Supporting Information

Photoinduced DNA Cleavage by Cyclopentadienyl Metal Complexes Conjugated to DNA Recognition Elements

Allison L. Hurley,[‡] Mitchell P.; Maddox III,[‡] Tricia L. Scott,[†] Mark R. Flood,[§] and Debra L. Mohler*[‡]

[‡]*Department of Chemistry, Emory University, 1515 Pierce Dr., Atlanta GA 30322*
[†]*Department of Chemistry, West Virginia University, Morgantown, WV 26506*
[§]*Department of Biology, Fairmont State College, Fairmont, WV, 26554*

Experimental Details:

General. The netropsin derivative **2**, γ–aminobutyric acid tethered netropsin derivative **5**, *N*-Cbz-8–aminocaprylic acid, [η^5-((succinimidooxy)carbonyl)cyclopentadienyl]methyl-tricarbonyltungsten (**4**), [η^5-(carboxy)cyclopentadienyl]methyltricarbonyltungsten (**1**) and $PdPhI(PPh_3)_2$ were prepared according to the literature procedures cited in the paper. Tungsten hexacarbonyl and NaCp were used as purchased from Aldrich. $ZnCl_2$ was purchased from Aldrich and purified by melting under vacuum to remove residual HCl. Anhydrous DMF was purchased from Aldrich and used without further purification. DECP was purchased from Acros and used without further purification. Triethylamine was distilled from calcium hydride immediately prior to use. Tetrahydrofuran was distilled from benzophenone ketal immediately prior to use.

Tungsten netropsin conjugate 3. The aminopyrrole **2** (0.284 g, 0.820 mmol) and the tungsten acid **1** (0.144 g, 0.367 mmol) were placed in a round bottom flask which was flushed thoroughly with argon. Anhydrous DMF (25 ml) was added and the reaction mixture was cooled to 0°C. DECP (0.189 mL, 1.25 mmol) and triethylamine (0.695 mL, 4.98 mmol) were added and the reaction mixture was stirred at 0°C for 2 hours and at room temperature for 16 hours. The DMF was removed under vacuum and the resulting residue was dissolved in CH_2Cl_2 (100 mL) and washed with 2% aqueous Na_2CO_3 (100 mL). The organic layer was dried with K_2CO_3 and the solvent was removed under reduced pressure. Purification of the residue by preparative thin layer chromatography on silica gel using 1% NH_4OH in methanol yielded a glassy yellow solid (0.099 g, 0.138 mmol, 38%).; IR (NaCl) 3284, 2014, 1916, 1652, 1539 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 7.17 (t, *J* = 1.5 Hz, 2H), 6.96 (d, *J* = 1.8 Hz, 1H), 6.81 (d, *J* = 1.5 Hz, 2H), 6.09 (t, *J* = 2.4 Hz, 2H), 5.67 (t, *J* = 2.4 Hz, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 3.33 (t, *J* = 6.9 Hz, 2H), 2.52 (br t, *J* = 7.8 Hz, 2H), 2.36 (s, 6H), 1.80 (m, *J* = 7.5 Hz, 2H), 0.47 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 227.9 ,215.1, 162.4, 160.3, 159.2, 123.9, 122.8, 121.4, 121.2, 120.8, 119.9, 104.2, 103.8, 101.5, 92.4, 91.8, 58.2, 45.3, 39.0, 36.7, 36.6, 26.0, -31.8. FAB HRMS *m/z* calcd for $C_{27}H_{33}N_6O_6W$ (MH^+): 721.1971; Found 721.1959.

Tungsten γ-aminobutyric acid-tethered netropsin conjugate 6. The γ-aminobutyric acid-substituted pyrrole **5** (0.201 g, 0.465 mmol) and the tungsten succinimide ester **4** (0.192 g, 0.392 mmol) were placed in a round bottom flask which was flushed thoroughly with argon. Anhydrous DMF (25 mL) was added and the reaction mixture was stirred at room temperature for 20 hours. The DMF was removed under vacuum and the resulting residue was dissolved in CH_2Cl_2 (25 mL) and washed with 2% aqueous Na_2CO_3 (25 mL). The organic layer was dried with K_2CO_3 and the solvent was removed under reduced pressure. Purification by preparative thin layer chromatography on silica gel using 1% NH_4OH in methanol yielded a glassy yellow solid (0.070 g, 0.087 mmol, 52%); IR (NaCl) 3293, 2014, 1916, 1645, 1540, 1436, 1258, 731 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 7.17 (d, *J* =2 Hz, 1H), 7.15 (d, *J* = 2 Hz, 1H), 6.82 (at, *J* = 2.4 Hz, 2H), 5.96 (t, *J*

= 2.4 Hz, 2H), 5.62 (t, *J* = 2.4 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.36 (m, 4H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.60 (s, 6H), 2.39 (t, *J* = 7.2 Hz, 2H), 1.88 (m, 4H), 0.44 (s, 3H); ^{13}C NMR (400 MHz, CD_3OD): δ 229.5, 216.8, 172.7, 165.4, 164.6, 161.5, 124.7, 124.5, 123.5, 123.4, 120.8, 120.7, 106.4, 106.0, 102.2, 94.4, 93.1, 57.8, 44.8, 40.4, 38.0, 37.0, 34.8, 27.7, 27.1, 26.3, -32.1; FAB HRMS *m/z* calcd. for $C_{31}H_{40}N_7O_7W$ (MH^+): 806.2499; Found 806.2517.

***N*-Cbz-8-aminocaprylic acid tethered netropsin analog (precursor to compound 7).** The aminopyrrole **2** (0.115 g, 0.332 mmol) and *N*-Cbz-protected 8-aminocaprylic acid (0.097 g, 0.332 mmol) were placed in a round bottom flask which was flushed thoroughly with argon. Anhydrous DMF (5 mL) was added and the reaction mixture was cooled to 0°C. DECP (0.079 mL, 0.518 mmol) and triethylamine (0.289 mL, 2.07 mmol) were added and the reaction mixture was warmed to room temperature and stirred for 16 hours. The solvent was removed under vacuum. The remaining residue was dissolved in CH_2Cl_2 (10 mL) which was washed with 2% Na_2CO_3 (10 mL). The organic layer was dried over K_2CO_3 and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel using 1% NH_4OH in methanol to yield a light yellow solid (0.145 g, 0.233 mmol, 65%). ^{1}H NMR (300 MHz, CD_3OD): δ 7.33 (m. 5H), 7.16 (d, *J* = 1.8 Hz, 1H), 7.14 (d, *J* = 1.8 Hz, 1H), 6.83 (d, *J* = 1.8 Hz, 1H), 6.80 (d, *J* = 1.8 Hz, 1H), 5.05 (s, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.10 (t, *J* = 6.9 Hz, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 2.36 (s, 6H), 2.30 (t, *J* = 7.8 Hz, 2H), 1.80 (m, *J* = 7.5 Hz, 2H), 1.67 (br m, 2H), 1.49 (br m, 2H), 1.35 (m, 8H); ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 171.3, 162.1, 159.2, 156.8, 136.4, 128.5, 128.1, 128.0, 123.4, 123.0, 122.0, 121.8, 119.0, 118.5, 104.0, 103.6, 66.6, 58.0, 50.1, 45.0, 41.0, 38.5, 36.6, 36.6, 29.9, 29.2, 28.9, 26.5, 26.1, 25.5; FAB HRMS *m/z* calcd. for $C_{33}H_{48}N_7O_5$ (MH^+): 622.3717; Found 622.3696.

8-Aminocaprylic acid-substituted netropsin analog 7. The *N*-Cbz-protected 8-aminocaprylic acid-substituted netropsin derivative (0.061 g, 0.098 mmol) was dissolved in methanol (5 mL) in a round bottom flask, and palladium on carbon (0.010 g) was added. The solution was thoroughly flushed with argon and the flask was capped with a septum. Hydrogen gas was bubbled through the solution for 1 minute and the reaction mixture was stirred under an atmosphere of hydrogen (via a balloon) for 21 hours. The solution was then filtered through celite under argon. The solvent was removed under reduced pressure and the resulting residue was dried under vacuum to yield a glassy solid (0.081 g, 0.0166 mmol, 71%). The compound was used immediately without further purification or characterization.

Tungsten aminocaprylic acid-tethered netropsin conjugate 8. The 8-aminocaprylic acid-substituted pyrrole **7** (0.094 g, 0.194 mmol) and the tungsten acid **1** (0.076 g, 0.193 mmol) were placed in a round bottom flask which was flushed thoroughly with argon. Anhydrous DMF (7 mL) was added and the reaction mixture was cooled to 0°C. DECP (0.056 mL, 0.369 mmol) and triethylamine (0.210 mL, 1.51 mmol) were added and the reaction mixture was stirred at 0°C for 2 hours and at room temperature for 16 hours. The DMF was removed under vacuum and the resulting residue was dissolved in CH_2Cl_2 (10 mL) and washed with 2% aqueous Na_2CO_3 (10 mL). The organic layer was dried with K_2CO_3 and the solvent was removed under reduced pressure. Purification by preparative thin layer chromatography on silica gel using 1% NH_4OH in methanol yielded a glassy yellow solid (0.090 g, 0.104 mmol, 54%); IR (NaCl) 3295, 2933, 2014, 1918, 1645, 1539, 1436, 731 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD): δ 7.17 (s, 1H), 7.14 (s, 1H), 6.84 (s, 1H), 6.82 (s, 1H), 5.96 (t, *J* = 2.4 Hz, 2H), 5.61 (t, *J* = 2.4 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.29 (t, *J* = 5.2 Hz, 2H), 2.62 (t, *J* = 8.4 Hz, 2H), 2.45 (s, 6H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.83 (m, 2H), 1.68 (m, 2H), 1.52 (m, 2H), 1.37-1.29 (m, 8H), 0.43 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 229.6, 216.8, 173.6, 165.1, 164.6, 161.5, 129.6, 129.1, 128.9, 124.7, 124.6, 123.5, 106.4, 106.1, 102.4, 94.5, 93.1, 58.0, 45.0, 40.7, 38.2, 37.4, 37.0, 30.9, 30.4, 30.3, 28.0, 27.9, 27.2, 27.1, -32.2; FAB HRMS *m/z* calcd. for $C_{45}H_{48}N_7O_7W$ (MH^+): 862.3125; Found 862.3152.

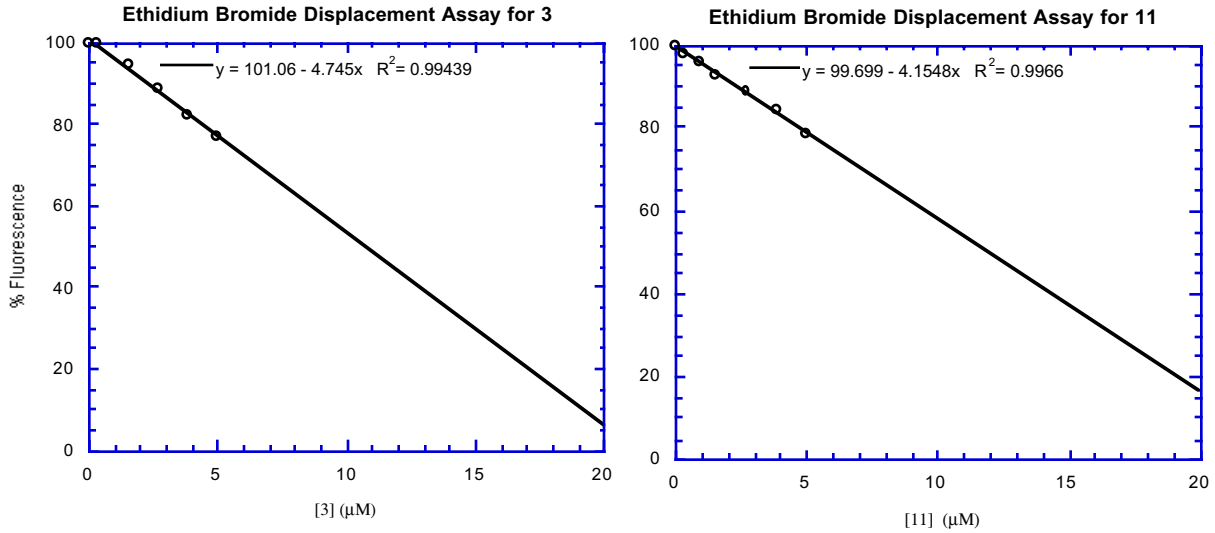
Preparation of benzyl-protected phenyltungsten complex 9. Tungsten hexacarbonyl (0.833 g, 2.37 mmol) was placed into an oven dried three neck round bottom flask which was fitted with a reflux condenser. This was then flushed with nitrogen. THF (20 mL) was then added followed by NaCp (1.42 mL of a 2.0 M solution, 2.84 mmol). The mixture was then heated at reflux for 18 h. The reaction mixture was then cooled to room temperature and $ZnCl_2$ (4.73 mL of a 0.5 M solution in THF, 2.37 mmol) was added, and the mixture was stirred at room temperature for 2 h. Benzyl protected 4-iodobenzoic acid (0.400 g, 1.18 mmol) was placed in a separate dry three neck round bottom flask fitted with a dry addition funnel containing $PdPhI(PPh_3)_2$ (0.059 g, 0.071 mmol). The flask was then flushed with nitrogen and an additional 20 mL of THF was added. The $CpW(CO)_3Zn$ solution was then transferred via cannulation into this second flask and the Pd catalyst was then added. The mixture was allowed to stir at room temperature for 4 h. The solvent was evaporated to dryness and the remaining residue was dried under vacuum. Purification was accomplished via chromatography on silica gel with 20% ethyl acetate/hexanes to give a yellow solid (0.606 g, 94%). IR (NaCl) 3111, 2019, 1916, 1712, 1580, 1276, 1195, 1106, 1005, 829, 754, 698 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.10 (m, 3H), 5.24 (s, 2H), 4.42 (s, 5H); ^{13}C NMR (100 MHz, C_6D_6): δ 228.4, 219.2, 167.8, 147.4, 138.4, 137.3, 129.1, 129.0, 128.8, 128.5, 127.3, 92.8, 66.8; FAB HRMS *m/z* calcd. for $C_{22}H_{17}O_5W$ (MH^+): 544.0507; Found 544.0511.

Preparation of phenyltungsten acid 10. Compound **9** (0.200 g, 0.368 mmol) and potassium hydroxide (0.103 g, 1.84 mmol) were placed in a round bottom flask. This was then flushed with nitrogen and a 1:1:1.5 mixture of THF/water/methanol (3.7 mL) was then added. The flask was then wrapped in aluminum foil and the mixture was stirred at room temperature for 21 h. After cooling, the reaction mixture was extracted with methylene chloride to remove starting material. The aqueous layer was then acidified with 1M HCl. The product was then extracted into methylene chloride, which was then dried over $MgSO_4$. The solvent was evaporated to dryness and the residue was dried under vacuum to give a yellow solid (0.090 g, 54%). IR (NaCl) 3437 (s, br), 2019, 1917, 1675, 1653, 1581, 1419, 1289 cm^{-1}; ^1H NMR (100 MHz, C_6D_6): δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 4.40 (s, 5H); ^{13}C NMR (400 MHz, C_6D_6): δ 228.3, 219.0, 173.0, 147.4, 139.7, 138.3, 129.3, 92.6; FAB HRMS *m/z* calcd. for $C_{15}H_{10}O_5WLi$ (MLi^+): 461.0198; Found 461.0207.

Preparation of phenyltungsten-netropsin conjugate 11. Phenyltungsten complex **10** (0.090 g, 0.367 mmol) and netropsin derivative **2** (0.127 g, 0.367 mmol) were added to a round bottom flask and flushed with nitrogen. DMF (5 mL) was then added and the reaction mixture was cooled to 0°C. Triethylamine (0.116 mL, 2.20 mmol) was then added, followed by DECP (0.048ml, 0.587 mmol). The mixture was stirred at room temperature for 19 h. The solvent was removed and the residue was dried under vacuum. The product was purified via preparative silica gel TLC with 1% NH_4OH/MeOH to give a yellow solid (0.100 g, 64%). IR (NaCl) 2017, 1917, 1653, 1540 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.25 (s, 1H), 7.16 (s, 1H), 6.98 (s, 1H), 6.79 (s, 1H), 5.70 (s, 5H), 3.89 (s, 3H), 3.85 (s, 3H), 3.32 (m, 2H), 2.45 (br t, 2H), 2.30 (s, 6H), 1.77 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ 229.6, 220.6, 168.4, 164.4, 161.6, 148.1, 136.6, 131.6, 127.0, 124.9, 124.8, 123.7, 123.4, 121.2, 120.6, 106.7, 106.3, 94.4, 58.4, 45.4, 38.6, 37.0, 36.9, 28.3; FAB HRMS *m/z* calcd. for $C_{32}H_{34}N_6O_6W$ (MH^+): 783.2128; Found 783.2151.

Ethidium bromide displacement assays. Fluorescence intensity was determined using a Turner Model 430 Spectrofluorometer with a Xenon lamp at an excitation wavelength of 540 nm and emission wavelength of 590 nm. Ultrapure ethidium bromide was purchased from Gibco BRL and was dissolved in 20 mM tris-HCl reaction buffer (pH 8) . Poly[d(AT)•(d(AT)] (ε_{260} = 6600 $M^{-1}cm^{-1}bp^{-1}$) was purchased from Sigma and dissolved in 20 mM tris HCl, 100 mM NaCl (pH 8) buffer. The exact DNA concentration was determined using a Cary 50 UV spectrophotometer.

To a 3 mL optical glass cell of 10 mm pathlength was added 36.8 μL of poly[d(AT)•(d(AT)] solution (0.325 mM), 30.0 μL of ethidium bromide solution (125 μM), and 2.93 mL of tris-HCl reaction buffer (pH 8). The fluorescence of this solution (4.0 μM in bp DNA, 1.26 μM ethidium bromide) was determined and then aliquots (5 – 20 μL) of the appropriate tungsten compound (180 μM in DMSO) were added. The fluorescence intensity was recorded after the addition of each aliquot. The addition of the tungsten solution was repeated until the fluorescence intensity decreased to approximately 20% of its original value. A plot relating % fluorescence intensity to concentration of tungsten compound was constructed using Kaleidagraph Version 3.09. The apparent binding constant (K_{app}) was calculated from the following equation: $K_{EtBr}[EtBr] = K_{app}[W]$, where [W] is the concentration of tungsten compound at 50% decrease in fluorescence and $K_{EtBr} = 9.5 \times 10^6\ M^{-1}$. The following graphs gave $K_{app} = 1.11 \times 10^6\ M^{-1}$ for **3** and $K_{app} = 1.00 \times 10^6\ M^{-1}$ for **11**. No decrease in fluorescence was observed for $CpW(CO)_3CH_3$.



DNA cleavage studies-general. Purified, deionized water was obtained by filtration with a four cartridge Barnstead E-Pure apparatus and was used for all aqueous reactions and dilutions. Plasmid pBR322 DNA (4361 bp) was obtained from New England Biolabs. α-^{32}P dATP (3000 Ci/mmol) was obtained from New England Nuclear. High Strength Analytical Grade Agarose was purchased from Bio-Rad. Gel electrophoresis was carried out with 1% agarose gels and 90 mM TBE buffer in a Gibco BRL Horizon 20:25 electrophoresis apparatus. The concentrated loading buffer for agarose gels consisted of 35% (w/v) sucrose solution containing 0.20% bromophenol and 0.20% xylene cyanol FF. The 3'-^{32}P labeling of the Eco R1 and Rsa 1 DNA restriction fragments was carried out according to standard literature procedures. Calf thymus DNA and methidiumpropyl-EDTA was purchased from Sigma. $Fe(NH_4)_2(SO_4)_2$, dimethylsulfate, and β–mercaptoethanol were purchased from Aldrich. The 40% acrylamide solution (19:1 acrylamide:bisacrylamide) was purchased from Bio-Rad. Polyacrylamide gel electrophoresis was carried with a 10% denaturing polyacrylamide gel and 90 mM TBE buffer on a CBS Scientific dual nucleic acid sequencer. Loading buffer for polyacrylamide gels was 80% formamide containing 0.2% bromophenol blue and xylene cyanol. The positively charged membrane was purchased from Boehringer Mannheim. The Kodak X-Ray film and intensifying screen were purchased from Sigma.

Cleavage with tungsten-netropsin conjugate 3 and high-resolution gel of electrophoresis of restriction fragments. Reactions were carried out in 1.5 mL plastic microcentrifuge tubes. A DMSO solution (2 μL) of the tungsten-netropsin derivative **3** was added to 18 μL of a solution containing 3'-^{32}P labeled restriction fragment (50,000 cpm) and carrier calf thymus DNA (100 μM

bp) in tris acetate buffer (pH 8). The microcentrifuge tubes were strapped to the outside of a water-cooled Pyrex photolysis reactor and irradiated with light from a 450 W medium pressure mercury arc lamp for 20 minutes. After the photolysis, the DNA was precipitated by adding 2 μL NaOAc (3 M, pH 5) and 50 μL absolute ethanol. The samples were cooled at -20°C for one hour and then centrifuged at 4°C at 13,000 rpm for 10 minutes. The supernatant was removed and the samples were resuspended in 5 μL formamide loading buffer. Each sample was heated at 95°C for 3 minutes and immediately cooled on ice for 1 minute prior to loading onto a 10% denaturing polyacrylamide gel (1:19 crosslinking, 7 M urea) along with the Maxam-Gilbert G sequencing reaction and footprinting assays (see below). The samples were electrophoresed at 55 W and 55°C for 1.5 hours. After electrophoresis, the gel was blotted with a positively charged membrane for 20 minutes. After crosslinking each section of the membrane for 3 minutes with UV light, the membrane was exposed to X-Ray film with an intensifying screen for 72 hours at -40°C.

MPE•Fe(II) Footprinting assay. A 250 μM solution of MPE•Fe(II) was prepared by mixing 5 μL of 1 mM $Fe(NH_4)_2(SO_4)_2$ with 5 μL of 1 mM methidiumpropyl EDTA. This solution was diluted with 10 μL of H_2O for a final concentration of 250 μM. To a tube containing the 2 μL of a DMSO solution of the tungsten netropsin derivative and 18 μL of a solution of 3'-^{32}P labeled restriction fragment (50,000 cpm) and carrier calf thymus DNA (100 μM bp) in tris acetate buffer (pH 8), 4 μL MPE•Fe(II) (250 μM) and 4 μL dithiothreitiol (20 mM) was added. This mixture was incubated at room temperature for 10 min and then precipitated with NaOAc and ethanol as previously described. The sample was then loaded onto a polyacrylamide gel and electrophoresed as previously described.

Sequence-selectivity of DNA cleavage by conjugate 3.

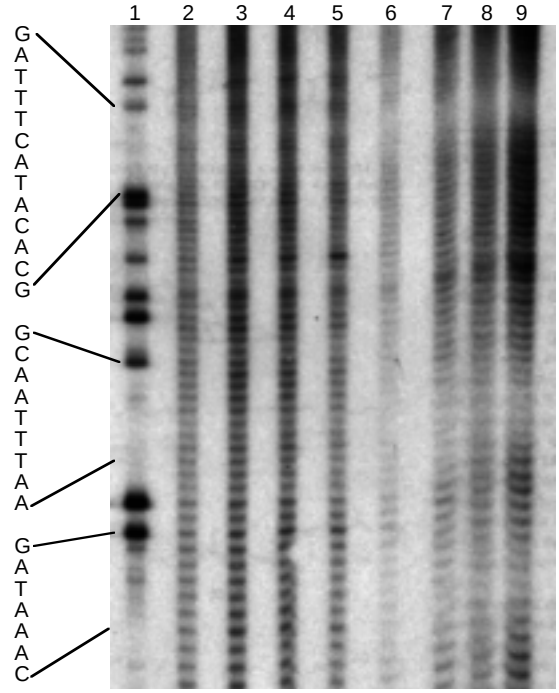


Figure S1. Autoradiogram of a 10% denaturing polyacrylamide gel for binding and photoinduced cleavage of the 3'-^{32}P-end-labeled 167 bp restriction fragment (*Eco*RI/*Rsa*I) of pBR322 DNA/calf thymus DNA (105 μM/bp in 10% DMSO/10 mM Tris buffer, pH 8) by **3**. Lane 1, Maxam-Gilbert G reaction; lanes 2 through 5, DNA + complex (2.88, 1.44, 0.72, and 0.36 mM, respectively), irradiated; lanes 6 through 9, MPE-EDTA/Fe(II)/DTT/O_2 footprinting of DNA + complex (2.88, 1.44, 0.72, and 0.36 mM, respectively). Reactions in lanes 2–5 were irradiated with Pyrex-filtered light from a 450 W medium pressure mercury arc lamp for 20 minutes.

Plasmid relaxation assays. A DMSO solution was made of the compound of interest and serial dilutions were made. The appropriate DMSO solution was added to a 1.5 mL plastic centrifuge tube containing 9 times the volume of a solution containing either 33.3 or 66.6 μM/bp DNA (pBR322) in 20 mM tris-HCl reaction buffer pH 8 (final concentration = 30.0 or 60.0 μM/bp). The tubes were then strapped to the outside of a water-jacketed reaction vessel for a Hanovia photolysis apparatus with a Pyrex filter and irradiated with light from a 450 W medium pressure mercury arc lamp for 20 minutes. After the irradiation, 5 μL of loading buffer was added to each tube and the contents of the tube were loaded onto a 1% agarose gel and electrophoresed for 12 h at 30 V. The gel was then stained in a diltue solution of ethidium bromide (~0.5 μg/mL) for 10 minutes and then destained with water. The DNA was visualized with UV light and photographed using a Polaroid DS34 camera with black and white Polaroid 667 film.

Plasmid relaxation by 3 in the presence of cysteine.

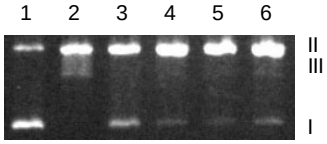


Figure S2. Cysteine inhibition of photoinduced cleavage of pBR322 DNA (30 μM/bp in 10% DMSO/10 mM Tris buffer, pH 8) by hybrid compound **3**. Lanes 1 through 6, DNA + complex (45 μM) + cysteine (0, 0, 3600, 1800, 900, and 450 μM, respectively). Reactions in 2 through 6 lanes were irradiated with Pyrex-filtered light from a 450 W medium pressure mercury arc lamp for 20 minutes.

Controls for plasmid relaxation by 11.

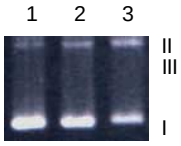


Figure S3. Controls for photoinduced cleavage of pBR322 DNA (60 μM/bp in 10% DMSO/10 mM Tris buffer, pH 8) by hybrid compound **11**. Lanes 1 and 2, DNA alone; lane 3, DNA + complex (360 μM). Reaction in lane 2 was irradiated with Pyrex-filtered light from a 450 W medium pressure mercury arc lamp for 20 minutes; and all samples were precipitated and resuspended in buffer prior to electrophoresis.

Plasmid Assay Quantitation Data. The bands in the scanned gels were quantitated with the NIH ImageJ program to give the following data:

pBR322 cleavage by netropsin conjugate **3** (Figure 1a):

Lane	Form I (%)	Form II (%)	Form III (%)
1 (control)	96.8	3.2	0.0
2 (control)	95.4	4.6	0.0
3 (control)	95.7	4.3	0.0
4	0.0	0.0	0.0
5	0.0	64.6	35.4
6	0.0	87.2	12.8
7	3.3	88.5	8.2
8	8.9	85.8	5.3
9	29.4	70.6	0.0
10	58.7	41.3	0.0
11	62.8	37.2	0.0

pBR322 cleavage by netropsin conjugate **6** (Figure 1b):

Lane	Form I (%)	Form II (%)	Form III (%)
1 (control)	96.5	3.5	0.0
2 (control)	86.5	13.5	0.0
3 (control)	93.9	6.1	0.0
4	0.0	88.7	11.3
5	6.2	87.0	6.8
6	38.7	58.6	2.7
7	59.4	40.6	0.0
8	61.8	38.2	0.0
9	68.5	31.5	0.0
10	93.4	6.6	0.0

pBR322 cleavage by netropsin conjugate **8** (Figure 1c):

Lane	Form I (%)	Form II (%)	Form III (%)
1 (control)	96.5	3.5	0.0
2 (control)	86.6	13.4	0.0
3 (control)	91.5	8.5	0.0
4	9.8	90.2	0.0
5	42.5	57.5	0.0
6	60.4	39.6	0.0
7	69.6	30.4	0.0
8	73.0	27.0	0.0
9	73.8	26.2	0.0
10	87.7	12.3	0.0
11	88.9	11.1	0.0