# An ExBox [2]Catenane

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# Supporting Information

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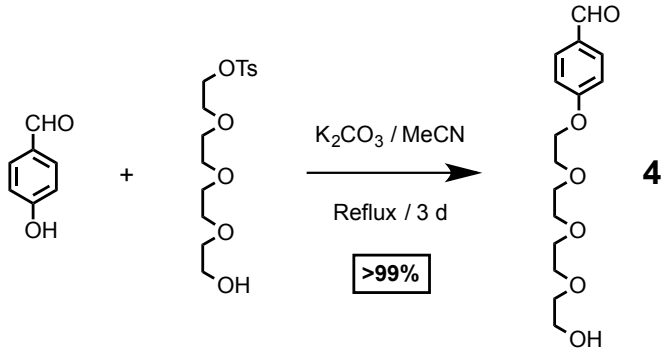
## S1. Materials and methods

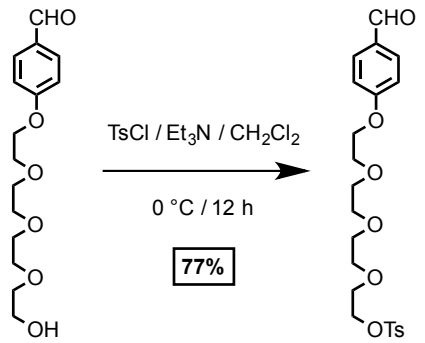
All reagents were purchased from commercial suppliers and used without further purification unless stated otherwise. Di(1*H*-pyrrol-2-yl)methane,[S1] **ExBox•**$4PF_6$,[S2,S3] and 2-(2-(2-(2-hydroxy-ethoxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate[S4] were synthesised as previously reported. Thin-layer chromatography (TLC) was performed on Merck™ TLC plates (F254 indicator). Column chromatography was carried out on Merck™ silica gel 60 (Merck Grade 9385, 0.040–0.063 mm). Analytical and preparative high-performance liquid chromatography (HPLC) was performed on reverse-phase HPLC (RP-HPLC) instruments, using a $C_{18}$ column and a binary solvent system (MeCN and $H_2O$ with 0.1% TFA). UV/Vis absorbance spectra were recorded using a UV-3600 Shimadzu spectrophotometer and a 2-mm cuvette at 298 K. One- (1D) and two-dimensional (2D) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III 600 MHz and Bruker Avance III 500 MHz NMR spectrometers, with working frequencies of 600.168 ($^1$H), 499.842 ($^1$H), and 125.579 ($^{13}$C) MHz, respectively. The signal corresponding to the residual non-deuterated solvent ($CDCl_3$: $\delta_H$ = 7.26 ppm and $\delta_C$ = 77.16 ppm; MeCN-$d_3$: $\delta_H$ = 1.94 ppm; $Me_2CO$-$d_6$: $\delta_H$ = 2.05 ppm and $\delta_C$ = 29.84 ppm) was used as a reference. High-resolution mass spectra (HRMS) were measured on an Agilent 6210 Time-of-Flight (TOF) LC-MS, using an ESI source, coupled with Agilent 1100 HPLC stack, using direct infusion (0.6 mL/min). Cyclic voltammetry (CV) experiments were carried out at room temperature in argon-purged solutions in DMF and MeCN with a Gamry Multipurpose instrument (Reference 600) interfaced to a PC. All CV experiments were performed using a glassy-carbon working electrode (0.071 $cm^2$). The electrode surface was polished routinely with 0.05-μm alumina–water slurry on a felt surface immediately before use. The counter electrode was a Pt coil and the reference electrode was a Ag/AgCl electrode. The concentration of the sample and supporting electrolyte, tetrabutylammonium hexafluoro-phosphate ($TBAPF_6$), were 1.0 mM and 0.10 M, respectively. The CV cell was dried in an oven immediately before use and argon was flushed continually through the cell as it was cooled down to room temperature to avoid condensation of water. Isothermal titration calorimetry (ITC) experiments were performed on a MicroCal system, VP-ITC model. The ITC measurements were performed in dry, deoxygenated $Me_2CO$ at 298 K. A solution of **ExBox•**$4PF_6$ (0.40 mM in $Me_2CO$) was used as

the host solution in a 1.8-mL cell. A solution of **2**-$H_2$ (4.0 mM in $Me_2CO$) was added by injecting 10 μL of titrant successively over 20 s (25×) with 300-s intervals between each injection. Experiments were repeated three times (Figures S9). Thermodynamic information was calculated using a one-site binding model utilising data, from which the heat of dilution of the guest was subtracted, with the average of three runs being reported.

## S2. Synthesis and characterisation

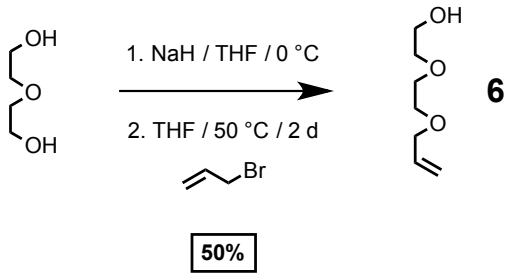



**4-(2-(2-(2-(2-Hydroxyethoxy)ethoxy)ethoxy)ethoxy)benzaldehyde (4).** A mixture of 4-hydroxybenzaldehyde (0.736 g, 6.03 mmol), 2-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (2.10 g, 6.03 mmol), $K_2CO_3$ (2.50 g, 18.1 mmol), and dry MeCN (50 mL) was heated at reflux under a nitrogen atmosphere for 3 d. After the addition of $CH_2Cl_2$ (50 mL), the mixture was filtered and the precipitate was washed with $CH_2Cl_2$ (2 × 50 mL). The organic filtrates were combined and the solvents were evaporated to afford the crude product **4** (1.80 g, >99%) as a pale orange oil. The product was used in the next step without further purification. $^1$H NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 9.88 (s, 1H), 7.86–7.80 (AA' of AA'XX', $J$ = 8.4 Hz, 2H), 7.05–6.99 (XX' of AA'XX', $J$ = 8.4 Hz, 2H), 4.25–4.20 (m, 2H), 3.92–3.87 (m, 2H), 3.77–3.56 (m, 12H), 2.60 (t, $J$ = 5.9 Hz, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 191.0, 163.9, 132.1, 130.2, 115.0, 72.6, 71.0, 70.8, 70.7, 70.4, 69.6, 67.8, 61.9. HRMS (ESI): *m/z* calcd for $[M + H]^+$: 299.1489; found 299.1498.



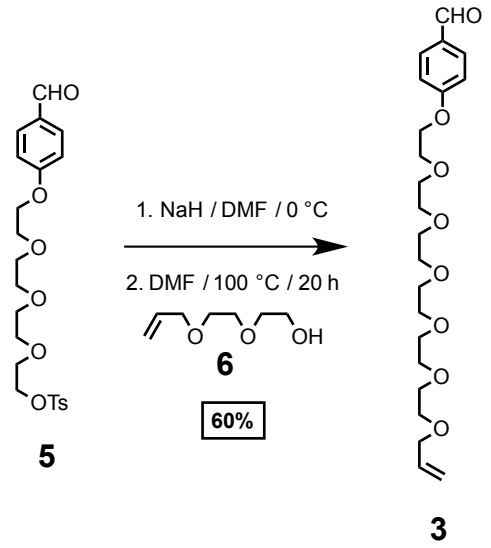

**4** **5**

**2-(2-(2-(2-(4-Formylphenoxy)ethoxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (5).** A mixture of **4** (1.80 g, 6.03 mmol), TsCl (1.73 g, 9.05 mmol), $Et_3N$ (1.7 mL, 12 mmol), and $CH_2Cl_2$ (75 mL) was left standing in the refrigerator (0 °C) for 12 h. After the solvents had been evaporated, the residue was purified by column chromatography over silica gel using $CH_2Cl_2$ and $CH_2Cl_2/Me_2CO$ (98:2) as the eluents to afford the pure product **5** (2.11 g, 77%) as a pale yellow oil. $^1$H NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 9.88 (s, 1H), 7.85–7.81 (AA' of AA'XX', $J$ = 8.7 Hz, 2H), 7.81–7.76 (AA' of AA'XX', $J$ = 8.3 Hz, 2H), 7.35–7.31 (XX' of AA'XX', $J$ = 8.0 Hz, 2H), 7.04–6.99 (XX' of AA'XX', $J$ = 8.7 Hz, 2H), 4.23–4.19 (m, 2H), 4.17–4.12 (m, 2H), 3.91–3.86 (m, 2H), 3.75–3.63 (m, 6H), 3.62–3.57 (m, 4H), 2.44 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 191.0, 164.0, 145.0, 133.0, 132.1, 130.1, 130.0, 128.1, 115.0, 71.0, 70.9, 70.8, 70.7, 69.6, 69.4, 68.8, 67.9, 21.8. HRMS (ESI): *m/z* calcd for $[M + Na]^+$: 475.1397; found 475.1414.



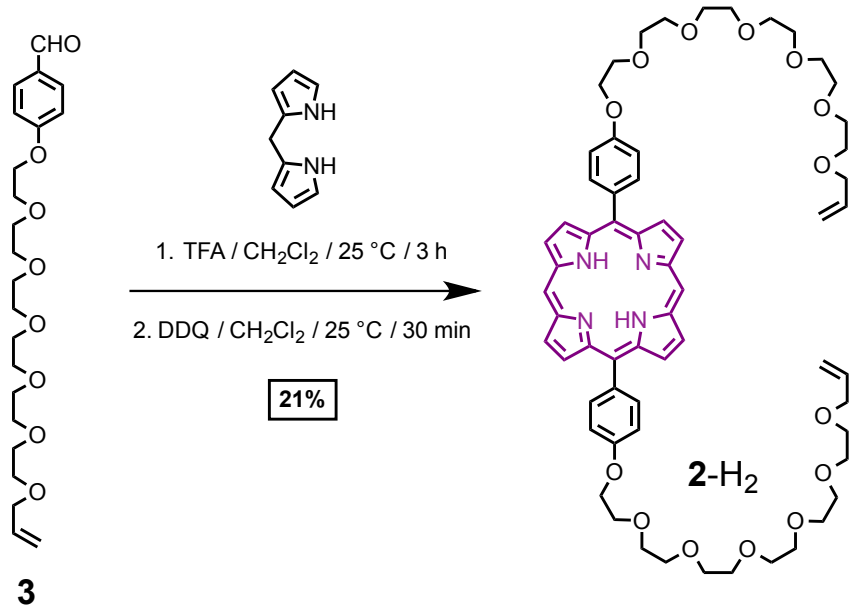

**2-(2-(Vinyloxy)ethoxy)ethanol (6).** NaH (1.50 g, 37.4 mmol, 60% suspension in oil) was added in small portions with stirring to a cooled (0 °C) solution of diethylene glycol (3.97 g, 37.4

mmol) in dry THF (150 mL) during 10 min. Next, allyl bromide (3.24 mL, 37.4 mmol) was added and the resulting mixture was heated at 50 °C under a nitrogen atmosphere for 2 d. The reaction mixture was filtered and the precipitate was washed with $Me_2CO$. The organic filtrates were combined, the solvents were evaporated, and the residue was purified by column chromatography over silica gel using $CH_2Cl_2/Me_2CO$ (98:2 to 95:5) as the eluent to afford the pure product **6** (2.74 g, 50%) as a pale yellow oil. $^1$H NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 5.92 (ddt, $J$ = 17.3, 10.4, 5.7 Hz, 1H), 5.29 (ddt, $J$ = 17.3, 1.6, 1.6 Hz, 1H), 5.20 (ddt, $J$ = 10.4, 1.4, 1.3 Hz, 1H), 4.03 (ddd, $J$ = 5.8, 1.4, 1.4 Hz, 2H), 3.77–3.71 (m, 2H), 3.71–3.66 (m, 2H), 3.64–3.59 (m, 4H), 2.45 (t, $J$ = 6.2 Hz, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 134.6, 117.6, 72.6, 72.4, 70.6, 69.6, 62.0. HRMS (ESI): *m/z* calcd for $[M + Na]^+$: 169.0835; found 169.0859.



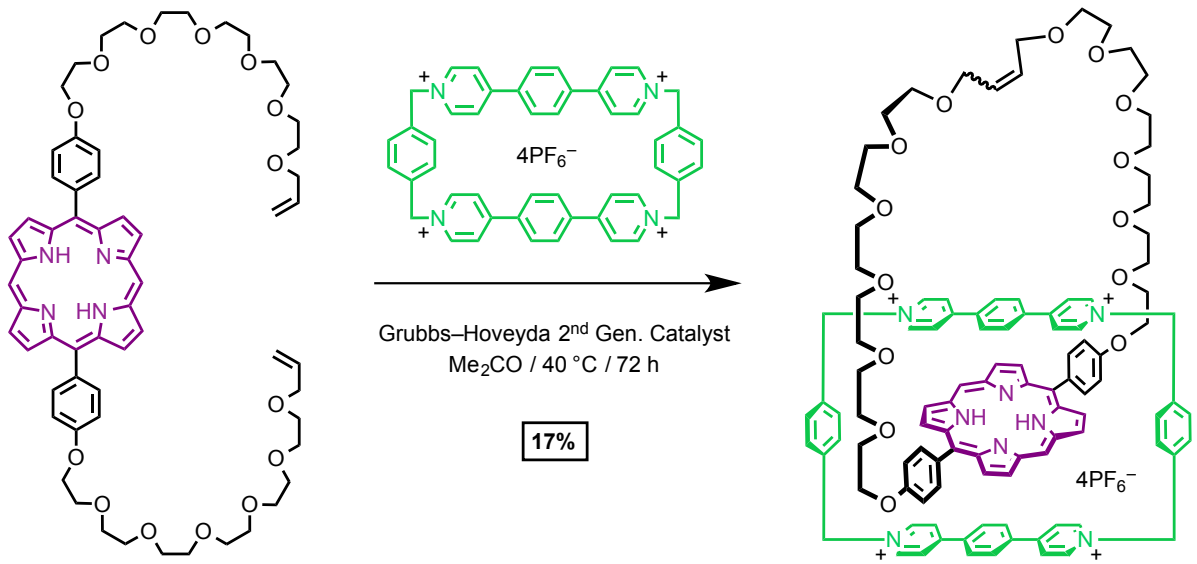

**4-(3,6,9,12,15,18-Hexaoxahenicos-20-en-1-yloxy)benzaldehyde (3).** NaH (133 mg, 3.33 mmol, 60% suspension in oil) was added in small portions with stirring to a cooled (0 °C) solution of **6** (360 mg, 2.47 mmol) in dry DMF (20 mL) over 10 min. Next, a solution of **5** (1.24 g, 2.74 mmol) in dry DMF (5 mL) was added and the resulting mixture was heated at 100 °C under a nitrogen atmosphere for 20 h. [Compound **5** (1.1 equiv) was used in a small excess relative to **6** (1 equiv) because **6** and **3** are inseparable by column chromatography.] The solvent was removed under the reduced pressure and the residue was purified by column chromatography over silica

gel using $CH_2Cl_2$/$Me_2CO$ (95:5 to 90:10) as the eluent to afford the pure product **3** (0.63 g, 60%) as a pale yellow oil. $^1$H NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 9.88 (s, 1H), 7.85–7.80 (AA' of AA'XX', $J$ = 8.7 Hz, 2H), 7.04–7.00 (XX' of AA'XX', $J$ = 8.6 Hz, 2H), 5.91 (ddt, $J$ = 16.4, 11.0, 5.7 Hz, 1H), 5.27 (ddt, $J$ = 17.1, 1.7, 1.7 Hz, 1H), 5.17 (ddt, $J$ = 10.6, 1.4, 1.4 Hz, 1H), 4.23–4.19 (m, 2H), 4.01 (ddd, $J$ = 5.6, 1.4, 1.4 Hz, 2H), 3.91–3.87 (m, 2H), 3.76–3.57 (m, 20H). $^{13}$C NMR (125 MHz, $CDCl_3$, ppm): $\delta$ (6 signals could not be detected because of their overlapping with each other) 191.0, 164.0, 134.9, 132.1, 130.1, 117.3, 115.0, 72.4, 71.0, 70.8, 70.7, 69.6, 69.5, 67.9. HRMS (ESI): *m/z* calcd for $[M + Na]^+$: 449.2146; found 449.2159.




**5,15-Bis(4-(3,6,9,12,15,18-Hexaoxahenicos-20-en-1-yloxy)phenyl)porphyrin (2-$H_2$).** A mixture of **3** (250 mg, 0.586 mmol), di(1*H*-pyrrol-2-yl)methane (86 mg, 0.586 mmol), TFA (0.03 mL, 0.4 mmol), and $CH_2Cl_2$ (125 mL) was stirred at room temperature under an argon atmosphere for 3 h in the dark. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ; 67 mg, 0.59 mmol) was then added and the reaction mixture was stirred for an additional 30 min at room temperature. The dark purple solution was washed with $K_2CO_3$ (sat. aq.) and dried ($K_2CO_3$). After the removal of the solvent, the residue was dissolved in MeOH (2–3 mL; 5% TFA) and purified by RP-HPLC ($H_2O$/MeCN/0.1% TFA; 0–100% MeCN in 25 min). The product-

containing fractions were combined, diluted with $H_2O$, and extracted with $CH_2Cl_2$. The combined organic layers were washed with $K_2CO_3$ (sat. aq.) and dried ($K_2CO_3$). Evaporation of the solvent afforded the pure product **2**-$H_2$ (67 mg, 21%) as a dark purple sticky solid. $^1$H NMR (500 MHz, $Me_2CO$-$d_6$, ppm): $\delta$ 10.53 (s, 2H), 9.58 (d, $J$ = 4.5 Hz, 4H), 9.12 (d, $J$ = 4.6 Hz, 4H), 8.24–8.19 (AA' of AA'XX', $J$ = 8.4 Hz, 4H), 7.50–7.43 (XX' of AA'XX', $J$ = 8.5 Hz, 4H), 5.85 (ddt, $J$ = 17.4, 10.6, 5.4 Hz, 2H), 5.22 (ddt, $J$ = 17.3, 1.8, 1.8 Hz, 2H), 5.07 (ddt, $J$ = 10.4, 1.5, 1.5 Hz, 2H), 4.51–4.45 (m, 4H), 4.08–4.02 (m, 4H), 3.93 (ddd, $J$ = 5.3, 1.5, 1.5 Hz, 4H), 3.85–3.46 (m, 40H), –3.04 (s, 2H). $^{13}$C NMR (125 MHz, $Me_2CO$-$d_6$, ppm): $\delta$ (2 signals could not be detected because of their overlapping with each other) 160.0, 136.7, 136.3, 134.3, 132.9, 131.7, 119.7, 116.3, 114.2, 106.2, 72.3, 71.6, 71.37, 71.35, 71.30, 71.26, 71.25, 71.22, 71.21, 71.15, 70.5, 70.3, 68.7. HRMS (ESI): *m/z* calcd for $[M + H]^+$: 1103.5587; found 1103.5585.




**2**-$H_2$ **1**-$H_2$· $4PF_6$

**1-$H_2$•$4PF_6$. ExBox•**$4PF_6$ (107 mg, 85.2 μmol) was added into a solution of **2**-$H_2$ (47 mg, 43 μmol) in $Me_2CO$ (50 mL). The colour of the solution changed immediately from purple to red, indicating the binding of **2**-$H_2$ inside **ExBox**$^{4+}$. Argon was passed through the solution (~1 mM) of **2**-$H_2$⊂**ExBox**$^{4+}$ in $Me_2CO$ for 2 h before the Grubbs–Hoveyda Catalyst (2$^{nd}$ Gen.; 1.3 mg, 2.1

μmol) was added. The reaction was heated at 40 °C for 46 h before the second portion (3.9 mg, 6.3 μmol) of the catalyst was added. The reaction mixture was then heated at 40 °C for an additional 26 h before it was cooled to room temperature and quenched with ethoxyethene (2 mL). After stirring at room temperature for 30 min, the solvents were evaporated and the residue was dissolved in $Me_2SO$ (5 mL; 10% TFA) and purified by RP-HPLC ($H_2O$/MeCN/0.1% TFA; 0–100% MeCN in 25 min). The product-containing fractions were combined and MeCN was removed under the reduced pressure. The **1**-$H_2$•4$PF_6$ (17 mg, 17%) was precipitated with $NH_4PF_6$ (5% (w/v)) and collected by filtration as a dark red solid and as a mixture of the *cis* and *trans* isomers (presumably in a ~1:1 ratio). Since $^1$H and $^{13}$C NMR signals of both isomers overlap within the resolution limits of the NMR spectroscopic techniques, only a set of signals for one isomer is reported. $^1$H NMR (500 MHz, $Me_2CO$-$d_6$, ppm): $\delta$ 9.31–9.27 (AA' of AA'XX', $J$ = 6.7 Hz, 8H), 8.84 (s, 8H), 8.81 (d, $J$ = 4.5 Hz, 4H), 8.18 (d, $J$ = 5.1 Hz, 4H), 8.18–8.14 (AA' of AA'XX', $J$ = 8.6 Hz, 4H), 7.62 (s, 2H), 7.60–7.56 (XX' of AA'XX', $J$ = 8.6 Hz, 4H), 6.74–6.70 (XX' of AA'XX', $J$ = 6.9 Hz, 8H), 6.24 (s, 8H), 5.07 (tt, $J$ = 3.1, 1.3 Hz, 2H), 4.65–4.60 (m, 4H), 4.27 (s, 8H), 4.15–4.09 (m, 4H), 3.92–3.86 (m, 4H), 3.84–3.69 (m, 16H), 3.68–3.63 (m, 4H), 3.61–3.56 (m, 4H), 3.50–3.45 (m, 4H), 3.41–3.32 (m, 8H), 3.18–3.12 (m, 4H), –4.47 (s, 2H). $^1$H NMR (500 MHz, MeCN-$d_3$, ppm): $\delta$ 8.78–8.75 (AA' of AA'XX', $J$ = 6.2 Hz, 8H), 8.74 (d, $J$ = 4.4 Hz, 4H), 8.54 (s, 8H), 8.14–8.09 (AA' of AA'XX', $J$ = 8.3 Hz, 4H), 7.92 (d, $J$ = 4.4 Hz, 4H), 7.59–7.53 (XX' of AA'XX', $J$ = 8.3 Hz, 4H), 7.16 (s, 2H), 6.34–6.30 (XX' of AA'XX', $J$ = 6.5 Hz, 8H), 5.89 (s, 8H), 5.03–5.00 (m, 2H), 4.61–4.56 (m, 4H), 4.09–4.04 (m, 4H), 3.95 (s, 8H), 3.86–3.81 (m, 4H), 3.77–3.59 (m, 20H), 3.56–3.51 (m, 4H), 3.46–3.41 (m, 4H), 3.37–3.33 (m, 4H), 3.30–3.26 (m, 4H), 3.11–3.07 (m, 4H), –4.78 (s, 2H). $^{13}$C NMR (125 MHz, $Me_2CO$-$d_6$, ppm): $\delta$ (4 signals could not be detected because of their overlapping with each other) 160.4, 152.2, 144.6, 139.5, 136.9, 133.5, 133.0, 132.7, 132.3, 132.0, 129.3, 125.7, 125.3, 120.1, 114.9, 104.2, 71.8, 71.6, 71.5, 71.3, 71.2, 71.1, 70.76, 70.75, 70.7, 70.1, 69.1, 65.3. HRMS (ESI): *m/z* calcd for $[M - 2PF_6]^{2+}$: 1018.3864; found 1018.3879.

## S3. Nuclear magnetic resonance spectroscopic data

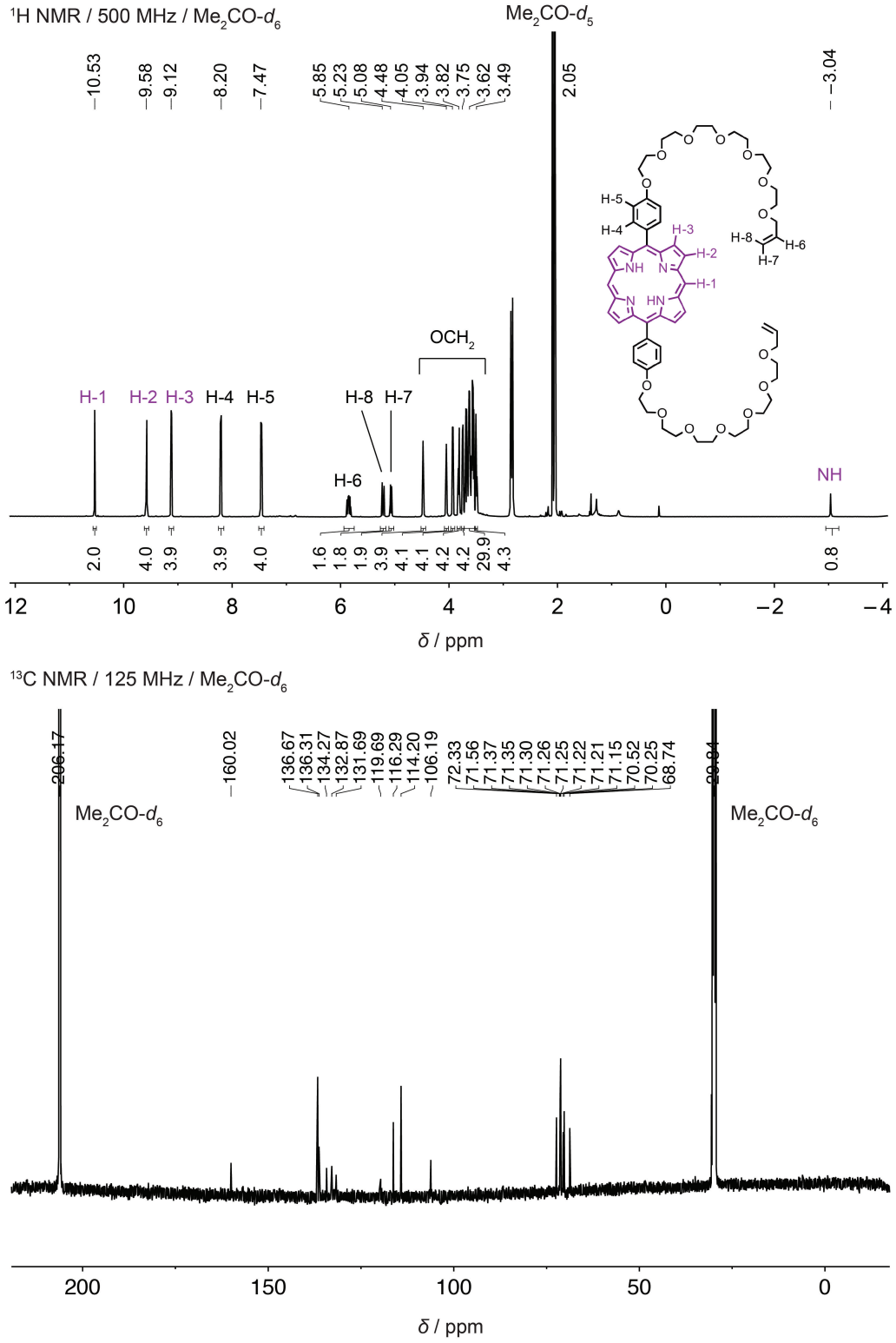



**Fig. S1** $^1$H and $^{13}$C NMR spectra of **2**-$H_2$ in $Me_2CO$-$d_6$.

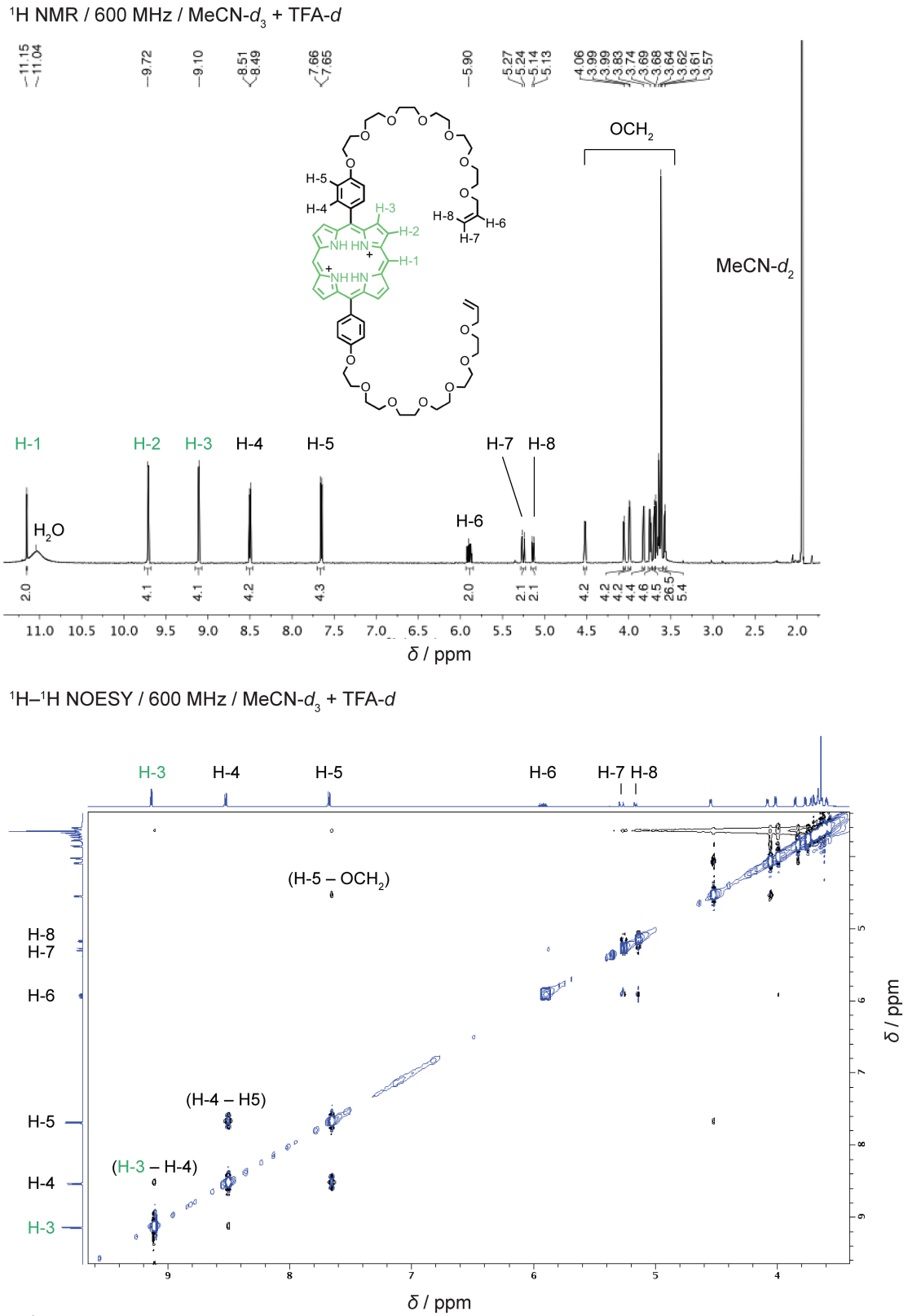



**Fig. S2** $^1$H and 2-D NOESY spectra of **2**-H$_4$•2TFA in CD$_3$CN.

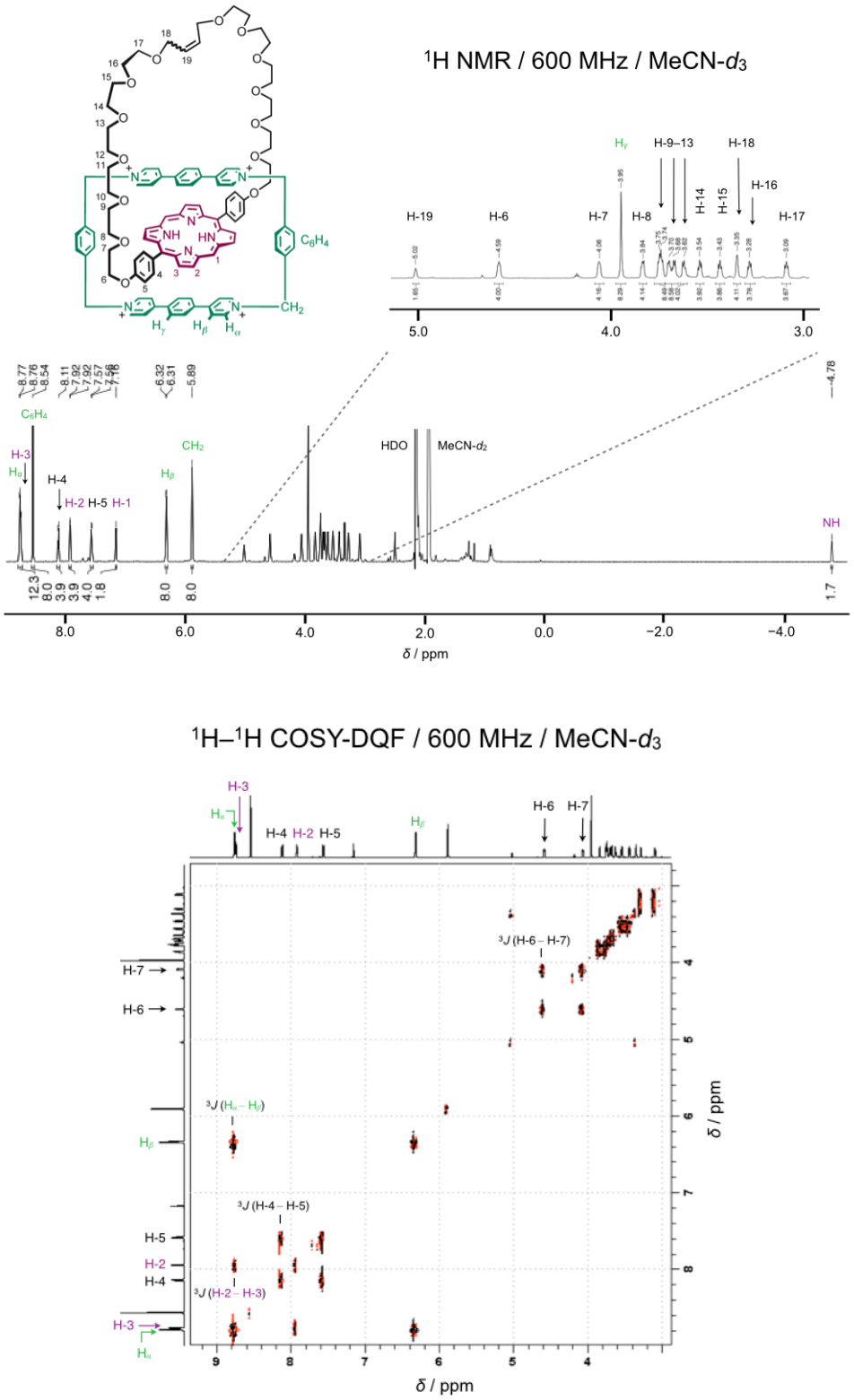



**Fig. S3** Assigned $^1$H NMR and $^1$H–$^1$H COSY-DQF spectra of **1**-$H_2$•4$PF_6$ in MeCN-$d_3$.

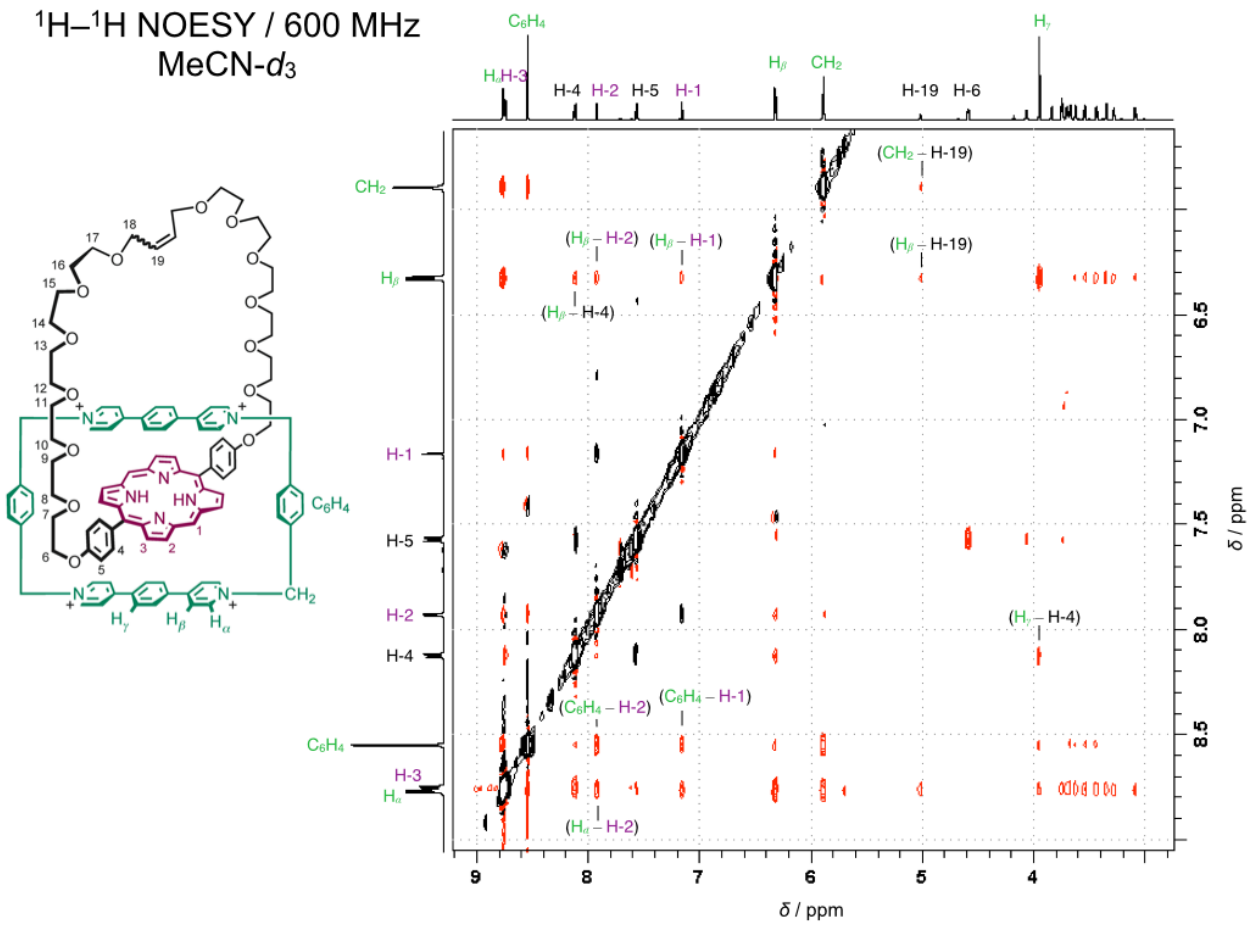



**Fig. S4** Assigned $^1$H–$^1$H NOESY spectra of **1**-$H_2$•4$PF_6$ in MeCN-$d_3$.

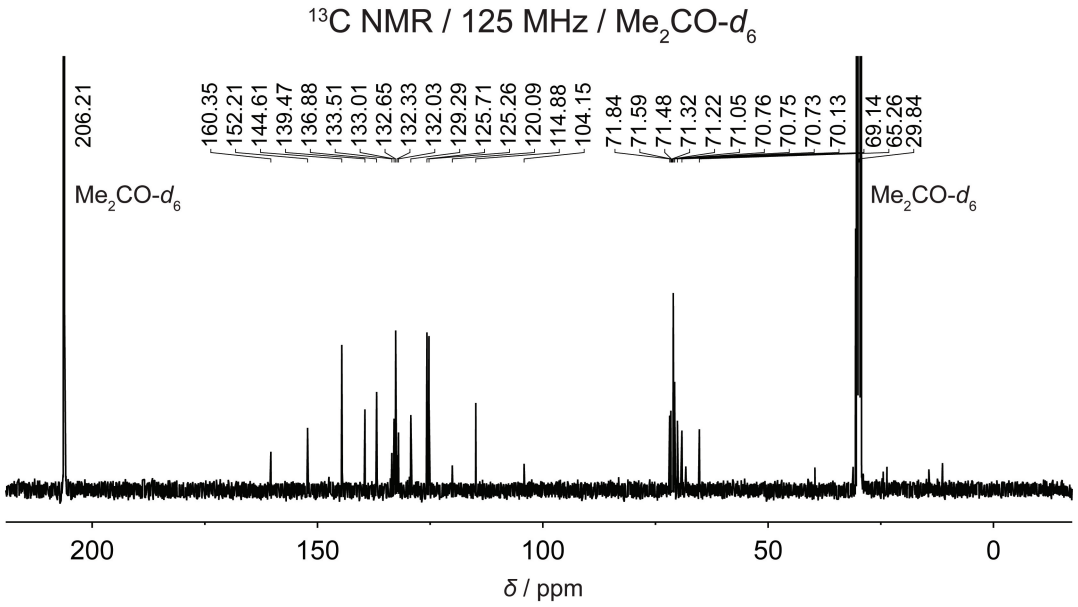



**Fig. S5** $^{13}$C NMR Spectra of **1**-$H_2$•4$PF_6$ in $Me_2CO$-$d_6$.

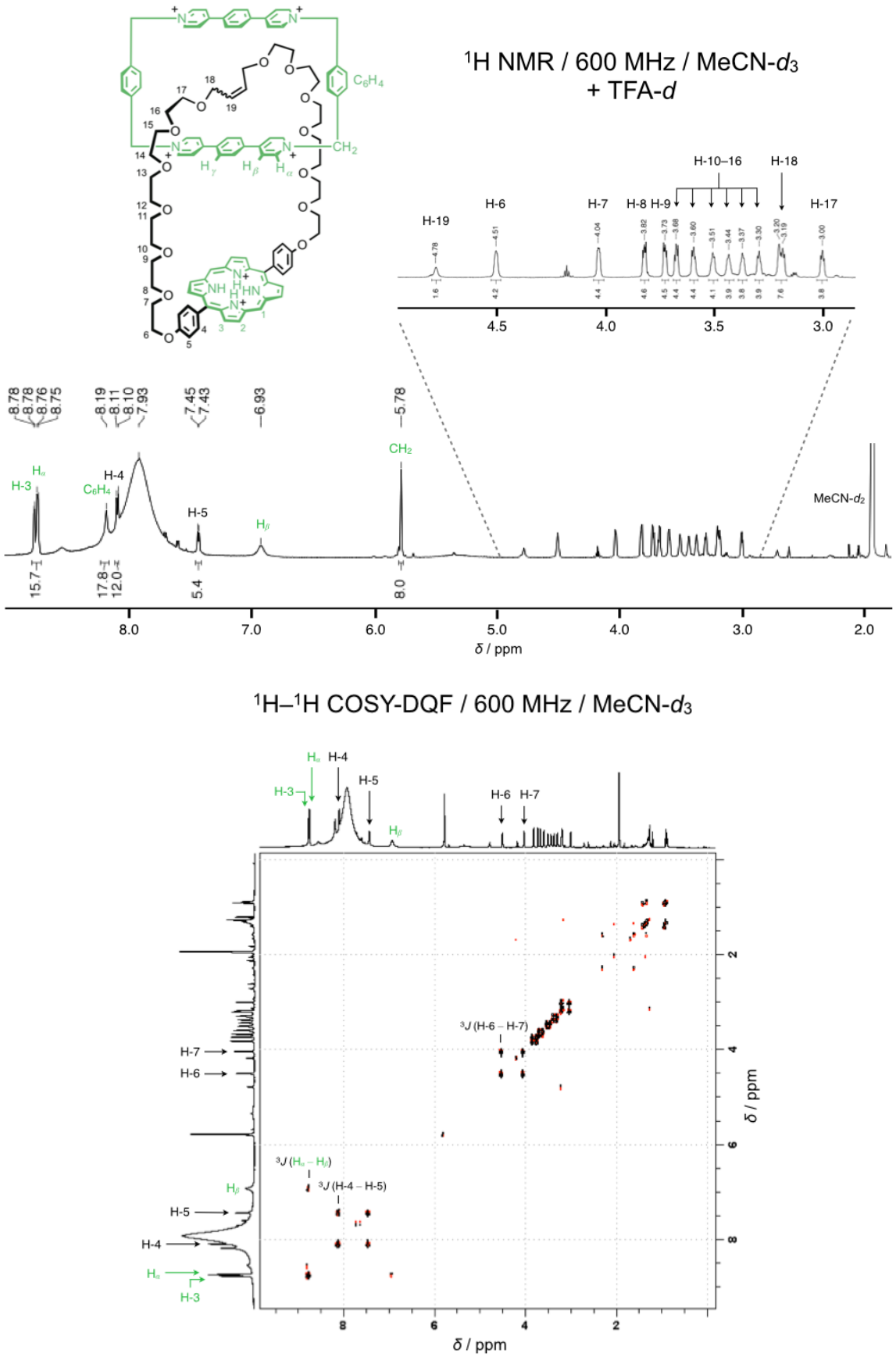



**Fig. S6** Assigned $^1$H NMR and $^1$H–$^1$H COSY-DQF spectra of **1**-$H_4$•6TFA in MeCN-$d_3$.

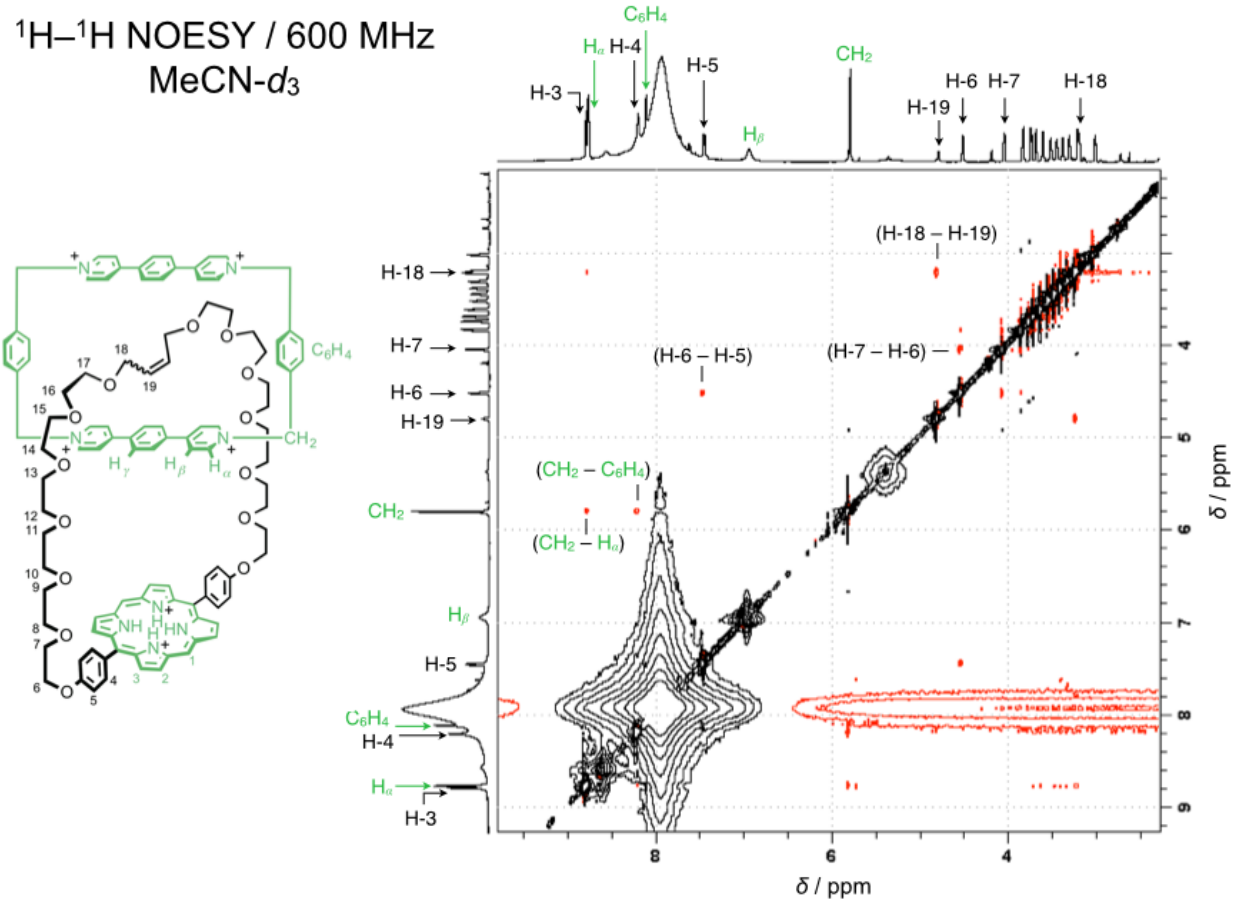



**Fig. S7** Assigned $^1$H–$^1$H NOESY spectra of **1**-$H_4$•6TFA in MeCN-$d_3$.

## S4. Acid-base switching

Switching (Figs. 2 and 3 of main text) between **1**-$H_2^{4+}$ and **1**-$H_4^{6+}$, which was performed by adjusting the pH of a sample of **1**-$H_2$•4$PF_6$ (0.8 mM, 0.75 mL, MeCN-$d_3$) through successive additions of deuterated trifluoroacetic acid (TFA-*d*, 15 μL) and cross-linked poly-4-vinylpyridine (Reilly Chemicals, Lot 11012, 100 mg), was followed by $^1$H NMR spectroscopy. The cross-linked poly-4-vinylpyridine was filtered off from the sample before acquiring an $^1$H NMR spectrum. The stacked $^1$H NMR spectra are shown in Figure S7. The signals for protons H-18 and H-19 shift significantly (by 0.2 ppm) upfield when the pH is lowered, suggesting that the cyclophane is located in the proximity of the alkene group once the porphyrin ring becomes charged. Analogously, the resonance for proton H-2 shifts downfield when TFA-*d* is added, as the aromatic groups of the cyclophane no longer provide the shielding induced current effect. The signals for the cyclophane protons $H_{C6H4}$ and $H_{CH2}$ are shifted upfield on moving away from

the deshielding induced current of the porphyrin ring. Proton $H_\beta$ occupies the space directly above and below the shielding induced current of the porphyrin ring at higher pH and thus its resonance is shifted downfield once the cyclophane no longer encircles the porphyrin ring at low pH. Although these changes in chemical shift on account of the adjustment of pH are reversible throughout the three-cycle NMR spectroscopic experiment, there are signs (Figure S7) of degradation of the **1**-$H_2$•$4PF_6$ upon the completion of the third cycle.

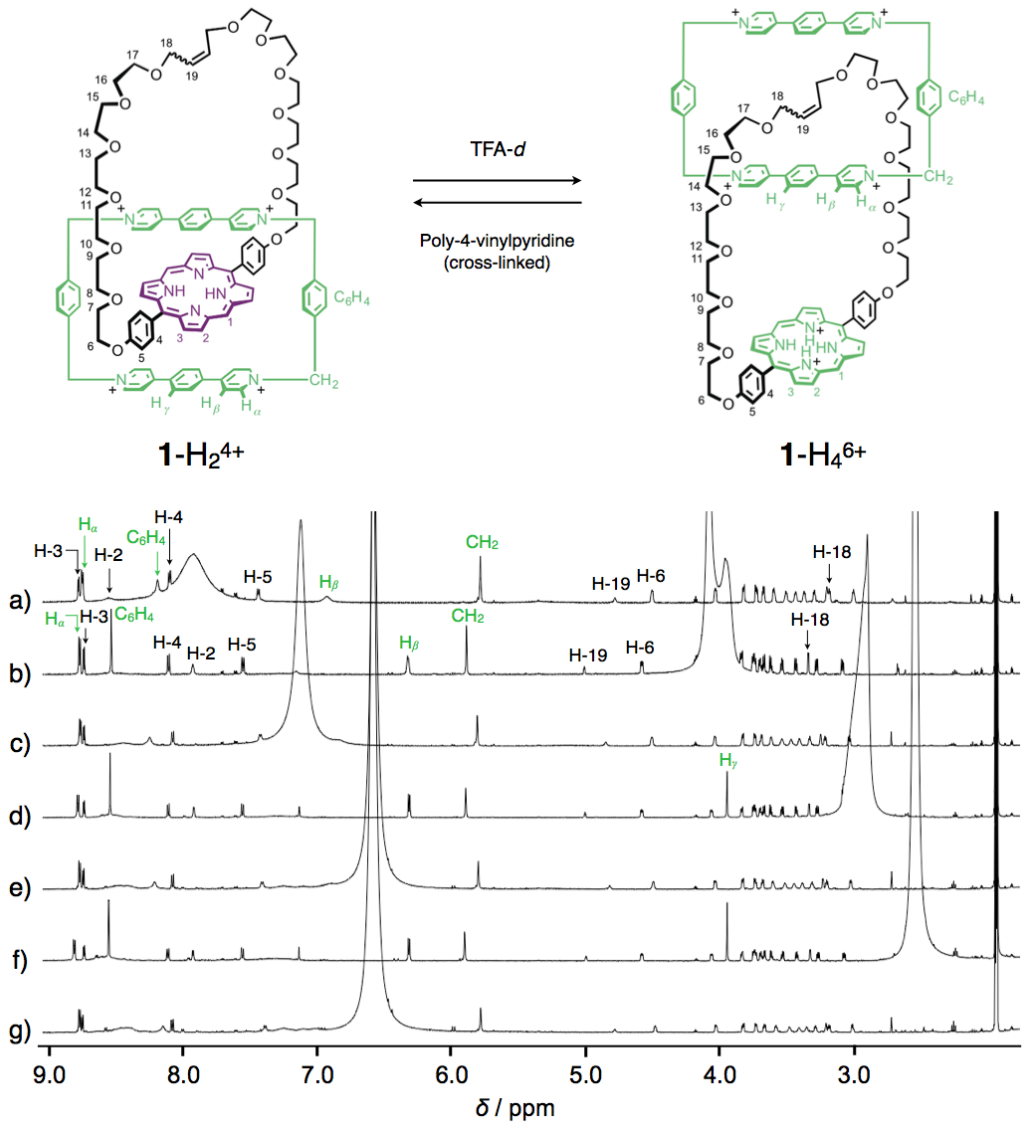



**Fig. S8** Stacked $^1$H NMR spectra demonstrating the switching behaviour of **1**-$H_2^{4+}$ in MeCN-$d_6$ at 25 °C. Using a single sample of **1**-$H_2$•$4PF_6$, the pH was lowered (a, c, e, g) through the addition of deuterated trifluoroacetic acid (TFA-*d*) and raised (b, d, f) by exposing the sample to cross-linked poly-4-vinylpyridine over three complete cycles.

## S5. RP-HPLC data

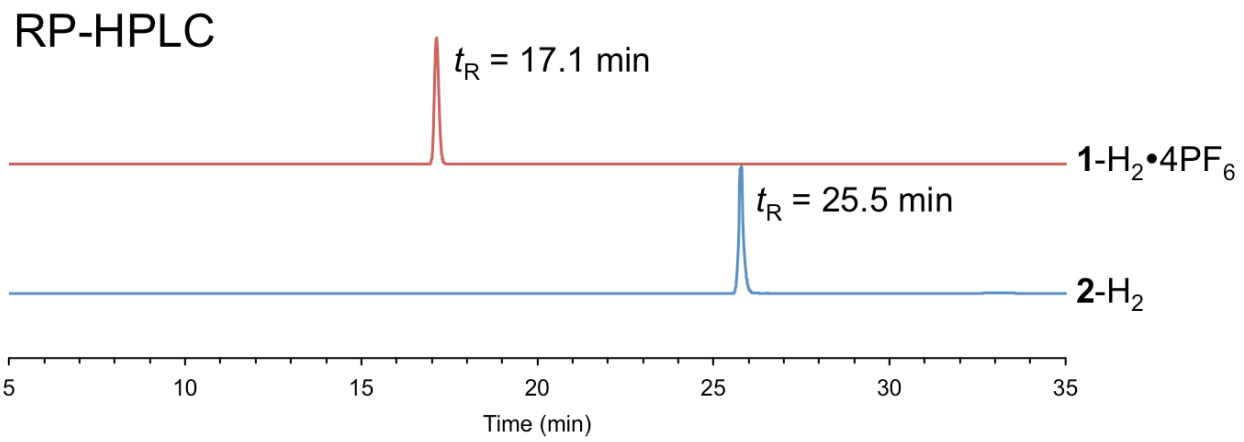



**Fig. S9** RP-HPLC Traces of the pure **1**-$H_2$•$4PF_6$ and **2**-$H_2$ ($C_{18}$ column, binary solvent system: MeCN and $H_2O$ with 0.1% TFA).

## S6. Isothermal titration calorimetric data

$$K_a = 5.48 \times 10^3 \pm 72\ M^{-1}$$
$$\Delta H = -5.94 \pm 0.03\ kcal\ mol^{-1}$$
$$\Delta S = -2.82\ cal\ mol^{-1}\ K^{-1}$$
$$\Delta G = -5.10 \pm 0.03\ kcal\ mol^{-1}$$

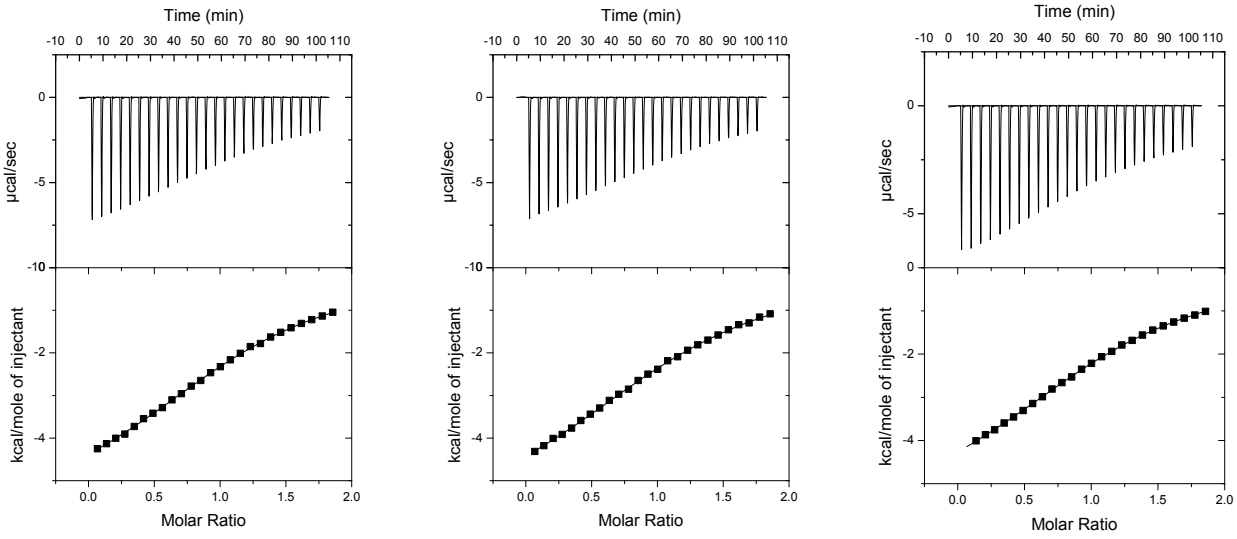



**Fig. S10** ITC data for **ExBox**•$4PF_6$ and **2**-$H_2$ in $Me_2CO$ at 298 K.

## S7. Cyclic voltammetric data

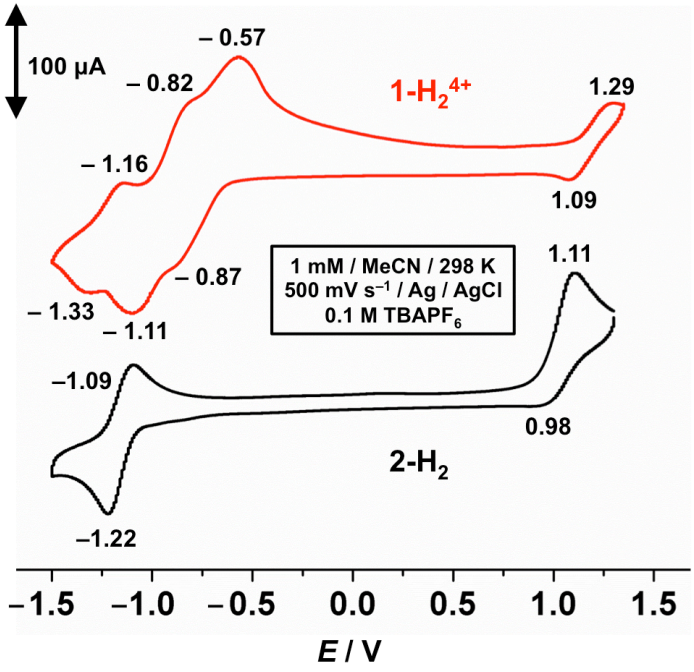



**Fig S11.** CV Data for **1**-$H_2$•4$PF_6$ and **2**-$H_2$ in MeCN at 298 K at 500 mV $s^{-1}$ (full redox cycle).

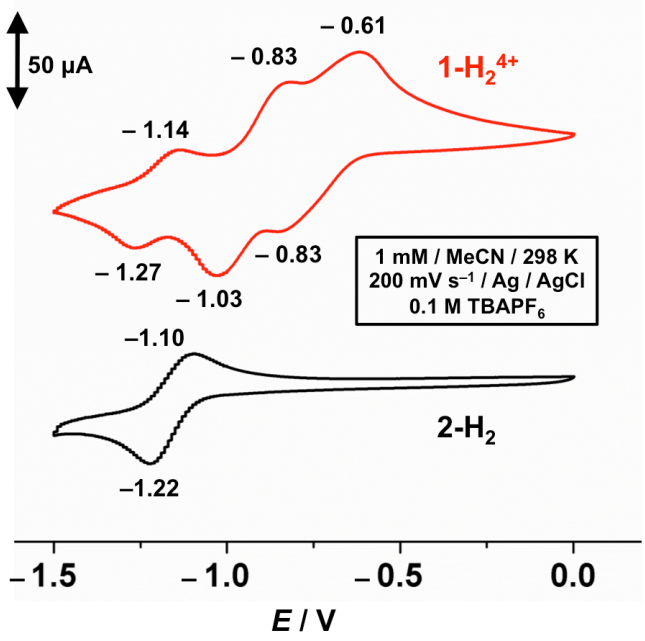



**Fig S12.** CV Data for **1**-$H_2$•4$PF_6$ and **2**-$H_2$ in MeCN at 298 K at 200 mV $s^{-1}$ (reduction cycle).

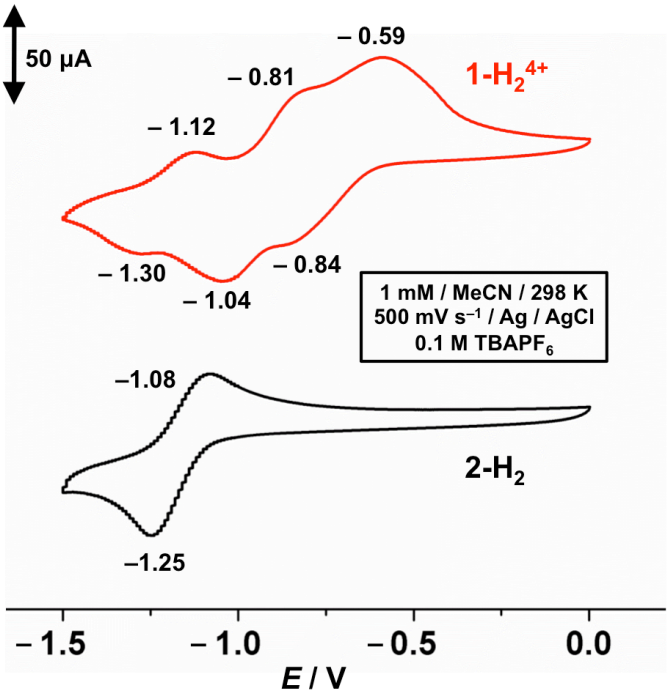



**Fig S13.** CV Data for **1**-$H_2$•4$PF_6$ and **2**-$H_2$ in MeCN at 298 K at 500 mV $s^{-1}$ (reduction cycle).

## S8. References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