Supporting Information

Synthesis and structure-activity relationships of cyanoguanidine-type and structurally related histamine H_4 receptor agonists

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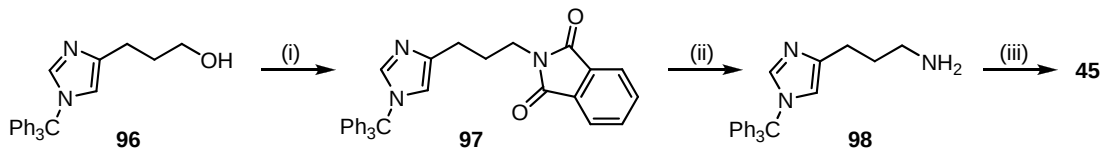
1. Overview about the preparation of the amines 45 and 46

Amines **45** and **46** were synthesized as shown in Schemes 4 and 5, amines **85** and **47** were prepared according to Durant et al.[1] and Vollinga et al.[2]. **45** was synthesized starting from the imidazolylpropanol **96**[3, 4] (Scheme 3). Conversion of the alcohol to the primary amine **98** was carried out by introduction of a phthalimide group under *Mitsunobu*-conditions[5] to give **97**, followed by hydrazinolysis.[6] Acidic hydrolysis of the trityl protecting group produced **45**.

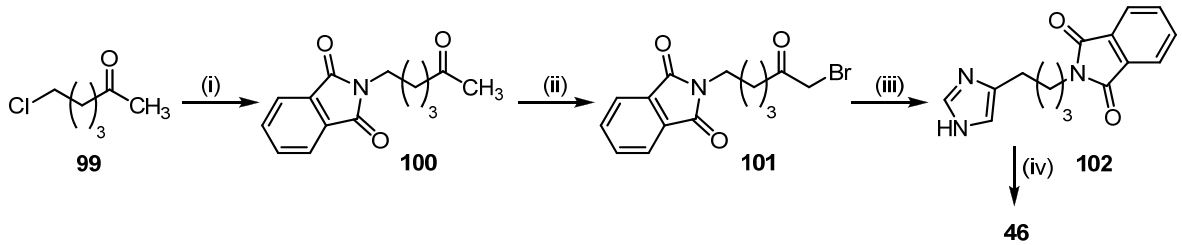
Scheme 3. Synthesis of 3-(1*H*-imidazol-4-yl)propan-1-amine (**45**).[a]



[a] Reagents and conditions: (i) phthalimide (1.5 eq), PPh_3 (1.5 eq), DIAD (2 eq), THF, 1 h, 0 °C → rt; (ii) $N_2H_4 \cdot H_2O$ (6.3 eq), *n*-BuOH, 1h, reflux; (iii) HCl 1N, 30 min, reflux.

The higher homolog of **45**, 4-(1*H*-imidazol-4-yl)butan-1-amine (**46**), was prepared as outlined in Scheme 4 by analogy with a synthetic pathway proposed for the synthesis of homohistamine.[7] 6-Phthalimidohexan-2-one (**100**) was obtained from the reaction of 6-chlorohexan-2-one (**99**) with phthalimide.[8] Regioselective bromination of **100** was achieved by employing methanol as solvent in the presence of urea according to Zav'yalov and Kravchenko.[9] Cyclization of formamidine with the α-bromoketone **101** in a *Bredereck* synthesis[10] gave the imidazole **102** which was converted to **46** by acidic hydrolysis of the phthalimide group.

Scheme 4. Synthesis of 4-(1*H*-imidazol-4-yl)butan-1-amine (**46**).[a]



[a] Reagents and conditions: (i) phthalimide (1 eq), K_2CO_3 (1.5 eq), KI (cat.), 12 h, 100 °C; (ii) urea (1 eq), Br_2 (1 eq), MeOH, 24h, rt; (iii) formamidine, 5 h, 160 °C; (iv) HCl 20%, overnight, reflux.

2. Preparation of the isoureas 27-31 and 33-43

The isoureas **27-31** and **33-43** were prepared according to the general procedure described in the main article.

1-Cyano-2-phenyl-3-(3-phenylpropyl)isourea (27). The title compound was prepared from **10** (0.68 g, 5.0 mmol) and **9** (1.19 g, 5.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.2 g, 86%); mp 92 – 95 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.91 – 2.10 (m, 2H, Ph-CH_2-C$\boldsymbol{H}_2$), 2.73 (t, 2H, ^3J = 7.6 Hz, Ph-C$\boldsymbol{H}_2$), 3.39 – 3.54 (m, 2H, Ph-$(CH_2)_2$-C$\boldsymbol{H}_2$), 6.86 (t, 1H, ^3J = 6.0 Hz, N-***H***), 7.00 – 7.51 (m, 10H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 30.97 (-, Ph-CH_2-***C***H_2), 32.88 (-, Ph-***C***H_2), 42.27 (-, Ph-$(CH_2)_2$-***C***H_2), 115.68 (C_{quat}, ***C***≡N), 121.48 (+, 2 Ph-***C***), 126.30 (+, 1 Ph-***C***), 126.67 (+, 1 Ph-***C***), 128.36 (+, 2 Ph-***C***), 128.64 (+, 2 Ph-***C***), 129.60 (+, 2 Ph-***C***), 140.66 (C_{quat}, Ph-***C***), 151.04 (C_{quat}, 1 Ph-***C***), 164.05 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3190 (N-H), 3061, 2942, 2187 (C≡N), 1635 (C=N), 1598, 1419, 1203. CI-MS (NH_3) *m/z* (%): 280 (100) $[M + H]^+$. Anal. ($C_{17}H_{17}N_3O$) C, H, N. $C_{17}H_{17}N_3O$ (279.34).

1-Cyano-2-phenyl-3-phenylethylisourea (28).[11] The title compound was prepared from **11** (0.97 g, 8.0 mmol) and **9** (1.91 g, 8.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.3 g, 85%); mp 126 – 128 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.96 (t, 2H, ^3J = 7.1 Hz, Ph-C$\boldsymbol{H}_2$), 3.63 – 3.78 (m, 2H, Ph-CH_2-C$\boldsymbol{H}_2$), 6.90 (d, 2H, ^3J = 7.8 Hz, Ph-***H***), 7.07 (t, 1H, ^3J = 6.1 Hz, N-***H***), 7.19 – 7.44 (m, 8H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 36.18 (-, Ph-***C***H_2), 43.93 (-, Ph-CH_2-***C***H_2), 115.69 (C_{quat}, ***C***≡N), 121.45 (+, 2 Ph-***C***), 126.63 (+, 1 Ph-***C***), 126.93 (+, 1 Ph-***C***), 128.87 (+, 2 Ph-***C***), 128.97 (+, 2 Ph-***C***), 129.53 (+, 2 Ph-***C***), 137.81 (C_{quat}, 1 Ph-***C***), 151.96 (C_{quat}, Ph-***C***), 164.03 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3188 (N-H), 3063, 2189 (C≡N), 1646 (C=N), 1448, 1419, 1196. CI-MS (NH_3) *m/z* (%): 264 (100) $[M – H^+]^-$. Anal. ($C_{16}H_{15}N_3O$) C, H, N. $C_{16}H_{15}N_3O$ (265.31).

1-Cyano-2-phenyl-3-(4-phenylbutyl)isourea (29). The title compound was prepared from **12** (1.19 g, 8.0 mmol) and **9** (1.91 g, 8.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (2.0 g, 85%); mp 134 – 136 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.61 – 1.81 (m, 4H, Ph-CH_2-(C$\boldsymbol{H}_2$)$_2$, 2.67 (t, 2H, ^3J = 6.7 Hz, Ph-C$\boldsymbol{H}_2$), 3.38 – 3.50 (m, 2H, Ph-$(CH_2)_3$-C$\boldsymbol{H}_2$), 6.99 (t, 1H, ^3J = 5.8 Hz, N-***H***), 7.01 – 7.51 (m, 10H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 28.32, 29.06 (-, Ph-CH_2-(***C***H_2)$_2$), 35.34 (-, Ph-***C***H_2), 42.56 (-, Ph-$(CH_2)_3$-***C***H_2), 115.77 (C_{quat}, ***C***≡N), 121.51 (+, 2 Ph-***C***), 125.99 (+, 1 Ph-***C***), 126.63 (+, 1 Ph-***C***), 128.45 (+, 2 Ph-***C***), 128.47 (+, 2 Ph-***C***), 129.58 (+, 2 Ph-***C***), 141.73 (C_{quat}, 1 Ph-***C***), 151.09 (C_{quat}, 1 Ph-***C***), 164.04 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3190 (N-H), 3057, 2934, 2187 (C≡N), 1644 (C=N), 1446,

1417, 1192. EI-MS (70 eV) *m/z* (%): 293 (10) [$M^{+\bullet}$], 91 (100) [$C_7H_7^+$]. Anal. ($C_{18}H_{19}N_3O$) C, H, N. $C_{18}H_{19}N_3O$ (293.36).

1-Cyano-3-(3,3-diphenylpropyl)-2-phenylisourea (30).[12] The title compound was prepared from **13** (1.06 g, 4.0 mmol) and **9** (0.95 g, 4.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.3 g, 91%); mp 166 – 168 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.37 – 2.52 (m, 2H, Ph_2CH-C***H***$_2$), 3.33 – 3.46 (m, 2H, Ph_2CH-CH_2-C***H***$_2$), 4.03 (t, 1H, ^3J = 7.9 Hz, Ph_2C***H***), 6.97 – 7.11 (m, 3H, 2 Ph-***H*** + N-***H***), 7.13 – 7.49 (m, 13H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 35.11 (-, Ph_2CH-CH_2-***C***H_2), 41.48 (-, Ph_2CH-***C***H_2), 48.63 (+, Ph_2***C***H), 115.62 (C_{quat}, ***C***≡N), 121.46 (+, 2 Ph-***C***), 126.66 (+, 3 Ph-***C***), 127.70 (+, 4 Ph-***C***), 128.78 (+, 4 Ph-***C***), 129.57 (+, 2 Ph-***C***), 143.61 (C_{quat}, 2 Ph-***C***), 151.03 (C_{quat}, 1 Ph-***C***), 163.93 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3184 (N-H), 3061, 2187 (C≡N), 1641 (C=N), 1447, 1208. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 356 (100) $[M + H]^+$. Anal. ($C_{23}H_{21}N_3O$) C, H, N. $C_{23}H_{21}N_3O$ (355.43).

1-Cyano-3-(3-cyclohexylpropyl)-2-phenylisourea (31). The title compound was prepared from **14** (1.13 g, 8.0 mmol) and **9** (1.91 g, 8.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.75 g, 77%); mp 101 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 0.76 – 1.03 (m, 2H), 1.04 – 1.42 (m, 6H), 1.54 – 1.94 (m, 7H), 3.31 – 3.58 (m, 2H, cHex-$(CH_2)_2$-C***H***$_2$), 6.80 (t, 1H, ^3J = 5.8 Hz, N-***H***), 7.03 – 7.61 (m, 5H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 26.33 (-, 2 ***C***H_2), 26.61 (-, ***C***H_2), 26.98 (-, ***C***H_2), 33.30 (-, 2 ***C***H_2), 34.32 (-, ***C***H_2), 37.30 (+, ***C***H), 43.13 (-, ***C***H_2), 115.77 (C_{quat}, ***C***≡N), 121.49 (+, 2 Ph-***C***), 126.62 (+, 1 Ph-***C***), 129.59 (+, 2 Ph-***C***), 151.11 (C_{quat}, 1 Ph-***C***), 164.05 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3183 (N-H), 3063, 2918, 2851, 2189 (C≡N), 1640 (C=N), 1446, 1416, 1207. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 286 (100) $[M + H]^+$. Anal. ($C_{17}H_{23}N_3O$) C, H, N. $C_{17}H_{23}N_3O$ (285.38).

1-Cyano-3-(1*H*-indol-3-yl)ethyl-2-phenylisourea (33)

The title compound was prepared from **16** (1.28 g, 8.0 mmol) and **9** (1.91 g, 8.0 mmol) in DCM (50 mL) according to the general procedure. The obtained solid was recrystallized from Et_2O/MeCN yielding a beige solid (2.1 g, 86%); mp 167 – 168 °C. ^{1}H-NMR (300 MHz, DMSO-d_6) isomers**:** δ [ppm] = 2.95 (t, 0.8H, ^3J = 7.4 Hz, indole-3-C***H***$_2$), 3.03 (t, 1.2H, ^3J = 7.0 Hz, indole-3-C***H***$_2$), 3.44 – 3.67 (m, 2H, indole-3-CH_2-C***H***$_2$), 6.77 – 7.62 (m, 10H, Ph-***H*** + indole-***H***), 8.49 (t, 0.4H, ^3J = 5.4 Hz, N-***H***), 8.88 (t, 0.6H, ^3J = 5.7 Hz, N-***H***), 10.89 (s, 1H, indole-N-***H***). ^{13}C-NMR (75 MHz, DMSO-d_6) isomers**:** δ [ppm] = 24.06, 25.44 (-, indole-3-***C***H_2), 42.81, 43.06 (-, ***C***H_2-NH), 110.66, 110.84 (C_{quat}, indole-***C***-3), 111.33 (+, indole-***C***-7), 114.77 (C_{quat}, ***C***≡N), 118.13, 118.27, 118.31, 119.84 (+, indole-***C***-4,5,6), 120.91, 121.46 (+, Ph-***C***), 123.00, 123.07 (+,

indole-***C***-2), 126.01, 126.04 (+, Ph-***C***), 127.05, 127.11 (C_{quat}, indole-***C***-3a), 129.24, 130.14 (+, Ph-***C***), 136.15, 136.21 (C_{quat}, indole-***C***-7a), 150.97, 151.42 (C_{quat}, Ph-***C***), 159.50, 162.62 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3354 (N-H), 3205 (N-H), 3058, 2180 (C≡N), 1640 (C=N), 1445, 1424, 1198. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 305 (100) $[M + H]^+$. Anal. ($C_{18}H_{16}N_4O$) C, H, N. $C_{18}H_{16}N_4O$ (304.35).

1-Cyano-3-[3-(4-fluorophenyl)propyl]-2-phenylisourea (34). The title compound was prepared from **17** (0.92 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.2 g, 67%); mp 104 – 106 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.88 – 2.06 (m, 2H, Ph-CH_2-C***H***$_2$), 2.69 (t, 2H, ^3J = 7.6 Hz, Ph-C***H***$_2$), 3.37 – 3.53 (m, 2H, Ph-$(CH_2)_2$-C***H***$_2$), 6.89 – 7.53 (m, 10H, Ph-***H*** + N-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 31.10, 32.07 (-, 4-F-Ph-***C***H_2-***C***H_2), 42.13 (-, 4-F-Ph-$(CH_2)_2$-***C***H_2), 115.38 (+, ^2J = 21.1 Hz, 4-F-Ph-***C***-3,5), 115.71 (C_{quat}, ***C***≡N), 121.47 (+, 2 Ph-***C***), 126.69 (+, 1 Ph-***C***), 129.62 (+, 2 Ph-***C***), 129.73 (+, ^3J = 7.9 Hz, 4-F-Ph-***C***-2,6), 136.36 (C_{quat}, ^4J = 3.2 Hz, 4-F-Ph-***C***-1), 151.05 (C_{quat}, 1 Ph-***C***), 161.46 (C_{quat}, ^2J = 244.0 Hz, 4-F-Ph-***C***-4), 164.04 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3205 (N-H), 3064, 2944, 2187 (C≡N), 1647 (C=N), 1448, 1429, 1203. CI-MS (NH_3) *m/z* (%): 298 (100) $[M + H]^+$. Anal. ($C_{17}H_{16}FN_3O$) C, H, N. $C_{17}H_{16}FN_3O$ (297.33).

1-Cyano-2-phenyl-3-[3-(pyridin-2-yl)propyl]isourea (35). The title compound was prepared from **18** (0.82 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.2 g, 71%); mp 96 – 98 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.07 – 2.21 (m, 2H, Pyr-2-CH_2-C***H***$_2$), 3.04 (t, 2H, ^3J = 6.2 Hz, Pyr-2-C***H***$_2$), 3.54 – 3.64 (m, 2H, Pyr-2-$(CH_2)_2$-C***H***$_2$), 6.95 – 7.88 (m, 8H, Ph-***H*** + Pyr-3,4,5-***H***), 8.49 (dd, 1H, ^3J = 5.9 Hz, ^4J = 1.6 Hz, Pyr-6-***H***), 9.41 (brs, 1H, N-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 26.94 (-, Pyr-2-CH_2-***C***H_2), 35.97 (-, Pyr-2-***C***H_2), 43.57 (-, Pyr-2-$(CH_2)_2$-***C***H_2), 115.89 (C_{quat}, ***C***≡N), 121.61 (+, Pyr-***C***-5 + 2 Ph-***C***), 123.05 (+, Pyr-***C***-3), 126.41 (+, 1 Ph-***C***), 129.50 (+, 2 Ph-***C***), 136.97 (+, Pyr-***C***-4), 149.76 (+, Pyr-***C***-6), 151.29 (C_{quat}, 1 Ph-***C***), 160.12 (C_{quat}, Pyr-***C***-2), 163.44 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3060, 2190 (C≡N), 1607 (C=N), 1326, 1208. CI-MS (NH_3) *m/z* (%): 281 (100) $[M + H]^+$. Anal. ($C_{16}H_{16}N_4O$) C, H, N. $C_{16}H_{16}N_4O$ (280.32).

1-Cyano-2-phenyl-3-[3-(pyridin-3-yl)propyl]isourea (36). The title compound was prepared from **19** (0.82 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.1 g, 65%); mp 90 – 91 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.91 – 2.09 (m, 2H, Pyr-3-CH_2-C***H***$_2$), 2.72 (t, 2H, ^3J = 7.7 Hz, Pyr-3-C***H***$_2$), 3.38 – 3.53 (m, 2H, Pyr-3-$(CH_2)_2$-C***H***$_2$), 7.00 – 7.58 (m, 8H, Ph-***H*** + Pyr-4,5-***H*** + N-***H***), 8.42 – 8.50 (m, 2H, Pyr-2,6-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 30.07, 30.67 (-, Pyr-3-***C***H_2-***C***H_2), 42.06 (-,

Pyr-3-$(CH_2)_2$-***C***H_2), 115.71 (C_{quat}, ***C***≡N), 121.46 (+, 2 Ph-***C***), 123.50 (+, Pyr-***C***-5), 126.67 (+, 1 Ph-***C***), 129.61 (+, 2 Ph-***C***), 135.81 (+, Pyr-***C***-4), 136.17 (C_{quat}, Pyr-***C***-3), 147.79 (+, Pyr-***C***-6), 149.86 (+, Pyr-***C***-2), 151.06 (C_{quat}, 1 Ph-***C***), 163.99 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3185 (N-H), 3056, 2937, 2187 (C≡N), 1632 (C=N), 1421, 1198, 1190. CI-MS (NH_3) *m/z* (%): 281 (100) $[M + H]^+$. Anal. ($C_{16}H_{16}N_4O$) C, H, N. $C_{16}H_{16}N_4O$ (280.32).

1-Cyano-2-phenyl-3-[3-(pyridin-4-yl)propyl]isourea (37). The title compound was prepared from **20** (0.82 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.34 g, 80%); mp 120 – 121 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.86 – 2.11 (m, 2H, Pyr-4-CH_2-C***H***$_2$), 2.71 (t, 2H, ^3J = 7.7 Hz, Pyr-4-C***H***$_2$), 3.39 – 3.50 (m, 2H, Pyr-4-$(CH_2)_2$-C***H***$_2$), 7.02 – 7.18 (m, 4H, Ph-***H*** + Pyr-3,5-***H***), 7.24 – 7.46 (m, 3H, Ph-***H***), 7.71 (t, 1H, ^3J = 5.6 Hz, N-***H***), 8.49 (dd, 2H, ^3J = 4.4 Hz, ^4J = 1.6 Hz, Pyr-2,6-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 29.82, 32.21 (-, Pyr-4-***C***H_2-***C***H_2), 42.02 (-, Pyr-4-$(CH_2)_2$-***C***H_2), 115.76 (C_{quat}, ***C***≡N), 121.44 (+, 2 Ph-***C***), 123.82 (+, Pyr-***C***-3,5), 126.69 (+, 1 Ph-***C***), 129.62 (+, 2 Ph-***C***), 149.88 (+, Pyr-***C***-2,6), 149.93 (C_{quat}, Pyr-***C***-4), 151.06 (C_{quat}, Ph-***C***), 163.99 (C_{quat}, ***C***=N). IR (cm^{-1}) = 2959, 2823, 2181 (C≡N), 1600 (C=N), 1452, 1416, 1200. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 281 (100) $[M + H]^+$. Anal. ($C_{16}H_{16}N_4O$) C, H, N. $C_{16}H_{16}N_4O$ (280.32).

1-Cyano-2-phenyl-3-(3-phenylbutyl)isourea (38). The title compound was prepared from **21** (0.90 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (1.5 g, 82%); mp 132 – 134 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.31 (d, 3H, ^3J = 6.9 Hz, PhC***H***$_3$CH), 1.91 – 2.03 (m, 2H, PhCH_3CH-C***H***$_2$), 2.75 – 2.90 (m, 1H, PhCH_3C***H***), 3.18 – 3.42 (m, 2H, PhCH_3CH-CH_2-C***H***$_2$), 6.83 (t, 1H, ^3J = 5.2 Hz, N-***H***), 6.99 – 7.52 (m, 10H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 22.62 (+, Ph***C***H_3CH), 37.49, (-, ***C***H_2), 37.56 (+, PhCH_3***C***H), 41.25 (-, ***C***H_2), 115.62 (C_{quat}, ***C***≡N), 121.46 (+, 2 Ph-***C***), 126.54 (+, 1 Ph-***C***), 126.60 (+, 1 Ph-***C***), 126.87 (+, 2 Ph-***C***), 128.76 (+, 2 Ph-***C***), 129.56 (+, 2 Ph-***C***), 145.71 (C_{quat}, 1 Ph-***C***), 151.05 (C_{quat}, 1 Ph-***C***), 163.91 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3185 (N-H), 3055, 2955, 2184 (C≡N), 1642 (C=N), 1450, 1427, 1201. CI-MS (NH_3) *m/z* (%): 294 (100) $[M + H]^+$. Anal. ($C_{18}H_{19}N_3O$) C, H, N. $C_{18}H_{19}N_3O$ (293.36).

1-Cyano-2-phenylisourea (39).[13] The title compound was prepared from a 7 M solution of ammonia (**22**) in MeOH (0.86 mL, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (0.8 g, 83%); mp 149 – 151 °C. ^{1}H-NMR (300 MHz, DMSO-d_6): δ [ppm] = 7.13 – 7.20 (m, 2H, Ph-***H***), 7.24 – 7.32 (m, 1H, Ph-***H***), 7.37 – 7.46 (m, 2H, Ph-***H***), 8.58 (brs, 2H, N-***H***). ^{13}C-NMR (75 MHz, DMSO-d_6): δ [ppm] = 114.86 (C_{quat}, ***C***≡N), 121.60 (+, 2 Ph-***C***), 126.09 (+, 1 Ph-***C***), 129.50 (+, 2 Ph-***C***), 151.03 (C_{quat}, 1

Ph-***C***), 164.53 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3321 (N-H), 3174, 3056, 2200 (C≡N), 1646 (C=N), 1576, 1452, 1203. CI-MS (NH_3) *m/z* (%): 179 (100) $[M + NH_4]^+$, 162 (71) $[M + H]^+$. Anal. ($C_8H_7N_3O$) C, H, N. $C_8H_7N_3O$ (161.16).

1-Cyano-3-methyl-2-phenylisourea (40).[14] The title compound was prepared from a 8 M solution of methylamine (**23**) in MeOH (0.75 mL, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (0.8 g, 76%); mp 125 – 126 °C. ^{1}H-NMR (300 MHz, DMSO-d_6) isomers: δ [ppm] = 2.76 (s, 1.4 H, C***H***$_3$), 2.91 (s, 1.6 H, C***H***$_3$), 7.14 – 7.54 (m, 5H, Ph-***H***), 8.19 (brs, 0.45H, N-***H***), 8.66 (brs, 0.55H, N-***H***). ^{13}C-NMR (75 MHz, DMSO-d_6) isomers: δ [ppm] = 28.69, 29.15 (+, ***C***H$_3$), 114.43, 114.85 (C_{quat}, ***C***≡N), 120.12, 121.70 (+, 2 Ph-***C***), 126.13, 126.26 (+, 1 Ph-***C***), 129.39, 130.22 (+, 2 Ph-***C***), 151.14, 151.29 (C_{quat}, 1 Ph-***C***), 160.06, 163.16 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3189 (N-H), 3015, 2186 (C≡N), 1656 (C=N), 1628, 1386. CI-MS (NH_3) *m/z* (%): 193 (100) $[M + NH_4]^+$, 176 (68) $[M + H]^+$. Anal. ($C_9H_9N_3O$) C, H, N. $C_9H_9N_3O$ (175.19).

1-Cyano-3-ethyl-2-phenylisourea (41).[15] The title compound was prepared from a 30 – 40% solution of ethylamine (**24**) in MeOH (0.90 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (0.5 g, 45%); mp 117 – 118 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.29 (t, 3H, ^3J = 7.2 Hz, C***H***$_3$), 3.41 – 3.55 (m, 2H, C***H***$_2$), 6.99 (brs, 1H, N-***H***), 7.09 (d, 2H, ^3J = 7.8 Hz, Ph-***H***), 7.24 – 7.33 (m, 1H, Ph-***H***), 7.34 – 7.50 (m, 2H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 14.93 (+, ***C***H$_3$), 37.74, (-, ***C***H$_2$), 115.84 (C_{quat}, ***C***≡N), 121.50 (+, 2 Ph-***C***), 126.60 (+, 1 Ph-***C***), 129.57 (+, 2 Ph-***C***), 151.11 (C_{quat}, 1 Ph-***C***), 163.97 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3259 (N-H), 2979, 2182 (C≡N), 1626 (C=N), 1419, 1208. CI-MS (NH_3) *m/z* (%): 190 (100) $[M + H]^+$. Anal. ($C_{10}H_{11}N_3O$) C, H, N. $C_{10}H_{11}N_3O$ (189.21).

1-Cyano-3-isopropyl-2-phenylisourea (42).[16] The title compound was prepared from **25** (0.35 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (0.8 g, 68%); mp 124 – 126 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.33 (d, 6H, ^3J = 6.0 Hz, C***H***$_3$), 4.04 – 4.22 (m, 1H, C***H***), 6.17 (brs, 1H, N-***H***), 7.09 (d, 2H, ^3J = 7.8 Hz, Ph-***H***), 7.30 (d, 1H, ^3J = 7.2 Hz, Ph-***H***), 7.35 – 7.48 (m, 2H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 22.62 (+, ***C***H$_3$), 45.73, (+, ***C***H), 115.44 (C_{quat}, ***C***≡N), 121.43 (+, 2 Ph-***C***), 126.70 (+, 1 Ph-***C***), 129.60 (+, 2 Ph-***C***), 151.05 (C_{quat}, 1 Ph-***C***), 163.22 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3201 (N-H), 3068, 2980, 2189 (C≡N), 1642 (C=N), 1431, 1200. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 204 (100) $[M + H]^+$. Anal. ($C_{11}H_{13}N_3O$) C, H, N. $C_{11}H_{13}N_3O$ (203.24).

1-Cyano-3-isobutyl-2-phenylisourea (43). The title compound was prepared from **26** (0.44 g, 6.0 mmol) and **9** (1.43 g, 6.0 mmol) in DCM (50 mL) according to the general procedure yielding a white solid (0.8 g, 59%); mp 103 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.00 (d, 6H, ^3J = 6.7 Hz, C***H***$_3$), 1.86 – 2.03 (m, 1H, C***H***), 3.21 – 3.30 (m, 2H, CH_2), 6.91 (brs, 1H, N-***H***), 7.07 (d, 2H, ^3J = 7.8 Hz, Ph-***H***), 7.23 – 7.33 (m, 1H, Ph-***H***), 7.34 – 7.46 (m, 2H, Ph-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 19.92 (+, ***C***H$_3$), 28.79, (+, ***C***H), 49.90 (-, CH_2), 115.68 (C_{quat}, ***C***≡N), 121.46 (+, 2 Ph-***C***), 126.58 (+, 1 Ph-***C***), 129.56 (+, 2 Ph-***C***), 151.10 (C_{quat}, 1 Ph-***C***), 164.16 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3194 (N-H), 3063, 2955, 2190 (C≡N), 1635 (C=N), 1423, 1207. CI-MS (NH_3) *m/z* (%): 218 (100) [M + H]$^+$. Anal. ($C_{12}H_{15}N_3O$) C, H, N. $C_{12}H_{15}N_3O$ (217.27).

3. Preparation of the cyanoguanidines 48-66, 68-78, 86 and 87

The compounds were prepared according to the general procedure described in the main article.

2-Cyano-1-[2-(1*H*-imidazol-4-yl)ethyl]-3-(3-phenylpropyl)guanidine (48). The title compound was prepared from **27** (0.56 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.44 g, 75%); mp (hydrogenoxalate) 149 – 151 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.77 – 1.89 (m, 2H, Ph-CH_2-C***H***$_2$), 2.62 (t, 2H, ^3J = 7.7 Hz, Ph-C***H***$_2$), 2.93 (t, 2H, ^3J = 6.9 Hz, Im-4-C***H***$_2$), 3.19 (t, 2H, ^3J = 7.2 Hz, Ph-$(CH_2)_2$-C***H***$_2$), 3.51 (t, 2H, ^3J = 6.9 Hz, Im-4-CH_2-C***H***$_2$), 7.11 – 7.30 (m, 6H, Ph-***H*** + Im-5-***H***), 8.56 (d, 1H, ^4J = 1.3 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 26.29 (-, Im-4-***C***H$_2$), 32.14 (-, Ph-CH_2-***C***H$_2$), 33.93 (-, Ph-***C***H$_2$), 41.57 (-, Im-4-CH_2-***C***H$_2$), 42.46 (-, Ph-CH_2-CH_2-***C***H$_2$), 117.69 (+, Im-***C***-5), 119.86 (C_{quat}, ***C***≡N), 127.06 (+, Ph-***C***-4), 129.45 (+, 2 Ph-***C***), 129.52 (+, 2 Ph-***C***), 133.20 (C_{quat}, Im-***C***-4), 135.15 (+, Im-***C***-2), 142.78 (C_{quat}, Ph-***C***-1), 161.21 (C_{quat}, ***C***=N), 167.65 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3266 (N-H), 2972 (C-H), 2901 (C-H), 2160 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 297 (100) [M + H]$^+$. HRMS (EI-MS) calcd. for $C_{16}H_{19}N_6$ [M – H]$^+$ 295.1671; found 295.1675. Anal. ($C_{16}H_{20}N_6$ · 0.9 $C_2H_2O_4$ · 0.25 H_2O) C, H, N. $C_{16}H_{20}N_6$ (296.37).

2-Cyano-1-[2-(1*H*-imidazol-4-yl)ethyl]-3-(2-phenylethyl)guanidine (49). The title compound was prepared from **28** (0.53 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.40 g, 72%); mp (hydrogenoxalate) 149 – 151 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ

[ppm] = 2.78 – 2.92 (m, 4H, Im-4-C***H***$_2$ + Ph-C***H***$_2$), 3.38 – 3.50 (m, 4H, Im-4-CH$_2$-C***H***$_2$ + Ph-CH$_2$-C***H***$_2$), 7.14 – 7.32 (m, 6H, Ph-***H***, Im-5-***H***), 8.56 (d, 1H, ^4J = 1.2 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD$_3$OD, hydrogenoxalate): δ [ppm] = 26.26 (-, Im-4-***C***H$_2$), 36.59 (-, Ph***C***H$_2$), 41.59 (-, Im-4-CH$_2$-***C***H$_2$), 44.26 (-, Ph-CH$_2$-***C***H$_2$), 117.71 (+, Im-***C***-5), 119.76 (C$_{quat}$, ***C***≡N), 127.61 (+, Ph-***C***-4), 129.65 (+, 2 Ph-***C***), 130.03 (+, 2 Ph-***C***), 133.19 (C$_{quat}$, Im-***C***-4), 135.21 (+, Im-***C***-2), 140.03 (C$_{quat}$, Ph-***C***-1), 161.16 (C$_{quat}$, ***C***=N), 167.73 (C$_{quat}$, hydrogenoxalate). IR (cm^{-1}) = 3256 (N-H), 2939 (C-H), 2854 (C-H), 2160 (C≡N), 1576 (C=N). ES-MS (MeOH + NH$_4$OAc) *m/z* (%): 283 (100) [M + H]$^+$. HRMS (EI-MS) calcd. for C$_{15}$H$_{18}$N$_6$ [M$^{+\bullet}$] 282.1593; found 282.1588. Anal. (C$_{15}$H$_{18}$N$_6$ · 0.8 C$_2$H$_2$O$_4$ · 0.25 H$_2$O) C, H, N. C$_{15}$H$_{18}$N$_6$ (282.34).

2-Cyano-1-[2-(1*H*-imidazol-4-yl)ethyl]-3-(4-phenylbutyl)guanidine (50). The title compound was prepared from **29** (0.59 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography (CHCl$_3$/MeOH/7 M NH$_3$ in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.46 g, 74%); mp (hydrogenoxalate) 138 – 140 °C. ^{1}H-NMR (300 MHz, CD$_3$OD, hydrogenoxalate): δ [ppm] = 1.47 – 1.69 (m, 4H, Ph-CH$_2$-C***H***$_2$-C***H***$_2$), 2.62 (t, 2H, ^3J = 7.3 Hz, Ph-C***H***$_2$), 2.93 (t, 2H, ^3J = 6.8 Hz, Im-4-C***H***$_2$), 3.19 (t, 2H, ^3J = 6.9 Hz, Ph-(CH$_2$)$_3$-C***H***$_2$), 3.51 (t, 2H, ^3J = 6.8 Hz, Im-4-CH$_2$-C***H***$_2$), 7.08 – 7.29 (m, 6H, Ph-***H***, Im-5-***H***), 8.57 (d, 1H, ^4J = 1.3 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD$_3$OD, hydrogenoxalate): δ [ppm] = 26.31 (-, Im-4-***C***H$_2$), 29.75, 29.96 (-, Ph-CH$_2$-***C***H$_2$-***C***H$_2$), 36.51 (-, Ph-***C***H$_2$), 41.58 (-, Im-4-CH$_2$-***C***H$_2$), 42.70 (-, Ph-(CH$_2$)$_3$-***C***H$_2$), 117.73 (+, Im-***C***-5), 119.92 (C$_{quat}$, ***C***≡N), 126.90 (+, Ph-***C***-4), 129.43 (+, 2 Ph-***C***), 129.52 (+, 2 Ph-***C***), 133.16 (C$_{quat}$, Im-***C***-4), 135.15 (+, Im-***C***-2), 143.51 (C$_{quat}$, Ph-***C***-1), 161.22 (C$_{quat}$, ***C***=N), 167.44 (C$_{quat}$, hydrogenoxalate). IR (cm^{-1}) = 3257 (N-H), 2971 (C-H), 2930 (C-H), 2161 (C≡N), 1576 (C=N). ES-MS (H$_2$O/MeCN) *m/z* (%): 311 (100) [M + H]$^+$. HRMS (EI-MS) calcd. for C$_{17}$H$_{22}$N$_6$ [M$^{+\bullet}$] 310.1906; found 310.1897. Anal. (C$_{17}$H$_{22}$N$_6$ · C$_2$H$_2$O$_4$ · 0.25 H$_2$O) C, H, N. C$_{17}$H$_{22}$N$_6$ (310.40).

2-Cyano-1-(3,3-diphenylpropyl)-3-[2-(1*H*-imidazol-4-yl)ethyl]guanidine (51)

The title compound was prepared from **30** (0.71 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography (CHCl$_3$/MeOH/7 M NH$_3$ in MeOH 95/3/2 v/v/v) yielding a colorless resin that solidified over Et$_2$O (0.54 g, 72%); mp 178 – 180 °C. ^{1}H-NMR (300 MHz, CD$_3$OD): δ [ppm] = 2.23 – 2.34 (m, 2H, Ph$_2$CH-C***H***$_2$), 2.76 (t, 2H, ^3J = 7.2 Hz, Im-4-C***H***$_2$), 3.12 (t, 2H, ^3J = 7.3 Hz, Ph$_2$CH-CH$_2$-C***H***$_2$), 3.36 (t, 2H, ^3J = 7.2 Hz, Im-4-CH$_2$-C***H***$_2$), 3.97 (t, 1H, ^3J = 7.9 Hz, Ph$_2$C***H***), 6.84 (br s, 1H, Im-5-***H***), 7.10 – 7.31 (m, 10H, Ph-***H***), 7.55 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD$_3$OD): δ [ppm] = 28.07 (-, Im-4-***C***H$_2$), 36.01 (-, Ph$_2$CH-***C***H$_2$), 41.68 (-, Im-4-

CH_2-***C***H_2), 42.67 (-, Ph_2CH-CH_2***C***H_2), 50.09 (+, Ph_2***C***H), 120.16 (C_{quat}, ***C***≡N), 127.41 (+, 2 Ph-***C***-4), 128.89 (+, 4 Ph-***C***), 129.62 (+, 4 Ph-***C***), 136.28 (+, Im-***C***-2), 145.84 (C_{quat}, 2 Ph-***C***-1), 161.19 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3314 (N-H), 2939 (C-H), 2841 (C-H), 2172 (C≡N), 1584 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 273 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{22}H_{24}N_6$ $[M^{+\bullet}]$ 372.2062; found 372.2056. Anal. ($C_{22}H_{24}N_6$ · 0.25 H_2O) C, H, N. $C_{22}H_{24}N_6$ (372.47).

2-Cyano-1-(3-cyclohexylpropyl)-3-[2-(1*H*-imidazol-4-yl)ethyl]guanidine (52). The title compound was prepared from **31** (0.57 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.37 g, 60%); mp (hydrogenoxalate) 160 – 162 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 0.80 – 0.99 (m, 2H, cHex-C***H***$_2$), 1.08 – 1.35 (m, 6H, cHex), 1.46 – 1.60 (m, 2H, cHex-CH_2-C***H***$_2$), 1.61 – 1.79 (m, 5H, cHex), 2.96 (t, 2H, ^3J = 6.8 Hz, Im-4-C***H***$_2$), 3.14 (t, 2H, ^3J = 7.3 Hz, cHex-$(CH_2)_2$-C***H***$_2$), 3.53 (t, 2H, ^3J = 6.8 Hz, Im-4-CH_2-C***H***$_2$), 7.30 (d, 1H, ^4J = 1.4 Hz, Im-5-***H***), 8.68 (d, 1H, ^4J = 1.4 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 26.19 (-, Im-4-***C***H_2), 27.53 (-, 2 cHex-***C***), 27.78 (-, ***C***H_2), 27.82 (-, ***C***H_2), 34.57 (-, 2 cHex-***C***), 35.60 (-, ***C***H_2), 38.79 (+, cHex-***C***), 41.49 (-, Im-4-CH_2-***C***H_2), 43.24 (-, cHex-$(CH_2)_2$-***C***H_2), 117.75 (+, Im-***C***-5), 119.91 (C_{quat}, ***C***≡N), 132.97 (C_{quat}, Im-***C***-4), 135.09 (+, Im-***C***-2), 161.20 (C_{quat}, ***C***=N), 167.13 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3277 (N-H), 2921 (C-H), 2848 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (MeOH + NH_4OAc) *m/z* (%): 303 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{16}H_{26}N_6$ $[M^{+\bullet}]$ 302.2219; found 302.2218. Anal. ($C_{16}H_{26}N_6$ · $C_2H_2O_4$) C, H, N. $C_{16}H_{26}N_6$ (302.42).

2-Cyano-1-[2-(1*H*-imidazol-4-yl)ethyl]-3-[2-(phenylthio)ethyl]guanidine (53). The title compound was prepared from **32** (0.60 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.51 g, 82%); mp (hydrogenoxalate) 133 – 135 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 2.94 (t, 2H, ^3J = 6.8 Hz, Im-4-C***H***$_2$), 3.10 (t, 2H, ^3J = 6.9 Hz, S-CH_2-C***H***$_2$), 3.40 (t, 2H, ^3J = 6.9 Hz, S-C***H***$_2$), 3.49 (t, 2H, ^3J = 6.8 Hz, Im-4-CH_2-C***H***$_2$), 7.15 – 7.23 (m, 1H, Ph-4-***H***), 7.25 – 7.33 (m, 3H, Ph-***H*** + Im-5-***H***), 7.35 – 7.42 (m, 2H, Ph-***H***), 8.71 (d, 1H, ^4J = 1.4 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 25.95 (-, Im-4-***C***H_2), 33.61 (-, S-***C***H_2), 41.49 (-, Im-4-CH_2-***C***H_2), 42.28 (-, S-CH_2-***C***H_2), 117.79 (+, Im-***C***-5), 119.50 (C_{quat}, ***C***≡N), 127.47 (+, Ph-***C***-4), 130.23 (+, 2 Ph-***C***), 130.59 (+, 2 Ph-***C***), 132.70 (C_{quat}, Im-***C***-4), 135.08 (+, Im-***C***-2),

136.85 (C_{quat}, Ph-***C***-1), 161.16 (C_{quat}, ***C***=N), 166.73 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3246 (N-H), 2989 (C-H), 2900 (C-H), 2162 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 315 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{15}H_{18}N_6S$ $[M^{+\bullet}]$ 314.1314; found 314.1310. Anal. ($C_{15}H_{18}N_6S \cdot C_2H_2O_4$) C, H, N. $C_{15}H_{18}N_6S$ (314.41).

2-Cyano-1-[2-(1*H*-imidazol-4-yl)ethyl]-3-[2-(1*H*-indol-3-yl)ethyl]guanidine (54). The title compound was prepared from **33** (0.61 g, 2.0 mmol) and **44** (0.24 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless solid (0.41 g, 64%); mp 78 – 82 °C. ^{1}H-NMR (600 MHz, NOESY, CD_3OD): δ [ppm] = 2.69 (t, 2H, ^3J = 7.3 Hz, Im-4-C***H***$_2$), 2.99 (t, 2H, ^3J = 7.1 Hz, indole-3-C***H***$_2$), 3.34 (t, 2H, ^3J = 7.3 Hz, Im-4-CH_2-C***H***$_2$), 3.48 (t, 2H, ^3J = 7.1 Hz, indole-3-CH_2-C***H***$_2$), 6.82 (brs, 1H, Im-5-***H***), 7.03 (ddd, 1H, ^3J = 8.0 Hz, ^3J = 7.0 Hz , ^4J = 1.0 Hz, indole-5-***H***), 7.08 – 7.12 (m, 2H, indole-6-***H*** + indole-2-***H***), 7.34 (ddd, 1H, ^3J = 8.1 Hz, ^4J = 1.0 Hz, ^5J = 1.0 Hz, indole-7-***H***), 7.57 (ddd, 1H, ^3J = 8.0 Hz, ^4J = 1.2 Hz, ^5J = 1.0 Hz, indole-4-***H***), 7.59 (brs, 1H, Im-2-***H***). ^{13}C-NMR (150 MHz, HSQC, HMBC, CD_3OD): δ [ppm] = 26.33 (-, indole-3-***C***H_2), 27.88 (-, Im-4-***C***H_2), 42.58 (-, Im-4-CH_2-***C***H_2), 43.60 (-, indole-3-CH_2-***C***H_2), 112.32 (+, indole-***C***-7), 112.73 (C_{quat}, indole-***C***-3), 117.35 (+, Im-***C***-5), 119.28 (+, indole-***C***-4), 119.76 (+, indole-***C***-5), 120.19 (C_{quat}, ***C***≡N), 122.45 (+, indole-***C***-6), 123.77 (+, indole-***C***-2), 128.69 (C_{quat}, indole-***C***-3a), 136.21 (+, Im-***C***-2), 138.22 (C_{quat}, indole-***C***-7a), 161.21 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3253 (N-H), 2927 (C-H), 2847 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 322 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{17}H_{19}N_7$ $[M^{+\bullet}]$ 321.1702; found 321.1698. Anal. ($C_{17}H_{22}N_6 \cdot 0.25\ H_2O$) C, H, N. $C_{17}H_{19}N_7$ (321.38).

2-Cyano-1-[3-(1*H*-imidazol-4-yl)propyl]-3-(3-phenylpropyl)guanidine (55). The title compound was prepared from **27** (0.56 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.45 g, 72%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.80 – 1.95 (m, 4H, Im-4-CH_2-C***H***$_2$ + Ph-CH_2-C***H***$_2$), 2.59 – 2.72 (m, 4H, Im-4-C***H***$_2$ + Ph-C***H***$_2$), 3.17 – 3.28 (m, 4H, Im-4-$(CH_2)_2$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 7.04 (d, 1H, ^4J = 1.1 Hz, Im-5-***H***), 7.11 – 7.29 (m, 5H, Ph-***H***), 8.12 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 23.87 (-, Im-4-***C***H_2), 29.87 (-, Im-4-CH_2-***C***H_2), 32.23 (-, Ph-CH_2-***C***H_2), 33.98 (-, Ph-***C***H_2), 41.98 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.42 (-, Ph-$(CH_2)_2$-***C***H_2), 117.06 (+, Im-***C***-5), 120.18 (C_{quat}, ***C***≡N), 127.03 (+, Ph-***C***-4), 129.45 (+, 2 Ph-***C***), 129.50 (+, 2 Ph-***C***), 135.39 (+, Im-***C***-2), 136.74 (C_{quat}, Im-***C***-4), 142.84 (C_{quat}, Ph-***C***-1), 161.26 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3250 (N-H), 2937 (C-H), 2857 (C-H), 2157 (C≡N), 1576 (C=N). ES-

MS (DCM/MeOH + NH_4OAc) *m/z* (%): 311 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{17}H_{22}N_6$ $[M^{+\bullet}]$ 310.1906; found 310.1903. Anal. ($C_{17}H_{22}N_6 \cdot 0.25\ H_2O$) C, H, N. $C_{17}H_{22}N_6$ (310.40).

2-Cyano-1-[3-(1*H*-imidazol-4-yl)propyl]-3-(2-phenylethyl)guanidine (56). The title compound was prepared from **28** (0.53 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.37 g, 62%); mp (hydrogenoxalate) 146 – 149 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.78 – 1.91 (m, 2H, Im-4-CH_2-C$\boldsymbol{H}_2$), 2.69 (t, 2H, ^3J = 7.6 Hz, Im-4-C$\boldsymbol{H}_2$), 2.84 (t, 2H, ^3J = 7.2 Hz, Ph-C$\boldsymbol{H}_2$), 3.22 (t, 2H, ^3J = 7.0 Hz, Im-4-$(CH_2)_2$-C$\boldsymbol{H}_2$), 3.44 (t, 2H, ^3J = 7.2 Hz, Ph-CH_2-C$\boldsymbol{H}_2$), 7.11 – 7.33 (m, 6H, Ph-***H***, Im-5-***H***), 8.58 (d, 1H, ^4J = 1.3 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 22.96 (-, Im-4-***C***H_2), 29.47 (-, Im-4-CH_2-***C***H_2), 36.68 (-, Ph-***C***H_2), 41.80 (-, Im-4-$(CH_2)_2$-***C***H_2), 44.27 (-, Ph-CH_2-***C***H_2), 116.91 (+, Im-***C***-5), 120.02 (C_{quat}, ***C***≡N), 127.58 (+, Ph-***C***-4), 129.63 (+, 2 Ph-***C***), 130.05 (+, 2 Ph-***C***), 134.93 (+, Im-***C***-2), 135.43 (C_{quat}, Im-***C***-4), 140.12 (C_{quat}, Ph-***C***-1), 161.20 (C_{quat}, ***C***=N), 167.90 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3249 (N-H), 2940 (C-H), 2854 (C-H), 2159 (C≡N), 1576 (C=N). ES-MS (MeOH + NH_4OAc) *m/z* (%): 297 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{16}H_{20}N_6$ $[M^{+\bullet}]$ 296.1749; found 296.1747. Anal. ($C_{16}H_{20}N_6 \cdot 0.7\ C_2H_2O_4 \cdot 0.5\ H_2O$) C, H, N. $C_{16}H_{20}N_6$ (296.37).

2-Cyano-1-[3-(1*H*-imidazol-4-yl)propyl]-3-(4-phenylbutyl)guanidine (57). The title compound was prepared from **29** (0.59 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.51 g, 79%); mp (hydrogenoxalate) 128 – 130 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.49 – 1.72 (m, 4H, Ph-CH_2-C$\boldsymbol{H}_2$-C$\boldsymbol{H}_2$), 1.82 – 1.96 (m, 2H, Im-4-CH_2-C$\boldsymbol{H}_2$), 2.63 (t, 2H, ^3J = 7.2 Hz, Im-4-C$\boldsymbol{H}_2$), 2.71 (t, 2H, ^3J = 7.5 Hz, Ph-C$\boldsymbol{H}_2$), 3.17 – 3.30 (m, 4H, Im-4-$(CH_2)_2$-C$\boldsymbol{H}_2$ + Ph-$(CH_2)_3$-C$\boldsymbol{H}_2$), 7.08 – 7.27 (m, 6H, Ph-***H*** + Im-5-***H***), 8.50 (d, 1H, ^4J = 1.3 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 23.09 (-, Im-4-***C***H_2), 29.63 (-, Im-4-CH_2-***C***H_2), 29.75, 30.03 (-, Ph-CH_2-***C***H_2-***C***H_2), 36.50 (-, Ph-***C***H_2), 41.82 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.65 (-, Ph-$(CH_2)_3$-***C***H_2), 116.91 (+, Im-***C***-5), 120.19 (C_{quat}, ***C***≡N), 126.84 (+, Ph-***C***-4), 129.38 (+, 2 Ph-***C***), 129.48 (+, 2 Ph-***C***), 134.97 (+, Im-***C***-2), 135.59 (C_{quat}, Im-***C***-4), 143.51 (C_{quat}, Ph-***C***-1), 161.23 (C_{quat}, ***C***=N), 168.22 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3245 (N-H), 2934 (C-H), 2858 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 325 (100) $[M + H]^+$.

HRMS (EI-MS) calcd. for $C_{18}H_{24}N_6$ [$M^{+\bullet}$] 324.2062; found 324.2058. Anal. ($C_{18}H_{24}N_6 \cdot 0.85$ $C_2H_2O_4$) C, H, N. $C_{18}H_{24}N_6$ (324.42).

2-Cyano-1-(3,3-diphenylpropyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (58). The title compound was prepared from **30** (0.71 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 95/3/2 v/v/v) yielding a colorless foam-like solid (0.51 g, 66%); mp (hydrogenoxalate) 156 – 158 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.80 – 1.93 (m, 2H, Im-4-CH_2-C$\boldsymbol{H}_2$), 2.28 – 2.39 (m, 2H, Ph_2CH-C$\boldsymbol{H}_2$), 2.70 (t, 2H, ^3J = 7.6 Hz, Im-4-C$\boldsymbol{H}_2$), 3.15 (t, 2H, ^3J = 7.3 Hz, Ph_2CH-CH_2-C$\boldsymbol{H}_2$), 3.21 (t, 2H, ^3J = 7.0 Hz, Im-4-$(CH_2)_2$-C$\boldsymbol{H}_2$), 4.00 (t, 1H, ^3J = 7.9 Hz, Ph_2C$\boldsymbol{H}$), 7.31 – 7.11 (m, 11H, Ph-$\boldsymbol{H}$ + Im-5-$\boldsymbol{H}$), 8.59 (d, 1H, ^4J = 1.3 Hz, Im-2-$\boldsymbol{H}$). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 22.90 (-, Im-4-$\boldsymbol{C}H_2$), 29.46 (-, Im-4-CH_2-$\boldsymbol{C}H_2$), 35.98 (-, $Ph_2CH\boldsymbol{C}H_2$), 41.73, 41.78 (-, Im-4-$(CH_2)_2$-$\boldsymbol{C}H_2$ + Ph_2CHCH_2-$\boldsymbol{C}H_2$), 50.05 (+, $Ph_2\boldsymbol{C}H$), 116.87 (+, Im-$\boldsymbol{C}$-5), 120.12 (C_{quat}, $\boldsymbol{C}$≡N), 127.43 (+, 2 Ph-$\boldsymbol{C}$-4), 128.89 (+, 4 Ph-$\boldsymbol{C}$), 129.63 (+, 4 Ph-$\boldsymbol{C}$), 134.89 (+, Im-$\boldsymbol{C}$-2), 135.30 (C_{quat}, Im-$\boldsymbol{C}$-4), 145.81 (C_{quat}, 2 Ph-$\boldsymbol{C}$-1), 161.21 (C_{quat}, $\boldsymbol{C}$=N), 167.51 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3242 (N-H), 2989 (C-H), 2901 (C-H), 2159 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 387 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{23}H_{26}N_6$ [$M^{+\bullet}$] 386.2219; found 386.2214. Anal. ($C_{23}H_{26}N_6 \cdot 0.25$ H_2O) C, H, N. $C_{23}H_{26}N_6$ (386.49).

2-Cyano-1-(3-cyclohexylpropyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (59). The title compound was prepared from **31** (0.57 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 95/3/2 v/v/v) yielding a colorless foam-like solid (0.35 g, 55%); mp (hydrogenoxalate) 144 – 146 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 0.81 – 1.00 (m, 2H, cHex-C$\boldsymbol{H}_2$), 1.10 – 1.35 (m, 6H), 1.49 – 1.79 (m, 7H), 1.85 – 1.99 (m, 2H, Im-4-CH_2-C$\boldsymbol{H}_2$), 2.75 (t, 2H, ^3J = 7.5 Hz, Im-4-C$\boldsymbol{H}_2$), 3.16 (t, 2H, ^3J = 7.2 Hz, cHex-$(CH_2)_2$-C$\boldsymbol{H}_2$), 3.28 (t, 2H, ^3J = 7.0 Hz, Im-4-$(CH_2)_2$-C$\boldsymbol{H}_2$), 7.25 (d, 1H, ^4J = 1.3 Hz, Im-5-$\boldsymbol{H}$), 8.58 (d, 1H, ^4J = 1.3 Hz, Im-2-$\boldsymbol{H}$). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 23.03 (-, Im-4-$\boldsymbol{C}H_2$), 27.54 (-, 2 cHex-$\boldsymbol{C}$), 27.83 (-, $\boldsymbol{C}H_2$), 27.87 (-, $\boldsymbol{C}H_2$), 29.64 (-, Im-4-CH_2-$\boldsymbol{C}H_2$), 34.58 (-, 2 cHex-$\boldsymbol{C}$), 35.63 (-, $\boldsymbol{C}H_2$), 38.80 (+, cHex-$\boldsymbol{C}$), 41.81 (-, Im-4-$(CH_2)_2$-$\boldsymbol{C}H_2$), 43.21 (-, cHex-$(CH_2)_2$-$\boldsymbol{C}H_2$), 116.93 (+, Im-$\boldsymbol{C}$-5), 120.20 (C_{quat}, $\boldsymbol{C}$≡N), 134.97 (+, Im-$\boldsymbol{C}$-2), 135.47 (C_{quat}, Im-$\boldsymbol{C}$-4), 161.23 (C_{quat}, $\boldsymbol{C}$=N), 167.72 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3276 (N-H), 2919 (C-H), 2849 (C-H), 2159 (C≡N), 1580 (C=N). ES-MS (MeOH + NH_4OAc) *m/z* (%): 317 (100) [M +

H]$^+$. HRMS (EI-MS) calcd. for $C_{17}H_{28}N_6$ [$M^{+\bullet}$] 316.2375; found 316.2374. Anal. ($C_{17}H_{28}N_6$ · 0.8 $C_2H_2O_4$) C, H, N. $C_{17}H_{28}N_6$ (316.44).

2-Cyano-1-[3-(1*H*-imidazol-4-yl)propyl]-3-[2-(phenylthio)ethyl]guanidine (60). The title compound was prepared from **32** (0.60 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.52 g, 78%); mp (hydrogenoxalate) 126 – 129 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.83 – 1.96 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.73 (t, 2H, ^3J = 7.6 Hz, Im-4-C***H***$_2$), 3.11 (t, 2H, ^3J = 6.9 Hz, S-CH_2-C***H***$_2$), 3.22 (t, 2H, ^3J = 6.9 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 3.42 (t, 2H, ^3J = 6.9 Hz, S-C***H***$_2$), 7.13 – 7.21 (m, 1H, Ph-4-***H***), 7.22 – 7.34 (m, 3H, Ph-***H*** + Im-5-***H***), 7.34 – 7.43 (m, 2H, Ph-***H***), 8.65 (d, 1H, ^4J = 1.3 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 22.90 (-, Im-4-***C***H_2), 29.36 (-, Im-4-CH_2-***C***H_2), 33.62 (-, S-***C***H_2), 41.90 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.32 (-, S-CH_2-***C***H_2), 116.91 (+, Im-***C***-5), 119.82 (C_{quat}, ***C***≡N), 127.38 (+, Ph-***C***-4), 130.20 (+, 2 Ph-***C***), 130.48 (+, 2 Ph-***C***), 134.91 (+, Im-***C***-2), 135.22 (C_{quat}, Im-***C***-4), 136.97 (C_{quat}, Ph-***C***-1), 161.18 (C_{quat}, ***C***=N), 167.52 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3247 (N-H), 2938 (C-H), 2847 (C-H), 2160 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 329 (100) [M + H]$^+$. HRMS (EI-MS) calcd. for $C_{16}H_{20}N_6S$ [$M^{+\bullet}$] 328.1470; found 328.1467. Anal. ($C_{16}H_{20}N_6S$ · 0.75 $C_2H_2O_4$ · 0.25 H_2O) C, H, N. $C_{16}H_{20}N_6S$ (328.44).

2-Cyano-1-[3-(1*H*-imidazol-4-yl)propyl]-3-[2-(1*H*-indol-3-yl)ethyl]guanidine (61). The title compound was prepared from **33** (0.61 g, 2.0 mmol) and **45** (0.28 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.53 g, 79%); mp (hydrogenoxalate) 160 – 164 °C. ^{1}H-NMR (400 MHz, COSY, CD_3OD, hydrogenoxalate): δ [ppm] = 1.65 – 1.76 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.58 (t, 2H, ^3J = 7.6 Hz, Im-4-C***H***$_2$), 3.00 (t, 2H, ^3J = 6.9 Hz, indole-3-C***H***$_2$), 3.13 (t, 2H, ^3J = 6.9 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 3.50 (t, 2H, ^3J = 6.9 Hz, indole-3-CH_2-C***H***$_2$), 6.99 (ddd, 1H, ^3J = 7.8 Hz, ^3J = 7.0 Hz, ^4J = 1.1 Hz, indole-5-***H***), 7.05 (ddd, 1H, ^3J = 8.0 Hz, ^3J = 7.0 Hz, ^4J = 1.3 Hz, indole-6-***H***), 7.10 (s, 1H, indole-2-***H***), 7.15 (d, 1H, ^4J = 1.4 Hz, Im-5-***H***), 7.29 (ddd, 1H, ^3J = 8.0 Hz, ^4J = 1.1 Hz, ^5J = 0.8 Hz, indole-7-***H***), 7.56 (ddd, 1H, ^3J = 7.8 Hz, ^4J = 1.3 Hz, ^5J = 0.8 Hz, indole-4-***H***), 8.64 (d, 1H, ^4J = 1.4 Hz, Im-2-***H***). ^{13}C-NMR (100 MHz, HMQC, CD_3OD, hydrogenoxalate): δ [ppm] = 22.63 (-, Im-4-***C***H_2), 26.40 (-, indole-3-***C***H_2), 29.20 (-, Im-4-CH_2-***C***H_2), 41.61 (-, Im-4-$(CH_2)_2$-***C***H_2), 43.71 (-, indole-3-CH_2-***C***H_2), 112.37 (+, indole-***C***-7), 112.70 (C_{quat}, indole-***C***-3), 116.82 (+, Im-***C***-5), 119.33 (+, indole-***C***-4), 119.82 (+, indole-***C***-5), 120.12 (C_{quat}, ***C***≡N), 122.47 (+, indole-***C***-6),

123.98 (+, indole-***C***-2), 128.75 (C_{quat}, indole-***C***-3a), 134.74 (+, Im-***C***-2), 135.04 (C_{quat}, Im-***C***-4), 138.22 (C_{quat}, indole-***C***-7a), 161.29 (C_{quat}, ***C***=N), 167.11 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3280 (N-H), 2936 (C-H), 2854 (C-H), 2160 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 336 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{18}H_{21}N_7$ $[M^{+\bullet}]$ 335.1858; found 335.1854. Anal. ($C_{18}H_{21}N_7 \cdot C_2H_2O_4$) C, H, N. $C_{18}H_{21}N_7$ (335.41).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-(3-phenylpropyl)guanidine (62). The title compound was prepared from **27** (0.56 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.47 g, 72%); mp (hydrogenoxalate) 134 – 137 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.52 – 1.77 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 1.78 – 1.92 (m, 2H, Ph-CH_2-C***H***$_2$), 2.63 (t, 2H, ^3J = 7.7 Hz, Im-4-C***H***$_2$), 2.74 (t, 2H, ^3J = 7.3 Hz, Ph-C***H***$_2$), 3.15 – 3.27 (m, 4H, Im-4-$(CH_2)_3$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 7.10 – 7.30 (m, 6H, Im-5-***H*** + Ph-***H***), 8.61 (d, 1H, ^4J = 1.4 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 25.20 (-, Im-4-***C***H_2), 26.87 (-, Im-4-CH_2-***C***H_2), 29.84 (-, Im-4-$(CH_2)_2$-***C***H_2), 32.30 (-, Ph-CH_2-***C***H_2), 34.00 (-, Ph***C***H_2), 42.17 (-, Im-4-$(CH_2)_3$-***C***H_2), 42.43 (-, Ph-$(CH_2)_2$-***C***H_2), 116.87 (+, Im-***C***-5), 120.29 (C_{quat}, ***C***≡N), 127.05 (+, Ph-***C***-4), 129.47 (+, 2 Ph-***C***), 129.53 (+, 2 Ph-***C***), 134.80 (+, Im-***C***-2), 135.69 (C_{quat}, Im-***C***-4), 142.87 (C_{quat}, Ph-***C***-1), 161.22 (C_{quat}, ***C***=N), 167.65 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3250 (N-H), 2937 (C-H), 2857 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 325 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{18}H_{24}N_6$ $[M^{+\bullet}]$ 324.2062; found 324.2055. Anal. ($C_{18}H_{24}N_6 \cdot 0.9\ C_2H_2O_4$) C, H, N. $C_{18}H_{24}N_6$ (324.42).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-(2-phenylethyl)guanidine (63). The title compound was prepared from **28** (0.53 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.55 g, 88%); mp (hydrogenoxalate) 142 – 144 °C. ^{1}H-NMR (400 MHz, CD_3OD, COSY): δ [ppm] = 1.45 – 1.56 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.56 – 1.67 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.58 (t, 2H, ^3J = 7.3 Hz, Im-4-C***H***$_2$), 2.82 (t, 2H, ^3J = 7.2 Hz, Ph-C***H***$_2$), 3.14 (t, 2H, ^3J = 7.1 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 3.42 (t, 2H, ^3J = 7.2 Hz, Ph-CH_2-C***H***$_2$), 6.76 (s, 1H, Im-5-***H***), 7.15 – 7.30 (m, 5H, Ph-***H***), 7.53 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (100 MHz, CD_3OD, HSQC): δ [ppm] = 27.14 (-, Im-4-***C***H_2), 27.66 (-, Im-4-CH_2-***C***H_2), 29.86 (-, Im-4-$(CH_2)_2$-***C***H_2), 36.67 (-, Ph***C***H_2), 42.47 (-, Im-4-$(CH_2)_3$-***C***H_2), 44.15 (-, Ph-CH_2-***C***H_2), 117.74 (+, Im-***C***-5), 120.19 (C_{quat}, ***C***≡N), 127.51 (+, Ph-***C***-4), 129.56 (+, 2 Ph-***C***), 129.95 (+, 2 Ph-***C***), 135.73 (+, Im-***C***-2), 137.97 (C_{quat}, Im-***C***-4), 140.11 (C_{quat},

Ph-***C***-1), 161.13 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3245 (N-H), 2935 (C-H), 2857 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 311 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{17}H_{22}N_6$ $[M^{+\bullet}]$ 310.1906; found 310.1912. Anal. ($C_{17}H_{22}N_6 \cdot 0.75\ C_2H_2O_4 \cdot 0.5\ H_2O$) C, H, N. $C_{17}H_{22}N_6$ (310.40).

2-Cyano-1-{1-[4-(1*H*-imidazol-4-yl)butyl]}-3-(4-phenylbutyl)guanidine (64). The title compound was prepared from **29** (0.59 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.45 g, 66%); mp (hydrogenoxalate) 125 – 128 °C. ^{1}H-NMR (600 MHz, CD_3OD, NOESY): δ [ppm] = 1.54 – 1.61 (m, 4H, Im-4-$(CH_2)_2$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 1.62 – 1.69 (m, 4H, Im-4-CH_2-C***H***$_2$ + Ph-CH_2-C***H***$_2$), 2.61 (t, 2H, ^3J = 7.4 Hz, Im-4-C***H***$_2$), 2.63 (t, 2H, ^3J = 7.5 Hz, Ph-C***H***$_2$), 3.18 – 3.24 (m, 4H, Im-4-$(CH_2)_3$-C***H***$_2$ + Ph-$(CH_2)_3$-C***H***$_2$), 6.77 (s, 1H, Im-5-***H***), 7.13 – 7.21 (m, 5H, Ph-***H***), 7.55 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (150 MHz, CD_3OD, HSQC): δ [ppm] = 27.23 (-, Im-4-***C***H_2), 27.71 (-, Im-4-CH_2-***C***H_2), 29.73, 29.99, 30.05 (-, Im-4-$(CH_2)_2$-***C***H_2 + Ph-CH_2-***C***H_2-***C***H_2), 36.49 (-, Ph***C***H_2), 42.48, 42.54 (-, Im-4-$(CH_2)_3$-***C***H_2, Ph-$(CH_2)_3$-***C***H_2), 120.39 (C_{quat}, ***C***≡N), 126.83 (+, Ph-***C***-4), 129.37 (+, 2 Ph-***C***), 129.47 (+, 2 Ph-***C***), 135.74 (+, Im-***C***-2), 143.50 (C_{quat}, Ph-***C***-1), 161.19 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3266 (N-H), 2937 (C-H), 2858 (C-H), 2159 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 339 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{19}H_{26}N_6$ $[M^{+\bullet}]$ 338.2219; found 338.2224. Anal. ($C_{19}H_{26}N_6 \cdot 0.85\ C_2H_2O_4$) C, H, N. $C_{19}H_{26}N_6$ (338.45).

2-Cyano-1-(3,3-diphenylpropyl)-3-[4-(1*H*-imidazol-4-yl)butyl]guanidine (65). The title compound was prepared from **30** (0.71 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless resin that solidified from Et_2O (0.46 g, 57%); mp 80 – 84 °C. ^{1}H-NMR (400 MHz, COSY, CD_3OD): δ [ppm] = 1.48 – 1.58 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.58 – 1.68 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.27 – 2.36 (m, 2H, Ph_2CH-C***H***$_2$), 2.59 (t, 2H, ^3J = 7.2 Hz, Im-4-C***H***$_2$), 3.10 – 3.19 (m, 4H, Im-4-$(CH_2)_3$-C***H***$_2$ + Ph_2CH-CH_2-C***H***$_2$), 3.99 (t, 1H, ^3J = 7.8 Hz, Ph_2C***H***), 6.76 (d, 1H, ^4J = 1.1 Hz, Im-5-***H***), 7.11 – 7.19 (m, 2H, Ph-4-***H***), 7.23 – 7.30 (m, 8H, Ph-***H***), 7.52 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (100 MHz, HMQC, CD_3OD): δ [ppm] = 27.21 (-, Im-4-***C***H_2), 27.75 (-, Im-4-CH_2-***C***H_2), 29.96 (-, Im-4-$(CH_2)_2$-***C***H_2), 36.13 (-, Ph_2CH-***C***H_2), 41.70, 42.52 (-, Im-4-$(CH_2)_3$-***C***H_2 + Ph_2CH-CH_2-***C***H_2), 50.12 (+, Ph_2***C***H), 117.82 (+, Im-***C***-5), 120.39 (C_{quat}, ***C***≡N), 127.43 (+, 2 Ph-***C***-4), 128.91 (+, 4 Ph-***C***), 129.64 (+, 4 Ph-***C***), 135.79 (+, Im-***C***-2), 138.33 (C_{quat}, Im-***C***-4), 145.87 (C_{quat}, Ph-***C***-1),

161.21 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3277 (N-H), 2936 (C-H), 2858 (C-H), 2159 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN + NH_4OAc) *m/z* (%): 401 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{24}H_{28}N_6$ $[M^{+\bullet}]$ 400.2375; found 400.2372. Anal. ($C_{24}H_{28}N_6 \cdot 0.25\ H_2O$) C, H, N. $C_{24}H_{28}N_6$ (400.52).

2-Cyano-1-(3-cyclohexylpropyl)-3-[4-(1*H*-imidazol-4-yl)butyl]guanidine (66). The title compound was prepared from **31** (0.57 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.49 g, 75%); mp (hydrogenoxalate) 141 – 143 °C. ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 0.80 – 0.99 (m, 2H, cHex-C***H***$_2$), 1.09 – 1.35 (m, 6H), 1.46 – 1.79 (m, 11H), 2.60 (t, 2H, ^3J = 7.1 Hz, Im-4-C***H***$_2$), 3.15 (t, 2H, ^3J = 7.2 Hz, cHex-$(CH_2)_2$-C***H***$_2$), 3.21 (t, 2H, ^3J = 6.8 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 6.77 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.54 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 27.23 (-, Im-4-***C***H_2), 27.54 (-, 2 cHex-***C***), 27.76 (-, Im-4-CH_2-***C***H_2), 27.83 (-, ***C***H_2), 27.90 (-, ***C***H_2), 30.07 (-, Im-4-$(CH_2)_2$-***C***H_2), 34.57 (-, 2 c-Hex-***C***), 35.61 (-, ***C***H_2), 38.79 (+, cHex-***C***), 42.48 (-, Im-4-$(CH_2)_3$-***C***H_2), 43.09 (-, cHex-$(CH_2)_2$-***C***H_2), 117.81 (+, Im-***C***-5), 120.44 (C_{quat}, ***C***≡N), 135.77 (+, Im-***C***-2), 138.00 (C_{quat}, Im-***C***-4), 161.19 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3265 (N-H), 2922 (C-H), 2848 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 331 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{18}H_{30}N_6$ $[M^{+\bullet}]$ 330.2532; found 330.2533. Anal. ($C_{18}H_{30}N_6 \cdot 0.8\ C_2H_2O_4 \cdot 0.25\ H_2O$) C, H, N. $C_{18}H_{30}N_6$ (330.47).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-[2-(1*H*-indol-3-yl)ethyl]guanidine (68)

The title compound was prepared from **33** (0.61 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a beige foam-like solid (0.58 g, 83%); mp (hydrogenoxalate) 154 – 156 °C. ^{1}H-NMR (400 MHz, COSY, CD_3OD): δ [ppm] = 1.33 – 1.44 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.48 – 1.60 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.52 (t, 2H, ^3J = 7.4 Hz, Im-4-C***H***$_2$), 2.97 (t, 2H, ^3J = 7.0 Hz, indole-3-C***H***$_2$), 3.06 (t, 2H, ^3J = 7.2 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 3.47 (t, 2H, ^3J = 7.0 Hz, indole-3-CH_2-C***H***$_2$), 6.73 (d, 1H, ^4J = 1.4 Hz, Im-5-***H***), 7.00 (ddd, 1H, ^3J = 8.0 Hz, ^3J = 7.0 Hz, ^4J = 1.0 Hz, indole-5-***H***), 7.05 – 7.10 (m, 2H, indole-6-***H*** + indole-2-***H***), 7.32 (ddd, 1H, ^3J = 8.0 Hz, ^4J = 1.0 Hz, ^5J = 0.8 Hz, indole-7-***H***), 7.52 (d, 1H, ^4J = 1.2 Hz, Im-2-***H***), 7.55 (ddd, 1H, ^3J = 8.0 Hz, ^4J = 1.2 Hz, ^5J = 0.8 Hz, indole-4-***H***). ^{13}C-NMR (100 MHz, CD_3OD, HSQC): δ [ppm] = 26.37 (-, indole-3-***C***H_2), 27.07 (-, Im-4-***C***H_2), 27.60 (-, Im-4-CH_2-***C***H_2), 29.74 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.43 (-, Im-4-$(CH_2)_3$-***C***H_2), 43.59 (-, indole-3-CH_2-***C***H_2), 112.34 (+, indole-***C***-7), 112.73 (C_{quat}, indole-***C***-3), 117.85 (+, Im-***C***-5), 119.26 (+,

indole-***C***-4), 119.79 (+, indole-***C***-5), 120.41 (C_{quat}, ***C***≡N), 122.47 (+, indole-***C***-6), 123.80 (+, indole-***C***-2), 128.68 (C_{quat}, indole-***C***-3a), 135.69 (+, Im-***C***-2), 138.09 (C_{quat}, Im-***C***-4), 138.20 (C_{quat}, indole-***C***-7a), 161.20 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3249 (N-H), 2936 (C-H), 2849 (C-H), 2158 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 350 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{19}H_{23}N_7$ $[M^{+\bullet}]$ 349.2015; found 349.2010. Anal. ($C_{19}H_{23}N_7 \cdot C_2H_2O_4$) calcd. C: 57.39, H: 5.73, N: 22.31, found C: 56.50, H: 6.37, N: 21.57. $C_{19}H_{23}N_7$ (349.43).

2-Cyano-1-[3-(4-fluorophenyl)propyl]-3-[4-(1*H*-imidazol-4-yl)butyl]guanidine (69). The title compound was prepared from **34** (0.59 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a pale yellow foam-like solid (0.55 g, 80%); mp (hydrogenoxalate) 132 – 134 °C. ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.49 – 1.73 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 1.76 – 1.90 (m, 2H, Ph-CH_2-C***H***$_2$), 2.54 – 2.67 (m, 4H, Im-4-C***H***$_2$ + Ph-C***H***$_2$), 3.12 – 3.26 (m, 4H, Im-4-$(CH_2)_3$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 6.77 (d, 1H, ^4J = 1.2 Hz, Im-5-***H***), 6.92 – 7.03 (m, 2H, Ph-***H***), 7.14 – 7.23 (m, 2H, Ph-***H***), 7.53 (d, 1H, ^4J = 1.2 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 27.29 (-, Im-4-***C***H_2), 27.76 (-, Im-4-CH_2-***C***H_2), 30.01 (-, Im-4-$(CH_2)_2$-***C***H_2), 32.36 (-, 4-F-Ph-CH_2-***C***H_2), 33.15 (-, 4-F-Ph***C***H_2), 42.30 (-, Im-4-$(CH_2)_3$-***C***H_2), 42.53 (-, 4-F-Ph-$(CH_2)_2$-***C***H_2), 116.04 (+, ^2J = 21.3 Hz, 4-F-Ph-***C***-3,5), 120.34 (C_{quat}, ***C***≡N), 131.04 (+, ^3J = 7.8 Hz, 4-F-Ph-***C***-2,6), 135.78 (+, Im-***C***-2), 138.79 (C_{quat}, ^4J = 3.1 Hz, Ph-***C***-1), 161.22 (C_{quat}, ***C***=N), 162.83 (C_{quat}, ^1J = 271.7 Hz, 4-F-Ph-***C***-4). IR (cm^{-1}) = 3256 (N-H), 2970 (C-H), 2865 (C-H), 2158 (C≡N), 1576 (C=N), 1219 (C-F). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 343 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{18}H_{23}FN_6$ $[M^{+\bullet}]$ 342.1968; found 342.1969. Anal. ($C_{18}H_{23}FN_6 \cdot C_2H_2O_4 \cdot H_2O$) C, H, N. $C_{18}H_{23}FN_6$ (342.41).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-[3-(pyridin-2-yl)propyl]guanidine (70). The title compound was prepared from **35** (0.56 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.59 g, 91%); mp (hydrogenoxalate) 156 – 158 °C. ^{1}H-NMR (600 MHz, CD_3OD, COSY): δ [ppm] = 1.54 – 1.61 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.61 – 1.70 (m, 2H, Im-4-CH_2-C***H***$_2$), 1.90 – 1.97 (m, 2H, Pyr-2-CH_2-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.3 Hz, Im-4-C***H***$_2$), 2.81 (t, 2H, ^3J = 7.5 Hz, Pyr-2-C***H***$_2$), 3.21 (t, 2H, ^3J = 7.1 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 3.24 (t, 2H, ^3J = 7.0 Hz, Pyr-2-$(CH_2)_2$-C***H***$_2$), 6.76 (d, 1H, ^4J = 1.1 Hz, Im-5-***H***), 7.24 (ddd, 1H, ^3J = 7.5 Hz, ^3J = 5.0 Hz, ^4J = 1.2 Hz, Pyr-5-***H***), 7.30 (ddd, 1H, ^3J = 7.8 Hz, ^4J = 1.2 Hz, ^5J = 1.0 Hz, Pyr-3-***H***), 7.53 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***), 7.74 (ddd, 1H, ^3J = 7.8 Hz, ^3J = 7.5 Hz, ^4J = 1.8 Hz, Pyr-4-***H***), 7.74 (ddd, 1H, ^3J = 5.0 Hz, ^4J = 1.8 Hz, ^5J =

1.0 Hz, Pyr-6-***H***). ^{13}C-NMR (150 MHz, CD_3OD, HSQC, HMBC): δ [ppm] = 27.14 (-, Im-4-***C***H_2), 27.72 (-, Im-4-CH_2-***C***H_2), 29.99 (-, Im-4-$(CH_2)_2$-***C***H_2), 30.48 (-, Pyr-2-***C***H_2), 35.61 (-, Pyr-2-CH_2-***C***H_2), 42.20 (-, Pyr-2-$(CH_2)_2$-***C***H_2), 42.52 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.87 (+, Im-***C***-5), 120.24 (C_{quat}, ***C***≡N), 122.94 (+, Pyr-***C***-5), 124.73 (+, Pyr-***C***-3), 135.73 (+, Im-***C***-2), 138.20 (C_{quat}, Im-***C***-4), 138.83 (+, Pyr-***C***-4),149.64 (+, Pyr-***C***-6), 161.23 (C_{quat}, ***C***=N), 162.37 (C_{quat}, Pyr-***C***-2). IR (cm^{-1}) = 3242 (N-H), 2938 (C-H), 2857 (C-H), 2159 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 326 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{17}H_{23}N_7$ $[M^{+\bullet}]$ 325.2015; found 325.2009. Anal. ($C_{17}H_{23}N_7 \cdot 2\ C_2H_2O_4 \cdot H_2O$) C, H, N. $C_{17}H_{23}N_7$ (325.41).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-[3-(pyridin-3-yl)propyl]guanidine (71). The title compound was prepared from **36** (0.56 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.34 g, 52%); mp (hydrogenoxalate) 156 – 158 °C. ^{1}H-NMR (400 MHz, CD_3OD, COSY): δ [ppm] = 1.52 – 1.61 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.61 – 1.70 (m, 2H, Im-4-CH_2-C***H***$_2$), 1.82 – 1.93 (m, 2H, Pyr-3-CH_2-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.2 Hz, Im-4-C***H***$_2$), 2.68 (t, 2H, ^3J = 7.8 Hz, Pyr-3-C***H***$_2$), 3.19 (t, 2H, ^3J = 7.0 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 3.24 (t, 2H, ^3J = 7.1 Hz, Pyr-3-CH_2-CH_2-C***H***$_2$), 6.76 (d, 1H, ^4J = 1.1 Hz, Im-5-***H***), 7.35 (ddd, 1H, ^3J = 7.9 Hz, ^3J = 4.9 Hz, ^5J = 0.9 Hz, Pyr-5-***H***), 7.53 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***), 7.70 (ddd, 1H, ^3J = 7.9 Hz, ^4J = 2.3 Hz, ^4J = 1.6 Hz, Pyr-4-***H***), 8.35 (dd, 1H, ^3J = 4.9 Hz, ^4J = 1.6 Hz, Pyr-6-***H***), 8.39 (dd, 1H, ^4J = 2.3 Hz, ^5J = 0.9 Hz, Pyr-2-***H***). ^{13}C-NMR (100 MHz, CD_3OD, HSQC, HMBC): δ [ppm] = 27.17 (-, Im-4-***C***H_2), 27.73 (-, Im-4-CH_2-***C***H_2), 29.94 (-, Im-4-$(CH_2)_2$-***C***H_2), 30.94 (-, Pyr-3-***C***H_2), 31.81 (-, Pyr-3-CH_2-***C***H_2), 42.17 (-, Pyr-3-$(CH_2)_2$-***C***H_2), 42.52 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.72 (+, Im-***C***-5), 120.20 (C_{quat}, ***C***≡N), 125.22 (+, Pyr-***C***-5), 135.75 (+, Im-***C***-2), 138.24 (+, Pyr-***C***-4), 139.31 (C_{quat}, Pyr-***C***-3), 147.73 (+, Pyr-***C***-6), 150.06 (+, Pyr-***C***-2), 161.22 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3265 (N-H), 2931 (C-H), 2863 (C-H), 2160 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 326 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{17}H_{23}N_7$ $[M^{+\bullet}]$ 325.2015; found 325.2014. Anal. ($C_{17}H_{23}N_7 \cdot 2\ C_2H_2O_4 \cdot 1.3\ H_2O$) C, H, N. $C_{17}H_{23}N_7$ (325.41).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-[3-(pyridin-4-yl)propyl]guanidine (72). The title compound was prepared from **37** (0.56 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.34 g, 52%); mp (hydrogenoxalate) 155 – 157 °C. ^{1}H-NMR (400 MHz, CD_3OD, COSY): δ [ppm] = 1.51 – 1.61 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.61 – 1.70 (m, 2H, Im-4-CH_2-C***H***$_2$), 1.84 – 1.95 (m, 2H,

Pyr-4-CH_2-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.2 Hz, Im-4-C***H***$_2$), 2.69 (t, 2H, ^3J = 7.8 Hz, Pyr-4-C***H***$_2$), 3.19 (t, 2H, ^3J = 7.0 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 3.24 (t, 2H, ^3J = 7.1 Hz, Pyr-4-$(CH_2)_2$-C***H***$_2$), 6.77 (d, 1H, ^4J = 1.1 Hz, Im-5-***H***), 7.28 (dd, 2H, ^3J = 4.5 Hz, ^5J = 1.6 Hz, Pyr-3,5-***H***), 7.53 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***), 8.39 (dd, 2H, ^3J = 4.5 Hz, ^5J = 1.6 Hz, Pyr-2,6-***H***). ^{13}C-NMR (100 MHz, CD_3OD, HSQC, HMBC): δ [ppm] = 27.17 (-, Im-4-***C***H_2), 27.72 (-, Im-4-CH_2-***C***H_2), 29.94 (-, Im-4-$(CH_2)_2$-***C***H_2), 31.02 (-, Pyr-4-CH_2-***C***H_2), 33.25 (-, Pyr-4-***C***H_2), 42.18 (-, Pyr-4-$(CH_2)_2$-***C***H_2), 42.51 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.58 (+, Im-***C***-5), 120.18 (C_{quat}, ***C***≡N), 125.62 (+, Pyr-***C***-3,5), 135.75 (+, Im-***C***-2), 138.26 (C_{quat}, Im-***C***-4), 149.95 (+, Pyr-***C***-2,6), 153.69 (C_{quat}, Pyr-***C***-4), 161.20 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3244 (N-H), 2933 (C-H), 2864 (C-H), 2160 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 326 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{17}H_{23}N_7$ $[M^{+\bullet}]$ 325.2015; found 325.2007. Anal. ($C_{17}H_{23}N_7$ · 2 $C_2H_2O_4$ · 2 H_2O) C, H, N. $C_{17}H_{23}N_7$ (325.41).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-(3-phenylbutyl)guanidine (73). The title compound was prepared from **38** (0.59 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.53 g, 78%); mp (hydrogenoxalate) 135 – 137 °C. ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.25 (d, 3H, ^3J = 6.9 Hz, PhC***H***$_3$CH), 1.54 – 1.60 (m, 2H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 1.78 – 1.90 (m, 2H, PhCH_3CH-C***H***$_2$), 2.59 (t, 2H, ^3J = 7.2 Hz, Im-4-C***H***$_2$), 2.68 – 2.83 (m, 1H, PhCH_3C***H***), 2.97 – 3.20 (m, 4H, PhCH_3CH-CH_2-C***H***$_2$ + Im-4-$(CH_2)_3$-C***H***$_2$), 6.76 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.11 – 7.32 (m, 5H, Ph-***H***), 7.53 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 23.09 (+, ***C***H_3), 27.21 (-, Im-4-***C***H_2), 27.74 (-, Im-4-CH_2-***C***H_2), 29.97 (-, Im-4-$(CH_2)_2$-***C***H_2), 38.58, (-, PhCH_3CH-***C***H_2), 38.93 (+, PhCH_3***C***H), 41.43 (-, PhCH_3CH-CH_2-***C***H_2), 42.48 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.69 (+, Im-***C***-5), 120.39 (C_{quat}, ***C***≡N), 127.32 (+, Ph-***C***-4), 128.05 (+, 2 Ph-***C***), 129.64 (+, 2 Ph-***C***), 135.77 (+, Im-***C***-2), 138.03 (C_{quat}, Im-***C***-4), 147.85 (C_{quat}, Ph-***C***-1), 161.14 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3250 (N-H), 2930 (C-H), 2866 (C-H), 2159 (C≡N), 1576 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 339 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{19}H_{26}N_6$ $[M^{+\bullet}]$ 338.2219; found 338.2210. Anal. ($C_{19}H_{26}N_6$ · 0.85 $C_2H_2O_4$) C, H, N. $C_{19}H_{26}N_6$ (338.45).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]guanidine (74). The title compound was prepared from **39** (0.32 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 87.5/10.5/2 v/v/v) yielding a colorless foam-like solid (0.35 g, 85%); mp

(hydrogenoxalate) 172 – 174 °C. ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.46 – 1.74 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 2.61 (t, 2H, ^3J = 7.3 Hz, Im-4-C***H***$_2$), 3.17 (t, 2H, ^3J = 6.9 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 6.80 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.62 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 27.05 (-, Im-4-***C***H_2), 27.71 (-, Im-4-CH_2-***C***H_2), 29.95 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.23 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.81 (+, Im-***C***-5), 120.22 (C_{quat}, ***C***≡N), 135.72 (+, Im-***C***-2), 137.99 (C_{quat}, Im-***C***-4), 161.13 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3312 (N-H), 2940 (C-H), 2858 (C-H), 2164 (C≡N), 1558 (C=N). ES-MS (MeCN + TFA) *m/z* (%): 207 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_9H_{14}N_6$ $[M^{+\bullet}]$ 206.1280; found 206.1281. Anal. ($C_9H_{14}N_6 \cdot C_2H_2O_4 \cdot 0.1\ H_2O$) C, H, N. $C_9H_{14}N_6$ (206.25).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-methylguanidine (75).[1] The title compound was prepared from **40** (0.35 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless foam-like solid (0.34 g, 77%); mp (hydrogenoxalate) 143 – 145 °C. ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.49 – 1.73 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.1 Hz, Im-4-C***H***$_2$), 2.77 (s, 3H, C***H***$_3$), 3.20 (t, 2H, ^3J = 6.9 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 6.77 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.55 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 27.18 (-, Im-4-***C***H_2), 27.75 (-, Im-4-CH_2-***C***H_2), 28.73 (+, C***H***$_3$), 30.07 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.50 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.89 (+, Im-***C***-5), 120.32 (C_{quat}, ***C***≡N), 135.77 (+, Im-***C***-2), 138.21 (C_{quat}, Im-***C***-4), 161.99 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3277 (N-H), 2972 (C-H), 2901 (C-H), 2158 (C≡N), 1577 (C=N). ES-MS (MeCN + TFA) *m/z* (%): 221 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{10}H_{16}N_6$ $[M^{+\bullet}]$ 220.1436; found 220.1439. Anal. ($C_{10}H_{16}N_6 \cdot C_2H_2O_4 \cdot 0.4\ H_2O$) C, H, N. $C_{10}H_{16}N_6$ (220.27).

2-Cyano-1-ethyl-3-[4-(1*H*-imidazol-4-yl)butyl]guanidine (76). The title compound was prepared from **41** (0.38 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.39 g, 83%); mp (hydrogenoxalate) 130 – 133 °C. ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.14 (t, 3H, ^3J = 7.2 Hz, C***H***$_3$), 1.50 – 1.72 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.1 Hz, Im-4-C***H***$_2$), 3.16 – 3.27 (m, 4H, CH_3C***H***$_2$ + Im-4-$(CH_2)_3$-***C***H_2), 6.77 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.55 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 15.13 (+, ***C***H_3), 27.20 (-, Im-4-***C***H_2), 27.77 (-, Im-4-CH_2-***C***H_2), 30.04 (-, Im-4-$(CH_2)_2$-***C***H_2), 37.62 (-, ***C***H_2-CH_3), 42.51 (-, Im-4-$(CH_2)_3$-***C***H_2), 117.95 (+, Im-***C***-5), 120.48 (C_{quat}, ***C***≡N), 135.79 (+, Im-***C***-2), 138.15 (C_{quat}, Im-***C***-4), 161.10 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3264 (N-H), 2934 (C-H), 2858 (C-H), 2155 (C≡N), 1572

(C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 235 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{11}H_{18}N_6$ $[M^{+\bullet}]$ 234.1593; found 234.1590. Anal. ($C_{11}H_{18}N_6$ · 0.75 $C_2H_2O_4$) C, H, N. $C_{11}H_{18}N_6$ (234.30).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-isopropylguanidine (77). The title compound was prepared from **42** (0.41 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.39 g, 79%); mp (hydrogenoxalate) 129 – 131 °C. ^{1}H-NMR (600 MHz, CD_3OD): δ [ppm] = 1.25 (d, 6H, ^3J = 6.5 Hz, C***H***$_3$), 1.46 – 1.69 (m, 2H, Im-4-$(CH_2)_2$-C***H***$_2$), 1.62 – 1.69 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.4 Hz, Im-4-C***H***$_2$), 3.22 (t, 2H, ^3J = 7.4 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 3.86 (sep, 1H, ^3J = 6.5 Hz, C***H***), 6.77 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.54 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 22.83 (+, ***C***H_3), 27.20 (-, Im-4-***C***H_2), 27.75 (-, Im-4-CH_2-***C***H_2), 30.02 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.50 (-, Im-4-$(CH_2)_3$-***C***H_2), 45.06 (+, ***C***H), 117.87 (+, Im-***C***-5), 120.42 (C_{quat}, ***C***≡N), 135.78 (+, Im-***C***-2), 138.15 (C_{quat}, Im-***C***-4), 160.37 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3241 (N-H), 2937 (C-H), 2860 (C-H), 2157 (C≡N), 1569 (C=N). ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 249 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{12}H_{20}N_6$ $[M^{+\bullet}]$ 248.1749; found 248.1746. Anal. ($C_{12}H_{20}N_6$ · 0.75 $C_2H_2O_4$ · 0.25 H_2O) C, H, N. $C_{12}H_{20}N_6$ (248.33).

2-Cyano-1-[4-(1*H*-imidazol-4-yl)butyl]-3-isobutylguanidine (78). The title compound was prepared from **43** (0.43 g, 2.0 mmol) and **46** (0.31 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielding a colorless foam-like solid (0.28 g, 53%); mp (hydrogenoxalate) 140 – 143 °C. ^{1}H-NMR (600 MHz, CD_3OD, COSY): δ [ppm] = 0.90 (d, 6H, ^3J = 6.7 Hz, C***H***$_3$), 1.54 – 1.60 (m, 2H, Im-4-$(CH_2)_2$-***C***H_2), 1.62 – 1.69 (m, 2H, Im-4-CH_2-C***H***$_2$), 1.79 – 1.87 (m, 1H, C***H***), 2.60 (t, 2H, ^3J = 7.3 Hz, Im-4-C***H***$_2$), 2.99 (d, 2H, ^3J = 7.2 Hz, $(CH_3)_2CHC$***H***$_2$), 3.21 (t, 2H, ^3J = 7.1 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 6.76 (d, 1H, ^4J = 1.1 Hz, 1H, Im-5-***H***), 7.54 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (150 MHz, CD_3OD, HSQC): δ [ppm] = 20.83 (+, ***C***H_3), 27.15 (-, Im-4-***C***H_2), 27.70 (-, Im-4-CH_2-***C***H_2), 29.55 (+, ***C***H), 30.00 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.47 (-, Im-4-$(CH_2)_3$-***C***H_2), 50.07 (+, $(CH_3)_2CH$-***C***H_2)), 117.65 (+, Im-***C***-5), 120.36 (C_{quat}, ***C***≡N), 135.72 (+, Im-***C***-2), 138.10 (C_{quat}, Im-***C***-4), 161.28 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3280 (N-H), 2955 (C-H), 2871 (C-H), 2157 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 263 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{13}H_{22}N_6$ $[M^{+\bullet}]$ 262.1906; found 262.1906. Anal. ($C_{13}H_{22}N_6$ · 0.75 $C_2H_2O_4$ · 0.25 H_2O) C, H, N. $C_{13}H_{22}N_6$ (262.35).

2-Cyano-1-{2-[(5-methyl-1*H*-imidazol-4-yl)methylthio]ethyl}-3-(3-phenylpropyl)guanidine (86). The title compound was prepared from **27** (0.56 g, 2.0 mmol) and **85**[1] (0.38 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 95/3/2 v/v/v) yielding a pale yellow foam-like solid (0.42 g, 61%); mp (hydrogenoxalate) 148 – 150 °C. ^{1}H-NMR (300 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 1.79 – 1.93 (m, 2H, Ph-CH_2-C***H***$_2$), 2.34 (s, 3H, Im-5-C***H***$_3$), 2.58 – 2.69 (m, 4H, Ph-C***H***$_2$ + Im-4-CH_2-S-C***H***$_2$), 3.20 (t, 2H, ^3J = 7.1 Hz, Ph-$(CH_2)_2$-C***H***$_2$), 3.36 (t, 2H, ^3J = 7.1 Hz, Im-4-CH_2-S-CH_2-C***H***$_2$), 3.84 (s, 2H, Im-4-C***H***$_2$), 7.10 – 7.30 (m, 5H, Ph-***H***), 8.61 (s, 1H, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD, hydrogenoxalate): δ [ppm] = 9.12 (+, ***C***H_3), 24.74 (-, Im-4-***C***H_2), 31.99 (-, Im-4-CH_2-S-***C***H_2), 32.16, 33.96 (-, Ph***C***H_2-***C***H_2), 41.95 (-, Im-4-CH_2-S-CH_2-***C***H_2), 42.48 (-, Ph-$(CH_2)_2$-***C***H_2), 119.95 (C_{quat}, ***C***≡N), 127.08 (+, Ph-***C***-4), 127.86, 128.03 (C_{quat}, Im-***C***-4,5), 128.03 (+, 2 Ph-***C***), 129.54 (+, 2 Ph-***C***), 133.92 (+, Im-***C***-2), 142.80 (C_{quat}, Ph-***C***-1), 161.14 (C_{quat}, ***C***=N), 167.00 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3253 (N-H), 2989 (C-H), 2901 (C-H), 2161 (C≡N), 1576 (C=N). ES-MS (H_2O/MeCN) *m/z* (%): 357 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{18}H_{24}N_6S$ $[M^{+\bullet}]$ 356.1783; found 356.1781. Anal. ($C_{18}H_{24}N_6S \cdot 0.85\ C_2H_2O_4 \cdot 0.25\ H_2O$) C, H, N. $C_{18}H_{24}N_6S$ (356.49).

2-Cyano-1-(3,3-diphenylpropyl)-3-{2-[(5-methyl-1*H*-imidazol-4-yl)methylthio]ethyl}-guanidine (87). The title compound was prepared from **30** (0.71 g, 2.0 mmol) and **85**[1] (0.38 g, 2.2 mmol) in MeCN (50 mL) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/7 M NH_3 in MeOH 98/2 v/v) yielding a pale yellow foam-like solid (0.63 g, 73%); mp (hydrogenoxalate) 144 – 146 °C. ^{1}H-NMR (400 MHz, COSY, CD_3OD, hydrogenoxalate): δ [ppm] = 2.29 – 2.38 (m, 5H, Ph_2CH-C***H***$_2$ + Im-5-C***H***$_3$), 2.60 (t, 2H, ^3J = 7.0 Hz, Im-4-CH_2-S-C***H***$_2$), 3.14 (t, 2H, ^3J = 7.2 Hz, Ph_2CH-CH_2-C***H***$_2$), 3.32 (t, 2H, ^3J = 7.0 Hz, Im-4-CH_2-S-CH_2-C***H***$_2$), 3.81 (s, 2H, Im-4-C***H***$_2$), 4.01 (t, 1H, ^3J = 7.9 Hz, Ph_2C***H***), 7.12 – 7.19 (m, 2H, Ph-4-***H***), 7.23 – 7.31 (m, 8H, Ph-***H***), 8.60 (s, 1H, Im-2-***H***). ^{13}C-NMR (100 MHz, HMQC, CD_3OD, hydrogenoxalate): δ [ppm] = 9.05 (+, Im-5-***C***H_3), 24.66 (-, Im-4-***C***H_2), 31.94 (-, Im-4-CH_2-S-***C***H_2), 35.84 (-, Ph_2CH-***C***H_2), 41.70 (-, Ph_2CH-CH_2-***C***H_2), 41.94 (-, Im-4-CH_2-S-CH_2-***C***H_2), 49.96 (+, Ph_2***C***H), 119.92 (C_{quat}, ***C***≡N), 127.45 (+, 2 Ph-***C***-4), 127.76, 128.01 (C_{quat}, Im-***C***-4,5), 128.89 (+, 4 Ph-***C***), 129.64 (+, 4 Ph-***C***), 133.87 (+, Im-***C***-2), 145.74 (C_{quat}, 2 Ph-***C***-1), 161.11 (C_{quat}, ***C***=N), 166.77 (C_{quat}, hydrogenoxalate). IR (cm^{-1}) = 3245 (N-H), 2927 (C-H), 2822 (C-H), 2161 (C≡N), 1576 (C=N). ES-MS (MeOH + NH_4OAc) *m/z* (%): 433 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{24}H_{28}N_6S$ $[M^{+\bullet}]$ 432.2096; found 432.2101. Anal. ($C_{24}H_{28}N_6S \cdot C_2H_2O_4 \cdot 0.5\ H_2O$) C, H, N. $C_{24}H_{28}N_6S$ (432.58).

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General procedure. The respective isourea (1 eq) and **47**[2] (1 eq) in 10 mL MeCN was heated under microwave irradiation at 170 °C for 3 min. After addition of 10 mL MeOH, the solvent was removed under reduced pressure and the residue purified by flash chromatography.

2-Cyano-1-[5-(1*H*-imidazol-4-yl)pentyl]-3-(3-phenylpropyl)guanidine (79). The title compound was prepared from **27** (0.279 g, 1.0 mmol) and **47**[2] (0.153 g, 1.0 mmol) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/NH_3(aq.) 32% 90/8/2 v/v/v) yielding a pale yellow oil (0.31 g, 92%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.35 (m, 2H, C***H***$_2$), 1.56 (m, 2H, C***H***$_2$), 1.65 (m, 2H, C***H***$_2$), 1.85 (m, 2H, CH_2C***H***$_2$$CH_2$Ph), 2.60 (m, 4H, Im-4-C***H***$_2$ + Ph-C***H***$_2$), 3.18 (m, 4H, Im-4-$(CH_2)_4$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 6.74 (s, 1H, Im-5-***H***), 7.12-7.28 (m, 5H, Ph-***H***), 7.52 (s, 1H, Im-2-***H***). ^{13}C-NMR (300 MHz, CD_3OD): δ [ppm] = 27.32 (-, Im-4-***C***H_2 + Im-$(CH_2)_2$***C***H2), 30.27 (-, 2 ***C***H_2), 32.28 (-, ***C***H_2), 34.00 (-, Ph-***C***H_2), 42.36 (-, ***C***H_2), 42.68 (-, ***C***H_2), 118.25 (+, Im-***C***-5), 120.37 (C_{quat}, ***C***≡N), 127.02 (+, Ph-***C***-4), 129.50 (+, 4 Ph-***C***), 135.67 (+, Im-***C***-2), 137.27 (C_{quat}, Im-***C***-4), 142.87 (C_{quat}, Ph-***C***), 161.18 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3250 (N-H), 2932 (C-H), 2857 (C-H), 2159 (C≡N), 1578 (C=N). HRMS (EI-MS) calcd. for $C_{19}H_{26}N_6$ [$M^{+\bullet}$] 338.2219; found 338.2217. $C_{19}H_{26}N_6$ (338.45).

2-Cyano-1-[5-(1*H*-imidazol-4-yl)pentyl]-3-(2-phenylthioethyl)guanidine (80). The title compound was prepared from **32** (0.297 g, 1.0 mmol) and **47**[2] (0.153 g, 1.0 mmol) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/NH_3(aq.) 32% 90/8/2 v/v/v) yielding a pale yellow oil (0.29 g, 81%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.34 (m, 2H, C***H***$_2$), 1.54 (m, 2H, C***H***$_2$), 1.64 (m, 2H, C***H***$_2$), 2.57 (t, 2H, ^3J = 7.5 Hz, Im-4-C***H***$_2$), 3.09 (m, 4H, Im-4-$(CH_2)_4$-C***H***$_2$ + Ph-S-CH_2-C***H***$_2$), 3.40 (t, 2H, ^3J = 7.4 Hz, Ph-S-C***H***$_2$), 6.75 (s, 1H, Im-5-***H***), 7.17 (m, 1H, Ph-***H***), 7.28 (m, 2H, Ph-***H***), 7.39 (m, 2H, Ph-***H***), 7.54 (s, 1H, Im-2-***H***). ^{13}C-NMR (300 MHz, CD_3OD): δ [ppm] = 27.31 (-, Im-4-***C***H_2 + Im-$(CH_2)_2$-***C***H_2), 30.08 (-, 2 ***C***H_2), 30.25 (-, ***C***H_2), 33.54 (-, Ph-S-CH_2***C***H_2), 42.27 (-, ***C***H_2), 42.77 (-, ***C***H_2), 118.24 (+, Im-***C***-5), 120.02 (C_{quat}, ***C***≡N), 127.32 (+, Ph-***C***), 130.16 (+, 2 Ph-***C***), 130.40 (+, 2 Ph-***C***), 135.68 (+, Im-***C***-2), 137.02 (C_{quat}, Im-***C***-4 + Ph-***C***), 161.10 (C_{quat}, ***C***=N). IR (cm^{-1}) = 3250 (N-H), 2933 (C-H), 2858 (C-H), 2160 (C≡N), 1578 (C=N). HRMS (EI-MS) calcd. for $C_{18}H_{24}N_6S$ [$M^{+\bullet}$] 356.1783; found 356.1786. $C_{18}H_{24}N_6S$ (356.49).

2-Cyano-1-[5-(1*H*-imidazol-4-yl)pentyl]-3-methylguanidine (81).[17] The title compound was prepared from **40** (0.175 g, 1.0 mmol) and **47**[2] (0.153 g, 1.0 mmol) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/NH_3(aq.) 32% 90/8/2 v/v/v) yielding a pale yellow solid (0.17 g, 73%); mp 180 °C (ref[17]:199-200°C). ^{1}H-

NMR (300 MHz, CD_3OD): δ [ppm] = 1.25 (m, 2H, C***H***$_2$), 1.46 (m, 2H, C***H***$_2$), 1.55 (m, 2H, C***H***$_2$), 2.48 (t, 2H, ^3J = 7.6 Hz, Im-4-C***H***$_2$), 2.65 (s, 3H, C***H***$_3$), 3.06 (t, 2H, ^3J = 7.1 Hz, C***H***$_2$-NH), 6.70 (s, 1H, Im-5-***H***), 7.50 (s, 1H, Im-2-***H***). ^{13}C-NMR (300 MHz, CD_3OD): δ [ppm] = 25.73 (-, Im-4-***C***H$_2$), 25.98 (-, Im-4-(CH$_2$)$_2$-***C***H$_2$), 28.01 (+, ***C***H$_3$), 28.62 (-, ***C***H$_2$), 28.68 (-, ***C***H$_2$), 40.75 (-, Im-4-(CH$_2$)$_4$-***C***H$_2$), 117.14 (+, Im-***C***-5), 118.22 (C$_{quat}$, ***C***≡N), 134.18 (+, Im-***C***-2), 135.60 (C$_{quat}$, Im-***C***-4), 159.81 (C$_{quat}$, ***C***=N). IR (cm^{-1}) = 3226 (N-H), 2948 (C-H), 2857 (C-H), 2169 (C≡N), 1594 (C=N). HRMS (EI-MS) calcd. for $C_{11}H_{18}N_6$ [M$^{+\bullet}$] 234.1593; found 234.1588. $C_{11}H_{18}N_6$ (234.30).

2-Cyano-1-ethyl-3-[5-(1*H*-imidazol-4-yl)pentyl]guanidine (82). The title compound was prepared from **41** (0.228 g, 1.2 mmol) and **47**[2] (0.18 g, 1.2 mmol) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/NH_3(aq.) 32% 90/8/2 v/v/v) yielding a pale yellow oil (0.25 g, 83%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.14 (t, 3H, ^3J = 7.2 Hz, CH$_2$C***H***$_3$), 1.36 (m, 2H, C***H***$_2$), 1.57 (m, 2H, C***H***$_2$), 1.66 (m, 2H, C***H***$_2$), 2.57 (t, 2H, ^3J = 7.5 Hz, Im-4-C***H***$_2$), 3.20 (m, 4H, Im-4-(CH$_2$)$_4$-C***H***$_2$ + C***H***$_2$CH$_3$), 6.75 (s, 1H, Im-5-***H***), 7.53 (s, 1H, Im-2-***H***). ^{13}C-NMR (300 MHz, CD_3OD): δ [ppm] = 15.06 (+, CH$_2$***C***H$_3$), 27.31 (-, Im-4-***C***H$_2$ + Im-4-(CH$_2$)$_2$***C***H$_2$), 30.26 (-, 2 ***C***H$_2$), 37.55 (-, ***C***H$_2$-CH$_3$), 42.65 (-, Im-4-(CH$_2$)$_4$***C***H$_2$), 118.42 (+, Im-***C***-5), 120.38 (C$_{quat}$, ***C***≡N), 135.66 (+, Im-***C***-2), 137.56 (C$_{quat}$, Im-***C***-4), 161.08 (C$_{quat}$, ***C***=N). IR (cm^{-1}) = 3235 (N-H), 2932 (C-H), 2859 (C-H), 2163 (C≡N), 1575 (C=N). HRMS (EI-MS) calcd. for $C_{12}H_{20}N_6$ [M$^{+\bullet}$] 248.1749; found 248.1748. $C_{12}H_{20}N_6$ (248.33).

2-Cyano-1-[5-(1*H*-imidazol-4-yl)pentyl]-3-isopropylguanidine (83). The title compound was prepared from **42** (0.122 g, 0.6 mmol) and **47**[2] (0.092 g, 0.6 mmol) according to the general procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/NH_3(aq.) 32% 90/8/2 v/v/v) yielding a colorless oil (0.11 g, 70%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.17 (d, 6H, ^3J = 6.5 Hz, C***H***$_3$), 1.36 (m, 2H, C***H***$_2$), 1.57 (m, 2H, C***H***$_2$), 1.66 (m, 2H, C***H***$_2$), 2.59 (t, 2H, ^3J = 7.5 Hz, Im-4-C***H***$_2$), 3.19 (t, 2H, ^3J = 7.1 Hz, Im-4-(CH$_2$)$_4$-C***H***$_2$), 3.87 (m, 1H, C***H***), 6.75 (s, 1H, Im-5-***H***), 7.54 (s, 1H, Im-2-***H***). ^{13}C-NMR (300 MHz, CD_3OD): δ [ppm] = 22.79 (+, 2 ***C***H$_3$), 27.31 (-, Im-4-***C***H$_2$), 27.37 (-, Im-4-(CH$_2$)$_2$***C***H$_2$), 30.27 (-, 2 ***C***H$_2$), 42.65 (-, Im-4-(CH$_2$)$_4$***C***H$_2$), 45.01 (+, ***C***H), 118.03 (+, Im-***C***-5), 120.40 (C$_{quat}$, ***C***≡N), 135.67 (+, Im-***C***-2), 138.06 (C$_{quat}$, Im-***C***-4), 160.36 (C$_{quat}$, ***C***=N). IR (cm^{-1}) = 3263 (N-H), 2933 (C-H), 2857 (C-H), 2158 (C≡N), 1574 (C=N). HRMS (EI-MS) calcd. for $C_{13}H_{22}N_6$ [M$^{+\bullet}$] 262.1906; found 262.1901. $C_{13}H_{22}N_6$ (262.35).

2-Cyano-1-[5-(1*H*-imidazol-4-yl)pentyl]-3-isobutylguanidine (84). The title compound was prepared from **43** (0.14 g, 0.65 mmol) and **47**[2] (0.1 g, 0.65 mmol) according to the general

procedure. The crude product was purified by flash chromatography ($CHCl_3$/MeOH/NH_3(aq.) 32% 90/8/2 v/v/v) yielding a pale yellow oil (0.15 g, 84%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 0.91 (d, 6H, ^3J = 6.7 Hz, CH(C***H***$_3$)$_2$), 1.36 (m, 2H, C***H***$_2$), 1.58 (m, 2H, C***H***$_2$), 1.66 (m, 2H, C***H***$_2$), 1.83 (m, 1H, C***H***(CH$_3$)$_2$), 2.58 (t, 2H, ^3J = 7.6 Hz, Im-4-C***H***$_2$), 2.99 (d, 2H, ^3J = 7.2 Hz, C***H***$_2$-CH(CH$_3$)$_2$), 3.19 (t, 2H, ^3J = 7.1 Hz, Im-4-(CH$_2$)$_4$***C***H$_2$), 6.75 (s, 1H, Im-5-***H***), 7.54 (s, 1H, Im-2-***H***). ^{13}C-NMR (300 MHz, CD_3OD): δ [ppm] = 20.30 (+, 2 ***C***H$_3$), 27.33 (-, Im-4-***C***H$_2$), 27.39 (-, Im-CH$_2$CH$_2$***C***H$_2$), 29.57 (+, CH$_2$***C***H(CH$_3$)$_2$), 30.28 (-, ***C***H$_2$), 30.31 (-, ***C***H$_2$), 42.67 (-, Im-4-(CH$_2$)$_4$***C***H$_2$), 50.05 (-, ***C***H$_2$-CH(CH$_3$)$_2$), 118.04 (+, Im-***C***-5), 120.37 (C$_{quat}$, ***C***≡N), 135.66 (+, Im-***C***-2), 138.14 (C$_{quat}$, Im-***C***-4), 161.29 (C$_{quat}$, ***C***=N). IR (cm^{-1}) = 3250 (N-H), 2930 (C-H), 2868 (C-H), 2157 (C≡N), 1575 (C=N). HRMS (EI-MS) calcd. for $C_{14}H_{24}N_6$ [$M^{+\bullet}$] 276.2062; found 276.2056. $C_{14}H_{24}N_6$ (276.38).

5. Preparation of the carbamoylguanidines 89-91

The compounds were prepared according to the general procedure described in the main article.

2-Carbamoyl-1-[3-(1*H*-imidazol-4-yl)propyl]-3-(3-phenylpropyl)guanidine (89). The title compound was prepared from **55** (0.20 g, 0.64 mmol) according to the general procedure. Purification by preparative HPLC (MeCN/0.1% TFA (aq.): 25/75) followed by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielded a colorless semisolid compound (0.20 g, 95%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.79 – 1.94 (m, 4H, Im-4-CH$_2$-C***H***$_2$ + Ph-CH$_2$-C***H***$_2$), 2.57 – 2.72 (m, 4H, Im-4-C***H***$_2$ + Ph-C***H***$_2$), 3.12 – 3.27 (m, 4H, Im-4-(CH$_2$)$_2$-C***H***$_2$ + Ph-CH$_2$-CH$_2$-C***H***$_2$), 6.79 (s, 1H, Im-5-***H***), 7.10 – 7.31 (m, 5H, Ph-***H***), 7.55 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 24.83 (-, Im-4-***C***H$_2$), 30.46 (-, Im-4-CH$_2$-***C***H$_2$) 32.34 (-, Ph-CH$_2$-***C***H$_2$), 34.05 (-, Ph-***C***H$_2$), 41.31, 41.38 (-, Im-4-(CH$_2$)$_2$-***C***H$_2$ + Ph-CH$_2$-CH$_2$-***C***H$_2$), 117.87 (+, Im-***C***-5), 127.02 (+, Ph-***C***-4), 129.50 (+, 2 Ph-***C***), 129.53 (+, 2 Ph-***C***), 135.93 (+, Im-***C***-2), 137.62 (C$_{quat}$, Im-***C***-4), 142.90 (C$_{quat}$, Ph-***C***-1), 160.96 (C$_{quat}$, ***C***=N), 169.32 (C$_{quat}$, ***C***=O). IR (cm^{-1}) = 3206, 2933, 2864, 1570, 1397, 1369. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 329 (100) [M + H]$^+$. HRMS (EI-MS) calcd. for $C_{17}H_{24}N_6O$ [$M^{+\bullet}$] 328.2012; found 328.2088. $C_{17}H_{24}N_6O$ (328.41).

2-Carbamoyl-1-[3-(1*H*-imidazol-4-yl)propyl]-3-(4-phenylbutyl)guanidine (90). The title compound was prepared from **57** (0.20 g, 0.62 mmol) according to the general procedure. Purification by preparative HPLC (MeCN/0.1% TFA (aq.): 25/75) followed by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 90/8/2 v/v/v) yielded a colorless semisolid compound (0.17 g, 80%). ^{1}H-NMR (600 MHz, COSY, CD_3OD, trifluoroacetate): δ [ppm] = 1.62

– 1.74 (m, 4H, Ph-CH_2-C***H***$_2$-C***H***$_2$), 1.96 – 2.03 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.66 (t, 2H, ^3J = 7.7 Hz, Ph-C***H***$_2$), 2.80 (t, 2H, ^3J = 7.2 Hz, Im-4-C***H***$_2$), 3.31 (t, 2H, ^3J = 7.0 Hz, Ph-$(CH_2)_3$-C***H***$_2$), 3.38 (t, 2H, ^3J = 6.6 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 7.12 – 7.27 (m, 5H, Ph-***H***), 7.33 (brs, 1H, Im-5-***H***), 8.79 (d, 1H, ^4J = 1.3 Hz, Im-2-***H***). ^{13}C-NMR (150 MHz, HSQC, HMBC, CD_3OD, trifluoroacetate): δ [ppm] = 22.56 (-, Im-4-***C***H_2), 28.59 (-, Im-4-CH_2-***C***H_2), 29.17, 29.52 (-, Ph-CH_2-***C***H_2-***C***H_2), 36.29 (-, Ph***C***H_2), 41.76 (-, Im-4-$(CH_2)_2$-***C***H_2), 42.75 (-, Ph-$(CH_2)_3$-***C***H_2), 117.02 (+, Im-***C***-5), 126.98 (+, Ph-***C***-4), 129.43 (+, 2 Ph-***C***), 129.45 (+, 2 Ph-***C***), 134.35 (C_{quat}, Im-***C***-4), 134.96 (+, Im-***C***-2), 143.09 (C_{quat}, Ph-***C***-1), 154.55 (C_{quat}, ***C***=N), 156.86 (C_{quat}, ***C***=O). IR (cm^{-1}) = 3192, 2934, 2858, 1723, 1576, 1594, 1399, 1370. ES-MS (H_2O/MeCN) *m/z* (%): 343 (100) $[M + H]^+$. HRMS (EI-MS) calcd. for $C_{18}H_{26}N_6O$ $[M + H]^+$ 343.2241; found 343.2250. $C_{18}H_{26}N_6O$ (342.44).

2-Carbamoyl-1-[4-(1*H*-imidazol-4-yl)butyl]-3-(3-phenylpropyl)guanidine (91). The title compound was prepared from **62** (0.48 g, 1.48 mmol) according to the general procedure. Purification by preparative HPLC (MeCN/0.1% TFA (aq.): 0 min: 10/90, 20 min: 40/60) followed by flash chromatography ($CHCl_3$/MeOH/7 M NH_3 in MeOH 92.5/5.5/2 v/v/v) yielded a colorless foam-like solid (0.29 g, 57%). ^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = 1.49 – 1.74 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 1.78 – 1.93 (m, 2H, Ph-CH_2-C***H***$_2$), 2.55 – 2.70 (m, 4H, Im-4-C***H***$_2$ + Ph-C***H***$_2$), 3.11 – 3.27 (m, 4H, Im-4-$(CH_2)_3$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 6.76 (d, 1H, ^4J = 1.1 Hz, Im-5-***H***), 7.10 – 7.29 (m, 5H, Ph-***H***), 7.53 (d, 1H, ^4J = 1.1 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, CD_3OD): δ [ppm] = 27.17 (-, Im-4-***C***H_2), 27.88 (-, Im-4-CH_2-***C***H_2), 30.14 (-, Im-4-$(CH_2)_2$-***C***H_2), 32.38 (-, Ph-CH_2-***C***H_2), 34.06 (-, Ph***C***H_2), 41.40, 41.69 (-, Im-4-$(CH_2)_3$-C***H***$_2$ + Ph-$(CH_2)_2$-C***H***$_2$), 117.61 (+, Im-***C***-5), 127.00 (+, Ph-***C***-4), 129.49 (+, 2 Ph-***C***), 129.53 (+, 2 Ph-***C***), 135.75 (+, Im-***C***-2), 142.95 (C_{quat}, Ph-***C***-1), 160.96 (C_{quat}, ***C***=N), 169.38 (C_{quat}, ***C***=O). IR (cm^{-1}) = 3200, 2989, 2932, 1569, 1394, 1367. ES-MS (DCM/MeOH + NH_4OAc) *m/z* (%): 343 (100) $[M + H]^+$. HRMS (LSI-MS) calcd. for $C_{18}H_{27}N_6O$ $[M + H]^+$ 343.2241; found 343.2255. $C_{18}H_{26}N_6O$ (342.43).

6. Preparation of 3-(1*H*-imidazol-4-yl)propan-1-amine 45.

2-[3-(1-Trityl-1*H*-imidazol-4-yl)propyl]isoindoline-1,3-dione (97).[6] To a cold solution (0 °C) of **96**[3, 4] (10.00 g, 27.1 mmol) in THF_{abs} (250 mL), phthalimide (6.00 g, 40.8 mmol) and triphenylphosphine (10.7 g, 40.8 mmol) were added. Under ice cooling DIAD (11.00 g, 54.2 mmol) in THF_{abs} (200 mL) was added dropwise. The mixture was allowed to warm to ambient temperature, stirred for 1 h and concentrated *in vacuo*. The precipitated product was filtered, washed twice with cold THF (20 mL) and recrystallized from THF/MeCN yielding the title compound as white solid (13.0 g, 96%); mp 212 °C (ref.[6]: 217 – 219 °C). ^{1}H-NMR (300 MHz,

$CDCl_3$): δ [ppm] = 1.93 – 2.09 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.60 (t, 2H, ^3J = 7.7 Hz, Im-4-C***H***$_2$), 3.73 (t, 2H, ^3J = 7.2 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 6.57 (d, 1H, ^4J = 1.3 Hz, Im-5-***H***), 7.09 – 7.18 (m, 6H, Ph-***H***), 7.28 – 7.37 (m, 10H, Ph-***H*** + Im-2-***H***), 7.64 – 7.72 (m, 2H, Phth-***H***), 7.77 – 7.85 (m, 2H, Phth-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 26.03 (-, Im-4-CH_2-***C***H_2), 28.34 (-, Im-4-***C***H_2), 37.70 (-, Im-4-$(CH_2)_2$-***C***H_2), 75.11 (C_{quat}, ***C***Ph_3), 118.04 (+, Im-***C***-5), 123.15 (+, Phth-***C***-4, 7), 127.95 (+, 3 Ph-***C***-4), 128.02 (+, 6 Ph-***C***), 129.84 (+, 6 Ph-***C***), 132.23 (C_{quat}, Im-***C***-4), 133.82 (+, Phth-***C***-5, 6), 138.39 (+, Im-***C***-2), 140.65 (C_{quat}, Phth-***C***-3a, 7a), 142.61 (C_{quat}, 3 Ph-***C***-1), 168.39 (C_{quat}, 2 ***C***=O). ES-MS (DCM/MeOH + NH_4OAc) m/z (%): 498 (100) $[M + H]^+$. Anal. ($C_{33}H_{27}N_3O_2$) C, H, N. $C_{33}H_{27}N_3O_2$ (497.59).

3-(1-Trityl-1*H*-imidazol-4-yl)propan-1-amine (98). [18] A mixture of **97** (12.80 g, 25.7 mmol) and hydrazine monohydrate (8.0 mL, 164.6 mmol) in *n*-butanol was refluxed for 1 h. After removal of insoluble material, the filtrate was evaporated giving a pale brownish oil that solidified (9.11 g, 96%); mp 106 – 108 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.70 – 1.82 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.57 (t, 2H, ^3J = 7.5 Hz, Im-4-C***H***$_2$), 2.70 (t, 2H, ^3J = 7.0 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 6.52 (d, 1H, ^{4}J = 1.4 Hz, Im-5-***H***), 7.08 – 7.18 (m, 6H, Ph-***H***), 7.27 – 7.37 (m, 10H, Ph-***H*** + Im-2-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 25.83 (-, Im-4-***C***H_2), 33.42 (-, Im-4-CH_2-***C***H_2), 41.85 (-, Im-4-$(CH_2)_2$-***C***H_2), 75.09 (C_{quat}, ***C***Ph_3), 117.79 (+, Im-***C***-5), 127.97 (+, 3 Ph-***C***-4), 128.00 (+, 6 Ph-***C***), 129.81 (+, 6 Ph-***C***), 138.35 (+, Im-***C***-2), 141.45 (C_{quat}, Im-***C***-4), 142.63 (C_{quat}, 3 Ph-***C***-1). ES-MS (DCM/MeOH + NH_4OAc) m/z (%): 368 (100) $[M + H]^+$. Anal. ($C_{25}H_{25}N_3 \cdot 0.5\ H_2O$) C, H, N. $C_{25}H_{25}N_3$ (367.49).

3-(1*H*-Imidazol-4-yl)propan-1-amine (45). 98 (8.00 g, 21.8 mmol) was heated under reflux in 1M HCl for 30 min. The cooled mixture was filtered and the solvent was removed *in vacuo*. The obtained residue was recrystallized from EtOH yielding a white solid (3.37 g, 78%); mp (**45** · 2 HCl) 151 °C (ref.[19]: 155 – 157 °C). ^{1}H-NMR (300 MHz, D_2O, dihydrochloride): δ [ppm] = 1.89 – 2.03 (m, 2H, Im-4-CH_2-C***H***$_2$), 2.76 (t, 2H, ^3J = 7.7 Hz, Im-4-C***H***$_2$), 2.96 (t, 2H, ^3J = 7.8 Hz, Im-4-$(CH_2)_2$-C***H***$_2$), 7.19 (d, 1H, ^4J = 1.4 Hz, Im-5-***H***), 8.51 (d, 1H, ^4J = 1.4 Hz, Im-2-***H***). ^{13}C-NMR (75 MHz, D_2O, dihydrochloride): δ [ppm] = 20.93 (-, Im-4-***C***H_2), 25.62 (-, Im-4-CH_2-***C***H_2), 38.49 (-, Im-4-$(CH_2)_2$-***C***H_2), 115.57 (+, Im-***C***-5), 131.98 (C_{quat}, Im-***C***-4), 133.10 (+, Im-***C***-2). EI-MS (70 eV) m/z (%): 125 (11) $[M^{+\bullet}]$, 95 (100) $[M - CH_2\text{-}NH_2]^+$. Anal. ($C_6H_{11}N_3 \cdot 2$ HCl) C, H, N. $C_6H_{11}N_3 \cdot 2$ HCl (198.09).

7. Preparation of 4-(1*H*-imidazol-4-yl)butan-1-amine 46.

2-(5-Oxohexyl)isoindoline-1,3-dione (100). A mixture of **99** (25.00 g, 185.7 mmol), finely powdered K_2CO_3 (38.50 g, 277.8 mmol), phthalimide (27.32 g, 185.7 mmol) and catalytical amounts of KI (0.1 g, 0.6 mmol) in DMF was stirred for 12 h at 100 °C. The cooled mixture was poured in ice-cold water (1000 mL) and extracted with $CHCl_3$ (1 x 600 mL, 2 x 200 mL). The combined organic layers were washed with saturated $NaHCO_3$ (400 mL), 2% HCl (2 x 400 mL), brine (400 mL) and dried over Na_2SO_4. Evaporation to dryness yielded a yellowish oil that crystallized from EtOH/H_2O as white solid (41.1 g, 91%); mp 63 °C (ref.[20] 57 °C). ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.54 – 1.77 (m, 4H, Phth-CH_2-C***H***$_2$-C***H***$_2$), 2.13 (s, 3H, C***H***$_3$), 2.49 (t, 2H, ^3J = 7.0 Hz, Phth-$(CH_2)_3$-C***H***$_2$), 3.69 (t, 2H, ^3J = 6.9 Hz, Phth-C***H***$_2$), 7.67 – 7.75 (m, 2H, Phth-***H***), 7.79 – 7.87 (m, 2H, Phth-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 20.82 (-, ***C***H_2), 27.97 (-, ***C***H_2), 30.00 (+, ***C***H_3), 37.53 (-, ***C***H_2), 42.91 (-, ***C***H_2), 123.24 (+, Phth-***C***-4,7), 132.12 (C_{quat}, Phth-***C***-3a,7a), 133.95 (+, Phth-***C***-5,6), 168.43 (C_{quat}, Phth-***C***-1,3), 208.38 (C_{quat}, ***C***OCH_3). CI-MS (NH_3) m/z (%): 264 (100) $[M + NH_4]^+$. Anal. ($C_{14}H_{15}NO_3$) C, H, N. $C_{14}H_{15}NO_3$ (245.27).

2-(6-Bromo-5-oxohexyl)isoindoline-1,3-dione (101).[21] To a solution of **100** (93.30 g, 380.4 mmol) and urea (22.85 g, 380.4 mmol) in MeOH (400 mL), bromine (60.79 g, 380.4 mmol) was rapidly added and stirred for 24 h. The precipitated product was filtered, washed with MeOH (20 mL), dried and crystallized from DCM/hexane yielding the title compound as a white solid (50.7 g, 41%); mp 112 – 113 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.58 – 1.79 (m, 4H, Phth-CH_2-C***H***$_2$-C***H***$_2$), 2.72 (t, 2H, ^3J = 6.9 Hz, Phth-$(CH_2)_3$-C***H***$_2$), 3.70 (t, 2H, ^3J = 6.8 Hz, Phth-C***H***$_2$), 3.88 (s, 2H, C***H***$_2$Br), 7.68 – 7.75 (m, 2H, Phth-***H***), 7.80 – 7.88 (m, 2H, Phth-***H***). ^{13}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 20.89 (-, ***C***H_2), 27.81 (-, ***C***H_2), 34.20 (-, ***C***H_2), 37.36 (-, ***C***H_2), 38.98 (-, ***C***H_2), 123.28 (+, Phth-***C***-4,7), 132.10 (C_{quat}, Phth-***C***-3a,7a), 133.99 (+, Phth-***C***-5,6), 168.42 (C_{quat}, Phth-***C***-1,3), 201.55 (C_{quat}, ***C***OCH_3). CI-MS (NH_3) m/z (%): 343 (13) $[M + NH_4]^+$, 341 (13) $[M + NH_4]^+$, 263 (100) $[M – Br + H + NH_4]^+$. Anal. ($C_{14}H_{14}BrNO_3$) C, H, N. $C_{14}H_{14}BrNO_3$ (324.17).

2-(4-(1*H*-Imidazol-4-yl)butyl)isoindoline-1,3-dione (102). 101 (50.00 g, 154.2 mmol) was stirred for 5 h at 160 °C in formamidine (300 mL). After removal of the solvent *in vacuo*, the residue was basified with saturated $NaHCO_3$ (400 mL) and extracted with $CHCl_3$ (1 x 600 mL, 2 x 200 mL). The combined organic layers were extracted with 5% HCl (3 x 300 mL), the aqueous solution alkalized with $NaHCO_3$ and extracted with $CHCl_3$ (3 x 200 mL). After drying the combined organic layers over Na_2SO_4, the solvent was evaporated yielding a beige solid that was used with further purification (21.5 g, 52%); mp 158 – 160 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.54 – 1.82 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 2.67 (t, 2H, ^3J = 6.9 Hz, Im-4-C***H***$_2$), 3.71 (t, 2H, ^3J = 6.9 Hz, Im-4-$(CH_2)_3$-C***H***$_2$), 6.78 (d, 1H, ^4J = 1.3 Hz, Im-5-***H***), 7.54 (d, 1H, ^{4}J = 0.9 Hz,

Im-2-***H***), 7.67 – 7.88 (m, 4H, Phth-***H***). CI-MS (NH_3) m/z (%): 270 (100) $[M + H]^+$. $C_{15}H_{15}N_3O_2$ (269.30).

4-(1*H*-Imidazol-4-yl)butan-1-amine (46).[22] **102** (17.00 g, 63.1 mmol) was refluxed overnight in 20% HCl (350 mL). Insoluble material was filtered off and the solvent was evaporated. The remaining dark oil was basified by addition of NH_3 (aq.) 32%, evaporated to dryness and purified by flash chromatography (DCM/MeOH/NH_3 (aq.) 32% 67/25/8 v/v/v) yielding the title compound as brownish oil (6.7 g, 76%). For analytical purposes a small amount was converted to the dihydrobromide and crystallized from EtOAc/EtOH (beige solid); mp (**46** · 2 HBr) 176 – 177 °C. ^{1}H-NMR (300 MHz, DMSO-d_6, dihydrobromide): δ [ppm] = 1.49 – 1.74 (m, 4H, Im-4-CH_2-C***H***$_2$-C***H***$_2$), 2.67 (t, 2H, ^3J = 7.1 Hz, Im-4-C***H***$_2$), 2.73 – 2.89 (m, 2H, Im-4-$(CH_2)_3$-C***H***$_2$), 7.48 (d, 1H, ^4J = 1.4 Hz, Im-5-***H***), 7.82 (brs, 3H, N***H***$_3^+$), 9.09 (d, 1H, ^4J = 1.4 Hz, Im-2-***H***), 14.14 (brs, 2H, Im-N-***H***). ^{13}C-NMR (75 MHz, DMSO-d_6, dihydrobromide): δ [ppm] = 23.05, 24.68, 25.90 (-, Im-4-***C***H_2-***C***H_2-***C***H_2), 38.22 (-, Im-4-$(CH_2)_3$-***C***H_2), 115.54 (+, Im-***C***-5), 132.73 (C_{quat}, Im-***C***-4), 133.62 (+, Im-***C***-2). CI-MS (NH_3) m/z (%): 140 (100) $[M + H]^+$. Anal. ($C_7H_{13}N_3$ · 2 HBr) C, H, N. $C_7H_{13}N_3$ (139.20).

8. Elemental Analysis (C, H, N)

No	formula	calculated			found		
		C	H	N	C	H	N
27	$C_{17}H_{17}N_3O$	73.10	6.13	15.04	73.02	6.07	15.12
28	$C_{16}H_{15}N_3O$	72.43	5.70	15.84	72.37	5.67	15.95
29	$C_{18}H_{19}N_3O$	73.69	6.53	14.32	73.41	6.57	14.25
30	$C_{23}H_{21}N_3O$	77.72	5.96	11.82	77.83	5.99	11.91
31	$C_{17}H_{23}N_3O$	71.55	8.12	14.72	71.56	7.95	14.89
32	$C_{16}H_{15}N_3OS$	64.62	5.08	14.13	64.57	5.07	14.16
33	$C_{18}H_{16}N_4O$	71.04	5.30	18.41	70.81	5.39	18.40
34	$C_{17}H_{16}FN_3O$	68.67	5.42	14.13	68.49	5.17	14.04
35	$C_{16}H_{16}N_4O$	68.55	5.75	19.99	68.51	5.69	20.29
36	$C_{16}H_{16}N_4O$	68.55	5.75	19.99	68.31	5.84	20.19
37	$C_{16}H_{16}N_4O$	68.55	5.75	19.99	68.32	5.43	20.39
38	$C_{18}H_{19}N_3O$	73.69	6.53	14.32	73.67	6.76	14.39
39	$C_8H_7N_3O$	59.62	4.38	26.07	59.68	4.34	26.32
40	$C_9H_9N_3O$	61.70	5.18	23.99	61.53	5.08	24.09
41	$C_{10}H_{11}N_3O$	63.48	5.86	22.21	63.37	5.82	22.35
42	$C_{11}H_{13}N_3O$	65.01	6.45	20.68	65.17	6.21	20.97
43	$C_{12}H_{15}N_3O$	66.34	6.96	19.34	66.11	7.00	19.63
45	$C_6H_{11}N_3 \cdot 2\ HCl$	36.38	6.61	21.21	36.09	6.65	21.39
46	$C_7H_{13}N_3 \cdot 2\ HBr$	27.93	5.02	13.96	27.83	5.24	13.81
48	$C_{16}H_{20}N_6 \cdot 0.9\ C_2H_2O_4 \cdot 0.25\ H_2O$	55.98	5.89	22.01	55.71	5.72	22.39
49	$C_{15}H_{18}N_6 \cdot 0.8\ C_2H_2O_4 \cdot 0.25\ H_2O$	55.56	5.65	23.42	55.23	5.76	23.68
50	$C_{17}H_{22}N_6 \cdot C_2H_2O_4 \cdot 0.25\ H_2O$	56.36	6.10	20.75	56.28	6.05	20.93
51	$C_{22}H_{24}N_6 \cdot 0.25\ H_2O$	70.09	6.55	22.29	70.39	6.85	22.68

52	$C_{16}H_{26}N_6 \cdot C_2H_2O_4$	55.09	7.19	21.41	55.34	7.29	21.67
53	$C_{15}H_{18}N_6S \cdot C_2H_2O_4$	50.48	4.98	20.78	50.51	5.20	20.89
54	$C_{17}H_{22}N_6 \cdot 0.25\ H_2O$	62.65	6.03	30.09	62.58	6.31	29.91
55	$C_{17}H_{22}N_6 \cdot 0.25\ H_2O$	64.84	7.20	26.69	64.93	7.50	26.85
56	$C_{16}H_{20}N_6 \cdot 0.7\ C_2H_2O_4 \cdot 0.5\ H_2O$	56.73	6.13	22.81	56.97	6.45	22.50
57	$C_{18}H_{24}N_6 \cdot 0.85\ C_2H_2O_4$	59.01	6.46	20.96	58.98	6.81	21.30
58	$C_{23}H_{26}N_6 \cdot 0.25\ H_2O$	70.65	6.83	21.49	70.33	6.89	21.64
59	$C_{17}H_{28}N_6 \cdot 0.8\ C_2H_2O_4$	57.51	7.68	21.63	57.18	7.45	21.40
60	$C_{16}H_{20}N_6S \cdot 0.75\ C_2H_2O_4 \cdot 0.25\ H_2O$	52.49	5.54	20.99	52.20	5.61	21.14
61	$C_{18}H_{21}N_7 \cdot C_2H_2O_4$	56.46	5.45	23.05	56.51	5.20	22.82
62	$C_{18}H_{24}N_6 \cdot 0.9\ C_2H_2O_4$	58.65	6.41	20.73	58.73	6.64	20.83
63	$C_{17}H_{22}N_6 \cdot 0.75\ C_2H_2O_4 \cdot 0.5\ H_2O$	57.45	6.08	21.95	57.43	6.38	21.72
64	$C_{19}H_{26}N_6 \cdot 0.85\ C_2H_2O_4$	59.91	6.73	20.25	59.71	6.90	20.44
65	$C_{24}H_{28}N_6 \cdot 0.25\ H_2O$	71.17	7.09	20.75	70.89	7.24	20.94
66	$C_{18}H_{30}N_6 \cdot 0.8\ C_2H_2O_4 \cdot 0.25\ H_2O$	57.84	7.95	20.65	58.20	8.27	20.45
67	$C_{17}H_{22}N_6S \cdot 0.75\ C_2H_2O_4$	54.20	5.78	20.50	53.94	6.16	20.75
68	$C_{19}H_{23}N_7 \cdot C_2H_2O_4$	57.39	5.73	22.31	56.50	6.37	21.57
69	$C_{18}H_{23}FN_6 \cdot C_2H_2O_4 \cdot H_2O$	53.33	6.04	18.66	53.07	6.10	18.28
70	$C_{17}H_{23}N_7 \cdot 2\ C_2H_2O_4 \cdot H_2O$	48.18	5.58	18.73	48.30	5.92	18.49
71	$C_{17}H_{23}N_7 \cdot 2\ C_2H_2O_4 \cdot 1.3\ H_2O$	47.69	5.64	18.54	47.94	5.95	18.14
72	$C_{17}H_{23}N_7 \cdot 2\ C_2H_2O_4 \cdot 2\ H_2O$	46.58	5.77	18.11	46.97	5.94	17.92
73	$C_{19}H_{26}N_6 \cdot 0.85\ C_2H_2O_4$	59.91	6.73	20.25	59.58	7.04	20.39
74	$C_9H_{14}N_6 \cdot C_2H_2O_4 \cdot 0.1\ H_2O$	44.32	5.48	28.19	44.08	5.76	28.36
75	$C_{10}H_{16}N_6 \cdot C_2H_2O_4 \cdot 0.4\ H_2O$	45.39	5.97	26.47	45.66	6.22	26.28
76	$C_{11}H_{18}N_6 \cdot 0.75\ C_2H_2O_4$	49.74	6.51	27.84	49.79	6.87	27.64

77	$C_{12}H_{20}N_6 \cdot 0.75\ C_2H_2O_4 \cdot 0.25\ H_2O$	50.61	6.92	26.23	50.26	7.17	26.16
78	$C_{13}H_{22}N_6 \cdot 0.75\ C_2H_2O_4 \cdot 0.25\ H_2O$	52.08	7.23	25.13	51.88	7.60	25.47
86	$C_{18}H_{24}N_6S \cdot 0.85\ C_2H_2O_4 \cdot 0.25\ H_2O$	54.08	6.04	19.21	53.76	6.21	19.58
87	$C_{24}H_{28}N_6S \cdot C_2H_2O_4 \cdot 0.5\ H_2O$	58.74	5.88	15.81	59.01	6.24	15.62
93	$C_{30}H_{42}N_4O_8$	61.42	7.22	9.55	61.35	7.51	9.48
97	$C_{33}H_{27}N_3O_2$	79.66	5.47	8.44	79.35	5.31	8.10
98	$C_{25}H_{25}N_3 \cdot 0.5\ H_2O$	79.75	6.96	11.16	80.15	6.67	11.06
100	$C_{14}H_{15}NO_3$	68.56	6.16	5.71	68.63	6.25	5.61
101	$C_{14}H_{14}BrNO_3$	51.87	4.35	4.32	51.86	4.38	4.32

9. HPLC purity data of target compounds 79-84, 88-91 94 and 95

No.	t_R (min)	k'	purity (%)	No.	t_R (min)	k'	purity (%)
79[a]	15.26	3.60	98.0	**88**[b]	13.60	3.10	100
80[a]	15.05	3.54	99.0	**89**[b]	14.58	3.39	99.5
81[a]	7.57	1.28	97.6	**90**[b]	16.10	3.85	99.7
82[a]	8.75	1.64	95.9	**91**[b]	14.73	3.44	99.6
83[a]	10.15	2.06	97.5	**94**[c]	15.08	3.54	99.7
84[a]	11.84	2.57	98.0	**95**[b]	15.42	3.64	97.8

[a] TSP-system, gradient mode: MeCN/0.05% TFA (aq.): 0 min: 10/90, 30 min: 90/10, 31 min: 95/5, 40 min: 95/5. [b] TSP-system, gradient mode: MeCN/0.05% TFA (aq.): 0 min: 5/95, 25 min: 55/45, 30 min: 90/10, 40 min: 90/10. [c] TSP-system, gradient mode: MeCN/0.05% TFA (aq.): 0 min: 5/95, 25 min: 50/50, 30 min: 95/5, 35 min: 95/5.

10. References

1. Durant, G. J.; Emmett, J. C.; Ganellin, C. R.; Miles, P. D.; Parsons, M. E.; Prain, H. D.; White, G. R. Cyanoguanidine-Thiourea Equivalence in the Development of the Histamine H_2-Receptor Antagonist, Cimetidine. *J. Med. Chem.* **1977**, 20, 901-906.
2. Vollinga, R. C.; Menge, W. M. P. B.; Timmerman, H. A new convenient route for the synthesis of 4(5)-(ω-aminoalkyl)-1*H*-imidazoles. *Rec. Trav. Chim. Pays-Bas* **1993**, 112, 123-125.
3. Ghorai, P.; Kraus, A.; Keller, M.; Götte, C.; Igel, P.; Schneider, E.; Schnell, D.; Bernhardt, G.; Dove, S.; Zabel, M.; Elz, S.; Seifert, R.; Buschauer, A. Acylguanidines as Bioisosteres of Guanidines: N^G-Acylated Imidazolylpropylguanidines, a New Class of Histamine H_2 Receptor Agonists. *J. Med. Chem.* **2008**, 51, 7193–7204.
4. Stark, H.; Purand, K.; Hüls, A.; Ligneau, X.; Garbarg, M.; Schwartz, J.-C.; Schunack, W. [^{125}I]Iodoproxyfan and Related Compounds: A Reversible Radioligand and Novel Classes of Antagonists with High Affinity and Selectivity for the Histamine H_3 Receptor. *J. Med. Chem.* **1996**, 39, 1220-1226.
5. Mitsunobu, O.; Yamada, M.; Mukaiyama, T. Preparation of esters of phosphoric acid by the reaction of trivalent phosphorus compounds with diethyl azodicarboxylate in the presence of alcohols. *Bull. Chem. Soc. Jpn.* **1967**, 40, 935-939.
6. Bertinaria, M.; Stilo, A. D.; Tosco, P.; Sorba, G.; Poli, E.; Pozzoli, C.; Coruzzi, G.; Fruttero, R.; Gasco, A. [3-(1*H*-Imidazol-4-yl)propyl]guanidines Containing Furoxan Moieties: A New Class of H_3-Antagonists Endowed with NO-Donor Properties. *Bioorg. Med. Chem.* **2003**, 11, 1197-1205.
7. Buschauer, A.; Lachenmeyr, F.; Schunack, W. Synthesis and histamine H_2-receptor activity of heterocyclic impromidine analogues. *Pharmazie* **1992**, 47, 86-91.
8. Lee, C. H.; Lee, J. S.; Na, H. K.; Yoon, D. W.; Miyaji, H.; Cho, W. S.; Sessler, J. L. Cis- and Trans-Strapped Calix[4]pyrroles Bearing Phthalamide Linkers: Synthesis and Anion-Binding Properties. *J. Org. Chem.* **2005**, 70, 2067-2074.
9. Zav'yalov, S. I.; Kravchenko, N. E. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1984**, 33, 418.
10. Bredereck, H.; Theilig, G. Untersuchungen in der Oxazolreihe und Umwandlungen von Oxazolen in Imidazole mittels Formamids (Formamid-Reaktionen, I. Mitteil.). *Chem. Ber.* **1953**, 86, 96-109.
11. Webb, R. L.; Eggleston, D. S.; Labaw, C. S.; Lewis, J. J.; Wert, K. Diphenyl Cyancarbonimidate and Dichlorodiphenoxymethane as Synthons for the Construction of Heterocyclic Systems of Medicinal Interest. *J. Heterocycl. Chem.* **1987**, 24, 275 - 278.
12. Eriks, J. C.; Sterk, G. J.; Van der Goot, H.; Timmerman, H. Preparation of substituted thiazole derivative as drugs. WO 9110657, **1991**, *Chem. Abstr.* 115:183285.
13. Garratt, P. J.; Hobbs, C. J.; Wrigglesworth, R. One-carbon compounds as synthetic intermediates. The synthesis of hydropyrimidines and hydroquinazolines by sequential nucleophilic addition to diphenyl cyanocarbonimidate with concomitant cyclization. *J. Org. Chem.* **1989**, 54, 1062-1069.
14. Citterio, A.; Minisci, F. Process for the preparation of cimetidine. DE 3148103, **1983**, *Chem. Abstr.* 99:88200.

15. Martin, D.; Witke, K.; Reich, P.; Nadolski, K. Cyanic acid esters. XVI. Cleavage of the silicon-nitrogen bond by cyanic acid esters. Synthesis of *N*-trimethylsilyl- and *N*-cyanoisoureas. *Chem. Ber.* **1968**, 101, 3185-200.
16. Martin, D.; Tittelbach, F.; Nadolski, K. Cyanic acid ester. 32. Simple syntheses for aminoaryloxy-1,3,5-triazines. *J. Prakt. Chem. (Leipzig)* **1981**, 323, 694-699.
17. Hough, L. B.; de Esch, I. J. P.; Janssen, E.; Phillips, J.; Svokos, K.; Kern, B.; Trachler, J.; Abood, M. E.; Leurs, R.; Nalwalk, J. W. Antinociceptive activity of chemical congeners of improgan: Optimization of side chain length leads to the discovery of a new, potent, non-opioid analgesic. *Neuropharmacology* **2006**, 51, 447-456.
18. Wolin, R.; Connolly, M.; Afonso, A.; Hey, J. A.; She, H.; Rivelli, M. A.; Willams, S. M.; West, R. E. Novel H_3 receptor antagonists. Sulfonamide homologs of histamine. *Bioorg. Med. Chem. Lett.* **1998**, 8, 2157-2162.
19. Sellier, C.; Buschauer, A.; Elz, S.; Schunack, W. Zur Synthese von (*Z*)- und (*E*)-3-(1*H*-Imidazol-4-yl)-2-propenamin und einigen 3-(1*H*-Imidazol-4-yl)propanaminen. *Liebigs Ann. Chem.* **1992**, 1992, 317-323.
20. Ghorai, P. Arpromidine-related acylguanidines: synthesis and structure activity relationships of a new class of guanidine-type histamine H_2 receptor agonists with reduced basicity. Doctoral thesis, University of Regensburg, Germany, **2005**. http://www.opus-bayern.de/uni-regensburg/frontdoor.php?source_opus=561&la=de.
21. Pioch, R. P. 2,4-Disubstituted thiazole derivatives. EP 49618, **1982**, *Chem. Abstr.* 97:72354.
22. Akabori, S.; Kaneko, T. Amino acids and their derivatives. V. 3. Synthesis of 2 higher homologs of histamine. *J. Chem. Soc. Jpn.* **1932**, 53, 207-212 (*Chem. Abstr.* 27:2500).