An Amide-Linked Ferrocene Dimer, $[(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$. Formation of Inter- and Intramolecular NH···O═C Hydrogen Bonds

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Received June 18, 1998

An amide-linked ferrocene dimer, $[(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**7**), and a monomer, $[(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**5**), were synthesized, and their unique structures were determined by X-ray analysis. Amide planes are stacked with respect to each other in both crystal and dilute solution. These complexes form intermolecular NH···O═C hydrogen bonds in the crystal. On the other hand, they form intramolecular NH···O═C hydrogen bonds in a dilute solution as established by IR and ^{1}H NMR measurements. Spectral data suggest the presence of flapping structures in solution. Crystal data for **5**: triclinic, $P\bar{1}$, $a = 9.358(3)$ Å, $b = 9.947(4)$ Å, $c = 7.946(3)$ Å, $\alpha = 106.86(3)°$, $\beta = 113.15(3)°$, $\gamma = 76.59(3)°$, $V = 644.9(5)$ Å^3, $Z = 2$. **7**·$^1/_2$EtCN: orthorhombic, $Pna2_1$, $a = 7.467(4)$ Å, $b = 14.048(4)$ Å, $c = 23.400(5)$ Å, $Z = 4$.

Introduction

Organometallic polymers have been found to produce a wide variety of attractive materials with diverse applications. Especially, the incorporation of transition metal into polymer backbone has been known to provide unusual physical and chemical properties.[1] Ferrocene is one of the most promising candidates to construct such polymeric materials for its synthetic facility and potential utilities for electronic, electrochemical, magnetic and optical materials.[2,3] From this viewpoint, many organometallic polymers containing skeletal ferrocenes using various bridges such as silicon,[4−14] germanium,[9,15] hydrocarbon,[2,5,16−18] sulfur,[19,20] and phosphorus[21,22] have been reported.

On the other hand, some nonnatural amino acids, oligopeptides and polypeptides containing ferrocene moieties in the side chain or as the terminal residue, have been reported.[23−26] Attempts to incorporate them into native proteins are interesting from the biological viewpoints. Ferrocene derivatives have a remarkably flexible conformation caused by the free rotation of cyclopentadienyl moieties[24] and the redox active iron center is appropriate to obtain electron-transfer ability.[26,27]

Recently, the first synthesis of nonnatural amino acid containing a skeletal ferrocene, $[(NH_2C_5H_4)Fe(C_5H_4COOH)]$, has been reported.[28] However, the synthetic method caused a mixture of products to be produced, and even after purification, some contaminations were detected.

Here, we will report a modified synthetic route to obtain the ferrocene-containing amino acid and synthesis of its dimer by the techniques which are required for the stepwise polymerization of the amino acid, i.e., N- and/or C-terminal protection/deprotection and coupling reactions to construct novel polypeptides containing ferrocene cores in the backbone. In this paper, its unique folding molecular structure is presented.

Experimental Section

All the procedures were performed under argon atmosphere by the Schlenk technique except for chromatography. All solvents were dried and distilled under argon before use. Acetylaminoferrocene was prepared by the literature method.[29]

1-Acetylamino-1′-(2,6-dichlorobenzoyl)ferrocene. To a dichloromethane solution (80 mL) of acetylaminoferrocene (10.0 g, 41.1 mmol) and 2,6-dichlorobenzoyl chloride (6.4 mL, 41 mmol) was added slowly aluminum chloride (7.66 g, 57.4 mmol) in an ice bath. The deep blue solution was stirred for 30 min at 0 °C and for 2 h at room temperature. After the reaction mixture was cooled again in an ice bath, ice−water (80 mL) was added cautiously, and the resultant two-phase

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(1) *Metal-Containing Polymeric Materials*; Pittman, C. U., Jr., Carraher, C. E., Jr., Zeldin, M., Sheats, J. E., Culbertson, B. M., Eds.; Plenum Press: New York, 1996 and references cited therein.

(2) Southard, G. E.; Curtis, D. *Organometallics* **1997**, *16*, 5618−5620.

(3) Kanis, D. R.; Ratner, M. A.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 10338−10357.

(4) Rasburn, J.; Foucher, D. A.; Reynolds, W. F.; Manners, I.; Vancso, G. J. *J. Chem. Soc., Chem. Commun.* **1998**, 843−844.

(5) Nelson, J. M.; Nguyen, P.; Peterson, R.; Rengel, H.; Macdonald, P. M.; Lough, A. J.; Manners, I.; Raju, N. P.; Greedan, J. E.; Barlow, S.; O'Hare, D. *Chem. Eur. J.* **1997**, *3*, 573−584.

(6) Rulkens, R.; Resendes, R.; Verma, A.; Manners, I.; Murti, K.; Fosssum, E.; Miller, P.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 8165−8171.

(7) Rulkens, R.; J.Lough, A.; Manners, I.; Lovelace, S. R.; Grant, C.; Geiger, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 12683−12695.

(8) Foucher, D. A.; Tang, B.-Z.; Manners, I. *J. Am. Chem. Soc.* **1992**, *114*, 6246−6248.

(9) Foucher, D. A.; Edwards, M.; Burrow, R. A.; Lough, A. J.; Manners, I. *Organometallics* **1994**, *13*, 4959−4966.

(10) Nguyen, T.; Diaz, A. F. *Chem. Mater.* **1993**, *5*, 1389−1394.

(11) Dement'ev, V. V.; Cervantes-Lee, F.; Parkanyi, L.; Sharma, H.; Pannell, K. H. *Organometallics* **1993**, *12*, 1983−1987.

(12) Nguyen, M. T.; Diaz, A. F.; Dement'ev, V. V.; Pannell, K. H. *Chem. Mater.* **1994**, *6*, 952−954.

(13) Pannell, K. H.; Dementiev, V. V.; Li, H.; Cervantes-Lee, F.; Nguyen, M. T.; Diaz, A. F. *Organometallics* **1994**, *13*, 3644−3650.

(14) Pannell, K. H.; Sharma, H. K. *Organometallics* **1997**, *16*, 3077.

(15) Kapoor, R. N.; Crawford, G. M.; Mahmoud, J.; Dementiev, V. V.; Nguyen, M. T.; Diaz, A. F.; Pannell, K. H. *Organometallics* **1995**, *14*, 4944−4947.

(16) Heo, R. W.; Somoza, F. B.; Lee, T. R. *J. Am. Chem. Soc.* **1998**, *120*, 1621−1622.

(17) Buretea, M. A.; Tilley, T. D. *Organometallics* **1997**, *16*, 1507−1510.

10.1021/ic9806939 CCC: $15.00

Table 1. Crystallographic Data for [($CH_3CONHC_5H_4$)Fe($C_5H_4CONHCH_3$)] (**5**) and [($CH_3CONHC_5H_4$)Fe($C_5H_4CONHC_5H_4$)Fe($C_5H_4CONHCH_3$)]·$^1/_2$EtCN (**7**·$^1/_2$EtCN)

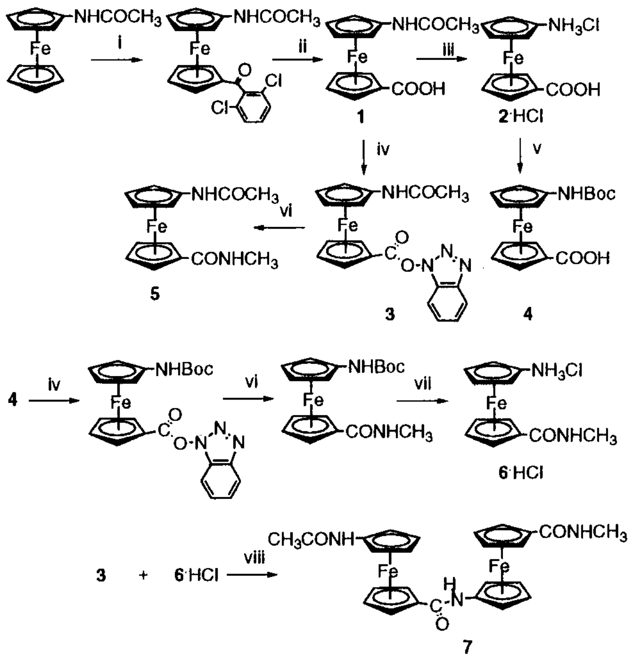
	5	**7**·$^1/_2$EtCN
empirical formula	$C_{14}H_{16}O_2N_2Fe$	$C_{26.50}H_{27.50}O_3N_{3.50}Fe_2$
fw	300.14	554.72
cryst syst	triclinic	orthorhombic
a, Å	9.358(3)	7.467(4)
b, Å	9.947(4)	14.048(4)
c, Å	7.946(3)	23.400(5)
α, deg	106.86(3)	90
β, deg	113.15(3)	90
γ, deg	76.59(3)	90
V, Å^3	644.9(5)	2454(1)
Z	2	4
space group	$P\bar{1}$ (No. 2)	$Pna2_1$ (No. 33)
μ, cm^{-1}	11.66	12.16
d_{calc}, g cm^{-3}	1.545	1.501
no. of reflecns measd	total: 3127 unique: 2985	total: 3041
no. of obsd reflecns	1070 ($I > 3\sigma(I)$)	1621 ($I > 2\sigma(I)$)
R[a]	0.064	0.068
R_w[b]	0.069	0.107

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$; $w = 1/\sigma(|F_o|)$.

mixture was stirred vigorously for 30 min at room temperature. The aqueous layer was extracted with dichloromethane. The combined dichloromethane solutions were washed once with water and twice with a 10% aqueous sodium hydroxide solution, dried over $MgSO_4$, and evaporated. The resulting red oil was purified by chromatography on silica gel with ethyl acetate−*n*-hexane (5:1) eluent. The eluate was concentrated under reduced pressure, and red powder was obtained. Yield 12.6 g (71%) ^{1}H NMR (chloroform-d_1) δ 2.09 (s, 3H), 4.15(t, 2H), 4.61 (m, 5H), 4.73 (t, 2H), 6.69 (br, 1H), 7.33 (m, 4H).

1-Acetylamino-1′-carboxy ferrocene (1). To a suspension of potassium *tert*-butoxide (13.9 g, 124 mmol) and water (0.7 mL) was slowly added a 1,2-dimethoxyethane solution (75 mL) of 1-acetylamino-1′-(2,6-dichlorobenzoyl)ferrocene (12.6 g, 29.1 mmol) in an ice bath, to give a red solution. This solution was stirred and refluxed for 1 h. The red solution was turned to tan. After cooling to room temperature, the reaction mixture was poured into water (300 mL). The resulting solution was washed with diethyl ether twice, and the washings were combined and back-extracted with a 10% aqueous sodium hydroxide solution. The combined aqueous phase was acidified with concentrated hydrochloric acid and extracted with ethyl acetate. The extract was washed with saturated NaCl (aq), dried over Na_2SO_4, and evaporated. The obtained oily product was washed with diethyl ether and dried in vacuo to give orange powder. Yield 4.9 g (41%) ^{1}H NMR (chloroform-d_1) δ 2.15 (s, 3H), 4.07 (t, 2H), 4.46 (t, 2H), 4.67 (t, 2H),4.83 (t, 2H) 7.06 (br, 1H). Anal. Calcd for $C_{13}H_{13}FeNO_3$: C, 54.39; H, 4.56; N, 4.88. Found: C, 54.29; H, 4.31; N, 4.95.

Scheme 1[a]



[a] (i) 2,6-$Cl_2C_6H_3COCl$ + $AlCl_3/CH_2Cl_2$. (ii) *t*-BuOK + H_2O/DME, reflux, 1 h. (iii) 6 N HCl (aq), reflux, 30 min. (iv) HOBt + DCC/CH_2Cl_2. (v) Boc_2O/phosphate buffer (pH ∼ 7). (vi) CH_3NH_2·HCl + NEt_3/THF. (vii) HCl gas/diethyl ether. (viii) NEt_3/DMF.

[(HCl·$NH_2C_5H_4$)Fe(C_5H_4COOH)] (2·HCl). 1-Acetylamino-1′-carboxyferrocene (1.60 g, 5.6 mmol) was suspended in 6 M HCl (100 mL) and refluxed for 30 min. The suspension turned to a clear brown solution. Insoluble materials were removed by filtration. The filtrate was evaporated under reduced pressure. The obtained crude product was washed with tetrahydrofuran and diethyl ether and dried in vacuo. Yield 1.50 g (96%). ^{1}H NMR (Me_2SO-d_6) δ 4.16 (t, 2H), 4.45 (t, 2H), 4.56 (t, 2H),4.82 (t, 2H) 10.02 (br, 4H).

[($CH_3CONHC_5H_4$)Fe(C_5H_4COOBt)] (3). The titled compound was synthesized in a similar way reported for carboxyferrocene derivative.[27]

To a solution of 1-acetylamino-1′-carboxyferrocene (0.63 g, 2.2 mmol) in dichloromethane (5 mL) was added solid dicyclohexylcarbodiimide (DCC) (0.45 g, 2.2 mmol) and *N*-hydroxybenztriazole (HOBt) (0.30 g, 2.2 mmol), and stirred for 1 day. The reaction mixture was filtered, and the filtrate was washed with 4% $NaHCO_3$ (aq), saturated NaCl (aq), 2% HCl (aq), and saturated NaCl (aq), dried over $MgSO_4$, and evaporated. The obtained brown oil was dissolved in ethyl acetate, and impurities was removed by chromatography on silica gel with ethyl acetate eluent. The elutate was concentrated under reduced pressure to give red powder. Yield 0.54 g (60%). ^{1}H NMR (chloroform-d_1) δ 1.98 (s, 3H), 4.13 (t, 2H), 4.72 (t, 2H), 4.94 (t, 2H) 5.09 (t, 2H), 7.47 (t, 1H), 7.53 (d, 1H), 7.59 (m, 2H), 8.10 (t, 1H). Anal. Calcd for $C_{19}H_{16}FeN_4O_3$: C, 56.46; H, 3.99; N, 13.86. Found: C, 55.69; H, 4.27; N, 13.17.

[($BocNHC_5H_4$)Fe(C_5H_4COOH)] (4). [(HCl·$NH_2C_5H_4$)Fe(C_5H_4-COOH)] (1.03 g, 3.7 mmol) was dissolved in a phosphate buffer and adjusted to pH ∼ 7 by the addition of 0.1 N aqueous sodium hydroxide. Di-*tert*-butyl dicarbonate (Boc_2O) (10.3 g, 47.3 mmol) was added to the solution cooling in an ice bath and then stirred overnight at room temperature. The reaction mixture was extracted with diethyl ether, washed with 4% $NaHCO_3$ (aq), 5% citric acid (aq), and saturated NaCl (aq), dried over Na_2SO_4, and evaporated. The crude product was washed with *n*-hexane and dried in vacuo. Yield 1.1 g (86%). ^{1}H NMR (chloroform-d_1) δ 1.57 (s, 9H), 3.98 (br, 2H), 4.41 (br, 2H), 4.56 (br, 2H) 4.91 (br, 2H), 6.16 (br, 1H).

[($CH_3CONHC_5H_4$)Fe($C_5H_4CONHCH_3$)] (5). To a solution of [($CH_3CONHC_5H_4$)Fe(C_5H_4COOBt)] (**4**) (0.54 g, 1.3 mmol) in tetrahydrofuran (THF) (3 mL) were added solid CH_3NH_2·HCl (0.14 g, 2.0 mmol) and NEt_3 (0.28 mmol, 2.0 mmol). After stirring for 1 day, the reaction mixture was concentrated to dryness. The obtained brown

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(18) Stanton, C. E.; Lee, T. R.; Grubbs, R. H.; Lewis, N. S. *Macromolecules* **1995**, *28*, 8713−8721.
(19) Pudelski, J. K.; Gates, D. P.; Rulkens, R.; Lough, A. J.; Manners, I. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1506−1503.
(20) Compton, D. L.; Rauchfuss, T. B. *Organometallics* **1994**, *13*, 4367−4376.
(21) Manners, I. *Adv. Organomet. Chem.* **1995**, *37*, 131−168.
(22) Honeymam, C. H.; Fourcher, D. A.; Dahmen, F. Y.; Rulkens, R.; Lough, A. J.; Manners, I. *Organometallics* **1995**, *14*, 5503−5512.
(23) Yli-Kauhaluoma, J. T.; Ashley, J. A.; Lo, C.-H.; Tucker, L.; Wolfe, M. M.; Janda, K. M. *J. Am. Chem. Soc.* **1995**, *117*, 7041−7047.
(24) Heine, A.; Stura, E. A.; Yli-Kauhaluoma, J. T.; Gao, C.; Deng, Q.; Beno, B. R.; Houk, K. N.; Janda, K. D.; Wilson, I. A. *Science* **1998**, *279*, 1934−1940.
(25) Carlström, A.-S.; Frejd, T. *J. Org. Chem.* **1990**, *55*, 4175−4180.
(26) Kira, M.; Matsubara, T.; Shinohara, H.; Sisido, M. *Chem. Lett.* **1997**, 89−90.
(27) Kraatz, H.-B.; Lusztyk, J.; Enright, G. D. *Inorg. Chem.* **1997**, *36*, 2400−2405.
(28) Butler, I. R.; Quayle, S. C. *J. Organomet. Chem.* **1998**, *552*, 63−68.
(29) Hall, D. W.; Richards, J. H. *J. Org. Chem.* **1963**, *28*, 1549−1554.

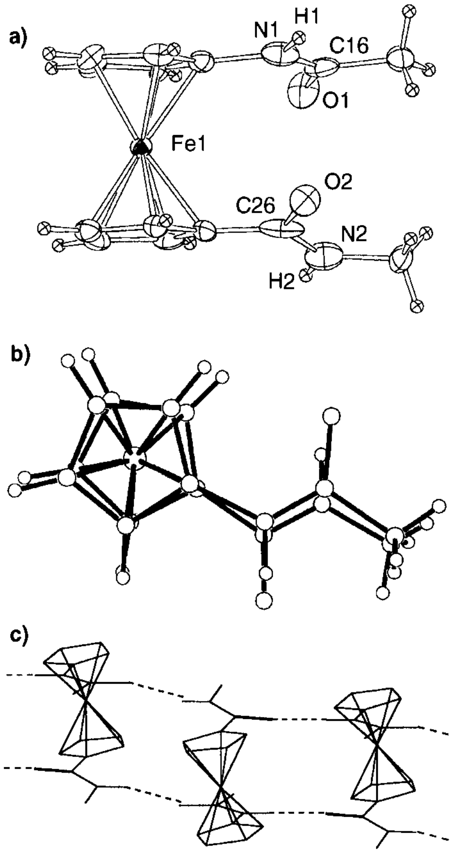

Figure 1. (a) ORTEP drawing of [($CH_3CONHC_5H_4$)Fe(C_5H_4-$CONHCH_3$)] (**5**). (b) Top view of the molecule **5**. (c) Intermolecular hydrogen bonds of **5** in the crystal.

powder was dissolved in acetone, and impurities were removed by chromatography on silica gel with acetone as eluent. Removal of solvent under reduced pressure gave orange powder. The crude product was recrystallized from dichloromethane. The product is soluble in water. Yield 0.15 g (23%). ^{1}H NMR (chloroform-*d*$_1$) δ 2.10 (s, 3H), 2.92 (d, 3H), 4.03 (t, 2H), 4.34 (t, 2H) 4.49 (t, 2H), 4.61 (t, 2H), 6.12 (br, 1H), 7.41 (br, 1H). Anal. Calcd for $C_{14}H_{16}FeN_2O_2$: C, 56.03; H, 5.37; N, 9.33. Found: C, 55.91; H, 5.27; N, 9.42.

[($BocNHC_5H_4$)Fe(C_5H_4COOBt)]. [($BocNHC_5H_4$)Fe(C_5H_4COOH)] (**4**) (2.49 g, 7.13 mmol), HOBt (1.95 g, 14.4 mmol), and dicyclohexylcarbodiimide (DCC) (2.95 g, 14.4 mmol) were dissolved in dichloromethane and the mixture was stirred overnight. The reaction mixture was filtered, and the filtrate was washed with 4% $NaHCO_3$ (aq), 5% citric acid (aq), and saturated NaCl (aq), dried over $MgSO_4$, and evaporated to dryness. The crude product was purified by chromatography on silica gel with ethyl acetate−*n*-hexane (1:1) eluent. The eluate was concentrated under reduced pressure. Yield 2.51 g (76%). ^{1}H NMR (chloroform-*d*$_1$) δ 1.57 (s, 9H), 4.13 (t, 2H), 4.63 (t, 2H), 4.79 (t, 2H) 5.08 (t, 2H), 6.42 (br, 1H), 7.44 (t, 1H), 7.51 (d, 1H), 7.56 (t, 1H), 8.10 (d, 1H).

[($BocNHC_5H_4$)Fe($C_5H_4CONHCH_3$)]. To a mixture of [($BocNHC_5H_4$)-Fe(C_5H_4COOBt)] (1.70 g, 3.67 mmol) and $CH_3NH_2\cdot HCl$ (0.40 g, 5.91 mmol) in THF (15 mL), was added NEt_3 (0.82 mL) which had been cooled in an ice bath. After stirring overnight, solvent was removed under reduced pressure. The crude product was purified as described for [($BocNHC_5H_4$)Fe(C_5H_4COOBt)] using silica gel and ethyl acetate eluent to give orange powder. Yield 1.26 g (96%). ^{1}H NMR (chloroform-*d*$_1$) δ 1.57 (s, 9H), 2.98 (d, 3H), 4.01 (t, 2H), 4.28 (t, 2H) 4.37 (t, 2H), 4.62 (t, 2H), 6.03 (br, 1H), 6.39 (br, 1H).

[($HCl\cdot NH_2C_5H_4$)Fe($C_5H_4CONHCH_3$)] (6·HCl). The compound, [($BocNHC_5H_4$)Fe($C_5H_4CONHCH_3$)] (1.40 g, 3.9 mmol) was suspended in ethyl acetate (30 mL). HCl gas was bubbled into the solution cooling in ice bath. After stirring for 1 h, orange powder was deposited. Excess HCl gas was removed under reduced pressure. The precipitate was collected with filtration, washed with diethyl ether, and dried in vacuo to give orange powder in a quantitative yield. ^{1}H NMR (Me_2SO-*d*$_6$) δ 2.71 (s, 3H), 4.15 (t, 2H), 4.41 (t, 2H), 4.47 (t, 2H) 4.86 (t, 2H), 8.01 (br, 1H), 6.03 (br, 1H), 9.06 (br, 3H).

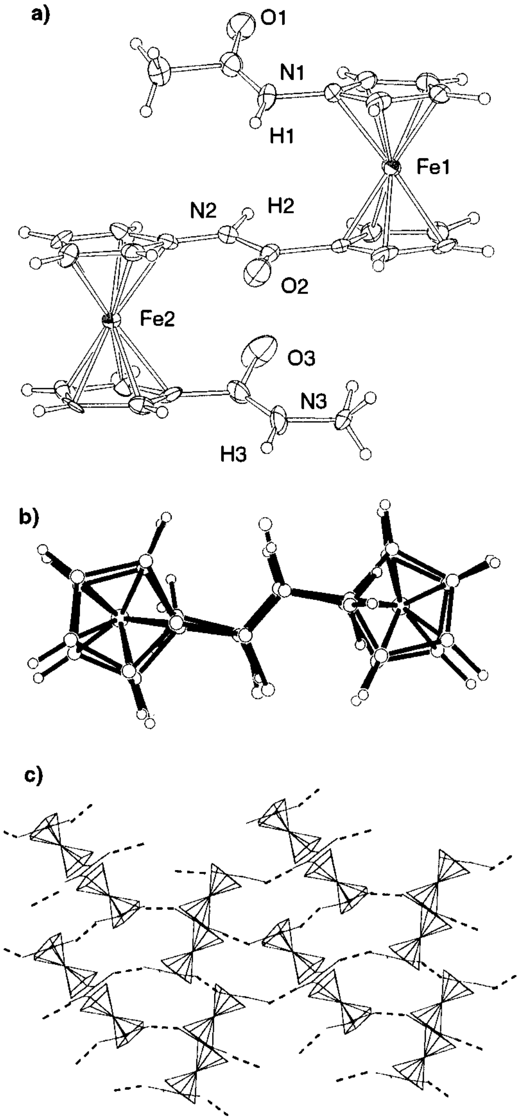

Figure 2. (a) ORTEP drawing of [($CH_3CONHC_5H_4$)Fe(C_5H_4-$CONHC_5H_4$)Fe($C_5H_4CONHCH_3$)] (**7**). (b) Top view of the molecule **7**. (c) Intermolecular hydrogen bonds of **7** in the crystal.

[($CH_3CONHC_5H_4$)Fe($C_5H_4CONHC_5H_4$)Fe($C_5H_4CONHCH_3$)] (7). The compounds [($CH_3CONHC_5H_4$)Fe(C_5H_4COOBt)] (**3**) (0.90 g, 1.96 mmol) and [($HCl\cdot NH_2C_5H_4$)Fe($C_5H_4CONHCH_3$)] (**6**·HCl) (0.58 g, 1.97 mmol) were dissolved in *N*,*N*-dimethylformamide (DMF) (3 mL). Triethylamine (0.4 mL) was added to the solution at 0 °C. After stirring overnight, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in a mixture of dichloromethane and water, the organic layer was washed with 4% $NaHCO_3$ (aq), 2% HCl (aq), and saturated NaCl (aq), dried over $MgSO_4$, and evaporated to dryness. The crude product was recrystallized from propionitrile to give orange crystals. Yield 0.60 g (80%). ^{1}H NMR (chloroform-*d*$_1$) δ 2.00 (s, 3H), 2.88 (t, 3H), 4.12 (m, 4H), 4.38 (t, 2H), 4.50 (t, 2H), 4.62 (m, 4H), 4.81 (t, 2H), 6.34 (br, 1H), 7.36 (br, 1H), 8.33 (br, 1H). Anal. Calcd for $C_{25}H_{25}Fe_2N_3O_3$: C, 56.96; H, 4.78; N, 7.97. Found: C, 56.32; H, 5.23; N, 7.59.

***N*-Methylcarbamoylferrocene, [(C_5H_5)Fe($C_5H_4CONHCH_3$)].** Methylamine hydrochloride was dissolved in a mixture of water (5 mL) and THF (5 mL), and NEt_3 (5.8 mL) was added to the solution. This solution was added to the THF solution (5 mL) of chlorocarbo-

Table 2. Selected Bond Distances (Å) and Dihedral Angles (deg) of [$(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)$] (**5**) and [$(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)$]·$^1/_2$EtCN (**7**)

5		7	
Fe1−C (mean, C11−C15)	2.02	Fe1−C (mean, C11−C15)	2.05
Fe1−C (mean, C21−C25)	2.02	Fe1−C (mean, C21−C25)	2.03
		Fe2−C (mean, C31−C35)	2.04
		Fe2−C (mean, C41−C45)	2.03
O1−C16−N1−C11	0(1)	O1−C16−N1−C11	5(3)
O2−C26−N2−C27	2(2)	O2−C36−N2−C31	−10(2)
		O2−C26−N2−C21	−8.7
		O3−C46−N3−C41	9.7
Cp1(C11−15) − Cp2(C21−25)[a]	1.84	Cp1(C11−15)−Cp2(C21−25)	2.55
		Cp2(C21−25)−Cp3(C31−35)	1.31
		Cp3(C31−35)−Cp4(C41−45)	2.00
Cp1−(N1O1C16)[b]	12.79	Cp1−(N1O1C16)	27.76
Cp2−(N2O2C26)	21.62	Cp2−(N2O2C26)	9.46
		Cp3−(N2O2C26)	10.56
		Cp4−(N3O3C46)	28.38
(N1O1C16)−(N2O2C26)	12.51	(N1O1C16)−(N2O2C26)	18.36
		(N2O2C26)−(N3O3C46)	23.29
		(N3O3C46)−(N1O1C16)	12.26
N1−O2	2.85(1)	N1−O3	2.74(2)
N2−O1	2.87(1)	N2−O1	2.90(2)
		N3−O2	2.80(2)
H1•••O2	1.89	H1•••O3	1.84
H2•••O1	1.95	H2•••O1	1.90
		H3•••O2	1.88

[a] Cp1(C11−15) indicates the least-squares plane called as Cp1 determned by five atoms, C11−C15. [b] (N1O1C16) indicates the amide plane determined by three atoms, N1, O1, and C16.

nylferrocene[30] (1.0 g, 4.0 mmol) with vigorous stirring. After overnight, the red solution changed to orange. After removal of the solvents, the residual solid was washed with water and dried over P_2O_5. The crude product was recrystallized from ethyl acetate. Yield 0.65 g (66%). ^{1}H NMR (chloroform-d_1) δ 2.94 (s, 3H), 4.20 (s, 5H), 4.32 (t, 2H), 4.64 (t, 2H), 5.63 (br, 1H). Anal. Calcd for $C_{12}H_{13}NOFe$: C, 59.29; H, 5.39; N, 5.76. Found: C, 59.22; H, 5.39; N, 5.73.

Physical Measurements. The ^{1}H NMR spectra were measured on a JEOL GSX-400 or a Varian UNITYplus 600 MHz spectrometer. Data processing of NOESY spectrum was performed using Felix 95.0 (Molecular Simulation Inc., San Diego, CA). Distances were estimated by the volume integration of cross-peaks. The cross-peak between neighboring protons on the Cp ring was used as a standard (2.5 Å). IR spectra were recorded on a Jasco FT/IR-8300 spectrometer. Samples were prepared as CH_2Cl_2 solution or Nujol mull. Electrochemical measurements were carried out on a BAS 100B/W using three electrode method. The sample was prepared as 2.5 mM CH_2Cl_2 solution including 0.2 M tetra-*n*-butylammonium perchlorate as a supporting electrolyte. The scan rate was 100 mV/s, and the $E_{1/2}$ value was referenced to the SCE electrode at room temperature.

X-ray Structure and Determination. Suitable single crystals of [$(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)$] (**5**) and [$(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)$] (**7**) were sealed in a glass capillaries under argon atmosphere. X-ray measurements were made at 23 °C on a Rigaku AFC5R diffractometer with graphite monochromated Mo Kα radiation (0.710 69 Å) using $\omega-2\theta$ scan up to $2\theta_{max} = 55°$. Unit cell dimensions were refined with 25 reflections. The basic crystallographic parameters are listed in Table 1. Three standard reflections were chosen and monitored with every 150 reflections and did not show any significant change. The structures were solved by the direct method (SHELXS86)[31] using the teXsan crystallographic software package of the Molecular Structure Corp. The non-hydrogen atoms except those of propionitrile molecule were refined anisotropically. Hydrogen atoms were placed on the calculated positions. During the refinement for **7**, the difference Fourier map showed the presence of propionitrile molecules but its position was highly disordered. Thus we used rigid group refinement for the propionitrile molecule (≡C−C = 1.47 Å, C−C = 1.53 Å, C≡N = 1.16 Å, C−H = 1.11 Å, C−C−H = 109.5°, C−C≡N = 180°). The final refinement was carried out using full-matrix least-squares techniques with non-hydrogen atoms. The final difference Fourier map showed no significant features. Atom scattering factors and dispersion corrections were taken from the *International Tables*.[32]

Results and Discussion

The synthetic route is shown in Scheme 1. The successful introduction of a carboxyl group to acetylaminoferrocene[29] was performed using 2,6-dichlorobenzoyl chloride.[33,34] The amino acid **2** was isolated as HCl salt which is reasonably stable in acidic condition. At pH > 7, the complex **2** immediately decomposes to deposit black precipitates through the dissociation of the ligands. Thus, the N-terminal protection by the Boc (*t*-butoxycarbonyl) group was carried out in phosphate buffer at pH ∼ 7. The active ester is stable enough to be purified by column chromatography and isolated as a pure product.

The molecular structures of [$(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)$] (**5**) and [$(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)$] (**7**) are shown in Figure 1a and Figure 2a, respectively. Selected dihedral angles and selected bond distances of **5** and **7** are listed in Table 2. The skeletal ferrocenes are found to have ordinary Fe−C bond distances. The dihedral angles indicate the coplanarity of amides and Cp rings. The three amide planes are stacked each other to cancel the amide dipole moments (Figures 1b and 2b). Significantly short intermolecular N•••O and NH•••O═C distances shown in Table 2 clearly indicate that all amide groups are intermolecularly NH•

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(30) Pauson, P. L.; Watts, W. E. *J. Chem. Soc.* **1963**, 2990−2997.

(31) Scheldrick, G. M. *Crystallographic Computing 3*; Oxford University Press:, 1985.

(32) Cromer, D. T. *International Tables for X-ray Crystallography*; The Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2A.

(33) Derenberg, M.; Hodge, P. *Tetrahedron Lett.* **1971**, *41*, 3835−3828.

(34) Reeves, P. C. *Org. Synth.* **1977**, *56*, 28−31.

Table 3. IR Spectral Data for Ferrocene Derivatives in the Solid State (Nujol Mull)

	ν(NH)/cm^{-1}			ν(C=O)/cm^{-1}		
	CH_3CO**NH**−	CH_3**NH**CO−	bridge **NH**	CH_3**CO**NH−	CH_3NH**CO**−	bridge **C=O**
$[(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**5**)	3281	3338	–	1667	1637	–
$[(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**7**)	3263	3330	3213	1675	1648	1635
$[(C_5H_5)Fe(C_5H_4NHCOCH_3)]$	3260, 3213[a]	–	–	1654	–	–
$[(C_5H_5)Fe(C_5H_4CONHCH_3)]$	–	3299	–	–	1631	–

[a] Two unequivalent molecules are present in the unit cell.

Table 4. Chemical Shifts (ppm) of Amide Protons for Ferrocene Derivatives in Dichlorimethane-d_2 at 303 K

	δ (NH)/ppm[a]
$[(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**5**)	6.24 (c) 7.30 (a)
$[(CH_3CONHC_5H_4)Fe(C_5H_4CONH)Fe(C_5H_4CONHCH_3)]$ (**7**)	6.34 (c) 7.36 (a) 8.33 (b)
$[(C_5H_5)Fe(C_5H_4CONHCH_3)]$	5.62
$[(C_5H_5)Fe(C_5H_4NHCOCH_3)]$	6.52

[a] Chemical shift from TMS. Characters in the parenthesis indicate the position of amide proton: (a) acetylamino group, (b) bridging amide group, and (c) *N*-methyl carbamoyl group.

••O=C hydrogen bonded in the crystal forming an effective hydrogen bond network (Figure 1c and 2c). Crystallographically distinguishable hydrogen bonded amides, two kinds for **5** and three for **7**, are also detected by the IR spectra (Table 3, Figure S1). The N- and C-terminal and bridging amide NHs are assignable on the basis of the ν(NH) bands of the analogous compounds, $[(C_5H_5)Fe(C_5H_4NHCOCH_3)]$ and $[(C_5H_5)Fe(C_5H_4CONHCH_3)]$. The value of ν(NH), i.e., the strength of NH bond is considered to reflect the acidity of amide NH. The adjacent ferrocenyl group contributes to the increase of acidity of NH resulting in the strong hydrogen bond formation.

When the complexes **5** and **7** were dissolved in nonpolar solvent such as dichloromethane or chloroform, they form *intramolecular* hydrogen bond as detected by IR and ^{1}H NMR spectroscopic analysis. The IR spectra of **5** and **7** in a dilute dichloromethane solution (<2 mM) are shown in Figure 3. Under the same condition, $[(C_5H_5)Fe(C_5H_4NHCOCH_3)]$ and $[(C_5H_5)Fe(C_5H_4CONHCH_3)]$ show *only free* ν(NH) and ν(C=O) bands, i.e., the former exhibits ν(NH) at 3432 and ν(C=O) at 1687 cm^{-1} and the latter does at 3466 and 1659 cm^{-1}. The complex **5** exhibits two free ν(NH) bands at 3459 and 3431 cm^{-1} and two broad hydrogen bonded ν(NH) bands at 3339 and 3272 cm^{-1}. ^{1}H NMR spectrum of **5** in dichloromethane-d_2 indicates amide NH signals at 6.24 and 7.30 ppm (Table 4, Figure S2). These signals are at the lower field than those of $[(C_5H_5)Fe(C_5H_4NHCOCH_3)]$ (6.45 ppm) and $[(C_5H_5)Fe(C_5H_4CONHCH_3)]$ (5.63 ppm). This low-field shift supports the presence of NH•••O=C hydrogen bonds. The NOESY spectrum of **5** shows the correlation peaks between the two methyl groups (Figure S2). Spectral analysis based on the volume integration of the cross-peaks revealed that the two amide planes are stacked each other in dichloromethane-d_2 (Figure 4). Even in polar solvents, e.g., Me_2SO-d_6, the cross-peak between the two methyl groups was detected (not shown).

To explain these results, we present here the conformational change as shown in Figure 5a. In the crystal, two amide planes are in antiparallel orientation to minimize total dipole moments and form *intermolecular* hydrogen bonds to realize the most stable conformation. In a dilute solution, however, the molecule is unable to form the *intermolecular* hydrogen bonds for the stabilization. Two conformers **A** and **B** forming the *intramolecular* hydrogen bonds are thus the most stable ones in solution. Any intermediate between the two conformers was not detected by spectral measurements. The observed two free ν(NH) bands at 3459 and 3431 cm^{-1} are assignable to free NH of **B** and **A**, respectively. The peaks at 3339 and 3272 cm^{-1} are hydrogen bonded ν(NH) of **A** and **B**, respectively. Two distinct C=O stretching bands are found at 1681 (CH_3**CO**NH-) and 1649 cm^{-1} (CH_3NH**CO**-) but two conformers are indistinguishable by the IR data.

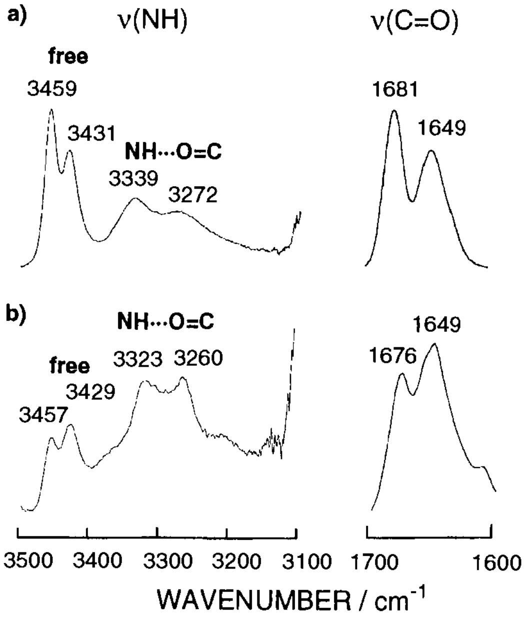

Figure 3. IR spectra (amide region) of (a) $[(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**5**) and (b) $[(CH_3CONHC_5H_4)Fe(C_5H_4CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**7**) in CH_2Cl_2 solution.

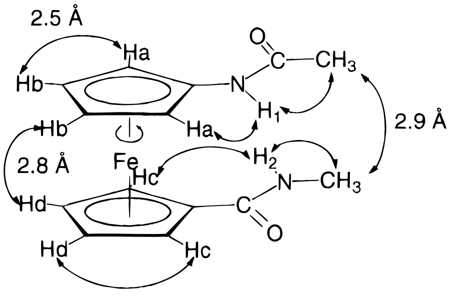

Figure 4. Estimated distances of $[(CH_3CONHC_5H_4)Fe(C_5H_4CONHCH_3)]$ (**5**) in 10 mM CD_2Cl_2 solution at 303 K. Observed NOE interactions are indicated by arrows.

The complex **7** exhibits two free ν(NH) bands at 3457 and 3429 cm^{-1} and two broad hydrogen-bonded ν(NH) bands at 3323 and 3260 cm^{-1} (Figure 3b). In the same manner as described above, these two free ν(NH) bands are considered to be assignable to two individual terminal amide NHs of each hydrogen bond chain of the two conformers (Figure 5b). The intensity of individual stretching bands indicates the validity

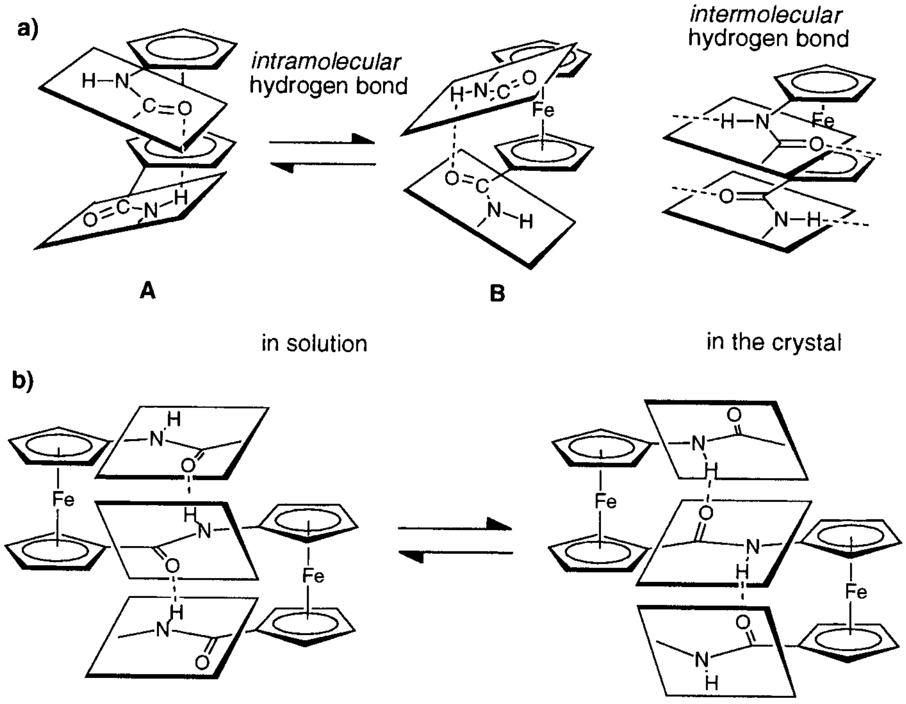

Figure 5. Proposed flapping structures of (a) **5** and (b) **7** which form intramolecular NH···O=C hydrogen bonds in solution.

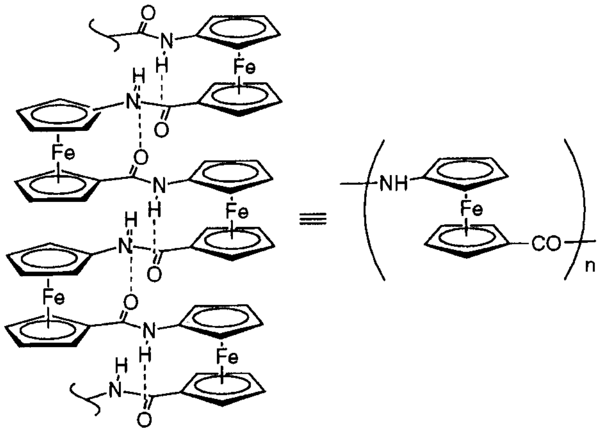

Figure 6. Proposed structure of the nonnatural organometallic polypeptide having skeletal ferrocenes.

of our assignments. The intensity ratio of free to hydrogen bonded ν(NH) is approximately 1:1 for **5** and 1:2 for **7**. The each ratio can be explained by assuming the presence of equal amounts of the two conformers shown in Figure 5.

The ^{1}H NMR spectrum of **7** in chloroform-d_1 indicates three amide NH signals at 8.33, 7.36, and 6.34 ppm that are assignable to bridged amide NH, acetylamino (CH_3CON**H**-) NH and *N*-methyl carbamoyl (CH_3N**H**CO-) NH, respectively. These results indicate the presence of intramolecular NH···O=C hydrogen bond as illustrated in Figure 5b. Since the bridging amide NH always forms intramolecular hydrogen bond during the conformational change, the peak was found at the lowest field. The other NH signals at moderately low field reflect an averaged situation with or without such hydrogen bonding. The conformational change between the two isomers is too fast to be detected as the distinct signals by ^{1}H NMR. However, it is slow enough to be detected by IR.

The dimeric complex **7** exhibits individual Fe(III)/ Fe(II) redox couples at +0.47 and +0.60 V vs SCE in CH_2Cl_2. The averaged value (+0.54 V) is close to that of the corresponding monomeric complex **5** (+0.51 V). These results are explained by the electronic effect as reported in the literature.[35]

The unique and appealing conformations led us to propose a unique structure for a novel organometallic nonnatural polypeptide with skeletal ferrocenes as shown in Figure 6. The folding structure reminds us of the secondary structures such as α-helix and *β*-sheet of polypeptides.

Supporting Information Available: IR spectra of **5** and **7** in the solid state (Figure S1) and 1D ^{1}H NMR and NOESY spectra of **5** (Figure S2) are available (2 pages). The X-ray crystallographic files, in CIF format, for **5** and **7**·1/2(EtCN) are available on the Internet only. Ordering and access information is given on any current masthead page.

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(35) Lu, S.; Strelets, V. V.; Ryan, M. F.; Pietro, W. J.; Lever, A. B. P. *Inorg. Chem.* **1996**, *35*, 1013−1023.