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Use of Ferrocene Scaffolds as Pendant Groups in Hairpin-Type Pyrrole-Imidazole Polyamide Molecules Showing Sequence-Selective Binding to DNA Duplexes

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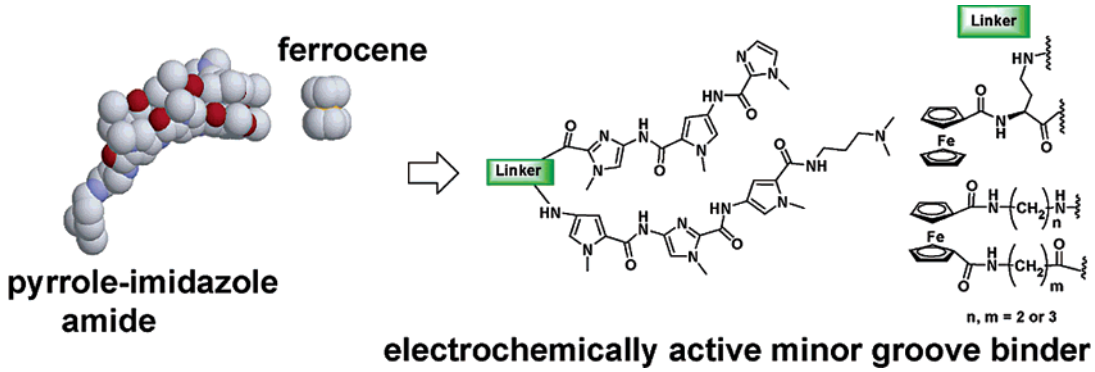
Received June 17, 2005



The synthesis and properties of new conjugate molecules, Fc-PIA, composed of ferrocene (Fc) and pyrrole-imidazole polyamides (PIA) are reported. As a PIA sequence, we chose Im-Py-Im/Py-Im-Py considering its future application to the SNPs detection of genes having a GCG/CGC sequence. Two types of Fc-containing linkers, i.e., ferrocene-1,1′-dicarboxamide and ferrocenecarboxamide, were designed, and several Fc-PIPA molecules having these linkers were synthesized. Titration studies by use of circular dichroism revealed that the carboxamide-type Fc-PIA could bind to the target DNA with an association constant of 10^7 M^{-1}. In contrast, ferrocene dicarboxamide-type compounds have slightly weaker affinity for the target DNA. However, the affinity could be recovered by replacing one of the pyrrole residues with β-alanine. We carried out the CV measurement and observed quasi-irreversible oxidation of the ferrocene moieties in the Fc-PIA compounds. These properties of Fc-PIA indicate the potential usefulness of these molecules in electrochemical detection of genes.

Introduction

Ferrocene is an organometallic compound in which an iron atom is flanked by two cyclopentadienyl (Cp) rings. The unique structural and conformational properties of ferrocene, an atomic ball bearing character[1], are characterized by the parallel alignment of the two Cp rings and the free rotation of the rings around the axis penetrating their centers. Because of such unique properties that cannot be obtained by use of simple organic molecules, ferrocene derivatives have been used as scaffolds to design new molecules that recognize various kinds of substances such as cation,[2] anion,[3] organic molecules,[4] nucleobases,[5] dinucleotides,[6] and amino acids.[7] The molecular recognition ability of these molecules together with the electrochemical properties of the ferrocene moiety has enabled the development of electrochemical molecular sensors. However, the development of DNA binding molecules utilizing the unique properties of ferrocene has so far not been reported.

In this paper, the development of new DNA binding molecules utilizing the structural and conformational

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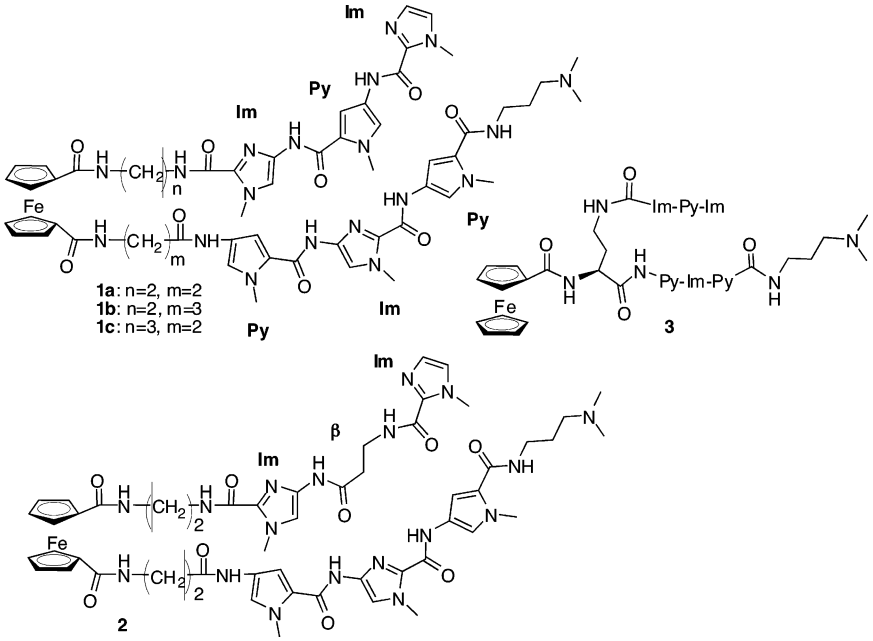
10.1021/jo051247n CCC: $30.25
Published on Web 11/08/2005

SCHEME 1. Ferrocene-Containing Minor Groove Binders Synthesized in this Study



properties of ferrocene is reported. Our design concept is based on the fact that the distance between the two Cp rings of ferrocene, ca. 3.3 Å,[8] is close to the distance between two aromatic rings stacked with each other. In addition, it is well-known that the minor groove of DNA can accommodate stacked aromatic rings, as established by the structural studies of natural or synthetic molecules that recognize the minor groove.[9] Therefore, it was expected that ferrocene derivatives could be a new type of DNA binding molecules if appropriately designed aromatic rings were attached to the Cp rings.

For this purpose we designed hybrid molecules (Fc-PIA; **1a**, **1b**, **1c**, **2**, and **3** in Scheme 1) combining ferrocene (Fc) and pyrrole-imidazole amides (PIA).[10] PIA derivatives are well recognized as molecules that can bind to the DNA minor groove as stacked dimers.[11] Therefore, PIA must be aromatic compounds of prime interest to design new ferrocene molecules having DNA binding ability. Compounds **1a**−**c** and **2** were designed by insertion of a ferrocene-1,1′-dicarboxamide moiety as part of the linker, and **3** was designed to clarify the properties of the pendant ferrocenylcarbonyl group on the amino group of the linker. In both types of compounds, strong affinity for DNA was expected because of the similarity in the whole structure between Fc-PIA and hairpin PIA.[12]

In addition to such DNA binding properties, the electrochemical properties of ferrocene can be utilized in the electrochemical detection of DNA hybridization.[13] There have been reported a number of strategies to detect DNA hybridization electrochemically. In most systems the target DNAs are hybridized to probe DNAs attached to an electrode, and the hybridization is detected by the electric current from electrochemical dyes covalently[14] or noncovalently[15] attached to the target−probe duplexes. The dyes used in the latter strategy included intercalators,[15a−d] minor groove binder,[15e,f] and other compounds that interact with DNA through electrostatic interactions.[15g,h] Among them, duplex-specific ligands have been sought and designed by several research

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groups. For example, duplex-specific threading-intercalators[15a−c] and an electrochemically active minor groove binder, Heochst 33258, were reported.[15e,f]

Because our Fc-PIAs are expected to bind to duplex DNA more tightly than single-stranded DNA, they could be new duplex-specific electrochemical dyes. Keeping such future applications in mind, the synthesis, DNA binding properties, and electrochemical properties of the Fc-PIA compounds are reported in this article.

Results and Discussion

Selection of Target Sequence. In this study, we chose a CGC/GCG triplet as the target sequence. Recently, it has been proposed that the CGC to CTC mutation in the promoter region of MxA gene could influence the response to interferon therapy for patients infected by the hepatitis C virus.[16] Therefore, rapid and accurate detection of the G/T SNP in the CXC sequence must be clinically important in the diagnosis of HCV infected patients.

Unfortunately, it is well-known that hairpin PIA binds to the CGC sequence with rather low affinity.[17] Therefore, the compounds targeting CGC sequences must be designed carefully to maintain the DNA binding affinity.

In this study, we used a DNA 11 mer, GACTGCGTAGG, as a model target in place of the GC-rich MxA promoter sequence and designed compounds **1a**, **1b**, **1c**, **2**, and **3**. Particularly, compound **2** was designed to increase the affinity of PIA for the GCG sequence by introduction of a β-alanine residue in place of a pyrrole residue.[18]

Can Ferrocene Moiety Fit the Minor Groove of DNA? Because ferrocene is a hydrophobic compound, the ferrocene moiety of Fc-PIAs **1a**−**c**, **2**, and **3** should be buried in the minor groove to avoid exposure to the bulk water on binding to the target DNA duplex. A number of molecular structures of ferrocene derivatives have been well characterized, and the typical distance between the two Cp rings has been proved to be approximately 3.3 Å,[8] which is close to the typical distance of two aromatic rings in parallel-stacking geometry. Because PIA can bind to the DNA minor groove as a stacked dimer, it is expected that the ferrocene moiety of Fc-PIA can fit the minor groove when they bind to the DNA duplex in a conformation similar to that of the conventional PIA dimers.

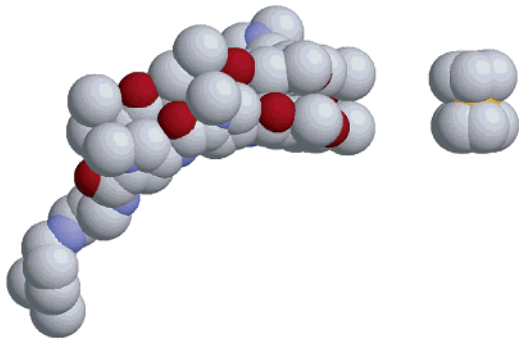

FIGURE 1. Comparison of the molecular structure and the size of a stacked dimer of a PIA (left) and ferrocene (right).

The idea is illustrated graphically by computer graphics, as shown in Figure 1. The structure of a PIA dimer extracted from a PIA-DNA complex[19] (PDB 408D) and a ferrocene residue extracted from the complex of a ferrocene dicarboxylic acid derivative and an antibody (PDB 1A3L)[20] was used. As shown in Figure 1, it is indicated that the thickness of the ferrocene and the stacked PIA dimer is almost identical so that they can bind to the minor groove together. This molecular model indicates that Fc-PIA could bind to the minor groove without severe structural distortion. Moreover, because the Cp rings can rotate almost freely, the important hydrogen bonds between the nucleobases and the PIA moiety could be maintained even if some structural perturbation exits. On the basis of these structural considerations, we tried to synthesize **1a**−**c**, **2**, and **3**.

Synthesis of Pyrrole-Imidazole Polyamides 10, 16, and 21. The synthesis of the upper-half pyrrole-imidazole triamide (Im-Py-Im in Scheme 1) was performed by use of pyrrole and imidazole building blocks **4**,[21] **5**,[22] **8**,[21] and **11**[22] (Scheme 2). The nitro group of **4** was converted to an amino group by hydrogenolysis, and the amino derivative was coupled with **5** to give **6**[23] in 78% yield. The hydrolysis of **6** followed by coupling with the 3-aminoimidazole derivative **8** gave the trimer **9**. Compound **9** thus obtained was hydrolyzed to give compound **10**.

Next, we synthesized the lower-half pyrrole-imidazole triamide (Py-Im-Py in Scheme 1), as shown in Scheme 3. The pyrrole derivative **11** was condensed with *N*,*N*-dimethyl-1,3-propanediamine to give **12**. The hydrogenolysis of **12** followed by reaction with the 1-(trichloroacetyl)imidazole derivative **13** gave the dimer **14**. Finally, the hydrogenolysis of **14** and the successive

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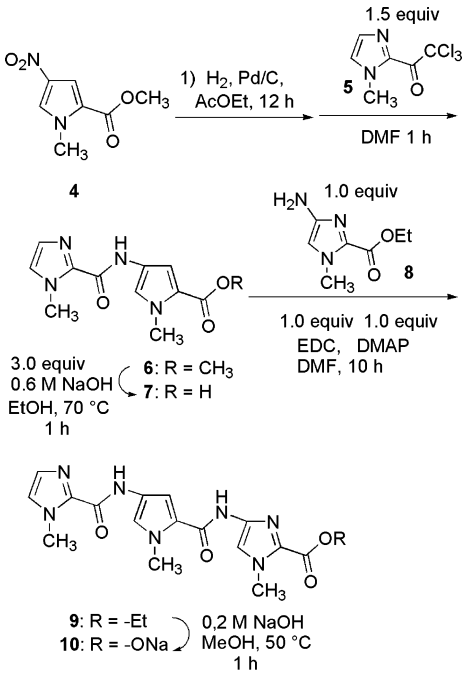
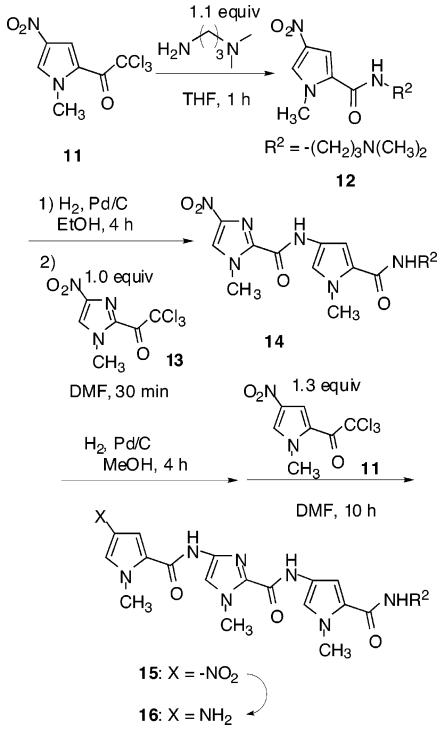
SCHEME 2



SCHEME 3



condensation with **11** gave the trimer **15**, which could be further converted to the amino derivative **16** by hydrogenolysis before the next reaction.

To synthesize an Fc-PIA derivative containing a β-alanine residue **2**, the triamide **20** was synthesized, as shown in Scheme 4. The pyrrole derivative **17**[21] was converted to the amino derivative by hydrogenolysis, and the following condensation with β-*N*-*t*-Boc-alanine gave the diamide **18**. After removal of the *t*-Boc group of **18**, the amino group was condensed with compound **5** to give the triamide **19** in 63% yield from **18**. Successively, the ethyl ester of **19** was hydrolyzed, and the resulting carboxylic acid was converted to the pentafluorophenyl ester **20** in 96% yield from **19**.

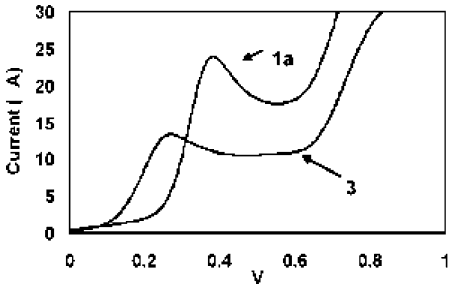


FIGURE 2. Anodic currents of CV profiles of Fc-PIA **1a** and **3** in DMF.

Synthesis of Fc-PIAs 1a−c. The ferrocene-1,1′-dicarboxylamide linkers **24a−c** were synthesized, as shown in Scheme 5. The monoester **21**[24] was condensed with the protected ethylenediamine and propylenediamine derivatives to give **22a** and **22b**, respectively. The methyl esters of **22a** and **22b** were hydrolyzed and then condensed with the ethyl esters of glycine or β-alanine to give compounds **23a**, **23b**, and **23c**, which could be converted to the ferrocene-dicarboxamide linkers **24a**, **24b**, and **24c**.

The synthesis of Fc-PIAs **1a**, **1b**, **1c**, and **2** was performed according to Scheme 6. Pyrrole-imidazole polyamide **15**, which was synthesized as described in Scheme 3, was converted to the amino derivative **16** by hydrogenolysis. The amine thus obtained was coupled with ferrocene-1,1′-decarboxamide linkers **24a**, **24b**, and **24c** to give the ferrocene-polyamide derivatives **25a**, **25b**, and **25c**, respectively. The *t*-Boc groups of **24a−c** were removed by acid treatment to give the amino derivatives **26a**, **26b**, and **26c**, which were further condensed with pyrrole-imidazole polyamide **10** to give the desired products **1a**, **1b**, and **1c**. Similarly, Fc-PIA **2** was synthesized by the condensation of **20** with **26a**.

Synthesis of PIA-Ferrocene Hybrid 3. Fc-PIA **3** was synthesized as shown in Scheme 7. The triamide **15** was subjected to hydrogenolysis followed by condensation with the commercially available diaminocarboxylic acid derivative **27**. During the reaction, partial cleavage of the fmoc group occurred probably due to the intramolecular attack by the dimethylaminopropyl group. Therefore, we isolated the product as **28** after the complete removal of the fmoc group by treatment with piperidine. The amino group of **28** was condensed with the triamide **10** to give the hairpin PIA **29**. Then, the *t*-Boc group of **29** was removed by treatment with 20% TFA, and the released amino group was coupled with ferrocene carboxylic acid derivative to give the desired product **3**.

Electrochemical Properties of Fc-PIAs. The electrochemical properties of Fc-PIA **1a**, **1b**, **1c**, **2**, and **3** were examined by use of cyclic voltammetry (CV). Shown in Figure 2 are the CV profiles of the Fc-PIA **1a** and **3** measured in DMF. In these cases, the electrochemical reactions were quasi-irreversible, giving rather large anodic currents of ferrocene and PIA. In contrast, the cathodic currents were much smaller than the corresponding anodic currents and are not shown in Figure 2.

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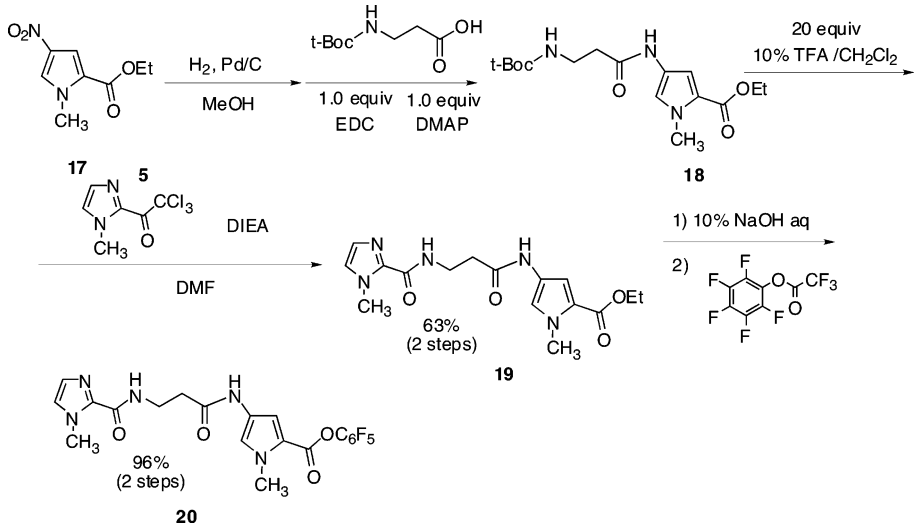
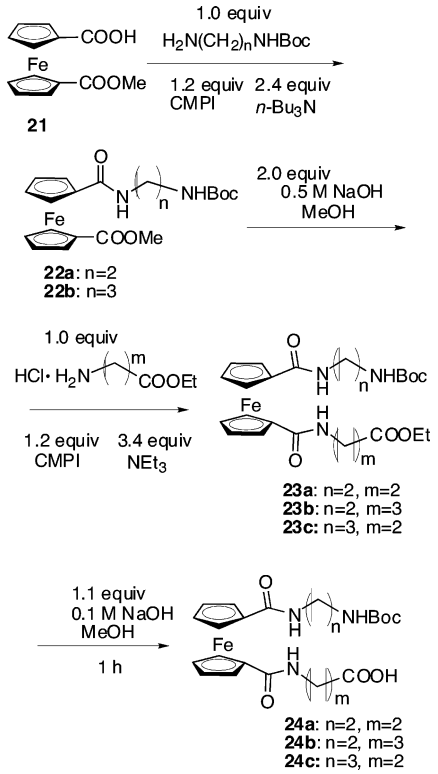
SCHEME 4



SCHEME 5



The anodic peak currents of the ferrocene moieties in **1a** and **3** were observed at around 0.38 and 0.24 V, respectively. The positions of the anodic peaks shifted to higher potentials than that of ferrocene (0.08 V) because of the presence of the electron-withdrawing carbonyl groups on the cyclopentadienyl rings. In the case of **1b**, **1c**, and **2**, the electrochemical behavior was similar to that of **1a** (data not shown). These results indicated that the electrochemical properties of the Fc-PIAs were dominated by the number of the carbonyl groups directly attached to the ferrocene moieties.

Binding of Ferrocene-PIAs (1a−c, 2, and 3) to Cognate DNA Duplexes. The binding of Fc-PIAs to DNA duplexes was studied by use of circular dichroism (CD) spectroscopy. Two DNA duplexes named **DNA1** (GACTGCGTAGG/CTGACGCATCC) and **DNA2** (GACTGAGTAGG/CTGACTCATCC) were prepared to study the DNA binding affinity of the Fc-PIAs and their difference

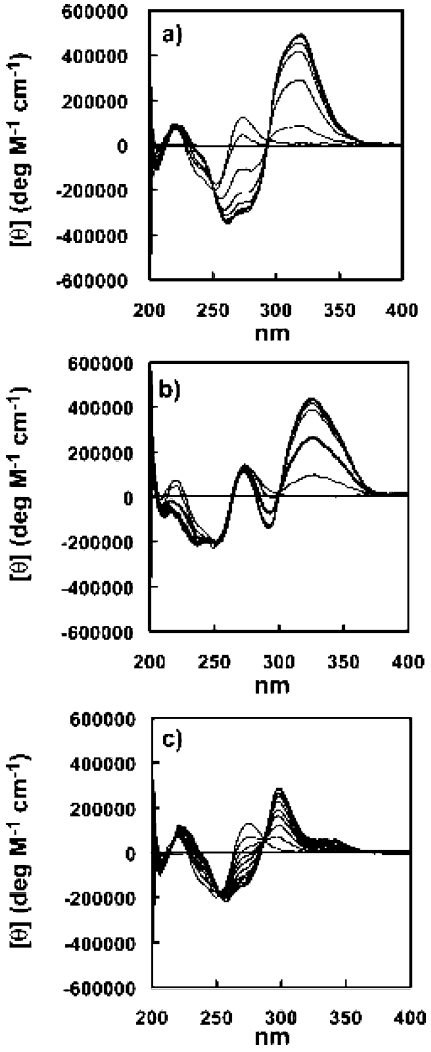
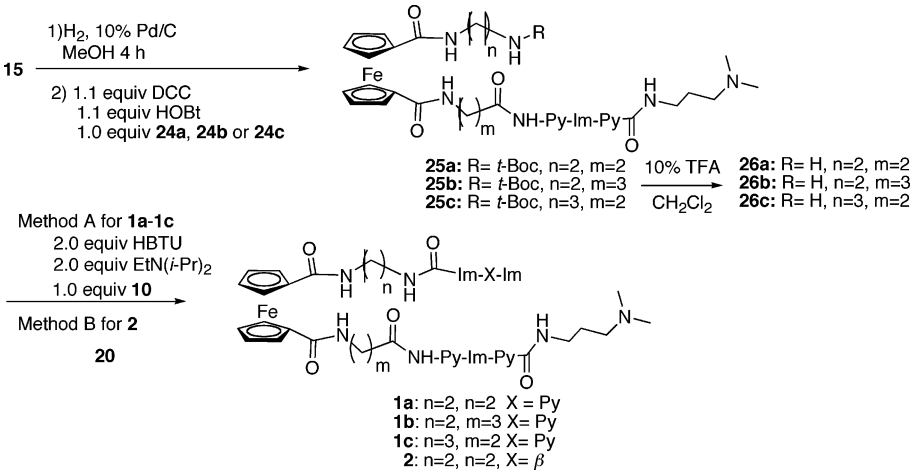
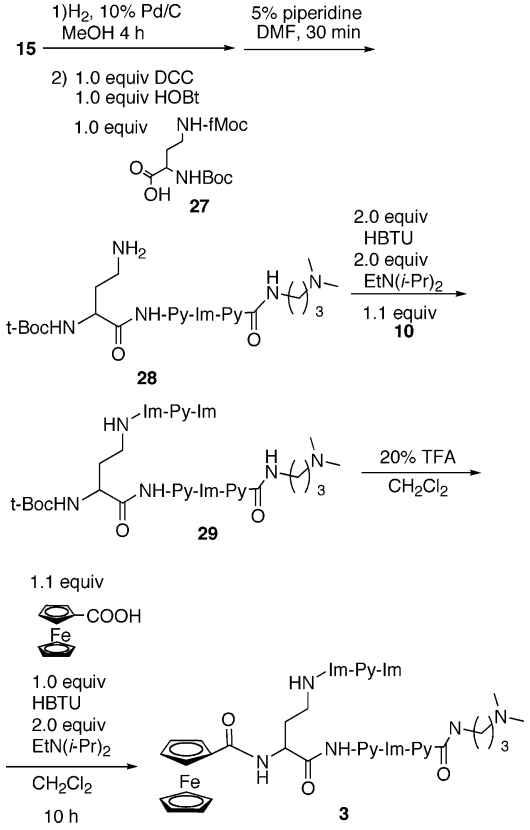


FIGURE 3. Titration of **DNA1** (5 μM) by (a) **1a** (0−1.8 equiv), (b) **3** (0−1.6 equiv), and (c) **2** (0−2.0 equiv).

SCHEME 6



SCHEME 7



in sequence selectivity between the cognate GCG/CGC and noncognate GAG/CTC sequences.

Initially, the binding properties of Fc-PIAs **1a**, **2**, and **3** were studied to clarify the influence of the linker structures and the insertion of β-alanine on their DNA-binding properties. Shown in Figure 3 are the CD-titration profiles of DNA duplexes **DNA1**. It is well-known that the binding of minor groove binders to DNA duplexes can be monitored by the positive Cotton effect at around 300−330 nm.[25] As shown in Figure 3a, addition of **1a** to a solution of **DNA1** showed dose-dependent increase of the Cotton effect in this range. The positive Cotton effect increases until the ratio of the cognate double strand DNA duplex (cog-dsDNA):**1a** reaches 1:1.8. Addition of **1a** beyond 1:1.8 stoichiometry did not lead to further increase of the peak intensity. Similarly, both Fc-PIAs **2** and **3** gave similar titration profiles showing saturation at 1:1.4 stoichiometry. In all these cases, single-binding modes are indicated by the presence of isosbestic points before the saturation is reached.

Next, we carried out the same CD titration experiments of the binding of **1b** and **1c** to **DNA1** (data not shown). In both cases, the titration was saturated at 1:3.4 stoichiometry of DNA and ligands. These results indicated that **1b** and **1c** have affinities for the DNA duplex lower than that of **1a**.

To compare the affinity of **1a**−**c** and **3** for the DNA duplex more quantitatively, the binding constants were estimated by fitting the theoretical titration curve and the experimental curves plotting the maximum Cotton effect vs concentration of the Fc-PIAs. The results are shown in Table 1. Compounds **3** and **2** gave the largest and the second largest binding constants of ca. 10^7 (M^{-1}), respectively. In both cases, the least-squares fit associated with correlation factors (R) of >0.989 supported the validity of the assumption of the formation of 1:1 complexes of the DNA target and Fc-PIA compounds **2** and **3**. In contrast, compound **1a**, which is a derivative of **2** having a pyrrole residue in place of the β-alanine residue, showed slightly weaker affinity compared with **2**. This observation clearly suggested that introduction of the β-alanine residue can improve the affinity of Fc-PIAs for the GC-rich sequence as described in the case of the original PIAs that were developed by Dervan P. et al. On the other hand, the same curve fitting and correlation analyses revealed that the titration by **1b** and **1c** gave a much smaller binding constant of ca. 1×10^6 probably because the linker length of these compounds was not optimal for the DNA binding.

Binding of Ferrocene-PIA Hybrids (1a, 2, and 3) to Noncognate DNA Duplex. On the basis of the above-mentioned binding properties of **1a**, **2**, and **3** to the cognate sequence, we examined the binding of Fc-PIAs **1a**, **2**, and **3** to the DNA duplex **DNA2** having a noncognate sequence. The results are shown in Figure

(25) (a) Pilch, D. S.; Poklar, N.; Baird, E. E.; Dervan, P. B.; Breslauer, K. J. *Biochemistry* **1999**, *38*, 2143−2151. (b) Pilch, D. S.; Poklar, N.; Gelfand, C. A.; Law, S. M.; Beslauer, K. J.; Baird, E. E. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 8306−8311.

TABLE 1. Binding Constants (K, M^{-1}) of Fc-PIA and Cognate DNA1

1a	1b	1c	2	3
$(7.4 \pm 1.1) \times 10^6$	$(1.3 \pm 0.2) \times 10^6$	$(1.5 \pm 0.2) \times 10^6$	$(1.4 \pm 0.6) \times 10^7$	$(2.3 \pm 0.8) \times 10^7$

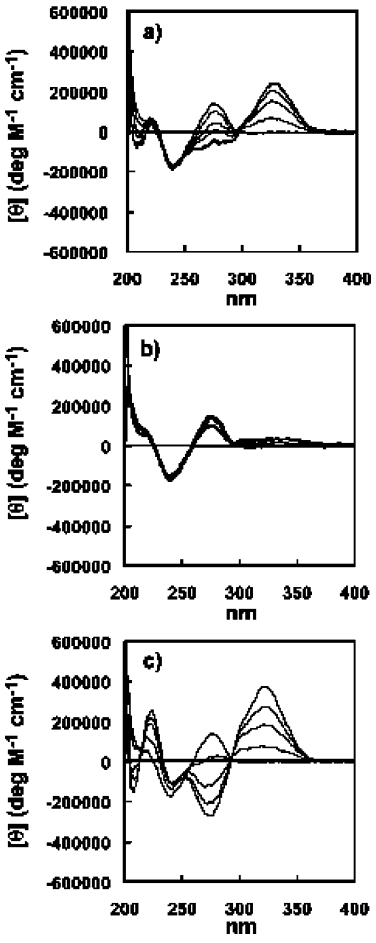


FIGURE 4. Titration of **DNA2** (5 μM) by (a) **1a** (0, 1, 2, 3, and 6 equiv), (b) **3** (0, 0.4, 0.8, and 2 equiv), and (c) **2** (0, 2, 4, 6, and 10 equiv).

4. Titration of **DNA2** with Fc-PIA **1a** showed increase of the positive Cotton effect at 315 nm until the stoichiometry of **DNA2**:**1a** approached 1:6.0. It should be noted that the magnitude of the induced CD signals was much smaller than that observed in the combination of **DNA1** and **1a**. The requirement of the high DNA to drug ratio for the saturation of the titration suggested the lower affinity of **1a** for the noncognate sequence.

Unfortunately, the quantitative binding constants of **1a** to the noncognate **DNA2** could not be determined because the peaks started to decrease on the addition of higher amounts of **1a** beyond 6 equiv. This phenomenon indicated the involvement of several binding modes having lower affinity at the higher concentration of **1a**.

On the other hand, compound **3** showed only small changes even after 1:2.0 stoichiometry had been reached. This small change in the spectra indicates the weak binding of **3** to the noncognate **DNA2**. As in the case of **1a**, the addition of higher amounts of **3** beyond 2.0 equiv led to decrease of the signals at around 330 nm to give a negative peak in this range.

Similarly, **2** showed only a small increase of the Cotton effect at around 330 nm before the 1:2.0 stoichiometry was reached. However, in this case, the further addition of **3** increased the Cotton effect almost linearly to the ligand concentration even after 10 equiv of **3** had been added.

From these observations, it is suggested that all of the Fc-PIAs **1a**, **2**, and **3** bind more strongly to the cognate **DNA1** than to the noncognate **DNA2**. In addition, it was also suggested **1a** and **3** and/or **2** bind to the noncognate **DNA2** in several binding modes at the higher concentrations.

Conclusion

There have been numerous studies on the use of ferrocene scaffolds to design molecules that recognize other chemical substances. We reported the synthesis and properties of new conjugate molecules (Fc-PIA), **1a**–**c**, **2**, and **3**, having ferrocene and pyrrole-imidazole polyamides (PIA). To our best knowledge, it is the first example of the development of DNA minor groove binders by use of the structural properties of ferrocene, i.e., the parallel alignment of the two Cp rings displaced by ca. 3.3 Å and the free rotation of the rings around the axis penetrating them. In addition, we also synthesized **3** to clarify the compatibility between the conventional hairpin PIA and the ferrocene moiety. As expected from the comparison between the minor groove width and the molecular size of ferrocene, the insertion of a ferrocene moiety did not interfere with the binding of the minor groove binder to target DNA duplex. Therefore, it must be possible to design new minor groove binders by the combination of various heteroaromatic compounds, other than pyrrole-imidazole amides, and ferrocene-type scaffolds.

The affinity of the Fc-PIA for the target DNA containing a CGC/GCG site depends on the linker structure that linked the ferrocene to PIA moieties. The CD titration studies revealed that **3** having a ferrocene carboxamide showed the strongest binding to the target DNA. Although the affinity of ferrocene-1,1′-dicarboxamide compounds **1a**–**c** was slightly lower, the affinity could be recovered by replacement of the pyrrole moiety by a β-alanine moiety as in the case of **1a** and **2**. Because the insertion of the β-alanine moiety was proved to be effective to improve the affinity of the original pyrrole-imidazole polyamide for GC-rich sequences, these observations suggest that the Fc-PIAs synthesized in this study recognize DNA in a similar way as do the original hairpin pyrrole-imidazole polyamides. It should be noted that similar CD titration experiments revealed that these Fc-PIA also had sequence selectivity in the binding to DNA duplexes.

The electrochemical properties of the ferrocene moiety in the Fc-PIA were also studied by cyclic voltammetry (CV). The CV studies in *N*,*N*-dimethylformamide revealed the irreversible oxidation of the ferrocene moiety at around 0.38 and 0.24 V for **1a** and **3**, respectively.

These strong DNA binding, sequence selectivity and electrochemical properties of Fc-PIA must be useful for the electrochemical detection of DNAs. Particularly, the ferrocene amide-type compound **3** should be a prototype of such a ligand because of its high affinity for duplex DNAs, low affinity for noncognate DNAs, and lower redox potential. The development of an electrochemical gene detection system by use of Fc-PIA is under way and will be reported elsewhere.

Experimental Section

1-Methyl-4-(1-methylimidazole-2-carboxamido)pyrrole-2-carboxylic Acid (7). Compound **6** (8.8 g, 34 mmol) was dissolved in ethanol (230 mL). To this solution was added 0.6 M aqueous NaOH (168 mL, 101 mmol), and the resulting solution was stirred at 70 °C for 1 h. The solution was cooled to ambient temperature and adjusted to pH 3.0 by addition of 3 M aqueous HCl. The resulting white precipitates were collected by filtration to give **7** (8.1 g, 97%): ^{1}H NMR (DMSO-d_6) δ 3.82 (3H, s), 3.97 (3H, s), 6.97 (1H, d, J = 2.0 Hz), 7.03 (1H, s), 7.38 (1H, s), 7.47 (1H, d, J = 2.0 Hz), 10.48 (1H, s), 12.19 (1H, s); ^{13}C NMR (DMSO-d_6) δ 35.3, 36.4, 109.1, 119.9, 120.7, 122.1, 126.6, 127.2, 138.8, 156.3, 162.1. Anal. Calcd for $C_{11}H_{12}N_4O_3$: C, 53.22; H, 4.89; N, 22.57. Found: C, 52.45; H, 4.72; N, 22.34.

2-Ethoxycarbonyl-1-methyl-4-{4-(1-methylimidazole-2-carboxamido)-1-methypyrrole-2-carboxamido)imidazole (9). 10% Pd/C (1.2 g) was added to a solution of 2-ethoxycarbonyl-1-methyl-4-nitroimidazole (4.7 g, 23.6 mmol) in methanol (94 mL). The suspension was stirred for 4 h under hydrogen atmosphere where a balloon filled with hydrogen gas was attached to a reaction vessel. The catalysts were removed by filtration, and the solvent was removed under reduced pressure. The residual methanol was removed by coevaporation with DMF, and the residue was finally dissolved in DMF (10 mL). To this solution were added **7** (5.9 g, 24 mmol), *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide (9.1 g, 47 mmol), and 4-dimethylaminopyridine (290 mg, 2.4 mmol). The resulting solution was stirred at ambient temperature for 10 h. Chloroform/ethyl acetate (15 mL/100 mL) was added to the reaction mixture, and the white powder was collected by filtration and washed with ethyl acetate to give **9** (5.9 g, 63%): ^{1}H NMR(DMSO-d_6) δ 1.28−1.30 (3H, t, J = 7.1 Hz), 3.85 (3H, s), 3.93 (3H, s), 3.98 (3H, s), 4.25−4.29 (2H, dd, J = 7.1 Hz), 7.03 (1H, d, J = 0.7 Hz), 7.22 (1H, d, J = 2.0 Hz), 7.38 (1H, s), 7.38(1H, s), 7.66 (1H, s), 10.35 (1H, s), 10.74 (1H, s); ^{13}C NMR (DMSO-d_6) δ 14.3, 35.3, 35.7, 36.5, 60.8, 106.4, 115.6, 119.8, 121.6, 122.2, 126.5, 127.2, 131.0, 138.0, 139.0, 156.3, 158.7, 158.9. Anal. Calcd for $C_{18}H_{12}N_4O_3 \cdot H_2O$: C, 53.22; H,4.89; N,22.57. Found: C, 50.88; H,4.88; N,23.13.

Sodium 1-Methyl-4-{4-(1-methylimidazole-2-carboxamido)-1-methypyrrole-2-carboxamido}imidazole-2-carboxylate (10). To a solution of compound **9** (3.0 g, 7.5 mmol) in methanol (38 mL) was added 0.2 M aqueous sodium hydroxide (38 mL, 7.6 mmol). The resulting solution was stirred for 1 h at 50 °C. The solution was cooled to ambient temperature and then acidified to pH 2.0 by addition of 1 M aqueous HCl. The product was separated by addition of 2-propanol. The resulting white precipitates were colleted by filtration and washed with 2-propanol to give **10** (2.9 g, 94%): ^{1}H NMR (DMSO-d_6) δ 3.86 (3H, s), 3.92 (3H, s), 4.01 (3H, s), 7.23 (1H, s), 7.25 (1H, s), 7.40 (1H, s), 7.52 (1H, s), 7.61 (1H, s), 10.70 (1H, s), 10.71 (1H, s); ^{13}C NMR (DMSO-d_6) δ 25.6, 35.7, 36.5, 106.2, 115.3, 119.9, 121.3, 122.4, 125.1, 126.6, 131.9, 137.3, 138.1, 154.7, 158.8, 160.1. MS *m/z* calcd for $C_{16}H_{18}N_7O_4^+$ 372.14203, found 394.11781 $[M + Na]^+$.

2-(3-Dimethylaminopropyl)aminocarbonyl-1-methyl-4-nitropyrrole (12). A solution of 3-dimethylaminopropylamine(12.6 g, 101 mmol) in THF (10 mL) was added dropwise to a stirred solution of compound **11** (25 g, 92 mmol) at 0 °C. The reaction mixture was warmed to room temperature, and stirring was continued for 1 h. The solvent was removed in vacuo, and the residual solid was recrystallized from ethanol to give compound **12** (19.6 g, 84%): ^{1}HNMR (DMSO-d_6) δ 1.6 (2H, t, J = 7.1 Hz), 2.1 (6H, s), 2.2 (2H, t, J = 7.1 Hz), 3.2 (2H, q, J = 7.1 Hz), 3.9 (3H, s), 7.9 (1H, s), 8.1 (1H, s), 8.4 (1H, t, J = 5.5 Hz); ^{13}CNMR (DMSO-d_6) δ 27.2, 37.2, 37.5, 45.4, 56.9, 107.3, 126.7, 127.9, 133.9, 159.9. MS *m/z* calcd for $C_{11}H_{19}N_4O_3^+$ 255.14572, found 255.13045 $[M + H]^+$.

1-Methyl-4-(1-methyl-4-nitroimidazole-2-carboxamido)-2-(3-dimethyl(aminopropyl)aminocarbonyl)pyrrole (14). Compound **12** (2.8 g, 10.9 mmol) was dissolved in ethanol (44 mL), and to this solution was added 10% Pd/C (545 mg). A balloon of hydrogen gas was attached, and the suspension was stirred under hydrogen atmosphere for 4 h at ambient temperature. The catalysts were removed by filtration, and the solvent was removed under reduced pressure. The residue was dissolved in DMF (10 mL) and concentrated to half of its original volume under reduced pressure to remove methanol completely. A solution of compound **13** (3.0 g, 10.9 mmol) in DMF (10 mL) was added with stirred at 0 °C. The temperature was allowed to rise to ambient temperature. The solvent was removed in vacuo. The resultant crystalline solid was collected and washed with 2-propanol to give compound **14** (3.68 g, 90%): ^{1}H NMR (DMSO-d_6) δ 1.6 (2H,t, J = 7.1 Hz), 2.1 (6H, s), 2.2 (2H, t, J = 7.1 Hz), 3.2 (2H, m), 3.8 (3H, s), 4.0 (3H, s), 7.0 (1H, d, J = 1.7 Hz), 7.3 (1H, d, J = 1.7 Hz), 8.1 (1H, t, J = 5.5 Hz), 8.6 (1H, s), 10.8 (1H, s); ^{13}C NMR (DMSO-d_6) δ 27.2, 36.2, 36.7, 37.4, 39.2, 45.4, 57.4, 104.5, 118.6, 121.1, 123.6, 126.8, 138.1, 144.5, 154.8, 161.2. MS *m/z* calcd for $C_{16}H_{24}N_7O_4^+$ 378.18898, found 378.18801 $[M + H]^+$.

1-Methyl-4-{1-methyl-4-(1-methyl-4-nitropyrole-2-carboxamido)imidazole-2-carboxamido}-2-(3-dimethyl(aminopropyl)aminocarbonyl)pyrrole (15). Compound **14** (3.6 g, 9.6 mmol) was dissolved in methanol (38 mL), and to this solution was added 10% Pd/C (481 mg). A balloon of hydrogen gas was attached, and the suspension was stirred under hydrogen atmosphere for 4 h at ambient temperature. The catalysts were removed by filtration, and the solvent was removed under reduced pressure. The residue was dissolved in DMF (10 mL) and concentrated to half of its original volume under reduced pressure to remove methanol completely. A solution of compound **11** (2.6 g, 9.6 mmol) in DMF (10 mL) was added with stirring at 0 °C. The temperature was allowed to rise to ambient temperature. The solvent was removed in vacuo. The resultant crystalline solid was collected and washed with 2-propanol to give compound **15** (3.5 g, 74%): ^{1}H NMR (DMSO-d_6) δ 1.58−1.62 (2H, t, J = 6.9 Hz), 2.1 (6H, s), 2.23−2.25 (2H, t, J = 6.9 Hz), 3.17−3.21 (2H, m), 3.81 (3H, s), 3.97 (3H, s), 3.98 (3H, s), 6.89 (1H, d, J = 1.7 Hz), 7.23 (1H, d, J = 1.5 Hz), 7.58 (1H, s), 7.76 (1H, d, J = 2.0 Hz), 8.11−8.14 (1H, t, J = 5.4 Hz), 8.21 (1H, s), 9.97 (1H, s), 10.82 (1H, s); ^{13}C NMR (DMSO-d_6) δ 27.3, 35.2, 36.3, 37.4, 37.9, 45.4, 57.4, 104.1, 108.8, 115.2, 118.1, 121.3, 123.6, 125.6, 128.9, 134.1, 134.7, 135.7, 155.9, 157.7, 161.2. MS *m/z* calcd for $C_{22}H_{30}N_9O_5^+$ 500.23699, found 500.23755 $[M + H]^+$.

2-Ethoxycarbonyl-1-methyl-4-{3-(*tert*-butoxycarbonylamino)propanamido}pyrrole (18). Compound **17** (546 mg, 2.7 mmol) was dissolved in methanol (11 mL), and to this solution was added 10% Pd/C (137 mg). A balloon of hydrogen gas was attached, and the suspension was stirred under hydrogen atmosphere for 1.5 h at ambient temperature. The catalysts were removed by filtration, and the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and *N*-(*tert*-butoxycarbonyl)-β-alanine (518 mg, 2.7 mmol), 1-(3-dimethylaminopropyl)-3-etylcarbodiimide hydrochloride (578 mg, 3.0 mmol), and 1-hydoxybenzotriazol (407 mg, 3.0 mmol) were added. The mixture was stirred at ambient temperature for 2 h. The mixture was extracted with ethyl acetate (50 mL), washed with water (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (11 g, hexane-

chloroform, 100: 20, v/v) to give **18** (510 mg, 56%): ^{1}H NMR (DMSO-d_6) δ 1.27−1.30 (t, J = 7.2 Hz), 1.36 (9H, s), 2.40−2.43 (2H, t, J = 7.2 Hz), 0.3.16−3.20 (2H, m), 3.90 (3H, s), 4.23−4.28 (2H, q, J = 7.1 Hz), 6.78 (1H, m), 7.51 (1H, s), 10.6 (1H, s); ^{13}C NMR (DMSO-d_6) δ 14.3, 28.4, 35.6, 35.8, 36.7, 60.8, 77.8, 115.1, 131.0, 137.6, 155.7, 158.7, 168.5. MS *m/z* calcd for $C_{15}H_{24}N_4NaO_5^+$ 363.16444, found 363.30490 $[M + Na]^+$.

2-Ethoxycarbonyl-1-methyl-4-{3-(1-methyimidazole-2-carboxamido)propanamido}pyrrole (19). Compound **18** (510 mg, 1.5 mmol) was dissolved in 10% trifluoroacetic acid/CH_2Cl_2 (24 mL, 30 mmol), and the solution was stirred at ambient temperature for 1 h. The solution was washed with water (15 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was dissolved in DMF, and ethyldiisopropylamine (128 μL, 0.75 mmol) and compound **5** (490 mg, 1.8 mmol) were added. The mixture was stirred at ambient temperature for 2 h. The mixture was extracted with chloroform (30 mL), washed with water (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was precipitated from chloroform and diisopropyl ether to give **19** (475 mg, 91%): ^{1}H NMR (DMSO-d_6) δ 1.26−1.38 (2H, t, J = 7.1 Hz), 2.53−2.56 (2H, t, J = 6.8 Hz), 3.45−3.49 (2H, m), 3.89 (3H, s), 3.92 (3H, s), 4.22−4.26 (2H, m), 6.94 (1H, s), 7.31 (1H, s), 7.53 (1H, s), 8.34 (1H, m), 10.7 (1H, s).^{13}C NMR (DMSO-d_6) δ 14.5, 35.4, 35.7, 36.2, 36.4, 61.6, 115.3, 125.6, 127.9, 131.7, 137.2, 139.2, 139.3, 159.0, 159.7, 168.7. MS *m/z* calcd for $C_{15}H_{21}N_6O_4^+$ 349.16243, found 349.16073 $[M + H]^+$.

2-Pentafluorophenoxycarbonyl-1-methyl-4-{3-(1-methyimidazole-2-carboxamido)propanamido}pyrrole (20). To a solution of compound **19** (65 mg, 0.19 mmol) in ethanol (1.9 mL) was added 0.4 M aqueous sodium hydroxide (1.4 mL, 0.56 mmol). The resulting solution was stirred for 1 h at 50 °C. The solution was cooled to ambient temperature and then acidified to pH 2.0 by addition of 1 M aqueous HCl. The product was separated by addition of 2-propanol, and the resulting white precipitates were colleted by filtration and washed with 2-propanol. The filtrate was concentrated in vacuo. The residue was dissolved in DMF (1.3 mL). Pentafluorophenyl trifluoromethyl acetate (68 μL, 0.39 mmol) and pyridine (32 μL, 0.39 mmol) were added to the solution under argon atmosphere, and the resulting mixture was stirred at ambient temperature for 1 h. The solution was washed with 0.1 M aqueous HCl (10 mL × 3), 5% $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried over Na_2SO_4. The residue was concentrated under reduced pressure to give **20** (88 mg, 96%): ^{1}H NMR (DMSO-d_6) δ 2.58−2.61 (2H, t, J = 7.0 Hz), 3.49−3.53 (2H, m), 3.94 (3H, s), 3.98 (3H, s), 6.96 (1H, d, J = 1.0 Hz), 7.37 (1H, d, J = 0.6 Hz), 8.37−8.39 (1H, t, J = 6.0 Hz), 10.9 (1H, s).^{13}C NMR (DMSO-d_6) δ 35.0, 35.1, 35.2, 35.9, 118.3, 126.2, 127.2, 127.6, 138.8, 138.8, 154.0, 159.0, 169.0. MS *m/z* calcd for $C_{19}H_{16}F_5N_6O_4^+$ 487.11532, found 487.10453 $[M + H]^+$.

General Procedure for the Synthesis of Ferrocene Derivatives 22a and 22b. To a solution of monoester **21** (1.0 g, 3.47 mmol) in 35 mL of CH_2Cl_2 were added *N-tert*-butoxycarbonyl ethylenediamine (0.56 g, 3.47 mmol) and *n*-tributylamine (2.0 mL, 8.3 mmol), followed by 2-chloro-1-methylpyridinium iodide (1.1 g, 4.16 mmol). The organic layer was washed successively with water (20 mL) and brine (20 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated in vacuo. Chromatography of the residue on a column of silica gel with hexane/chloroform (70:30−65:45, v/v) gave **22a** (1.3 g, 87% yield): ^{1}H NMR (DMSO-d_6) δ 1.38 (9H, s), 3.07−3.11 (2H, q, J = 6.1 Hz), 3.20−3.23 (2H, q, J = 6.1 Hz), 3.73 (3H, s), 4.37−4.44 (4H, m), 4.71−4.81 (4H, m), 6.84−6.86 (1H, t, J = 5.4 Hz), 7.82−7.85 (1H, t, J = 5.6 Hz); ^{13}CNMR (DMSO-d_6) δ 28.4, 39.1, 40.2, 51.7, 69.7, 71.2, 71.6, 72.2, 73.0, 77.9, 78.4, 155.9, 167.9, 170.5. MS *m/z* calcd for $C_{20}H_{27}FeN_2O_5^+$ 431.12694, found 431.12623 $[M + H]^+$.

Compound **22b** was synthesized according to the general procedure described above by use of *N-tert*-butoxycarbonyl-propylenediamine in place of *N-tert*-butoxycarbonyl-ethylenediamine in 88% yield: ^{1}H NMR (DMSO-d_6) δ 1.38 (9H, s), 1.57−1.63 (2H, q, J = 6.3 Hz), 2.97−3.01 (2H, q, J = 6.3 Hz, 6.6 Hz), 3.14−3.18 (2H, q, J = 6.3 Hz), 3.72 (3H, s), 4.37−4.44 (4H, m), 4.71−4.81 (4H, m), 6.81−6.83 (1H, t, J = 5.6 Hz), 7.77−7.80 (1H, t, J = 5.6 Hz); ^{13}C NMR (DMSO-d_6) δ 28.3, 29.8, 36.5, 37.7, 51.5, 69.5, 70.9, 71.5, 72.0, 72.8, 77.5, 78.5, 155.7, 167.5, 170.3. MS *m/z* calcd for $C_{21}H_{29}FeN_2O_5^+$: 445.14259, found $[M + H]^+$ 445.14270.

General Procedure for the Synthesis of Ferrocene Derivatives 23a, 23b, and 23c. Synthesis of 23a. To a solution of **22a** (1.1 g, 2.55 mmol) in methanol (26 mL) was added 0.5 M aqueous NaOH (26 mL, 2.55 mmol). The mixture was stirred at 80 °C for 12 h and then cooled to ambient temperature. The solution was acidified to pH 3.0 by addition of citric acid, diluted with ethyl acetate (20 mL), and washed with water (20 mL). The organic layer was collected and dried over Na_2SO_4. The solvents were removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 (22 mL). Ethyl 3-aminopropionate hydrochloride (354 mg, 2.31 mmol), *n*-tributylamine (1.87 mL, 7.85 mmol), and 2-chloro-1-methylpyridinium iodide (710 mg, 2.77 mmol) were added to the solution under argon atmosphere, and the resulting mixture was stirred at ambient temperature for 2 h. The solution was washed with water (50 mL), and the organic layer was dried over Na_2SO_4. The salt was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (20 g, hexane/chloroform, 50:50, v/v) to give **23a** (741 mg, 56%): ^{1}H NMR ($CDCl_3$) δ 1.18−1.21 (3H, t, J = 7.1 Hz), 1.32 (9H, s), 2.59−2.61 (2H, t, J = 6.3 Hz), 3.32 (2H, m), 3.42−3.45 (2H, dd, J = 5.4 Hz), 3.57−3.60 (2H, dd, J = 6.3 Hz), 4.07−4.12 (2H, dd, J = 7.1 Hz), 4.27 (3H, t, J = 2.0 Hz), 4.29−4.30 (3H, t, J = 1.8 Hz), 4.46 (4H, d, J = 1.5 Hz), 5.89 (1H, m), 7.34−7.37 (1H, t, J = 1.8 Hz), 7.55−7.57 (1H, t, J = 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 28.2, 33.9, 35.3, 40.2, 40.5, 60.4, 70.4, 70.5, 70.9, 71.0, 77.6, 78.0, 78.9, 156.5, 170.4, 170.5, 172.2. MS *m/z* calcd for $C_{23}H_{34}FeN_3O_6^+$ 516.17970, found 516.23203.

Compounds **23b** and **23c** were prepared in 84% and 98%, respectively, according to general procedure by use of **22a** and **22b** and appropriate amino acid esters. **Data for 23b**: ^{1}H NMR (500 MHz, DMSO) δ 1.16−1.19 (3H, t, J = 7.1 Hz), 1.38 (9H, s), 1.75−1.78 (2H, m, J = 7.1 Hz), 2.35−2.38 (2H, m), 3.09−3.11 (2H, m, J = 5.9, 6.1 Hz), 3.18−3.23 (2H, q, J = 5.9, 6.1, 6.6 Hz), 4.03−4.08 (2H, q, J = 7.1 Hz), 4.29−4.31 (4H, m), 4.69−4.72 (4H, m), 6.90 (1H, t), 7.86−7.88 (1H, t, J = 5.6 Hz), 7.90−7.92 (1H, t. J = 5.6 Hz); ^{13}C NMR (500 MHz, DMSO-d_6) δ 14.1, 24.7, 24.7, 28.3, 30.8, 31.1, 38.2, 51.3, 59.8, 69.6, 69.6, 71.4, 71.5, 77.7, 77.8, 77.9, 155.8, 168.5, 168.7, 172.8, 173.3. **Data for 23c**: ^{1}H NMR (500 MHz, DMSO) δ 1.18−1.21 (3H, t, J = 7.1 Hz), 1.38 (9H, s), 1.59−1.62 (2H, m, J = 7.1 Hz), 2.56−2.59 (2H, t, J = 6.8 Hz), 2.97−3.01 (2H, q, J = 6.6 Hz), 3.15−3.19 (2H, q, J = 6.6, 6.8 Hz), 3.39−3.43 (2H, q, J = 6.6, 7.1 Hz), 4.07−4.11 (2H q, J = 7.1 Hz), 4.28−4.30 (4H, m), 4.69−4.70 (4H, m), 6.81−6.83 (1H, t), 7.82−7.85 (1H, t, J = 5.9 Hz), 7.96−7.98 (1H, t, J = 5.8 Hz); ^{13}C NMR (500 MHz, DMSO-d_6) δ 14.1, 28.3, 29.8, 34.0, 35.2, 36.5, 37.7, 60.0, 69.5, 71.5, 71.6, 77.5, 77.6, 78.0, 155.7, 168.4, 168.6, 171.5.

General Procedure for the Synthesis of Ferrocene Derivatives 24a, 24b, and 24c. Synthesis of 24a. To a solution of **23a** (2.0 g, 3.9 mmol) in methanol (39 mL) was added 0.1 M aqueous NaOH (41 mL, 4.1 mmol), and the resulting solution was stirred at ambient temperature for 12 h. The solution was acidified to pH 3.0 by addition of 1 M aqueous HCl and partitioned between chloroform (100 mL) and water (100 mL). The organic layer was collected and dried over Na_2SO_4. The solvents were removed under reduced pressure, and the residue was chromatographed on a column of silica gel (22 g, chloroform/methanol, 100:2, v/v) to give **24a** (1.84 g, 97%): ^{1}H NMR (DMSO-d_6) δ 1.37 (9H, s), 2.49−2.53 (2H, m), 3.07−3.10 (2H,dd, J = 6.1 Hz), 3.19−3.22 (2H, dd, J = 6.1 Hz), 3.36−3.40 (2H, dd, J = 6.3 Hz), 4.28−4.29 (4H, t,, J = 1.7 Hz), 4.69−4.71 (4H, m), 6.91−6.94 (1H, t, J = 5.6 Hz),

7.83−7.86 (1H, t, J = 5.7 Hz), 7.93−7.95 (1H, t, J = 5.4 Hz), 12.25 (1H, s); ^{13}C NMR (DMSO-d_6) δ 28.5, 34.3, 35.5, 38.8, 69.8, 71.7, 71.8, 72.2, 77.8, 77.8, 77.9, 79.4, 155.9, 168.7, 168.8, 173.3. MS m/z calcd for $C_{22}H_{30}FeN_3O_6^+$ 488.14840, found 488.22584.

Compounds **24b** and **24c** were prepared according to general procedure by use of **23b** and **23c**, respectively. **Data for 24b**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.38 (9H, s), 1.72−1.77 (2H, m, J = 7.1, 7.3 Hz), 2.28−2.31 (2H, t, J = 7.3 Hz), 3.08−3.11 (2H, q, J = 6.3 Hz), 3.18−3.24 (4H, m, J = 6.3 Hz), 4.29−4.30 (4H, s), 4.69−4.72 (4H, m), 6.91−6.93 (1H, t, J = 5.6 Hz), 7.87−7.92 (2H, m, J = 5.6, 5.8 Hz), 12.1 (1H, s); ^{13}C NMR (500 MHz, DMSO) δ 25.4, 29.0, 31.9, 39.0, 70.2, 70.3, 72.1, 72.2, 78.3, 78.5, 78.6,156.4, 169.1, 169.3, 175.0. **Data for 24c**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.38 (9H, s), 1.59−1.63 (2H, m, J = 6.8 Hz), 2.97−3.01 (2H, m, J = 6.6 Hz), 3.15−3.19 (2H, q, J = 6.6, 6.8 Hz), 3.36−3.40 (2H, m, J = 6.8 Hz), 4.28−4.29 (4H, t), 4.70−4.72 (4H, m), 6.81−6.83 (1H, t, J = 5.6 Hz), 7.81−7.83 (1H, t, J = 5.9 Hz), 7.92−7.94 (1H, t, J = 5.4 Hz), 12.2 (1H, s); ^{13}C NMR (500 MHz, DMSO-d_6) δ 28.3, 29.8, 34.1, 35.3, 36.5, 37.7, 69.5, 69.5, 71.5, 71.6, 77.5, 77.7, 78.0, 155.6, 168.4, 168.4, 168.5, 173.0, 173.1.

General Procedure for the Synthesis of Ferrocene Derivatives 25a, 25b, and 25c. Synthesis of 25a. To a solution of **15** (1.6 g, 3.3 mmol) in methanol (13 mL) was added 10% Pd/C (164 mg). A balloon of hydrogen gas was attached, and the suspension was stirred under hydrogen atmosphere for 4 h. The catalysts were removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, and to this solution was added **24a** (1.6 g, 3.3 mmol), N,N'-dicyclohexylcarbodiimide (744 mg, 3.6 mmol), and 1-hydroxybenzotriazole (488 mg, 3.6 mmol). After 1 h, the white precipitates were removed by filtration. The filtrate was washed with water (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (32 g, chloroform/methanol.conc NH_3 aq, 100:7:0.2, v/v/v) to give **25a** (2.5 g, 82%): ^{1}H NMR(DMSO-d_6) δ 1.37 (9H, s), 1.70−1.73 (2H, t, J = 7.1 Hz), 2.42 (6H, s), 2.55−2.61 (4H, m), 3.09−3.47 (16H, m), 3.80 (3H, s), 3.83 (3H, s), 3.95 (3H, s), 4.28−4.29 (4H, m), 4.71−4.73 (4H, m), 6.92 (1H, d, J = 1.5 Hz), 6.94 (1H, d, J = 1.7 Hz), 7.21 (1H, d, J = 1.7 Hz), 7.29 (1H, d, J = 1.5 Hz), 7.51 (1H, s), 7.88−7.91 (1H, t, J = 5.5 Hz), 8.00−8.01 (1H, t, J = 5.5 Hz), 8.14−8.16 (1H, t, J = 5.4 Hz), 8.31 (1H, s), 9.95 (1H, s), 10.23 (1H, s); ^{13}C NMR(DMSO-d_6) δ 26.1, 28.4, 35.0, 36.0, 36.0, 36.2, 36.4, 36.6, 43.9, 56.2, 69.8, 71.7, 77.8, 77.9, 79.3, 104.3, 104.8, 114.9, 118.1, 119.3, 121.4, 122.0, 122.3, 123.3, 134.3, 136.2, 155.9, 158.8, 161.4, 168.1, 168.7, 168.8. MS m/z calcd for $C_{44}H_{59}FeN_{12}O_8^+$ 939.39282, found 939.2523.

Compounds **25b** and **25c** were synthesized according to the general procedure by use of **24b** and **24c**, respectively. **Data for 25b**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.38 (9H, s), 1.59−1.63 (2H, m, J = 7.1 Hz), 1.81−1.84 (2H, m, J = 7.3 Hz), 2.14 (6H, s), 2.23−2.26 (2H, t, J = 7.1 Hz), 2.31−2.34 (2H, m, J = 7.3 Hz), 3.09−3.12 (2H, m, J = 5.9 Hz), 3.17−3.25 (6H, m), 3.80 (3H, s), 3.84 (3H, s), 3.97 (3H, s), 4.32 (4H, s), 4.70−4.73 (4H, m), 6.89−6.93 (3H, m, J = 1.7, 1.9 Hz), 7.22 (1H, d, J = 1.7 Hz), 7.28 (1H, d, J = 1.7 Hz), 7.53 (1H, s), 7.89−7.94 (2H, m, J = 5.6, 5.9 Hz), 8.09−8.11 (1H, t, J = 5.6 Hz), 9.88 (1H, s), 9.95 (1H, s), 10.22 (1H, s); ^{13}C NMR (500 MHz, DMSO-d_6) δ 25.7, 27.1, 28.2, 33.2, 34.9, 36.0, 36.2, 37.2, 38.6, 45.2, 57.2, 69.6, 69.6, 71.4, 77.7, 77.8, 78.0, 79.2, 103.9, 104.6,114.7, 117.8, 119.1, 121.2, 121.8, 122.2, 123.4, 134.2, 136.1, 155.7, 158.7, 161.0, 168.4, 168.7, 169.3. **Data for 25c**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.38 (9H, s), 1.58−1.64 (4H, m, J = 6.8, 7,1 Hz), 2.14 (6H, s), 2.23−2.26 (2H, t, J = 7.1 Hz), 2.56−2.58 (2H, t, J = 7.1 Hz), 2.98−3.02 (2H, m, J = 6.3, 6.6 Hz), 3.16−3.21 (4H, m, J = 6.3, 6.6 Hz), 3.43−3.47 (2H, m, J = 6.6, 6.8 Hz), 3.80 (3H, s), 3.84 (3H, s), 3.97 (3H, s), 4.28−4.29 (4H, m), 4.71−4.73 (4H, m) 6.81−6.83 (1H, t, J = 5.6 Hz), 6.89 (1H, d, J = 2.0 Hz), 6.93 (1H, d, J = 2 0.0 Hz), 7.22 (1H, d, J = 1.7 Hz), 7.30 (1H, d, J = 1.7 Hz), 7.52 (1H, s), 7.83−7.85 (1H, t, J = 5.9 Hz), 7.96−7.97 (1H, t, J = 5.6 Hz), 8.08−8.11 (1H, t, J = 5.6 Hz), 9.95 (1H, s), 9.97 (1H, s), 10.23 (1H, s); ^{13}C NMR (500 MHz, DMSO-d_6) δ 27.1, 28.2, 29.8, 34.8, 35.8, 36.0, 36.3, 36.5, 37.2, 37.7, 45.2, 57.2, 69.5, 71.5, 71.6, 77.5, 77.8, 77.9, 103.9, 104.6, 109.3, 114.7, 117.8, 119.1, 121.2, 121.8, 122.1, 123.4, 134.2, 136.0, 155.6, 155.7, 158.7, 161.0, 167.9, 168.4, 168.4.

General Procedure for the Synthesis of Ferrocene Derivatives 26a, 26b, and 26c. Synthesis of 26a. Compound **25a** (1.5 g, 1.6 mmol) was dissolved in 10% trifluoroacetic acid/CH_2Cl_2 (25 mL, 32 mmol), and the solution was stirred at ambient temperature for 5 h. The mixture was washed with water (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (30 g, chloroform/methanol, 100:3, v/v) to give **26a** (1.0 g, 78%): ^{1}H NMR ($CDCl_3$) δ1.66−1.71 (2H, m), 2.20 (6H, s), 2.35−2.38 (2H, t, J = 6.4 Hz), 2.74 (2H, s), 2.97 (2H, m), 3.39−3.40 (2H, m), 3.47 (2H, m), 3.69 (2H, s), 3.84 (3H, s), 3.87 (3H, s), 3.97 (3H, s), 4.27 (2H, s), 4.31 (2H, s), 4.58−4.60 (4H, d, J = 7.3 Hz), 6.70 (1H, s), 6.90 (1H, s), 7.20 (1H, s), 7.23 (1H, s), 7.38 (1H, s), 7.45−7.46 (1H, m), 7.76 (2H, m), 7.83 (1H, m), 9.07 (1H, br), 9.21 (1H, br), 9.88(1H, s); ^{13}C NMR($CDCl_3$) δ 26.2, 35.4, 36.3, 36.5, 36.6, 38.9, 41.2, 42.1, 45.3, 58.4, 70.3, 70.4, 71.0, 71.2, 77.3, 77.5, 78.1, 103.2, 104.5, 114.0, 118.4, 120.0, 120.8, 121.7, 122.3, 123.8, 133.9, 136.1, 156.0, 158.6, 161.7, 169.4, 170.4, 170.6. MS m/z calcd for$C_{39}H_{51}FeN_{12}O_6^+$ 839.34039, found 839.33831.

Compounds **26b** and **26c** were synthesized according to general procedure by use of **25b** and **25c**, respectively. **Data for 26b**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.58−1.64 (2H, m, J = 7.1 Hz), 1.80−1.85 (2H, m), 2.14 (6H, s), 2.23−2.27 (2H, t, J = 7.1 Hz), 2.31−2.36 (2H, m, J = 7.1 Hz), 2.69−2.72 (2H, t, J = 6.6 Hz), 3.17−3.23 (6H, m), 3.81 (3H, s), 3.84 (3H, s), 3.97 (3H, s), 4.29−4.33 (4H, m), 4.70−4.73 (4H, m), 6.88 (1H, s), 6.93 (1H, s), 7.22 (1H, s), 7.29 (1H, m), 7.53 (1H, s), 7.86−7.88 (1H, t, J = 5.6 Hz), 7.92−7.97 (2H, m), 8.10−8.12 (1H, t, J = 5.6 Hz), 9.90−9.91 (1H, d), 9.97 (1H, s); ^{13}C NMR (500 MHz, DMSO-d_6) δ 27.1, 33.2, 34.9, 36.0, 36.2, 37.2, 45.2, 57.2, 69.6, 69.7, 71.3, 71.5, 77.9, 78.1, 78.1, 103.9, 104.6, 114.7, 114.7, 117.8, 119.1, 121.2, 121.8, 122.2, 123.4, 134.2, 136.1, 136.1, 155.7, 158.7, 161.0, 167.3, 168.4, 168.4, 168.5, 168.6, 169.3. **Data for 26c**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.59−1.62 (4H, m), 2.14 (6H, s), 2.23−2.26 (2H, t, J = 7.1 Hz), 2.57−2.59 (2H, t), 3.19−3.20 (2H, m), 3.24−3.25 (2H, m), 3.45−3.47 (2H, m), 3.80 (3H, s), 3.84 (3H, s), 3.97 (3H, s), 4.29 (4H, s), 4.71 (4H, d), 6.89 (1H, d, J = 1.5 Hz), 6.94 (1H, s), 7.22 (1H, s), 7.30 (1H, s), 7.53 (1H, s), 7.93−7.95 (1H, t, J = 5.4 Hz), 7.99−8.10 (2H, m, J = 5.1 Hz), 9.99−10.02 (1H, m, J = 5.1 Hz); ^{13}C NMR (500 MHz, DMSO-d_6) δ 27.1, 32.6, 34.9, 35.9, 36.0, 36.3, 36.5, 37.2, 45.2, 57.2, 69.5, 69.5, 71.4, 71.5, 77.8, 78.1, 79.2, 103.9, 104.6, 114.7, 117.8, 119.1, 121.2, 121.8, 122.1, 123.4, 134.2, 136.1, 155.7, 158.7, 161.0, 167.9, 168.4, 168.5, 168.5.

Polyamide (28). Compound **15** (806 mg, 1.6 mmol) was dissolved in methanol (6.5 mL), and to this solution was added 10% Pd/C (81 mg). A balloon of hydrogen gas was attached, and the suspension was stirred under hydrogen atmosphere for 4 h at ambient temperature. The catalysts were removed by filtration, and the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2, and the protected γ-butyric acid **27** (710 mg, 1.6 mmol), N,N'-dicyclohexyl carbodiimide (332 mg, 1.6 mmol) ,and 1-hydroxybenzotriazole (218 mg, 1.6 mmol) were added. The mixture was stirred at ambient temperature for 1 h. The precipitation was removed by filtration, and to the filtrate was added 5% piperidine/DMF (28 mL, 16 mmol). After 30 min, the solution was washed with water (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (16 g, chloroform/methanol/conc NH_3 aq,100:10:1, v/v/v) to give **28** (453 mg, 42%): ^{1}HNMR ($CDCl_3$) δ 1.44 (9H, s), 1.71−1.76 (2H, t, J = 6.3 Hz), 1.91−1.98 (2H, t, J = 6.3 Hz), 2.26 (6H, s), 2.41−2.44 (2H, t, J = 6.3 Hz), 2.90−2.95 (2H, m), 3.44−3.47 (2H, dd, J = 5.7 Hz), 3.83 (3H, s), 3.91 (3H, s), 4.01 (3H, s), 4.52 (1H, s), 6.46 (1H, s), 6.63 (1H, s), 6.67 (1H, s), 7.15 (1H, s), 7.26

(1H, s), 7.37 (1H, s), 7.77 (1H, s), 8.24 (1H, s), 9.10 (1H, s), 9.64 (1H, s); ^{13}C NMR (DMSO-d_6) δ 27.1, 28.2, 34.9, 35.7, 36.0, 36.2, 37.2, 38.4, 45.2, 57.2, 78.0, 79.2, 104.0, 114.7, 115.7, 117.8, 119.2, 121.2, 121.8, 121.9, 123.4, 134.2, 136.1, 155.4, 155.8, 158.7, 161.1, 169.7. MS *m/z* calcd for $C_{31}H_{48}N_{11}O_6^+$ 670.37890, found 670.33883.

Polyamide (29). To a solution of compound **10** (304 mg, 0.77 mmol) were added ethyldiisopopylamine (239 μL, 1.4 mmol) and *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (533 mg, 1.4 mmol), and the mixture was stirred at ambient temperature for 30 min. To this mixture was added **28** (470 mg, 0.70 mmol) in CH_2Cl_2 (7 mL), and the mixture was stirred for an additional 1 h. The solution was washed with water (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (10 g, chloroform/methanol/triethylamine, 100:5:0.5, v/v/v) to give **29** (673 mg, 94%): ^{1}H NMR (DMSO-d_6) δ 1.34 (9H, s), 1.70−1.73 (2H, t, J = 7.1 Hz) 1.75−193 (2H, m), 2.41 (6H, s), 2.61 (2H, m), 3.19−3.22 (2H,dd, J = 1.7 Hz), 3.27−3.37 (2H, m), 3.80 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.92 (3H, s), 3.96 (3H, s), 3.98 (3H, s), 4.08−4.13 (1H, m) 6.94 (1H, d, J = 1.5 Hz), 6.97 (1H, s), 7.02 (1H, s), 7.16 (1H, d, J = 1.5 Hz), 7.22 (1H, s), 7.26 (1H, d, J = 1.2 Hz), 7.37 (1H, s), 7.38 (1H, d, J = 1.5 Hz), 7.49 (1H, s), 7.53 (1H, s), 7.97−7.80 (1H, t, J = 5.5 Hz), 8.15−8.17 (1H, t, J = 5.5 Hz), 9.94 (1H, s), 9.99 (1H, s), 10.27 (1H, s), 10.34 (1H, s), 10.36 (1H, s); ^{13}C NMR(DMSO-d_6) δ 26.1, 28.4, 32.2, 35.1, 35.3, 35.7, 36.3, 36.4, 36.5, 36.6, 38.4, 43.9, 52.6, 56.1, 78.4, 79.4, 104.4, 105.0, 106.1, 114.5, 115.0, 118.2, 119.5, 119.7, 121.4, 121.7, 121.9, 122.1, 122.4, 123.3, 126.6, 127.2, 134.2, 134.4, 136.2, 136.2, 138.9, 155.6, 155.9, 156.3, 158.9, 158.9, 161.4, 169.4. MS *m/z* calcd for $C_{47}H_{63}N_{18}O_9^+$ 1023.50254, found 1023.49821.

General Procedure for the Synthesis of Fc-PIAs 1a, 1b, 1c, and 2 (3). Synthesis of 1a. To a solution of **10** (188 mg, 0.48 mmol) were added ethyldiisopopylamine (0.16 mL, 0.95 mmol) and *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (362 mg, 0.95 mmol), and the mixture was stirred at ambient temperature for 30 min. To this mixture was added **26a** (400 mg, 0.48 mmol) in CH_2Cl_2 (4.8 mL), and the mixture was stirred for an additional 1 h. The solution was washed with water (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (10 g, chloroform/methanol/triethylamine, 100:5:0.5, v/v/v) to give **1a** (349 mg, 61%): ^{1}H NMR (DMSO-d_6) δ 1.59−1.65 (2H, m), 2.15 (6H, s), 2.26−2.28 (2H, t, J = 7.1 Hz), 2.56−2.59 (2H, t, J = 7.0 Hz), 3.18−3.22 (2H, m), 3.37−3.50 (6H, m), 3.81(3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.94 (3H, s), 3.97 (3H, s), 3.99 (3H, s), 4.27−4.30 (4H, m), 4.73 (4H, s), 6.88 (1H, d, J = 1.7 Hz), 6.94 (1H, d, J = 1.5 Hz), 7.02 (1H, s), 7.16 (1H, d, J = 1.7 Hz), 7.19 (1H, d, J = 1.5 Hz), 7.26 (1H, d, J = 1.7 Hz), 7.35−7.36 (2H, m), 7.46 (1H, s), 7.49 (1H, s), 7.86−7,87 (1H, t, J = 5.6 Hz), 7.91−7.93 (1H, t, J = 5.5 Hz), 7.98−7.80 (1H, t, J = 5.5 Hz), 8.05−8.08 (1H, t, J = 5.7 Hz), 9.77 (1H, s), 9.88 (1H, s), 10.03 (1H, s), 10.06 1H, s), 10.19 (1H, s); ^{13}C NMR (DMSO-d_6) δ 27.2, 35.1, 35.1, 35.3, 36.0, 36.1, 36.2, 36.4, 36.5, 37.4, 38.8, 39.0, 45.3, 57.3, 69.8, 71.7, 71.8, 77.9, 78.0, 79.3, 104.1, 104.8, 106.1, 114.6, 114.9, 118.0, 119.4, 119.6, 121.4, 1221.7, 122.2, 122.3, 122.4, 123.5, 126.6, 127.2, 134.1, 134.4, 136.2, 138.9, 155.9, 156.3, 158.9, 158.9, 159.2, 161.2, 168.2, 168.6, 169.0. MS *m/z* calcd for$C_{55}H_{66}FeN_{19}O_9^+$ 1192.46403, found 1192.37089.

Compounds **1b** and **1c** were synthesized according to general procedure by use of **26b** and **26c**, respectively. Compound **2** was synthesized by the reaction of **26a** (138 mg, 0.17 mmol) and **20** (88 mg, 0.18 mmol) in the presence of ethyldiisopropylamine (31 mL, 0.18 mmol) in CH_2Cl_2. The product was purified according to the general procedure to give **2** (152 mg, 81%). **Data for 1b**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.59−1.63 (2H, m), 1.80−1.83 (2H, m), 2.14 (6H, s), 2.23−2.26 (2H, t, J = 6.8 Hz), 2.31−2.34 (2H, t, J = 7.2 Hz), 3.18−3.23 (4H, m), 3.44−3.50 (4H, m), 3.80 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.94 (3H, s), 3.96 (3H, s), 3.99 (3H, s), 4.29−4.32 (4H, d), 4.74 (4H, s), 6.90 (1H, s), 6.93 (1H, s), 7.04 (1H, s), 7.16 (1H, s), 7.22 (1H, s), 7.28 (1H, s), 739 (1H, m), 7.50 (1H, s), 7.53 (1H, s), 7.91−7.93 (1H, t, J = 5.0 Hz), 8.04 (1H, t), 8.11−8.12 (1H, t, J = 5.1 Hz), 8.14−8.16 (1H, t, J = 5.3 Hz), 9.89 (1H, s), 9.98 (1H, s), 10.23 (1H, s), 10.24 (1H, s), 10.38 (1H, s); ^{13}C NMR (500 MHz, DMSO-d_6) δ 26.4, 27.8, 33.9, 35.6, 35.7, 35.8, 35.8, 36.8, 36.9, 37.0, 37.9 39.3, 39.5, 45.9, 57.9, 63.5, 70.3, 70.3, 72.2, 72.3, 78.4, 78.8, 104.6,105.3, 106.6, 115.1, 115.4, 118.5, 119.8, 120.2, 121.9, 122.2, 122.5, 122.9, 124.1, 127.1, 127.7, 134.6, 134.9, 136.8, 139.4, 156.4, 156.8, 159.4, 159.4, 159.7, 161.8, 169.1, 169.5, 170.1. **Data for 1c**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.58−1.63 (2H, m, J = 7.1 Hz), 1.72−1.75 (2H, m, J = 6.7 Hz), 2.13 (6H, s), 2.22−2.25 (2H, t, J = 7.1 Hz), 2.56−2.58 (2H, t, J = 7.0 Hz), 3.17−3.21 (2H, q, J = 6.1, 6.6 Hz), 3.22−3.26 (2H, q, J = 6.1, 6.6 Hz), 3.44−3.48 (2H, q, J = 6.1, 6.8 Hz), 3.80 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.94 (3H, s), 3.96 (3H, s), 3.99 (3H, s), 4.30−4.32 (4H, m), 4.72−4.75 (4H, m), 6.89 (1H, d, J = 2.0 Hz), 6.92 (1H, d, J = 1.7 Hz), 7.03 (1H, d, J = 1.7 Hz), 7.17 (1H, d, J = 1.7 Hz), 7.21 (1H, d, J = 1.7 Hz), 7.30 (1H, d, J = 1.7 Hz), 7.39 (2H, d, J = 2.2 Hz), 7.50 (1H, s), 7.52 (1H, s), 7.93−7.95 (1H, t, J = 5.9 Hz), 7.99−8.01 (1H, t, J = 5.9 Hz), 8.09−8.12 (1H, t, J = 5.6 Hz), 8.14−8.16 (1H, t, J = 5.9 Hz), 9.97 (1H, s), 9.99 (1H, s), 10.24 (1H, s), 10.27 (1H, s), 10.38 (1H, s); ^{13}C NMR (500 MHz, DMSO-d_6) δ 27.1, 29.7, 34.9, 34.9, 35.1, 35.8, 35.9, 36.0, 36.1, 36.2, 36.3, 36.3, 37.2, 45.2, 57.2, 69.5, 71.6, 71.6, 77.8, 77.9, 103.9, 104.6, 105.9, 114.4, 114.7, 117.8, 119.2, 119.5, 121.2, 121.5, 121.8, 122.1, 122.2, 123.4, 126.4, 127.0, 134.0, 134.2, 136.0, 136.0, 134.7,155.7, 156.1, 158.7, 158.8, 161.0, 167.9, 168.5, 168. **Data for 2**: ^{1}H NMR (DMSO-d_6) δ 1.59−1.62 (2H, t, J = 7.0 Hz), 2.14 (6H, s), 2.23−2.25 (2H, t, J = 7.0 Hz), 2.55−2.60 (4H, m), 3.17−3.21 (2H, m), 3.35−3.37 (2H, m), 3.42−3.50 (6H, m), 3.80 (3H, s), 3.83 (3H, s), 3.91 (3H, s), 3.93 (3H, s), 3.96 (3H, s), 4.25−4.26 (2H, m), 4.29 (2H, m), 4.72−4.73 (2H, m), 4.74−4.75 (2H, m), 6.89 (1H, d, J = 1.8 Hz), 6.93-(1H, d, J = 1.7 Hz), 6.95 (1H, s), 7.21 (1H, d, J = 1.7 Hz), 7.31 (1H, d, J = 1.6 Hz), 7.32 (1H, s), 7.41 (1H, s), 7.52 (1H, s), 7.99−8.01 (2H, m), 8.10−8.12 (2H, m), 8.34 (1H, t, J = 6.0 Hz), 9.95 (1H, s), 10.0 (1H, s), 10.2 (1H, s), 10.2 (1H, s), 10.3 (1H, s).

Fc-PIA 3. Compound **30** (300 mg, 0.29 mmol) was dissolved in 20% trifluoroacetic acid /CH_2Cl_2 (1.2 mL, 2.9 mmol). After 1 h, the solution was washed with water (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (2.9 mL), and to this solution were added ethyldiisopropylamine (0.10 mL, 0.59 mmol), ferrocenecarboxylic acid (67 mg, 0.29 mmol), and *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (111 mg, 0.29 mmol). The solution was stirred at ambient temperature for 10 h, then washed with water (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel (7 g, chloroform/methanol/triethylamine, 100:5:0.5, v/v/v) to give **3** (204 mg, 61%): ^{1}HNMR(DMSO-d_6) δ 1.57−1.62 (2H, m), 2.12 (6H, s), 2.22−2.24 (2H, t, J = 7.0 Hz), 3.16−3.20 (2H, m), 3.37−3.43 (2H, m), 3.80 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.93 (3H, s), 3.96 (3H, s), 3.98 (3H, s), 4.22 (5H, s), 4.36−4.37 (2H, m), 4.85 (2H, m), 4.94 (2H, m), 6.86 (1H, d, J = 1.7 Hz), 6.99 (1H, d, J = 1.7 Hz), 7.02 (1H, d, J = 1.0 Hz), 7.17 (1H, d, J = 1.7 Hz), 7.20(1H, d, J = 1.7 Hz), 7.28 (1H, d, J = 1.7 Hz), 7.37 (1H, s), 7.38 (1H, d, J = 1.7 Hz), 7.49 (1H, s), 7.52 (1H, s), 7.86−7.87 (1H, d, J = 1.7 Hz), 8.05−8.10 (2H, m), 9.95 (1H, s), 10.04 (1H, s), 10.24 (1H, s), 10.25 (1H, s), 10.27 (1H, s), 10.36 (1H, s); ^{13}C NMR (DMSO-d_6) δ 27.2, 35.1, 35.1, 35.3, 36.0, 36.1, 36.2, 36.4, 36.5, 37.4, 38.8, 39.0, 45.3, 57.3, 69.8, 71.7, 71.8, 77.9, 78.0, 79.4, 104.1, 104.8, 106.1, 114.6, 114.9, 118.0, 119.4, 119.6, 121.4, 121.7, 122.0, 122.3, 122.4, 123.5, 126.6, 127.2, 134.1, 134.4, 136.2, 138.9, 155.9, 156.3, 158.9, 158.9, 159.2, 161.2, 168.2, 168.6, 169.0. MS *m/z* calcd for $C_{53}H_{63}FeN_{18}O_8^+$ 1135.44257, found 1135.43889.

CD Spectra. Solutions (1 mM) of Fc-PIA were prepared by addition of 0.1 M HCl (8.8 μL) to a suspension of Fc-PIA (10 mg, 8.8μmol) in a buffer composed of 10 mM sodium cacodylate (pH6.9), 10 mM KCl, 10 mM $MgCl_2$, and 5 mM $CaCl_2$ (8.8 mL). The titration was performed at 20 °C by incrementally adding 1.5 μL aliquots of the Fc-PIA solution into a 1.5 mL solution of 5 μM duplex (**DNA1** or **DNA2**). The spectra were recorded from 200 to 400 nm. The titration curves were drawn by plotting the molar ellipticity at the wavelength that gave maximum Cotton effects within a 300−350 nm range.

Cyclic Voltammetry in DMF. Fc-PIA (200 μL, 5 mM) was dissolved in DMF (10 mL). The CV profiles were measured by a general three-electrode system by use of a Pt electrode (6 mm) and platinum wire as working electrode and counter electrode, respectively. Ag/AgCl in CH_3CN was used as a reference.

Acknowledgment. This work was supported by CREST of JST (Japan Science and Technology Agency) and supported by The Sumitomo Foundation. We thank Dr. Yoshio Ishimori and Dr. Jun Okada (Toshiba Co. Ltd.) for fruitful discussion on the electrochemical detection of DNA hybridization in this study.

Supporting Information Available: ^1H and ^{13}C NMR spectra of all of the newly synthesized compounds and th procedure and results of curve fitting of the CD titration. This material is available free of charge via the Internet at http://pubs.acs.org.

JO051247N