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Hydrogen-bonding-directed molecular assembly of ferrocene bearing dipeptide chains (-L-Ala-L-Pro-NHPyMe) as an organometallic crystal architecture

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Abstract

The ferrocene **1** bearing the dipeptide chains, -L-Ala-L-Pro-NHPyMe, which was characterized by two intramolecular interchain hydrogen bondings between CO (Ala) and NH (another Ala) of each dipeptide chain to induce the chirality organized structure, was demonstrated to form a 1:2 complex with (1*R*,3*S*)-camphoric acid (**CA**). The single-crystal X-ray structure determination revealed a polymeric cocrystal composed of alternating units of **1** and two **CA**, which are linked by a network of hydrogen bonds to create the double-helical-like hydrogen-bonded molecular arrangement.

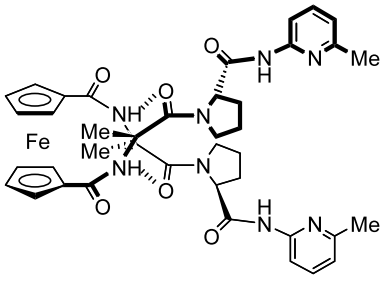
Keywords: Ferrocene; Dipeptide; Hydrogen bond; Chirality organized structure; Cocrystal; Hydrogen-bonded network; Bioorganometallic chemistry

1. Introduction

Solid-state properties are related to molecular arrangement of component molecules. The design of structurally defined molecular arrangement in a solid state is an area of intense current interest as crystal engineering [1]. Architectural control of molecular self-organization is of importance for the development of functional materials [2]. Control of hydrogen bonding has attracted much attention in the design of various molecular assemblies by virtue of the directionality and specificity [3]. In a previous paper, the introduction of amino acid derivatives into the molecular scaffold such as a ferrocene [4], a 2,6-pyridinedicarboxamide [5], and a urea [6], has been demonstrated to permit chirality organization through multiple hydrogen bondings. We herein report hydrogen-bonding-directed molecular assembly of the ferrocene bearing the dipeptide chains, -L-Ala-L-Pro-NHPyMe, with (1*R*,3*S*)-camphoric acid (**CA**).

2. Results and discussion

The ferrocene **1** bearing the dipeptide chains, -L-Ala-L-Pro-NHPyMe, was designed to self-associate with dicarboxylic acid through hydrogen bondings, in which the amide pyridyl moieties serve as binding sites for the carboxyl moieties. Complexation of **1** with two equivalents of dicarboxylic acid is expected to lead to an extended hydrogen bonding network.



1 **CA**

Crystallization of a 1:2 mixture of **1** and **CA** gave the 1:2 complex **1**·(**CA**)$_2$ as orange crystals by slow diffusion

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of hexane into chloroform. The single-crystal X-ray structure determination of **1**·(**CA**)$_2$ revealed a polymeric cocrystal composed of alternating units of **1** and two molecules of **CA**, which are connected by continuous intermolecular hydrogen bonds to form the double-helical-like hydrogen-bonded molecular arrangement (Fig. 1 and Table 1). Each **CA** was found to serve as a hydrogen bonding bridge. One carboxyl moiety of **CA** binds to the amide pyridyl binding site of **1** while another carboxyl moiety of **CA** interacts with the carbonyl group adjacent to the ferrocene unit of another molecule **1**. As a result, each molecule of **1** is bridged by two molecules of **CA** as depicted in Fig. 2. Furthermore, each hydrogen-bonded molecular assembly is linked by face-to-face π–π interactions between pyridyl moieties in a solid state (Fig. 3).

Another interesting feature is that the ferrocene **1** adopted the chirality organized structure based on the formation of two intramolecular hydrogen bondings between CO (Ala) and NH (another Ala) of each podand dipeptide chain (N···O, 2.97 and 2.95 Å) as observed in previously reported ferrocene derivatives [4]. The chirality organized structure of **1** was preserved in spite of complexation with **CA**.

In conclusion, hydrogen-bonding-directed molecular assembly of the chirality organized ferrocene bearing the dipeptide chains, -L-Ala-L-Pro-NHPyMe, was achieved by employing **CA** as a hydrogen bonding bridge to create the double-helical-like hydrogen-bonded molecular arrangement. We are currently investigating how the chirality organized ferrocene scaffold affects the hydrogen-bonding-directed self-organization.

Table 1
Crystallographic data for **1**·(**CA**)$_2$

Empirical formula	$C_{60}H_{78}FeN_8O_{14}\cdot 3CHCl_3$
Molecular weight	1549.30
T (°C)	23
λ(Mo–K$_\alpha$) (Å)	0.71069
Crystal system	Orthorhombic
Space group	$P2_12_12_1$ (No. 19)
a (Å)	21.445 (4)
b (Å)	23.049 (6)
c (Å)	15.358 (3)
V (Å^3)	7590(2)
Z	4
D_{calc} (g cm^{-3})	1.356
μ(Mo–K$_\alpha$) (cm^{-1})	5.78
R_1 [a]	0.094
wR_2 [b]	0.315

[a] $R_1 = \Sigma\ ||F_o| - |F_c||/\Sigma\ |F_o|$.
[b] $wR_2 = [\Sigma\ w(F_o^2 - F_c^2)^2/\Sigma\ w(F_o^2)^2]^{1/2}$.

3. Experimental

All reagents and solvents were purchased from commercial sources and purified by the standard methods, if necessary. Melting points were determined on a Yanagimoto Micromelting Point Apparatus and were uncorrected. IR spectra were obtained with a Perkin–Elmer Model 1605 FT-IR. ^{1}H-NMR spectra were recorded on a Varian MERCURY 300 (300 MHz) spectrometer with Me_4Si as an internal standard. Mass spectra were run on a JEOL JMS-DX303HF mass spectrometer.

H-L-Ala-L-Pro-NHPyMe was prepared with normal method by coupling of Boc-L-Ala-L-Pro-OH with 2-amino-6-methylpyridine using EDCI, followed by removal of the t-butyloxycarbonyl protective group [4].

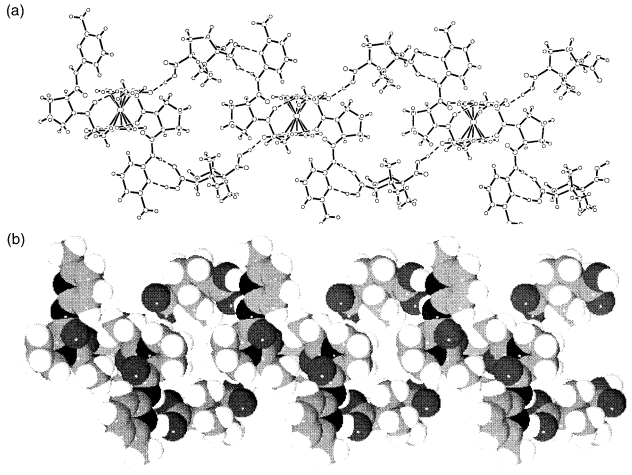

Fig. 1. A portion of a layer containing the double-helical-like hydrogen-bonded molecular assembly in the crystal packing of **1**·(**CA**)$_2$. (a) Ball and stick and (b) space-filling representations.

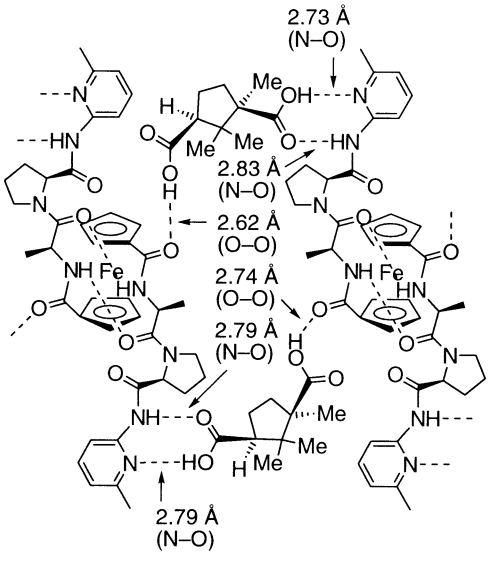

Fig. 2. Schematic representation of the crystal packing of **1**·(**CA**)$_2$.

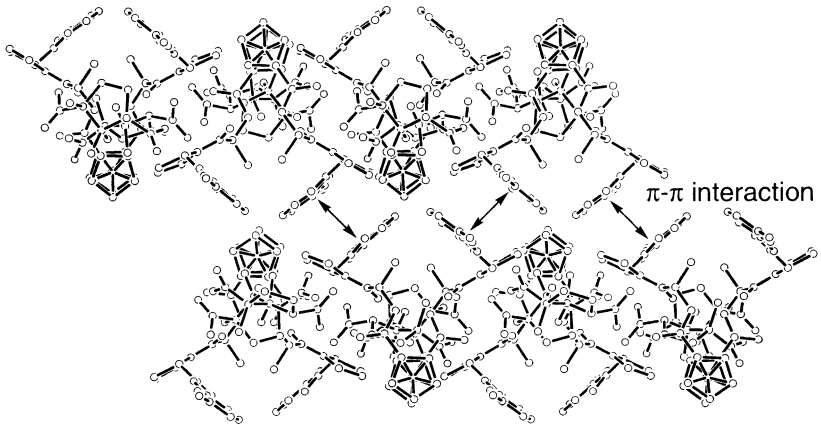

Fig. 3. Projection down the *b* axis of the crystal packing of **1**·(**CA**)$_2$. A hydrogen-bonded network is linked by π–π interactions between the pyridyl moieties.

1,1′-Bis(chlorocarbonyl)ferrocene was prepared according to the literature method [7].

3.1. Synthesis of the ferrocene *1* bearing the dipeptide chain, -L-Ala-L-Pro-NHPyMe

To a stirred mixture of H-L-Ala-L-Pro-NHPyMe (138.2 mg, 0.50 mmol) and Et_3N (348 μl, 2.5 mmol) in CH_2Cl_2 (5 ml) was dropwise added 1,1′-bis(chlorocarbonyl)ferrocene (77.7 mg, 0.25 mmol) in CH_2Cl_2 (5 ml) under Ar at 0 °C. The mixture was stirred at 0 °C for 1 h and then at room temperature for 4 h. The resulting mixture was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ aq. solution and brine, and then dried over Na_2SO_4. The solvent was evaporated in vacuo. Purification was performed by a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns, eluting with $CHCl_3$. The ferrocene **1** was isolated in 70% yield by recrystallization from $CHCl_3$. M.p. 148–150 °C (uncorrected); IR (CH_2Cl_2, 1.0×10^{-3} M): 3399, 3307, 1697, 1634 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$, 5.0×10^{-3} M): δ 8.84 (d, 2H, *J* = 7.2 Hz, N*H* of Ala), 8.78 (s, 2H, N*H*Py), 7.91 (d, 2H, *J* = 8.4 Hz, Py), 7.55 (dd, 2H, *J* = 8.4, 7.5 Hz, Py), 6.87 (d, 2H, *J* = 7.5 Hz, Py), 4.90–4.88 (m, 4H, Cp), 4.86–4.74 (m, 4H, Ala and Pro), 4.54–4.52 (m, 2H, Cp), 4.31–4.29 (m, 2H, Cp), 3.99–3.91 (m, 2H, Pro), 3.71–3.66 (m, 2H, Pro), 2.45–2.11 (m, 8H, Pro), 2.40 (s, 6H, Py*Me*), 1.33 (d, 6H, *J* = 7.2 Hz, Ala); ^{13}C-NMR (100 MHz, $CDCl_3$, 1.0×10^{-2} M): 175.3 (*C*=O of Ala), 170.6 (Cp*C*=O), 169.7 (*C*=O of Pro), 156.9 (Py), 150.4 (Py), 138.4 (Py), 119.3 (Py), 110.7 (Py), 75.4 (Cp), 71.9 (Cp), 71.2 (Cp), 70.2 (Cp), 61.2 (Pro), 47.6 (Ala), 47.3 (Pro), 27.7 (Pro), 25.4 (Pro), 23.9 (Py*Me*), 15.4 (Ala) ppm; MS (FAB): *m*/*z* 791 [$M^+ + 1$]; Anal. Calc. for $C_{40}H_{46}FeN_8O_6 \cdot H_2O$: C, 59.41; H, 5.98; N, 13.86. Found: C, 59.07; H, 5.64; N, 13.47%.

3.2. Preparation of cocrystal of *1*·(*CA*)$_2$

Cocrystal of **1**·(**CA**)$_2$ as orange crystals was obtained by crystallization of the ferrocene bearing the dipeptide chains (-L-Ala-L-Pro-NHPyMe) (**1**) with two equivalents of **CA** by slow diffusion of hexane into $CHCl_3$. Anal. Calc. for $C_{60}H_{78}FeN_8O_{14} \cdot 3CHCl_3$: C, 48.84; H, 5.27; Cl, 20.59; N, 7.23. Found: C, 49.20; H, 5.35; Cl, 20.28; N, 7.39%.

3.3. X-ray structure analysis

All measurements for **1**·(**CA**)$_2$ were made on a Rigaku AFC5R diffractometer with graphite monochromated Mo–K_α radiation. The structure of **1**·(**CA**)$_2$ was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms excluding Cl2, Cl3, Cl7, Cl8, Cl9, and C41 atoms were refined anisotropically. Some of the Cl as well as C atoms in the $CHCl_3$ solvent molecules were tried for modelling the disorder, but a good result was not obtained probably due to the data quality. In this context, Cl2, Cl3, Cl7, Cl8, Cl9, and C41 atoms were refined isotropically. The H atoms involved in hydrogen bonding were located in electron density maps. The remainder of the H atoms were placed in idealized positions and allowed to ride with the C atoms to which each was bonded. Crystallographic details are given in Table 1.

4. Supplementary material

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 188299 for **1**·(**CA**)$_2$. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK

(Fax: +44-1223-336033; email: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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