



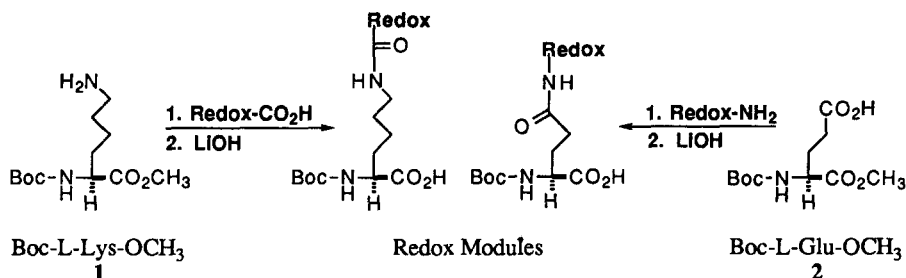
## Synthesis of Redox Derivatives of Lysine and Their Use in Solid-Phase Synthesis of a Light-Harvesting Peptide

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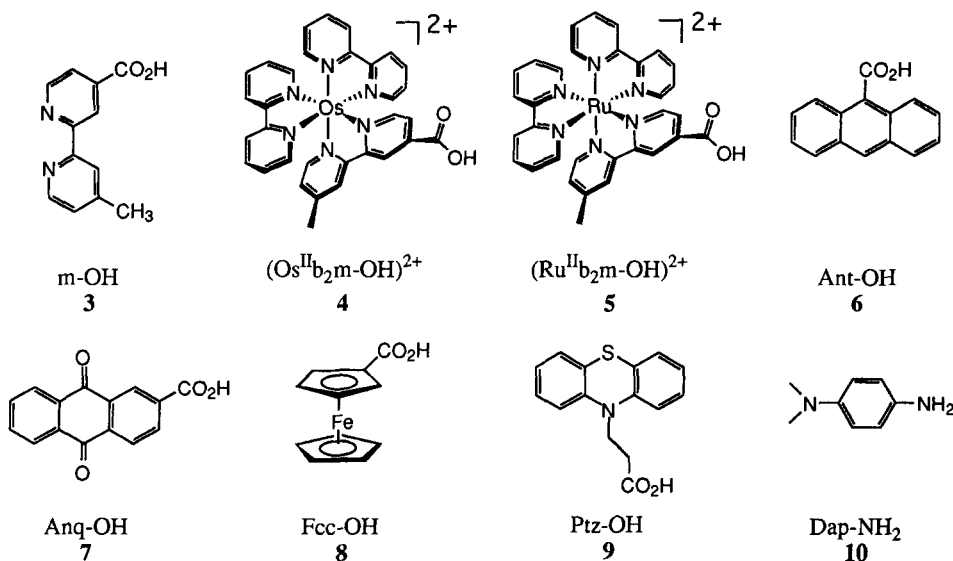
**Abstract:** Redox-active amino acids were synthesized for incorporation into peptide assemblies to study photoinitiated electron or energy transfer. 4'-Methyl-2,2'-bipyridine-4-carboxylic acid was obtained in 72% yield by consecutive  $\text{SeO}_2$  and  $\text{Ag}_2\text{O}$  oxidation without isolation of intermediates. The side chain  $\epsilon$ -amino group of Boc-L-lysine methyl ester or  $\gamma$ -carboxyl group of Boc-L-glutamic acid  $\alpha$ -methyl ester was coupled to a redox moiety (transition-metal chromophore, electron donor, electron acceptor, metal ligand, or triplet-energy transmitter) using 4-(dimethylamino)pyridine, (1-benzotriazoleoxy)tris(dimethylamino)phosphonium hexafluorophosphate, *N*-methylmorpholine, and 1-hydroxybenzotriazole. Use of one equivalent of 4-(dimethylamino)pyridine provided the amide coupling product in 80-97% isolated yield. Selective hydrolysis of the methyl esters with lithium hydroxide provided the redox Boc-amino acids in 70-98% yield. These redox modules are suitable for solid-phase assembly of light-harvesting peptides, as illustrated by the synthesis of the partially  $\alpha$ -helical 11-residue redox triad that contains a phenothiazine electron donor, a ruthenium(II)tris(bipyridine) chromophore, and an anthraquinone electron acceptor. Upon laser excitation at 420 nm, the peptide triad underwent photoinduced electron transfer to create a charge-separated state with a lifetime of 53 ns and decayed with a first-order rate constant of  $1.9 \times 10^8 \text{ s}^{-1}$ .

Photosynthesis converts light into useful chemical energy by creating spatially separated oxidizing and reducing sites. We wish to synthesize peptide assemblies that efficiently undergo photoinitiated redox separation and light harvesting.<sup>1</sup> We have already prepared amino acid assemblies containing several redox sites that undergo photoinitiated intramolecular electron transfer.<sup>2-4</sup> We have designed several peptide-based structures for study of the photoinduced formation of spatially isolated oxidizing and reducing sites by efficient long-range electron transfer to yield a long-lived redox-separated state. These peptides will be engineered to contain several redox sites in specific spatial arrangements that should enhance the photoinduced formation and prolong the lifetime of the redox-separated state.



Scheme 1

**Redox Modules.** This paper describes the synthesis of Boc-amino acids bearing a side chain redox group (Scheme 1) and their use in the solid-phase synthesis of an 11-residue light-harvesting peptide. Using stoichiometric amounts of the acylation catalyst 4-(dimethylamino)pyridine (DMAP), the dehydrating agent (1-benzotriazoleoxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP), 1-hydroxybenzotriazole (HOBt), and the base *N*-methylmorpholine (NMM), a redox-active carboxylic acid was coupled to the side chain amino group of Boc-L-lysine methyl ester (**1**) to form a stable amide bond (Scheme 1). Alternatively, a redox-active amine was coupled to the side chain carboxyl group of Boc-L-glutamic acid  $\alpha$ -methyl ester (**2**). Subsequent saponification of the methyl ester with lithium hydroxide provided a redox Boc-amino acid for use in solid-phase peptide synthesis.<sup>5</sup> The redox component was a metal ligand (bipyridine **3**), a chromophore (the osmium(II) complex **4** or the ruthenium(II) complex **5**), a triplet-energy transmitter (anthracene **6**), an electron acceptor (anthraquinone **7**), or an electron donor (ferrocene **8**, phenothiazine **9**, or aniline **10**).



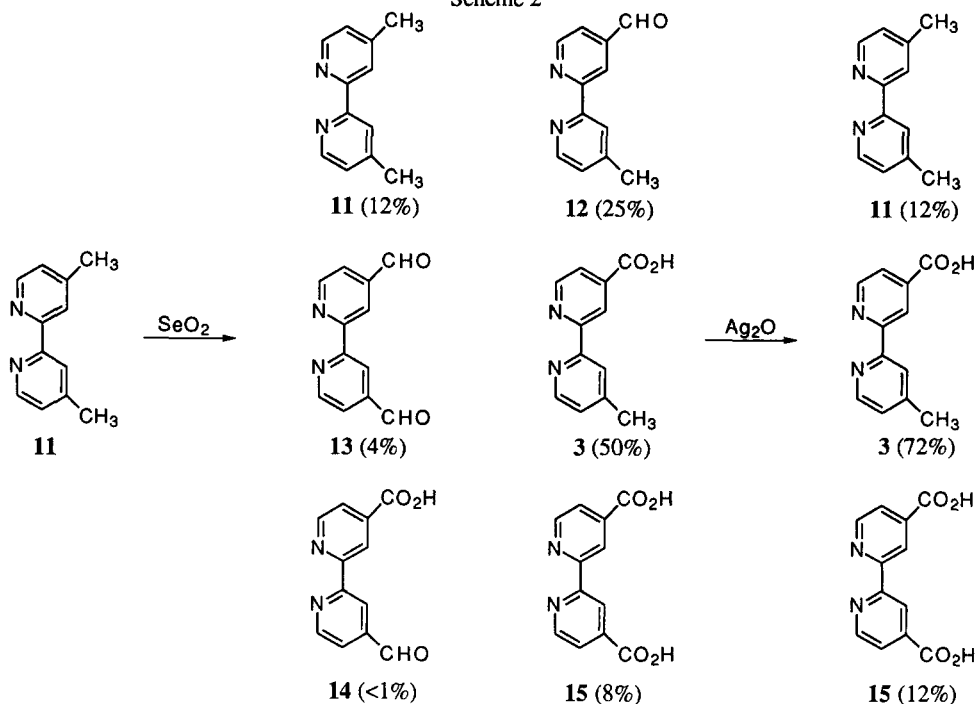
## RESULTS AND DISCUSSION

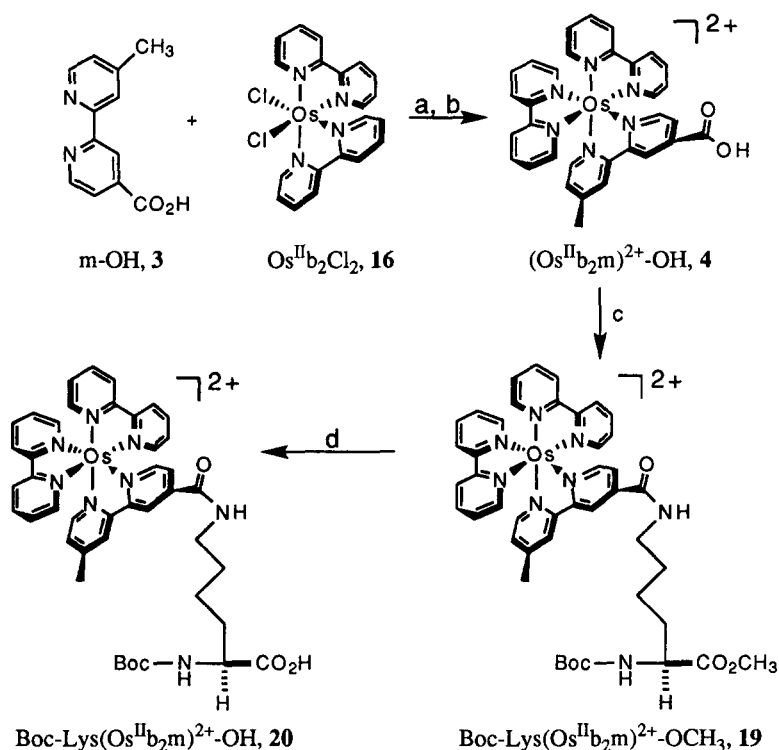
## Synthesis of Three Redox Acids

**Improved Synthesis of Bipyridine Acid 3.** Recently we reported<sup>6</sup> a two-step oxidative synthesis of 4'-methyl-2,2'-bipyridine-4-carboxylic acid (**3**, m-OH) in 45% overall yield from commercially available 4,4'-dimethyl-2,2'-bipyridine (**11**). Selective SeO<sub>2</sub> oxidation of bipyridine **11** to the monoaldehyde **12** was followed by Ag<sub>2</sub>O oxidation of the latter to the monoacid **3**. After the SeO<sub>2</sub> step, the aldehydes were isolated together as bisulfite addition compounds. However, SeO<sub>2</sub> oxidation occasionally yielded as much as 13% of the dialdehyde **13**, which was isolated along with the monoaldehyde **12** and subsequently converted into the diacid **15** during the Ag<sub>2</sub>O oxidation. Varying the number of equivalents of SeO<sub>2</sub> used or the reaction time decreased the isolated yield of the monoaldehyde **12** and increased the yields of acidic products such as **3** and **15**.

Since SeO<sub>2</sub> oxidation of bipyridine **11** produces significant amounts of both the monoaldehyde **12** and the monoacid **3**, we developed an improved procedure for synthesis of the latter that avoids the unnecessary separation of the aldehydic products. As shown in Scheme 2, the crude mixture of products from the SeO<sub>2</sub> oxidation was directly oxidized with Ag<sub>2</sub>O, which reduced the number of compounds from six to three. Specifically, monoaldehyde **12** was converted into monoacid **3** and both dialdehyde **13** and aldehydic acid **14** were converted into diacid **15**. Unreacted bipyridine **11** was easily separated from the salts of the acids **3** and **15** by chloroform extraction of the alkaline oxidation mixture. Then the desired monoacid **3** was separated from the diacid **15** by Soxhlet extraction with acetone.<sup>7</sup> When this two-step oxidation procedure was

Scheme 2





Scheme 3. Reagents and conditions: (a) ethylene glycol, reflux; (b) 1:1 (v/v) 1 N KOH/ethanol; (c) Boc-Lys-OCH<sub>3</sub> (**1**), BOP/HOBt/NMM/DMAP; (d) LiOH, 3:1 (v/v) methanol/water.

conducted on a 23-mmol scale, the pure monoacid **3** was isolated in 72% overall yield and the diacid **15** in 12% overall yield. Based on the 12% recovery of the starting bipyridine **11**, the net yield of the desired bipyridine monoacid **3** was 82%, which represents a significant improvement over previous procedures.<sup>6,8</sup>

*Synthesis of the Redox-Active Chromophoric Acid ( $\text{Os}^{\text{II}}\text{b}_2\text{m}$ )<sup>2+</sup>-OH ( $\text{PF}_6^-$ )<sub>2</sub> (**4**).* Redox acid **4** is a monocarboxylic acid derivative of tris(2,2'-bipyridine)osmium(II). It was synthesized by a mixed-ligand substitution<sup>9</sup> between *cis*-dichlorobis(2,2'-bipyridine)osmium(II) ( $\text{Os}^{\text{II}}\text{b}_2\text{Cl}_2$ , **16**) and the bipyridine monoacid **3** (m-OH; Scheme 3). This reaction was monitored by the appearance of the characteristic metal-to-ligand charge-transfer (MLCT) absorbance at 488 nm and was complete after 90 min. Since the reaction was conducted in ethylene glycol at reflux, the major reaction product, ( $\text{Os}^{\text{II}}\text{b}_2\text{m}$ )<sup>2+</sup>-OH ( $\text{Cl}^-$ )<sub>2</sub>, was accompanied by significant amounts of ethylene glycol esters. Saponification of the ester groups with aqueous KOH followed by protonation of the resulting potassium salt with 60% HPF<sub>6</sub> provided the pure redox acid **4** in 85% yield as black crystals.

*Synthesis of the Redox-Active Chromophoric Acid ( $\text{Ru}^{\text{II}}\text{b}_2\text{m}$ )<sup>2+</sup>-OH ( $\text{PF}_6^-$ )<sub>2</sub> (**5**).* Redox acid **5** is the analogous monocarboxylic acid derivative of tris(2,2'-bipyridine)ruthenium(II). Following the method of Peek and co-workers,<sup>6</sup> a suspension of *cis*-dichlorobis(2,2'-bipyridine)ruthenium(II) and the bipyridine monoacid **3**

Table 1. Percentage Yields for the Synthesis and Selective Ester Hydrolysis of Eight Compounds:  
Effect of 4-(Dimethylamino)pyridine during Amine Acylation

Code	Structure	DMAP present during amine acylation			Ester hydrolysis
		1.0 equiv	0.1 equiv	None	
17	Boc-Lys(m)-OCH <sub>3</sub>	84	76	69	74
19	Boc-Lys(Os <sup>II</sup> b <sub>2</sub> m) <sup>2+</sup> -OCH <sub>3</sub>	94	92	64	82
21	Boc-Lys(Ru <sup>II</sup> b <sub>2</sub> m) <sup>2+</sup> -OCH <sub>3</sub>	87	55	32	70
23	Boc-Lys(Ant)-OCH <sub>3</sub>	97	55	17	98
25	Boc-Lys(Anq)-OCH <sub>3</sub>	81	69	50	70
27	Boc-Lys(Fcc)-OCH <sub>3</sub>	90	60	5	80
29	Boc-Lys(Ptz)-OCH <sub>3</sub>	90	87	80	87
31	Boc-Glu(Dap)-OCH <sub>3</sub>	80	75	70	75

in 70% ethanol was heated at reflux for 6 h. Acidification with 60% HPF<sub>6</sub> provided the pure redox acid **5** in 96% yield as a blood-red solid.

#### DMAP-Assisted Side Chain Acylation

We have synthesized<sup>6</sup> lysine derivatives containing either an electron acceptor or a chromophore by coupling the succinimido ester of a redox acid to the ε-amino group of Boc-Lys. Due to limitations of reaction scale and difficulties in product purification, this approach was not applicable to many carboxylic acids. In order to increase the yield and variety of the redox derivatives, we have developed a more general method for attaching carboxylic acids to the side chain amino group of Boc-Lys.

The acylation catalyst<sup>10</sup> 4-(dimethylamino)pyridine (DMAP) has occasionally been used during peptide synthesis. For example, DMAP has been used with *N,N'*-dicyclohexylcarbodiimide (DCC) to accelerate the formation of peptide bonds between α-amino acids during solid-phase peptide synthesis.<sup>11</sup> The yield from a DCC/DMAP coupling generally is markedly increased over the DCC coupling with no added DMAP. But the presence of DMAP can cause significant racemization of the amino acid being coupled.<sup>12,13</sup> BOP/DMAP couplings were used during a total synthesis of cyclotheonamide B.<sup>14</sup>

We have studied the use of DMAP during coupling of an amine and an acid by the combined action of the dehydrating agent BOP, the alcohol HOBt, and the base NMM. Either a catalytic (0.1 equiv) or stoichiometric (1.0 equiv) amount of DMAP was present during BOP/HOBt/NMM coupling of the amine **1** (Boc-Lys-OCH<sub>3</sub>) and each of the acids **3-9**. The coupling yields were lowest (5-80%) in the absence of DMAP, higher (55-92%) using the catalytic amount of DMAP, and highest (81-97%) using the stoichiometric amount of DMAP (Table 2). The amides (**21**, **23**, and **27**) that formed poorly in the absence of DMAP (5-32%), coupled much better using 1.0 equiv of DMAP (87-97%) than using only 0.1 equiv (55-60%). The yields of the amides **17** and **29** and of the glutamine derivative **31** from coupling of amine **10** and the glutamic acid derivative **2** (Boc-Glu-OCH<sub>3</sub>) were nearly the same under all three conditions (Table 1).

### Synthesis of Eight Redox Modules

**Synthesis of the Metal-Ligating Module Boc-Lys(m)-OH (18).** Amino acid derivatives that contain the bidentate ligand 2,2'-bipyridine (b) are used in protein engineering because binding of a metal ion to this ligand can promote protein folding<sup>15</sup> or provide a potential catalytic site.<sup>16</sup> Coupling of the bipyridine monoacid 3 (m-OH) to the side chain amino group of Boc-Lys-OH would provide the metal-ligating module Boc-Lys(m)-OH for use in the solid-phase assembly of redox-active proteins. This module was synthesized in two steps. BOP/HOBt/NMM/DMAP coupling of monoacid 3 to the  $\epsilon$ -amino group of Boc-Lys-OCH<sub>3</sub> (1) produced Boc-Lys(m)-OCH<sub>3</sub> (17). The isolated yield of ester 17 was 84% using 1.0 equiv of DMAP, 76% using 0.1 equiv of DMAP, and 69% using no DMAP. Selective hydrolysis of ester 17 with LiOH afforded the corresponding acid Boc-Lys(m)-OH (18) in 74% yield. The overall yield of the metal-ligating module 18 from the commercially available ester 1 was 62%.

**Synthesis of the Chromophoric Module Boc-Lys(Os<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OH (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (20).** Acid 4 was activated by treatment with BOP, HOBt, NMM, and DMAP in 1:1 (v/v) *N,N*-dimethylformamide (DMF)/dichloromethane and coupled to amine 1 to afford Boc-Lys(Os<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OCH<sub>3</sub> (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (19; Scheme 3). Ester 19 was purified by flash chromatography on an alumina column eluted with 2:1 (v/v) acetonitrile/toluene. The isolated yield of ester 19 was 94% using 1.0 equiv of DMAP and 92% using 0.1 equiv of DMAP but only 64% using no DMAP. Selective hydrolysis of ester 19 with LiOH followed by protonation of the carboxylate with 0.1 M HPF<sub>6</sub> (instead of 60% HPF<sub>6</sub> to prevent loss of the Boc protecting group) gave the corresponding acid Boc-Lys(Os<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OH (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (20; Scheme 3) in 80% yield. The overall yield of the chromophoric module 20 was 77% from redox acid 4 and 66% from osmium complex 16. Osmium complexes 4, 19 and 20 were precipitated as solids or crystals by slow evaporation over 2-3 days from 1:1 (v/v) acetone/water and their purity was assessed by cation-exchange HPLC.

**Synthesis of the Chromophoric Module Boc-Lys(Ru<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OH (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (22).** Acid 5 was activated by treatment with BOP, HOBt, NMM, and DMAP in DMF and coupled to amine 1 to afford Boc-Lys(Ru<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OCH<sub>3</sub> (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (21). Ester 21 was also purified by flash chromatography on alumina eluted with 2:1 (v/v) acetonitrile/toluene. The isolated yield of ester 21 was 87% using 1.0 equiv of DMAP, 56% using 0.1 equiv of DMAP, and only 38% using no DMAP. Selective hydrolysis of ester 21 with LiOH followed by protonation with 0.1 M HPF<sub>6</sub> provided the corresponding acid Boc-Lys(Ru<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OH (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (22) in 70% yield. The overall yield of the chromophoric module 22 was 61% from acid 5. Ruthenium complexes 5, 21, and 22 were precipitated as orange or red solids by dissolving in a minimal volume of acetonitrile and adding this solution dropwise to cold diethyl ether with rapid stirring. Their purity was assessed by cation-exchange HPLC.

**Synthesis of the Triplet-Energy Transmitting Module Boc-Lys(Ant)-OH (24).** Anthracene has been used in soluble polymer assemblies to transmit triplet energy from an osmium chromophore to a ruthenium chromophore.<sup>17</sup> Thus a module containing anthracene was synthesized for use in the solid-phase assembly of triplet-energy transmitting peptides and proteins. The BOP/HOBt/NMM/DMAP coupling of anthracene-9-carboxylic acid (Ant-OH; 6) to the  $\epsilon$ -amino group of Boc-Lys-OCH<sub>3</sub> (1) produced Boc-Lys(Ant)-OCH<sub>3</sub> (23). The yield of ester 23 was 97% using 1.0 equiv of DMAP, 55% using 0.1 equiv of DMAP, but only 17% using no DMAP. Selective hydrolysis of ester 23 with LiOH afforded the acid Boc-Lys(Ant)-OH (24) in 98% yield. The overall yield of the triplet-energy transmitting module 21 was 95%.

**Synthesis of the Electron-Accepting Module Boc-Lys(Anq)-OH (26).** The electron acceptor

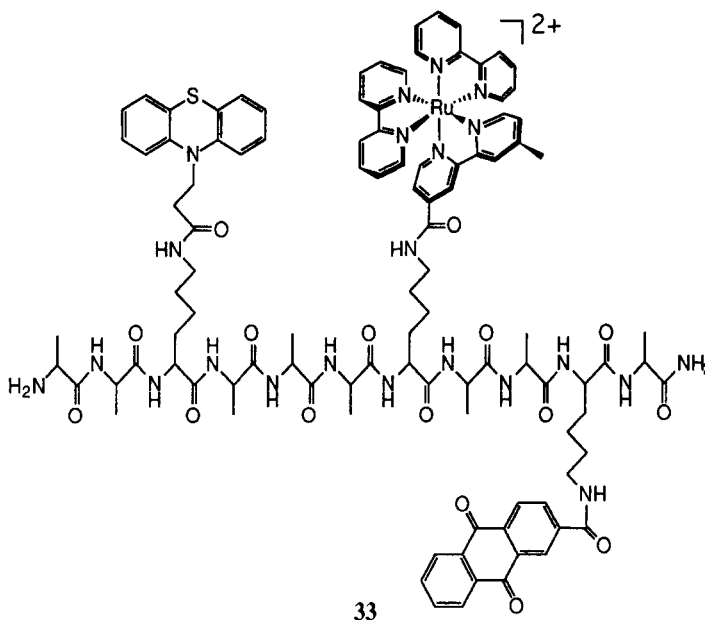
anthraquinone has also been incorporated into light-harvesting assemblies.<sup>4</sup> BOP/HOBt/NMM/DMAP coupling of anthraquinone-2-carboxylic acid (Anq-OH; **7**) to the  $\epsilon$ -amino group of Boc-Lys-OCH<sub>3</sub> (**1**) produced Boc-Lys(Anq)-OCH<sub>3</sub> (**25**). The yield of ester **25** was 81% using 1.0 equiv of DMAP, 69% using 0.1 equiv of DMAP, and 50% using no DMAP. Selective hydrolysis of ester **25** with LiOH afforded the corresponding acid Boc-Lys(Anq)-OH (**26**) in 70% yield. The overall yield of the electron-accepting module **26** was 57%.

*Synthesis of the Electron-Donating Module Boc-Lys(Fcc)-OH (28).* Derivatives of the electron donor ferrocene have been attached to amino acids to increase lipophilicity or to act as markers for chromophoric or electrochemical detection.<sup>18,19</sup> Amide derivatives of ferrocene-1-carboxylic acid (Fcc-OH; **8**) are more difficult to prepare due to the lack of reactivity of activated acyl derivatives<sup>18</sup> to nucleophilic attack. Reaction of ferrocene-1-carbonyl chloride<sup>20</sup> with amine **1** resulted in a low yield of the desired amide. In contrast, coupling of ferrocene-1-carboxylic acid (**8**) to Boc-Lys-OCH<sub>3</sub> (**1**) using BOP/HOBt/NMM/DMAP activation furnished Boc-Lys(Fcc)-OCH<sub>3</sub> (**27**) in good to excellent yield. The isolated yield of ester **27** was 90% using 1.0 equiv of DMAP, 60% using 0.1 equiv of DMAP, but only 5% using no DMAP. Selective hydrolysis of ester **27** with LiOH afforded the corresponding acid Boc-Lys(Fcc)-OH (**28**) in 80% yield as a rust-colored solid. The overall yield of the electron-donating module **28** was 54%. Like other ferrocene derivatives,<sup>21</sup> the ferrocene-containing ester **27** and acid **28** were unstable to treatment with mineral acids, such as HCl or HF, but were stable to treatment with neat trifluoroacetic acid (TFA) or 1:1 (v/v) TFA/dichloromethane.

*Synthesis of the Electron-Donating Module Boc-Lys(Ptz)-OH (30).* The electron donor phenothiazine has previously been incorporated into redox-active amino acids and peptides.<sup>2-4,22</sup> The BOP/HOBt/NMM/DMAP coupling of 10*H*-(phenothiazine-10)propionic acid<sup>23</sup> (Ptz-OH; **9**) to the  $\epsilon$ -amino group of Boc-Lys-OCH<sub>3</sub> (**1**) produced Boc-Lys(Ptz)-OCH<sub>3</sub> (**29**). The yield of ester **29** was 90% using 1.0 equiv of DMAP, 87% using 0.1 equiv of DMAP, and 80% using no DMAP. Selective hydrolysis of ester **29** with LiOH afforded the corresponding acid Boc-Lys(Ptz)-OH (**30**) in 87% yield. The overall yield of the electron-accepting module **30** was 79%. All reactions involving a phenothiazine derivative were run in the dark to prevent oxidation of the sulfur atom by O<sub>2</sub> in the presence of light.<sup>3</sup>

*Synthesis of the Electron-Donating Module Boc-Glu(Dap)-OH (32).* A protected amino acid derivative of the electron donor phenylenediamine was recently prepared by N-acylation of the redox amine **10** with 4-(Boc-amino)butanoic acid using DCC activation.<sup>24</sup> We have synthesized a glutamic acid derivative of **10** similarly. BOP/HOBt/NMM/DMAP coupling of the amino group of 4-(dimethylamino)aniline (Dap-NH<sub>2</sub>; **10**) to the  $\gamma$ -carboxylic acid group of Boc-Glu-OCH<sub>3</sub> (**2**) produced Boc-Glu(Dap)-OCH<sub>3</sub> (**31**). A clear purple solution of ester **31** in CDCl<sub>3</sub> turned into a black gel within 15 min probably due to light-initiated free-radical processes. Thereafter, the Glu(Dap) derivatives **31** and **32** were kept away from light and halogenated solvents at all times. The yield of ester **31** was 80% using 1.0 equiv of DMAP, 75% using 0.1 equiv of DMAP, and 70% using no DMAP. Selective hydrolysis of ester **31** with LiOH afforded the corresponding acid Boc-Glu(Dap)-OH (**32**) in 75% yield. The overall yield of the electron-accepting module **32** was 60%.

*Electrochemistry.* The half-wave reduction potentials measured by cyclic voltammetry for six redox-active methyl esters (Table 2), were shifted only slightly from the parent acids and amine.<sup>3,4</sup> For **19**, the O<sub>S</sub><sup>III/II</sup> couple occurs at  $E = 0.74$  eV in CH<sub>3</sub>CN (vs Ag/AgNO<sub>3</sub>) and the first ligand reduction at  $E = -1.52$  eV. For **21**, the Ru<sup>III/II</sup> couple occurs at  $E = 0.94$  eV in CH<sub>3</sub>CN (vs Ag/AgNO<sub>3</sub>) and the first ligand reduction at  $E = -1.56$  eV. The reductive couple for quinone **25** occurs at  $E = -1.10$  eV. Oxidative couples for the electron donors **27**, **29** and **31** occur  $E = 0.36$  eV, 0.41 eV, and 0.50 eV, respectively.





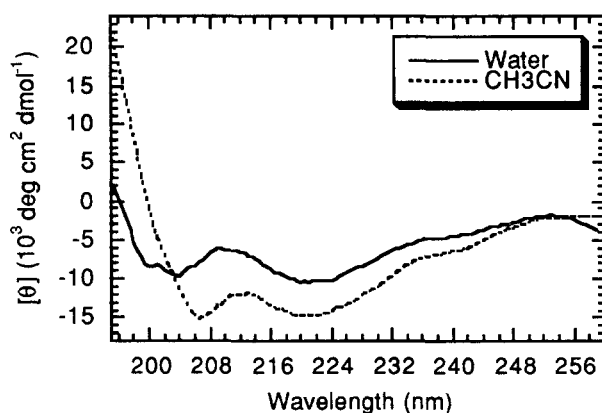
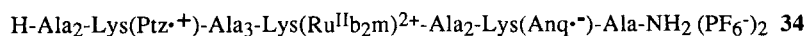
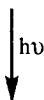
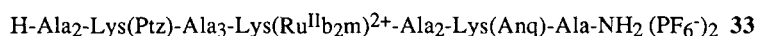


Figure 1. CD spectra of **33** at 25 °C in water (67  $\mu$ M) and in acetonitrile (64  $\mu$ M).

**Circular Dichroism and  $\alpha$ -Helical Structure.** The solution conformation of peptide **33** was studied by circular dichroic spectroscopy. The CD spectrum of **33** in water showed minima at 203 nm and 222 nm. In acetonitrile, the spectrum showed minima at 208 nm and 222 nm, which are characteristic of an  $\alpha$  helix.<sup>25</sup> According to Chen et al.,<sup>26</sup> the theoretical maximum amplitude of the negative band near 222 nm for a fully  $\alpha$ -helical 11-residue peptide is  $[\theta] = -30,270 \text{ deg cm}^2 \text{ dmol}^{-1}$ . By this criterion, peptide **33** was 49%  $\alpha$ -helical in acetonitrile and 34% in water.

**Photoinduced Electron Transfer.** For emission lifetimes and nanosecond transient absorption spectra and kinetics, a solution of **33** in acetonitrile was excited with 1.2-mJ pulses from a 420-nm laser using instrumentation and methods described previously.<sup>3,4</sup> Emission from the MLCT excited state of the chromophore was largely quenched with a single-exponential rate constant of  $2 \times 10^8 \text{ s}^{-1}$  (lifetime of 5 ns). By 30 ns after the laser pulse, the transient absorbance difference spectrum corresponded to a superposition of the spectra of  $\text{Ptz}^+$  (515 nm) and  $\text{Anq}^{\cdot-}$  (590 nm), consistent with the formation of the redox-separated state **34** having Ptz as the radical cation and Anq as the radical anion. The redox-separated state decayed with single-exponential kinetics,  $k = 1.9 \times 10^7 \text{ s}^{-1}$ , and persisted for 53 ns. This lifetime is shorter than that seen for the redox-separated state of  $\text{Anq-Lys(Ru}^{\text{II}}\text{b}_2\text{m)}^{2+}\text{-pPtz}$  (174 ns).<sup>4</sup> Based on the measured redox potentials of the donor and acceptor of the triad, the energy stored in the redox-separated state **34** was 1.5 eV.



## EXPERIMENTAL PROCEDURES

**Materials and Methods.** NMM was distilled from ninhydrin and stored in the dark. Boc-amino esters **1** and **2** were purchased from Bachem Biosciences; acids **6**, **7**, and **8** and amine **10** were bought from Aldrich Chemical. Acids **5** and **9** were prepared as described.<sup>6,23</sup> Uncorrected melting points, cyclic voltammetry, elemental analysis, cation-exchange HPLC, and ultraviolet-visible (UV-VIS), infrared, and NMR spectroscopy were performed as previously described.<sup>3,6</sup> The melting point (mp) and spectral data for bipyridine monoacid **3** and diacid **15**, the Ru complexes **21** and **22**, anthraquinone **26**, and phenothiazine **30** were consistent with literature values.<sup>3,4,6,22</sup> CD spectra were recorded with an AVIV Model 62DS CD spectrophotometer (Lakewood, NJ). The ellipticity  $\theta_{\text{obs}}(\lambda, 25^\circ\text{C})$  of a solution of **33** was measured at integral values of wavelength ( $\lambda$ ) over the range of 185–260 nm using an averaging time of 4 s. Protein concentrations were determined by quantitative amino acid analysis of stock solutions.

**4'-Methyl-2,2'-bipyridine-4-carboxylic Acid, 3.** A suspension of  $\text{SeO}_2$  (3.07 g, 27.7 mmol, 1.2 equiv) and 4,4'-dimethyl-2,2'-bipyridine (**11**, 4.25 g, 23.1 mmol, 1.0 equiv) in 1,4-dioxane (250 mL) was heated at reflux for 24 h with stirring and filtered hot through a pad of diatomaceous earth (Celite) to remove elemental selenium. The filtrate was cooled to room temperature and freed of solvent by rotary evaporation. The residual yellow solid was suspended in 95% ethanol (150 mL). A solution of  $\text{AgNO}_3$  (4.31 g, 25.3 mmol, 1.1 equiv) in water (40 mL) was added. The yellow suspension was stirred rapidly as 1.00 M NaOH (100 mL) was added dropwise over 20 min to form  $\text{Ag}_2\text{O}$ . The black reaction mixture was stirred rapidly for 15 h. Ethanol was removed by rotary evaporation and the aqueous residue was filtered through a fine-porosity glass frit to remove  $\text{Ag}_2\text{O}$  and elemental silver. The solids were washed with 1.3 M NaOH (2 x 30 mL) and water (30 mL). The combined basic filtrates were extracted with dichloromethane (4 x 100 mL) to remove unreacted bipyridine **11** and adjusted to pH 3.5 with 1:1 (v/v) 4.0 N HCl/acetic acid, which produced a white precipitate. After the mixture was kept at  $-10^\circ\text{C}$  overnight, the white solid was collected, vacuum dried, placed into the thimble of a Soxhlet apparatus, and continuously extracted with dry acetone for 72 h. Rotary evaporation of the acetone provided the title compound (m-OH, **3**, 3.57 g, 72% yield) as a white solid whose mp, UV, infrared, and NMR data agreed with those reported previously.<sup>6</sup>

**Bis(2,2'-bipyridine)(4'-methyl-2,2'-bipyridine-4-carboxylic acid)osmium(II) bis(hexafluorophosphate), 4.** A suspension of solid *cis*-dichlorobis(2,2'-bipyridyl)osmium(II) (**16**, 0.948 g, 1.56 mmol, 1.0 equiv) and 4'-methyl-2,2'-bipyridine-4-carboxylic acid (m-OH, **3**, 0.500 g, 2.33 mmol, 1.5 equiv) in argon-degassed ethylene glycol (15 mL) was heated at reflux under argon for 1.5 h and cooled to room temperature. Saturated aqueous  $\text{NH}_4\text{PF}_6$  (30 mL) was added. The resulting black precipitate was collected on a fine-porosity glass frit, dissolved in 1:1 (v/v) 1.0 N KOH/ethanol and heated at  $50^\circ\text{C}$  for 6 h to hydrolyze the ethylene glycol esters. After rotary evaporation of the ethanol, the aqueous solution was acidified to pH 2 with 60% HPF<sub>6</sub>. The resulting black precipitate was dissolved in 50% acetone and the solvent was allowed to evaporate slowly over 2–3 days, which precipitated the title compound (**4**, 1.33 g, 85% yield) as black microcrystals: mp  $230.0\text{--}232.0^\circ\text{C}$ ; UV-VIS ( $\text{CH}_3\text{CN}$ )  $\lambda$  (e) 248 (13,900), 292 (36,000), 374 (4,500), and 488 nm (6,700  $\text{L cm}^{-1} \text{mol}^{-1}$ ); NMR (400 MHz,  $\text{CD}_3\text{CN}$ )  $\delta$  2.66 (s, 3 H, m  $\text{CH}_3$ ), 7.22 (d  $J_{5',6'} = 6.3$  Hz, d  $J_{3',5'} = 1.1$  Hz, 1 H, m5'), 7.30–7.36 (m, 4 H, 4 x b5), 7.48 (d  $J_{5,6} = 5.9$  Hz, 1 H, m5), 7.60–7.64 (m, 5 H, 4 x b6, m6'), 7.83–7.91 (m, 5 H, 4 x b4, m6), 8.48–8.51 (m, 4 H, 4 x b3), 8.54 (s, 1 H, m3'), and 8.89 ppm (d  $J = 1.5$  Hz, 1 H, m3); anal. (calcd

C 38.18, H 2.60, N 8.35) found C 38.71, H 2.57, N 7.97.

**BOP/HOBt/NMM/DMAP Acylation of Boc-Lys-OCH<sub>3</sub> (1).** N<sup>α</sup>-Boc-L-lysine methyl ester hydrochloride (Boc-Lys-OCH<sub>3</sub>·HCl, 1.0 equiv), (1-benzotriazoleoxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP, 1.1 equiv), 1-hydroxybenzotriazole hydrate (HOBt·H<sub>2</sub>O, 1.1 equiv), 4-(dimethylamino)pyridine (DMAP, 1.0 equiv), *N*-methylmorpholine (NMM, 2.1 equiv), and a redox-active carboxylic acid (Redox-OH, 1.0 equiv) were dissolved in a minimum amount of DMF with stirring. The solution was stirred at room temperature for 24 h. After the DMF was removed by rotary evaporation under high vacuum (0.2 torr), the residue was partitioned between ethyl acetate and 0.5 M H<sub>2</sub>SO<sub>4</sub>. The organic phase was washed four times with 0.5 M H<sub>2</sub>SO<sub>4</sub> and five times each with saturated NaCl, 1.0 M NaHCO<sub>3</sub>, and saturated NaCl, dried over anhydrous MgSO<sub>4</sub>, and freed of solvent by rotary evaporation. The residual Boc-Lys-(Redox)-OCH<sub>3</sub> was preparatively purified by recrystallization or by flash chromatography on silica developed with hexanes/ethyl acetate or alumina developed with toluene/acetonitrile. Analytical samples of the Os complex **19** and the Ru complex **21** were prepared by cation-exchange HPLC.

**Selective Hydrolysis of Boc-Lys-(Redox)-OCH<sub>3</sub>.** A suspension of Boc-Lys-(Redox)-OCH<sub>3</sub> (1.0 equiv) in 75% methanol was cooled to 0°C with stirring. Solid lithium hydroxide (5.0 equiv) was added and the mixture was stirred without cooling for 16 h, during which it warmed to room temperature. After the methanol was removed by rotary evaporation, the alkaline solution was acidified with 0.1 M HCl, 0.5 M H<sub>2</sub>SO<sub>4</sub> (Fe complex **28**) or 0.1 M HPF<sub>6</sub> (Os complex **20** and Ru complex **22**), and extracted with ethyl acetate or dichloromethane. The organic phase was dried over anhydrous MgSO<sub>4</sub> and freed of solvent to provide the free acid, Boc-Lys-(Redox)-OH.

**N<sup>α</sup>-(1,1-Dimethylethoxycarbonyl)-N<sup>ε</sup>-(bis(2,2'-bipyridine)(4'-methyl-2,2'-bipyridine-4-carbonyl)osmium(II))-L-lysine Methyl Ester Bis(hexafluorophosphate), **19**:** mp 150-153 °C; UV-VIS (CH<sub>3</sub>CN) λ (ε) 248 (17,800), 292 (47,500), 374 (5,100), and 488 nm (6,700 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (400 MHz, CD<sub>3</sub>CN) δ 1.37 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.30-1.45 (m, 4 H, C<sup>β</sup>H<sub>2</sub> & C<sup>δ</sup>H<sub>2</sub>), 1.64 (m, 2 H, C<sup>γ</sup>H<sub>2</sub>), 2.66 (s, 3 H, mCH<sub>3</sub>), 3.39 (m, 2 H, C<sup>ε</sup>H<sub>2</sub>), 3.62 (s, 3 H, OCH<sub>3</sub>), 4.05 (m, 1 H, C<sup>α</sup>H), 7.19 (d *J*<sub>5',6'</sub> = 6.0 Hz, 1 H, m5'), 7.25-7.36 (m, 4 H, 4 × b5), 7.44 (d *J*<sub>5,6</sub> = 7.6 Hz, 1 H, m5), 7.49-7.64 (m, 6 H, 4 × b6 & m6' & N<sup>α</sup>H), 7.75 (d *J*<sub>5,6</sub> = 6.0 Hz, 1 H, m6), 7.80-7.91 (m, 5 H, 4 × b4 & N<sup>ε</sup>H), 8.42-8.53 (m, 4 H, 4 × b3), 8.75 (br s, 1 H, m3'), and 8.85 ppm (br s, 1 H, m3); anal. (calcd for the monohydrate C 41.70, H 4.00, N 9.47) found C 41.66, H 4.01, N 9.47.

**N<sup>α</sup>-(1,1-Dimethylethoxycarbonyl)-N<sup>ε</sup>-(bis(2,2'-bipyridine)(4'-methyl-2,2'-bipyridine-4-carbonyl)osmium(II))-L-lysine Bis(hexafluorophosphate), **20**:** mp 260 °C dec; UV-VIS (CH<sub>3</sub>CN) λ (ε) 248 (13,900), 292 (36,000), 374 (4,500), and 488 nm (6,700 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR ((CD<sub>3</sub>)<sub>2</sub>CO) δ 1.36 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.32-1.45 (m, 6 H, C<sup>β</sup>H<sub>2</sub>-C<sup>γ</sup>H<sub>2</sub>-C<sup>δ</sup>H<sub>2</sub>), 2.60 (s, 3 H, mCH<sub>3</sub>), 3.40 (m, 2 H, C<sup>ε</sup>H<sub>2</sub>), 4.00 (m, 1 H, C<sup>α</sup>H), 7.20 (m, 1 H, m5'), 7.23-7.37 (m, 4 H, 4 × b5), 7.52 (d *J*<sub>5,6</sub> = 6.0 Hz, 1 H, m5), 7.49-7.64 (m, 6 H, 4 × b6 & m6' & N<sup>α</sup>H), 7.74 (d *J*<sub>5,6</sub> = 5.8 Hz, 1 H, m6), 7.79-7.99 (m, 5 H, 4 × b4 & N<sup>ε</sup>H), 8.48-8.51 (m, 4 H, 4 × b3), 8.55 (br s, 1 H, m3'), and 8.85 ppm (br s, 1 H, m3); anal. (calcd for the monohydrate C 41.81, H 3.84, N 9.07) found C 41.58, H 3.94, N 9.37.

**N<sup>α</sup>-(1,1-Dimethylethoxycarbonyl)-N<sup>ε</sup>-(anthracene-9-carbonyl)-L-lysine Methyl Ester, **23**:** mp 130.0-132.0 °C; UV-VIS (CH<sub>3</sub>CN) λ (ε) 220 (35,100), 252 (178,200), 330 (11,400), 344 (15,800), 362 (19,800), and 382 nm (18,500 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO) δ 1.37 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C),

1.47 (m, 2 H, C $\gamma$ H<sub>2</sub>), 1.64 (m, 4 H, C $\beta$ H<sub>2</sub> & C $\delta$ H<sub>2</sub>), 3.44 (m, 2 H, C $\epsilon$ H<sub>2</sub>), 3.62 (m, 3 H, OCH<sub>3</sub>), 4.00 (m, 1 H, C $\alpha$ H), 7.28 (d  $J$  = 7.7 Hz, 1 H, N $\alpha$ H), 7.55 (m, 4 H, 2,3,6,7-Ant), 7.93 (d  $J_{3,4}$  =  $J_{5,6}$  = 8.1 Hz, 2 H, 4,5-Ant), 8.12 (d  $J_{1,2}$  =  $J_{7,8}$  = 8.0 Hz, 2 H, 1,8-Ant), 8.64 (s, 1 H, 10-Ant), and 8.80 ppm (m, 1 H, N $\epsilon$ H); <sup>13</sup>C NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  182.8, 173.9, 165.2, 156.3, 140.2, 137.6, 135.4, 135.2, 133.8, 133.5, 127.7, 127.5, 126.1, 78.9, 54.2, 52.4, 31.1, 29.2, 28.8, and 23.7 ppm; anal. (calcd C 69.81, H 6.94, N 6.03) found C 69.92, H 6.98, N 5.98.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\epsilon$ -(anthracene-9-carbonyl)-L-lysine, 24:** mp 186 °C dec; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  (e) 220 (17,600), 254 (134,000), 316 (3,800), 330 (5,800), 334 (9,300), 362 (12,500), and 382 nm (12,300 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  1.37 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.48-1.64 (m, 6 H, C $\beta$ H<sub>2</sub>-C $\gamma$ H<sub>2</sub>-C $\delta$ H<sub>2</sub>), 3.44 (m, 2 H, C $\epsilon$ H<sub>2</sub>), 3.88 (m, 1 H, C $\alpha$ H), 7.08 (d  $J$  = 8.1 Hz, 1 H, N $\alpha$ H), 7.53 (m, 4 H, 2,3,6,7-Ant), 7.92 (d  $J_{3,4}$  =  $J_{5,6}$  = 8.1 Hz, 2 H, 4,5-Ant), 8.11 (d  $J_{1,2}$  =  $J_{7,8}$  = 8.2 Hz, 2 H, 1,8-Ant), 8.64 (s, 1 H, 10-Ant), and 8.80 ppm (m, 1 H, N $\epsilon$ H); <sup>13</sup>C NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  183.6, 174.9, 168.7, 156.4, 134.2, 131.4, 129.0, 127.9, 127.7, 127.1, 126.2, 125.9, 78.7, 54.3, 31.2, 29.4, 28.9, and 24.1 ppm; anal. (calcd C 69.31, H 6.71, N 6.22) found C 69.14, H 6.74, N 6.20.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\epsilon$ -(9,10-dihydro-9,10-dioxoanthracene-2-carbonyl)-L-lysine Methyl Ester, 25:** mp 152.2-155.0 °C; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  (e) 210 (41,100), 256 (60,500), and 326 nm (7,500 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (200 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  1.37 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.28-1.76 (m, 6 H, C $\beta$ H<sub>2</sub>-C $\gamma$ H<sub>2</sub>-C $\delta$ H<sub>2</sub>), 3.31 (m, 2 H, C $\epsilon$ H<sub>2</sub>), 3.63 (s, 3 H, OCH<sub>3</sub>), 3.88-4.02 (m, 1 H, C $\alpha$ H), 7.28 (d  $J$  = 7.7 Hz, 1 H, N $\alpha$ H), 7.77-8.02 (m, 2 H, 6,7-Anq), 8.16-8.36 (m, 4 H, 3,4,5,8-Anq), 8.63 (s, 1 H, 1-Anq), and 8.97 ppm (t  $J$  = 5.4 Hz, 1 H, N $\epsilon$ H); <sup>13</sup>C NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  173.9, 168.7, 156.3, 137.6, 135.6, 134.2, 131.4, 129.1, 127.9, 127.8, 127.1, 126.2, 125.9, 78.9, 54.3, 52.4, 31.1, 29.4, 28.9, and 24.0 ppm; anal. (calcd C 65.58, H 6.11, N 5.67) found C 65.46, H 5.99, N 5.61.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\epsilon$ -(9,10-dihydro-9,10-dioxoanthracene-2-carbonyl)-L-lysine, 26:** mp 105 °C dec; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  (e) 256 (33,900), and 326 nm (4,800 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (200 MHz, CDCl<sub>3</sub>)  $\delta$  1.39 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.30-1.97 (m, 6 H, C $\beta$ H<sub>2</sub>-C $\gamma$ H<sub>2</sub>-C $\delta$ H<sub>2</sub>), 3.51-3.56 (m, 2 H, C $\epsilon$ H<sub>2</sub>), 4.35-4.36 (m, 1 H, C $\alpha$ H), 5.42 (d  $J$  = 7.8 Hz, 1 H, N $\alpha$ H), 7.15 (m, 1 H, N $\epsilon$ H), 7.72 (d  $J_{5,6}$  =  $J_{7,8}$  = 5.8 Hz, d  $J_{5,7}$  =  $J_{6,8}$  = 3.4 Hz, 2 H, 6,7-Anq), 8.18-8.29 (m, 4 H, 3,4,5,8-Anq), and 8.52 ppm (s, 1 H, 1-Anq); <sup>13</sup>C NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  184.1, 176.2, 166.4, 157.6, 141.2, 140.8, 136.9, 136.6, 136.4, 135.0, 134.7, 128.9, 128.8, 127, 79.9, 55.4, 32.4, 30.5, 30.1, and 25.1 ppm; anal. (calcd C 64.99, H 5.87, N 5.83) found C 65.04, H 5.89, N 5.84.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\epsilon$ -(ferrocene-1-carbonyl)-L-lysine Methyl Ester, 27:** mp 118-120 °C; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  (e) 260 (31,100), 302 (14,000), and 428 (7,300 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (250 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  1.34 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.32-1.63 (m, 6 H, C $\beta$ H<sub>2</sub>-C $\gamma$ H<sub>2</sub>-C $\delta$ H<sub>2</sub>), 3.15 (d  $J$  = 12.4 Hz, t  $J$  = 6.3 Hz, 2 H, C $\epsilon$ H<sub>2</sub>), 3.62 (s, 3 H, OCH<sub>3</sub>), 3.93 (m, 1 H, C $\alpha$ H), 4.14 (s, 5 H, C<sub>5</sub>H<sub>5</sub>), 4.32 (t  $J$  = 1.9 Hz, 2 H, 3,4-C<sub>5</sub>H<sub>4</sub>-CO), 4.77 (t  $J$  = 1.9 Hz, 2 H, 2,5-C<sub>5</sub>H<sub>4</sub>-CO), 7.23 (d  $J$  = 7.7 Hz, 1 H, N $\alpha$ H), and 7.77 ppm (t  $J$  = 5.7 Hz, 1 H, N $\epsilon$ H); <sup>13</sup>C NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  183.6, 174.0, 169.4, 156.3, 139.6, 78.8, 77.6, 70.5, 70.0, 68.8, 68.7, 54.3, 52.4, 31.0, 29.7, 28.9, and 23.6 ppm; anal. (calcd C 58.49, H 6.83, N 5.93) found C 58.33, H 6.78, N 5.89.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\epsilon$ -(ferrocene-1-carbonyl)-L-lysine, 28:** mp 90.5 °C dec; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  (e) 260 (27,300), 302 (12,000), and 428 (7,000 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (200 MHz,

(CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  1.37 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.33-1.80 (m, 6 H, C $\beta$ H<sub>2</sub>-C $\gamma$ H<sub>2</sub>-C $\delta$ H<sub>2</sub>), 3.14 (m, 2 H, C $\epsilon$ H<sub>2</sub>), 3.85 (m, 1 H, C $\alpha$ H), 4.15 (s, 5 H, C<sub>5</sub>H<sub>5</sub>), 4.33 (t  $J$  = 1.9 Hz, 2 H, 3,4-C<sub>5</sub>H<sub>4</sub>-CO), 4.77 (t  $J$  = 1.9 Hz, 2 H, 3,4-C<sub>5</sub>H<sub>4</sub>-CO), 7.06 (d  $J$  = 7.9 Hz, 1 H, N $\alpha$ H), and 7.79 ppm (t  $J$  = 5.8 Hz, 1 H, N $\epsilon$ H); <sup>13</sup>C NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  183.6, 170.1, 157.5, 139.6, 78.6, 77.6, 70.5, 70.0, 68.8, 68.7, 58.1, 29.9, and 28.9 ppm; anal. (calcd: C 57.65, H 6.60, N 6.11) found C 57.76, H 6.65, N 6.03.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\epsilon$ -(5-(10*H*-phenothiazine-10)propanoyl)-L-lysine Methyl Ester, 29:** mp 75.0-77.2 °C; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  ( $\epsilon$ ) 232 (16,200), 254 (46,500), and 308 nm (5,800 L cm<sup>-1</sup> mol<sup>-1</sup>); NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  1.37 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.22-1.47 (m, 6 H, C $\beta$ H<sub>2</sub>-C $\gamma$ H<sub>2</sub>-C $\delta$ H<sub>2</sub>), 2.54 (t  $J_{2,3}$  = 7.0 Hz, 2 H, 2'-CH<sub>2</sub>), 3.04 (m, 2 H, C $\epsilon$ H<sub>2</sub>), 3.61 (m, 3 H, OCH<sub>3</sub>), 3.89 (m, 1 H, C $\alpha$ H), 4.10 (t  $J_{2,3}$  = 7.0 Hz, 2 H, 3'-CH<sub>2</sub>), 6.89-7.26 (m, 8 H, C<sub>8</sub>H<sub>8</sub>NS), and 7.92 ppm (m, 1 H, N $\epsilon$ H); anal. (calcd C 63.14, H 6.89, N 8.18) found C 63.21, H 6.98, N 8.20.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\delta$ -(4-(dimethylamino)phenyl)-L-glutamine Methyl Ester, 31:** mp 129-130 °C; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  ( $\epsilon$ ) 276 (4,200 L cm<sup>-1</sup> mol<sup>-1</sup>), and 320 nm (sh); NMR (400 MHz, (CD<sub>3</sub>)<sub>2</sub>SO)  $\delta$  1.38 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.80 (m, 1 H, C $\beta$ H<sub>2</sub>), 2.01 (m, 1 H, C $\beta$ H<sub>2</sub>), 2.34 (t  $J$  = 7.4 Hz, 2 H, C $\gamma$ H<sub>2</sub>), 2.83 (s, 6 H, N(CH<sub>3</sub>)<sub>2</sub>), 3.63 (s, 3 H, OCH<sub>3</sub>), 3.95 (m, 1 H, C $\alpha$ H), 6.66 (d  $J_{2,3}$  =  $J_{5,6}$  = 9.1 Hz, 2 H, 3,5-C<sub>6</sub>H<sub>4</sub>), 7.32 (d  $J$  = 6.4 Hz, N $\alpha$ H), 7.39 (d  $J_{2,3}$  =  $J_{5,6}$  = 8.5 Hz, 2 H, 2,6-C<sub>6</sub>H<sub>4</sub>), and 9.7 ppm (s, 1 H, N $\delta$ H); anal. (calcd C 60.14, H 7.70, N 11.07) found C 59.95, H 7.65, N 11.06.

**N $\alpha$ -(1,1-Dimethylethoxycarbonyl)-N $\delta$ -(4-(dimethylamino)phenyl)-L-glutamine, 32:** mp 110.5 °C dec; UV-VIS (CH<sub>3</sub>CN)  $\lambda$  ( $\epsilon$ ) 276 (2,000 L cm<sup>-1</sup> mol<sup>-1</sup>), and 320 nm (sh); NMR (250 MHz, CD<sub>3</sub>CN)  $\delta$  1.40 (s, 9 H, (CH<sub>3</sub>)<sub>3</sub>C), 1.96-2.21 (m, 2 H, C $\beta$ H<sub>2</sub>), 2.34-2.46 (m, 2 H, C $\gamma$ H<sub>2</sub>), 2.88 (s, 6 H, N(CH<sub>3</sub>)<sub>2</sub>), 4.05-4.20 (m, 1 H, C $\alpha$ H), 5.86 (d  $J$  = 8.0 Hz, N $\alpha$ H), 6.76 (d  $J_{2,3}$  =  $J_{5,6}$  = 9.1 Hz, 2 H, 3,5-C<sub>6</sub>H<sub>4</sub>), 7.35 (d  $J_{2,3}$  =  $J_{5,6}$  = 9.1 Hz, 2 H, 2,6-C<sub>6</sub>H<sub>4</sub>), and 8.22 ppm (br s, 1 H, N $\delta$ H); anal. (calcd C 59.16, H 7.45, N 11.50) found C 59.05, H 7.47, N 11.46.

**H-Ala-Ala-Lys(Ptz)-Ala-Ala-Ala-Lys(Ru<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-Ala-Ala-Lys(Anq)-Ala-NH<sub>2</sub> (PF<sub>6</sub><sup>-</sup>)<sub>2</sub>, 33.** This redox-triad undecapeptide was assembled by the solid-phase method<sup>5,6</sup> using Boc-Ala, redox modules **22**, **26**, and **30**, and methylbenzhydrylamine-*copoly*-(styrene-1% divinylbenzene) beads (MBHA resin, Applied Biosystems, 0.5 mmol). The synthetic cycle of Fournier and co-workers<sup>27</sup> was used except that NMM was used for neutralization and the Boc-amino acid (4.0 equiv), BOP (2.2 equiv), HOBT (2.2 equiv), and NMM (4.2 equiv) were used for coupling. Boc-Lys(Ru<sup>II</sup>b<sub>2</sub>m)<sup>2+</sup>-OH (PF<sub>6</sub><sup>-</sup>)<sub>2</sub> (2.0 equiv) was coupled for 18 h.<sup>6</sup> After cleavage from the resin with 10:1 (v/v) HF/anisole (1 h, 4 °C), the crude peptide was purified by reversed-phase HPLC on a butyl-silica column (Vydac C<sub>4</sub>) eluted over 90 min with a linear gradient of 25-39% acetonitrile in 0.5% trifluoroacetic acid/water. The center fractions were freed of solvent to provide pure peptide **33** as an orange oil. By electrospray-ionization mass spectrometry, peptide **33** was found to have an average mass of 2065.9 Da, which agreed well with the value of 2067.2 Da calculated for the C-terminal amide derivative of AlaLys(Anq)Lys(Ptz)Lys(Rub<sub>2</sub>m)<sup>2+</sup>.

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