Supporting Information

Direct guanylation of amino groups by cyanamide in water:
Catalytic generation and activation of unsubstituted carbodiimide by Sc(OTf)₃

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General Methods. All commercially available reagents were used without further purification. Otherwise noted, the preparative separation was performed by column chromatography on silica gel (Merck, Silica gel 60 F254). Preparative reverse phase HPLC employed a Shimadzu Prominence system equipped with a Nacalai tesque column (SC18-AR300, 10 × 250 mm). Two solvent systems, namely, A: H2O containing 0.1% TFA and B: MeCN containing 0.1% TFA, were applied. 1H and 13C NMR spectra were recorded on a JEOL AL400 NMR spectrometer and a JEOL AL300 NMR spectrometer. Chemical shifts of 1H and 13C NMR spectra were referenced to the solvent peaks: δH 3.31 and δC 49.0 for CD3OD, and δH 4.79 for D2O. IR spectra were recorded on a Thermo Nicolet iS5. ESI-mass spectra including the high resolution mass spectra (HRMS) were recorded on a Waters Synapt G2. Only the guanidines 2g and 2n are the new compounds.

N-(p-Tert-butylphenyl)guanidine (2c)

Reaction was performed in a mixed solvent of water and 1,4-dioxane (1 : 1) according to the general procedure described above. The product was purified by column chromatography on silica gel (chloroform : methanol = 15 : 1) to give 2c as a white solid (67% yield): IR (neat, cm⁻¹) 3225, 2965, 1673, 1603, 1226, 1028; 1H NMR (400 MHz, CD3OD, 25 °C) δ 7.48 (d, J = 6.7 Hz, 2H), 7.16 (d, J = 6.7 Hz, 2H), 1.29 (s, 9H); 13C NMR (100 MHz, CD3OD, 25 °C) δ 158.1, 152.2, 133.1, 128.0, 126.3, 35.5, 31.6; ESI-MS m/z calcd for C11H17N3 (M+H)+ 192.1, found 192.1.

N-(p-Trifluoromethylphenyl)guanidine (2d)

After the reaction was performed according to the general procedure, the product was purified by column chromatography on silica gel (chloroform : methanol = 30 : 1) to give 2d as a brown solid (88% yield): IR (neat, cm⁻¹) 3359, 1658, 1603, 1324, 1246, 1027; 1H NMR (400 MHz, CD3OD, 25 °C) δ 7.67 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H); 13C NMR (100 MHz, CD3OD, 25 °C) δ 157.8, 140.2, 129.8 (q, J = 32.7 Hz), 128.1 (q, J = 3.3 Hz), 126.0, 125.3 (q, J = 270.9 Hz); ESI-MS m/z calcd for C8H8N3 (M+H)+ 204.1, found 204.1.

N-(p-Methoxycarbonylphenyl)guanidine (2e)

The product was purified by column chromatography on silica gel (chloroform : methanol = 20 : 1) to give 2e as a yellow solid (47% yield): IR (neat, cm⁻¹) 3226, 2924, 1678, 1603, 1260, 1173, 1032; 1H NMR (400 MHz, CD3OD, 25 °C) δ 8.00 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H); 13C NMR (100 MHz, CD3OD, 25 °C) δ 167.6, 157.7, 142.1, 132.3, 129.6, 120.1, 52.8; ESI-MS m/z calcd for C9H11N3O2 (M+H)+ 194.1, found 194.1.

6-Guanidino quinoline (2f)

Reaction was performed in a mixed solvent of water and 1,4-dioxane (1 : 1) according to the general procedure described above. The product was purified by column chromatography on silica gel (chloroform :
methanol = 5 : 1) to give 2f as a brown solid (57% yield): IR (neat, cm⁻¹) 3227, 1603, 1260, 1173, 1036; ¹H NMR (400 MHz, CD₃OD, 25 °C) δ 8.87 (dd, J = 4.4, 1.6 Hz, 1H), 8.40 (dd, J = 8.3, 1.6 Hz, 1H), 8.12 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 2.4 Hz, 1H); ¹H NMR (400 MHz, CD₃OD, 25 °C) δ 8.40 (dd, J = 8.3, 1.6 Hz, 1H), 7.59 (dd, J = 8.3, 4.4 Hz, 1H); ¹³C NMR (100 MHz, CD₃OD, 25 °C) δ 151.9, 147.4, 138.3, 134.7, 131.3, 130.3, 128.5, 124.6, 123.5, 123.4; ESI-MS m/z calcd for C₁₀H₁₀N₄ (M+H)⁺ 187.1, found 187.1.

6-Guanidino indole (2g)

After the reaction was performed according to the general procedure, the product was purified by column chromatography on silica gel (chloroform : methanol = 5 : 1) to give 2g as a brown solid (quantitative yield): IR (neat, cm⁻¹) 3370, 2165, 1630, 1468, 1384, 1090; ¹H NMR (400 MHz, CD₃OD, 25 °C) δ 7.59 (d, J = 9.1 Hz, 1H), 7.28 (d, J = 3.2 Hz, 1H), 7.26 (m, 1H), 6.86 (dd, J = 8.3, 2.0 Hz, 1H), 6.46 (dd, J = 2.8, 1.2 Hz, 1H); ¹³C NMR (100 MHz, CD₃OD, 25 °C) δ 161.4, 138.5, 126.1, 125.1, 121.6, 119.9, 117.9, 107.2, 102.1; ESI-MS m/z calcd for C₉H₁₀N₄ (M+H)⁺ 175.1, found 175.1; HRESI-MS m/z calcd for C₉H₁₀N₄ (M+H)⁺ 175.0984, found 175.0986.

2-Guanidino benzo[α]thiazole (2h)

Reaction was performed in a mixed solvent of water and 1,4-dioxane (1 : 1) according to the general procedure described above. The product was purified by the reverse phase HPLC (10–70 % of B over 60 min) to give 2h as a white solid (31% yield): IR (neat, cm⁻¹) 3226, 1673, 1203, 1139; ¹H NMR (300 MHz, CD₃OD, 25 °C) δ 7.77 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.38 (dd, J = 7.8, 7.8 Hz, 1H), 7.24 (dd, J = 7.8, 7.8 Hz, 1H); ¹³C NMR (75 MHz, CD₃OD, 25 °C) δ 162.3, 157.1, 149.9, 132.8, 127.2, 124.5, 122.2, 120.8; HRESI-MS m/z calcd for C₈H₉N₄S (M+H)⁺ 193.1, found 193.1.

N-(4-Phenylbutyl)guanidine (2i)

Reaction was performed in a mixed solvent of water and 1,4-dioxane (1 : 1) according to the general procedure. The product was purified by column chromatography on silica gel (chloroform : methanol = 30 : 1) to give 2i as a white solid (68% yield): IR (neat, cm⁻¹) 3365, 1668, 1253, 1171, 1029; ¹H NMR (400 MHz, CD₃OD, 25 °C) δ 7.27-7.15 (m, 5H), 3.17 (t, J = 6.7 Hz, 2H), 2.65 (t, J = 7.5 Hz, 2H), 1.71-1.59 (m, 4H); ¹³C NMR (100 MHz, CD₃OD, 25 °C) δ 164.9, 143.2, 129.4 (2C), 126.9, 42.3, 36.3, 29.7, 29.4; ESI-MS m/z calcd for C₁₁H₁₆N₃ (M+H)⁺ 192.1, found 192.1.

N-(2-Pycolyl)guanidine (2j)

The product was purified by the reverse phase HPLC (0–100 % of B over 60 min) to give 2j as a white solid (56% yield). IR (neat, cm⁻¹) 3333, 2159, 1668, 1183, 1127, 1033; ¹H NMR (400 MHz, CD₃OD, 25 °C) δ 8.53 (d, J = 6.3 Hz, 1H), 8.42 (dd, J = 8.1, 8.1 Hz, 1H), 7.82 (m, 2H), 4.57 (s, 2H); ¹³C NMR (100 MHz, CD₃OD, 25 °C) δ 164.9, 158.3, 145.1 (2C), 125.7, 125.5, 43.8; ESI-MS m/z calcd for C₇H₉N₄ (M+H)⁺ 151.1,
Cbz-Arg-OH (2k)
After the reaction was performed according to the general procedure, the product was purified by the reverse phase HPLC (20–100% of B over 30 min) to give 2k as a white solid (68% yield): IR (neat, cm\(^{-1}\)) 3247, 2940, 1668, 1203, 1131, 1033; \(^1\)H NMR (400 MHz, D\(_2\)O, 25 °C) \(\delta\) 7.35-7.26 (m, 5H), 5.01 (d, \(J = 4.0\) Hz, 2H), 3.95 (m, 1H), 3.17 (brs, 2H), 1.97 (m, 1H), 1.78-1.67 (m, 3H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD, 25 °C) \(\delta\) 172.3, 162.0, 158.7, 138.3, 129.4 (2C), 129.0, 128.9 (2C), 67.6, 52.4, 42.8, 29.1, 22.4; ESI-MS m/z calcd for C\(_{14}\)H\(_{20}\)N\(_4\)O\(_4\) (M+H\(^+\)) 309.2, found 309.2.

N,N'-Dibenzyl guanidine (2l)
Reaction was performed in a mixed solvent of water and 1,4-dioxane (1 : 1) according to the general procedure described above. The product was purified by column chromatography on silica gel (Fuji Silysa, NH-DM1020SG, eluent: water) to give 2l as a white solid (46% yield): IR (neat, cm\(^{-1}\)) 3137, 2155, 1601, 1452, 1027; \(^1\)H NMR (400 MHz, CD\(_3\)OD, 25 °C) \(\delta\) 7.35 (m, 4H), 7.32 (m, 2H), 7.20 (m, 4H), 4.55 (s, 4H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD, 25 °C) \(\delta\) 159.0, 135.9, 130.1, 129.2, 128.2, 52.3; ESI-MS m/z calcd for C\(_{15}\)H\(_{17}\)N\(_3\) (M+H\(^+\)) 240.1, found 240.1.

Morpholine-4-carboximidamide (2m)
The product was purified by column chromatography on silica gel (Nacalai tesque, Cosmosil 75C\(_{18}\)-OPN, eluent: water) to give 2m as a white solid (83% yield): IR (neat, cm\(^{-1}\)) 3226, 2190, 1645, 1251, 1109, 1029; \(^1\)H NMR (400 MHz, CD\(_3\)OD, 25 °C) \(\delta\) 3.63 (dd, \(J = 4.7, 4.7\) Hz, 4H), 3.36 (dd, \(J = 4.7\) Hz, 4H), 3.36 (dd, \(J = 4.7\) Hz, 4H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD, 25 °C) \(\delta\) 161.4, 67.6, 45.2; ESI-MS m/z calcd for C\(_5\)H\(_{11}\)N\(_3\)O (M+H\(^+\)) 130.1, found 130.0.

Ac-Gly-Leu-Arg-Ala-Gly-OH (2n)
After the reaction was performed according to the general procedure, the product was purified by the reverse phase HPLC (0–60 % B over 60 min) to give 2n as a white solid (56% yield): IR (neat, cm\(^{-1}\)) 2931, 1652, 1204, 1056, 1033; \(^1\)H NMR (400 MHz, CD\(_3\)OD, 25 °C) \(\delta\) 4.35-4.22 (m, 3H), 4.00-3.74 (m, 4H), 3.16-3.08 (m, 2H), 2.02 (s, 3H), 1.86 (m, 1H), 1.75-1.54 (m, 6H), 1.38, (d, \(J = 7.1\) Hz, 3H), 0.94 (dd, \(J = 16.6, 6.3\) Hz, 6H); ESI-MS m/z calcd for C\(_{21}\)H\(_{38}\)N\(_8\)O\(_7\) (M+Na\(^+\)) 537.3, found 537.3; HRESI-MS m/z calcd for C\(_{21}\)H\(_{38}\)N\(_8\)O\(_7\) (M+Na\(^+\)) 537.2756, found 537.2756.