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Increased dipeptoid diversity resulting from post-condensational manipulation of the Ugi reaction products

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Characterization data for the compounds synthesized in this work:

N-*[1-(4-Isopropylphenyl)-2-(2-methoxyethylamino)-2-oxoethyl]*-N-*(4-methoxybenzyl)-5-(4-methylphenyl)-1*H-*pyrazole-3-carboxamide* **7a**. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 13.29 (s, 1H), 7.54- 7.80 (m, 2H), 7.00-7.34 (m, 6H), 6.75-6.94 (m, 3H), 6.53-6.68 (m, 2H), 6.20 (s, 1H), 5.07 (s, 1H), 4.57 (m, 1H), 3.67 (s, 3H), 3.15-3.45 (m, 6H), 2.97 (m, 2H), 2.84 (m, 1H), 2.34 (s, 3H), 1.18 (d, J = 6.7 Hz, 6H); ^{13}C NMR (d_6-DMSO, 75 Hz) δ 169.5, 164.5, 157.4, 148.0, 142.8, 137.8, 134.0, 132.8, 130.9, 129.7, 129.5, 128.5, 127.8, 126.0, 125.8, 125.1, 112.8, 104.6, 70.3, 63.8, 61.8, 57.8, 54.8, 49.6, 47.4, 33.0, 23.8, 23.6, 20.8. Found (%): C, 71.70; H, 7.02; N, 10.16. Calc. for $C_{33}H_{38}N_4O_4$ (%): C, 71.48; H, 6.91; N, 10.10.

N-*[2-Benzylamino-1-(4-isopropylphenyl)-2-oxoethyl]*-N-*(4-methoxybenzyl)-5-(4-methylphenyl)-1*H-*pyrazole-3-carboxamide* **7b**. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 13.35 (s, 1H), 8.19 (s, 1H), 7.51- 7.70 (m, 2H), 7.02-7.35 (m, 11H), 6.75-6.95 (m, 3H), 6.50-6.67 (m, 2H), 4.57 (m, 1H), 4.31 (d, J = 5.5 Hz, 2H), 3.65 (s, 3H), 3.59 (s, 1H), 2.8 (m, 1H), 2.34 (s, 3H), 1.20-1.30 (m, 1H), 1.18 (d, J = 7.0 Hz, 6H); ^{13}C NMR (d_6-DMSO, 75 Hz) δ 168.8, 164.2, 157.8, 154.8, 148.7, 138.0, 132.7, 131.3, 129.9, 129.7, 129.5, 128.5, 127.8, 127.5, 127.3, 126.7, 126.5, 125.8, 125.5, 114.1, 113.1, 66.5, 65.6, 60.9, 60.4, 55.3, 55.1, 45.0, 44.0, 43.0, 33.0, 23.7, 23.5, 20.7, 14.4. Found (%): C, 75.69; H, 6.40; N, 9.46. Calc. for $C_{37}H_{38}N_4O_3$ (%): C, 75.74; H, 6.53; N, 9.55.

N^2-*(4-Methoxybenzyl)*-N^2-*[(5-methyl-1*H-*pyrazol-3-yl)carbonyl]*-N^1-*[(tetrahydrofuran-2-yl)methyl]valinamide* **7c**. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 12.77 (s, 1H), 7.92 (s, 1H), 7.18 (d, J = 6.4 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 6.34 (s, 1H), 4.30-5.00 (m, 2H), 3.75-3.86 (m, 2H), 3.72 (s, 3H), 3.58-3.67 (m, 1H), 3.07-3.24 (m, 2H), 3.03 (s, 1H), 2.32-2.45 (m, 1H), 2.28 (s, 3H), 1.70-1.91 (m, 3H), 1.39-1.56 (m, 1H), 0.83 (d, J = 6.0 Hz, 3H), 0.71 (d, J = 5.1 Hz, 3H); ^{13}C NMR (d_6-DMSO, 75 Hz) δ 169.7, 165.0, 158.2, 147.6, 130.8, 129.0, 113.4, 106.5, 76.9, 67.3, 66.4, 55.2, 42.8, 28.6, 26.7, 25.3, 19.6, 18.6, 10.2. Found (%): C, 69.61; H, 7.59; N, 13.19. Calc. for $C_{23}H_{32}N_4O_4$ (%): C, 69.47; H, 7.53; N, 13.07.

N^1-*Benzyl*-N^2-*(4-methoxybenzyl)*-N^2-*[(5-methyl-1*H*-pyrazol-3-yl)carbonyl]valinamide* **7d**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 12.73 (s, 1H), 8.37 (s, 1H), 7.20-7.35 (m, 5H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.74 (d, *J* = 8.5 Hz, 2H), 6.33 (s, 1H), 4.82 (s, 2H), 4.18-4.35 (m, 2H), 3.72 (s, 3H), 3.04 (s, 1H), 2.34-2.47 (m, 1H), 2.26 (s, 3H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.74 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 169.7, 158.2, 139.0, 130.7, 129.0, 128.3, 127.3, 126.8, 113.4, 106.4, 66.3, 55.1, 42.4, 26.9, 19.6, 18.6, 10.2. Found (%): C, 69.40; H, 7.06; N, 12.96. Calc. for $C_{25}H_{30}N_4O_3$(%): C, 69.10; H, 6.96; N, 12.89.

N-*[1-(4-Isopropylphenyl)-2-oxo-2-(pyrrolidin-1-yl)ethyl]*-N-*(4-methoxybenzyl)-5-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide* **8b**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 7.63 and 7.26 (ABq, *J* = 7.8 Hz, 4H), 7.18 and 7.10 (ABq, *J* = 8.0 Hz, 4H), 6.88 (s, 1H), 6.80 и 6.60 (ABq, *J* = 8.3 Hz, 4H), 5.04 (m, 1H), 4.61 (m, 1H), 3.67 (s, 3H), 3.22 (s, 1H), 2.98 (m, 5H), 2.85 (m, 1H), 2.35 (s, 3H), 1.71 (m, 4H), 1.18 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 167.9, 167.6, 163.7, 157.4, 148.2, 148.0, 138.0, 137.7, 132.4, 131.0, 130.7, 129.8, 129.5, 129.0, 128.6, 127.6, 126.3, 125.9, 125.2, 125.0, 112.7, 62.6, 60.2, 54.8, 49.3, 47.5, 45.6, 45.2, 33.0, 25.4, 23.8, 23.6, 23.4, 20.8. Found (%): C, 74.19; H, 7.01; N, 10.13. Calc. for $C_{34}H_{38}N_4O_3$ (%): C, 74.16; H, 6.96; N, 10.17.

N-*[2-(4-Ethoxycarbonylpiperazin-1-yl)-1-(4-isopropylphenyl)-2-oxoethyl]*-N-*(4-methoxybenzyl)-5-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide* **8c**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 13.36 (s, 1H), 7.60- 7.68 (m, 2H), 7.21-7.30 (m, 2H), 7.04-7.19 (m, 4H), 6.93 (s, 1H), 6.75 and 6.57 (ABq, *J* = 8.5 Hz, 4H), 4.04 (m, 2H), 3.65 (s, 3H), 3.59 (s, 1H), 3.09-3.52 (m, 10H), 2.83 (m, 1H), 2.34 (s, 3H), 1.10-1.24 (m, 9H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 168.8, 164.2, 157.8, 154.8, 148.7, 138.0, 132.7, 131.3, 129.9, 129.7, 129.5, 128.5, 127.8, 127.5, 127.3, 126.7, 126.5, 125.8, 125.5, 114.1, 113.1, 66.5, 65.6, 60.9, 60.4, 55.3, 55.1, 45.0, 44.0, 43.0, 33.0, 23.7, 23.5, 20.7, 14.4. Found (%): C, 69.75; H, 6.77; N, 10.83. Calc. for $C_{37}H_{43}N_5O_5$ (%): C, 69.68; H, 6.80; N, 10.98.

N-*(4-Methoxybenzyl)*-N-*[(5-methyl-1*H*-pyrazol-3-yl)carbonyl]-3-methyl-1-(morpholin-4-yl)-1-oxobutan-2-amine* **8d**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 12.94 (s, 1H), 7.19 and 6.83 (ABq, *J* = 8.4 Hz, 2H), 6.96 and 6.77 (ABq, *J* = 8.2 Hz, 2H), 6.34-6.50 (m, 1H), 6.06 and 5.48 (ABq, *J* = 12.9 Hz, 1H), 5.17 and 4.88 (ABq, *J* = 12.5 Hz, 1H), 4.50 and 4.16 (ABq, *J* = 14.9 Hz, 1H), 3.70 (d, *J* = 7.9 Hz, 3H), 3.52-3.63 (m, 1H), 3.35-3.49 (m, 4H), 3.14-3.30 (m, 2H), 2.25 (d, *J* = 7.9 Hz, 3H), 1.25 (s, 1H), 0.72-0.90 (m, 6H), 0.68 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 167.3, 164.1, 158.0, 147.4, 138.9, 130.4, 129.1, 113.1, 107.4, 65.7, 60.4, 57.5, 55.0, 46.4, 45.0,

41.6, 30.9, 27.5, 21.9, 19.8, 17.9, 13.8, 10.1. Found (%): C, 63.64; H, 7.12; N, 13.36. Calc. for $C_{22}H_{30}N_4O_4$ (%): C, 63.75; H, 7.30; N, 13.52.

N^2-*[(5-cyclopropyl-1*H*-pyrazol-3-yl)carbonyl]*-N^1-*ethyl*-N^2-*(4-methoxybenzyl)*-N^1-*methylvalinamide* **8e**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 12.59 (s, 1H), 7.04 (s, 2H), 6.75 (d, *J* = 8.2 Hz, 2H), 6.32 (s, 1H), 4.57 (s, 1H), 3.72 (s, 3H), 3.01-3.20 (m, 2H), 2.94 (s, 3H), 2.35-2.46 (m, 1H), 2.25 (s, 3H), 0.70-1.09 (m, 11H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 167.9, 164.4, 163.7, 157.8, 138.7, 130.5, 128.8, 128.0, 113.0, 107.9, 106.7, 57.9, 54.9, 46.3, 44.7, 42.8, 41.8, 33.6, 32.4, 27.6, 19.8, 17.9, 13.8, 11.3, 10.0. Found (%): C, 65.33; H, 7.87; N, 14.66. Calc. for $C_{21}H_{30}N_4O_3$ (%): C, 65.26; H, 7.82; N, 14.50.

N-*[1-(4-Cyclopentylpiperazin-1-yl)-3-methyl-1-oxobut-2-yl]*-N-*(4-methoxybenzyl)-5-methyl-1*H-*pyrazole-3-carboxamide* **8f**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 12.93 (s, 1H), 7.19 and 6.81 (ABq, *J* = 8.5 Hz, 2H), 6.94 and 6.74 (ABq, *J* = 8.3 Hz, 2H), 6.40 (s, 1H), 6.07 and 5.42 (ABq, *J* = 12.4 Hz, 1H), 5.18 and 4.83 (ABq, *J* = 12.4 Hz, 1H), 4.54 and 4.20 (ABq, *J* = 15.0 Hz, 1H), 3.70 (d, *J* = 7.5 Hz, 3H), 3.45-3.61 (m, 1H), 3.20-3.41 (m, 5H), 3.14 и 2.89 (m, 1H), 1.93-2.45 (m, 8H), 1.37-1.78 (m, 5H), 1.25 (s, 2H), 0.73-0.88 (m, 4H), 0.68 (d, *J* = 6.7 Hz, 1H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 166.8, 164.0, 158.0, 147.5, 138.9, 130.5, 129.5, 128.7, 113.1, 107.9, 106.8, 66.3, 60.3, 57.6, 54.9, 51.5, 50.8, 46.4, 44.5, 41.3, 29.5, 27.9, 27.1, 23.5, 19.8, 17.9, 10.0. Found (%): C, 67.42; H, 8.24; N, 14.58. Calc. for $C_{27}H_{39}N_5O_3$ (%): C, 67.33; H, 8.16; N, 14.54.

N-*[1-(4-Cyclohexylpiperazin-1-yl)-5-cyclopropyl*-N-*(4-methoxybenzyl)-1*H-*pyrazole-3-carboxamide* **8g**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 12.76 (s, 1H), 6.90-7.50 (m, 5H), 6.23 (s, 1H), 5.28 (s, 1H), 4.62 (s, 1H), 3.20-3.65 (m, 3H), 2.85-3.20 (m, 3H), 2.10-2.45 (m, 5H), 1.90 (s, 1H), 1.64-1.81 (m, 4H), 1.57 (d, *J* = 10.1 Hz, 1H), 1.03-1.33 (m, 5H), 0.58-1.01 (m, 10H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 167.3, 166.7, 138.8, 127.6, 127.3, 127.1, 126.3, 118.7, 104.2, 62.6, 48.8, 48.6, 48.3, 48.1, 45.4, 45.2, 44.9, 42.1, 28.5, 27.7, 25.9, 25.3, 24.6, 19.8, 18.1, 7.6, 6.4, 6.2; LCMS ($M+H^+$) 492; calc. for $C_{29}H_{41}N_5O_2$.

N-*Benzyl-5-cyclopropyl*-N-*[3-methyl-1-oxo-1-(piperidin-1-yl)but-2-yl]-1*H-*pyrazole-3-carboxamide* **8h**. ^{1}H NMR (*d*$_6$-DMSO, 300 MHz) δ 12.74 (s, 1H), 6.85-7.38 (m, 5H), 6.10-6.40 (m, 1H), 5.10-5.50 (m, 1H), 4.40-4.90 (m, 1H), 3.19-3.55 (m, 2H), 1.80-2.45 (m, 1H), 1.10-1.60 (m, 8H), 0.55-1.00 (m, 12H); ^{13}C NMR (*d*$_6$-DMSO, 75 Hz) δ 167.3, 164.5, 146.2, 138.9, 127.5, 126.3, 103.8, 47.4, 45.9, 45.5, 42.4, 28.9, 27.9, 27.7, 25.9, 25.6, 25.3, 23.9, 21.9, 19.8, 18.1, 7.6, 6.2. Found (%): C, 70.63; H, 7.92; N, 13.76. Calc. for $C_{24}H_{32}N_4O_2$ (%): C, 70.56; H, 7.90; N, 13.71.