

ORGANIC & BIOMOLECULAR CHEMISTRY

Probing the tolerance of cucurbit[7]uril inclusion complexes to small structural changes in the guest

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Synthetic Details

Synthesis of Ferrocenylamine. FcNH₂ was synthesized by adapting the literature procedures,^{1,2} starting from 1-bromoferrocene, which was prepared by reaction of monolithioferrocene and bromine in THF at -80 °C.¹

Under an atmosphere of Ar, a stirred mixture containing 1-bromoferrocene (4 g, 15.2 mmol), freshly distilled and deoxygenated pyridine (27 mL), phthalimide (3.67 g, 24.9 mmol) and Cu₂O (1.07 g, 7.48 mmol), was heated under reflux for 48 hours. During this time, the initial red color changed to black. The pyridine was removed in vacuo, and the resulting dark solid was extracted in a Soxhlet apparatus, using diethyl ether as solvent. Solvent removal afforded a red solid, which was recrystallized from hot ethanol. The intermediated product, *N*-ferrocenyl phthalimide, was isolated as dark red crystals. Yield: 4.4 g (87 %). ¹H NMR (CDCl₃): δ 4.20 (m, 2H, C₅H₄), 4.22 (s, 5H, C₅H₅), 5.01 (m, 2H, C₅H₄), 7.74 (m, 2H, C₆H₄), 7.90 (m, 2H, C₆H₄). MS (EI⁺): *m/z* 331.03 [M⁺].

To a suspension of *N*-ferrocenyl phthalimide (2.3 g, 6.95 mmol) in deoxygenated dry ethanol (45 mL), hydrazine monohydrate (15 mL) was added and the resulting mixture was heated under reflux for 4 hours. The reaction mixture was cooled to 0 °C, and deoxygenated water (80 mL) was added. Then, the mixture was extracted several times with diethyl ether, until the organic extract was no longer yellow. The combined ether extracts were dried over anhydrous Na₂SO₄, filtered, and then the solvent was removed in vacuo, to give a yellow solid. Yield: 1.15 g, (82%). C₁₀H₁₁NFe (201.05): calcd. C 59.69, H 5.51, N 6.97; found C 59.64, H 5.46, N 7.07. ¹H NMR (CDCl₃, 300MHz): δ 2.59 (br, 2H, NH₂), 3.85 (m, 2H, C₅H₄), 4.00 (m, 2H, C₅H₄), 4.10 (s, 5H, C₅H₅). IR (KBr): ν(N-H) 3393, 3325 cm⁻¹, ν(C-H) 3077, 2963 cm⁻¹, δ(N-H) 1497 cm⁻¹, δ(C-H) 801 cm⁻¹, ρ(Fe-ring) 483 cm⁻¹. MS (EI⁺): *m/z* 201.02 [M⁺].

Synthesis of ferrocenyltrimethyl ammonium iodide (FcO⁺ I⁻).

Ferrocenylamine (100 mg, 0.50 mmol) was dissolved in 5mL CH₃OH/CHCl₃ (3:1, v/v), followed by filtration through a 0.45-μm syringe membrane filter to remove

any undissolved species. To the resulting filtrate, iodomethane (0.8 mL, 12.9 mmol) and Na₂CO₃ (530 mg, 5.0 mmol) were added, and then the reaction mixture was stirred overnight at room temperature. After filtration, the solvent was removed under vacuum to obtain a brown mixture, followed by two recrystallizations from methanol/chloroform/diethyl ether (1:1:20, v/v/v). The yellowish solid was collected as the final product. Yield: 85.6 mg, (46 %). ESI-HRMS (*m/z*) calcd for [C₁₃H₁₈NFe]⁺: 244.0783, found: 244.0795. ¹H NMR (D₂O, 500 MHz): δ 3.37 (s, 9H), 4.34 (t, 2H), 4.38 (s, 5H), 4.54 (t, 2H). ¹³C NMR (D₂O, 125 MHz, referenced to methanol): δ 58.04, 60.82, 68.67, 71.05.

Synthesis of 2-(Ferrocenyl)ethylamine. Fc(CH₂)₂NH₂ was synthesized in two reaction steps from *N,N,N*-trimethylferrocenylmethyamonium iodide, by adapting the literature procedures.^{3,4}

1-Cyanomethylferrocene, FcCH₂CN,⁴ (5.55 g, 24.4 mmol) in dry diethyl ether (90 mL) was added dropwise to a stirred suspension of LiAlH₄ (1.63 g, 43 mmol) in 100 mL of dry diethyl ether and heated at 35 °C. After being stirred for 3 h under reflux, the reaction mixture was externally cooled with an ice bath, and cold water was slowly added dropwise until H₂ release stopped. Once decanted, the solution was acidified by addition of 6M H₂SO₄. The solid formed was separated by filtration and treated with an 6N NaOH aqueous solution to adjust the pH ~ 11. The dark orange mixture was extracted with diethyl ether, the organic phases were combined, dried (over Na₂CO₃), filtered and the solvent was removed under vacuo. A viscous, brown oil was obtained which was dissolved in *n*-hexane and filtered to remove any solid impurities. Solvent removal afforded Fc(CH₂)₂NH₂ as a viscous oily dark amber-brown product, which can be purified by distillation in vacuo. Yield: 3.7 g (66%). ¹H NMR (CDCl₃, 300MHz): δ 1.30 (br, 2H, NH₂), 2.50 (t, ³*J* = 7.0 Hz, 2H, Fc-CH₂), 2.80 (t, ³*J* = 7.0 Hz, 2H, CH₂-NH₂), 4.07, 4.08 (m, 4H, C₅H₄), 4.10 (s, 5H, C₅H₅). ¹³C NMR (CDCl₃, 75 MHz): δ 34.1 (Fc-CH₂), 43.6 (CH₂-NH₂), 67.4, 68.4, 86.3 (C₅H₄), 68.6 (C₅H₅). IR (CsI): ν(N-H) 3368, 3292 cm⁻¹, ν(C-H) 3091, 2927, 2853 cm⁻¹, δ(N-H) 1587 cm⁻¹, δ(C-H) 818 cm⁻¹, ρ(Fe-ring) 483 cm⁻¹. MS (FAB⁺): *m/z* 229.1 [M⁺].

Synthesis of ferrocenylethyltrimethylammonium iodide (**Fc2⁺I⁻**).

Fc2⁺I⁻ was prepared using a similar procedure to that for **Fc0⁺I⁻**. Yield: 57%. ESI-HRMS (*m/z*) calcd for [C₁₅H₂₂NFe]⁺: 272.1096, found: 272.1113. ¹H NMR (D₂O, 500 MHz): δ 2.78 (t, 2H), 3.03 (s, 9H), 3.37 (t, 2H), 4.11 (s, 2H), 4.13 (s, 7H). ¹³C NMR (D₂O, 125 MHz, referenced to methanol): δ 23.33, 53.59, 67.36, 68.79, 68.91, 69.56.

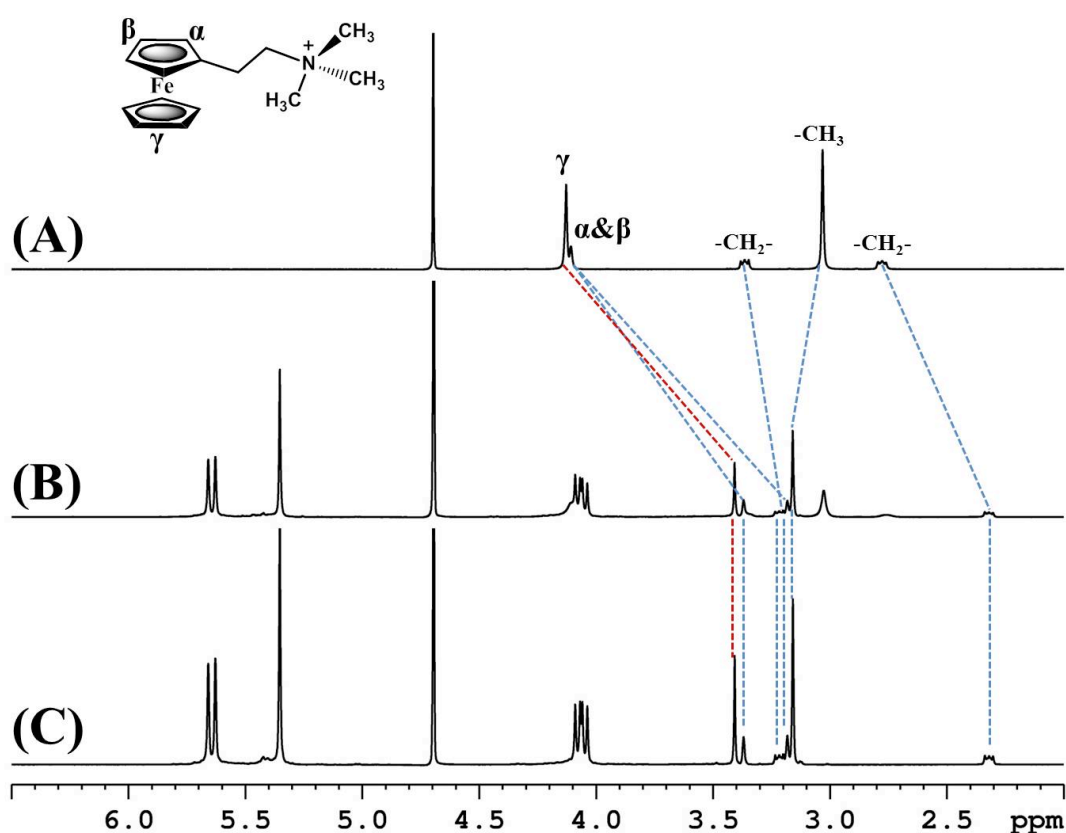


Figure S1. ¹H NMR spectra (500 MHz, D₂O) of 0.5 mM **Fc2⁺** (a) in the absence and in the presence of (b) 0.5 equiv and (c) 1.0 equiv CB7.

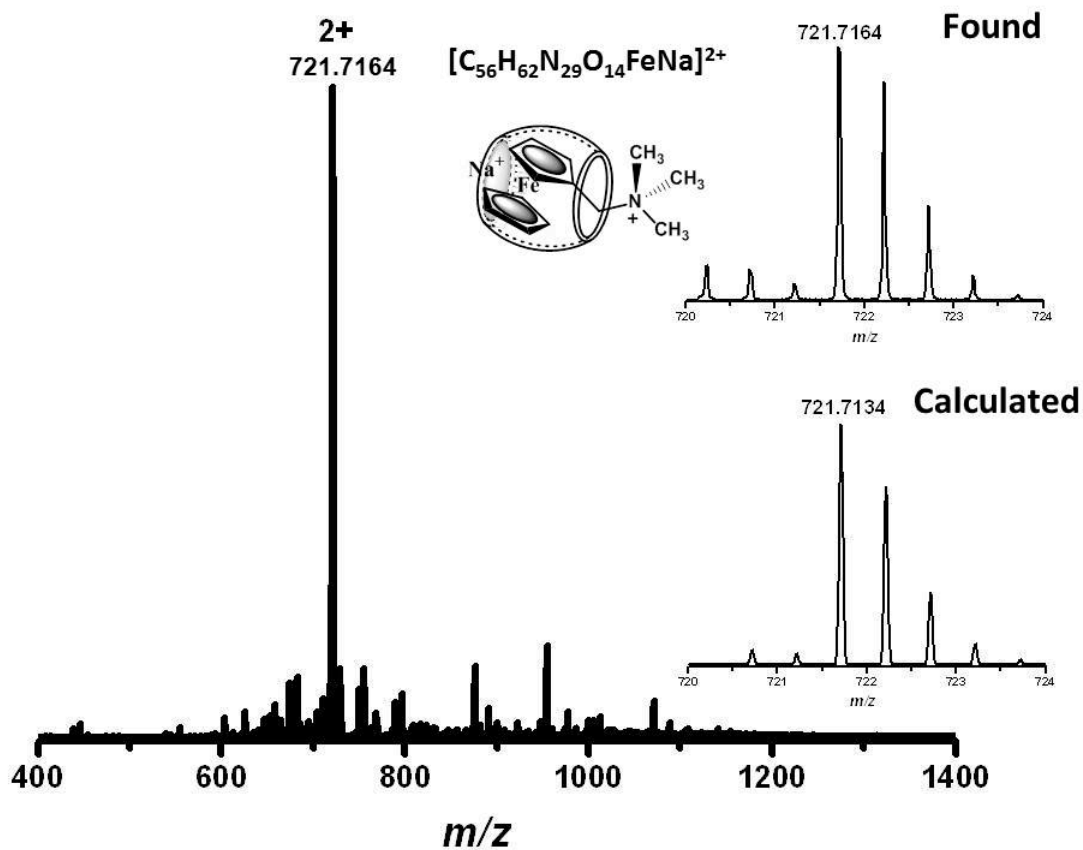


Figure S2. High-resolution ESI-TOF mass spectrum obtained with an aqueous solution containing equal concentrations of **Fc1**⁺ and CB7. The insert shows the experimental (top) and calculated (bottom) isotopic distributions corresponding to the main peak.

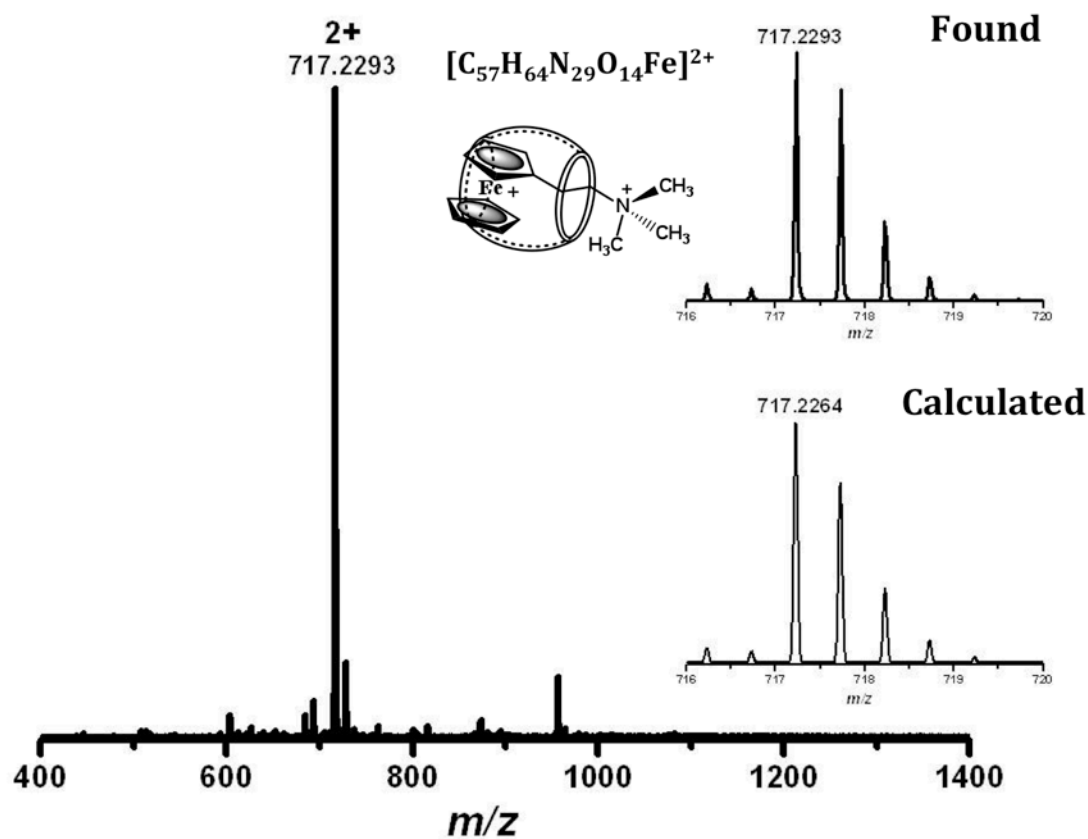


Figure S3. High-resolution ESI-TOF mass spectrum obtained with an aqueous solution containing equal concentrations of **Fc2⁺** and CB7. The insert shows the experimental (top) and calculated (bottom) isotopic distributions corresponding to the main peak.

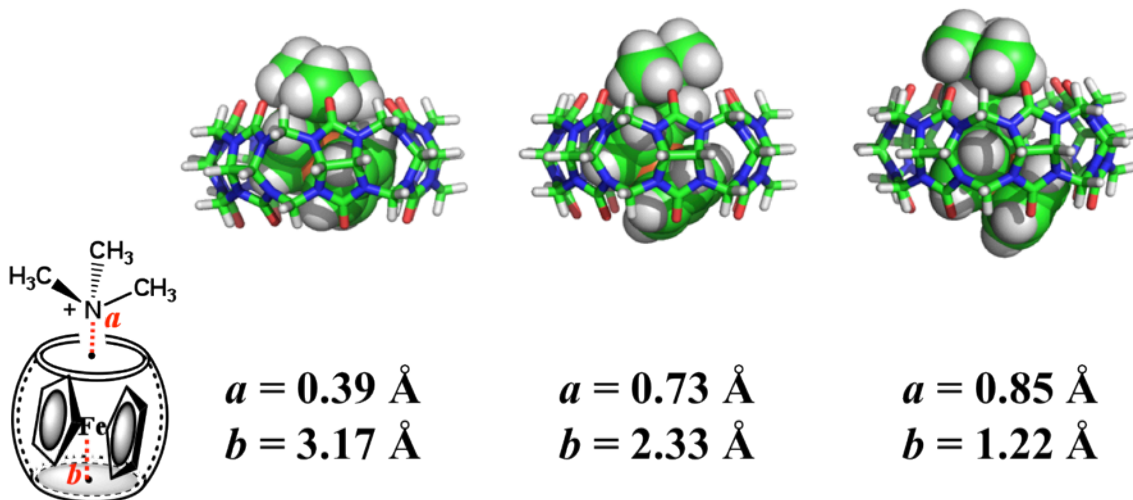


Figure S4. Energy minimized structures (B3LYP/3-21G*) computed for the CB7•Fc0⁺, CB7•Fc1⁺ and CB7•Fc2⁺ complexes (from left to right). Computed distances from (a) the ammonium nitrogen (a) and (b) the ferrocene iron to the nearest portal, defined by the plane formed by the carbonyl oxygens.

References

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