Supplementary Material (ESI) for Chemical Communications

Decelerated chirality interconversion of an optically inactive 3_{10}-helical peptide by metal chelation

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Electronic supplementary information

1. Measurements

^{1}H NMR spectra were recorded on a JEOL model JNM-A500 (500 MHz) spectrometer, where chemical shifts were determined with respect to tetramethylsilane as internal reference. MALDI-TOF MS spectrum was recorded on an Applied Biosystems model Voyager-DE mass spectrometer using 1,8,9-anthracenetriol matrix and NaI salt for sample preparation. ESI mass spectra were recorded on a Mariner™ ESI-TOF Biospectrometry Workstation.

2. Materials

Synthetic procedure of peptide **1** has been already reported.[7d] Pyridine-3-carboxylic acid (Kanto Chemical Co., INC.) was used without further purification. Coupling reagents such as 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC: Kokusan Chemical Co. Ltd.) and 1-hydroxy-1H-benzotriazole, monohydrate (HOBt: Wako Pure Chemical Industries Ltd) were used without further purification. $Pd(en)(ONO_2)_2$ was purchased from Wako Pure Chemical Industries Ltd., and used without further purification. $Pt(en)(ONO_2)_2$ was prepared according to the literature method.[S1] N,N-diisopropylethylamine (DIEA: Sigma-Aldrich INC.) and 4N solution of HCl in 1,4-dioxane (Kokusan Chemical Co. Ltd.) were used without further purification. N,N-dimethylformamide (DMF) was obtained as dehydrated-grade reagents from Wako Pure Chemical Industries Ltd.

3. Synthesis of 2

2: To a solution of pyridine-3-carboxylic acid (38 mg, 0.31 mmol), HOBt (57 mg, 0.37 mmol), EDC (59 mg, 0.31 mmol), and Cbz-[Aib_2-Api(HCl)]$_2$-Aib_2-OMe (0.089 mmol) [obtained by treatment of **1** (100 mg, 0.089 mmol) with 4N solution of HCl in 1,4-dioxane] in DMF (1 mL) at 0 °C, DIEA (71 μL, 0.44 mmol) was added. The reaction mixture was stirred at 0 °C for 3 h, and at room temperature for 4 days. Then, the solution was evaporated to dryness under reduced pressure. The residue was purified by a column chromatography on silica gel (chloroform/methanol = 9/1), and size-exclusion column chromatography in DMF. Then, recrystallization from ethyl acetate/hexane provided peptide **2** (74 mg, 73 %) as a white solid. ^{1}H NMR (500 MHz, CD_3CN, 20 °C): δ = 8.62 (bs, 1H), 8.57 (m, 3H), 7.87 (bs, 1H), 7.72 (m, 2H), 7.62 (s+s, 2H), 7.59 (bs, 1H), 7.53 (s, 1H), 7.43 (s, 1H), 7.41-7.31 (m+m, 7H), 7.18 (s, 1H), 6.50 (s, 1H), 5.13 (s, 2H), 4.45 (bs, 1H), 4.34 (bs, 1H), 3.58 (s, 3H), 3.55 (bs, 1H), 3.46 (bs, 1H), 3.31+3.10 (bs+bs, 2H), 2.85 (bs, 1H), 2.20-1.89 (closely overlapping with H_2O and solvent), 1.44+1.41+1.39+1.39 (s+s+s+s, 36H, partially overlapping). MALDI-TOF-MS: $[M+Na]^+$ (calcd. 1161.57): found. 1160.89.

4. Additional Spectroscopic Data and Energy-Minimized Structure of 2.

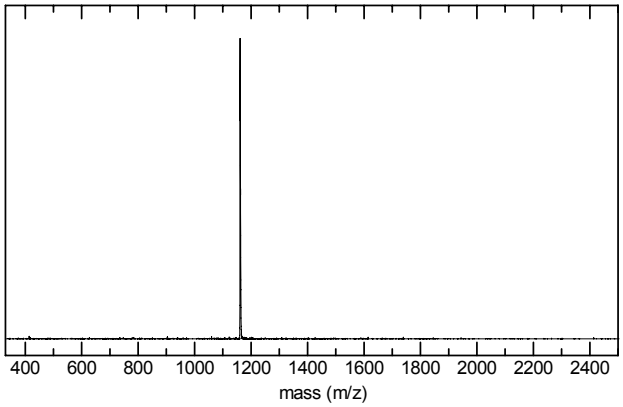

Fig. S1 MALDI-TOF mass spectrum of **2**.

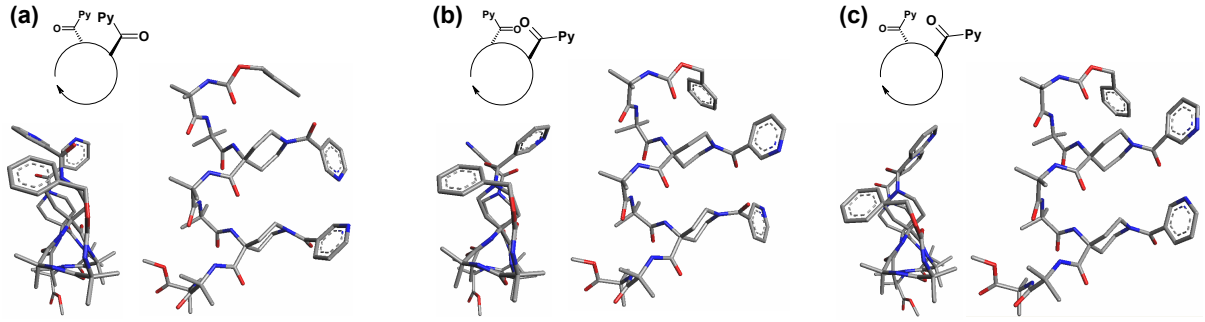

Fig. S2 Side (left) and top (right) views of right-handed **2** [type I (a), III (b), and IV (c)] energy-minimized by the semi-empirical MO calculation (PM 6 method[14]).[17] Hydrogen atoms are omitted for clarity. The schematic representations indicate the side-chain orientations of amide carbonyl.

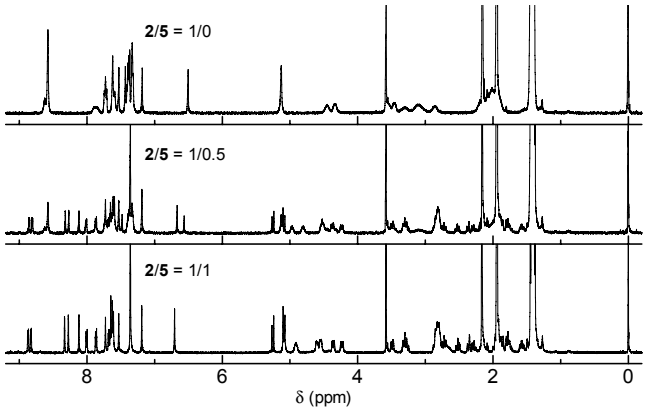

Fig. S3 ^{1}H NMR monitored titration of **2** with **5** in CD_3CN at 20 °C. Initial concentration of **2** is set to 4.8 mM (2.7 mg/500 μL). A desired amount of the CD_3CN solution of **2** (3.1 mg/400 μL) was directly added to the NMR tube. After titration of **5**, final peptide concentration is 4.0 mM.

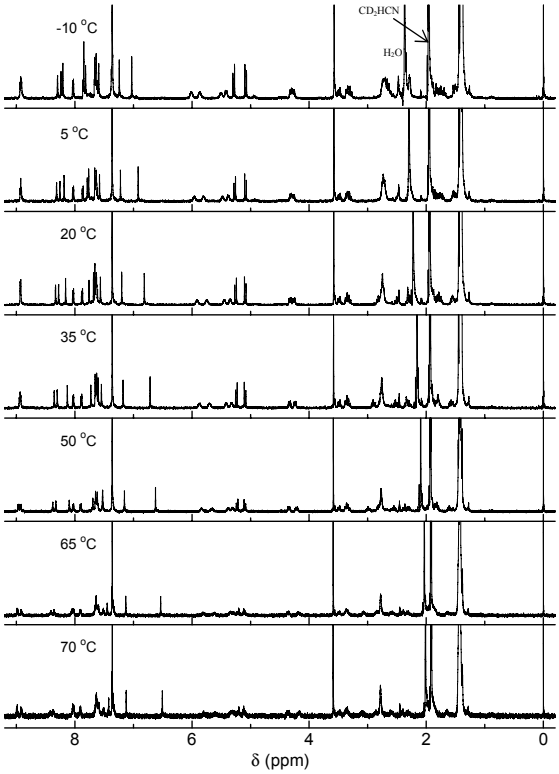

Fig. S4 Variable temperature ^{1}H NMR spectra of **4** in CD_3CN/DMSO-d_6 (100/1; v/v); [**4**] = 3.5 mM. The complex **4** was obtained by the following procedure; a 1:1 mixture of **2** (4.0 mg, 3.5 μmol) and [Pt(en)$(ONO_2)_2$] (1.3 mg, 3.5 μmol) in CD_3CN/DMSO-d_6 (1.0 mL/10 μL; v/v) was heated at 55−60 °C for overnight.

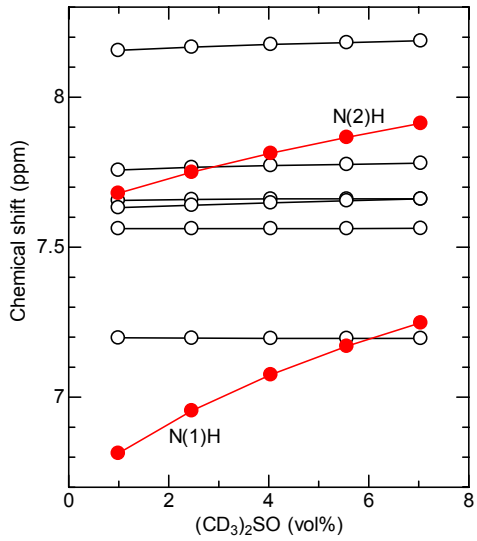

Fig. S5 Solvent dependence on NH chemical shifts of peptides **4** in CD_3CN/DMSO-d_6 mixture at 20 °C in 500 MHz ^{1}H NMR spectra.

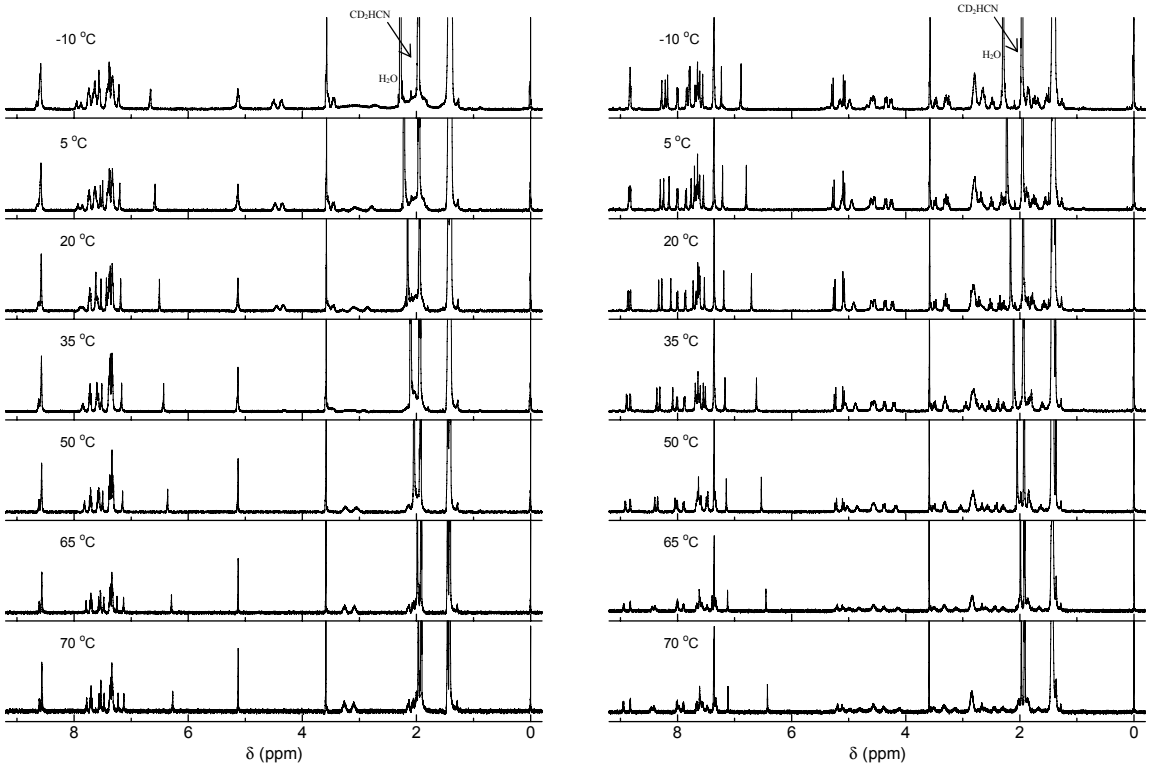

Fig. S6 Wide-range variable temperature ^{1}H NMR spectra of **2** (left) and **3** (right) in CD_3CN. These spectra correspond to Fig. 3.

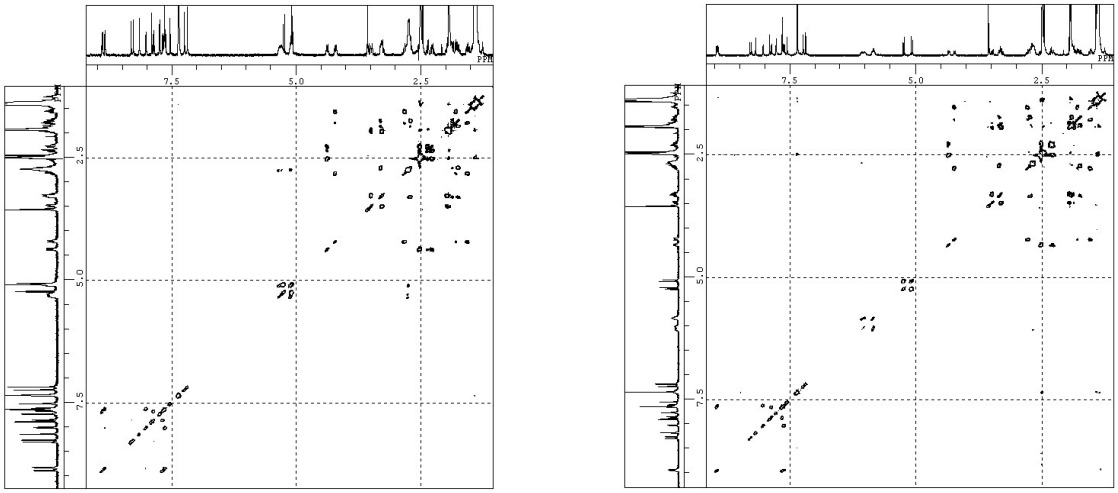

Fig. S7 ^{1}H-^{1}H COSY (500 MHz) spectra of **3** (left) and **4** (right) in $CDCN_3$/DMSO-d_6 (DMSO-d_6 = 7 vol%) at 20 °C.

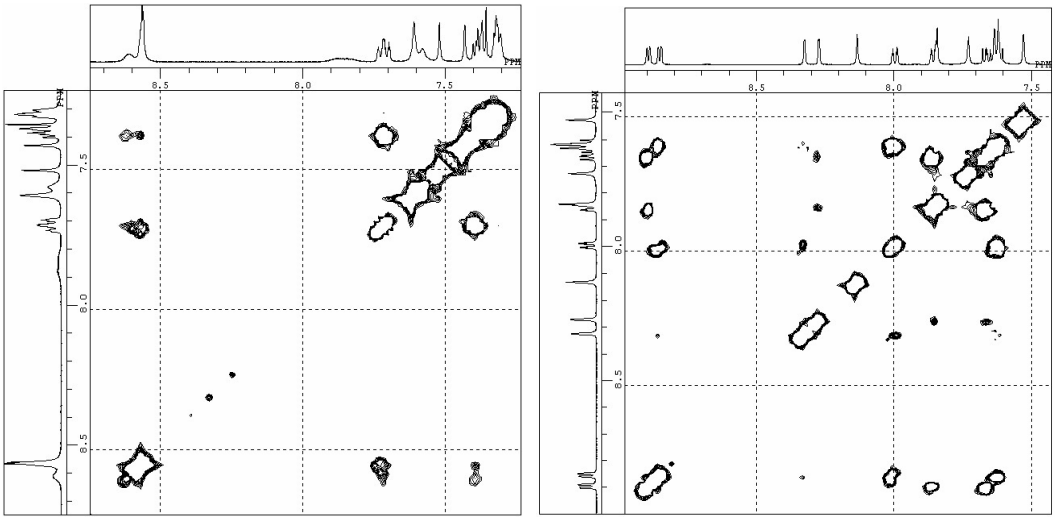

Fig. S8 Expanded TOCSY (500 MHz) spectrum of **2** (left) in CD_3CN and **3** (right) in $CDCN_3$/DMSO-d_6 (DMSO-d_6 = 4 vol%) for 3 at room temperature; [**2**] = 6.0 mM, [**3**] = 9.6 mM.

5. Reference

(S1) F. Basolo, J. C. Bailar and B. R. Tarr, *J. Am. Chem. Soc*., 1950, **72**, 2433.