Electronic Supplementary Information

Heterogeneous Assembly of Silver(I) and Calcium(II) Ions Accompanying a Dimer Formation of cyclo(l-Ala-l-Met)₃
Tomoko Okada,¹ Kentaro Tanaka,ᵃᵇ Motoo Shiro,ᶜ and Mitsuhiko Shionoya,ᵃ*¹

¹ Department of Chemistry, Graduate School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan. Fax: +81 3 5841 8061; Tel: +81 3 5841 8061; E-mail: shionoya@chem.s.u-tokyo.ac.jp
ᵇ PRESTO, Japan Science and Technology Agency (JST), Japan
ᶜ Rigaku Corporation, 3-9-12 Matsubaracho, Akishima, Tokyo 196-8666, Japan

General: NMR spectra were recorded on a Bruker DRX 500 (500 MHz for ¹H; 125 MHz for ¹³C) spectrometer and the spectra were referenced to tetramethylsilane. Electrospray ionization-time-of-flight (ESI-TOF) mass spectra were recorded on a Micromass-LCT spectrometer. Linear peptides were prepared by the standard Fmoc chemistry on an Applied Biosystems peptide synthesizer (Model 433A). Fmoc-l-Ala-OH, Fmoc-l-Met-OH and Wang resin were obtained from Watanabe Chemical Industries. 1-Ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC·HCl) and N-methylmorpholine (NMM) were purchased from TCI, and 1-hydroxy-1H-benzotriazole monohydrate (HOBt) was obtained from Dojindo. Ag(CF₃SO₃) and Ca(CF₃SO₃)₂ were purchased from Aldrich.

Linear hexapeptide, H₂-(l-Ala-l-Met)₃-OH(CF₃CO₂): The resins of linear hexapeptide, H-(l-Ala-l-Met)₃-OH, were prepared on the peptide synthesizer via FastMoc (HBTU/HOBt, 0.25 mmol scale) based methods. The obtained on-resin peptide was treated with trifluoroacetic acid (TFA) for 30 min at room temperature to cleave the peptide from the resins. The product was precipitated when the TFA solution was poured into ice-cooled diethyl ether (40 mL). The resulting colorless precipitation was collected by centrifugation and washed with diethyl ether (40 mL) twice. The precipitate was dissolved into CH₂OH and then the solution was evaporated and dried under vacuo to obtain colorless solid (84 mg, 46%). ¹H NMR (CD₃OD, 500 MHz): δ = 4.55 (dd, J = 4.0, 9.0 Hz, 1H; CH(Met)), 4.50 (dd, J = 5.0, 8.5 Hz, 1H; CH(Met)), 4.45 (dd, J = 8.5, 11.0 Hz, 1H; CH(Met)), 4.36 (q, J = 5.5 Hz, 1H;
Cyclic hexapeptide (1), cyclo(l-Ala-l-Met)₃: To a solution of H₂-(l-Ala-l-Met)₃-OH·(CF₃CO₂) (63 mg, 85 mmol) in CH₂Cl₂/MeOH (8:9, 0.2 mM in concentration) were added NMM (90 mL, 940 mmol, 11 equiv), EDC·HCl (162 mg, 850 mmol, 10 equiv) and HOBt (13 mg, 85 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature for 31 h and then the resulting pale yellow solution was evaporated to dryness. The crude product was purified by silica gel column chromatography (Merck silica gel 60, eluent: CHCl₃/MeOH 30:1–20:1) (20 mg, 38%). ¹H NMR (CD₃OD, 500 MHz): δ = 4.31 (dd, J = 5.0, 9.0 Hz, 3H; CH(Met)), 4.22 (q, J = 7.0 Hz, 3H; CH(Ala)), 4.16 (q, J = 7.5 Hz, 3H; CH(Ala)), 3.90 (dd, J = 4.0, 12.0 Hz, 3H; SCH₂CHH (Met)), 2.25 – 2.18 (m, 3H; SCH₂CH₂ (Met)), 2.14 – 2.05 (m, 3H; SCH₂CHH (Met)), 2.09 (s, 9H; SCH₃) 1.43 ppm (d, J = 7.1 Hz, 9H; C₃H₃); ¹³C NMR (CD₃OD, 125 MHz): δ = 173.1, 171.8, 53.3, 50.2, 30.1, 29.7, 16.1, 13.8 ppm; HRMS: m/z: exact mass 629.220 [M + Na]⁺.

Preparation of [Ag₃Ca₁₂](CF₃CO₂)₅ (2), for NMR studies: Ag(CF₃SO₃) (0.64 mg, 2.5 mmol) and Ca(CF₃SO₃)₂ (0.28 mg, 0.82 mmol) were added to a solution of cyclo(l-Ala-l-Met)₃ (1) (1.0 mg, 1.6 mmol) in acetone-d₆/CD₃OD (5:1, 0.40 mL), and the mixture was left stand at room temperature for 5 min. ¹H NMR (acetone-d₆/CD₃OD (5:1), 500 MHz): δ = 5.56 (dd, J = 3.0, 12.0 Hz, 3H; CH(Met)), 4.22 (q, J = 7.0 Hz, 3H; CH(Ala)), 4.16 (q, J = 7.5 Hz, 3H; CH(Ala)), 3.90 (dd, J = 4.0, 12.0 Hz, 3H;
CH(Met), 3.06 (dd, J = 3.0, 12.0 Hz, 3H; SCHHCH2 (Met)), 2.88 (dd, J = 6.0, 12.0 Hz, 3H; SCHHCH2 (Met)), 2.76 (t, J = 11.5 Hz, 3H; SCH2CHH (Met)), 2.66 – 2.34 (m, 3H; SCH2CHH (Met)), 2.52 (s, 9H; SCH3), 2.49 (s, 9H; SCH3), 1.51 (d, J = 8.0 Hz, 9H; CH3), 1.46 ppm (d, J = 7.5 Hz, 9H; CH3); 13C NMR (acetone-d6/CD3OD (5:1), 125 MHz): δ = 175.57, 175.49, 174.97, 172.85, 55.78, 54.31, 52.75, 34.63, 33.34, 32.65, 18.55, 17.54, 17.19 ppm; ESI-MS: m/z: 1180.9 \([\text{Ag}_3\text{Ca}_2^+ (\text{CF}_3\text{SO}_3)_3]^{2+}\), 2173.3 \([\text{Ag}_3\text{Ca}_2^+ (\text{CF}_3\text{SO}_3)_4]^-\).