

Electrostatic Kinetic Barriers in the Threading/Dethreading Motion of a Rotaxane-like Complex

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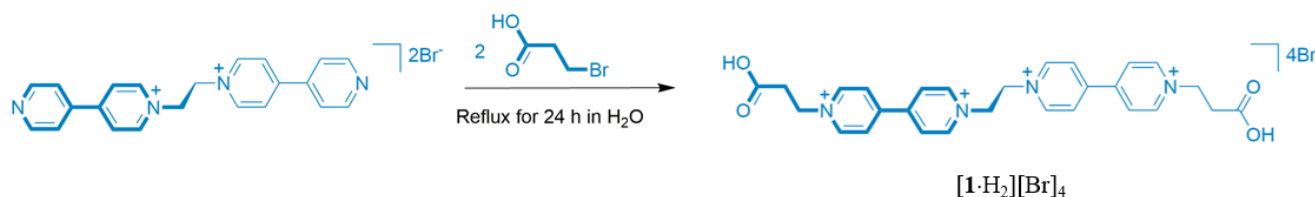
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1. General

All chemicals were purchased from Aldrich and used without further purification. NMR spectra were recorded on a Jeol ECA 500 MHz, locked to the deuterated solvent. Mass spectra were obtained on an Agilent G1969A electrospray-ionization time-of-flight spectrometer. Single-crystal X-ray diffraction experiments were performed in an Enraf–Nonius Kappa diffractometer fitted with a CCD based detector using MoK α radiation (0.71073 Å). Diffraction data and unit-cell parameters were consistent with the assigned space groups. The structures were solved by direct methods, completed by subsequent Fourier syntheses and refined with full-matrix least-squares methods against $|F^2|$ data. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were treated as idealized contributions. Scattering factors and anomalous dispersion coefficients are contained in the SHELXTL 5.03 program library. Ball-and-stick diagrams were prepared using DIAMOND 3.3. Stopped-flow experiments were performed in SX-20 from Applied Photophysics. Kinetic traces were fitted by using software Pro-Data SX by Applied Photophysics. Acid-base titration experiments and pH-measurements were followed on a Thermo Orion Dual-Star potentiometer using a micro pH electrode.

2. Synthesis and characterization of thread and rotaxane-like complexes

Synthesis of [1·H₂][Br]₄



Compound [1·H₂][Br]₄ was synthesized by reacting 0.5 g (1 mmol) of 1,2-bis(4,4'-bipyridinium)ethane dibromide with 1.5 g (10 mmol) of 3-bromopropionic acid in 1 mL of water. The solution was brought to reflux for 24 h. The reaction mixture was cooled to room temperature. 15 mL of acetonitrile were added and a beige powder precipitated from the solution. The product was isolated via filtration and washed with acetonitrile to remove any unreacted 3-bromopropionic acid. Pure product was obtained after dried under vacuum. Yield: 0.73 g, 90%. ¹H NMR (500 MHz, D₂O, 298 K): δ (ppm) = 9.27 (d, ³J_{b-c} = 6.8 Hz, 4 H, H_b), 9.23 (d, ³J_{e-d} = 7.0 Hz, 4 H, H_e), 8.70 (d, ³J_{c-b} = 7.0 Hz, 4 H, H_c), 8.60 (d, 4 H, ³J_{d-e} = 6.8 Hz, H_d), 5.55 (s, 4 H, H_a), 5.02 (t, ³J_{f-g} = 6.1 Hz, 4 H, H_f), and 3.23 (t, ³J_{g-f} = 6.1 Hz, 4 H, H_g). ¹H NMR (500 MHz, D₂O), 278 K): δ (ppm) = 8.94 (d, ³J_{b-c} = 6.8 Hz, 4 H, H_b), 8.91 (d, ³J_{e-d} = 7.0 Hz, 4 H, H_e), 8.36 (d, ³J_{c-b} = 7.0 Hz, 4 H, H_d), 8.26 (d, ³J_{d-e} = 6.8 Hz, 4 H, H_c), 5.22 (s, 4 H, H_a), 4.79 (H_f – overlapping with HDO), and 2.95 (t, ³J_{g-f} = 6.1 Hz, 4 H, H_g). A 2.5 × 10⁻³ M solution of [1·H₂][Br]₄ in D₂O renders a pH = 3. ¹³C NMR (125.8 MHz, D₂O, 293 K): δ (ppm) = 173.80 (C_{carbonyl}), 151.73 (C_{ipso}), 149.90 (C_{ipso}), 146.27 (C_b, C_e), 128.01 (C_d), 127.05 (C_c), 59.86 (C_a), 57.47 (C_f), 34.62 (C_g). HR-ESI-MS: m/z [(1·H₂)(Br)₂]²⁺ calc.: 322.0311, found: 322.0309 (error: 0.75 ppm). Anal. Calc. for C₂₈H₃₀Br₄N₄O₄·H₂O: N, 6.80; C, 40.80; H, 3.91. Found: N, 6.59; C, 40.55; H, 3.86. M.P. Decomposes at 190 °C.

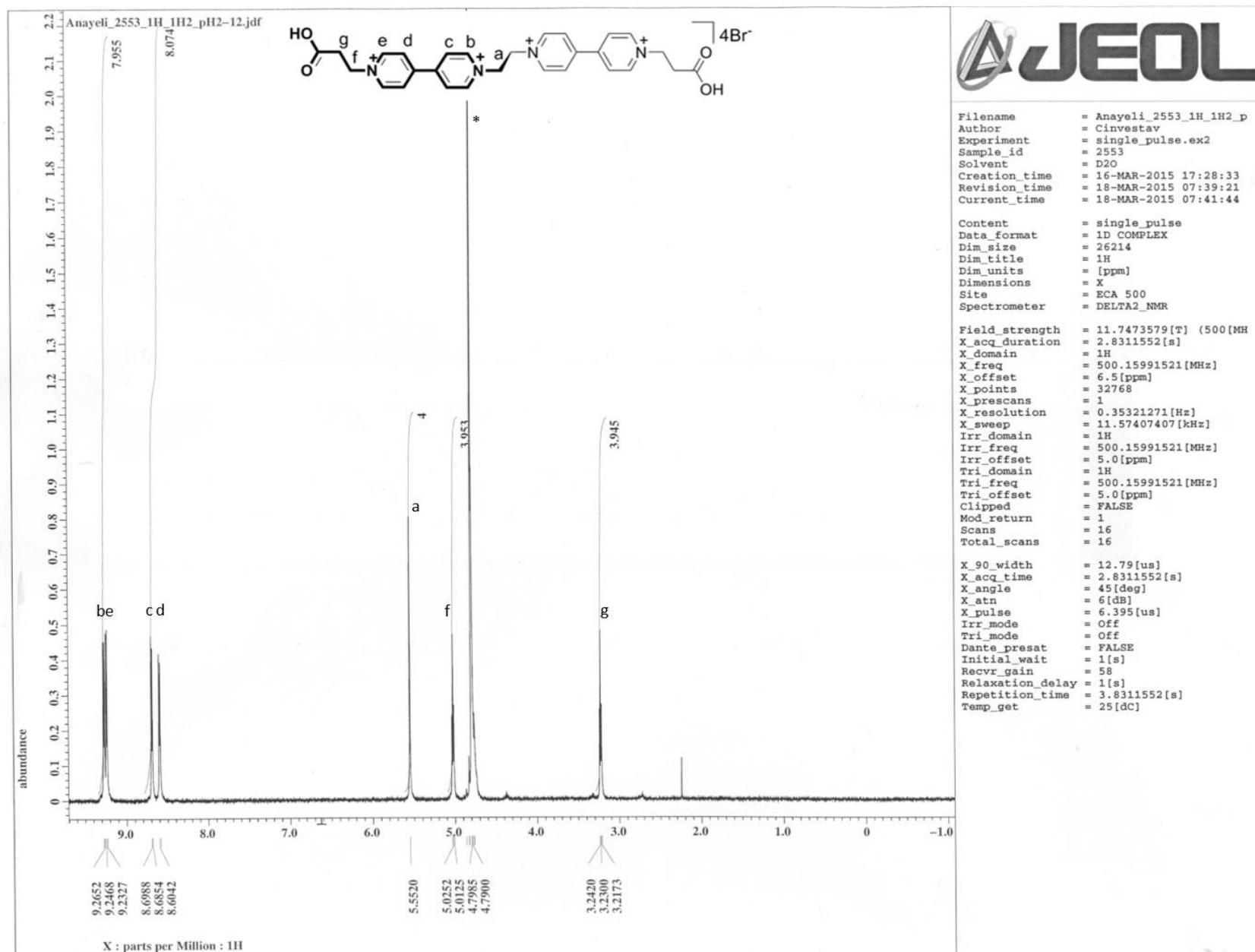


Figure S1: ¹H NMR 500 MHz spectrum in D₂O at 298 K and pH = 3 of [1·H₂][Br]₄; *solvent peak.

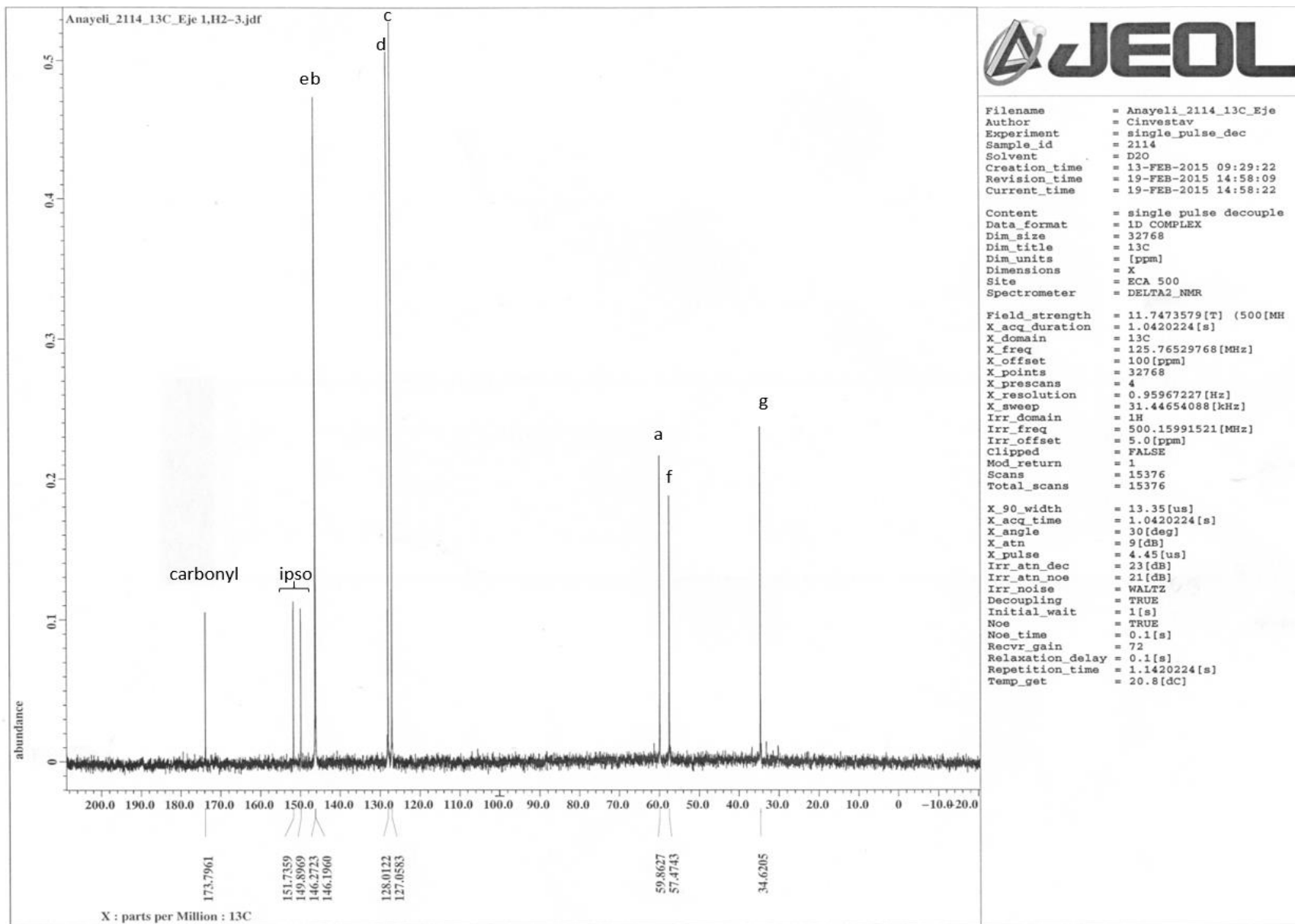


Figure S2: ^{13}C NMR spectrum acquired at 125.76 MHz and 293 K of $[\mathbf{1}\text{-H}_2][\text{Br}]_4$.

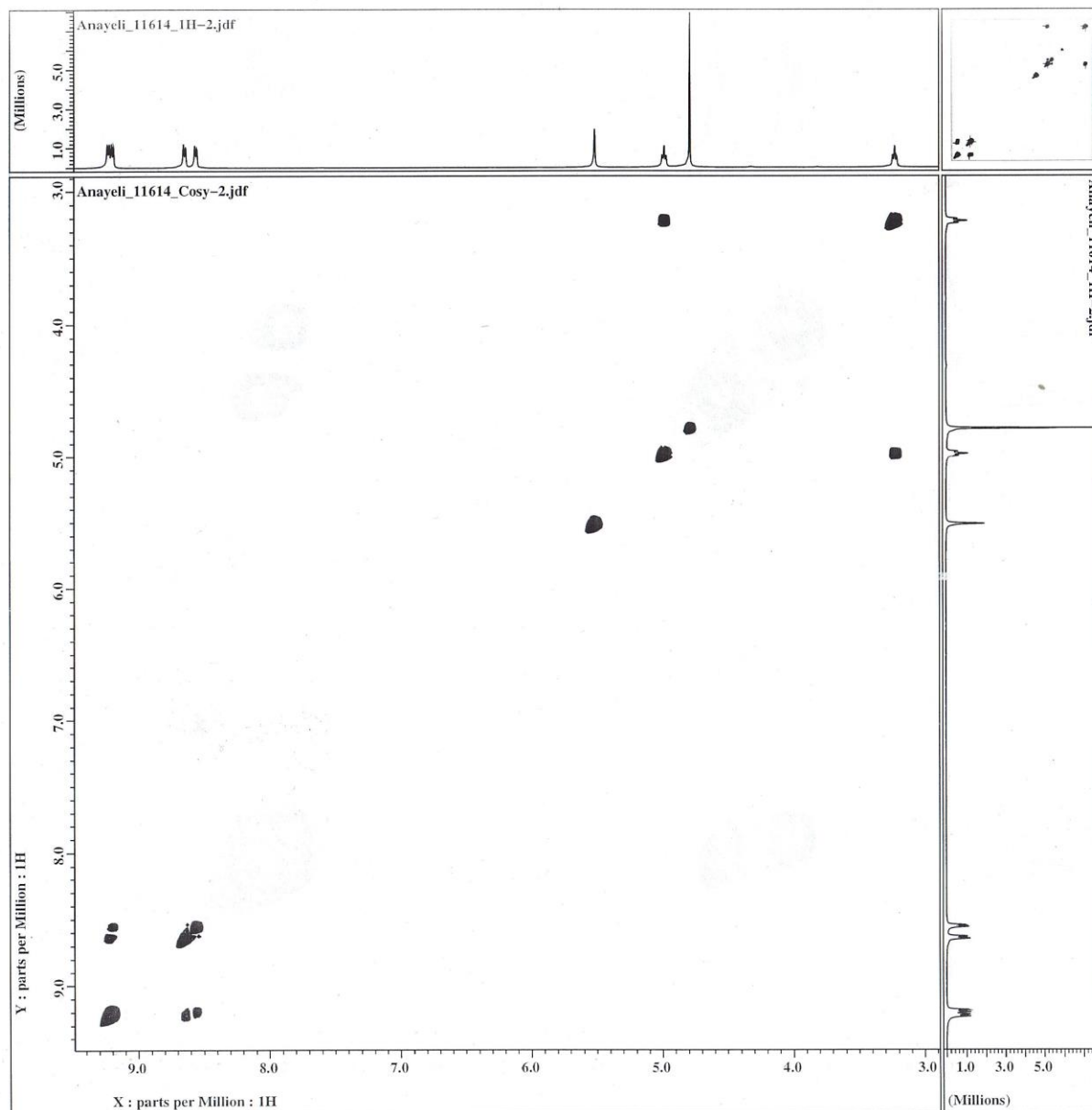


Figure S3: NMR 2D COSY 500 MHz spectrum in D₂O at 293 K of [1-H₂][Br]₄.

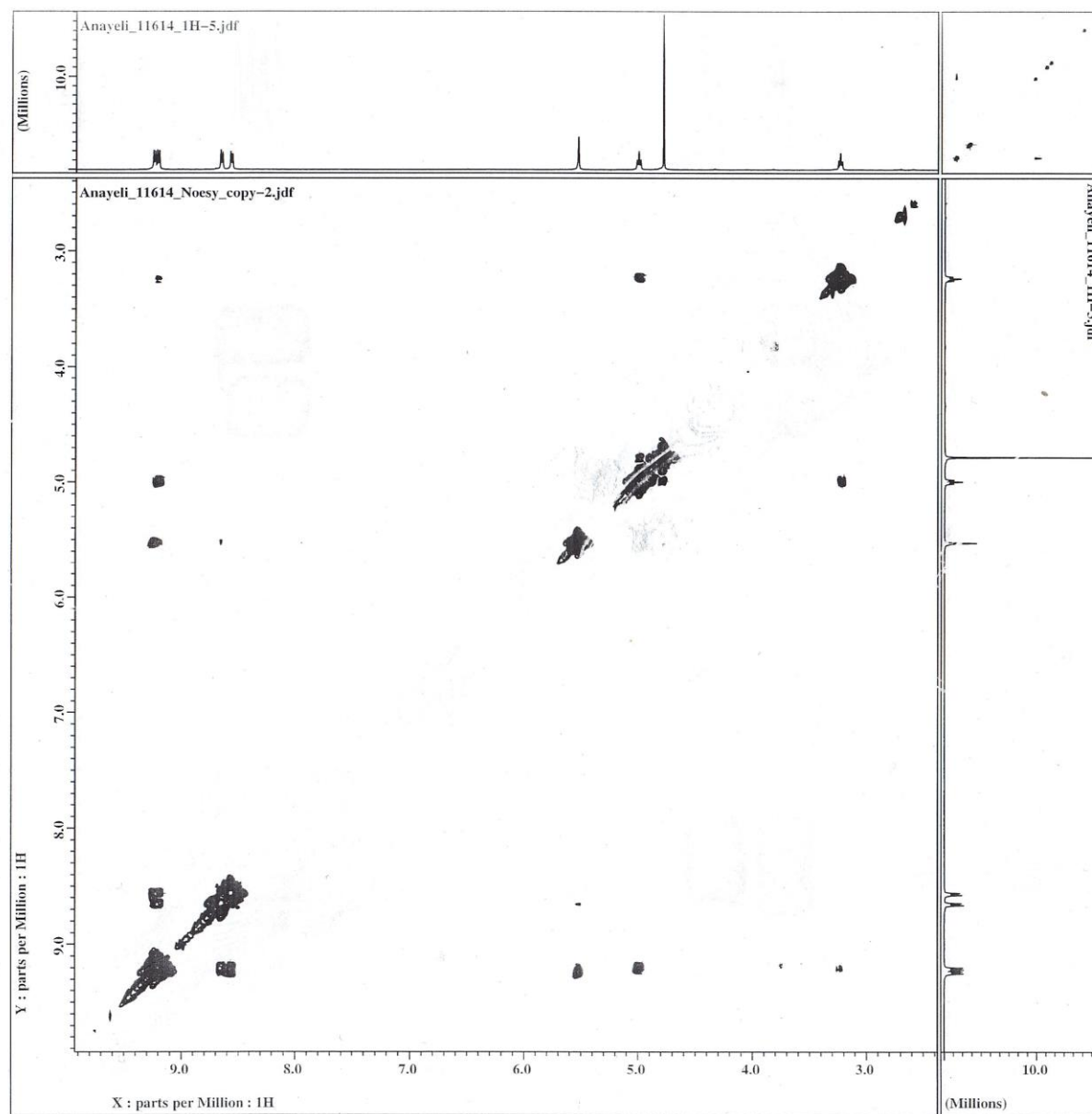


Figure S4: NMR 2D NOESY 500 MHz spectrum in D₂O at 293 K of [1-H₂][Br]₄.

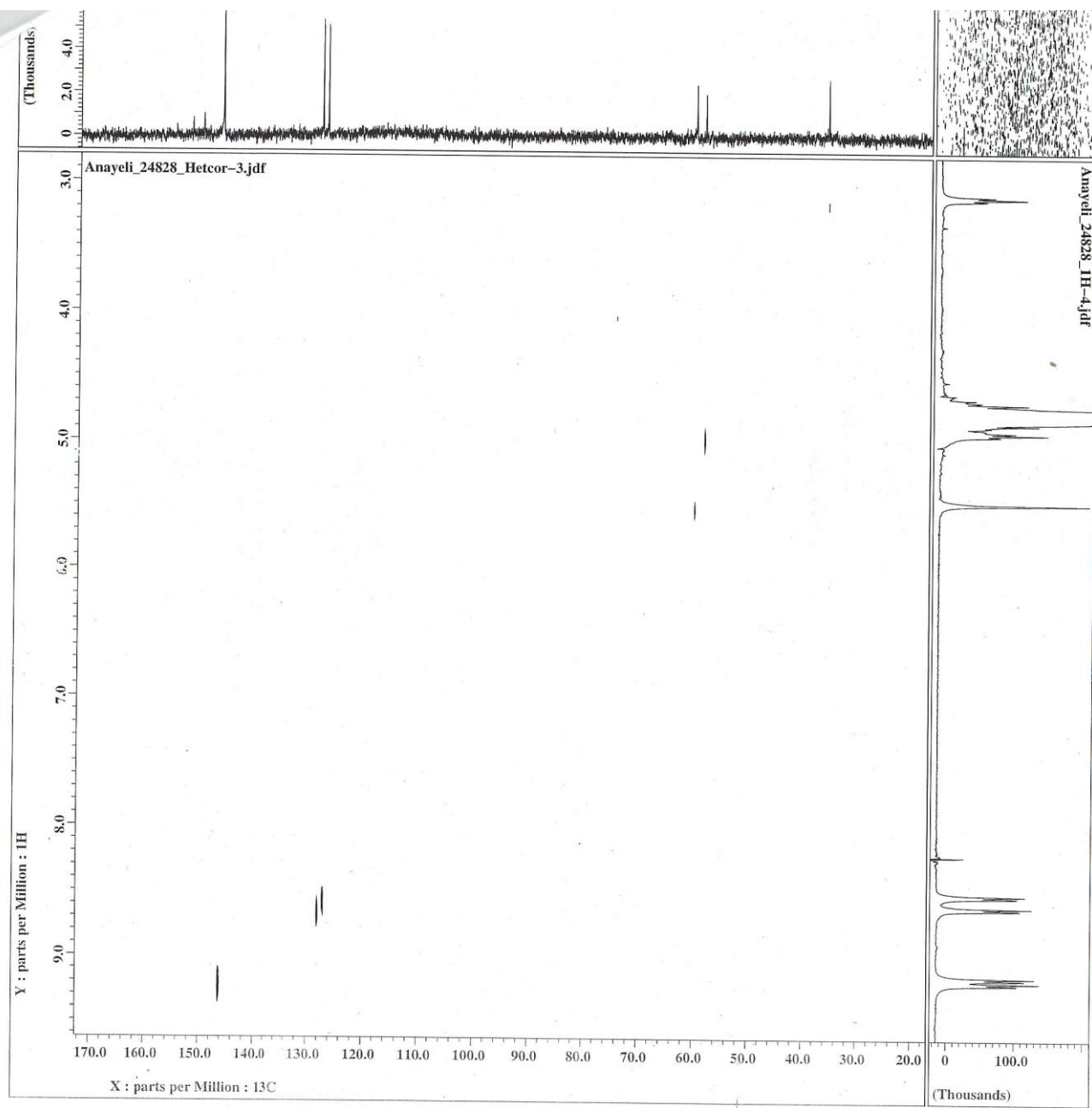


Figure S5: NMR 2D HETCOR spectrum in D_2O at 293 K of $[\text{1-H}_2][\text{Br}]_4$.

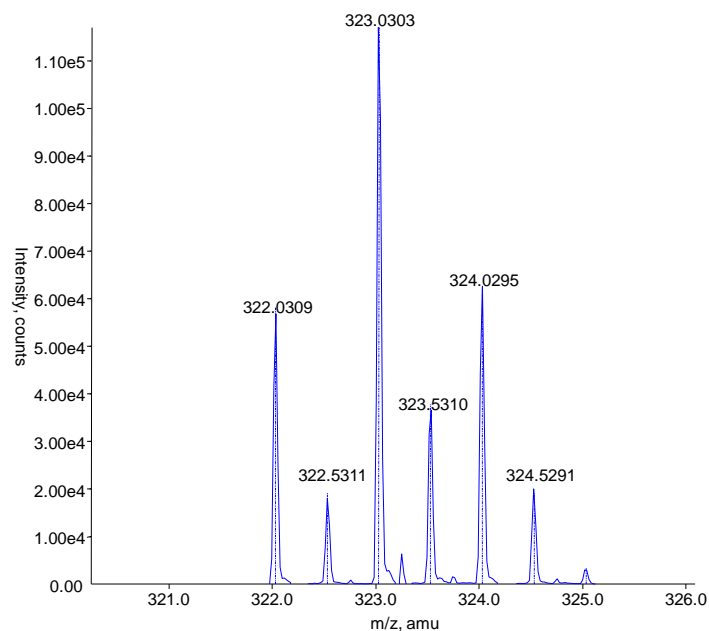


Figure S6: ESI-MS spectrum of $[1\cdot H_2][Br]_4$. Experimental molecular ion (continuous line) and calculated isotopic profile (broken line).

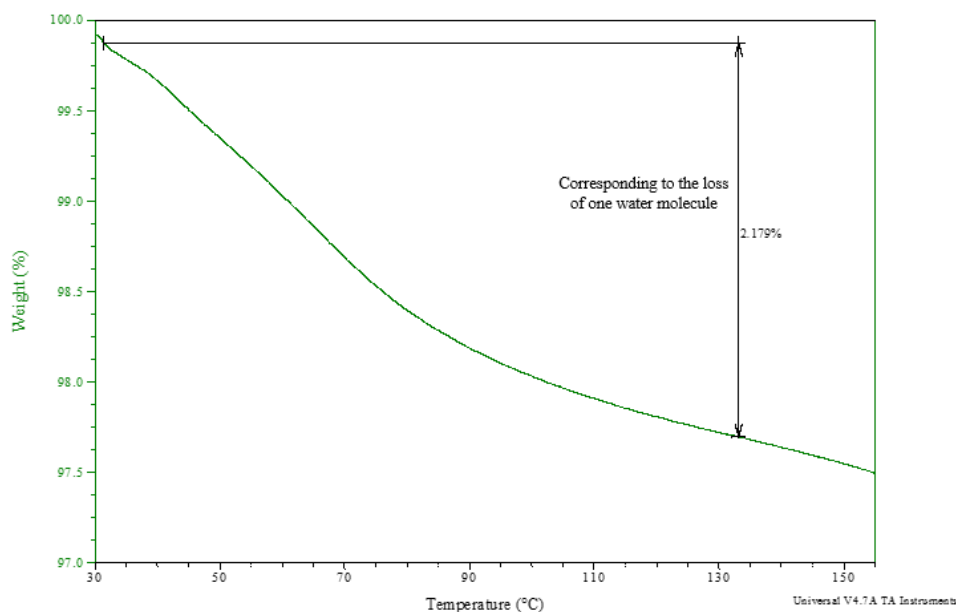


Figure S7: Thermogravimetric register for $[1\cdot H_2][Br]_4$.

Self-assembly of [2]rotaxane-like complex at pH = 1; $[1\cdot H_2\text{CDSDB24C8}][Br]_2$

[2]Rotaxane-like complex $[1\cdot H_2\text{CDSDB24C8}]^{2+}$ was obtained by combining 2.5 ml of an aqueous solution (50 mM) of $[1\cdot H_2][Br]_4$ with 2.5 ml of an aqueous solution (50 mM) of $[NMe_4]_2[DSDB24C8]$. The solution was stirred and left to cool for several days until rotaxane-like complex $[1\cdot H_2\text{CDSDB24C8}][Br]_2$ precipitated as a yellow crystalline solid. The product was isolated via filtration, washed with methanol and dried under vacuum. Yield 0.13 g, 84%. 1H NMR (500 MHz, D_2O , 278 K): δ (ppm) 9.21 (broad, 4 H, H_b), 8.90 (broad, 4 H, H_e), 8.20 (broad, 4 H, H_c), 8.03 (broad, 4 H, H_d), 6.72 and 6.66 (broad, 6 H, H_n , H_i , H_j), 5.42 (broad, 4 H, H_a), 4.79 (H_f overlapping with HDO), 4.10-3.55 (m, 24 H, H_k , H_l , H_m broad set of signals) and 2.94 (broad, 4H, H_g). The pH of the solution was adjusted to 1 by the addition of a 48% DBr in D_2O solution. HR-ESI-MS: m/z $[1\cdot H_2\text{CDSDB24C8}]^{2+}$ calc.: 546.1666, found: 546.1674 (error: 1.37 ppm).

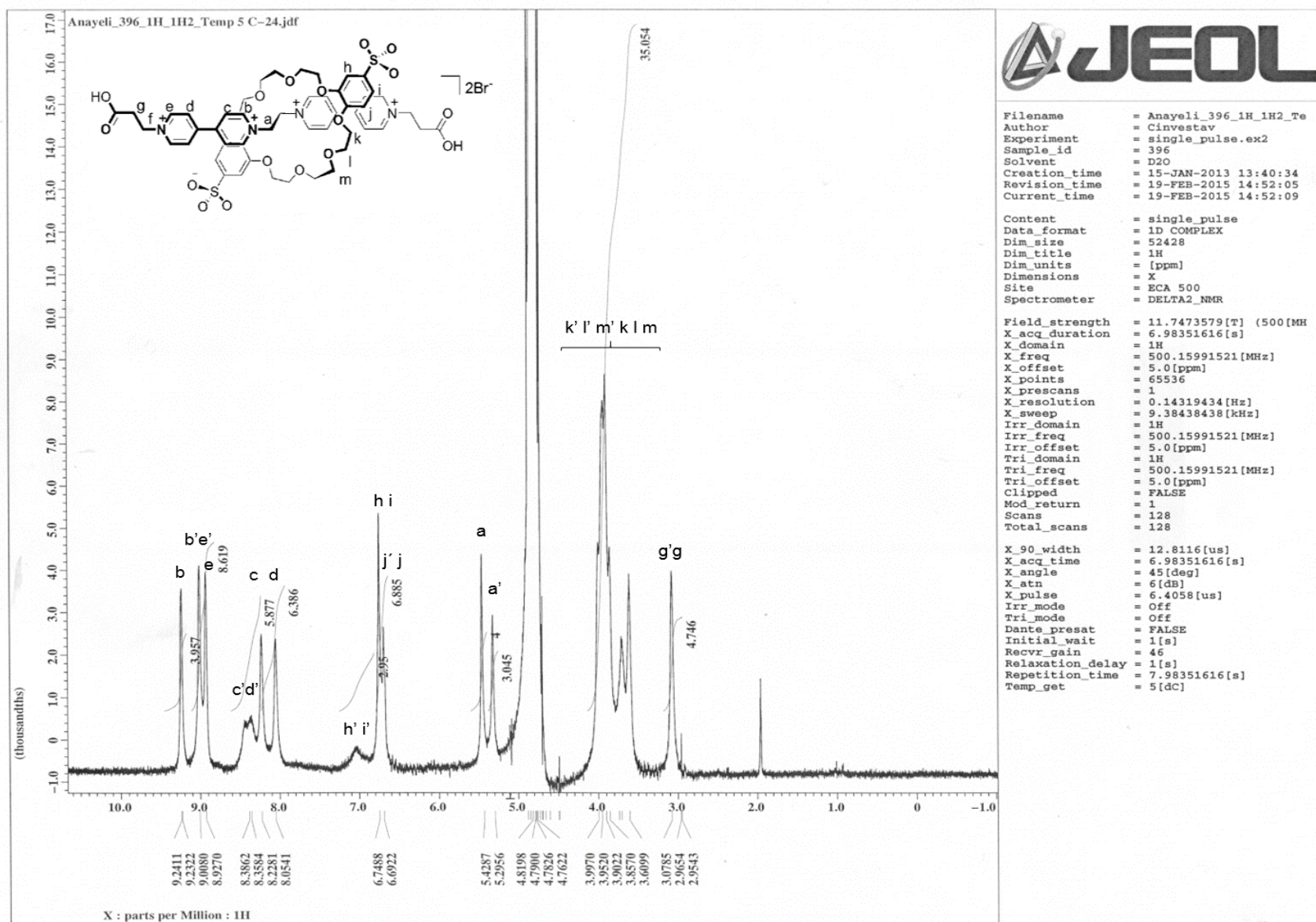


Figure S8: ^1H NMR 500 MHz spectrum in D_2O of $[1 \cdot \text{H}_2\text{CDSDB24C8}][\text{Br}]_2$ at 278 K, pH = 1. Labels without (') = complexed components of the [2]rotaxane-like complex $[1 \cdot \text{H}_2\text{CDSDB24C8}][\text{Br}]_2$, labels with (') = uncomplexed thread $[1 \cdot \text{H}_2]^{4+}$ and wheel $[\text{DSDB24C8}]^{2-}$.

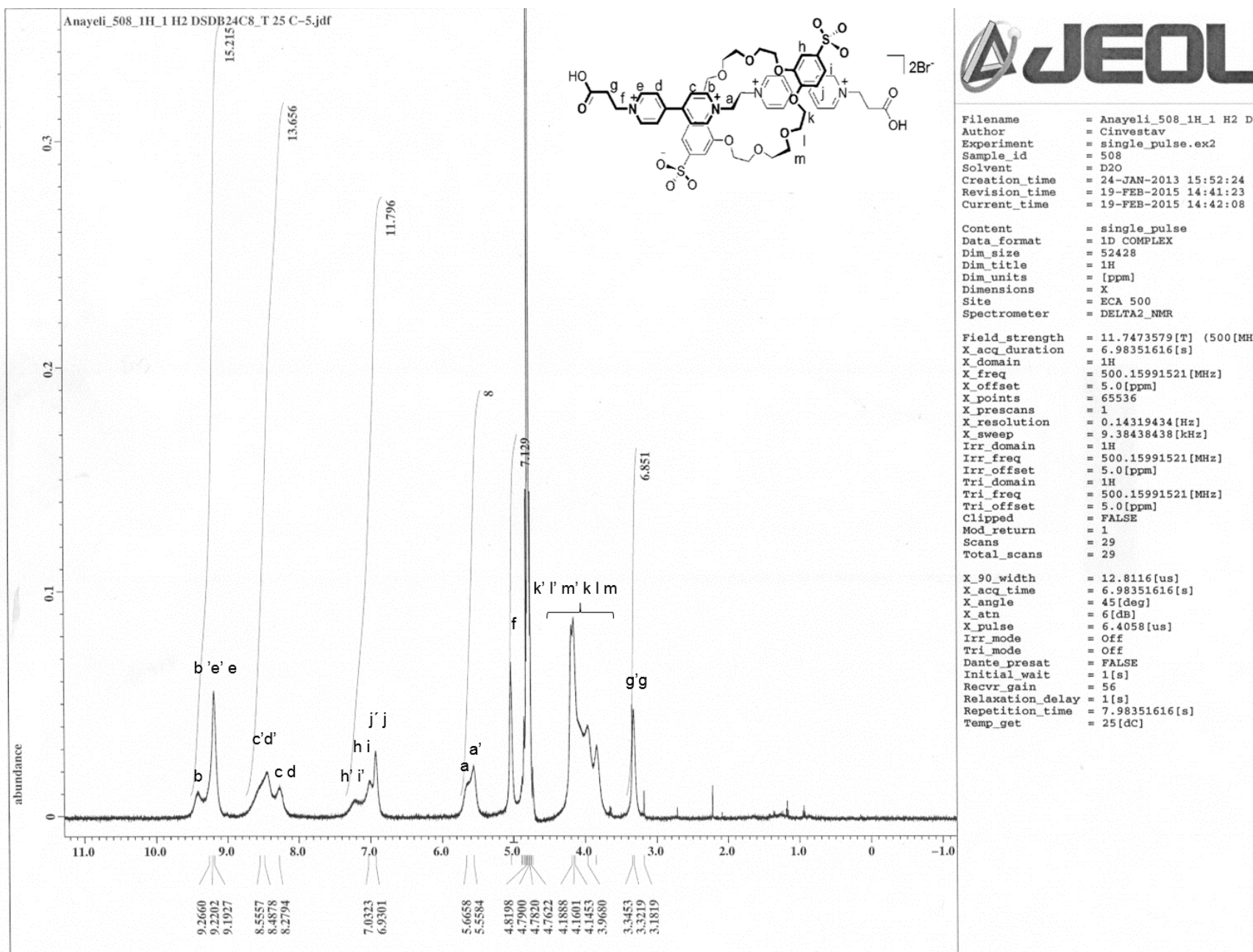


Figure S9: ¹H NMR 500 MHz spectrum in D₂O of [1·H₂CDSDB24C8][Br]₂ at 298 K and pH = 1.

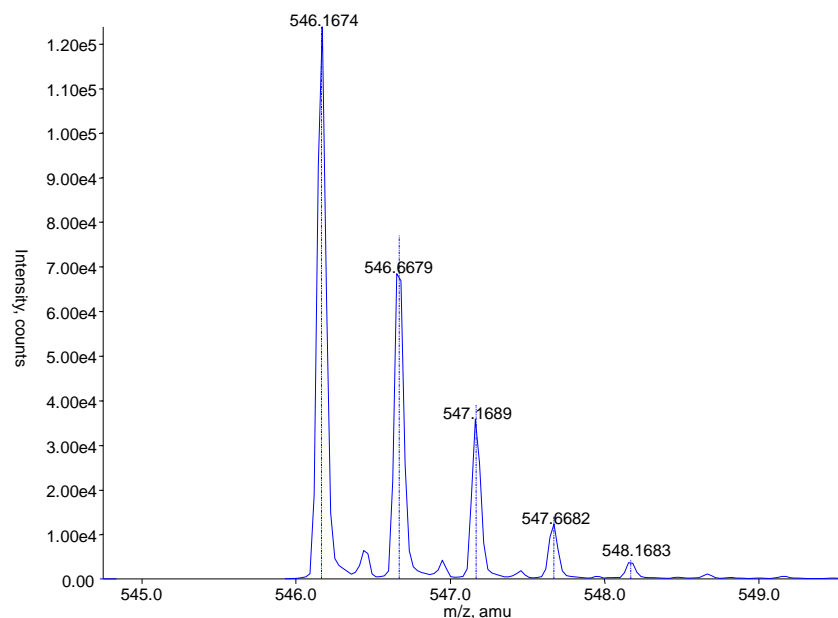


Figure S10: ESI-MS spectrum of $[1\cdot\text{H}_2\text{CDSDB24C8}][\text{Br}]_2$. Experimental molecular ion $[1\cdot\text{H}_2\text{CDSDB24C8}]^{2+}$ (continuous line) and calculated isotopic profile (broken line).

Self-assembly of [2]rotaxane-like complex at pH = 7; $[1\cdot\text{CDSDB24C8}]$

0.13 g (0.39mmol) of pyridine was mixed with 0.05 g (0.63mmol) $[1\cdot\text{H}_2\text{CDSDB24C8}][\text{Br}]_2$ in 5 mL of water. The solution was stirred and left to cool for several days until *pseudo*-rotaxane $[1\cdot\text{CDSDB24C8}]$ precipitated as a yellow crystalline solid. The product was isolated via filtration and washed with acetonitrile in order to remove any unreacted pyridine. Pure [2]rotaxane-like complex was obtained after drying under vacuum. Yield 0.03 g, 68%. ^1H NMR (500 MHz D_2O , 278 K): δ (ppm) 9.26 (broad, 4 H, H_b), 8.90 (broad, 4 H, H_e), 8.23 (broad, 4 H, H_c), 8.04 (broad, 4 H, H_d), 7.09 (broad, 2 H, H_h), 7.06 (d, 2 H, $J = 8.6$ Hz, H_i), 6.78 (d, 2 H, $J = 8.6$ Hz, H_j), 5.48 (broad, 4 H, H_a), 4.79 (H_f - overlapping with HDO), 4.02 - 3.60 (m, 24 H, H_k , H_l , H_m , broad set of signals) and 2.80 (broad, 4 H, H_g). The pH of the solution was adjusted to 7 by the addition of $\text{C}_5\text{D}_5\text{N}$. HR-ESI-MS: m/z $[1\cdot\text{H}_2\text{CDSDB24C8}]^{2+}$ calc.: 546.1666, found: 546.1672 (error: 0.1 ppm).

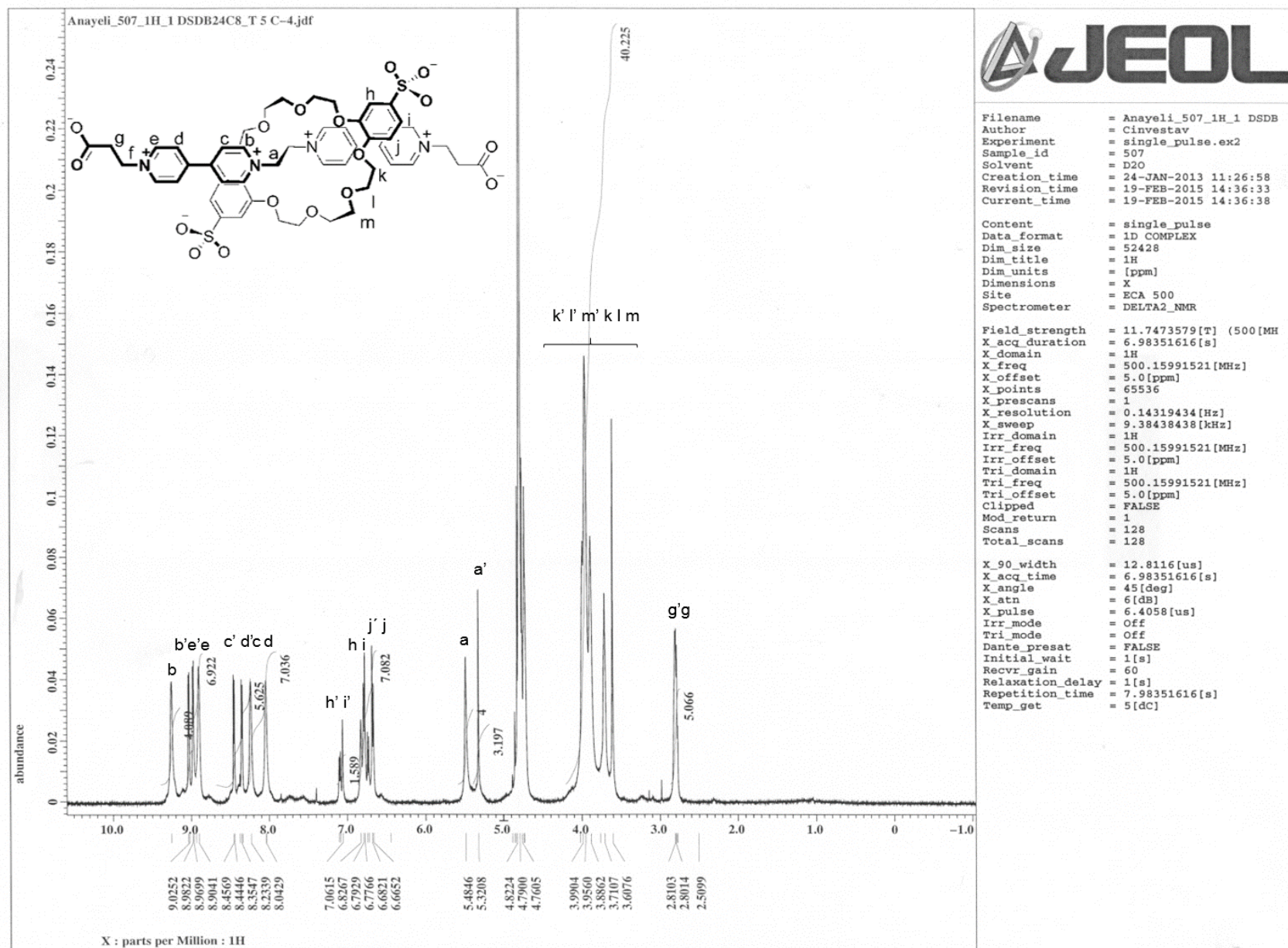


Figure S11: ^1H NMR 500 MHz spectrum in D_2O of $[1\text{-DSDB24C8}]$ at 278 K and pH = 7. Labels without (') = complexed components of the $[2]_{\text{pseudo-rotaxane}}$, labels with (') = uncomplexed thread $[1]^{2+}$ and wheel $[\text{DSDB24C8}]^{2-}$.

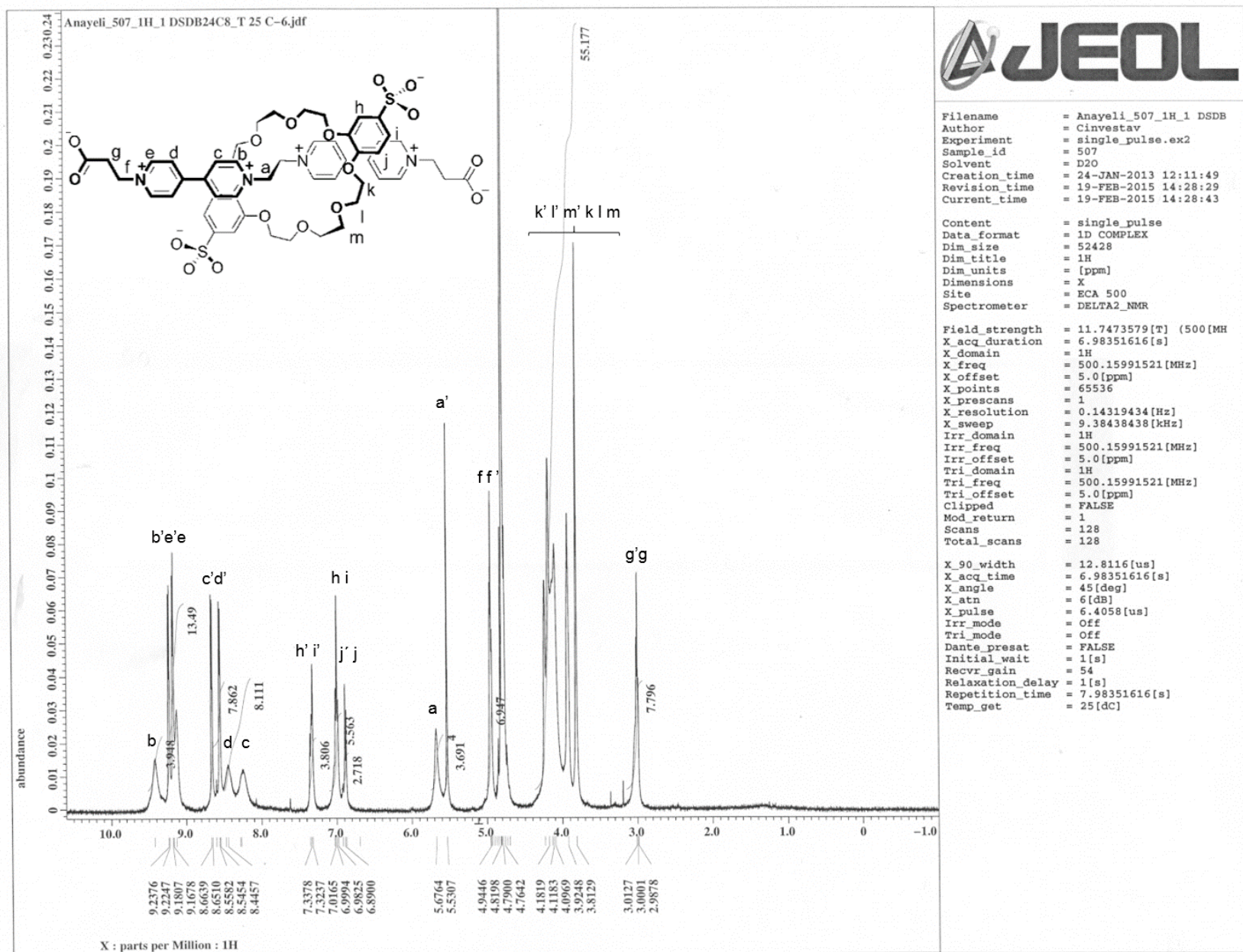


Figure S12: ^1H NMR 500 MHz spectrum in D_2O of [1-DSDB24C8] at 298 K and pH = 7.

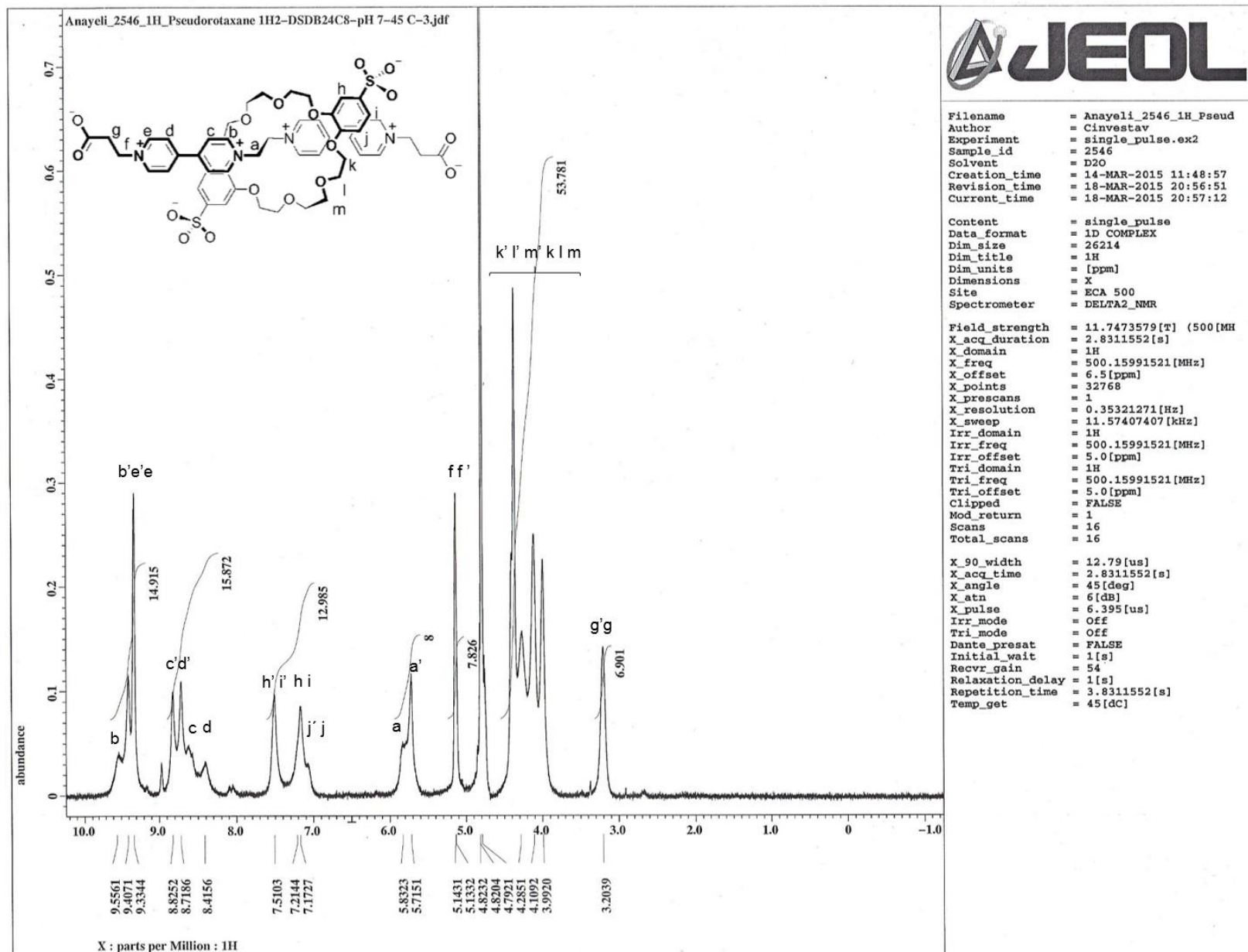


Figure S13: ^1H NMR 500 MHz spectrum in D_2O of [1-DSDB24C8] at 318 K and pH = 7.

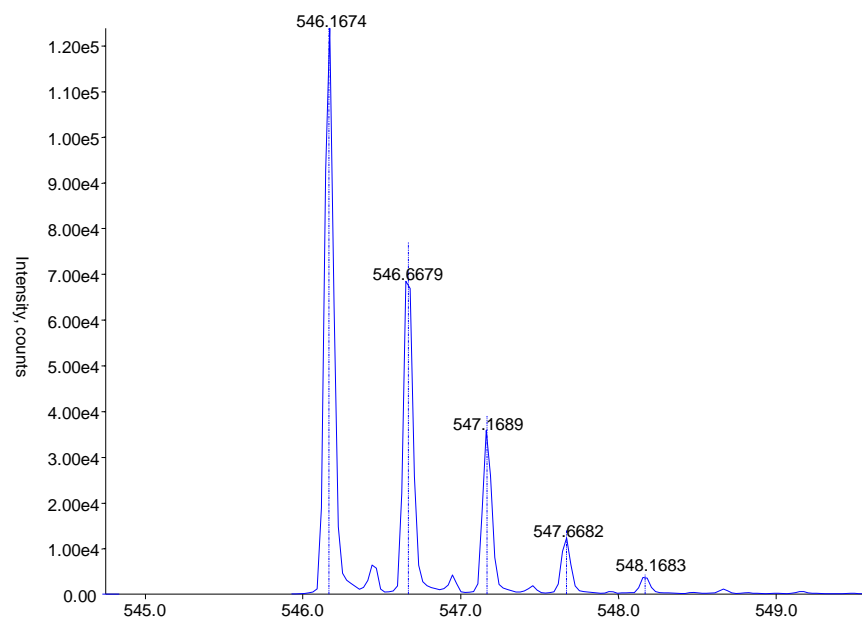


Figure S14: ESI-MS spectrum of [1-DSDB24C8]. Experimental molecular ion [1-DSDB24C8]²⁺ (continuous line) and calculated isotopic profile (broken line).

3. Thread acid-base solution behavior and pK_a determination

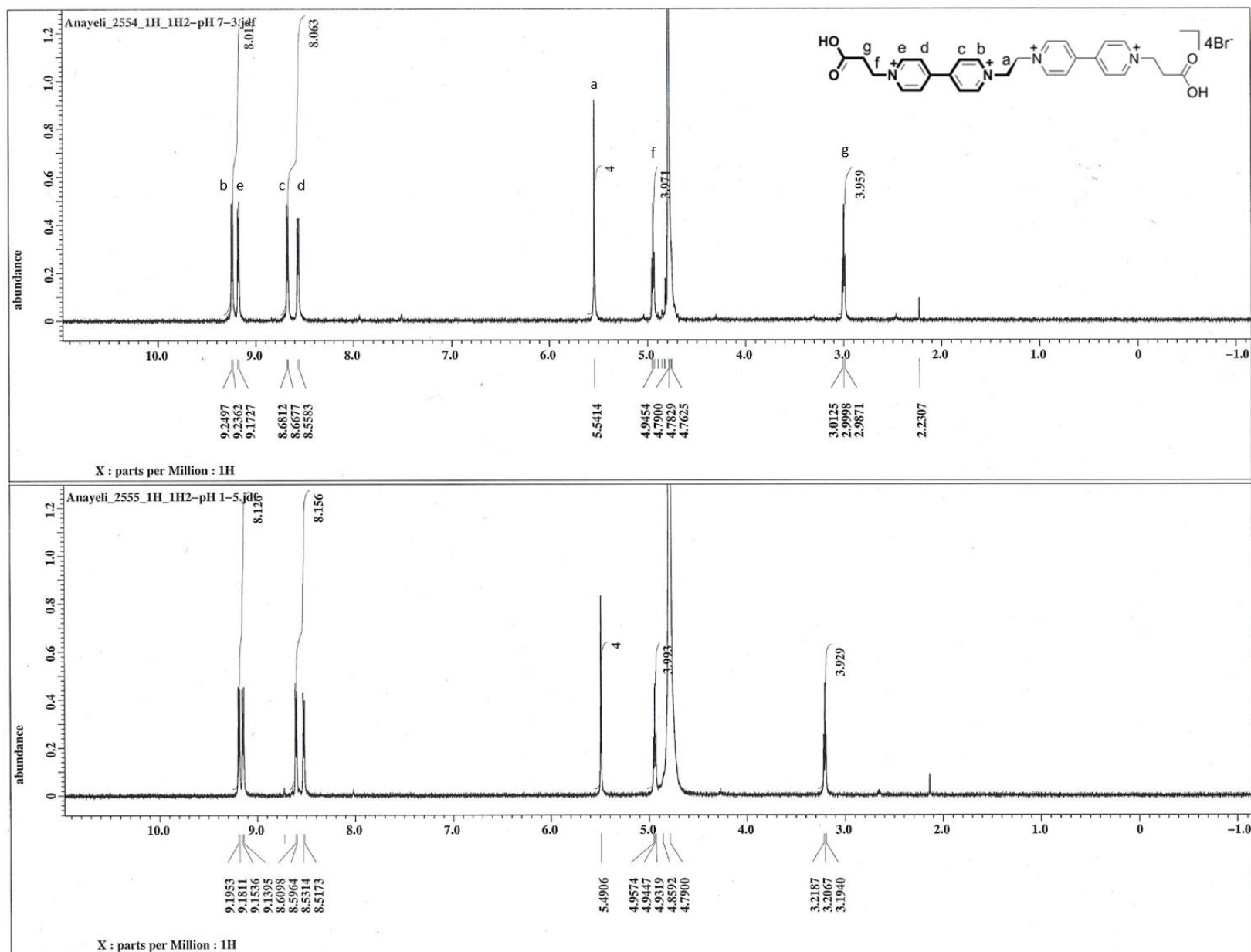


Figure S15. ^1H NMR 500 MHz spectra of $[\text{1-H}_2][\text{Br}]_4$ in D_2O at 298 K pH = 7 (top) and pH = 1 (bottom).

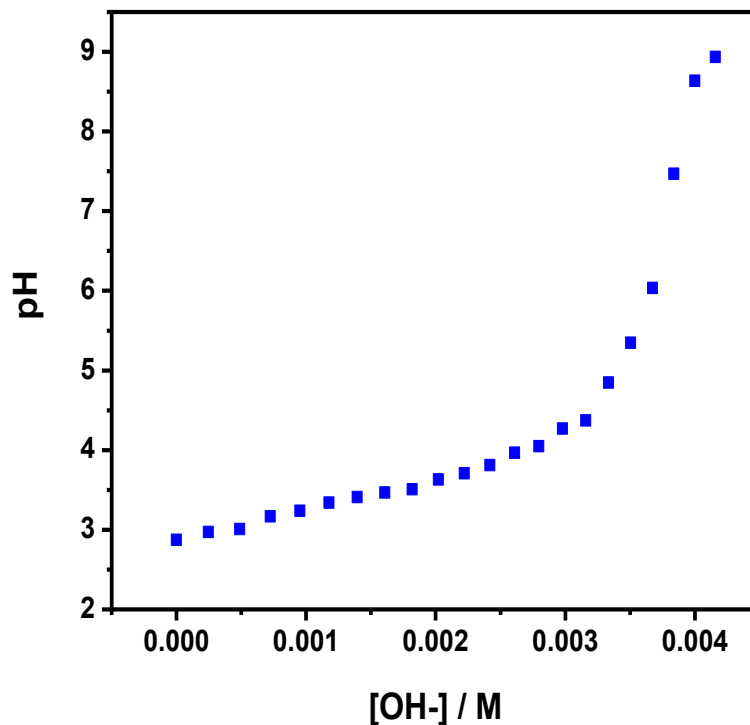
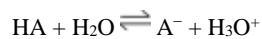


Figure S16: pH titration of an aqueous solution (2 mL, 2×10^{-3} M) of $[1\text{-H}_2][\text{Br}]_2$ with a normalized 2×10^{-2} M solution of NaOH. Data fitting renders an average pK_a value of 3.7 for both carboxylic acid groups.

Determination of ratio $[A^-]/[HA]$

For an specific equilibrium between the acid, HA and its conjugate base A^- , in water,



Assuming that the concentration of water, $[\text{H}_2\text{O}]$, is constant and writing $[\text{H}^+]$ for the concentration of the hydronium ion the expression of equilibrium is

$$K_a = \frac{[A^-][H^+]}{[HA]} \dots (1)$$

pK_a is defined as $-\log_{10} K_a$. After rearranging the expression defining K_a , and putting $\text{pH} = -\log [H^+]$, one obtains

$$\text{pH} = pK_a + \log \left(\frac{[A^-]}{[HA]} \right) \dots (2)$$

This is a form of the Henderson–Hasselbalch equation. If we solve $\left(\frac{[A^-]}{[HA]} \right)$

$$\log \left(\frac{[A^-]}{[HA]} \right) = \text{pH} - pK_a \dots (3)$$

$$\left(\frac{[A^-]}{[HA]} \right) = 10^{\text{pH} - pK_a} \dots (4)$$

In order to obtain $[A^-]$ and $[HA]$ values, the next expression can be used

$$C_0 = [A^-] + [HA] \dots (5)$$

Where C_0 is the initial concentration. If we solve $[A^-]$

$$A^- = C_0 - [HA] \dots (6)$$

When we substitute (6) in (4) we obtain

$$\left(\frac{C_0 - [HA]}{[HA]}\right) = 10^{pH-pKa} \dots (7)$$

If we solve $[HA]$

$$\frac{C_0}{[HA]} - 1 = 10^{pH-pKa} \dots (8)$$

$$\frac{C_0}{[HA]} = 10^{pH-pKa} + 1 \dots (9)$$

$$[HA] = \frac{C_0}{10^{pH-pKa} + 1} \dots (10)$$

With equation (10) and considering an obtained pK_a of 3.7 for $[1 \cdot H_2][Br]_4$, several $[HA]$ values were calculated at distinct pH values (Table S1).

Table S1: Calculated mole fraction of $[1 \cdot H_2][Br]_4$.

C_0 (mM)	pH	$[HA]$ (mM)	$[A^-]$ (mM)	% $[HA]$
1.0	1	0.9983	0.0017	99.83
	2	0.9836	0.0164	98.36
	3	0.8532	0.1468	85.32
	4	0.3416	0.6584	34.16
	5	0.0462	0.9538	4.62
	6	0.0048	0.9952	0.48
	7	0.0005	0.9995	0.05

4. Crown ether acid-base solution behavior and pK_a determination

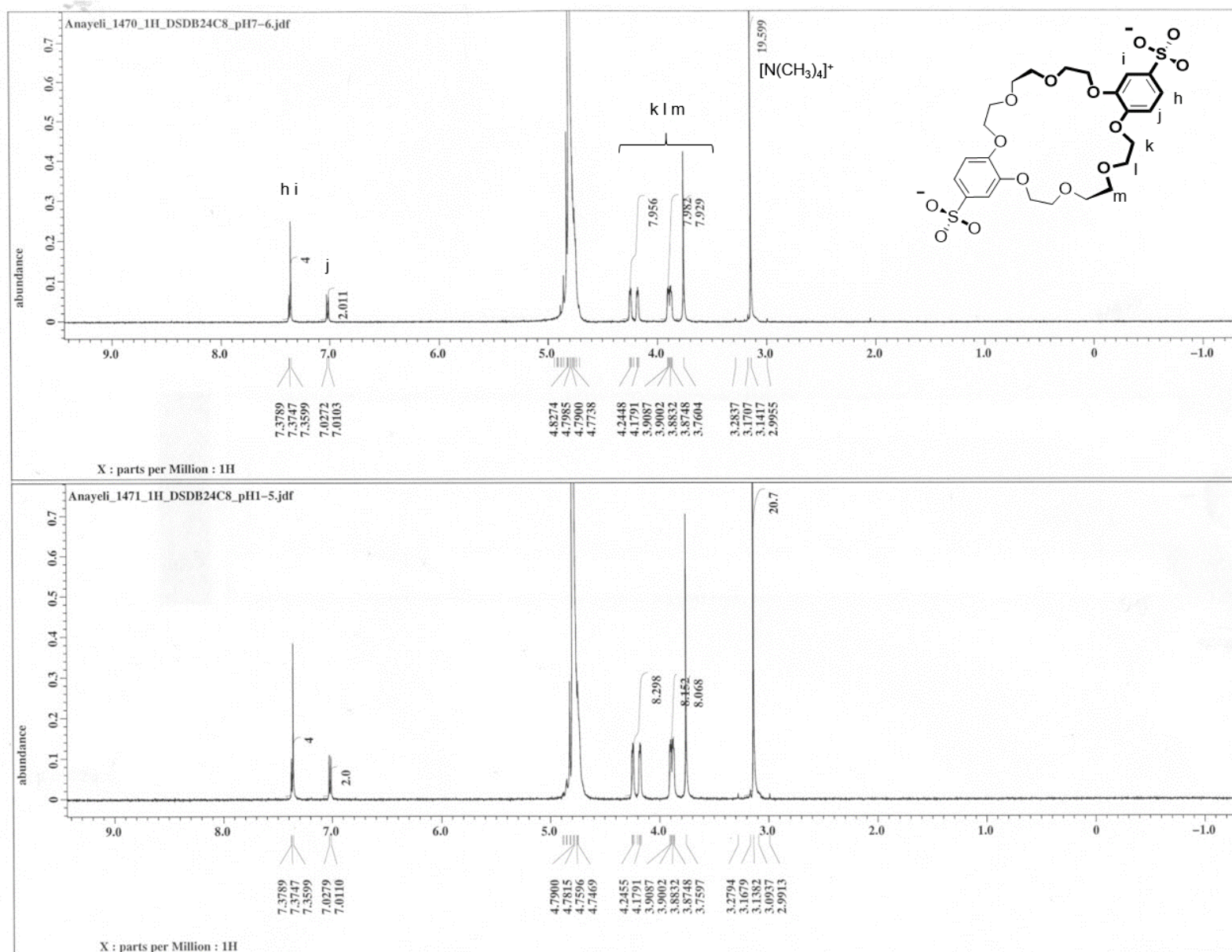


Figure S17: ^1H NMR 500 MHz spectra in D_2O of $[(\text{CH}_3)_4\text{N}]_2[\text{DSDB24C8}]$ at 293 K pH = 7 (top) and pH = 1 (bottom).

$$pK_a = -0.72 (\pm 0.20) \text{ at } 25^\circ\text{C}$$

Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2014 ACD/Labs). This calculation provides the same pK_a value for both sulfonate groups.

Table S2: Calculated mole fraction of H₂DSDB24C8.

C ₀ (mM)	pH	[H ₂ DSDB24C8]	[DSDB24C8] ²⁻	%[DSDB24C8] ²⁻
		(mM)	(mM)	
1.0	1	0.0187	0.9813	98.13
	7	1.9×10 ⁻⁸	0.9999	99.99

5. Model compound with pH-insensitive end groups

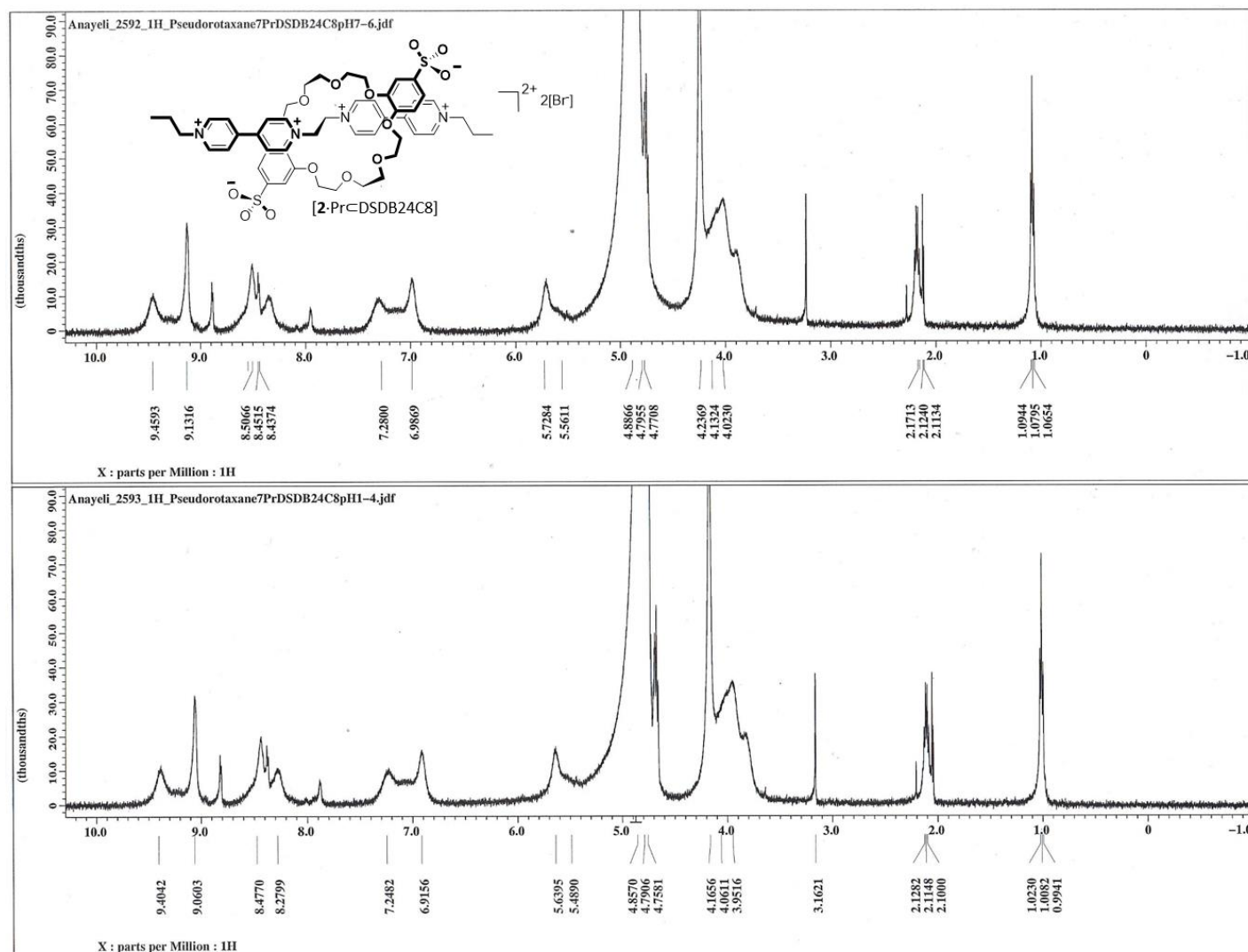


Figure S18: ¹H NMR 500 MHz spectra in D₂O of [2-Pr<DSDB24C8] at 298 K pH = 7 and (top) and pH = 1 (bottom).

6. Reversibility of threading/dethreading process

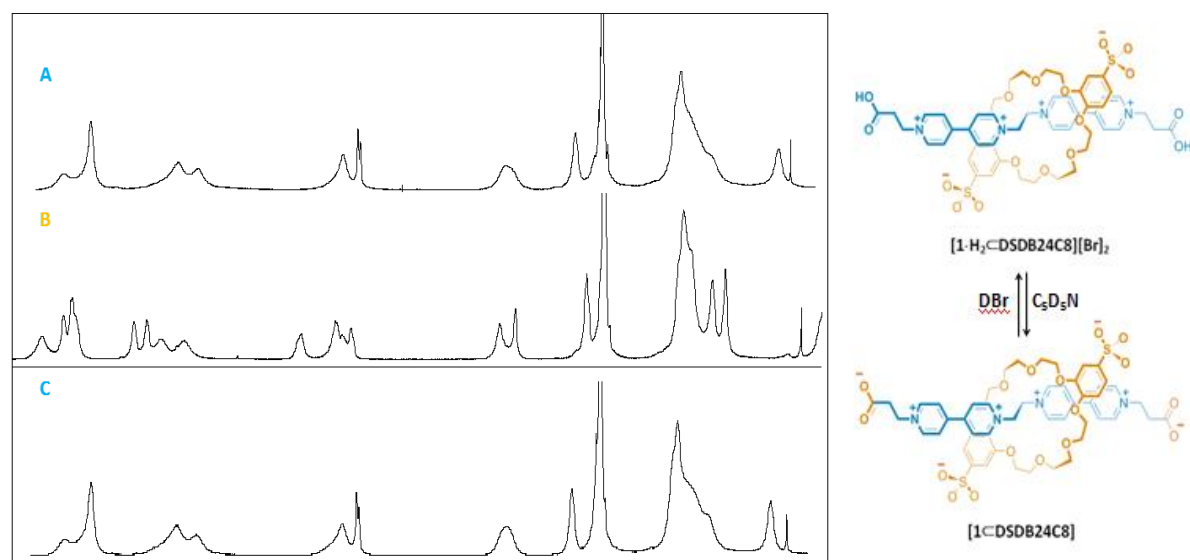


Figure S19: ^1H NMR spectra (400 MHz) of A) $[1\cdot\text{H}_2\text{C}\equiv\text{DSDB24C8}][\text{Br}]_2$; B) $[1\cdot\text{H}_2\text{C}\equiv\text{DSDB24C8}][\text{Br}]_2 + 2\text{eq. C}_5\text{D}_5\text{N}$; C) $[1\cdot\text{H}_2\text{C}\equiv\text{DSDB24C8}][\text{Br}]_2 + 2\text{eq. C}_5\text{D}_5\text{N} + 2\text{eq. DBr (48\% D}_2\text{O)}$. All spectra were recorded at 298 K.

7. Comparative table of chemical shifts at pH 1 and 7

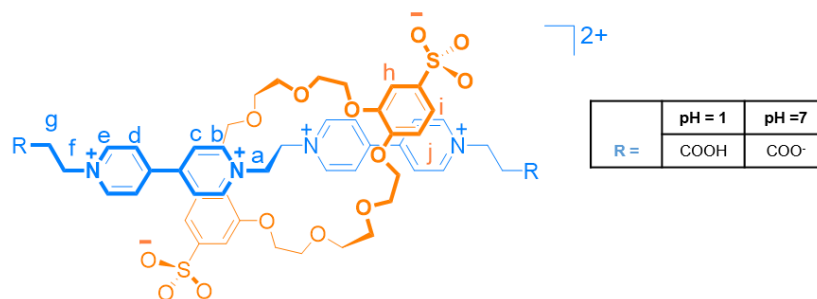


Table S3: Chemical shifts of the [2]rotaxane-like complex $[1\cdot\text{H}_2\text{C}\equiv\text{DSDB24C8}][\text{Br}]_2$ at pH = 1 and pH = 7.

Protons	Chemical shift (ppm)	
	pH = 1	pH = 7
b	9.21	9.26
e	8.90	8.90
c	8.20	8.23
d	8.03	8.03
h	7.01	7.09
I	7.01	7.06
J	6.66	6.68
A	5.43	5.48
F	*	*
G	3.10	2.80

* H_f – overlapping with HDO

8. Determination of equilibrium constants by UV/Vis

The equation used for determination of association constants is based on the Lambert-Beer and mass action laws using equimolar solutions of host (H) and guest (G). For a 1:1 complex:

Absorption of the complexes were monitored by UV/vis spectroscopy at 298 K. Stock solutions (2.5mM) for rotaxane-like complex at pH = 1 and pH = 7 were prepared in 2 mL volumetric flasks using deionized water as solvent. In order to ensure that the terminal group –COOH units are totally protonated and deprotonated pH values of the solution were adjusted at pH 1 and pH 7. After each measurement of the absorption spectrum, the solutions were diluted accurately by removing 250 μ L of the solution with a micropipette and replacing the same volume with fresh water. Dilutions were made from 2.5×10^{-3} M to 0.2×10^{-3} M.

All measurements were recorded against deionized water as a reference. The values of C_0/A were plotted against $A^{-1/2}$. The linear regression parameters were calculated and the association constants were determined.

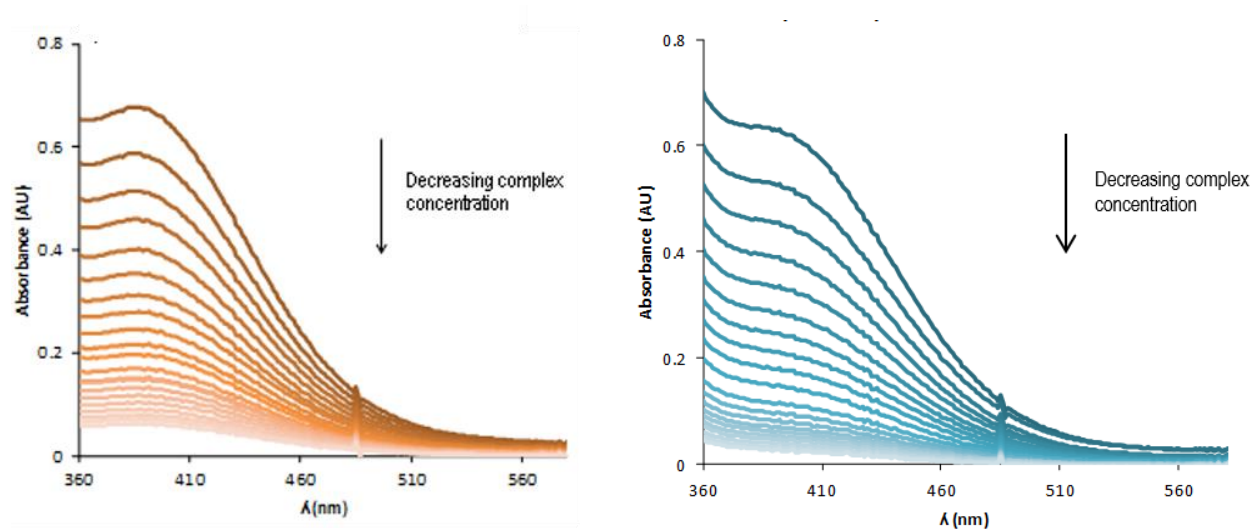


Figure S20: UV/vis spectra of *pseudo*-rotaxane complex recorded at 298 K, pH = 1 with $\lambda_{\text{max}} = 390$ nm (left) and pH = 7 (right); $\lambda_{\text{max}} = 384$ nm in deionized water.

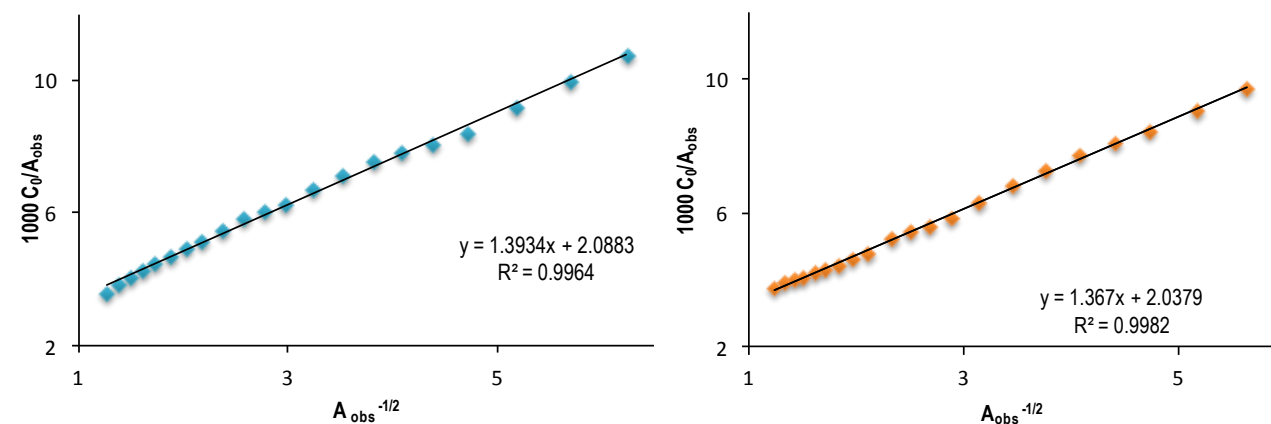


Figure S21: Linear plots of C_0/A versus $A^{-1/2}$ at pH = 1 (left); and C_0/A versus $A^{-1/2}$ at pH = 7 (right).

References: A. Ray, *J. Am. Chem. Soc.*, 1971, **93**, 7146; R. Cervantes, R. I. Sanchez, J. Tiburcio, *Chem. Eur. J.*, 2013, **19**, 4051.

9. Van't Hoff plots

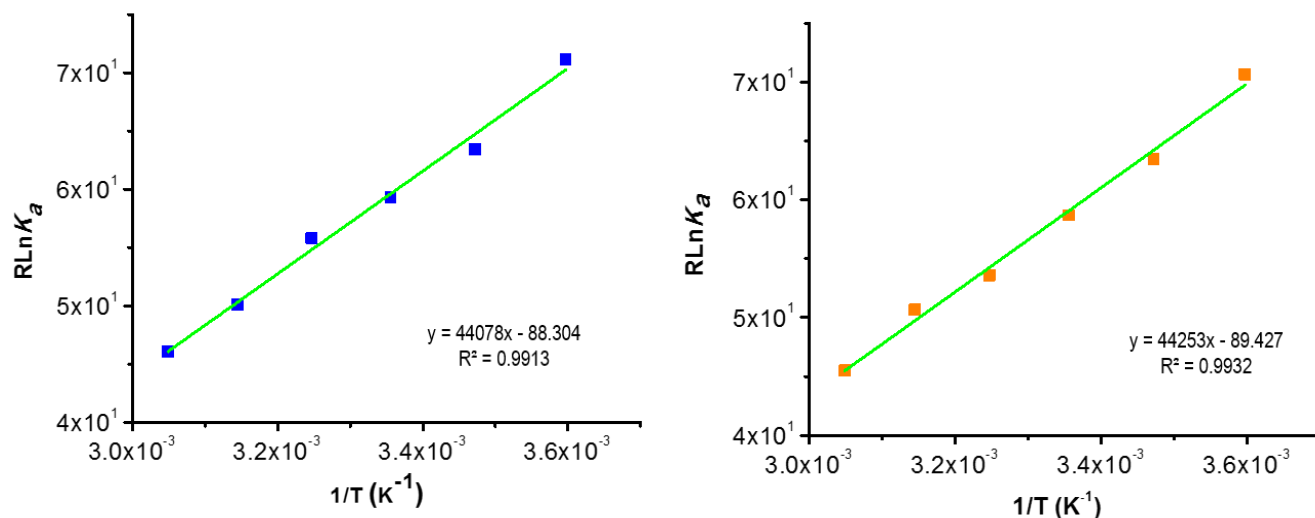
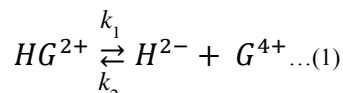


Figure S22: van't Hoff plots of [2]pseudo-rotaxane complex at pH = 1 (left) and pH = 7 (right).

10. Determination of the rate constants by concentration-jump kinetic experiments

Dilution method by stopped flow for determination of rate constants in [1-H₂C₂DSDB24C8][Br]₂ complex (HG²⁺) with equal concentrations of host (H²⁻) and guest (G⁴⁺). Assuming a 1:1 complex, the dissociation process could be defined as equation (1)



Dissociation of the complex assures an equimolar concentration between host and guest

$$[H^{2-}] = [G^{4+}]$$

The equilibrium constant is defined as

$$K_{eq} = \frac{[H^{2-}]_{eq}^2}{[HG^{2+}]_{eq}} \dots (2)$$

The rate equations are defined as

$$-\frac{d[HG^{2+}]}{dt} = k_1 [HG^{2+}] - k_2 [H^{2-}]^2 \dots (3)$$

$$-\frac{d[H^{2-}]}{dt} = k_2 [H^{2-}]^2 - k_1 [HG^{2+}] \dots (4)$$

If HG²⁺ and H²⁻ are related by the equilibrium in eq. (1), and the perturbation $\delta(t)$ in the concentration of complex HG²⁺ and host H²⁻ is defined according to eqs. (5) and (6),

$$[HG^{2+}]_t = [HG^{2+}]_{eq} + \delta(t) \dots (5)$$

$$[H^{2-}]_t = [H^{2-}]_{eq} - 2\delta(t) \dots (6)$$

When we substitute (5) and (6) in (4) the decay of $-\frac{d[\delta(t)]}{dt}$ is given by equation (7)

$$\begin{aligned}
-\frac{d[\delta(t)]}{dt} &= -\frac{d[H^{2-}]}{dt} = k_2 \{ [H^{2-}]_{eq} - 2\delta(t) \}^2 - k_1 \{ [HG^{2+}]_{eq} + \delta(t) \} \\
-\frac{d[\delta(t)]}{dt} &= -\frac{d[H^{2-}]}{dt} = k_2 \{ [H^{2-}]_{eq}^2 - 4[H^{2-}]_{eq}\delta(t) + 4\delta(t)^2 \} - k_1 \{ [HG^{2+}]_{eq} + \delta(t) \} \\
-\frac{d[\delta(t)]}{dt} &= -\frac{d[H^{2-}]}{dt} = k_2 [H^{2-}]_{eq}^2 - 4k_2 [H^{2-}]_{eq}\delta(t) + 4k_2 \delta(t)^2 - k_1 [HG^{2+}]_{eq} - k_1 \delta(t)
\end{aligned}$$

If we consider that at equilibrium the rate of occurrence of H^{2-} is equal to the rate of disappearance of HG^{2+} we obtain

$$\begin{aligned}
-\frac{d[\delta(t)]}{dt} &= -\frac{d[H^{2-}]}{dt} = -4k_2 [H^{2-}]_{eq}\delta(t) + 4k_2 \delta(t)^2 - k_1 \delta(t) \\
-\frac{d[\delta(t)]}{dt} &= -\frac{d[H^{2-}]}{dt} = -\{k_1 + 4k_2 [H^{2-}]_{eq}\}\delta(t) + 4k_2 \delta(t)^2 \dots (7)
\end{aligned}$$

If the perturbation $\delta(t)$ is sufficiently small that the term $\delta(t)^2$ in eq. (7) can be neglected, we can obtain the integrated equation (8)

$$\begin{aligned}
-\frac{1}{\delta(t)} d\delta(t) &= -\{k_1 + 4k_2 [H^{2-}]_{eq}\} \delta(t) dt \\
-\ln \delta(t) &= -\{k_1 + 4k_2 [H^{2-}]_{eq}\} t \dots (8)
\end{aligned}$$

Where $-\{k_1 + 4k_2 [H^{2-}]_{eq}\}$ is equal to $-k_{obs}$ so we can obtain a linear equation (9)

$$-k_{obs} = -\{k_1 + 4k_2 [H^{2-}]_{eq}\} \dots (9)$$

For determining $[H^{2-}]_{eq}$ we use the equation (2) if we solve $[H^{2-}]^2$

$$[H^{2-}]_{eq}^2 = K_{eq} * [HG^{2+}]_{eq} \dots (10)$$

The initial concentration C_0 is given by

$$C_0 = [HG^{2+}]_{eq} + [H^{2-}]_{eq} \dots (11)$$

If we solve $[HG^{2+}]_{eq}$

$$[HG^{2+}]_{eq} = C_0 - [H^{2-}]_{eq} \dots (12)$$

When we substitute (12) in (10) we obtain

$$[H^{2-}]_{eq}^2 = K_{eq} * \{C_0 - [H^{2-}]_{eq}\} \dots (13)$$

$$[H^{2-}]_{eq}^2 = K_{eq} C_0 - K_{eq} [H^{2-}]_{eq} \dots (14)$$

If we solve the second order equation we can calculate $[H^{2-}]_{eq}$ by the equation (15)

$$\begin{aligned}
[H^{2-}]_{eq}^2 + K_{eq} [H^{2-}]_{eq} - K_{eq} C_0 &= 0 \\
[H^{2-}]_{eq} &= \frac{-K_{eq} \pm \sqrt{K_{eq}^2 + 4K_{eq} [HG^{2+}]_0}}{2} \dots (15)
\end{aligned}$$

The stopped flow traces were treated by a conventional kinetic analysis with Pro-Data SX fitting program to afford the values of the rate constants.

Reference: S. S. Kristjánssdóttir, A. E. Moody and J. R. Norton, *Int. J. Chem. Kinet.*, 1992, **24**, 895.

11. Eyring plots

Activation parameters for threading and dethreading were obtained from the temperature-dependence Eyring plots of the rate constants values in the range of 278 – 328 K. Plots of $\ln(k/T)$ versus $1/T$ and corresponding linear fit, according to the Eyring equation for threading and dethreading processes, are shown in figure S18.

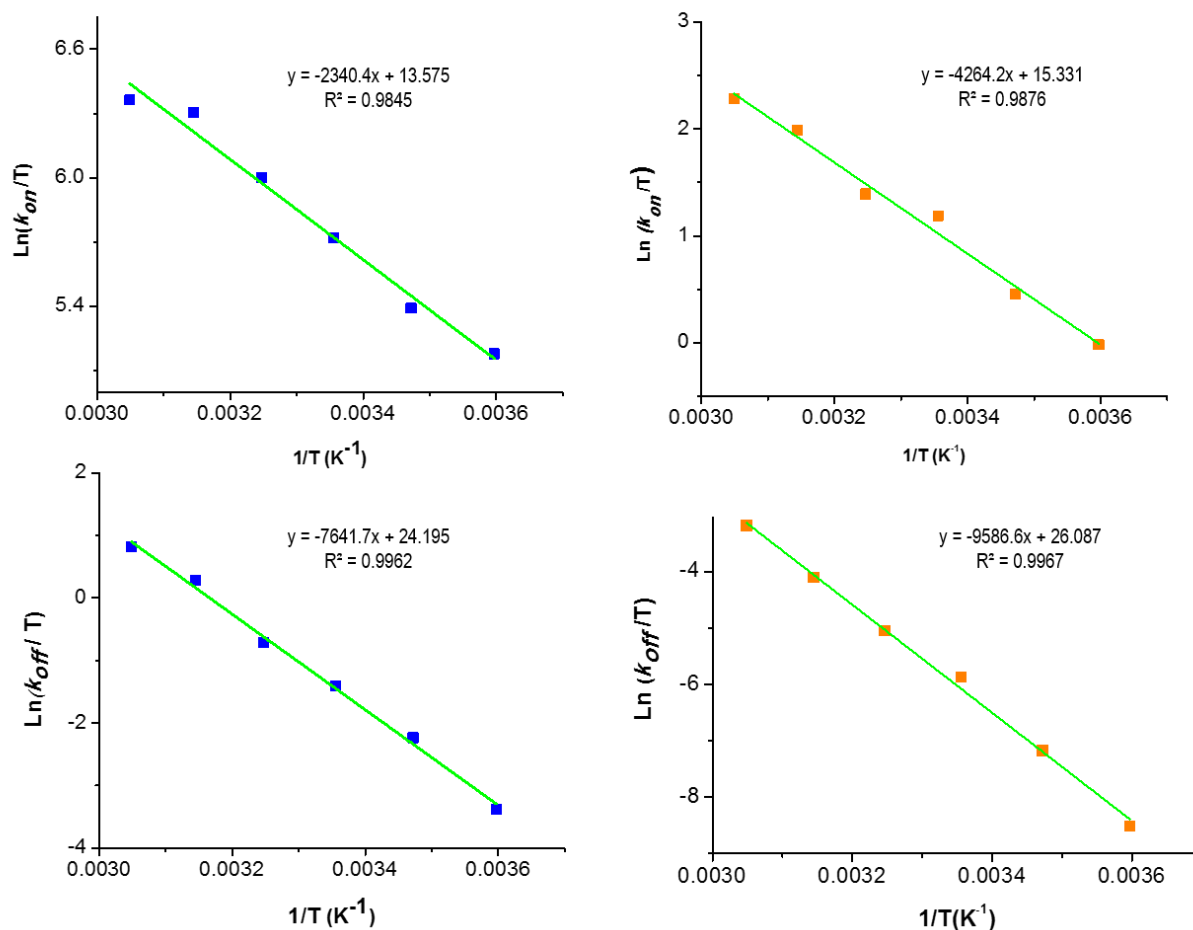


Figure S23: Eyring plots obtained for threading and dethreading processes at pH = 1 and pH = 7 in the temperature range 278 – 328 K.

12. Kinetic parameters for dethreading process

Kinetic parameters	pH = 1	pH = 7
$\Delta H_{off}^{\ddagger} / \text{kJmol}^{-1}$	63.5 (± 0.4)	79.7 (± 0.6)
$\Delta S_{off}^{\ddagger} / \text{Jmol}^{-1}\text{K}^{-1}$	3.6 (± 0.3)	19 (± 1)
$k_{off} / \text{M}^{-1}\text{s}^{-1}$ at 298 K	73 (± 8)	0.8 (± 0.1)
$\Delta G_{off}^{\ddagger} / \text{kJmol}^{-1}$ at 298 K	62.5 (± 0.6)	74 (± 1)