Supporting Information

EXPERIMENTAL

Photolysis of 4'-bromoacetophenones

4'-Bromoacetophenones were dissolved in 20 mL of solvent (concentration = 2 mM) in a vycor tube. Before the reaction was started, argon was bubbled through the reaction mixture for 15 minutes. The tube was then tightly closed with a septum and the reaction was performed under argon atmosphere, room temperature using a Hanovia 450W medium pressure mercury arc lamp, equipped with a Pyrex chamber,

DNA-cleaving experiment

Aqueous solutions of DNA plasmid pBR322 (from SIGMA or USB) or ϕX174RF (from USB) were prepared using a tris buffer at indicated pH. The final concentration of the supercoiled plasmid DNA was equal to 30 μM in base pairs for all experiments reported herein. THF, MeOH, or DMSO solutions of 4'-bromoacetophenone derivatives were added to the DNA solutions and their final concentrations ranged from 40 μM (1.3 eq/bp) to 50 mM. All the solvents were degassed before use. The 20 μL aliquots of the solution of DNA and 4'-bromoacetophenone were placed in microfuge tubes and were irradiated by a Pyrex-filtered light from a Hanovia 450W medium pressure mercury arc lamp for 25 or 30 min. After irradiation was complete, 5μL of loading buffer was added to reaction and the reactions were loaded onto a 1% agarose gel. The electrophoresis was carried out at 33V for 12-18 h. Gels were stained in a dilute ethidium bromide solution (0.5 μg/mL) for 30 min. The DNA was visualized by means of an UV transilluminator (300 nm UV light source) and photographed with a Polaroid DS 344 camera and Polaroid 667 film.

Preparation of the buffers

Borate running buffer : 108 g of Tris base, 25 g of boric acid and 6.8 g of EDTA were dissolved in deionized water. The volume was brought to 1 l. It was diluted 1: 9 for agarose gel preparation and buffer before use.

DNA buffer (1.0 M, pH 8.0) : 5.3 g of Tris base and 8.8 g of Tris•HCl were dissolved in deionized water. The volume was brought to 100 mL. It was diluted 1: 49 to 20 mM before use.

Preparation of the gels

2.3 g of agarose were dissolved in 230 mL of 10 times-diluted borate running buffer and placed in a 500 mL-erlern. The solution was heated until it got transparent. When the temperature was cooled down to 60°C, the solution was poured into a tray. After 1.5 hours, the gel was put in a vat and 10 times-diluted borate running buffer was poured into the vat to cover the gel.

Preparation of 3'-^{32}P End Labeled 167 Base Pair Restriction Fragment

Supercoiled pBR322 plasmid (15 μg) was linearized into 4 fragments with 40 U of Eco RI and 60 U of Rsa I restriction endonucleases on 60 μL of React 2 buffer (50 mM Tris-HCl, 10 mM $MgCl_2$, 50 mM NaCl, from Gibco BRL). The digest was allowed to proceed at 37 °C for 2h. To this DNA solution was added 5 μL of dTTP, 9 μL of a-32P dATP, and 26 U of Klenow Polymerase. The labeling reaction was incubated at room temperature for 30 min, after which time 8 μL of loading buffer were added, and the mixture directly loaded onto a 2% preparative agarose gel. Electrophoresis was carried out at 180V for 2.5 h. The labeled fragments were visualized by autoradiography; the 167 bp fragment was excised from the gel and recovered by centrifugation through Millipore Ultrafree MC 0.45 μm microcentrifuge filters.

Cleavage and High-Resolution Gel Electrophoresis

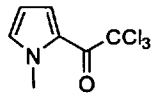
2 μL of an aqueous solution of conjugate were added to 18 μL of a solution containing 3'-^{32}P labeled restriction fragment and carrier calf thymus DNA (100 μM bp) in 50 mM Tris acetate buffer (pH 7.9). The microfuge tubes containing this reaction mixture were strapped to the outside of a Pyrex photolysis chamber and irradiated for 30 min with light from a 450W medium pressure mercury arc lamp. After photolysis was complete, the DNA was precipitated, and the pellets dissolved in 5 μL of loading buffer.

The samples were heat denatured at 95°C for 3 min, chilled immediately on ice, and loaded onto 10% denaturing polyacrylamide gel (7 M urea), in parallel with the Maxam-Gilbert G sequencing reaction.[25] Electrophoresis was carried out at constant power (P= 45-55W) for ca. 2 h. Gels were transferred to filter paper and subjected to autoradiography with an intensifying screen at -80°C.

Footprinting Reaction

2 μL of an aqueous solution of conjugate were added to 18 μL of a solution containing 3'-^{32}P labeled restriction fragment and carrier calf thymus DNA (100 μM bp) in DNase reaction buffer (20 mM Tris HCl, 2 mM $MgCl_2$, 50 mM KCl, pH 8.4). Reactions were incubated for 30 min at 37°C, after which time 2 μL of DNase I (0.1U/μL) were added. The enzyme digest proceeded for 2 min at 24°C and quenched by the addition of 1 μL of 0.5M EDTA. The DNA fragments were precipitated and electrophoresed as above.

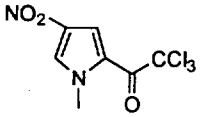
1-Methyl-2-trichloroacetylpyrrole (1)



To a well-stirred solution of trichloroacetyl chloride (44 g, 246 mmol) in 170 mL of ethyl ether in a 500 mL flask was added dropwise over a period of 1.5 h a solution of N-methylpyrrole (20g, 246 mmol) in 80 mL of anhydrous ethyl ether. The reaction mixture was stirred for an additional 3 h, and the reaction was quenched by the dropwise addition of a solution of 18 g of potassium carbonate in 70 mL water. The layers were seperated, and the ether layer was concentrated *in vacuo* to provide 1-methyl-2-trichloroacetylpyrrole 1 (53 g, 234 mmol, 95% yield) as a yellow crystalline solid sufficiently pure to be used without further purification.

IR ($CHCl_3$) 1662, 1522, 1456, 1365, 1333 cm^{-1}
^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.50 (dd, J = 4.4, 1.7 Hz, 1H), 6.97 (m, 1H), 6.22 (dd, J = 4.5, 2.5 Hz, 1H), 3.97 (s, 3H)
^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.9, 133.6, 124.0, 121.8, 108.9, 96.3, 38.5

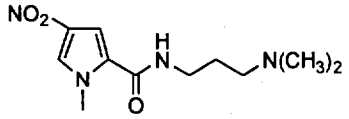
1-Methyl-4-nitro-2-trichloroacetylpyrrole (2)



To a cooled (-40°C) solution of 1-methyl-2-trichloroacetylpyrrole (53 g, 234 mmol) in acetic anhydride 300 mL in a 500 mL flask was added dropwise 20 mL of fuming nitric acid while a temperature (-40°C) was maintained. The reaction mixture was carefully allowed to warm to room temperature and stirred for an additional 4 h. The mixture was cooled to -30°C and isopropyl alcohol (300 mL) added. The solution was stirred at -20°C for 30 min, during which time a white precipitate formed. The solution was allowed to stand for 15 min and the resulting precipitate collected by vacuum filtration to provide compound **2** (39.4 g, 145 mmol, 62% yield).

IR ($CHCl_3$) 1691, 1538, 1316 cm^{-1}
^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.96 (d, J = 1.7 Hz, 1H), 7.76 (d, J = 1.7 Hz, 1H), 4.06 (s, 3H)
^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.5, 135.2, 130.3, 121.3, 117.4, 94.8, 39.7
MS (EI) *m/z* 270 (M^+,3), 207 (11), 153 (100), 107 (68), 79 (13)
HRMS (EI) *m/z* calcd for $C_7H_5Cl_3N_2O_3$ 269.9366, found 269.9371

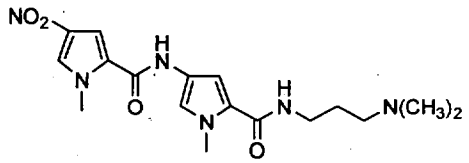
3-(1-Methyl-4-nitropyrrole-2-carboxamido)dimethyl aminopropane (3)



A solution of 3-dimethylaminopropylamine (597 mg, 5.85 mmol) in THF (2 mL) was added dropwise to a stirred solution of **2** (1.35 g, 5 mmol) in THF 3 mL at 0°C. The reaction mixture was warmed up to room temperature and stirring was continued for 1h. The solvent was removed *in vacuo* and the residual solid was recrystallized from ethanol to give pale yellow needles of **3** (1.23 g, 4.84 mmol, 96% yield).

IR ($CHCl_3$) 1647, 1546, 1305 cm^{-1}
^1H NMR ($CDCl_3$, 300 MHz) δ 8.77 (br s, 1H), 7.53 (d, J = 1.9 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 4.01 (s, 3H), 3.49 (q, J = 5.7 Hz, 2H), 2.51 (t, J = 5.7 Hz, 2H), 2.32 (s, 6H), 1.75-1.71 (m, 2H)
^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.4, 135.0, 127.1, 126.4, 106.5, 59.5, 45.3, 40.3, 37.8, 24.5
MS (EI) *m/z* 254(M^+,12), 153 (19), 107 (15), 84 (8), 72 (14), 58 (100)
HRMS (EI) *m/z* calcd for $C_{11}H_{18}N_4O_3$ 254.1379, found 254.1377

3-[1-Methyl-4-(1-methyl-4-nitropyrrole-2-carboxamido)pyrrole-2-carboxamido]dimethylaminopropane (4)



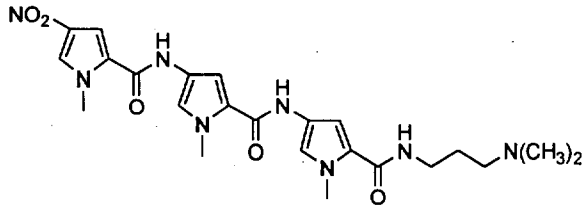
A suspension of 10% Pd-C (250 mg) in a solution of **3** (1 g, 3.91 mmol) in MeOH (10 mL) was stirred for 2h under a current of H_2 at room temperature, then filtered. The residual catalyst was washed thoroughly with methanol and the combined filtrate and washings were concentrated *in vacuo* to give the crude amine.

^1H NMR ($CDCl_3$, 300 MHz) δ 7.61 (br s, 1H), 6.27 (d, J = 2.0 Hz, 1H), 6.05 (d, J = 2.0 Hz, 1H), 3.83 (s, 3H), 3.41 (q, J = 6.0 Hz, 2H), 2.41 (t, J = 6.0 Hz, 2H), 2.27 (s, 6H), 1.72-1.68 (m, 2H)

The residual solid was dissolved in DMF (5 mL) and a solution of compound **2** (880 mg, 3.9 mmol) in DMF (5 mL) was added with stirring at 0°C. The temperature was allowed to rise to ambient temperature. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel with NH_4OH: MeOH: CH_2Cl_2 (3: 10: 90) as an eluent to give **4** (1.25 g, 3.32 mmol, 85% yield).

IR ($CHCl_3$) 1657, 1634, 1538, 1310 cm^{-1}
^1H NMR ($CDCl_3$, 300 MHz) δ 8.16 (s, 1H), 7.84 (br, 1H), 7.59 (d, J = 1.8 Hz, 1H), 7.28 (d, J = 1.6 Hz, 1H), 7.18 (d, 1H), 6.47 (d, J = 1.8 Hz, 1H), 4.03 (s, 3H), 3.92 (s, 3H), 3.46 (q, J = 5.8 Hz, 2H), 2.45 (t, J = 6.0 Hz, 2H), 2.29 (s, 6H), 1.74-1.69 (m, 2H)
^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.3, 159.2, 136.5, 128.5, 128.0, 125.7, 122.4, 120.3, 108.9, 104.6, 60.5, 46.9, 41.1, 39.4, 38.1, 27.1
MS (EI) *m/z* 376 (M^+,4), 358 (4), 291 (3), 275 (13), 259 (7), 153 (12), 149 (3), 138(2), 123 (3), 107 (9), 84 (8), 72 (13), 58 (100)
HRMS (EI) *m/z* calcd for $C_{17}H_{24}N_6O_4$ 376.1859, found 376.1853

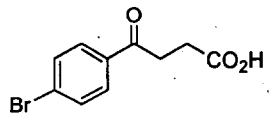
3-{1-Methyl-4-[1-methyl-4-(1-methyl-4-nitropyrrole-2-carboxamido)pyrrole-2-carboxamido]pyrrole-2-carboxamido}dimethylaminopropane (5)



By the same procedure as that described for **4**, **5** (407 mg, 0.82 mmol) was obtained from **4** (400 mg, 1.06 mmol), PtO_2 (10 mg), and **2** as a microcrystalline solid in 77% yield.

IR ($CHCl_3$) 1644, 1534, 1310 cm^{-1}
^1H NMR ($CDCl_3$, 300 MHz) δ 9.13 (br s, 1H), 8.07 (br, 1H), 7.70 (d, J = 1.7 Hz, 1H), 7.60 (d, J = 1.7 Hz, 1H), 7.33 (d, J = 1.7 Hz, 1H), 7.13 (s, 1H), 7.06 (d, J = 1.7 Hz, 1H), 6.48 (d, J = 1.7 Hz, 1H), 6.25 (d, J = 1.7 Hz, 1H), 4.06 (s, 3H), 3.92 (s, 3H), 3.83 (s, 3H), 3.54 (q, J = 5.7 Hz, 2H), 2.49 (t, J = 6.0 Hz, 2H), 2.31 (s, 6H), 1.81-1.73 (m, 2H)
^{13}C NMR (CD_3OD, 100 MHz) δ 164.2, 161.2, 159.5, 136.1, 128.7, 127.7, 124.6, 124.5, 123.2, 122.9, 120.7, 120.4, 108.7, 106.2, 106.1, 58.0, 45.1, 38.3, 38.1, 36.9, 36.8, 28.0
MS (EI) *m/z* 498 (M^+, 5), 480 (4), 453 (3), 413 (12), 397 (5), 395 (5), 370 (3), 291 (8), 273 (6), 245 (4), 159 (4), 138 (8), 58 (100)
HRMS (EI) *m/z* calcd for $C_{23}H_{30}N_8O_5$ 498.2339, found 498.2332

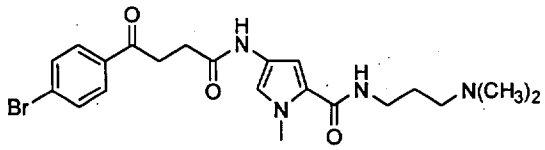
4-(4-Bromo-phenyl)-4-oxo-butyric acid (6)



To a mixture of anhydrous $AlCl_3$ (26.67 g, 200 mmol) and succinic anhydride (10 g, 100 mmol) in boiling cyclohexane (50 mL) was added, in one portion with manual stirring, 55 mL of bromobenzene. After about 15 min of further heating, the vigorous evolution of HCl had ceased. The viscous red reaction mixture was cooled, diluted with toluene and treated with ice and aqueous HCl. The keto acid was extracted from this mixture with hot toluene. The toluene extract was washed with water and then extracted with 2 M aqueous NaOH solution. The basic extract was acidified with aqueous HCl, and the keto acid was extracted with toluene. Rotary evaporation of the toluene extract yielded crude **6**. Recrstallization from a mixture of toluene and n-hexane gave 10.1 g (42 mmol, 42%) of 3-(4'-bromobenzoyl)propanoic acid **6** as a white solid.

IR ($CHCl_3$) 3034, 1699, 1673, 1411 cm^{-1}
^1H NMR ($CDCl_3$, 300 MHz) δ 7.85, 7.62 (AB quar, J = 8.6 Hz, 4H), 3.29 (t, J = 6.5 Hz, 2H), 2.82 (t, J = 6.5 Hz, 2H)
^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.2, 180.6, 137.4, 134.3, 131.8, 130.8, 35.2, 30.0
MS (EI) *m/z* 258, 256 (M^+, 9), 185 (98), 183 (100), 155 (27), 119 (19), 76 (24)
HRMS (EI) *m/z* calcd for $C_{10}H_9{}^{81}BrO_3$ 257.9715, found 257.9709
calcd for $C_{10}H_9{}^{79}BrO_3$ 255.9735, found 255.9730

3-{1-Methyl-4-[3-(4'-bromobenzoyl)propanoylamino]pyrrole-2-carboxamido}dimethylaminopropane (7)



3-(4'-bromobenzoyl)propanoic acid **6** (122 mg, 0.51 mmol) and 4-dimethylaminopyridine (63.5 mg, 0.52 mmol) was added to the aminopyrrole (90 mg, 0.4 mmol). The mixture was dissolved in dry DMF (1 mL) and chilled (0°C), followed by the addition of solution of dicyclohexylcarbodiimide(107 mg, 0.52 mmol) in dry DMF (1 mL). The reaction mixture was stirred under nitrogen atmosphere at 0°C for 15 min and at room temperature for 17 h. The precipitated urea was removed by filtration, and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel with NH_4OH: MeOH: CH_2Cl_2 (1: 10: 90) as an eluent to afford 7.

IR ($CHCl_3$) 1681, 1645, 1585, 1532, 1442, 1400 cm^{-1}

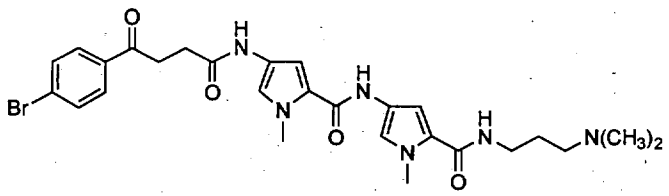
^1H NMR (DMSO, 300 MHz) δ 9.90 (s, 1H), 8.12 (t, J = 5.6 Hz, 1H), 7.91 (d, J = 8.6 Hz, 2H), 7.74 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 1.7 Hz, 1H), 6.70 (d, J = 1.7 Hz, 1H), 3.77 (s, 3H), 3.28 (t, J = 6.3 Hz, 2H), 3.21 (m, 2H), 2.78 (t, J = 7.6 Hz, 2H), 2.65 (t, J = 6.3 Hz, 2H), 2.56 (s, 6H), 1.74 (m, 2H)

^{13}C NMR (DMSO, 75 MHz) δ 198.3, 168.5, 161.5, 135.6, 131.8, 129.9, 127.2, 122.7, 122.1, 117.6, 103.5, 55.6, 43.3, 36.0, 33.3, 29.5, 25.6

MS (EI) *m/z* 464, 462 (M^+, 4), 446, 444 (2), 388, 386 (3), 363 (4), 361 (4), 241 (4), 239 (4), 185 (2), 183 (3), 139 (4), 123 (4), 101 (5), 72 (12)

HRMS (EI) *m/z* calcd for $C_{21}H_{27}{}^{79}BrN_4O_3$ 462.1266, found 462.1266
calcd for $C_{21}H_{27}{}^{81}BrN_4O_3$ 464.1246, found 464.1280

3-{1-Methyl-4-[1-methyl-4-(3-(4'-bromobenzoyl)propanoylamino)pyrrole-2-carboxamido]pyrrole-2-carboxamido}dimethylaminopropane (8)



By the same procedure as that described for **7**, **8** was obtained from dipyrrole amine (153 mg, 0.44 mmol), **6** (107 mg, 0.44 mmol), DCC (119 mg, 0.58 mmol), and DMAP (70 mg, 0.58 mmol).

IR ($CHCl_3$) 1682, 1651, 1634, 1585, 1557, 1538, 1466, 1435, 1403 cm^{-1}

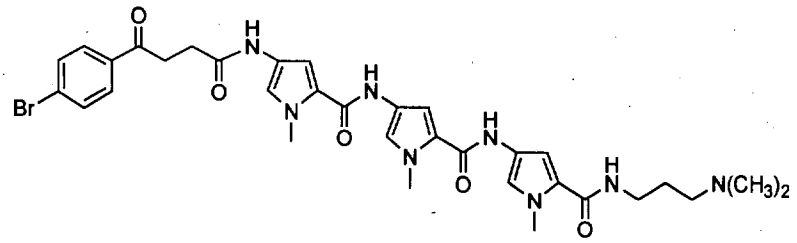
^1H NMR (DMSO, 500 MHz) δ 9.94 (s, 1H), 9.84 (s, 1H), 8.08 (t, J = 5.6 Hz, 1H), 7.91 (dd, J = 6.8, 2.0 Hz, 2H), 7.73 (d, J = 6.8, 2.0 Hz, 2H), 7.17 (d, J = 2.0 Hz, 1H), 7.11 (d, J = 2.0 Hz, 1H), 6.87 (d, J = 2.0 Hz, 1H), 6.83 (d, J = 1.5 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.28 (t, J = 6.3 Hz, 2H), 3.19 (m, 2H), 2.65 (t, J = 6.3 Hz, 2H), 2.38 (t, J = 7.3 Hz, 2H), 2.24 (s, 6H), 1.64 (m, 2H)

^{13}C NMR (DMSO, 125 MHz) δ 198.4, 168.6, 161.4, 158.5, 135.7, 131.9, 130.0, 127.3, 123.0, 122.8, 122.1, 118.1, 117.9, 104.2, 104.0, 56.7, 44.7, 36.9, 36.2, 36.0, 33.3, 29.5, 26.8

MS (EI) *m/z* 586, 584 (M^+, 1), 568 (4), 566 (4)

HRMS (EI) *m/z* calcd for $C_{27}H_{33}{}^{79}BrN_6O_4$ 584.1746, found 584.1760
calcd for $C_{27}H_{33}{}^{81}BrN_6O_4$ 586.1726, found 586.1639

3-{1-Methyl-4-[1-Methyl-4-<1-methyl-4-(3-(4'-bromobenzoyl)propanoylamino)pyrrole-2-carboxamido>pyrrole-2-carboxamido]pyrrole-2-carboxamido} dimethylaminopropane (9)



By the same procedure as that described for **8**, **9** was obtained from tripyrrole amine (355 mg, 0.758 mmol), **6** (183 mg, 0.7582 mmol), DCC (203 mg, 0.98 mmol), and DMAP (120 mg, 0.98 mmol).

IR ($CHCl_3$) 1682, 1674, 1668, 1659, 1652, 1644, 1634, 1585, 1557, 1538, 1464, 1434, 1403 cm^{-1}

^1H NMR (DMSO, 500 MHz) δ 9.93 (s, 1H), 9.89 (s, 1H), 9.88 (s, 1H), 8.08 (t, J = 5.4 Hz, 1H), 7.92 (dd, J = 6.8, 2.0 Hz, 2H), 7.75 (d, J = 6.8, 2.0 Hz, 2H), 7.23 (d, J = 1.5 Hz, 1H), 7.18 (d, J = 2.0 Hz, 1H), 7.12 (d, J = 1.5 Hz, 1H), 7.03 (d, J = 1.5 Hz, 1H), 6.89 (d, J = 2.0 Hz, 1H), 6.82 (d, J = 2.0 Hz, 1H) 3.84 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 3.29 (t, J = 6.3 Hz, 2H), 3.19 (m, 2H), 2.66 (t, J = 6.3 Hz, 2H), 2.25 (t, J = 6.8 Hz, 2H), 2.15 (s, 6H), 1.61 (m, 2H)

^{13}C NMR (DMSO, 125 MHz) δ 198.3, 168.5,161.2, 158.5, 135.6, 131.8, 129.9, 127.2, 123.0, 122.8, 122.7, 122.1, 118.4, 118.0, 117.7, 104.7, 104.0, 103.9, 57.1, 45.2, 37.1, 36.1, 35.9, 33.3, 29.5, 27.1

MS (+LSIMS) *m/z* 709, 707 (MH^+), 643, 533, 483, 369, 329, 232