132.0, 131.1, 130.6, 127.9, 125.9, 125.2, 107.0, 36.1, 26.1, 22.5, 17.7. HRMS calcd for C₂₁H₂₀³⁵Cl₂N₆O₃Na ([M+Na]⁺): 497.0867, found: 497.0866; calcd for C₂₁H₂₀³⁵Cl³⁷ClN₆O₃Na ([M+Na]⁺): 499.0835, found: 499.0838; calcd for C₂₁H₂₀³⁷Cl₂N₆O₃Na ([M+Na]⁺): 501.0802, found: 501.0815.

***N*-(4-chloro-2-methyl-6-(methylcarbamoyl)phenyl)-1-(3-chloropyridin-2-yl)-3-(methylsulfonamidomethyl)-1*H*-pyrazole-5-carboxamide 21b.** Yield 80.5%, white solid, mp 110-112 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.30 (s, 1H, CONHAr), 8.56 (dd, 1H, ⁴*J*_{HH}=1.6 Hz, ³*J*_{HH}=4.8 Hz, Ar-H), 7.86 (dd, 1H, ⁴*J*_{HH}=1.6 Hz, ³*J*_{HH}=8.0 Hz, Ar-H), 7.42 (dd, 1H, ³*J*_{HH}=4.8 Hz, ³*J*_{HH}=8.0 Hz, Ar-H), 7.31 (s, 1H, Ar-H), 7.08 (s, 1H, Ar-H), 7.07 (s, 1H, Ar-H), 6.44 (br s, 1H, CH₂*NH*), 6.03 (d, 1H, ³*J*_{HH}=4.8 Hz, *NHCH*₃), 4.46 (d, 2H, ³*J*_{HH}=6.8 Hz, CH₂), 3.00 (s, 3H, SO₂CH₃), 2.89 (d, 3H, ³*J*_{HH}=4.8 Hz, *NHCH*₃), 2.08 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 166.3, 156.6, 150.6, 149.3, 146.9, 139.0, 138.8, 138.3, 135.9, 131.9, 131.1, 130.7, 127.8, 126.1, 125.2, 107.2, 40.0, 39.9, 26.1, 17.7. HRMS calcd for C₂₀H₂₀³⁵Cl₂N₆O₄SNa ([M+Na]⁺): 533.0537, found: 533.0536; calcd for C₂₀H₂₀³⁵Cl³⁷ClN₆O₄SNa ([M+Na]⁺): 535.0505, found: 535.0508; calcd for C₂₀H₂₀³⁷Cl₂N₆O₄SNa ([M+Na]⁺): 537.0493, found: 537.0482.

***N*-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-3-((2,2,2-trifluoroacetamido)methyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamide 21c.** Yield 88.0%, white solid, mp 239-241 °C; ¹H NMR (400 MHz, DMSO-*d*₆): δ 10.23 (s, 1H, CONHAr), 10.18 (t, 1H, ³*J*_{HH}=6.4 Hz, CF₃CONH), 8.47 (d, 1H, ³*J*_{HH}=3.6 Hz, Ar-H), 8.23 (d, 1H, ³*J*_{HH}=4.0 Hz, *NHCH*₃), 8.13 (d, 1H, ³*J*_{HH}=7.2 Hz, Ar-H), 7.57 (dd, 1H, ³*J*_{HH}=4.8 Hz, ³*J*_{HH}=8.0 Hz, Ar-H), 7.46 (d, 1H, ⁴*J*_{HH}=1.6 Hz, Ar-H), 7.32 (d, 1H, ⁴*J*_{HH}=2.0 Hz, Ar-H), 7.19 (s, 1H, Ar-H), 4.50 (d, 2H, ³*J*_{HH}=5.6 Hz, Ar-CH₂), 2.65 (d, 3H, ³*J*_{HH}=4.8 Hz, *NHCH*₃), 2.15 (s, 3H, Ar-CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 166.3, 156.7, 156.6, 149.4, 149.2, 146.9, 139.0, 138.8, 138.4, 136.1, 131.8, 131.1, 130.7, 127.8, 126.1, 125.2, 116.0, 106.9, 36.7, 26.0, 17.7. HRMS calcd for C₂₁H₁₇³⁵Cl₂F₃N₆O₃Na ([M+Na]⁺): 551.0584, found: 551.0584; calcd for C₂₁H₁₇³⁵Cl³⁷ClF₃N₆O₃Na ([M+Na]⁺): 553.0553, found: 553.0556; calcd for C₂₁H₁₇³⁷Cl₂F₃N₆O₃Na ([M+Na]⁺): 555.0541, found: 555.0534.

***N*-(2-(methylcarbamoyl)-4-chloro-6-methylphenyl)-3-((benzamido)methyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamide 21d.** Yield 84.6%, white solid, mp 254-256 °C; ¹H NMR (400 MHz, DMSO): δ 10.18 (s, 1H, CONHAr), 8.22 (t, 1H, ³*J*_{HH}=5.8 Hz, CONHCH₂), 8.46 (d, 1H, ³*J*_{HH}=4.8 Hz, Ar-H), 8.21 (d, 1H, ³*J*_{HH}=4.4 Hz, *NHCH*₃), 7.56-7.53 (m, 2H, Ar-H), 7.49 (m,

1 2H, Ar-H), 7.43 (s, 1H, Ar-H), 7.30 (d, 1H, $^4J_{\text{HH}}=2.0$ Hz, Ar-H), 7.20 (s, 1H, Ar-H), 4.57 (d, 2H,
2 $^3J_{\text{HH}}=5.6$ Hz, Ar-CH₂), 2.63 (d, 3H, $^3J_{\text{HH}}=4.4$ Hz, NHCH₃), 2.13 (s, 3H, Ar-CH₃). ¹³C NMR (100
3 MHz, DMSO-*d*₆): δ 166.2 (2C), 156.7, 151.6, 149.4, 146.8, 138.9, 138.8, 138.1, 136.1, 134.1,
4 131.9, 131.4, 131.0, 130.6, 128.3, 127.9, 127.3, 125.9, 125.2, 107.0, 36.7, 26.0, 17.7. HRMS calcd
5 for C₂₆H₂₂³⁵Cl₂N₆O₃Na ([M+Na]⁺): 559.1024, found: 559.1023; calcd for C₂₆H₂₂³⁵Cl³⁷ClN₆O₃Na
6 ([M+Na]⁺): 561.0999, found: 561.0996; calcd for C₂₆H₂₂³⁷Cl₂N₆O₃Na ([M+Na]⁺): 563.1061,
7 found: 563.0977.