

## Supporting Information

### Probing the Dynamics of Imine-based Pentafoil Knot and Pentameric Circular Helicate Assembly

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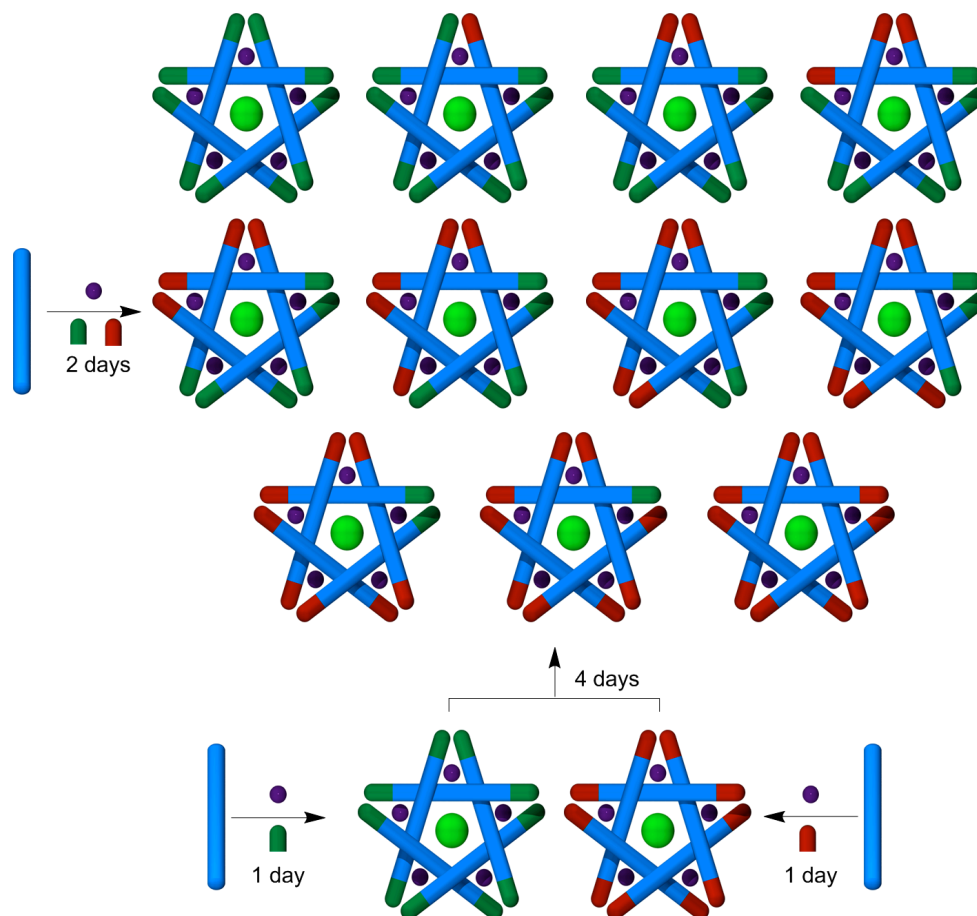
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Unless stated otherwise, all reagents and solvents were purchased from Aldrich Chemicals and used without further purification. NMR spectra were recorded on Bruker AV 400, and Bruker DMX 500 instruments. Chemical shifts are reported in parts per million (ppm) from low to high frequency and referenced to the residual solvent resonance. Coupling constants ( $J$ ) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = doublet, t = triplet, dd = double doublet, q = quartet, m = multiplet, b = broad, ddd = doublet of double doublets.  $^1\text{H}$  and  $^{13}\text{C}$  NMR assignments were made using 2D-NMR methods (COSY, ROESY, HSQC, HMBC) and are unambiguous unless stated otherwise. Low resolution ESI mass spectrometry was performed with a Finnigan LCQ-MS, Micromass Platform II or Waters Quattro Ultima LC-MS/MS mass spectrometers. High resolution ESI mass spectrometry were carried out by the mass spectrometry services at the University of Edinburgh and the EPSRC National Mass Spectrometry Service Centre, Swansea, UK. Compounds **1** and **S1** were prepared according to literature procedures.<sup>1</sup>

## 1. Amine Exchange on Pentameric Circular Helicates

### 1.1 Experimental Procedure for the Investigations of Amine Scrambling

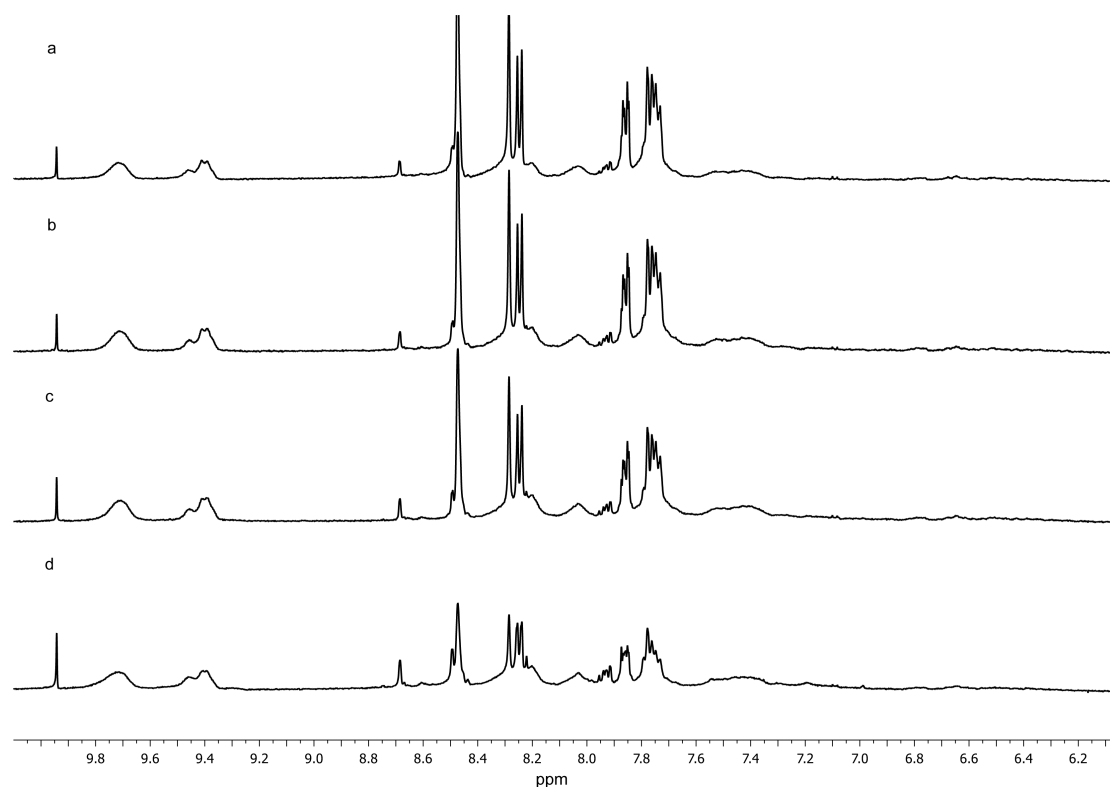


**Scheme S1.** Schematic diagram showing the synthesis of mixed amine pentameric cyclic helicates. Mixing the two amines (hexylamine **4**, green; 2-methoxyethylamine **7**, red) at the start of the reaction gives a statistical distribution of mixed amine helicates (only one positional isomer is shown where appropriate). Whereas two preformed homoamine helicates, when mixed, undergo exchange generating the same distribution of mixed species as above over the course of 4 days.

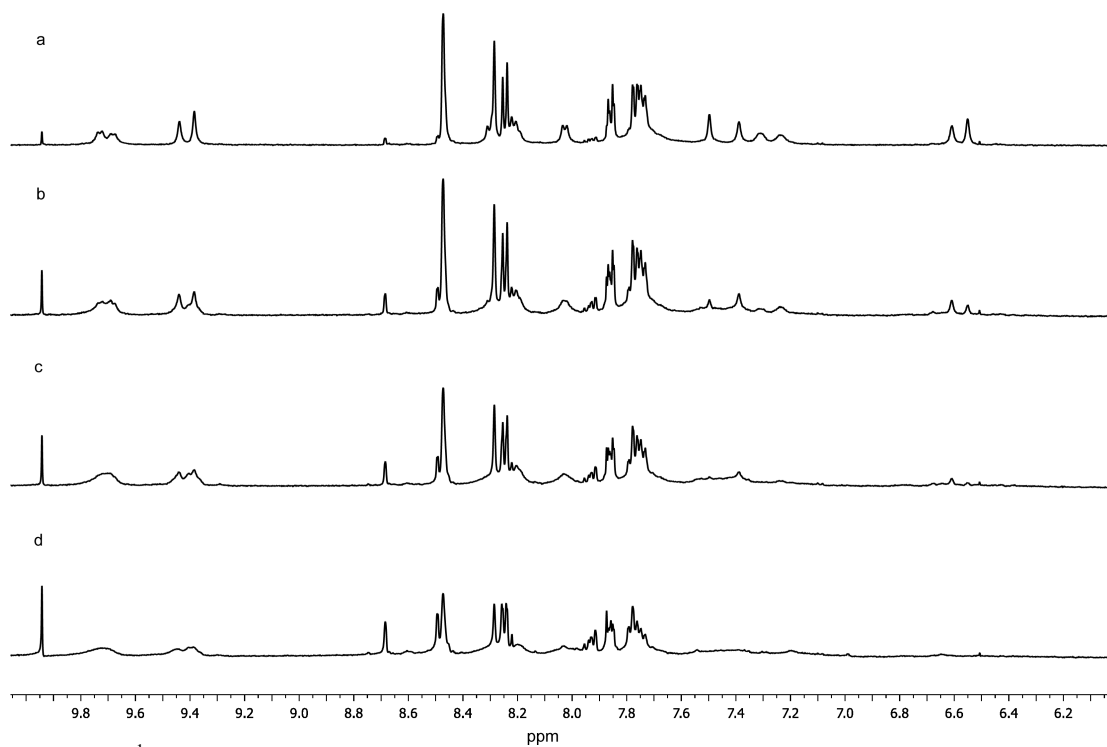
To two separate DMSO-*d*<sub>6</sub> solutions of **1** (4 mg, 9.5 μmol, in 2.0 mL) was added FeCl<sub>2</sub> (100 μL of a 0.10 M stock solution, 10.5 μmol). The purple solution was mixed thoroughly to ensure complete dissolution of the aldehyde. To a 1.0 mL aliquot of **1**+FeCl<sub>2</sub> was added hexylamine **4** (25 μL of a 0.20 M stock solution, 5.2 μmol) and 2-methoxyethylamine **7** (25 μL of a 0.20 M stock solution, 5.2 μmol) (sample A). To a 0.5 mL aliquot of **1**+FeCl<sub>2</sub> was added hexylamine **4** (25 μL of a 0.20 M stock solution, 5.2 μmol) only. To the remaining 0.5 mL aliquot of **1**+FeCl<sub>2</sub> was added 2-methoxyethylamine **7** (25 μL of a 0.20 M stock solution, 5.2 μmol) only. The three solutions were heated for 1d at 60 °C. The solutions of **1**+FeCl<sub>2</sub>+**4** and **1**+FeCl<sub>2</sub>+**7** were combined in a clean NMR tube and thoroughly mixed (sample B) before being heated at 60 °C for a further 4 days. Both samples (A and B) were monitored over

time (Figures S1 and S2). The two samples (A and B) were allowed to cool and the following purification procedure was applied to each sample individually: The reaction mixture was precipitated using  $\text{KPF}_6$  (saturated aqueous solution). The resulting purple powder was collected on celite and washed with water, EtOH,  $\text{CH}_2\text{Cl}_2$  and finally  $\text{Et}_2\text{O}$ . The product mixture was dissolved in  $\text{CH}_3\text{CN}$  and the solvent removed under reduced pressure. Both samples were dissolved in 0.5 mL of  $\text{CD}_3\text{CN}$  and compared by  $^1\text{H}$  NMR (Figure S3) and LRESI-MS (see Figure 1, main text).

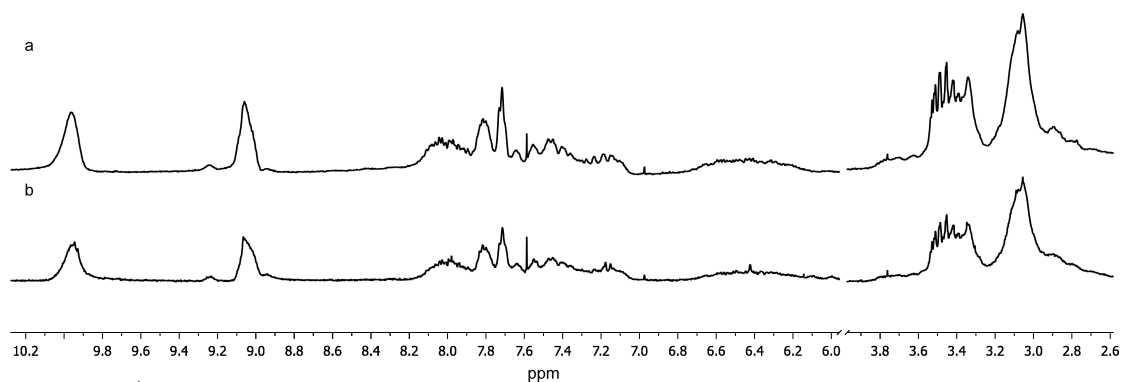
### 1.1.1 $^1\text{H}$ NMR Analysis of Amine Scrambling



**Figure S1.**  $^1\text{H}$ NMR ( $\text{CD}_3\text{SOCD}_3$ , 500 MHz) analysis of the crude mixture of sample A after heating at  $60^\circ\text{C}$  for; (a) 1 day, (b) 2 days, (c) 3 days, (d) 4 days.



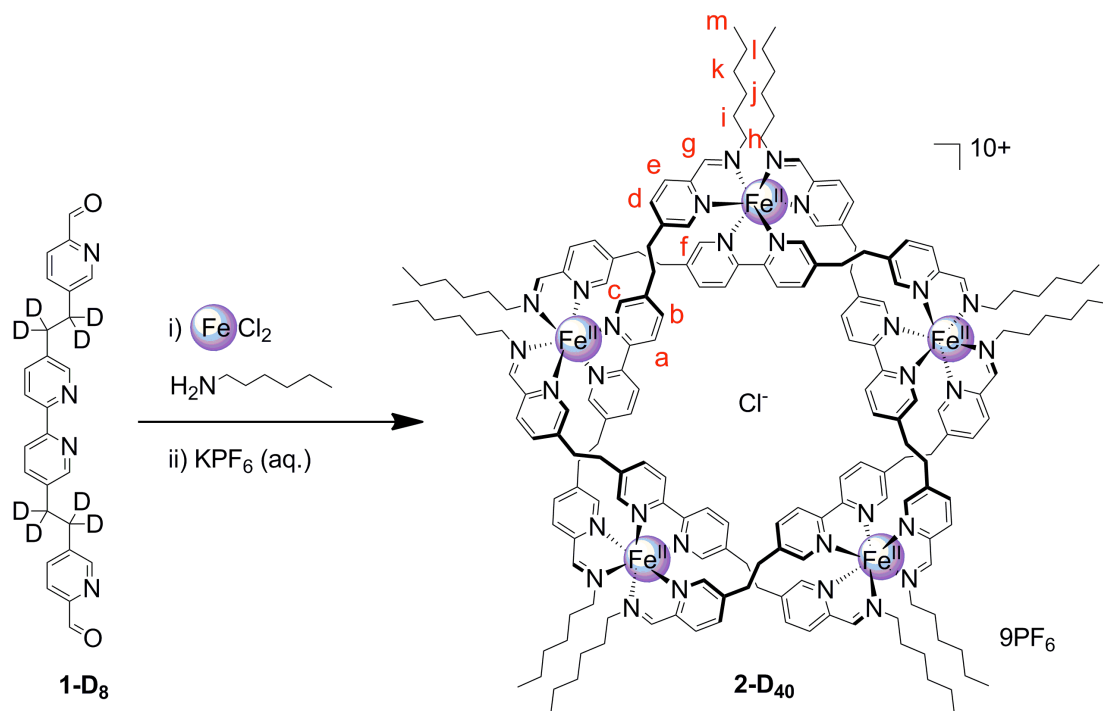
**Figure S2.**  $^1\text{H NMR}$  ( $\text{CD}_3\text{SOCD}_3$ , 500 MHz) analysis of the crude mixture of sample B after heating at  $60\text{ }^\circ\text{C}$  for; (a) 1 day, (b) 2 days, (c) 3 days, (d) 4 days.



**Figure S3.**  $^1\text{H NMR}$  ( $\text{CD}_3\text{CN}$ , 500 MHz) analysis after purification; (a) Sample A (b) Sample B.

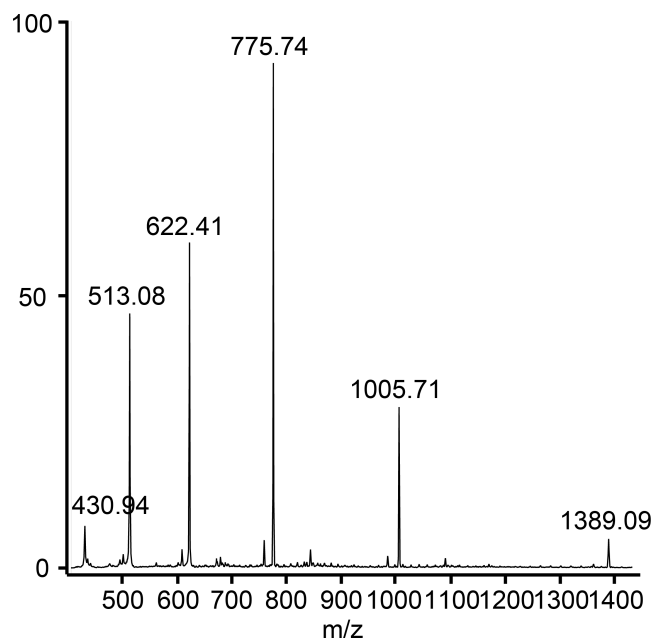


## 2.2 Experimental Procedure for the Synthesis of Helicate **2-D<sub>40</sub>**



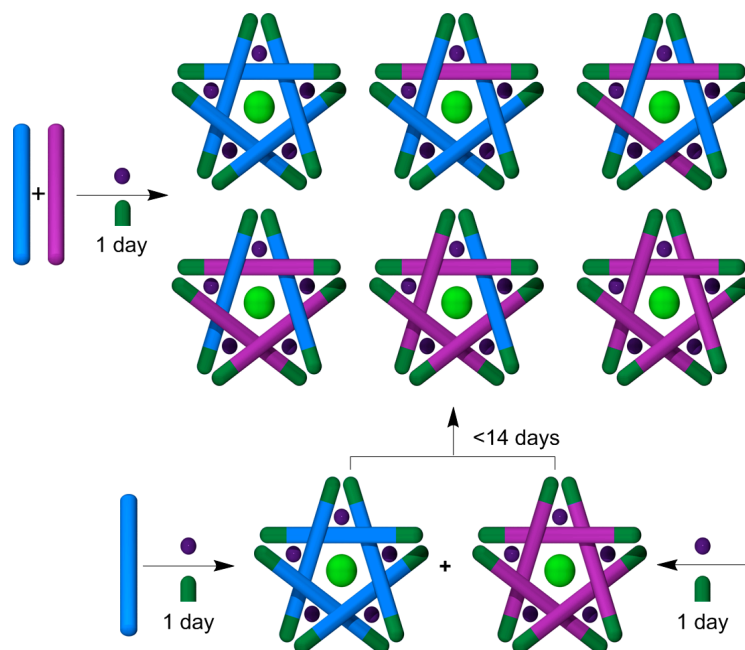
**Scheme S3.** Preparation of deuterated cyclic helicate **2-D<sub>40</sub>**. Reagents and conditions: (i)  $60\text{ }^\circ\text{C}$ ,  $\text{DMSO-d}_6$ , 1d. (ii) Precipitation by addition of an aqueous solution of  $\text{KPF}_6$ . Overall yield, 61%.

To a solution of dialdehyde **1-D<sub>8</sub>** (2.0 mg,  $4.6\text{ }\mu\text{mol}$ , 1.0 eq.) in  $\text{DMSO-d}_6$  (1.0 mL) was added a solution of anhydrous  $\text{FeCl}_2$  ( $50\text{ }\mu\text{L}$  of a  $0.1\text{ M}$   $\text{DMSO-d}_6$  solution,  $5.1\text{ }\mu\text{mol}$ , 1.1 eq.) followed by a  $\text{DMSO-d}_6$  solution of hexylamine **4** ( $50\text{ }\mu\text{L}$ ,  $0.2\text{ M}$ ,  $10.1\text{ }\mu\text{mol}$ , 2.2 eq.). The resulting dark purple reaction was thoroughly mixed and heated at  $60\text{ }^\circ\text{C}$  for one day. After cooling to room temperature, excess saturated aqueous  $\text{KPF}_6$  was added ( $5.0\text{ mL}$ ). A fine suspension of a purple material formed which was collected on celite, thoroughly washed with water, EtOH,  $\text{CH}_2\text{Cl}_2$  and diethylether. The purple solid was dissolved in acetonitrile and concentrated under reduced pressure to give **2-D<sub>40</sub>** as a purple powder (2.6 mg, 61 %).  $^1\text{H}$  NMR (500 MHz,  $\text{CD}_3\text{CN}$ )  $\delta$  9.94 (d,  $J = 8.3\text{ Hz}$ , 10H,  $\text{H}^a$ ), 9.06 (s, 10H,  $\text{H}^g$ ), 7.98 (d,  $J = 8.0\text{ Hz}$ , 10H,  $\text{H}^e$ ), 7.82 (d,  $J = 8.0\text{ Hz}$ , 10H,  $\text{H}^d$ ), 7.53 (d,  $J = 8.5\text{ Hz}$ , 10H,  $\text{H}^b$ ), 7.17 (s, 10H,  $\text{H}^c$ ), 6.42 (s, 10H,  $\text{H}^f$ ), 3.35 (m, 10H,  $\text{H}^h$ ), 3.05 (m, 10H,  $\text{H}^i$ ), 1.62–1.39 (m, 20H,  $\text{H}^j$ ), 1.19 (m, 20H,  $\text{H}^k$ ), 1.15–1.03 (m, 40H,  $\text{H}^l$  and  $\text{H}^m$ ), 0.84 (t,  $J = 7.2$ , 30H,  $\text{H}^n$ ).



**Figure S4.** LRESI MS analysis after purification of cyclic helicate **2-D<sub>40</sub>**. Peaks correspond to sequential loss of  $\text{PF}_6^-$  counter-ions.

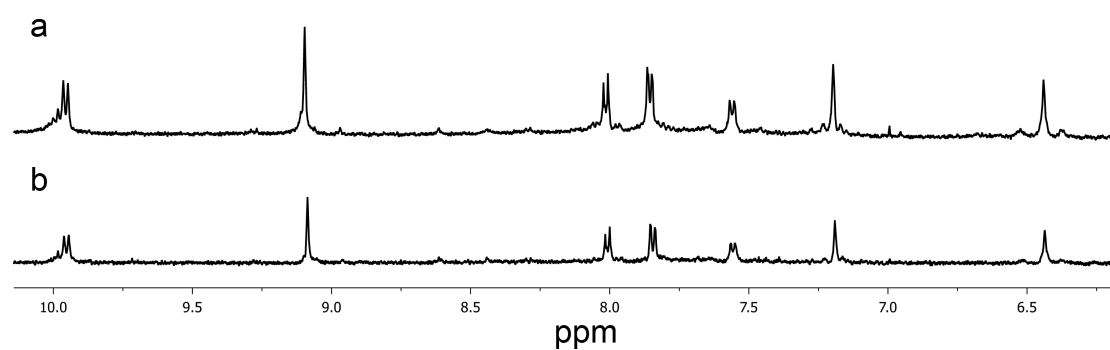
### 2.3 Experimental Procedure for the Investigations of Aldehyde Scrambling on Helicates **2** and **2-D<sub>40</sub>**



**Scheme S4.** Schematic diagram showing the synthesis of mixed aldehyde pentameric cyclic helicates. Mixing the two aldehydes (**1**, blue; **1-D<sub>8</sub>**, pink) at the start of the reaction gives a statistical distribution of mixed aldehyde helicates (only one positional isomer is shown where appropriate). Whereas two preformed homoaldehyde helicates, when mixed, undergo exchange generating a similar distribution of mixed species as above over the course of 13 days.

To two separate  $\text{DMSO-}d_6$  solutions of **1** (1.9 mg, 4.6  $\mu\text{mol}$ , in 1.0 mL) and **1-D<sub>8</sub>** (2.0 mg, 4.6  $\mu\text{mol}$  in 1.0 mL) was added  $\text{FeCl}_2$  (50  $\mu\text{L}$  of a 0.10 M stock solution, 5.1

$\mu\text{mol}$ ). The two purple solutions were mixed thoroughly to ensure complete dissolution of both aldehydes. A 0.5 mL aliquot of **1**+FeCl<sub>2</sub> was mixed with a 0.5 mL aliquot of **1-D**<sub>8</sub>+FeCl<sub>2</sub> in a clean NMR tube before addition of hexylamine **4** (50  $\mu\text{L}$  of a 0.21 M stock solution, 10.2  $\mu\text{mol}$ ) (Sample C). The remaining 0.5 mL aliquots of **1**+FeCl<sub>2</sub> and **1-D**<sub>8</sub>+FeCl<sub>2</sub> were separately reacted with hexylamine **3** (25  $\mu\text{L}$  of a 0.21 mM stock solution, 2.6  $\mu\text{mol}$ , for each reaction). The three solutions were heated for 1d at 60 °C. The solutions of **1**+FeCl<sub>2</sub>+**4** and **1-D**<sub>8</sub>+FeCl<sub>2</sub>+**4** were combined in a clean NMR tube and thoroughly mixed (Sample D) before being heated at 60 °C for a further 13 days. Both samples were monitored over time (Figure 2, main text). At each time point (1, 3, 6 and 13 days) a small sample (0.2 mL) was removed from each reaction mixture, allowed to cool and the following purification procedure was applied to each sample individually: The reaction mixture was precipitated using KPF<sub>6</sub> (saturated aqueous solution). The resulting purple powder was collected on celite and washed with water, EtOH, CH<sub>2</sub>Cl<sub>2</sub> and finally Et<sub>2</sub>O. The product mixture was dissolved in CH<sub>3</sub>CN and the solvent removed under reduced pressure. Both samples were dissolved in 0.5 mL of CH<sub>3</sub>CN and compared by LRESI MS (see Figure 2, main text).

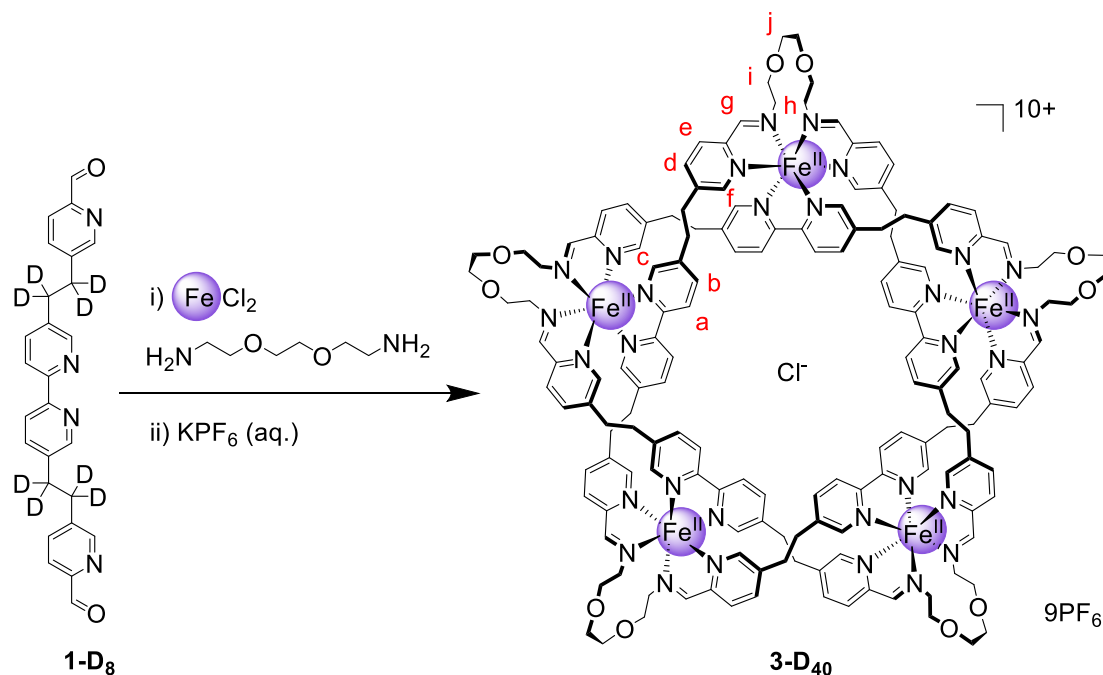


**Figure S5.** <sup>1</sup>H NMR (CD<sub>3</sub>CN, 500 MHz) analysis of (a) Sample C and (b) Sample D after 13 days of heating at 60 °C followed by purification.



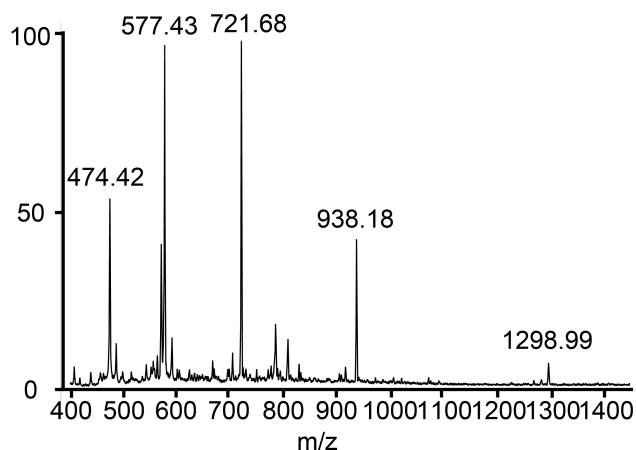
### 3. Aldehyde Exchange for Pentafoil Knot 6

#### 3.1 Experimental Procedure for the Synthesis of Pentafoil Knot 3-D<sub>40</sub>



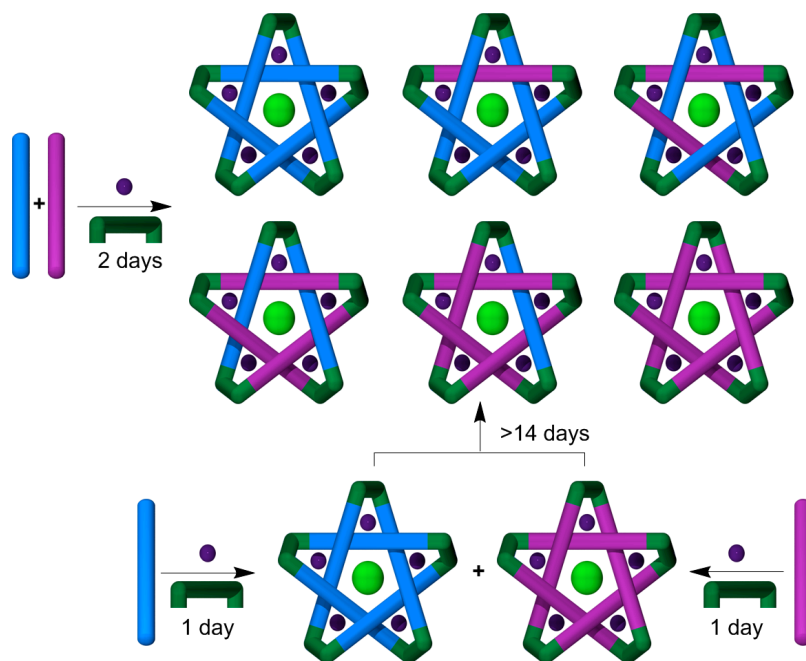
**Scheme S5.** Preparation of deuterated pentafoil knot **3-D<sub>40</sub>**. Reagents and conditions: (i) 60 °C, DMSO-*d*<sub>6</sub>, 2d. (ii) Precipitation by addition of an aqueous solution of KPF<sub>6</sub>. Overall yield, 39%.

To a solution of dialdehyde **1-D<sub>8</sub>** (2.0 mg, 4.6 μmol, 1.0 eq.) in DMSO-*d*<sub>6</sub> (1.0 mL) was added a solution of anhydrous FeCl<sub>2</sub> (50 μL of a 0.10 mM DMSO-*d*<sub>6</sub> solution, 5.1 μmol, 1.1 eq.) followed by a DMSO-*d*<sub>6</sub> solution of 2,2'-(ethylenedioxy)bis(ethylamine) **5** (50 μL, 0.10 M, 5.1 μmol, 1.1 eq.). The resulting dark purple reaction was thoroughly mixed and heated at 60 °C for 24 h. After cooling to room temperature, excess saturated aqueous KPF<sub>6</sub> was added (5.0 mL). A fine suspension of a purple material formed which was collected on celite, thoroughly washed with water, EtOH, CH<sub>2</sub>Cl<sub>2</sub> and diethylether. The purple solid was dissolved in acetonitrile and concentrated under reduced pressure to give **3-D<sub>40</sub>** as a purple powder (1.6 mg, 39 %). <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>CN) δ 9.92 (d, *J* = 8.3 Hz, 10H, H<sup>a</sup>), 9.04 (s, 10H, H<sup>g</sup>), 8.03 (d, *J* = 8.1 Hz, 10H, H<sup>c</sup>), 7.86 (d, *J* = 8.1 Hz, 10H, H<sup>d</sup>), 7.51 (d, *J* = 8.0 Hz, 10H, H<sup>b</sup>), 7.19 (s, 10H, H<sup>e</sup>), 6.43 (s, 10H, H<sup>f</sup>), 4.11 (m, 10H, H<sup>h</sup>), 3.67 (d, *J* = 10.0 Hz, 20H, H<sup>i</sup> and H<sup>j</sup>), 3.32 (d, *J* = 9.8 Hz, 10H, H<sup>i</sup>), 3.23 (d, *J* = 11.3 Hz, 10H, H<sup>h</sup>), 2.96 (m, 10H, H<sup>i</sup>).



**Figure S6.** LRESI MS analysis after purification of cyclic helicate **3-D<sub>40</sub>**. Peaks correspond to sequential loss of PF<sub>6</sub><sup>-</sup> counter-ions.

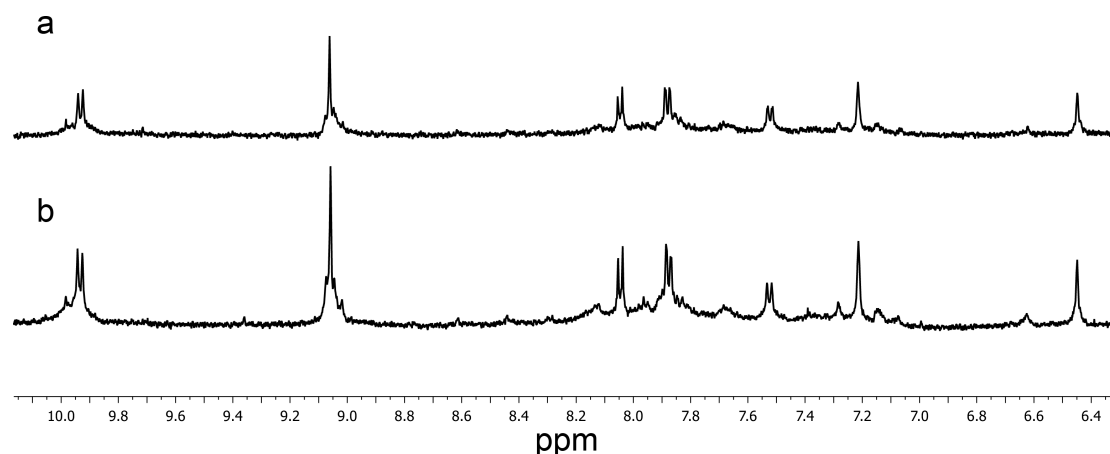
### 3.2 Experimental Procedure for the Investigations of Aldehyde Scrambling on Pentafoil Knots **3** and **3-D<sub>40</sub>**



**Scheme S6.** Schematic diagram showing the synthesis of mixed aldehyde pentafoil knots. Mixing the two aldehydes (**1**, blue; **1-D<sub>8</sub>**, pink) at the start of the reaction gives a statistical distribution of mixed aldehyde pentafoil knots (only one positional isomer is shown where appropriate). Whereas two preformed homoaldehyde helicates, when mixed, undergo slow exchange.

To two separate DMSO-*d*<sub>6</sub> solutions of **1** (1.9 mg, 4.6 μmol, in 1.0 mL) and **1-D<sub>8</sub>** (2.0 mg, 4.6 μmol in 1.0 mL) was added FeCl<sub>2</sub> (50 μL of a 0.10 M stock solution, 5.1 μmol). The two purple solutions were mixed thoroughly to ensure complete dissolution of both aldehydes. A 0.5 mL aliquot of **1**+FeCl<sub>2</sub> was mixed with a 0.5 mL aliquot of **1-D<sub>8</sub>**+FeCl<sub>2</sub> in a clean NMR tube before addition of 2,2'-(ethylenedioxy)bis(ethylamine) **5** (50 μL of a 0.10 mM stock solution, 5.1 μmol)

(Sample E). The remaining 0.5 mL aliquots of **1**+FeCl<sub>2</sub> and **1-D<sub>8</sub>**+FeCl<sub>2</sub> were separately reacted with 2,2'-(ethylenedioxy)bis(ethylamine) **5** (25 μL of a 0.10 mM stock solution, 2.6 μmol, for each reaction). The three solutions were heated for 1d at 60 °C. The solutions of **1**+FeCl<sub>2</sub>+**5** and **1-D<sub>8</sub>**+FeCl<sub>2</sub>+**5** were combined in a clean NMR tube and thoroughly mixed (Sample F) before being heated at 60 °C for a further 13 days. Both samples were monitored over time (Figure 3, main text). At each time point (1, 3, 6 and 13 days) a small sample (0.2 mL) was removed from each reaction mixture, allowed to cool and the following purification procedure was applied to each sample individually: The reaction mixture was precipitated using KPF<sub>6</sub> (saturated aqueous solution). The resulting purple powder was collected on celite and washed with water, EtOH, CH<sub>2</sub>Cl<sub>2</sub> and finally Et<sub>2</sub>O. The product mixture was dissolved in CH<sub>3</sub>CN and the solvent removed under reduced pressure. Both samples were dissolved in 0.5 mL of CH<sub>3</sub>CN and compared by LRESI MS (see Figure 3, main text).



**Figure S7.** <sup>1</sup>H NMR (CD<sub>3</sub>CN, 500 MHz) analysis of (a) Sample E and (b) Sample F after 13 days of heating at 60 °C followed by purification.

#### 4. Additional References

1. Ayme, J.-F.; Beves, J. E.; Leigh, D. A.; McBurney, R. T.; Rissanen, K.; Schultz, D. *Nat. Chem.* **2012**, *4*, 15-20.