Electronic Supplementary Material (ESI) for ChemComm.

Formation of a hetero[3]rotaxane by a dynamic component-swapping strategy

*Eleanor A. Wilson, Nicolaas A. Vermeulen, Paul R. McGonigal, Alyssa-Jennifer Avestro, Amy A. Sarjeant, Charlotte L. Stern and J. Fraser Stoddart**

Department of Chemistry, Northwestern University
2145 Sheridan Road, Evanston, IL 60208-3113, USA

Supporting Information

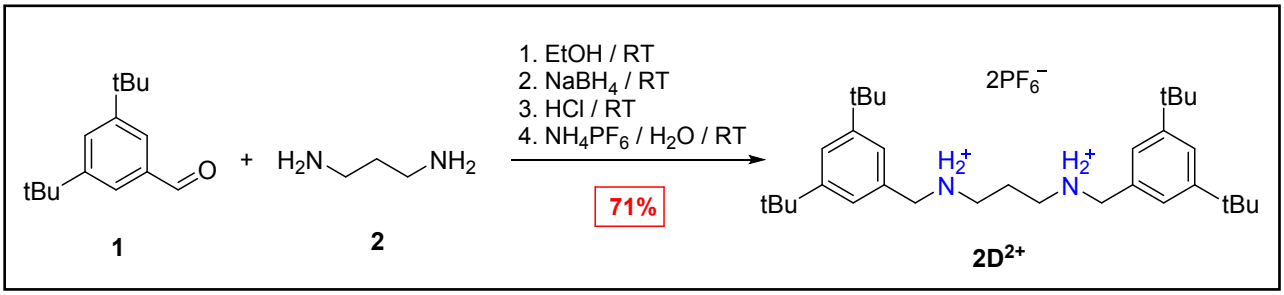
Table of Contents

1. Materials and Methods

Tetraethyleneglycol bis(2-aminophenyl)ether[S1] (**BA**) and 2,6-pyridinedicarboxaldehyde[S2] (**HDA**) were synthesised according to literature procedures. Anhydrous CH_2Cl_2 and dimethylformamide (DMF) were obtained after treatment of the reagent grade solvents on a SC Water USA Glass Contour Seca Solvent System. CD_3CN was obtained from Aldrich and used without further purification. All other reagents were purchased from commercial sources and were employed without further purification, unless otherwise stated. Thin-layer chromatography (TLC) was performed on aluminum sheets, precoated with silica gel 60-F254 (Merck 5554) which were inspected by UV light (254 nm). Column chromatography was carried out on silica gel 60F (Merck 9385, 0.040–0.063 mm). Preparative high-performance liquid chromatography (HPLC) was performed on a reverse-phase HPLC (RP-HPLC) instrument, using either a biphenyl (BiPh) column or a C_{18} column and a binary solvent system (MeCN and H_2O with 0.1% CF_3CO_2H). ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III 500 MHz spectrometer at ambient temperature, unless otherwise noted. The chemical shifts (δ) for ^1H spectra are given in ppm and are referenced to the residual proton signal of the deuterated solvent (CD_3CN: δ = 1.940 ppm). The chemical shifts (δ) for ^{13}C spectra are referenced relative to the signal from the carbon of the deuterated solvent (CD_3CN: δ = 118.260 ppm, 1.320 ppm). Abbreviations used to define multiplicities are as follows: s = singlet; d = doublet; t = triplet; m = multiplet; br = broad. High resolution mass spectra (HR-ESI) were measured on an Agilent (Wilmington, DE) 6210 ToF-LC/MS mass spectrometer.

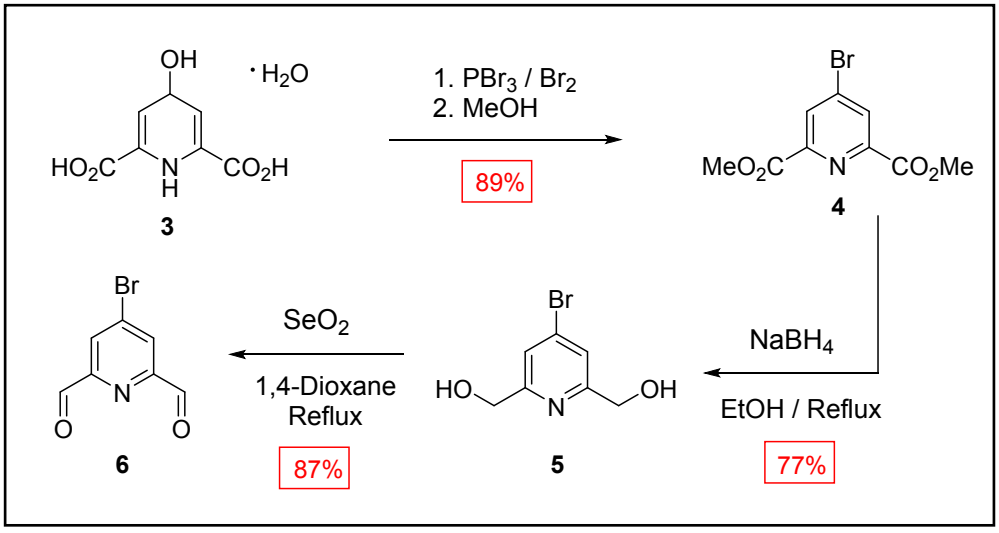
2. Synthesis and Characterisation of the Compounds

Scheme S1. Synthesis of **2D^{2+}**



2D^{2+}: 1,3-Diaminopropane (**2**) (0.250 g, 3.37 mmol, 1.0 equiv) was added to a solution of 3,5-di-*tert*-butylbenzaldehyde (**1**) (1.47 g, 6.74 mmol, 2.0 equiv) in absolute EtOH (17 mL) and the mixture was stirred for 14 h at room temperature. Sodium borohydride (0.510 g, 13.5 mmol, 4.0 equiv) was added and the solution was stirred for an additional 1 h before slowly quenching the reaction mixture with concentrated HCl (20 mL, 12 N). The solution was then stirred at room temperature for 4 h before being concentrated *in vacuo*. The residue was dissolved in H_2O and a saturated aqueous solution of NH_4PF_6 was added until precipitation ceased. The mixture was stirred for 24 h, followed by collection of the precipitate by filtration and rinsing thoroughly with H_2O. The product **2D^{2+}** was dried under vacuum and isolated as a white powder (1.85 g, 2.40 mmol, 71%). ^{1}H NMR (500 MHz, CD_3CN) δ = 7.58 (br, 4H), 7.53 (t, 2H, J = 1.8 Hz), 7.38 (d, 4H, J = 1.8 Hz), 4.12 (s, 4H), 3.13 (t, 4H, J = 7.0 Hz), 2.11 (m, 2H), 1.33 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN) δ = 152.8, 130.6, 125.2, 124.7, 53.3, 45.6, 35.6, 31.4, 23.3. HR-ESI: calcd for $[M–PF_6–HPF_6]^+$ *m/z* 479.4365, found *m/z* 479.4369.

Scheme S2. Synthesis of Dialdehyde Clipping Precursor **6**



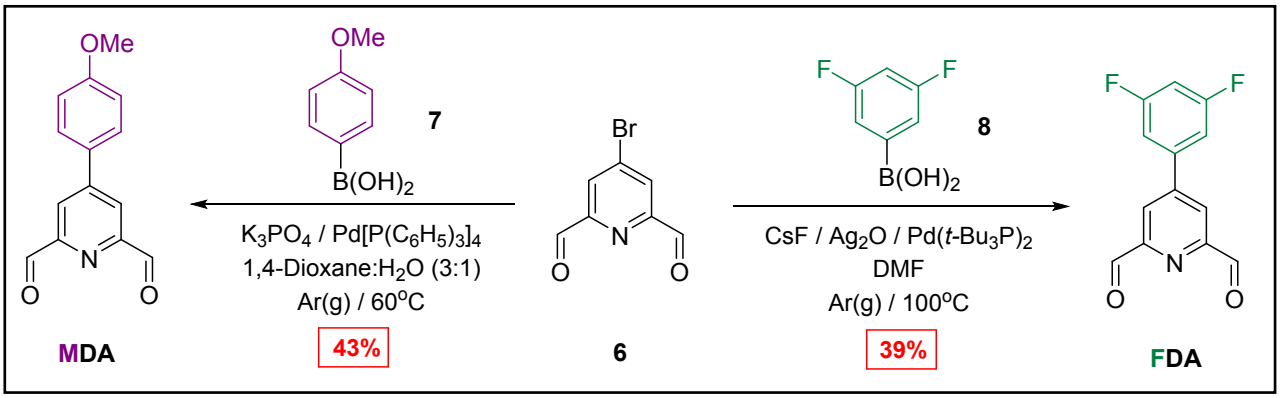
4: Compound **4** was synthesised following a modified literature procedure[S3]. Hexanes (40 mL) was degassed at 0 °C for 30 min in a dry flask, after which Br_2 (18.3 g, 0.115 mol, 3.3 equiv) was added under Ar. Phosphorus tribromide (37.3 g, 0.138 mol, 4.0 equiv) was added dropwise to the reaction flask over 30 min. The mixture was stirred for a further 5 min at room temperature followed by decantation of the hexanes. The mixture was washed with hexanes (3 x 20 mL) and any remaining hexanes were removed *in vacuo*. Chelidamic acid monohydrate (**3**)

(7.0 g, 34.8 mmol, 1.0 equiv), was added to the reaction flask and the mixture was heated to 130°C before being cooled to 90 °C and stirred for 2 h. The mixture was cooled to room temperature and dry CH_2Cl_2 (70 mL) was added. The resulting solution was stirred for 20 min before being cooled further to 0 °C. MeOH (100 mL) was added dropwise and the mixture was stirred for 1 h at room temperature. The solvent was evaporated and the resulting solid was collected by filtration and washed with MeOH until the pink colour was no longer present. Compound **4** was isolated (8.48 g, 30.9 mol, 89%) without further purification.

5: This compound was synthesised following a modified literature procedure[S4]. Sodium borohydride (2.75 g, 0.728 mol, 5.0 equiv) was added to a solution of compound **4** (3.99 g, 14.6 mmol, 1.0 equiv) in absolute EtOH (150 mL) and the mixture was stirred at room temperature for 15 min. The reaction mixture was heated under reflux for 16 h before being cooled to room temperature and slowly quenched with a saturated aqueous solution of $NaHCO_3$ (100 mL). The white precipitate was filtered off and the filtrate was concentrated *in vacuo* until a precipitate was formed. The white precipitate was filtered off and dried under vacuum to obtain the diol **5** (2.44 g, 11.2 mmol, 77%).

6: The diol **5** (1.98 g, 9.08 mmol, 1.0 equiv) and selenium dioxide (2.12 g, 19.1 mmol, 2.1 equiv) were suspended in 1,4-dioxane (90 mL) and the mixture was heated under reflux for 16 h. The solvent was evaporated and the residue was redissolved in CH_2Cl_2 and filtered through a pad of silica, flushing through with hot EtOAc. The filtrate was concentrated *in vacuo* to obtain the dialdehyde **6** (1.69 g, 7.90 mmol, 87%).

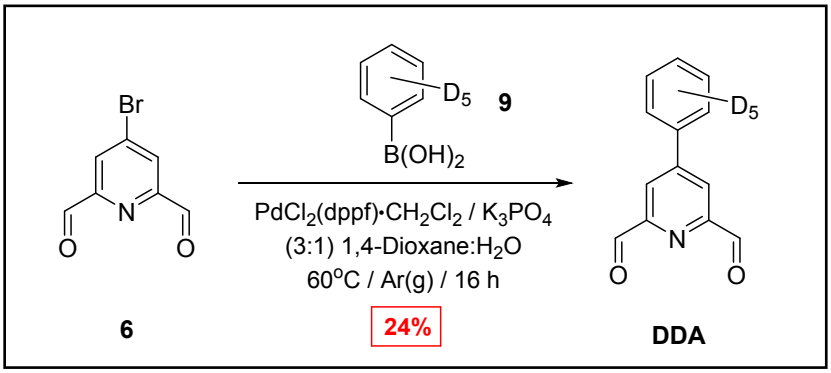
Scheme S3. Synthesis of **MDA** and **FDA**



MDA: A mixture of 3:1 1,4-dioxane:H_2O (25 mL) was degassed with Ar for 1 h before the addition of compound **6** (0.500 g, 2.34 mmol, 1.0 equiv), 4-methoxyphenylboronic acid (**7**) (0.355 g, 2.34 mmol, 1.0 equiv), K_3PO_4 (0.992 g, 4.67 mmol, 2.0 equiv), and tetrakis(triphenylphosphine)palladium(0) (0.135 g, 0.117 mmol, 0.05 equiv). The reaction mixture was stirred under Ar at 60 °C for 16 h. After cooling, the mixture was diluted with CH_2Cl_2 (250 mL) and washed with saturated $NH_4Cl_{(aq)}$ (250 mL), H_2O (250 mL), and brine (250 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography (SiO_2 / EtOAc:Hexane 30:70), affording **MDA** as a pale yellow solid (0.240 g, 0.994 mmol, 43% yield). ^{1}H NMR (500 MHz, CD_3CN): δ = 10.14 (s, 2H), 8.38 (s, 2H), 7.87 (m, 2H), 7.10 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (125 MHz, CD_3CN): δ = 193.7, 162.5, 154.6, 151.3, 129.7, 128.9, 123.0, 115.6, 56.1. HR-ESI: calcd for $[M+H]^+$ *m/z* 242.0812, found *m/z* 242.0803.

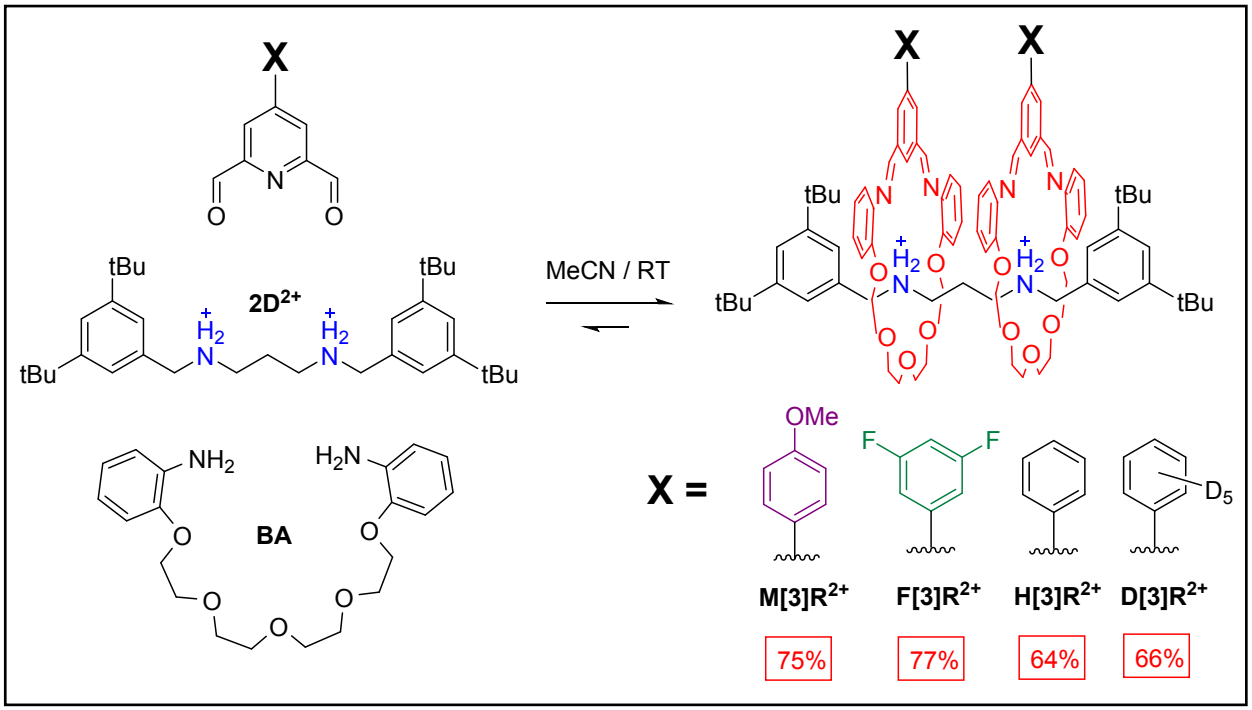
FDA: DMF (5 mL) was degassed with Ar for 1 h before the addition of compound **6** (0.100 g, 0.467 mmol, 1.0 equiv), 3,5-difluorophenylboronic acid (**8**) (0.111 g, 0.701 mmol, 1.5 equiv), cesium fluoride (0.142 g, 0.934 mmol, 2.0 equiv), silver oxide (0.130 g, 0.561 mmol, 1.2 equiv), and bis(tri-tert-butylphosphine)palladium(0) (11.9 mg, 23.4 μmol, 0.05 equiv). The reaction mixture was stirred under Ar at 100 °C for 16 h. After cooling, the mixture was diluted with CH_2Cl_2 (250 mL) and washed with H_2O (250 mL). The aqueous layer was extracted with CH_2Cl_2 (250 mL) and the organic layers were combined and extracted with dilute $NaHCO_{3(aq)}$ (250 mL) followed by H_2O (250 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude product was subjected to column chromatography (SiO_2 / EtOAc:Hexane 30:70), affording **FDA** as a white solid (39.3 mg, 0.139 mmol, 39% yield). ^{1}H NMR (500 MHz, CD_3CN): δ = 10.19 (s, 2H), 8.44 (s, 2H), 7.56 (m, 2H), 7.17 (tt, 2H, J = 9.1, 2.3 Hz). ^{13}C NMR (125 MHz, CD_3CN): δ = 193.3, 164.3 (dd, $J_{C\text{-}F}$ = 247.4, 13.2 Hz), 154.8, 149.4, 140.5 (t, $J_{C\text{-}F}$ = 9.9 Hz), 124.0, 111.9–111.6 (m), 106.1 (t, $J_{C\text{-}F}$ = 25.8 Hz). HR-ESI: calcd for $[M+H]^+$ *m/z* 248.0518, found *m/z* 248.0513.

Scheme S4. Synthesis of **DDA**



DDA: A mixture of 3:1 1,4-dioxane:H_2O (3 mL) was degassed with Ar for 1 h before the addition of compound **6** (44.8 mg, 0.209 mmol, 1.0 equiv), phenyl-d_5-boronic acid (**9**) (26.6 mg, 0.209 mmol, 1.0 equiv), K_3PO_4 (88.9 mg, 0.419 mmol, 2.0 equiv), and $PdCl_2(dppf)•CH_2Cl_2$ (8.5 mg, 10.4 µmol, 0.05 equiv). The reaction mixture was stirred under Ar at 60 °C for 16 h. After cooling, the mixture was diluted with CH_2Cl_2 (100 mL) and extracted with saturated $NH_4Cl_{(aq)}$ (2 x 100 mL), H_2O (100 mL), and brine (100 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude product was purified by preparative thin layer chromatography (CH_2Cl_2), affording **DDA** as a white solid (10.7 mg, 0.495 mmol, 24% yield). ^{1}H NMR (500 MHz, CD_3CN): δ = 10.15 (s, 2H), 8.41 (s, 2H). ^{13}C NMR (125 MHz, CD_3CN): δ = 193.5, 154.7, 151.8, 136.7, 130.7 (t), 129.8 (t), 127.8 (t), 123.8. HR-ESI: calcd for $[M+H]^+$ *m/z* 217.1020, found *m/z* 217.1022.

Scheme S5. Synthesis of Homo[3]Rotaxanes



Direct Mixing Protocol for the Formation of Homo[3]Rotaxanes. Diamine **BA** (2.0 equiv) and **2D**$^{2+}$ (1.0 equiv) were dissolved in CD_3CN (5 mM solution) and the mixture was allowed to stand at room temperature for 5 min. The requisite dialdehyde clipping precursor (2.0 equiv) was added, at which point the colour of the solution changed from colourless to yellow, indicating the formation of the [3]rotaxane. The solution was allowed to react at room temperature until equilibrium was established as determined by ^{1}H NMR spectroscopy. An excess of ^{i}Pr$_2$O (~5 times by volume) was added slowly to the solution and the mixture was left to precipitate at room temperature for 12 h. The resulting precipitate was collected by filtration, and dried under vacuum to afford the homo[3]rotaxane, typically as a yellow powder.

M[3]R^{2+}. This compound was prepared in 75% yield from **BA** (15.7 mg, 41.7 μmol), **2D**$^{2+}$ (16.1 mg, 20.8 μmol) and **MDA** (10.1 mg, 41.9 μmol) using the Direct Mixing Protocol above. ^{1}H NMR (500 MHz, CD_3CN): δ = 9.48 (br, 4H), 8.35 (s, 4H), 7.70 (s, 4H), 7.41 (d, J = 8.8 Hz, 4H), 7.20 (m, 4H), 7.02 (s, 4H), 7.01–6.99 (m, 2H), 6.93 (d, J = 1.8 Hz, 4H), 6.84 (d, J = 8.8 Hz, 4H), 6.77 (dd, J = 7.7, 1.7 Hz, 4H), 6.67 (m, 4H), 4.51–4.42 (m, 4H), 4.29 (t, J = 4.1 Hz, 8H), 3.89–3.79 (m, 8H), 3.76 (s, 6H), 3.56 (s, 10H), 3.41 (dq, J = 8.7, 5.6, 4.1 Hz, 4H), 2.30 – 2.18 (m, 2H),

0.83 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN) δ = 162.7, 162.4, 153.2, 152.4, 151.6, 150.6, 141.0, 132.8, 129.8, 128.8, 127.4, 127.3, 124.2, 123.8, 122.3, 121.6, 115.5, 113.4, 71.0, 70.9, 69.6, 68.9, 55.9, 52.3, 46.3, 34.9, 31.1. HR-ESI: calcd for $[M–2PF_6]^{2+}$ *m/z* 821.4742, found *m/z* 821.4757. Crystals suitable for X-ray crystal structure analysis were obtained by slow liquid diffusion of $^{i}Pr_2O$ into a MeCN solution of **M[3]R^{2+}**.

F[3]R^{2+}. This compound was prepared in 77% yield from **BA** (15.5 mg, 41.2 μmol), **2D^{2+}** (15.9 mg, 20.6 μmol) and **FDA** (10.2 mg, 41.3 μmol) using the Direct Mixing Protocol above. ^{1}H NMR (500 MHz, CD_3CN): δ = 9.37 (s, 4H), 8.37 (s, 4H), 7.81 (s, 4H), 7.23 (ddd, *J* = 8.8, 7.4, 1.6 Hz, 4H), 7.15 (d, *J* = 6.3 Hz, 4H), 7.03 (s, 4H), 7.03 – 7.00 (m, 2H), 6.96 (tt, *J* = 9.0, 2.3 Hz, 2H), 6.91 (d, *J* = 1.8 Hz, 4H), 6.77 (dd, *J* = 7.7, 1.7 Hz, 4H), 6.67 (td, *J* = 7.6, 1.2 Hz, 4H), 4.51 – 4.42 (m, 4H), 4.29 (dd, *J* = 4.0, 2.0 Hz, 8H), 3.90 – 3.78 (m, 8H), 3.66 – 3.50 (m, 16H), 3.47 – 3.37 (m, 4H), 2.25 (dd, *J* = 11.2, 6.4 Hz, 2H), 0.82 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN): δ = 164.3 (dd, $J_{C\text{-}F}$ = 248.0, 13.0 Hz), 162.1, 153.7, 152.5, 151.8, 148.2, 140.8, 138.6, 132.7, 130.1, 127.9, 124.1, 123.9, 122.3, 121.6, 113.5, 110.7–110.3 (m), 106.4 (t, $J_{C\text{-}F}$ = 25.7 Hz), 71.0, 70.9, 69.6, 68.9, 52.3, 46.3, 34.9, 31.1, 24.3. HR-ESI: calcd for $[M–2PF_6]^{2+}$ *m/z* 827.4448, found *m/z* 827.4466. Crystals suitable for X-ray crystal structure analysis were obtained by slow liquid diffusion of $^{i}Pr_2O$ into a MeCN solution of **F[3]R^{2+}**.

H[3]R^{2+}. This compound was prepared in 64% yield from **BA** (8.0 mg, 0.021 mmol), **2D^{2+}** (8.1 mg, 0.011 mmol) and **HDA** (4.5 mg, 0.021 mmol) using the Direct Mixing Protocol above. ^{1}H NMR (500 MHz, CD_3CN): δ = 9.45 (s, 4H), 8.36 (s, 4H), 7.80 (s, 4H), 7.48 (dd, *J* = 7.8, 1.9 Hz, 4H), 7.41 – 7.35 (m, 6H), 7.21 (ddd, *J* = 8.8, 7.4, 1.7 Hz, 4H), 7.03 (s, 4H), 7.01 (s, 2H), 6.95 (d, *J* = 1.8 Hz, 4H), 6.76 (dd, *J* = 7.8, 1.7 Hz, 4H), 6.69 (td, *J* = 7.5, 1.1 Hz, 4H), 4.51 – 4.44 (m, 4H), 4.35 – 4.25 (m, 8H), 3.87 – 3.76 (m, 8H), 3.66 – 3.62 (m, 2H), 3.58 – 3.47 (m, 16H), 3.43 – 3.38 (m, 4H), 0.84 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN): δ = 162.4, 153.4, 152.5, 151.6, 151.2, 140.9, 135.6, 132.8, 131.3, 130.2, 129.8, 128.2, 127.5, 124.1, 123.8, 122.3, 121.5, 113.4, 71.0, 70.9, 69.6, 69.0, 52.3, 46.3, 34.9, 31.1, 24.4. HR-ESI: calcd for $[M–2PF_6]^{2+}$ *m/z* 791.4636, found *m/z* 791.4642.

D[3]R^{2+}. This compound was prepared in 66% yield from **BA** (9.3 mg, 0.025 mmol), **2D^{2+}** (9.6 mg, 0.012 mmol) and **DDA** (5.4 mg, 0.025 mmol) using the Direct Mixing Protocol above. ^{1}H

NMR (500 MHz, CD_3CN): δ = 9.45 (s, 4H), 8.36 (s, 4H), 7.80 (s, 4H), 7.21 (ddd, J = 8.8, 7.4, 1.7 Hz, 4H), 7.03 (s, 4H), 7.01 (s, 2H), 6.95 (d, J = 1.9 Hz, 4H), 6.76 (dd, J = 7.7, 1.7 Hz, 4H), 6.69 (td, J = 7.6, 1.2 Hz, 4H), 4.51 – 4.44 (m, 4H), 4.36 – 4.24 (m, 8H), 3.87 – 3.76 (m, 8H), 3.66 – 3.62 (m, 2H), 3.59 – 3.47 (m, 16H), 3.44 – 3.37 (m, 4H), 0.84 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN): δ = 162.4, 153.4, 152.5, 151.6, 151.2, 140.9, 135.4, 132.8, 129.8, 128.2, 127.0 (t), 124.6 (t), 124.1, 123.8, 122.6 (t), 122.3, 121.5, 113.4, 71.0, 70.9, 69.6, 69.0, 52.3, 46.3, 34.9, 31.1, 24.4. HR-ESI: calcd for $[M–2PF_6]^{2+}$ *m/z* 796.4950, found *m/z* 796.4955.

Formation of Hetero[3]Rotaxane M-F[3]R^{2+} by Direct Mixing. Diamine **BA** (2.0 equiv) and **2D**$^{2+}$ (1.0 equiv) were dissolved in CD_3CN (8 mM or 3 mM soln) and the mixture was allowed to stand at room temperature for 5 min. The aldehyde clipping precursors **MDA** and **FDA** (1.0 equiv each) were added, at which point the colour of the solution changed from colourless to yellow, indicating the formation of [3]rotaxanes. The solution was allowed to react at room temperature until equilibrium was established as determined by ^{1}H NMR spectroscopy.

Formation of Hetero[3]Rotaxane M-F[3]R^{2+} by Acid-Catalysed Direct Mixing. Diamine **BA** (2.0 equiv) and the dialdehyde clipping precursors **MDA** and **FDA** (1.0 equiv each) were dissolved in CD_3CN (3 mM) and the mixture was allowed to stand at room temperature for 5 min. The dumbbell **2D**$^{2+}$ (1.0 equiv) was added, at which point the colour of the solution changed from colourless to yellow, indicating the formation of [3]rotaxane products. This addition was followed immediately by the further addition of an 80 mM solution of HPF_6 (5 mol% per imine bond) in CD_3CN. The mixture was allowed to react at room temperature until equilibrium was established (6 h) as determined by ^{1}H NMR spectroscopy. Insoluble material was removed by filtration and an excess of ^{i}Pr$_2$O (~10 times by volume) was added slowly to the filtrate, causingd precipiation of a yellow solid. The mixture of [3]rotaxanes was isolated by filtration with a 66% mass recovery.

Component-Swapping Protocol for the Formation of Hetero[3]Rotaxanes. An 80 mM solution of HPF_6 (5mol% per imine bond) in CD_3CN was added to a solution of two different homo[3]rotaxanes in CD_3CN or MeCN (3 mM). The components were allowed to undergo acid-catlysed dynamic exchange at room temperature until equilibrium was established as determined by ^{1}H NMR spectroscopy (2 days).

M-F[3]R^{2+}. This compound was prepared starting from the homo[3]rotaxanes **M[3]R^{2+}** and **F[3]R^{2+}** (1.0 equiv each) using the Component-Swapping Protocol above, and was obtained in 47% yield as determined by ^{1}H NMR spectroscopy using 2,4,6-triiodophenol as an internal standard.

H-M[3]R^{2+}. This compound was prepared starting from the isolated homo[3]rotaxanes **H[3]R^{2+}** and **M[3]R^{2+}** (1.0 equiv each) using the Component-Swapping Protocol above, and was obtained in 44% yield as determined by ^{1}H NMR spectroscopy using 2,4,6-triiodophenol as an internal standard.

H-F[3]R^{2+}. This compound was prepared starting from the isolated homo[3]rotaxanes **H[3]R^{2+}** and **F[3]R^{2+}** (1.0 equiv each) using the Component-Swapping Protocol above, and was obtained in 50% yield as determined by ^{1}H NMR spectroscopy using 2,4,6-triiodophenol as an internal standard.

General Procedure for the Isolation of Reduced [3]Rotaxanes. A solution of sodium borohydride (9 equiv. per imine bond) in MeOH was added quickly to the appropriate mixture of [3]rotaxanes in dry CH_2Cl_2, and the resulting mixture was stirred for 18 h at room temperature. The solution was concentrated *in vacuo*, the residue was dissolved in CH_2Cl_2 and the solid particulate was filtered off. The solution was concentrated *in vacuo* to yield the neutral and reduced [3]rotaxane product(s). The reduced [3]rotaxane(s) were treated with CF_3CO_2H and purified by RP-HPLC (isocratic method / 75% MeCN in H_2O with 0.1% CF_3CO_2H). Fractions were freeze-dried to afford the desired reduced [3]rotaxane as the diammonium CF_3CO_2H salt.

Reduced M[3]R^{2+}. The reduced homo[3]rotaxane **M[3]R^{2+}** was isolated as the CF_3CO_2H salt according to the General Procedure above, using a C_{18} column (32% yield). ^{1}H NMR (500 MHz, CD_3CN) δ = 8.85 (s, 4H), 7.54 (d, J = 8.7 Hz, 4H), 7.35 (t, J = 1.7 Hz, 2H), 7.32 (s, 4H), 6.97 (d, J = 8.7 Hz, 4H), 6.83 – 6.78 (m, 4H), 6.76 (d, J = 1.8 Hz, 4H), 6.60 – 6.49 (m, 12H), 4.50 (dt, J = 7.0, 3.4 Hz, 4H), 4.30 – 4.24 (m, 4H), 4.18 – 4.13 (m, 4H), 4.09 – 4.03 (m, 4H), 4.03 – 3.97 (m, 4H), 3.91 (s, 6H), 3.84 (t, J = 3.9 Hz, 8H), 3.77 (t, J = 4.0 Hz, 8H), 3.55 – 3.45 (m, 4H), 3.37 – 3.27 (m, 4H), 3.03 (d, J = 15.3 Hz, 4H), 1.64 (t, J = 12.6 Hz, 2H), 0.94 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN) δ = 162.2, 160.1, 153.2, 148.0, 137.3, 132.4, 132.4, 129.9, 129.4, 124.8, 124.6,

122.6, 121.3, 120.6, 115.6, 114.4, 111.4, 72.3, 71.9, 71.4, 68.9, 56.2, 54.2, 50.4, 46.5, 35.3, 31.3. HR-ESI: calcd for $[M–2CF_3CO_2]^{2+}$ *m/z* 825.5055, found *m/z* 825.5061.

Reduced F[3]R^{2+}. The reduced homo[3]rotaxane **F[3]R^{2+}** was isolated as the CF_3CO_2H salt according to the General Procedure above, using a C_{18} column (22% yield). ^{1}H NMR (500 MHz, CD_3CN) δ = 8.72 (s, 4H), 7.35 (t, *J* = 1.9 Hz, 2H), 7.32 (s, 4H), 7.30 – 7.26 (m, 4H), 7.08 (tt, *J* = 9.3, 2.3 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 4H), 6.76 (d, *J* = 1.8 Hz, 4H), 6.64 – 6.58 (m, 4H), 6.57 – 6.51 (m, 8H), 4.52 (dt, *J* = 6.9, 3.4 Hz, 4H), 4.32 – 4.24 (m, 4H), 4.18 – 4.11 (m, 4H), 4.10 – 3.98 (m, 8H), 3.85 (q, *J* = 2.8 Hz, 8H), 3.77 (dd, *J* = 4.8, 2.9 Hz, 8H), 3.51 (t, *J* = 9.2 Hz, 4H), 3.31 (d, *J* = 15.6 Hz, 4H), 3.06 (d, *J* = 15.8 Hz, 4H), 2.96 (br, 4H), 1.59 (q, *J* = 14.9, 12.3 Hz, 2H), 0.94 (s, 36H). ^{13}C NMR (125 MHz, CD_3CN) δ = 165.4, 163.4, 160.7, 153.2, 148.6, 148.0, 141.1 (t, $J_{C\text{-}F}$ = 10.1 Hz), 137.1, 132.3, 124.8, 124.7, 122.7, 121.4, 121.3, 114.4, 111.5, 111.3 – 110.9 (m), 105.9 (t, $J_{C\text{-}F}$ = 26.2 Hz), 72.3, 71.9, 71.4, 68.9, 54.9, 54.2, 50.3, 46.4, 46.3, 35.3, 31.5, 31.2, 25.6. HR-ESI: calcd for $[M–2CF_3CO_2]^{2+}$ *m/z* 831.4761, found *m/z* 831.4759.

Reduced M-F[3]R^{2+}. The reduced hetero[3]rotaxane **M-F[3]R^{2+}** was isolated from a mixture of reduced [3]rotaxanes as the CF_3CO_2H salt according to the General Procedure above, using a BiPh column (overall isolated yield of 24%, over two steps). ^{1}H NMR (600 MHz, CD_3CN) δ = 8.84 (s, 2H), 8.73 (s, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.37 – 7.35 (m, 3H), 7.34 (t, *J* = 1.8 Hz, 1H), 7.33 – 7.31 (m, 2H), 7.30 (s, 2H), 7.16 (tt, *J* = 9.0, 2.1 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.84 – 6.78 (m, 4H), 6.77 (d, *J* = 1.8 Hz, 2H), 6.75 (d, *J* = 1.8 Hz, 2H), 6.62 – 6.49 (m, 12H), 4.50 (dt, *J* = 7.1, 3.5 Hz, 4H), 4.27 (dt, *J* = 11.9, 6.5 Hz, 4H), 4.20 – 4.11 (m, 4H), 4.09 – 4.03 (m, 4H), 4.00 (dd, *J* = 11.8, 6.2 Hz, 4H), 3.89 (s, 3H), 3.86 – 3.82 (m, 8H), 3.79 – 3.75 (m, 8H), 3.54 – 3.42 (m, 4H), 3.31 (d, *J* = 15.4 Hz, 4H), 3.07 (d, *J* = 15.9 Hz, 2H), 3.01 (d, *J* = 15.7 Hz, 2H), 1.63 – 1.56 (m, 2H), 0.94 (s, 18H), 0.93 (s, 18H). ^{1}H NMR (500 MHz, CD_3CN) δ = 8.85 (s, 2H), 8.73 (s, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.36 (s, 3H), 7.34 (s, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.30 (s, 2H), 7.16 (t, *J* = 9.4 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 4H), 6.77 (s, 2H), 6.75 (s, 2H), 6.64 – 6.47 (m, 12H), 4.54 – 4.47 (m, 4H), 4.26 (dd, *J* = 11.0, 5.4 Hz, 4H), 4.15 (q, *J* = 9.5, 8.9 Hz, 4H), 4.06 (dt, *J* = 12.0, 5.9 Hz, 4H), 4.00 (dd, *J* = 11.4, 5.6 Hz, 4H), 3.89 (s, 3H), 3.84 (d, *J* = 5.4 Hz, 8H), 3.77 (t, *J* = 3.9 Hz, 8H), 3.47 (s, 4H), 3.31 (d, *J* = 15.9 Hz, 4H), 3.07 (d, *J* = 15.6 Hz, 2H), 3.04 – 2.97 (m, 2H), 1.64 – 1.55 (m, 2H), 0.94 (s, 18H), 0.93 (s, 18H). ^{13}C NMR (125 MHz, CD_3CN) δ = 160.7, 160.0, 153.1, 153.1, 148.0, 147.9, 137.2, 137.1, 132.4, 132.3, 129.4,

129.1, 124.8, 124.8, 124.6, 124.6, 122.6, 122.6, 121.4, 121.3, 121.3, 120.4, 115.4, 114.5, 114.4, 111.4, 111.4, 111.2, 72.3, 71.8, 71.3, 68.8, 56.1, 54.2, 54.2, 50.4, 50.3, 46.5, 46.4, 35.3, 35.3, 31.2, 31.2, 25.6. HR-ESI: calcd for $[M–2CF_3CO_2]^{2+}$ *m/z* 828.4908, found *m/z* 828.4907.

3. $^{1}H/^{13}C$ and ^{1}H-^{1}H COSY NMR Spectra

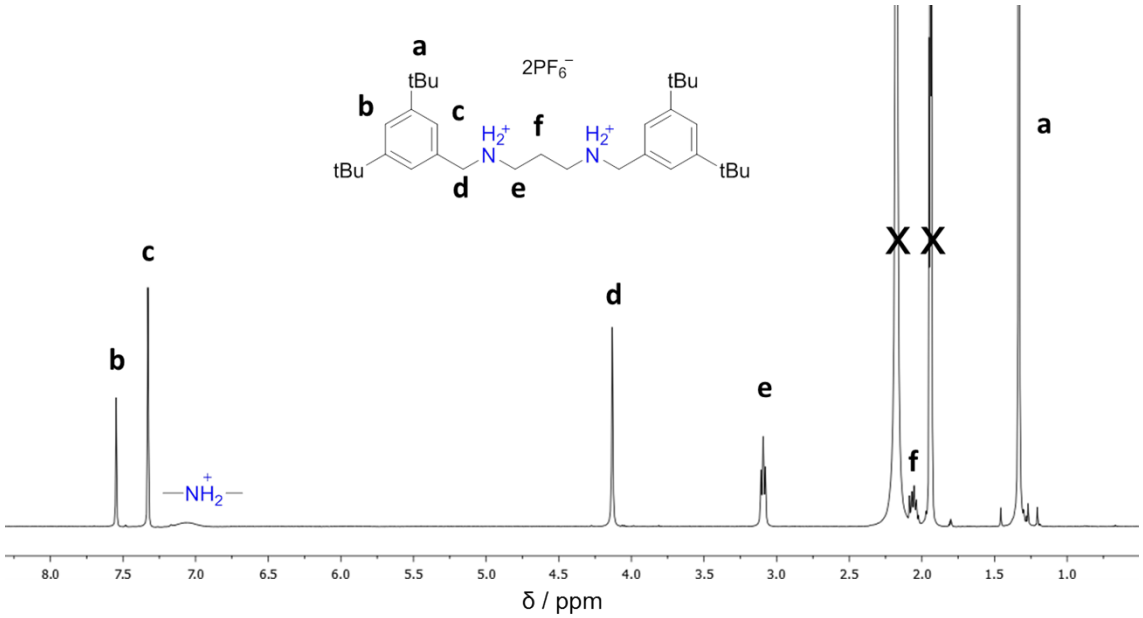


Figure S1. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **2D²⁺**

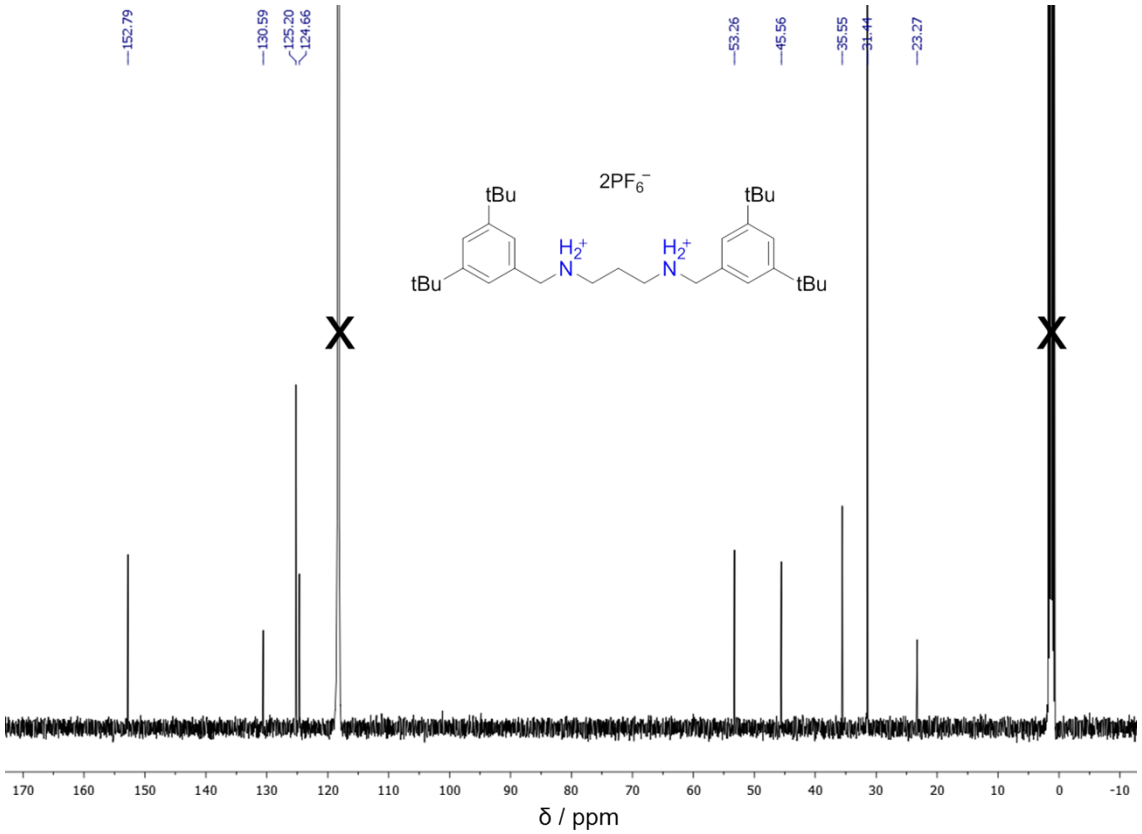


Figure S2. ^{13}C NMR Spectrum (125 MHz, CD_3CN, 298 K) of **$2D^{2+}$**

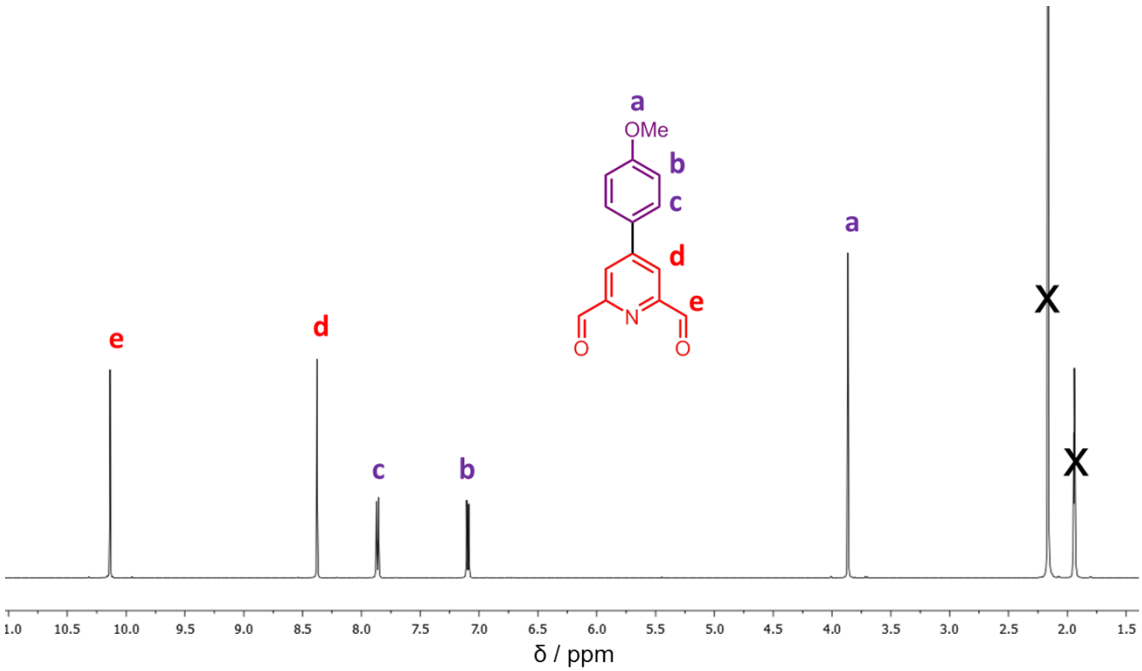


Figure S3. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **MDA**

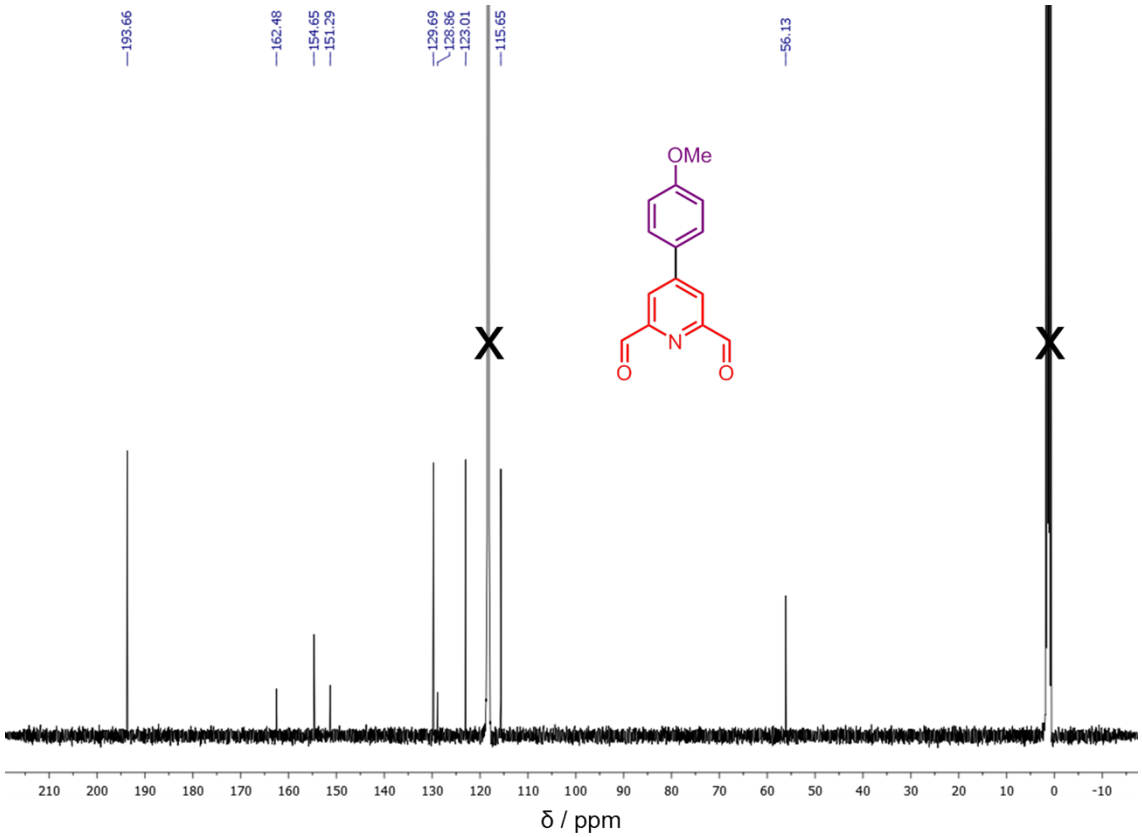


Figure S4. ^{13}C NMR Spectrum (125 MHz, CD_3CN, 298 K) of **MDA**

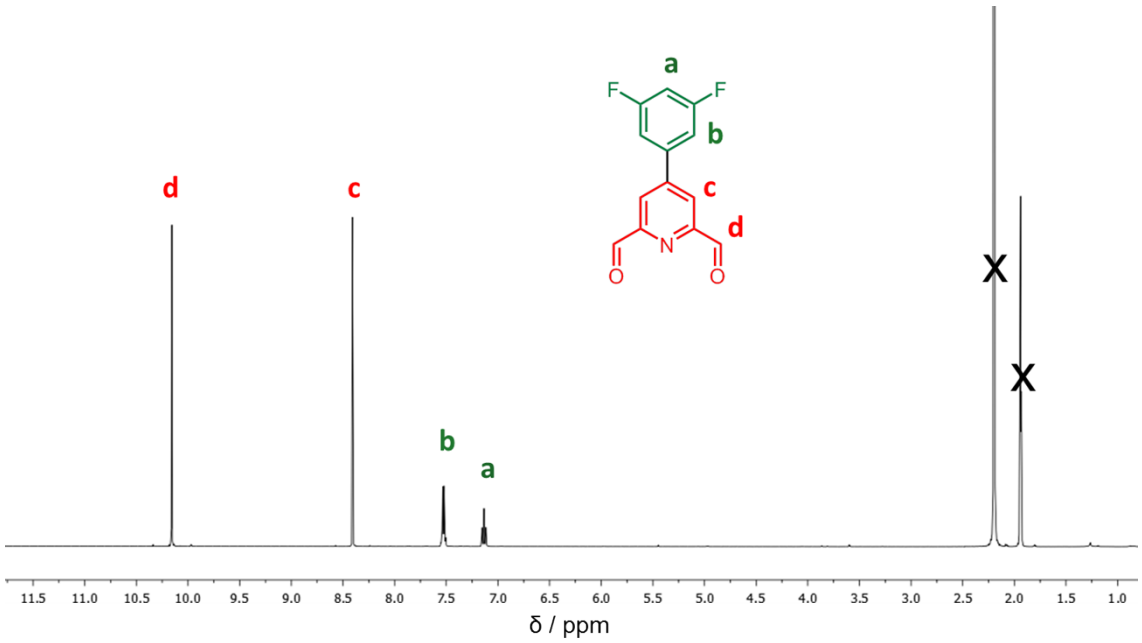


Figure S5. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **FDA**

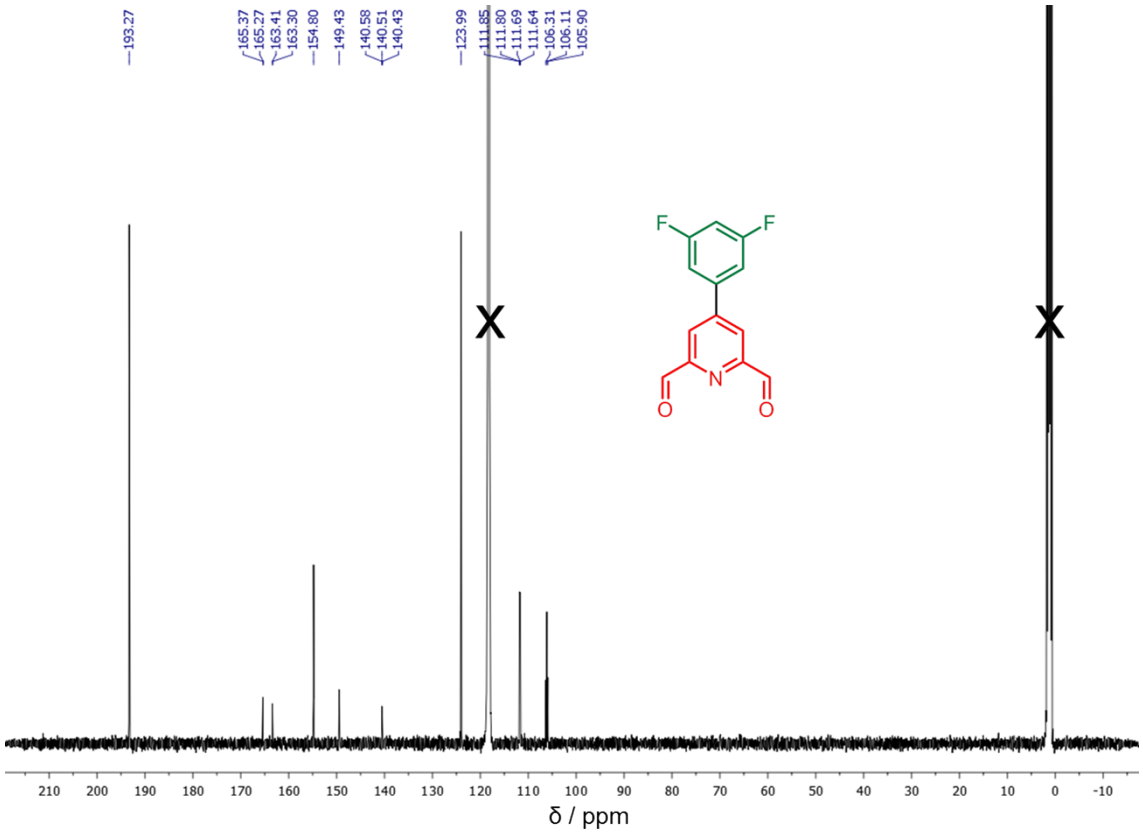


Figure S6. ^{13}C NMR Spectrum (125 MHz, CD_3CN, 298 K) of **FDA**

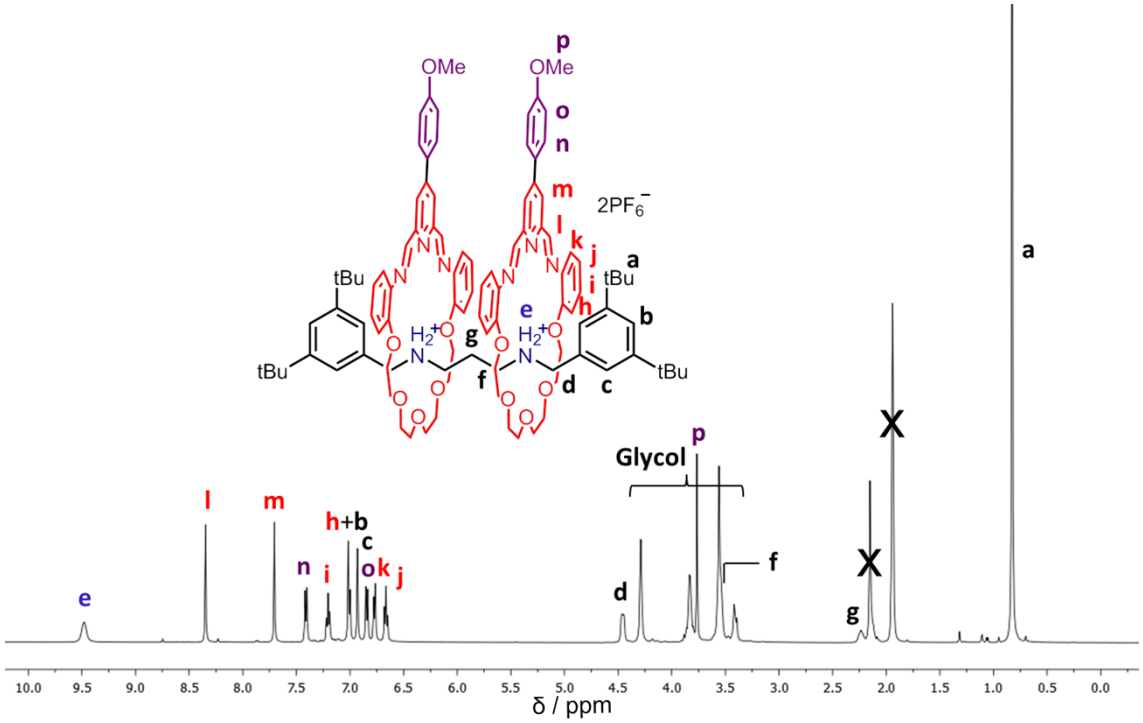


Figure S7. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **M[3]R^{2+}**

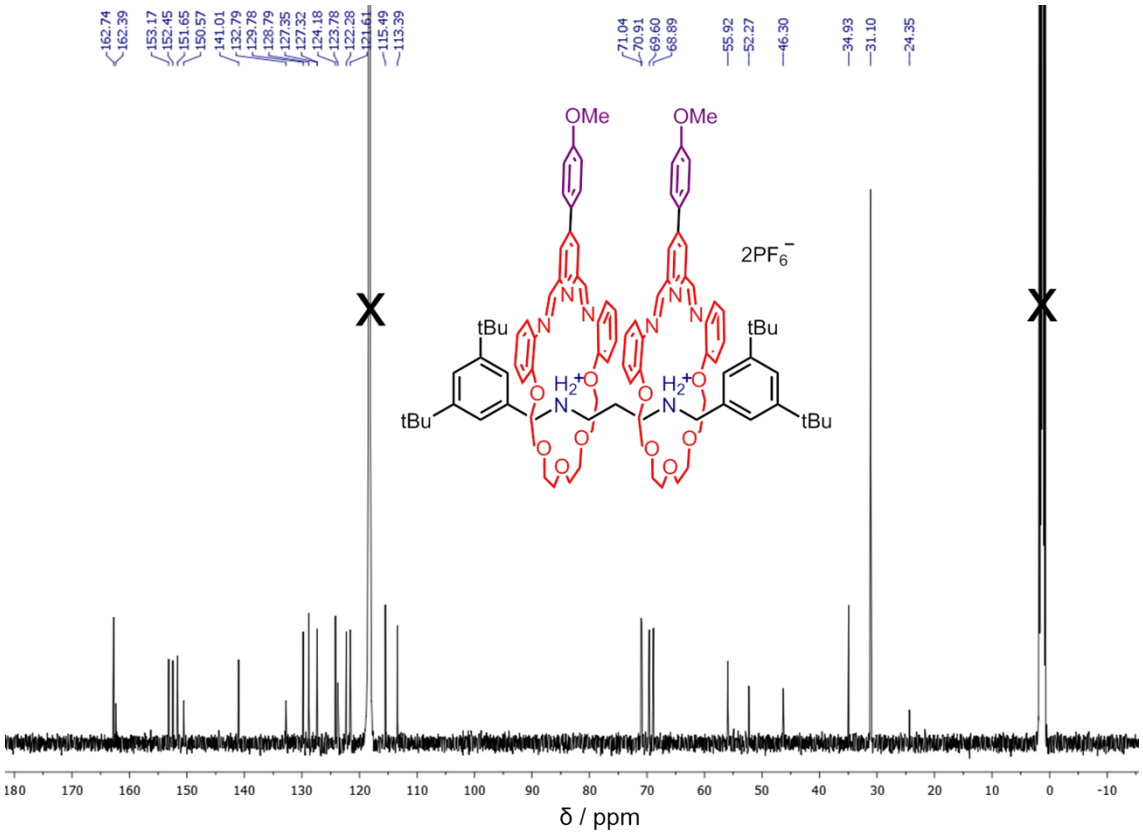


Figure S8. ^{13}C NMR Spectrum (125 MHz, CD_3CN, 298 K) of **M[3]R^{2+}**

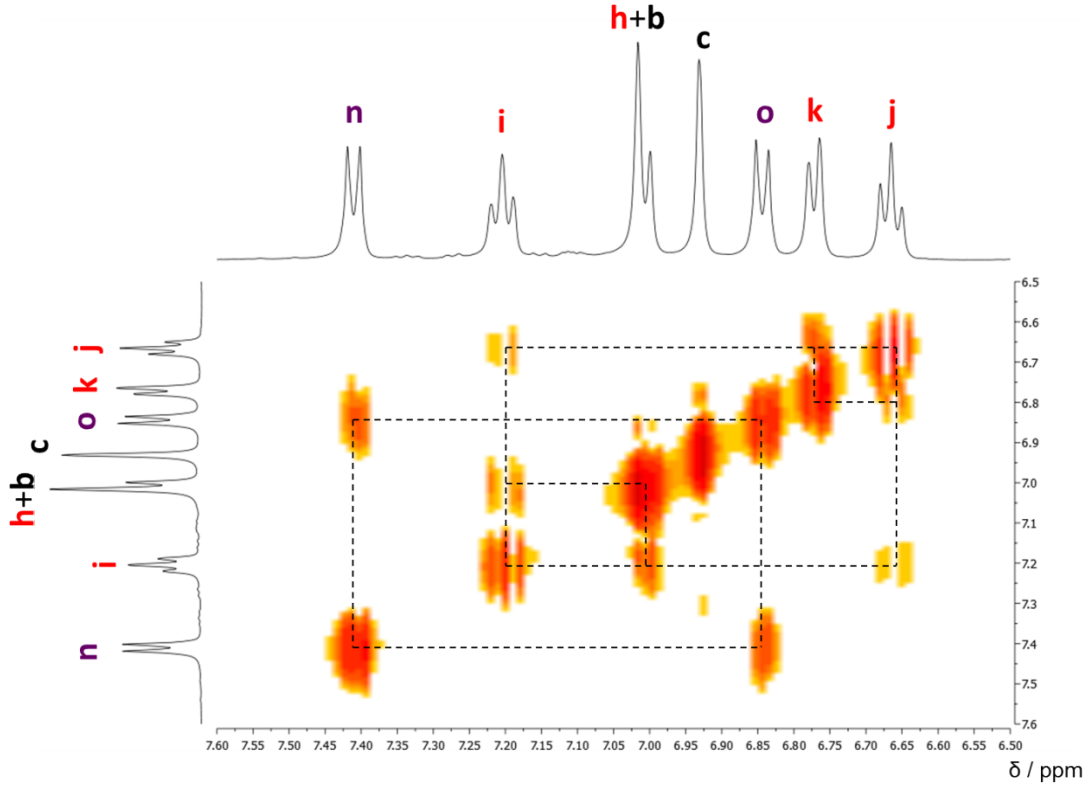


Figure S9. Partial ^1H–^1H COSY NMR Spectrum (500 MHz, CD_3CN, 298 K) of **M[3]R^{2+}**

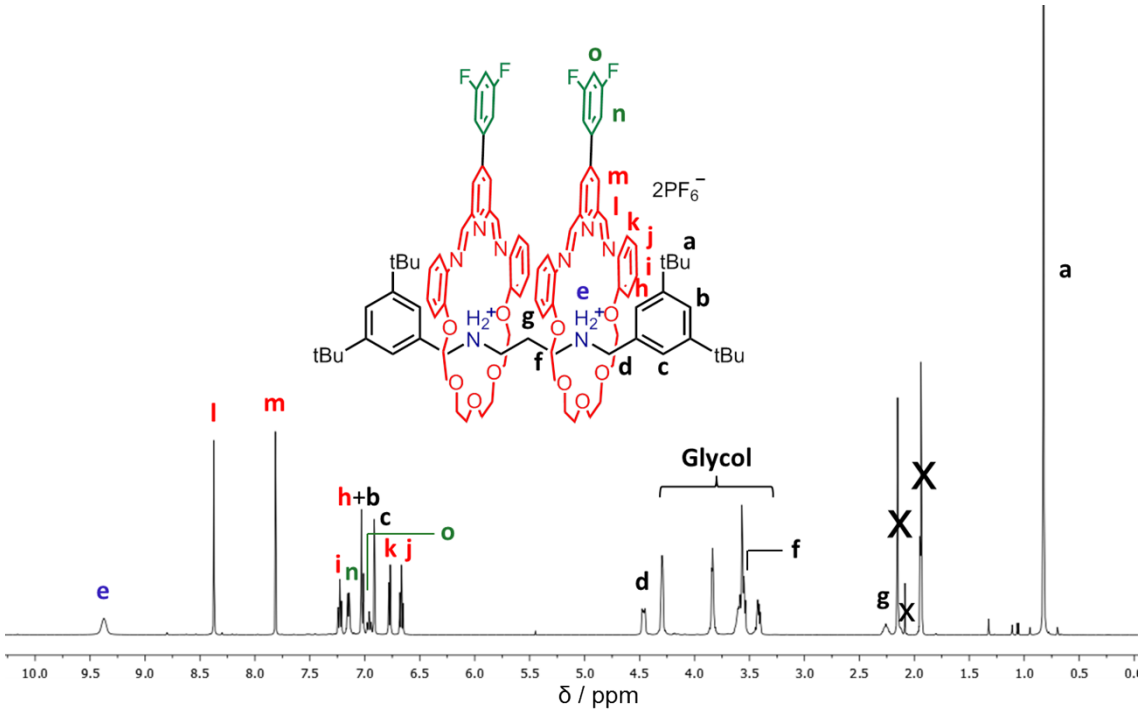


Figure S10. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **F[3]R^{2+}**

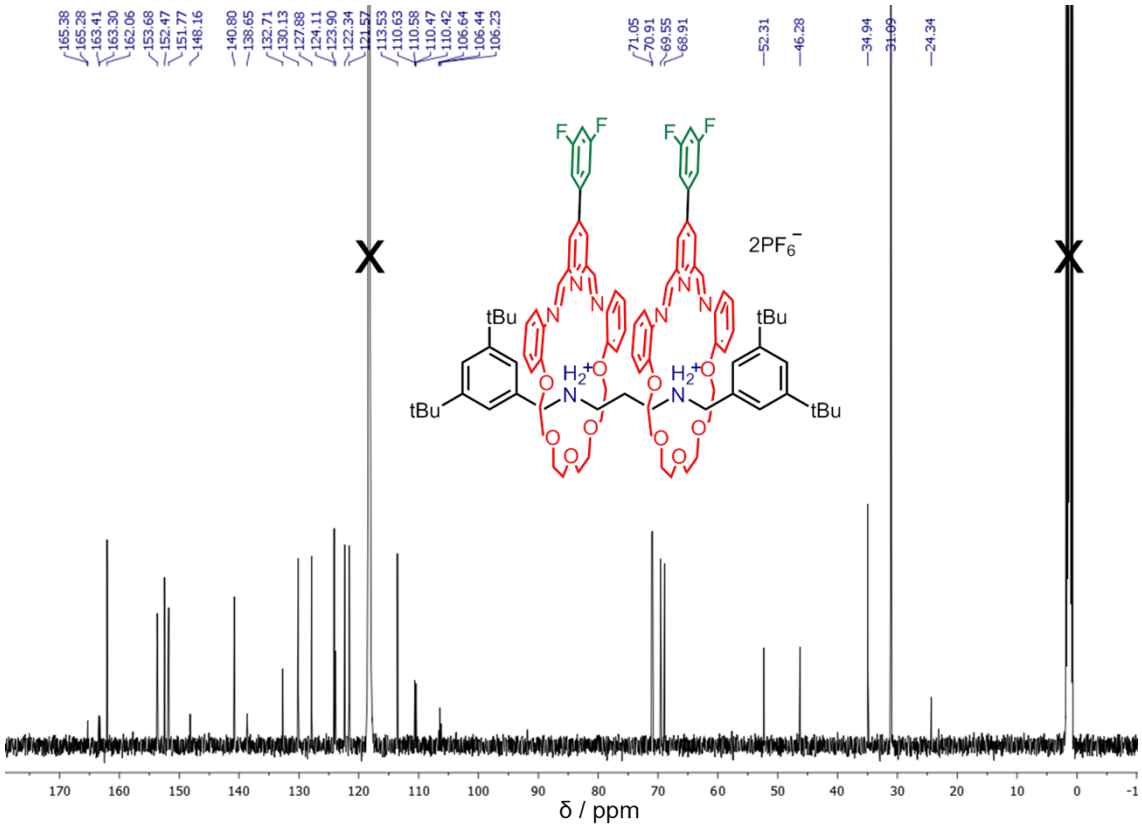


Figure S11. ^{13}C NMR Spectrum (125 MHz, CD_3CN, 298 K) of **F[3]R^{2+}**

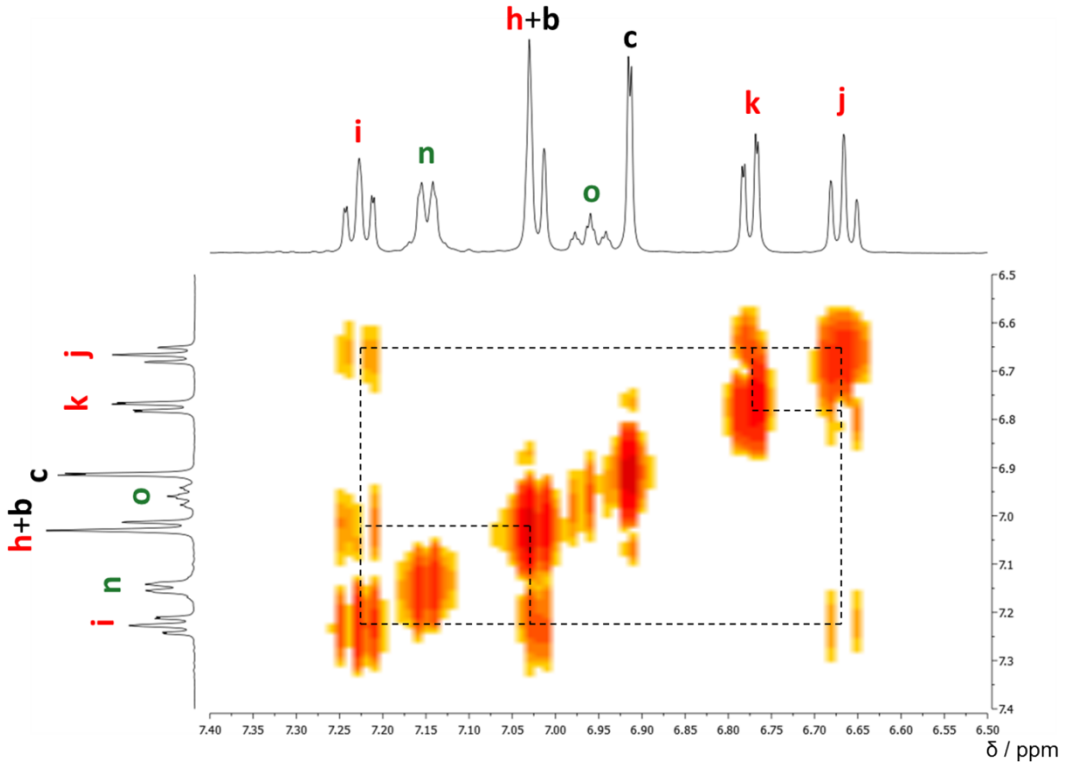


Figure S12. Partial ^{1}H–^{1}H COSY NMR spectrum (500 MHz, CD_3CN, 298 K) of **F[3]R^{2+}**

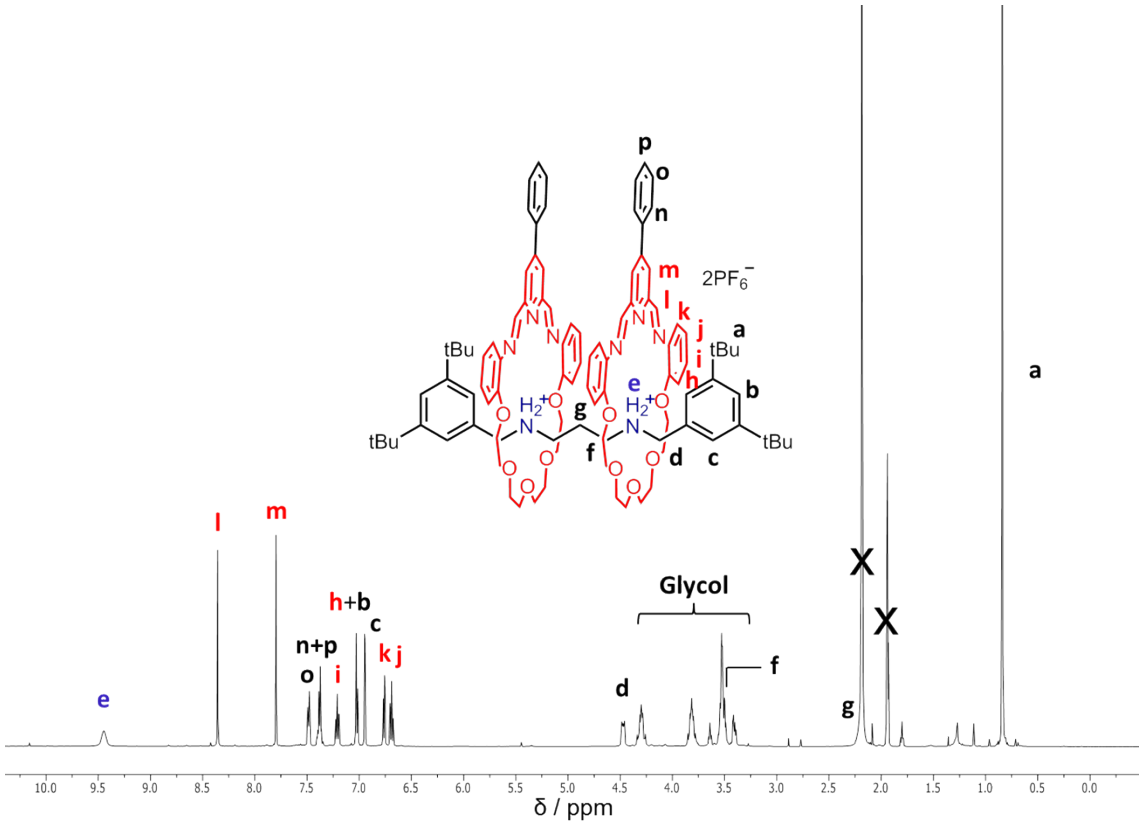


Figure S13. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **H[3]R^{2+}**

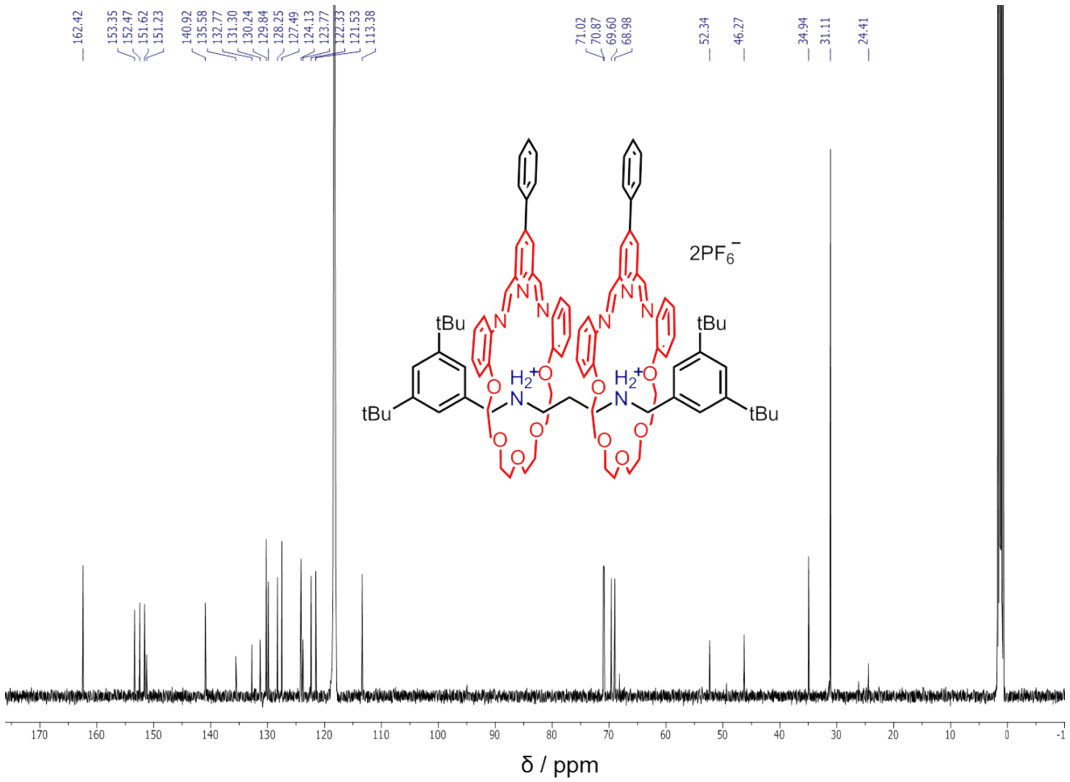


Figure S14. ^{13}C NMR Spectrum (500 MHz, CD_3CN, 298 K) of **H[3]R^{2+}**

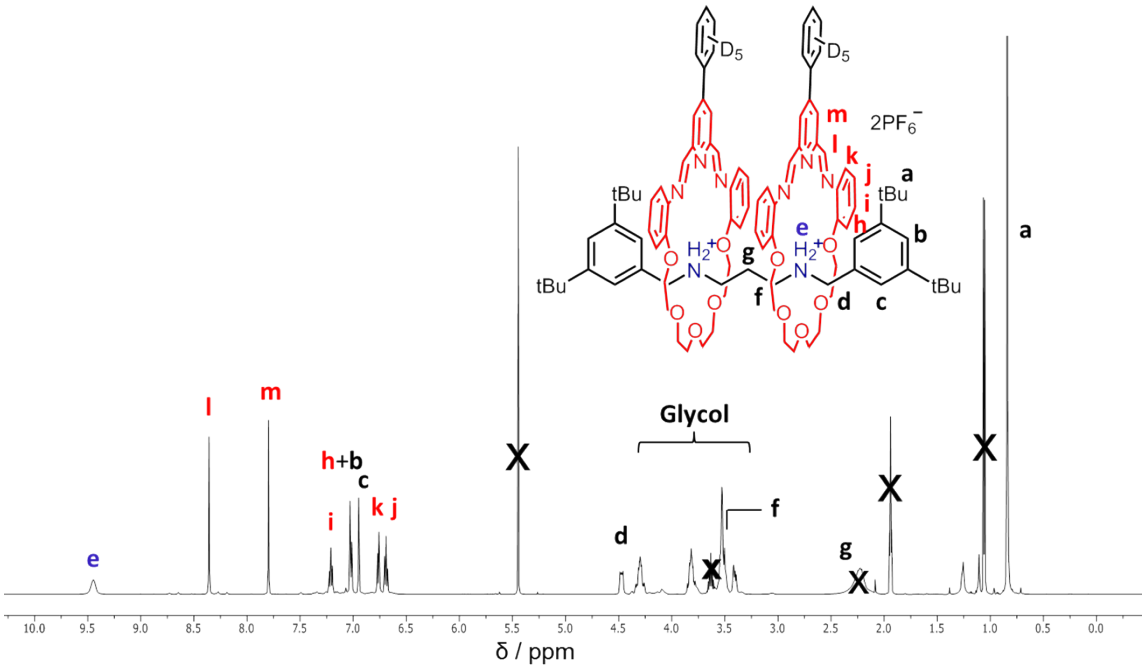


Figure S15. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of **D[3]R^{2+}**

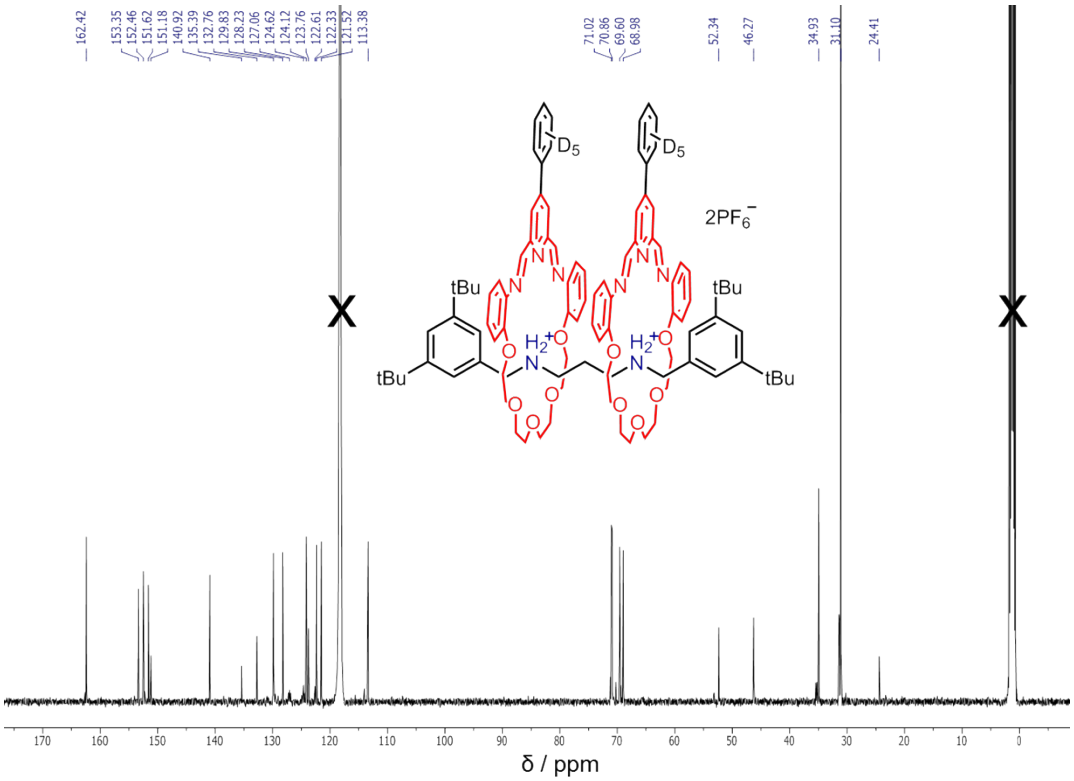


Figure S16. ^{13}C NMR Spectrum (500 MHz, CD_3CN, 298 K) of **D[3]R^{2+}**

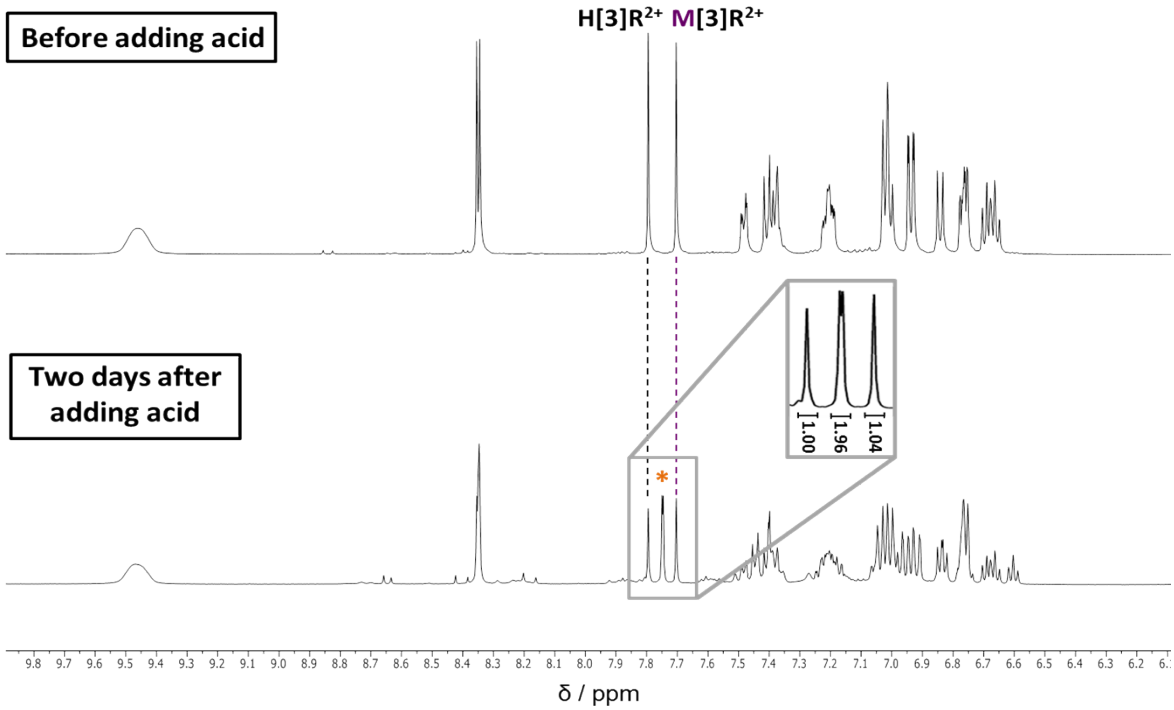


Figure S17. ^{1}H NMR Spectra (500 MHz, CD_3CN, 298 K) showing the acid-catalysed component-swapping of **H[3]R^{2+}** and **M[3]R^{2+}**

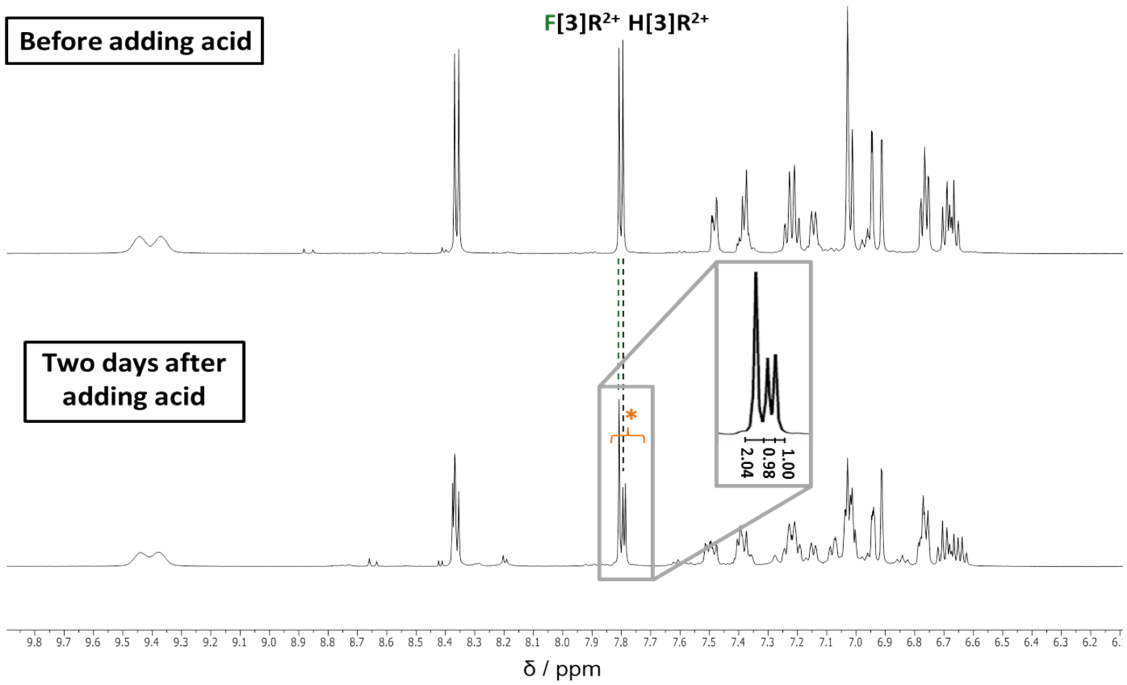


Figure S18. ^{1}H NMR Spectra (500 MHz, CD_3CN, 298 K) showing the acid-catalysed component-swapping of **H[3]R^{2+}** and **F[3]R^{2+}**

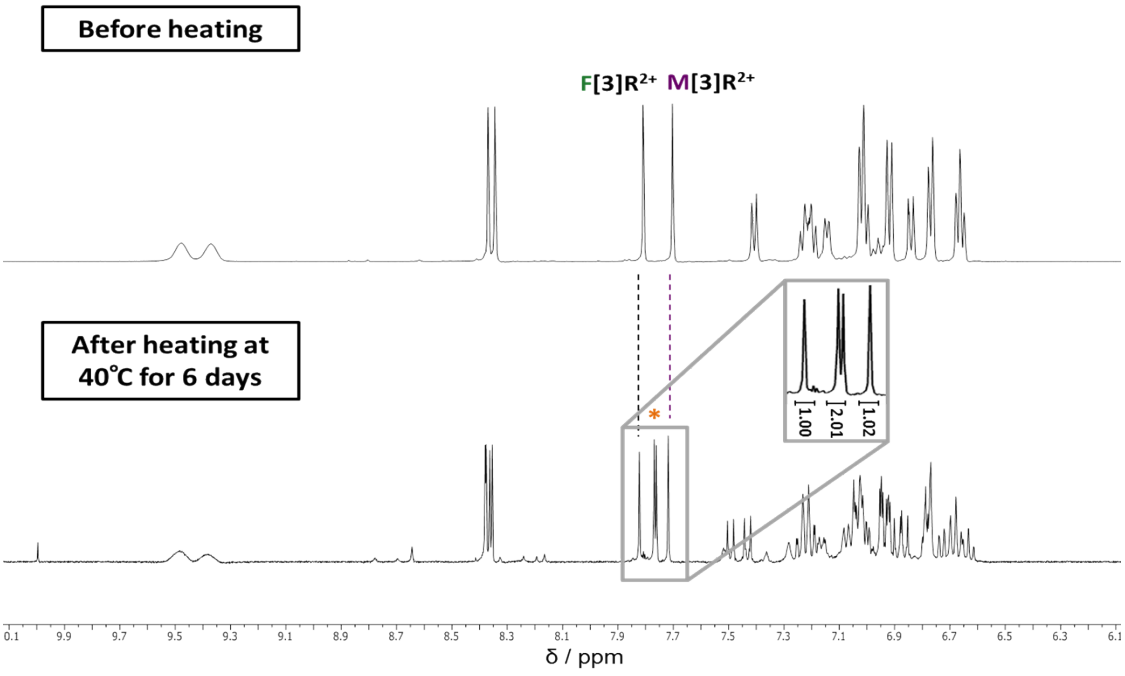


Figure S19. ^{1}H NMR Spectra (500 MHz, CD_3CN, 298 K) showing the dynamic exchange of **M[3]R^{2+}** and **F[3]R^{2+}** by heating at 40°C for 6 days

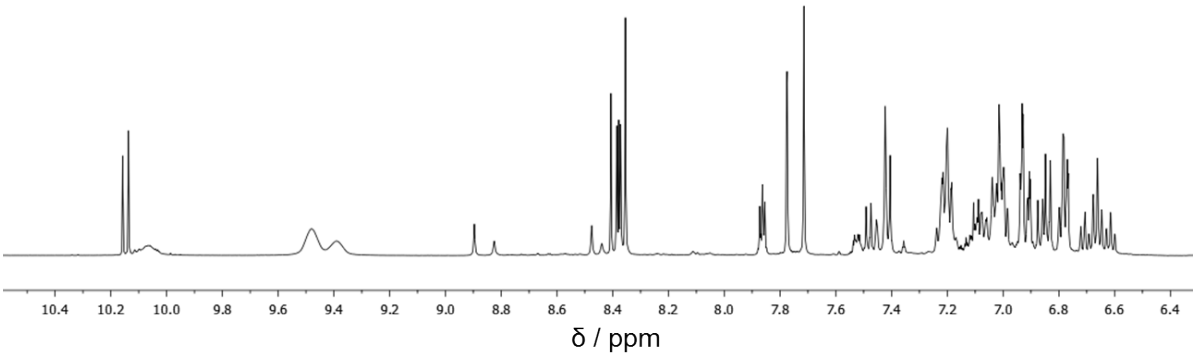


Figure S20. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) showing the direct mixing of 2.0 equiv **BA** and 1.0 equiv each of **2D²⁺**, **MDA** and **FDA** at 8.0 mM after 48 h.

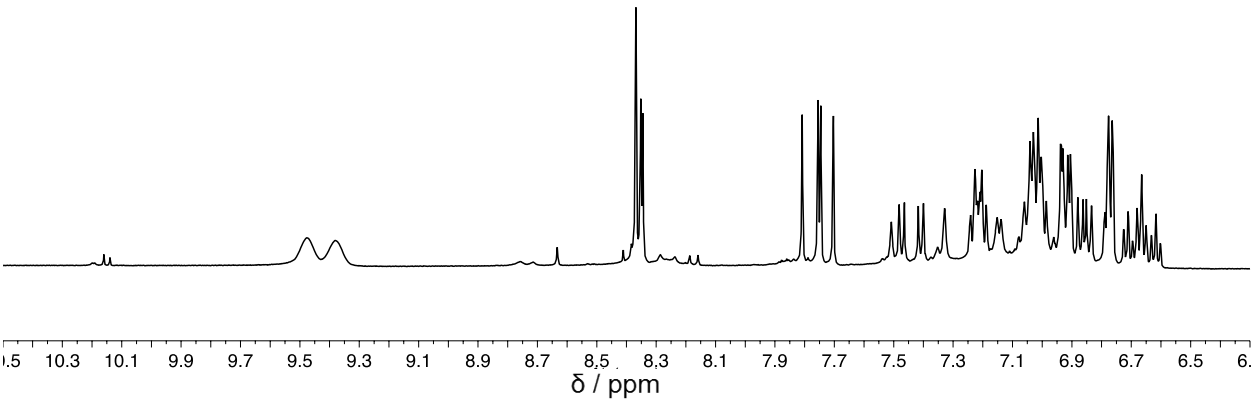


Figure S21. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) showing the acid-catalysed direct mixing of **BA, 2D²⁺, MDA** and **FDA** in the presence of HPF_6 (5 mol% per imine bond) after 48 h.

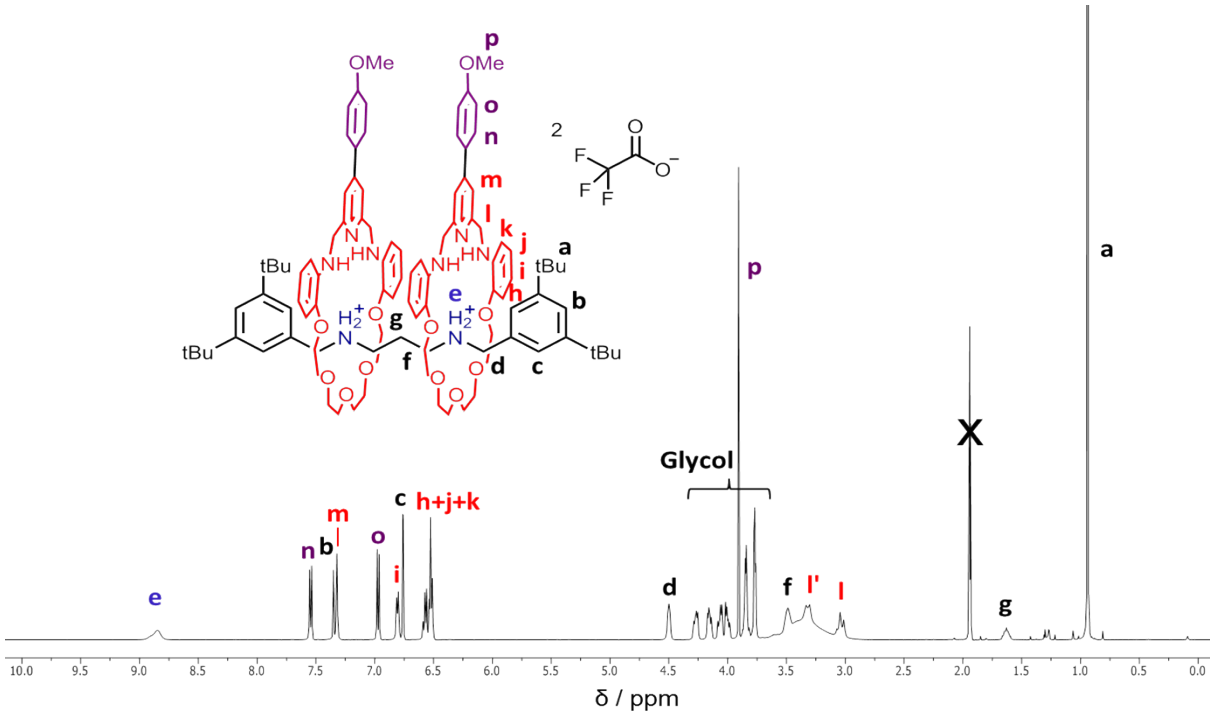


Figure S22. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **M[3]R^{2+}**

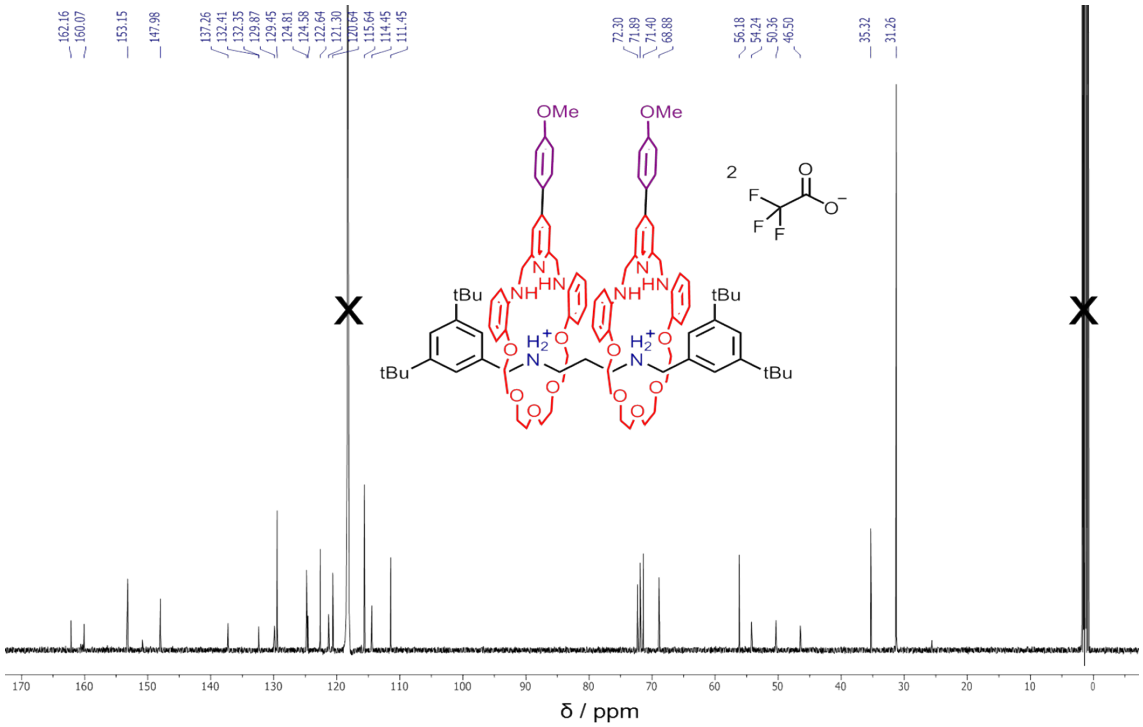


Figure S23. ^{13}C NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **M[3]R^{2+}**

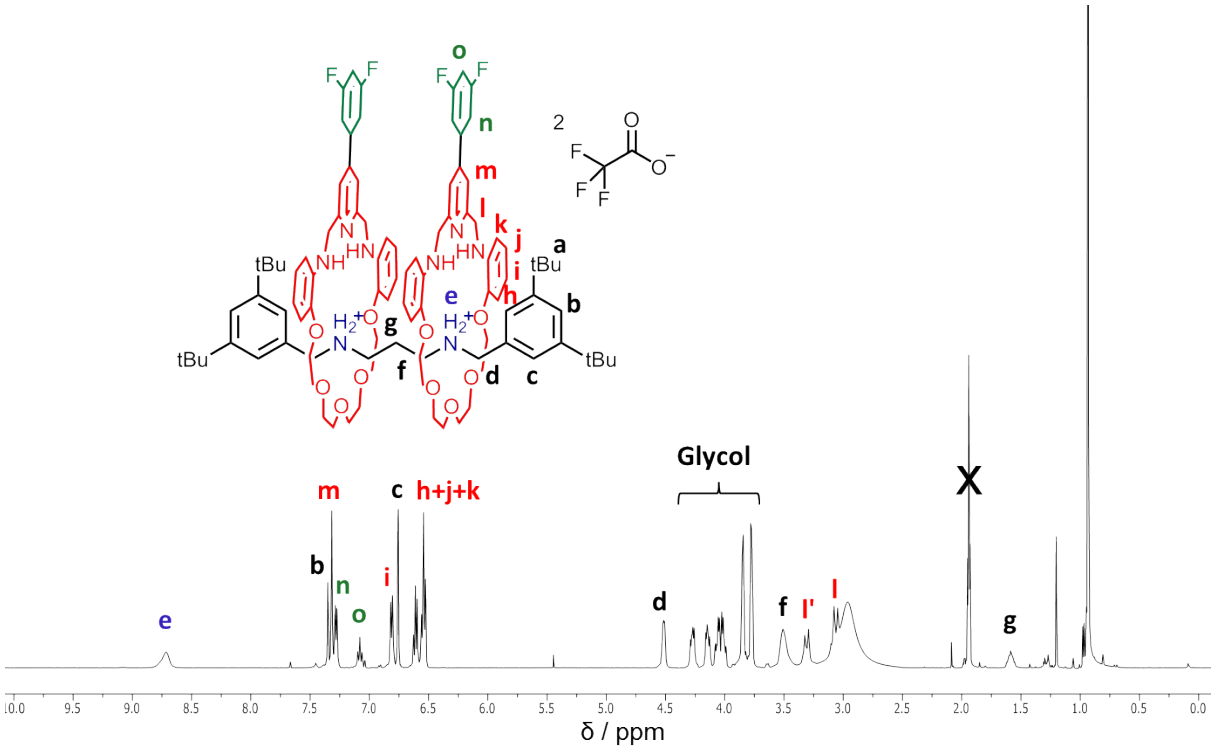


Figure S24. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **F[3]R^{2+}**

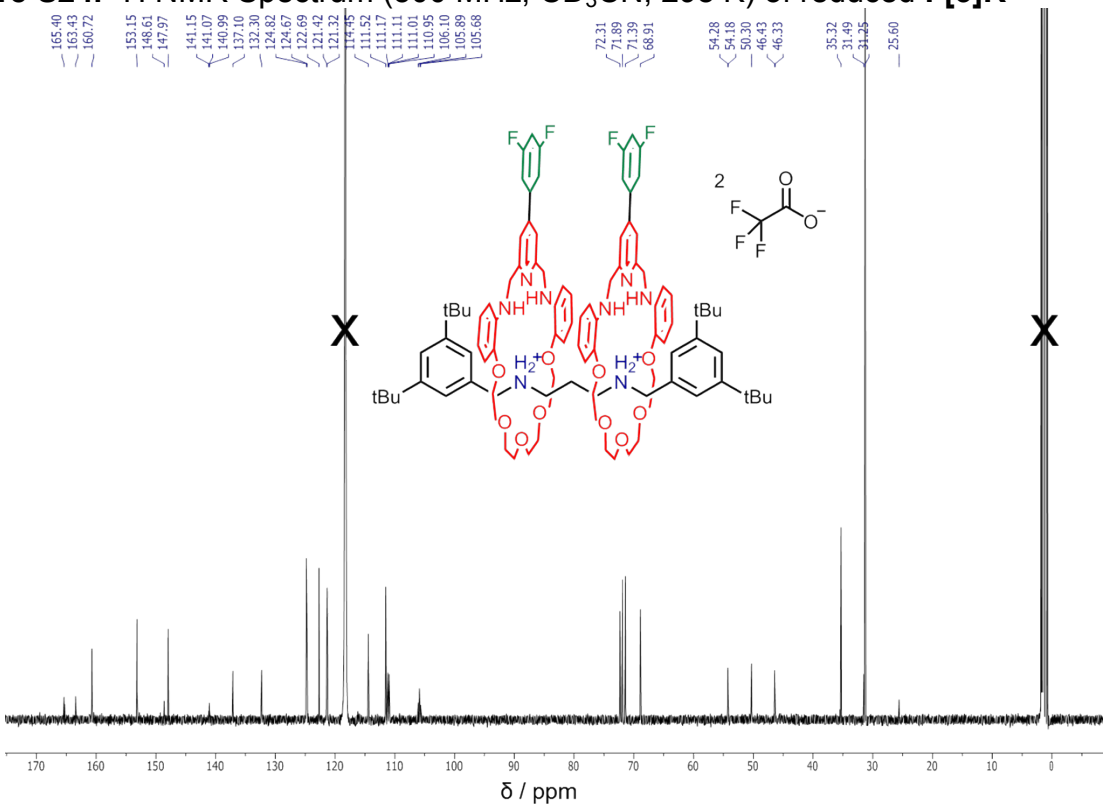


Figure S25. ^{13}C NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **F[3]R^{2+}**

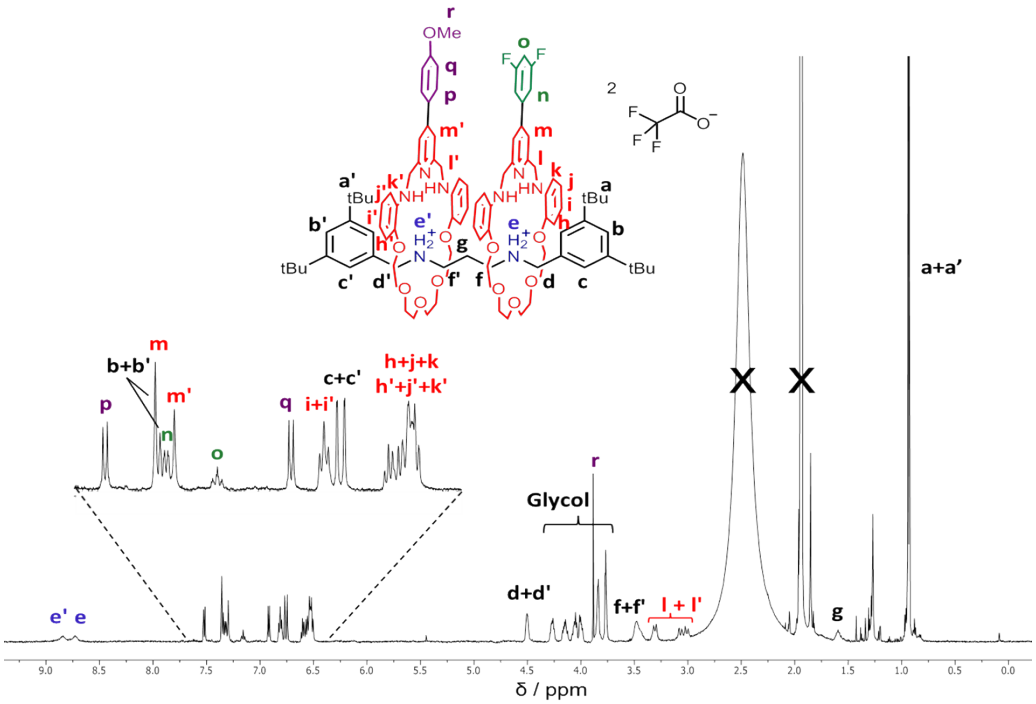


Figure S26. ^{1}H NMR Spectrum (600 MHz, CD_3CN, 298 K) of reduced **M-F[3]R^{2+}**

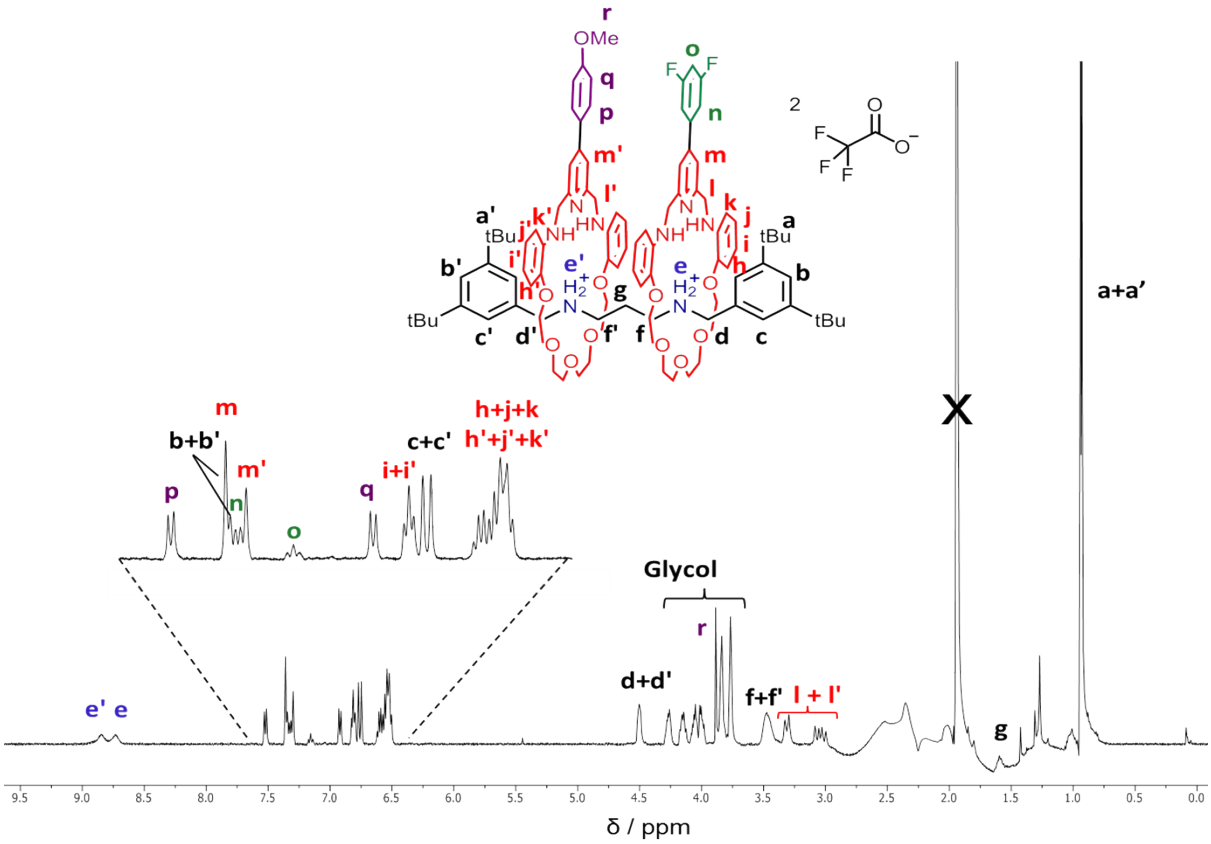


Figure S27. ^{1}H NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **M-F[3]R^{2+}** with H_2O signal at 2.5 ppm suppressed

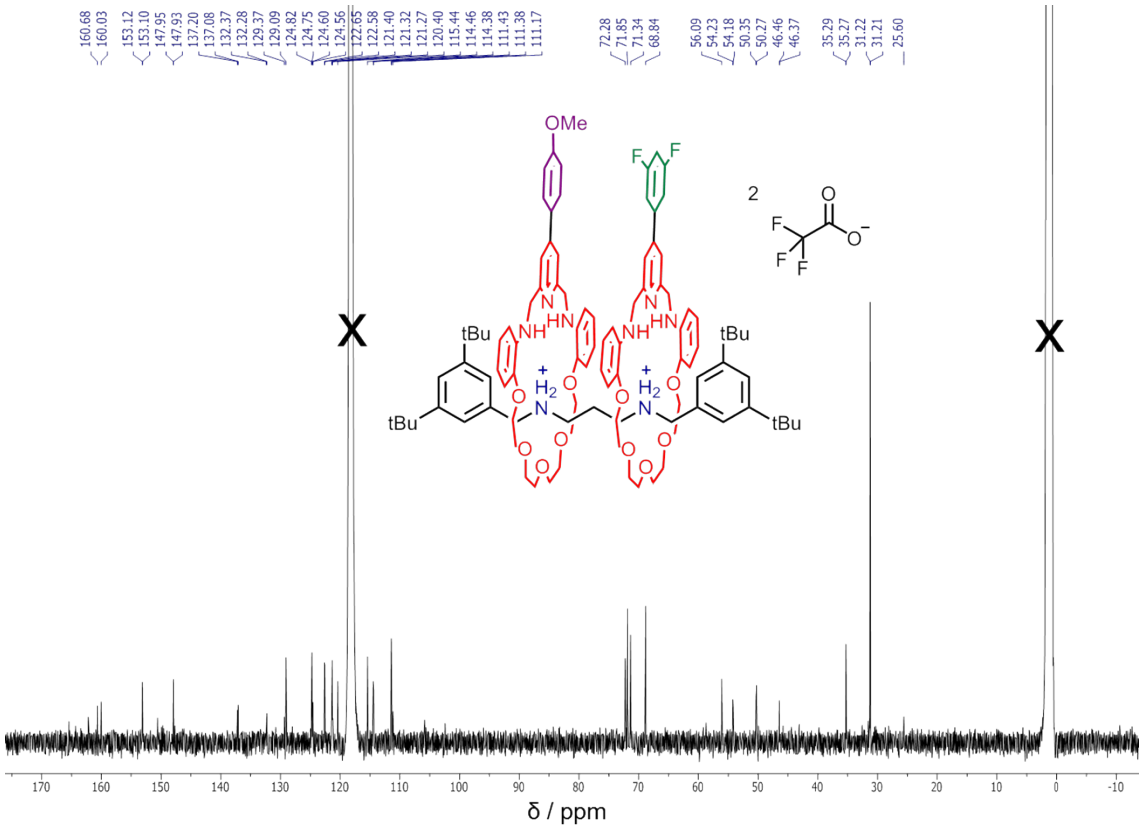


Figure S28. ^{13}C NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **M-F[3]R^{2+}**

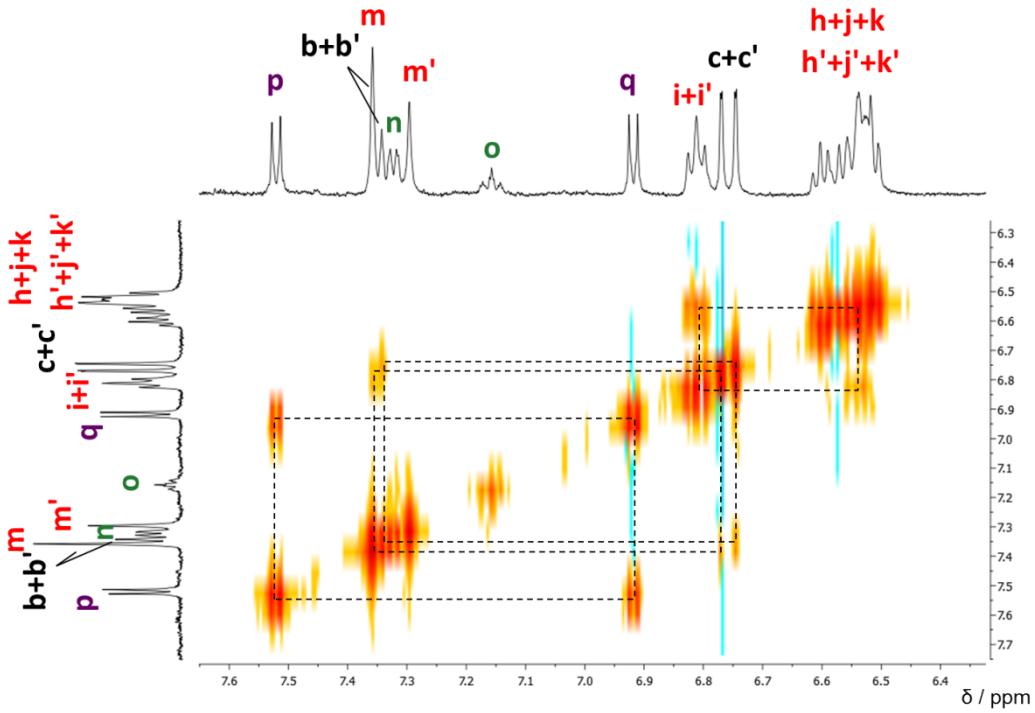


Figure S29. Partial ^1H–^1H COSY NMR Spectrum (500 MHz, CD_3CN, 298 K) of reduced **M-F[3]R^{2+}**

4. MS Spectra

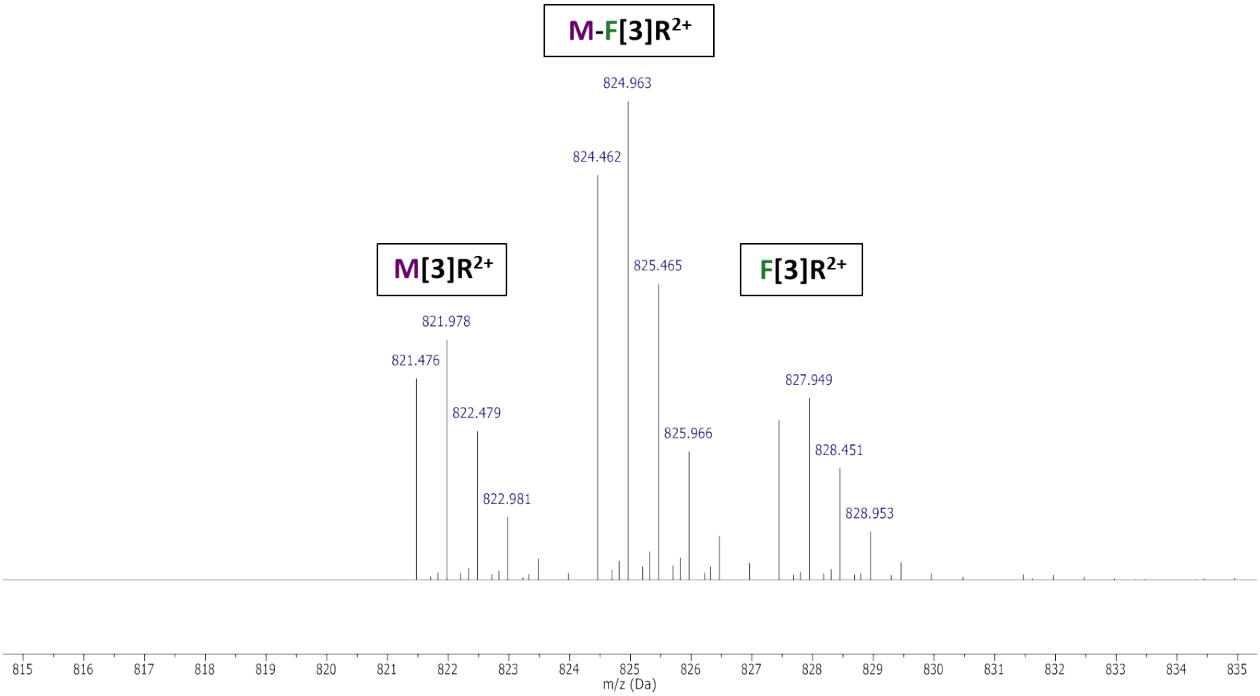


Figure S30. MS Spectrum of the dynamic mixture of **M[3]R^{2+}**, **F[3]R^{2+}** and **M-F[3]R^{2+}** showing the [*M*–2PF$_6$]$^{2+}$ signals

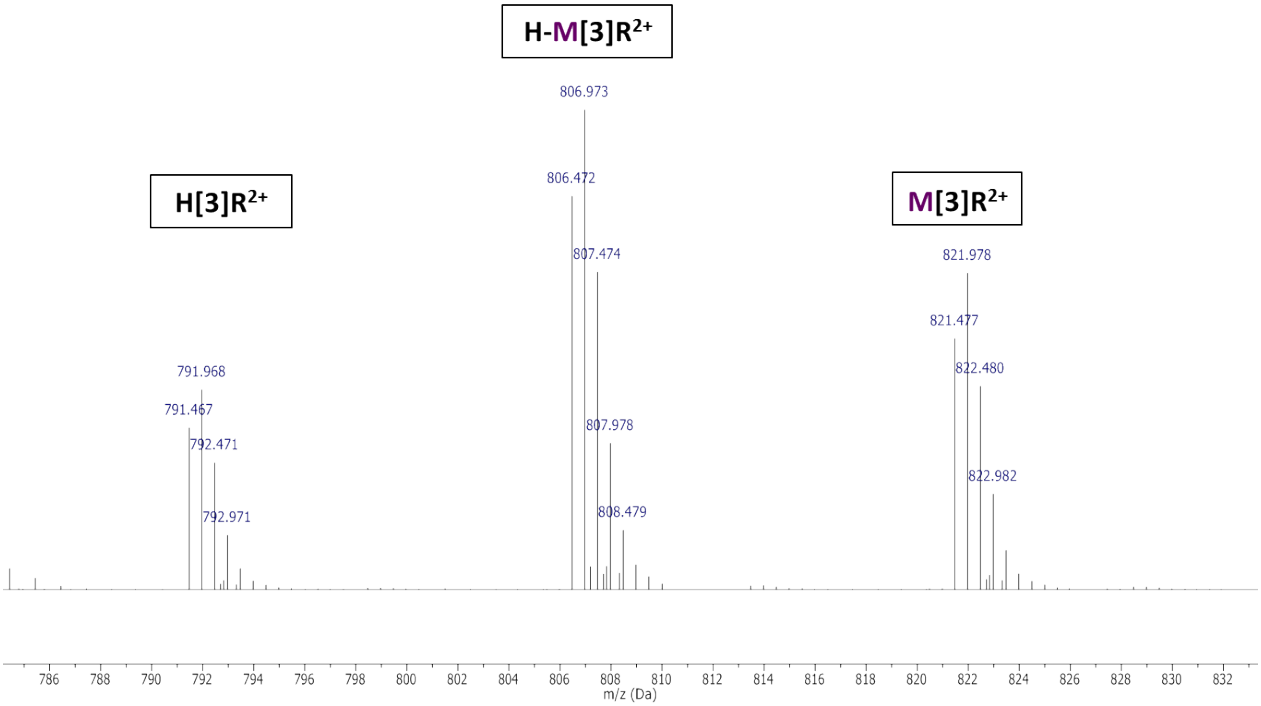


Figure S31. MS Spectrum of the dynamic mixture of **H[3]R^{2+}**, **M[3]R^{2+}** and **H-M[3]R^{2+}** showing the [*M*–2PF$_6$]$^{2+}$ signals

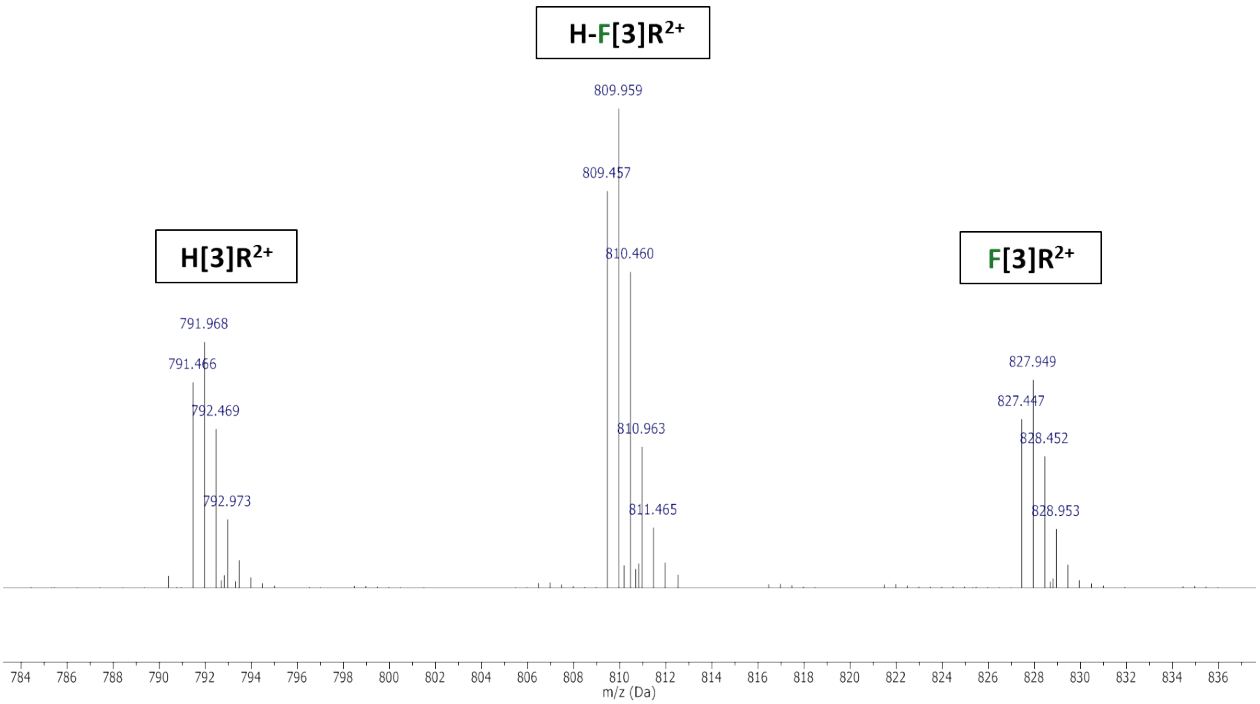


Figure S32. MS Spectrum of the dynamic mixture of **H[3]R^{2+}**, **F[3]R^{2+}** and **H-F[3]R^{2+}** showing the [*M*–2PF$_6$]$^{2+}$ signals

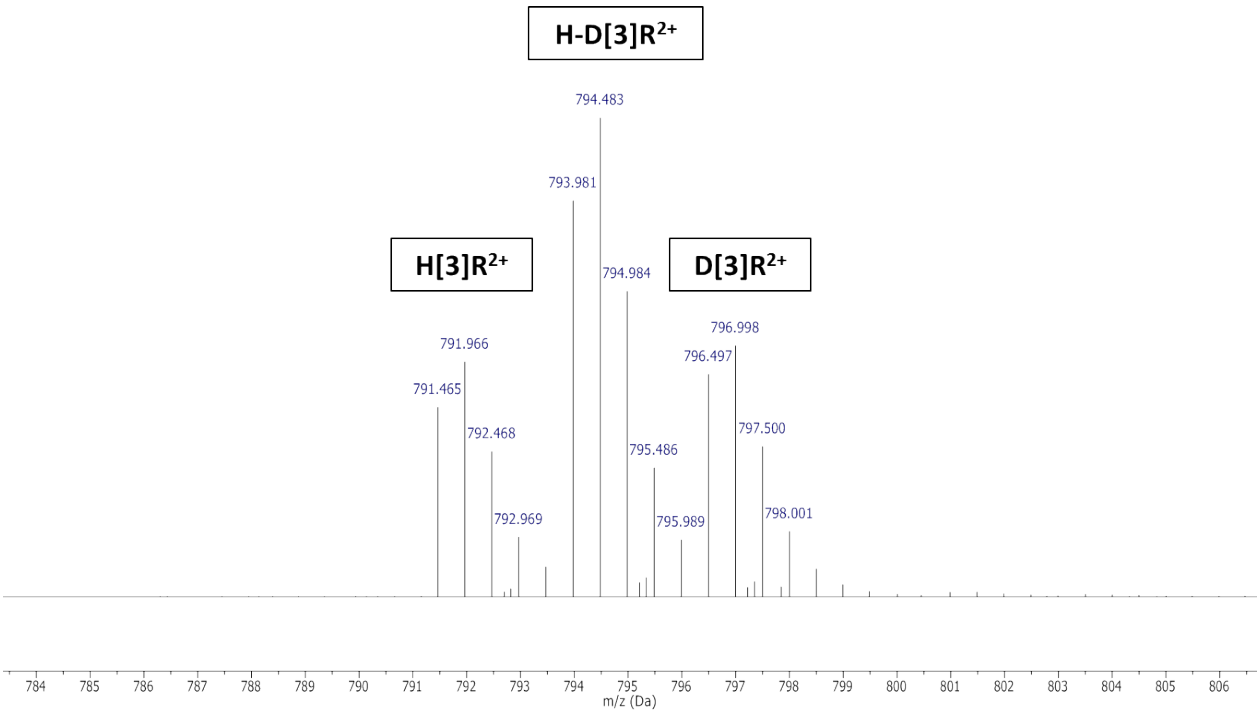


Figure S33. MS Spectrum of the dynamic mixture of **H[3]R^{2+}**, **D[3]R^{2+}** and **H-D[3]R^{2+}** showing the [*M*–2PF$_6$]$^{2+}$ signals in a 1:1:2 ratio

5. Single Crystal X-Ray Crystallographic Information

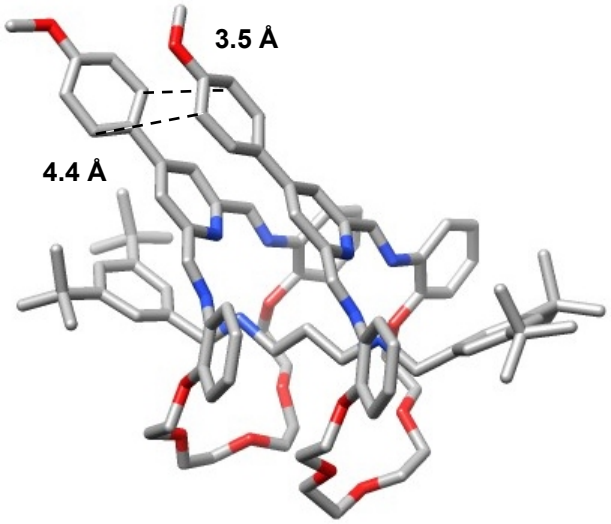


Figure S34. Single crystal XRD structure of **M[3]R^{2+}** (PF_6 counterions and hydrogen atoms omitted for clarity)

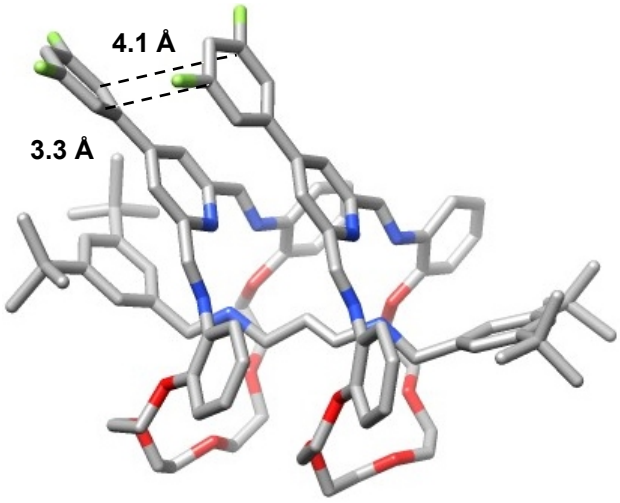


Figure S35. Single Crystal XRD structure of **F[3]R^{2+}** (PF_6 counterions and hydrogen atoms omitted for clarity)

Table S1. X-Ray Crystallographic Parameters for **M[3]R**$^{2+}$

formula	$C_{106}H_{136}F_{12}N_9O_{12.5}P_2$
formula weight (FW)	2026.227
crystal system	triclinic
space group	$P\bar{1}$
T [K]	100(2)
a [Å]	20.542(2)
b [Å]	23.791(3)
c [Å]	24.599(2)
α [deg]	91.402(10)
β [deg]	95.326(7)
γ [deg]	115.533(8)
V [Å^3]	10773(2)
Z	4
no. of reflections measured	20131
no. of observations	6275
no. of parameters refined	2635
$R1$	0.1475
$wR2$	0.4305
GOF	1.035
CCDC no.	999555

Table S2. X-Ray Crystallographic Parameters for **F[3]R^{2+}**

formula	$C_{105}H_{127}F_{16}N_{11}O_{10}P_2$
formula weight (FW)	2069.11
crystal system	triclinic
space group	$P\bar{1}$
T [K]	100(2)
a [Å]	17.5877(8)
b [Å]	18.0515(9)
c [Å]	19.1109(9)
α [deg]	73.981(2)
β [deg]	64.138(2)
γ [deg]	88.090(2)
V [Å^3]	5221.1(4)
Z	2
no. of reflections measured	17189
no. of observations	14403
no. of parameters refined	1525
$R1$	0.0922
$wR2$	0.2715
GOF	1.049
CCDC no.	999556

6. Supporting Information References

S1. H. Sieger and F. Vögtle, *Liebigs Ann.,* 1980, 425.

S2. A.-J. Avestro, D. M. Gardner, N. A. Vermeulen, E. A. Wilson, S. T. Schneebeli, A. C. Whalley, M. E. Belowich, R. Carmieli, M. R. Wasielewski and J. F. Stoddart, *Angew. Chem., Int. Ed.*, 2014, **53**, 4442.

S3. H. Takalo and J. Kankare, *Acta Chem. Scand. B,* 1987, **41**, 219.

S4. H. Takalo, *Acta Chem. Scand. B,* 1988, **42**, 373.