Supporting Information

A calix[4]pyrrole-based linear supramolecular polymer constructed by orthogonal self-assembly

## Contents

General Considerations

All solvents were dried before use according to standard procedures. Unless specifically indicated, all other chemicals and reagents used in this study were purchased from commercial sources and used as received. ^{1}H and ^{13}C NMR spectra were recorded on Agilent VNMRS 500 spectrometers using TMS as an internal reference. DOSY NMR spectra were recorded on a Bruker Ascend 500 MHz spectrometer. Mass spectra were measured on a Thermo Scientific Thermo Q Exactive HR mass spectrometer equipped with a LC unit. Viscosity measurements were carried out with an Ubbelohde micro dilution viscometer (Shanghai Liangjing Glass Instrument Factory, 0.40 mm inner diameter) in chloroform. Melting points were determined using a Stuart SMP10 instrument with 1 °C/min temperature increment under ambient conditions. Compounds **2** and TBAS was synthesized according to previously reported literature procedures.[1-2]

Synthesis and Characterization

Compound 1
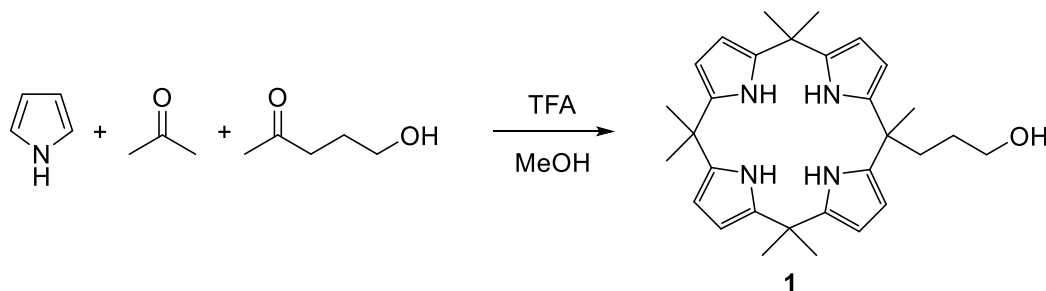
Methanol (150 mL) at 0 °C was bubbled with N_2 for 10 min. Then, pyrrole (6 mL, 86.8 mmol), 5-hydroxy-2-pentanone (2.19 mL, 21.62 mmol) and acetone (4.80 mL, 64.86 mmol) were added into the methanol at 0 °C. TFA (1.00 mL) was added dropwise over the course of ten minutes by shielding the reaction vessel from light. The resulting mixture was stirred at 0 °C for 3 hours and then overnight at room temperature. Pale yellow precipitate was filtered and washed with cold MeOH. Chromatographic purification (silica gel, DCM then DCM/MeOH: 99/1) yielded yellow solid (2.14 g, 21%). M.p. decomposes over 198 °C. ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): δ = 1.46 (s, 3H, −CH_3), 1.50-1.52 (m, 20H, −CH_2− and −CH_3), 1.92 (m, 2H, −CH_2−), 3.54 (t, J = 6 Hz, 2H, −CH_2−), 5.90 (s, 8H, pyrrole−CH), 7.03 (br, 4H, NH). ^{13}C NMR (126 MHz, CDCl$_3$): δ = 138.4, 137.1, 103.8, 102.8, 63.2, 38.6, 36.6, 35.2, 29.3, 29.0, 27.8, 26.3. HRMS (ESI): m/z calcd for $C_{30}H_{41}N_4O$ [M+H]$^+$: 473.32749; found: 473.32549.

ABA_547_PROTON_01

7.03

5.90

3.54
3.53
3.51

1.92
1.52
1.50
1.46

A (t)
3.53
J(6.4)

3.95

8.00

2.05

2.01

20.15
2.99

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
δ (ppm)
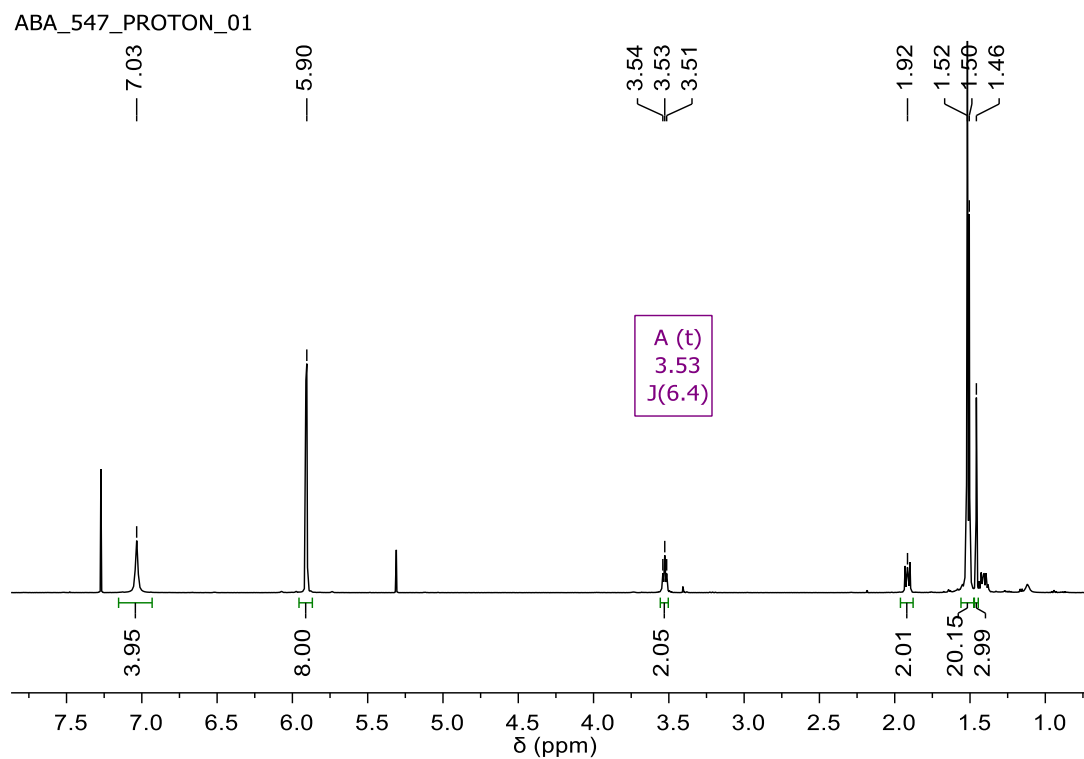
Figure S1. ^{1}H NMR spectrum of **1** recorded in CDCl$_3$ at 25 °C.

ABA_435_CARBON_01

138.4
137.1

103.8
102.8

63.2

38.6
36.6
35.2
29.3
29.0
27.8
26.3

150 140 130 120 110 100 90 80 70 60 50 40 30 20
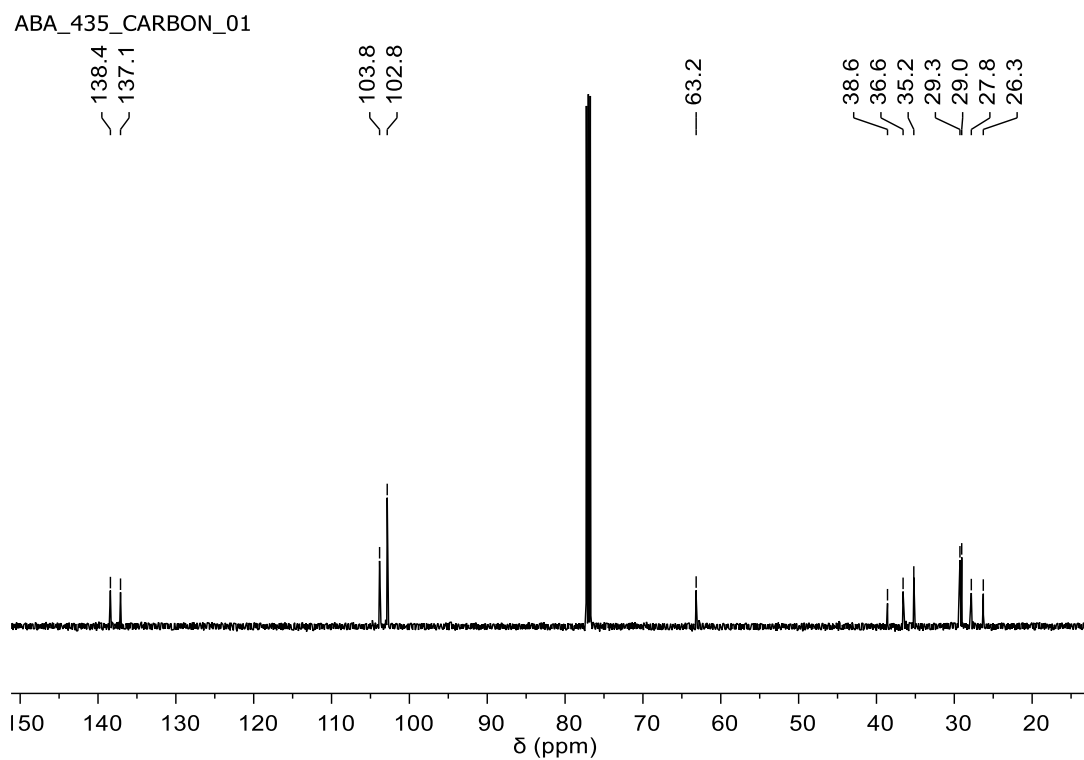δ (ppm)

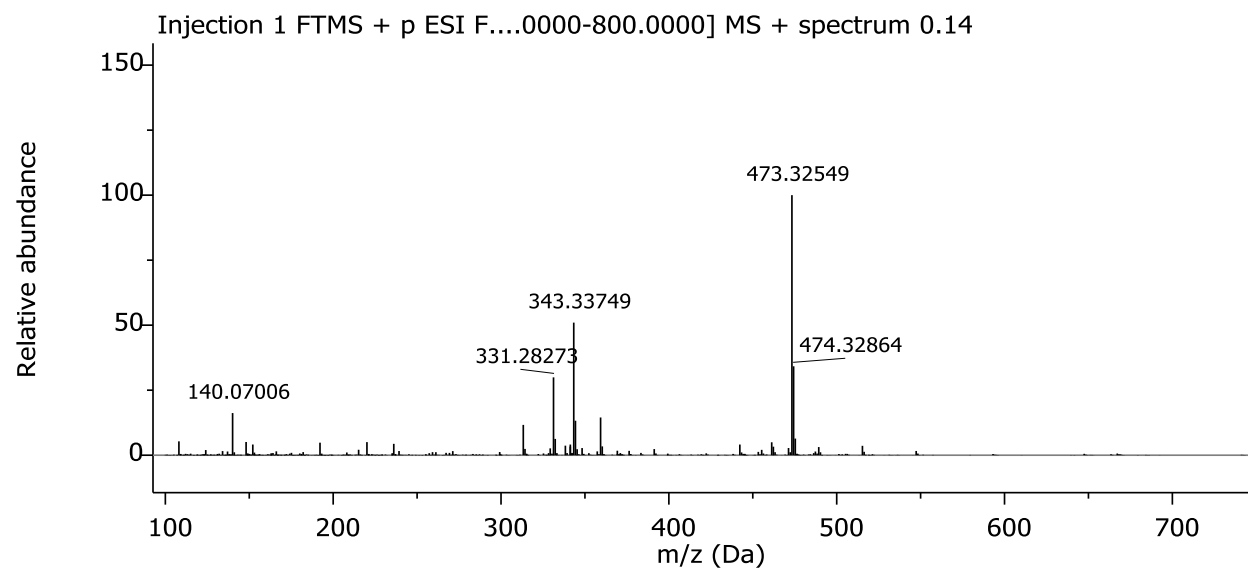**Figure S2.** ^{13}C NMR spectrum of **1** recorded in CDCl$_3$ at 25 °C.
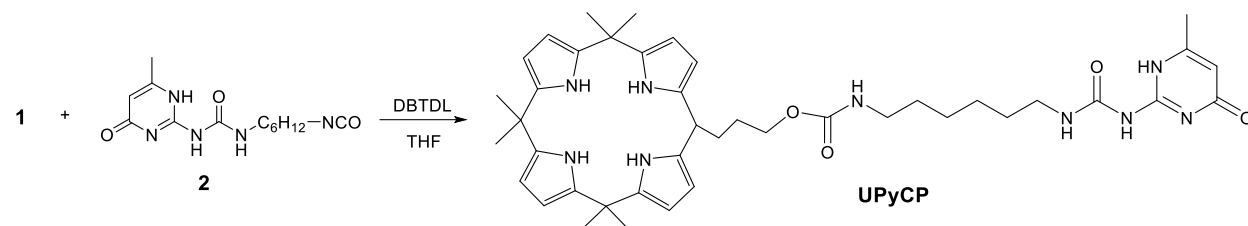
S3

Figure S3. HRESI-MS spectrum of **1**.

UPyCP

In a flask equipped with a condenser, **1** (150 mg, 0.32 mmol), **2** (186 mg, 0.63 mmol) and DBTDL (8 mg, 0.013 mmol) were dissolved in dry THF (20 mL) under an N_2 atmosphere. The resulting mixture was stirred at 70 °C for 18h. After completion of the reaction white precipitate was filtered. The supernatant was concentrated and precipitated into hexane. Precipitate was dissolved in DCM and precipitation into hexane afforded **UPyCP** as a pale-yellow solid (121 mg, 51%). M.p.: 127-129 °C. ^{1}H NMR (500 MHz, CDCl$_3$, 25 °C): δ = 1.38-1.88 (br m, 31H, *meso*–CH_3 and –CH_2–), 1.88 (br m, 2H, –CH_2–), 2.22 (s, 3H, –CH_3), 3.16 (td, 2H, –CH_2–), 3.25 (td, 2H, –CH_2–), 3.94 (t, 2H, –CH_2–), 4.82 (t, 1H, NH), 5.85 (s, 1H, CH), 5.90 (m, 8H, pyrrole CH), 7.00-7.02 (br d, 4H, pyrrole NH), 10.16 (s, 1H, NH) , 11.87 (s, 1H, NH) , 13.14 (s, 1H, NH). ^{13}C NMR (126 MHz, CDCl$_3$): δ = 173.1, 156.6, 154.7, 138.5, 138.4, 137, 106.7, 103.8, 102.8, 38.5, 35.2, 29.0, 26.2, 24.3, 18.9. HRMS (ESI): m/z calcd for C$_{43}$H$_{58}$N$_9$O$_4$ [M-H]$^-$: 764.46172; found: 764.46272.
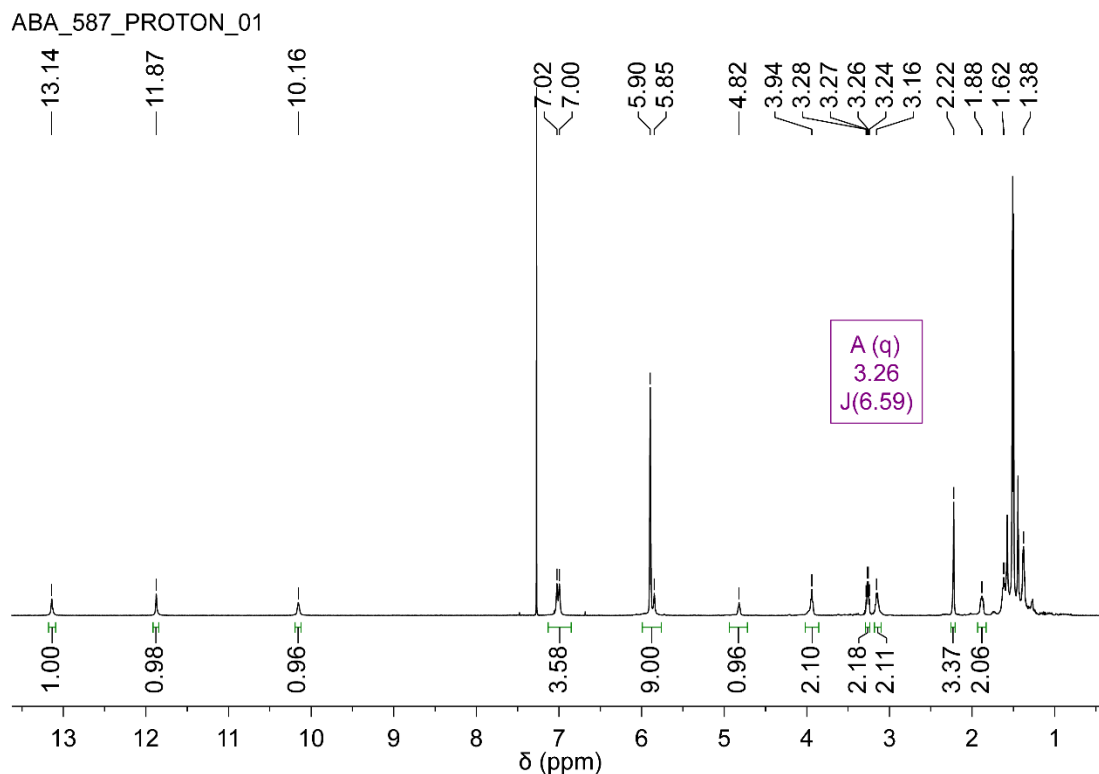
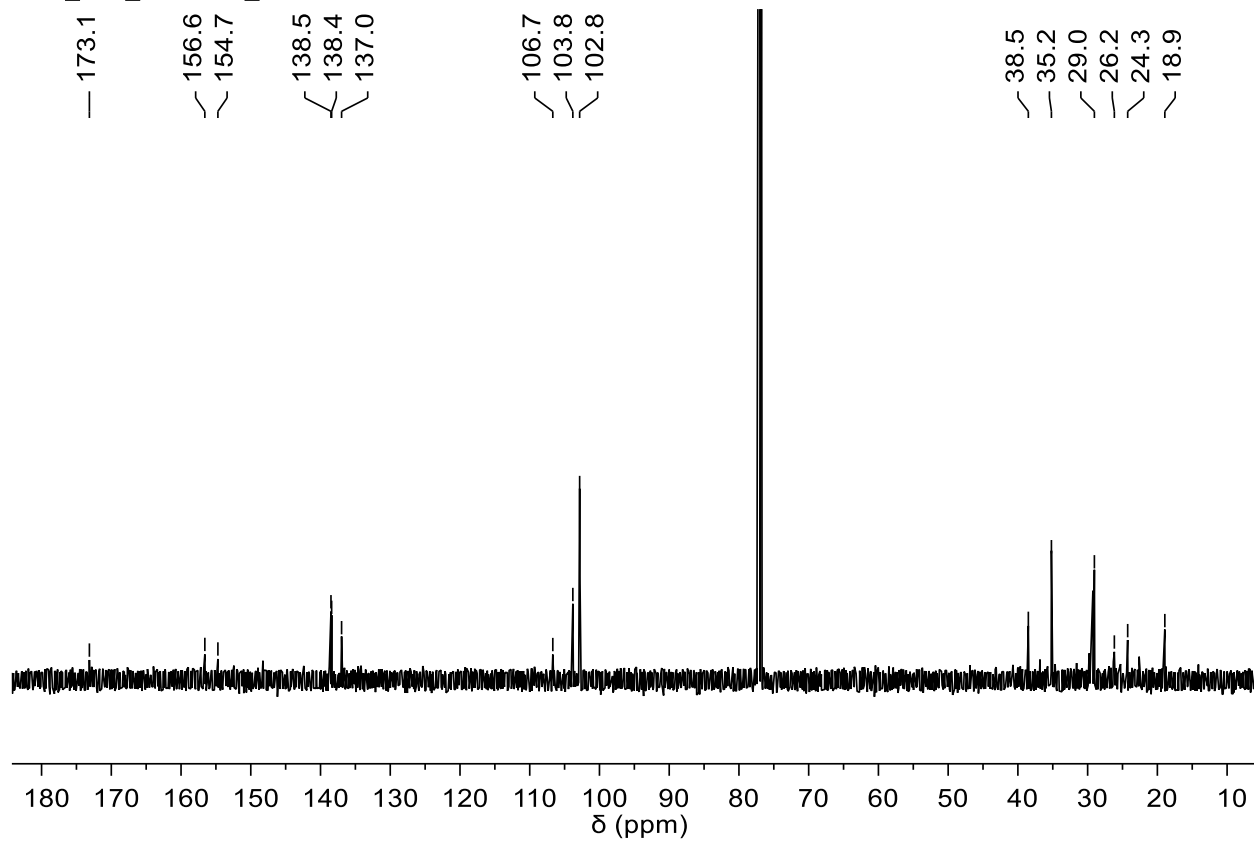**Figure S4.** ^{1}H NMR spectrum of **UPyCP$_2$** recorded in CDCl$_3$.

Figure S5. ^{13}C NMR spectrum of **UPyCP$_2$** recorded in CDCl$_3$.
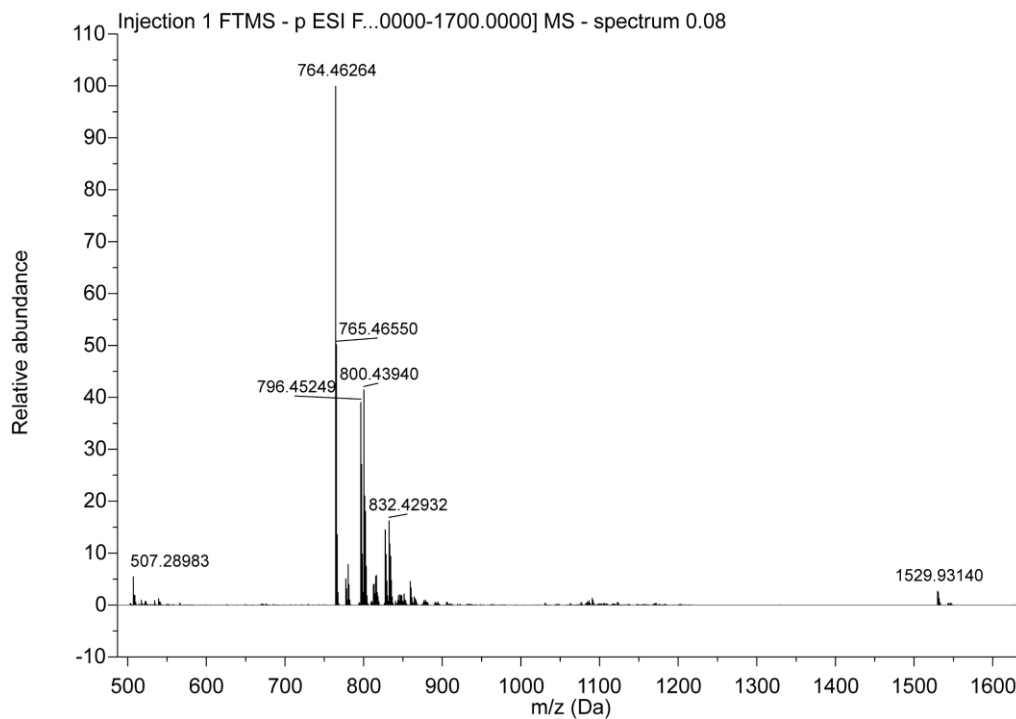
Figure S6. HRMS spectrum of **UPyCP** showing monomer and dimer (**UPyCP$_2$**) at 765 and 1530.
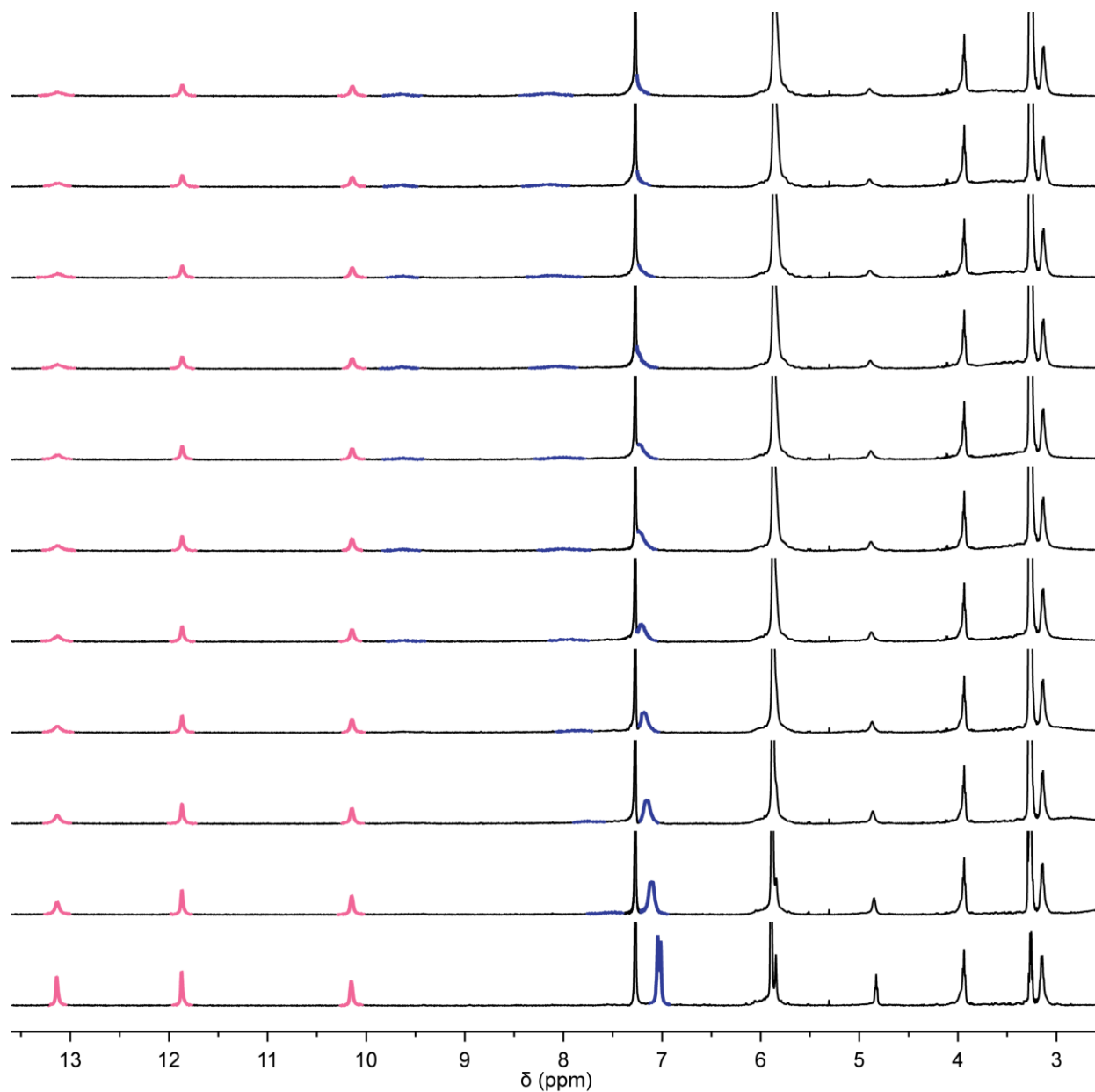
NMR Spectra

Figure S7. The stacked ^{1}H NMR (500 MHz, CDCl$_3$) spectra of **UPyCP$_2$** (8 mM) after addition of **TBAS**. Bottom to top: 0.00, 0.26, 0.42, 0.56, 0.66, 0.76, 0.82, 0.88, 0.92, 0.96, and 1.00 equiv. **TBAS**.
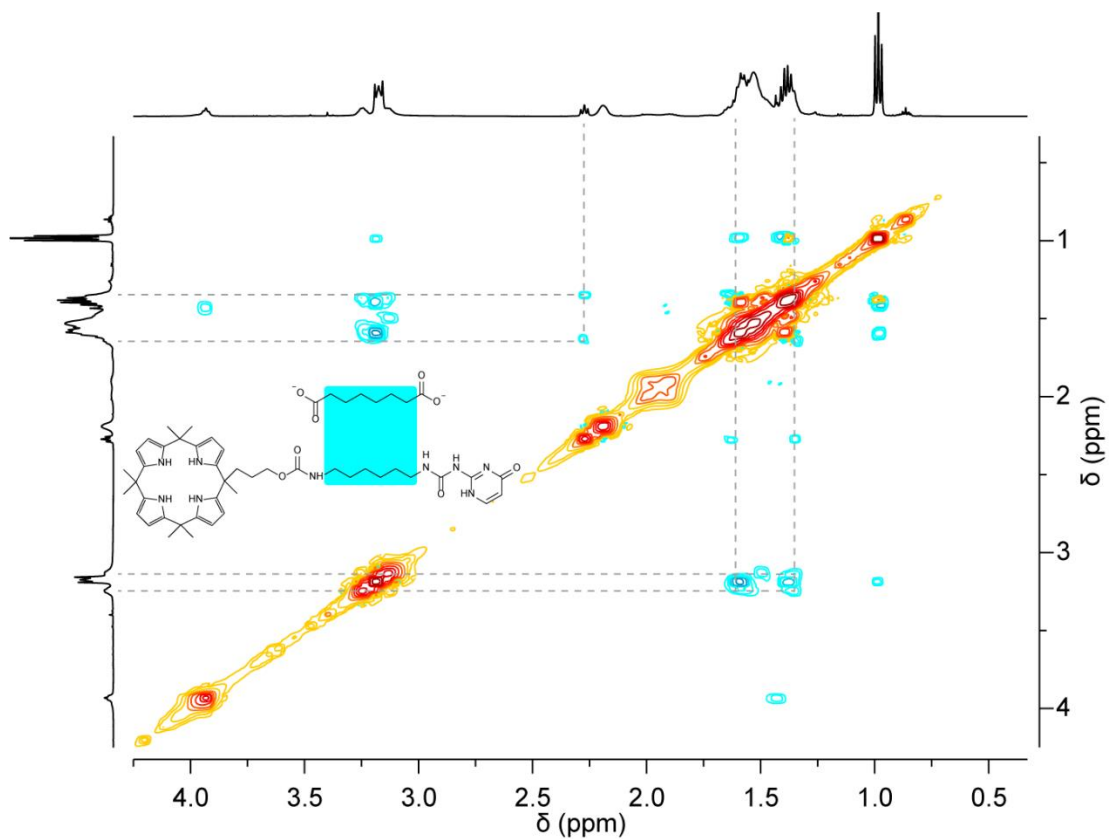
Figure S8. Partial ROESY spectrum of **UPyCP₂ + TBAS** (8 mM, CDCl₃) showing the existence of cyclic species via correlated 2D-ROSEY signals between methylene protons of **UPyCP₂** and **TBAS**.

Figure S9. DOSY NMR spectrum of **UPyCP₂** + **TBAS** (5 mM, CDCl3, 500 MHz, 25 °C).

Figure S10. Mono-exponential decay fit of pyrrole CH proton integrations of Figure S9 between 5.59 and 6.23 ppm, indicating a fast exchange between free host, open-, and cyclic-complex species.
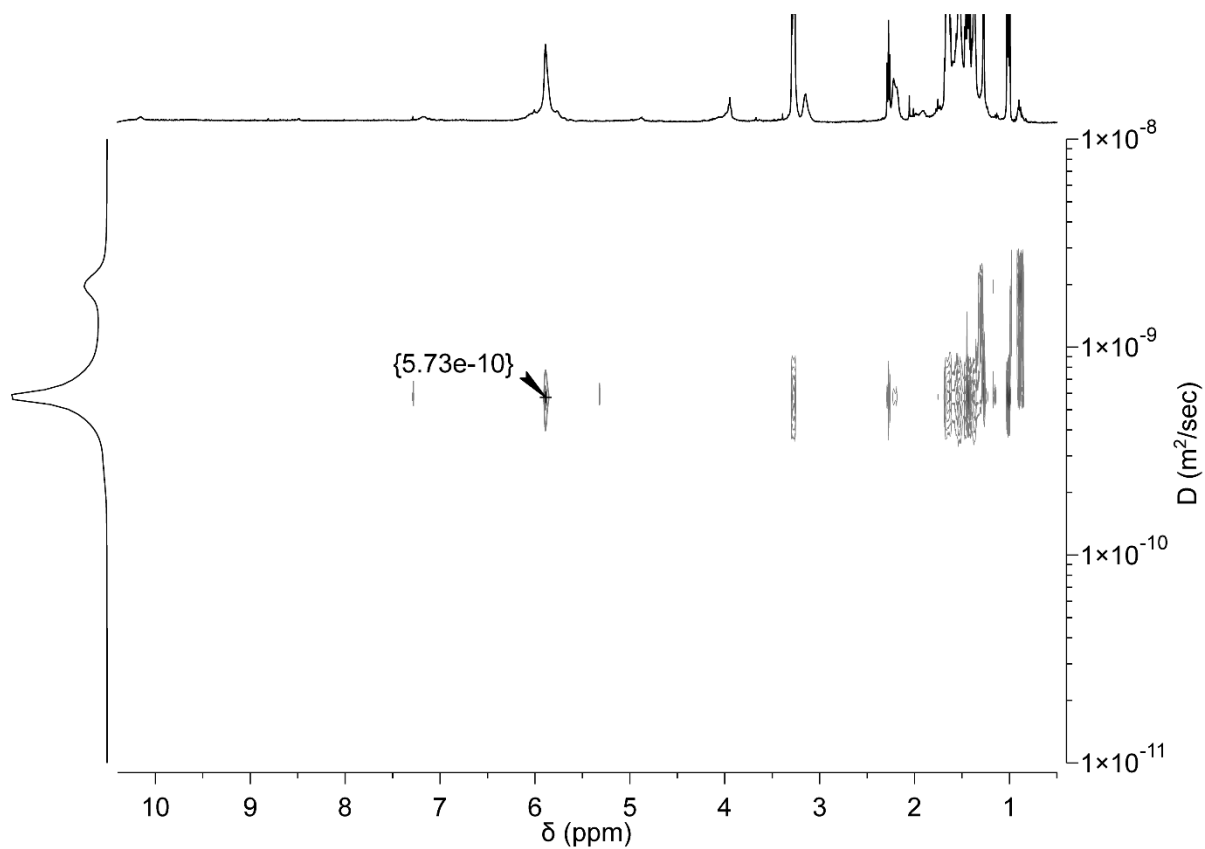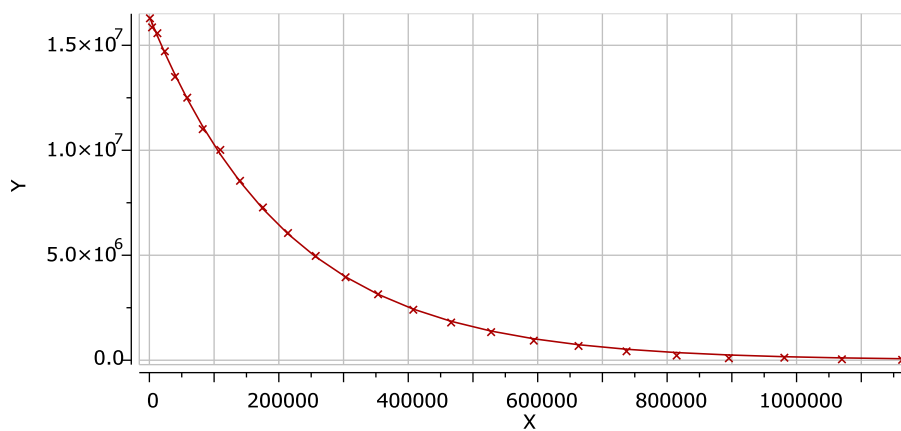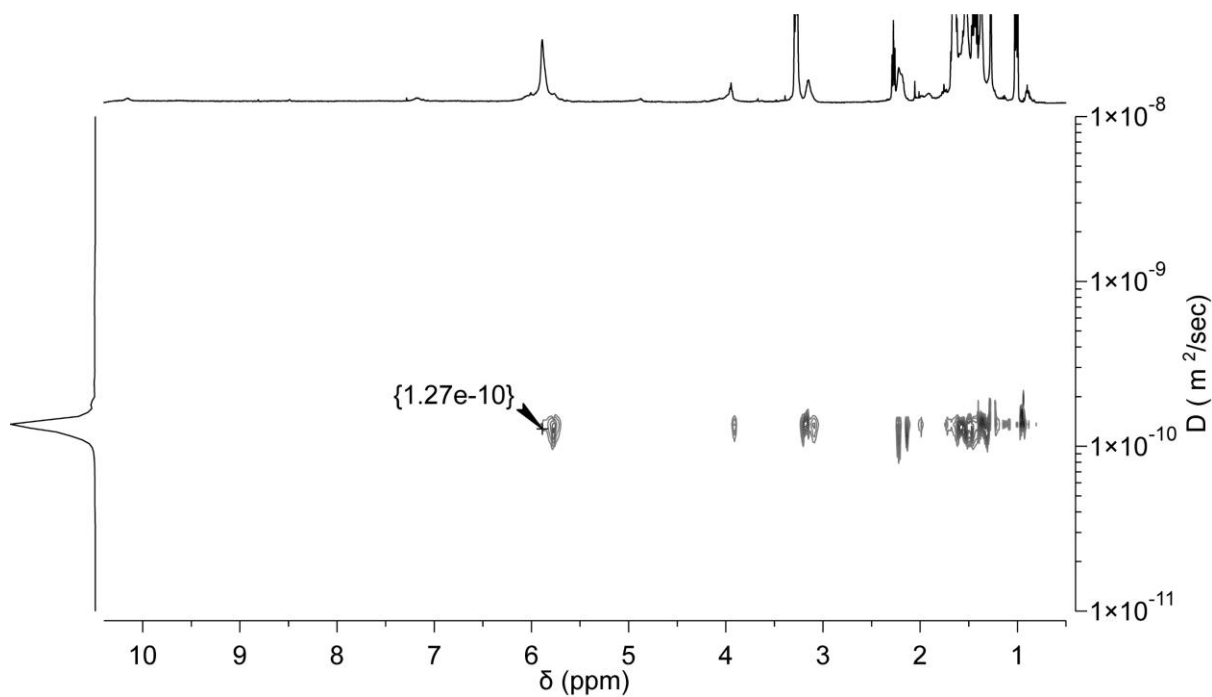
Figure S11. DOSY NMR spectrum of **UPyCP₂ + TBAS** (110.5 mM, CDCl3, 500 MHz, 25 °C).
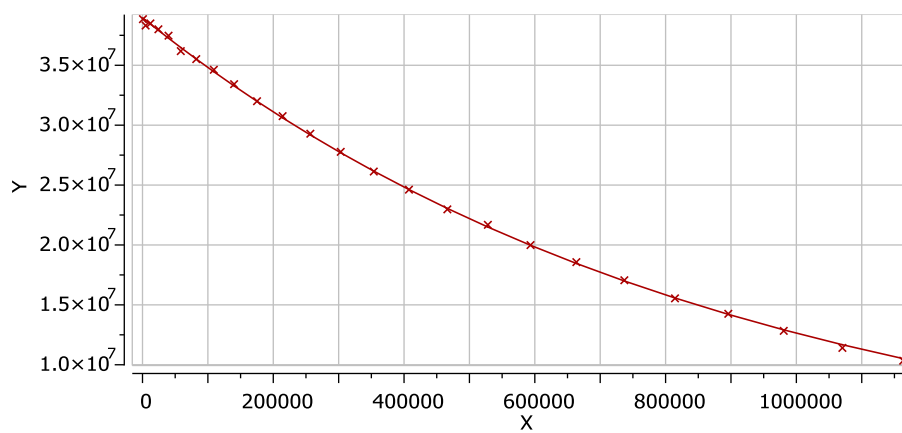
Figure S12. Mono-exponential decay fit of pyrrole CH proton integrations of Figure S11 between 5.59 and 6.23 ppm.
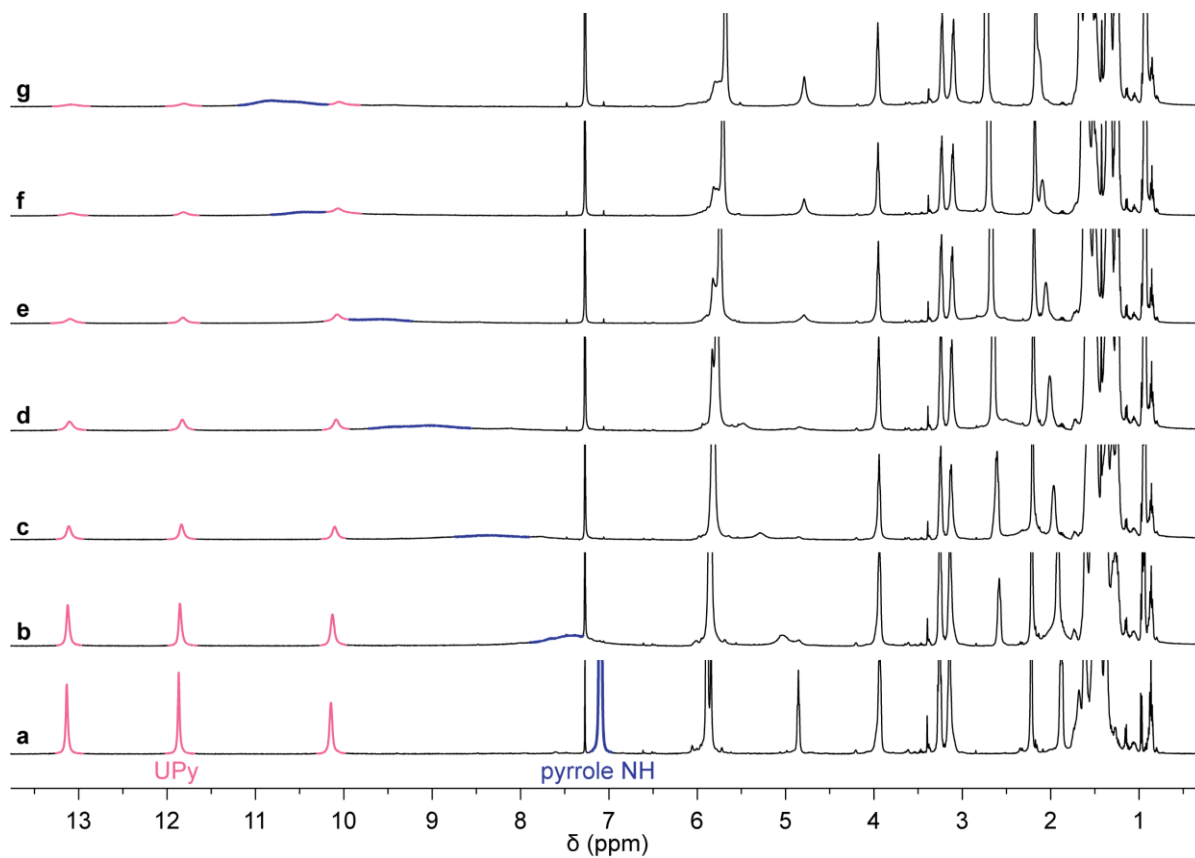
Figure S13. ^{1}H NMR spectra of **UPyCP$_2$** (76 mM, CDCl$_3$) after addition of (a) 0.0, (b) 0.2, (c) 0.4, (d) 0.6, (e) 0.8, (f) 1.0, (g) 1.2 equivalents of TBAF.

Figure S14. ^{1}H NMR spectra of **UPyCP$_2$ + TBAS** (76 mM, CDCl$_3$) after addition of (a) 0.0, (b) 0.2, (c) 0.4, (d) 0.6, (e) 0.8, (f) 1.0, (g) 1.2 equivalents of TBAF.

Assignment of Pyrrole-NH Resonance Signals

When two-site receptor **UPyCP₂** and divalent ligand **TBAS** were used in the formation of a supramolecular polymer, **UPyCP₂** may have different states in terms of its complexes to be formed with **TBAS**. Since **UPyCP₂** + **TBAS** system has three different 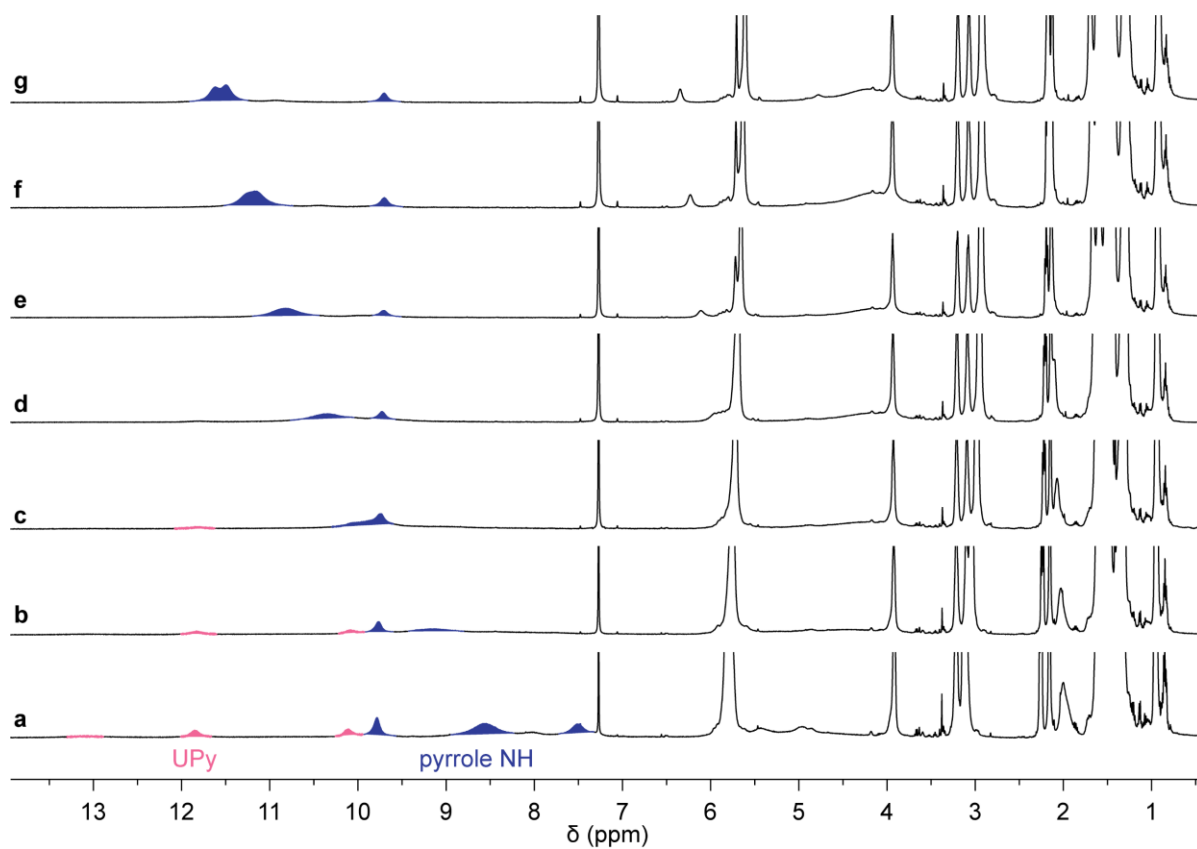pyrrole-NH resonance signals in its ^{1}H NMR spectra, these peaks could be assigned to free host, closed- and open-complex structures as illustrated in Scheme 1 (main text). For instance, **UPyCP₂** + **TBAS** system (8 mM) exhibits resonance signals at 7.26, 8.15, and 9.63 ppm in CDCl₃ (Fig. 1f, main text). It is obvious that the peak at 7.26 ppm represents the free **UPyCP₂** dimers in solution.
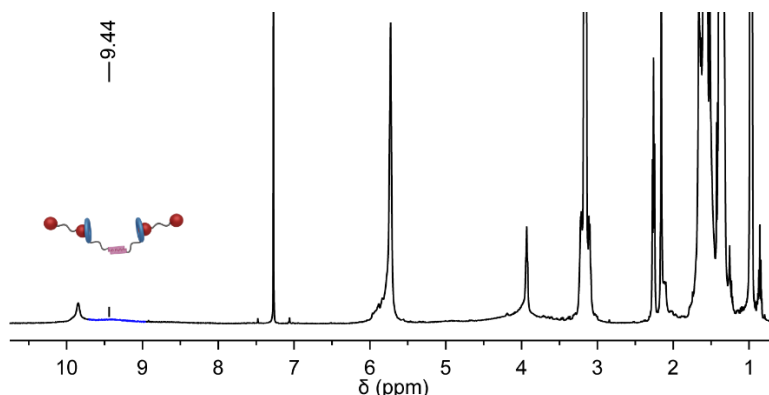
Figure S15. ^{1}H NMR spectrum of **UPyCP₂** + 2 **TBAS** (8 mM, CDCl₃).

We altered the ratio of **UPyCP₂** and **TBAS** and recorded an ^{1}H NMR spectrum to find the open complexed pyrrole NH resonance signals. As shown in Figure S15, when 2 equivalents of **TBAS** was used the pyrrole NH resonance signals of **UPyCP₂** was observed at 9.44 ppm. Thus, the resonance signals of **UPyCP₂** + **TBAS** at 8.15 ppm (Fig. 1f and Figure S7) corresponds to the closed complexes formed between **UPyCP₂** and **TBAS**. A cartoon representation of peak assignments is given in the figure below.

Figure S16. Partial ^{1}H NMR spectrum of **UPyCP₂** + **TBAS** (10 mM, CDCl₃) and the assignment of pyrrole NH resonance signals. See Fig. 2a, main text, for full spectrum.

Estimation of Effective Molarity (*EM*)
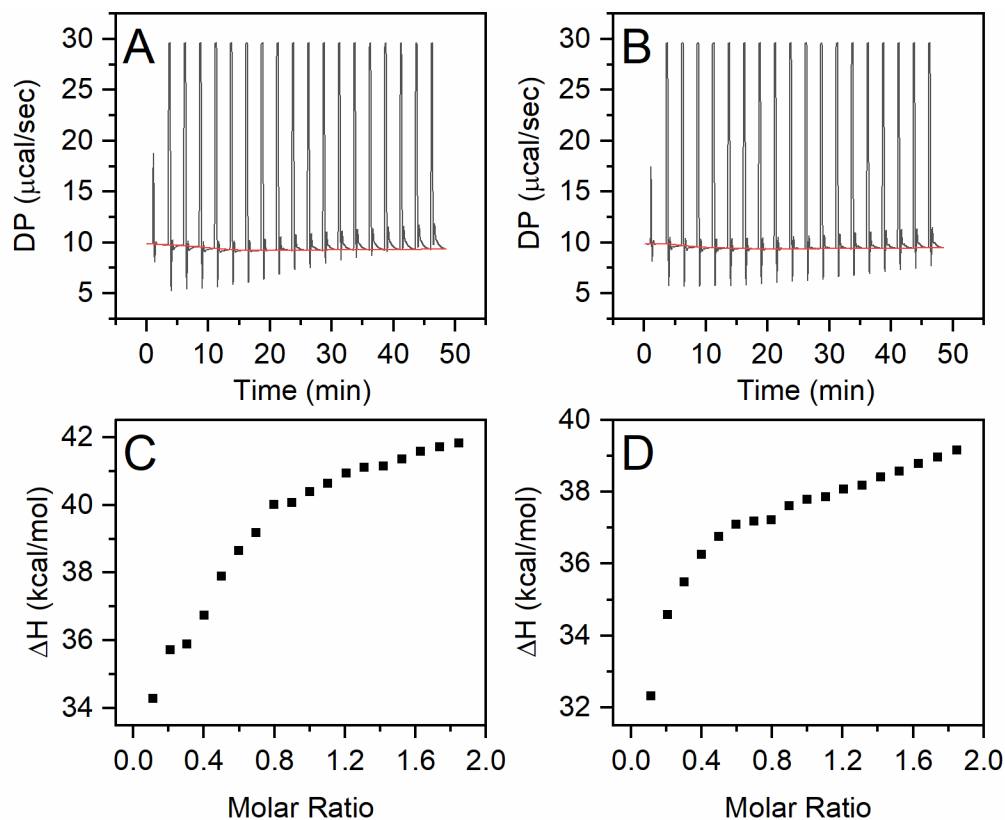
Figure S17. ITC titration curves obtained from the titration of **UPyCP$_2$** (0.4 mM) with **TBAS** (A, C) and TBAOAc (B, D) in CHCl$_3$ at 20 °C.
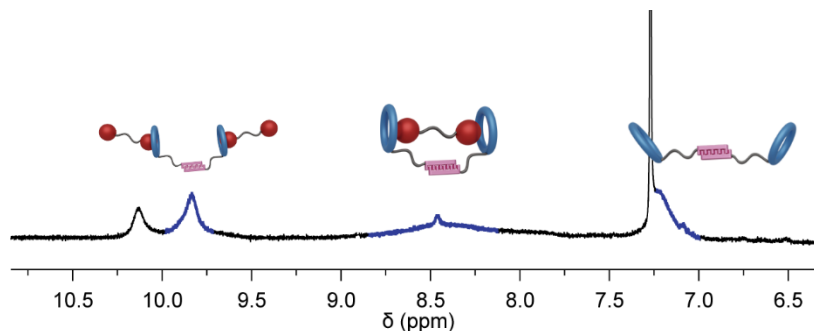
The *EM* parameter has been extensively utilized as a quantitative measure for the estimation of the ease of ring closure in supramolecular systems. For equilibrium studies *EM* is defined by Eq. 1.[3]

$$EM = \frac{K_{cyc}}{K_{open}} \tag{1}$$

The binding constant between model compound **CP** and tetrabutylammonium acetate (TBAOAc) could be used for K_{open} which was reported to be 1.65×10^3 M^{-1}.[1] We have performed a ^{1}H NMR titration experiment between **UPyCP$_2$** and TBAOAc to calculate the K_{cyc} by monitoring chemical shift of the peak corresponding to cyclic complexes in CDCl$_3$ (Figure S18).
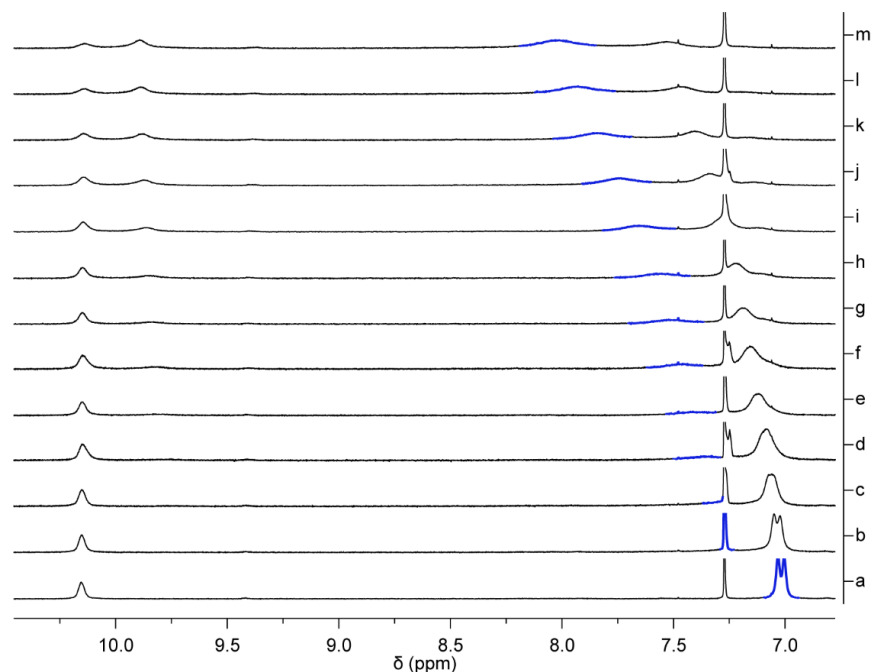
Figure S18. Partial ^{1}H NMR spectra (500 MHz, CDCl^3, 25 °C) of **UPyCP$_2$** at a constant concentration of 4.99 mM upon addition of TBAOAc at a) 0.00, b) 0.78, c) 1.54, d) 2.26, e) 2.96, f) 3.63, g) 4.28, h) 4.90, i) 6.03, j) 7.20, k) 8.24, l) 9.22, m) 10.01 mM concentrations.

By a non-linear curve-fitting method, the association constant between **UPyCP$_2$** and TBAOAc was determined to be 50.15 ± 0.78 M^{-1} (Figure S19). Based on the Eq. 1, *EM* for **UPyCP$_2$ + TBAS** system was estimated to be 30.4 mM.

K	50.14846 ± 0.77593
Reduced Chi-Sqr	6.09847E-4
R-Square (COD)	0.99356
Adj. R-Square	0.99356

Figure S19. Chemical shift changes of pyrrole NH protons (initially at 7.01 ppm) belonging to **UPyCP$_2$** (4.99 mM) upon addition of TBAOAc. The blue solid line was obtained from a non-linear curve fitting to calculate the binding constant K_{cyc}.

Concentration Dependence of Estimated Values of Maximum Polymerization Degree (*DP*)

OMCP

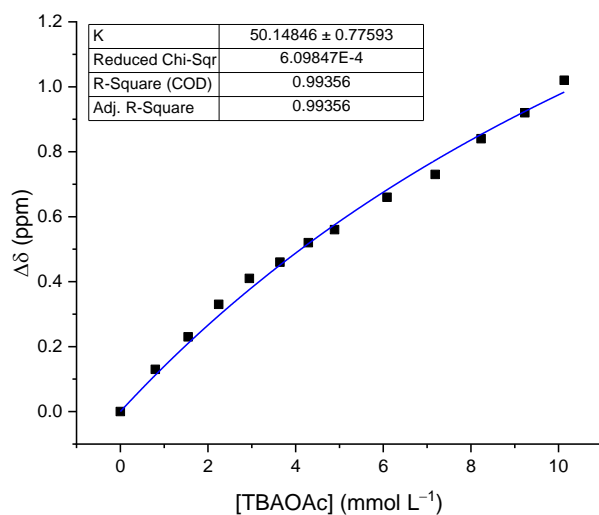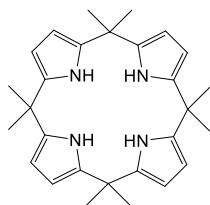Since the association constant between the **UPy** units of **UPyCP₂** is >10^7 M^{-1} in CHCl$_3$ and we were able to see the characteristic NH resonance signals of **UPyCP₂** between 10.15 and 13.13 ppm even at very low concentrations, we assume that **UPyCP** forms stable dimers at all concentration ranges. Therefore, we used the association constant between **OMCP** units of **UPyCP₂** and carboxylate units of **TBAS** to estimate the *DP*.

Using the Carothers equation and assuming that the same average association constant holds for each successive step (isodesmic model) and that cyclic species can either be ignored or considered, the average degree of polymerization, *DP*, may be derived from the equilibrium constant K_a between **UPyCP₂** and **TBAS** and the initial monomer concentration as follows:

$$DP = \frac{1}{1-p} \tag{2}$$

If p is defined as the extend of complexation,

$$K_a = \frac{p[\boldsymbol{UPyCP_2}]}{(1-p)^2[\boldsymbol{UPyCP_2}]^2}$$

Solving this quadratic equation results in

$$1 - p = \frac{(1 + 4K_a[\boldsymbol{UPyCP_2}])^{1/2} - 1}{2K_a[\boldsymbol{UPyCP_2}]}$$

$$DP = \frac{1}{1-p} = \frac{2K_a[\boldsymbol{UPyCP_2}]}{(1 + 4K_a[\boldsymbol{UPyCP_2}])^{1/2} - 1} \tag{3}$$

If $4K_a[\boldsymbol{UPyCP_2}] \gg 1$,

$$DP = \frac{2K_a[\boldsymbol{UPyCP_2}]}{(4K_a[\boldsymbol{UPyCP_2}])^{1/2} - 1}$$

and if $\sqrt{4K_a[\boldsymbol{UPyCP_2}]} \gg 1$,

$$DP = \sqrt{K_a[\boldsymbol{UPyCP_2}]}$$ (4)

In this system the initial concentration of $[\boldsymbol{UPyCP_2}]_0 = 2[\boldsymbol{UPyCP_2}]_0$ and DP can be estimated as:

$$DP = \sqrt{K_a 2[\boldsymbol{UPyCP_2}]}$$ (5)[4]

In this system p is the extend of complexation of **UPyCP₂** and **TBAS**. *DP* estimated in this way represents maximum values that in practice will be reduced by the presence of half-complexed, cyclic structures and reduction in the association constant (K_a) as the supramolecular polymer grows (the attenuation). Consequently, estimated size of supramolecular polymer converges to large values. Therefore, in addition to association constant ($K_a = 1.65 \times 10^3 \pm 54.3$ M^{-1}) between model compounds **OMCP** and TBAOAc,[1] maximum pyrrole-CH chemical shifts of **OMCP** + TBAOAc at varying concentrations were also used to estimate *DP*.
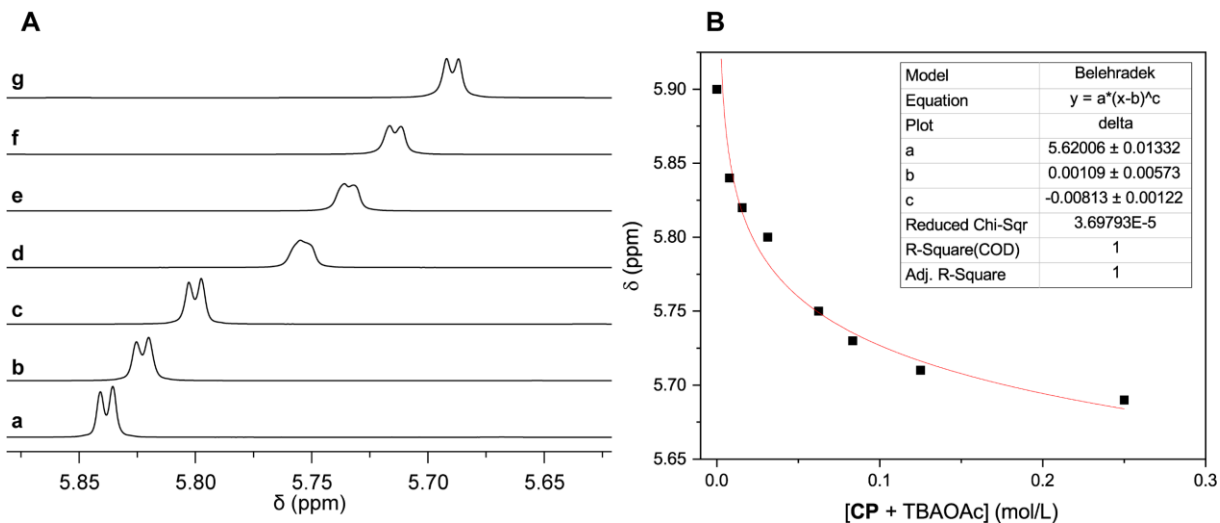

Figure S20. (A) Pyrrole-CH chemical shifts of **CP** + **TBAS** (excess) in CDCl₃ at varying concentrations: (a) 7.8, (b) 15.6, (c) 31.3, (d) 62.5, (e) 83.3, (f) 125, and (g) 250 mM. (B) Curve fitting based on Belehradek equation using the pyrrole-CH chemical shifts from A (pyrrole-CH chemical shift of free CP was taken as 5.90).

To encounter the attenuation during supramolecular polymerization, maximum chemical shifts of pyrrole-CH resonance signals were detected by conducting variable concentration ¹H NMR measurements on a mixture of **OMCP** + TBAOAc (excess). As shown in Figure S20B, the relationship between concentration and chemical shift of pyrrole-CH protons can be related by using Belehradek equation:

$$y = 5.62006(x - 0.00109)^{-0.00813}$$ (6)

where y is pyrrole-CH chemical shift and x is the concentration of **OMCP** + TBAOAc.

Hence, Eq. 6 could be used to estimate the maximum pyrrole-CH chemical shifts in **UPyCP$_2$** + **TBAS** system.
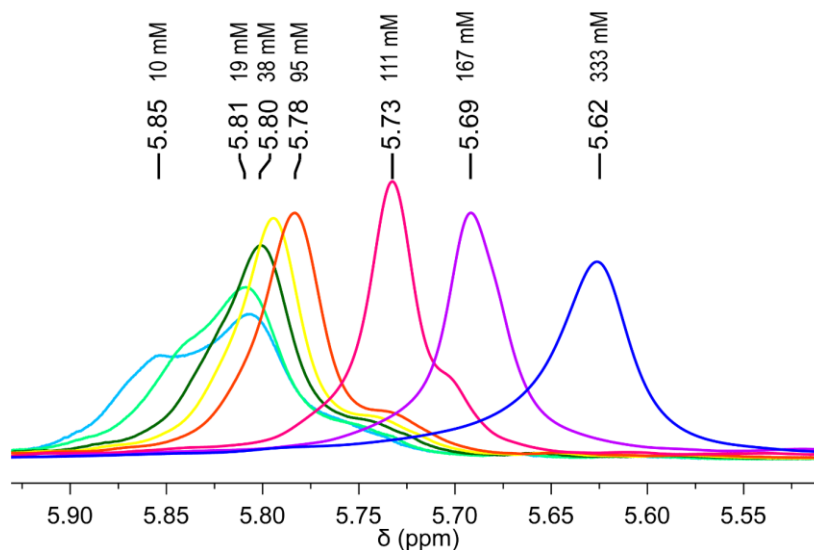

Figure S21. Pyrrole-CH chemical shifts of **UPyCP$_2$** + **TBAS** upon dilution in CDCl$_3$.

To calculate the extend of complexation (p) and the degree of polymerization (*DP*), Eq. 5 and observed pyrrole-CH chemical shifts of **UPyCP$_2$** + **TBAS** system (Figure S21) were used. Table S1 shows the results of estimated *DP*s using Egs. 2 and 5.

Table S1. Estimated values of *p* and *DP* at different concentrations of **UPyCP$_2$** + **TBAS** system.

[UPyCP$_2$+TBAS] (mmol L^{-1})	DP (Eq. 2)				DP$_{max}$ (Eq. 5)
	δ_{max} (ppm)[a]	δ_{obs} (ppm)[b]	p[c]	DP	
10	5.84	5.85	0.17 ± 0.001	1.20 ± 0.01	5.60 ± 0.02
19	5.81	5.81	0.62 ± 0.001	2.62 ± 0.01	7.92 ± 0.03
38	5.77	5.80	0.87 ± 0.002	7.94 ± 0.06	11.20 ± 0.05
95	5.73	5.79	0.93 ± 0.002	14.86 ± 0.12	17.71 ± 0.06
111	5.72	5.78	0.95 ± 0.002	18.20 ± 0.22	19.14 ± 0.07
167	5.70	5.73	0.96 ± 0.002	25.83 ± 1.15	23.44 ± 0.09
222	5.69	5.69	0.97 ± 0.002	29.92 ± 1.63	27.07 ± 0.12
333	5.67	5.62		33.15 ± 0.17[d]	33.15 ± 0.17

[a] From Figure S20A. [b] From Figure S21. [c] Calculated from $p = (\delta_{obs} - \delta_u)/(\delta_{max} - \delta_u)$ where chemical shifts of pyrrole CH protons; δ_u: chemical shift of free host (5.90 ppm). [d] DP$_{max}$ value was used. Error bars reflect the potential error of 0.003 ppm in δ.

DOSY NMR analyses could also provide information about the size of the model by calculating the degree of polymerization. If we assume that the formed supramolecular polymer is linear, cylinder-like structure model could be applied. Thus, the aggregate average size of **UPyCP$_2$ + TBAS** system can be estimated by using the Garcia de la Torre relationship:[5]

$$D = \frac{kT}{3\pi\eta L}\left[\ln\left(\frac{L}{d}\right) + \nu\right]$$

With,

$$\nu = 0.312 + 0.565\frac{d}{L} - 0.100\left(\frac{d}{L}\right)^2$$

Where:

D   Translational diffusion coefficient (m^2·s^{-1})

k   Boltzmann constant (J·K^{-1})

T   Temperature (K)

η   Viscosity of the liquid (Pa·s)

L   Length of cylinder (m)

d   Diameter of cylinder (m)

Introducing the isolating the terms and a finite aspect ratio ($P = L/d$), D can be expressed as:

$$\frac{3D\pi\eta d}{kT} = \frac{1}{P}\left[\ln(P) + 0.312 + \frac{0.565}{P} - \frac{0.100}{P^2}\right] \tag{7}$$

The right-hand side of this equation can be drawn as $y = f(P)$ and calculated value of left-hand side could be used to define P graphically (Figure S22).
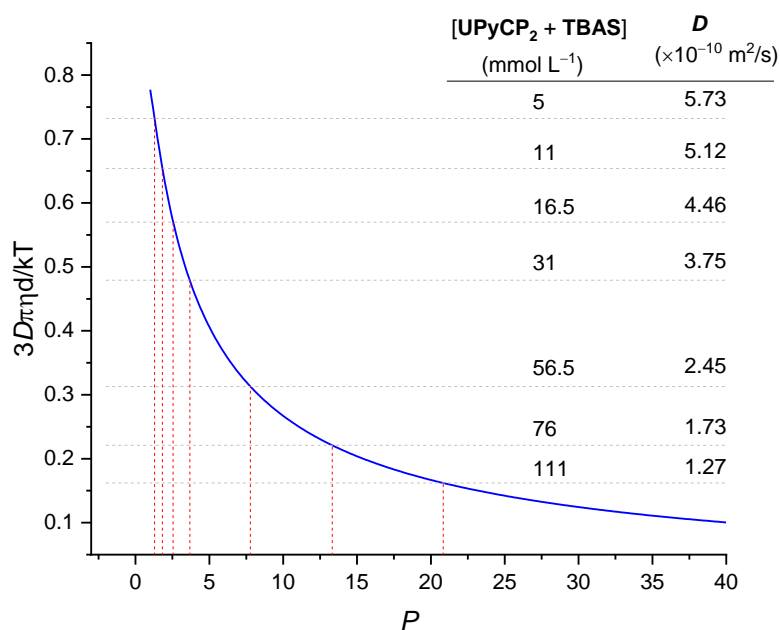
Figure S22. Calculation of P for **UPyCP$_2$ + TBAS** system for different concentrations (d was taken as 10.3 nm from X-ray crystal structure of **OMCP**[6]).

Calculated P values are listed in Table S2 by using the data given in Figure S22.

Table S2. Calculated P values based on diffusion coefficients of **UPyCP$_2$ +TBAS** system at different concentrations.

[UPyCP$_2$+TBAS] (mmol L^{-1})	P
5	1.29
11	1.82
16.5	2.55
31	3.68
56.5	7.78
76	13.32
111	20.84

Hence, DP of **UPyCP₂ + TBAS** system could be estimated at a given concentration by using corresponding P values by using the equation: $DP = P \times d/L$. Comparison of DP values are depicted in Figure S23.
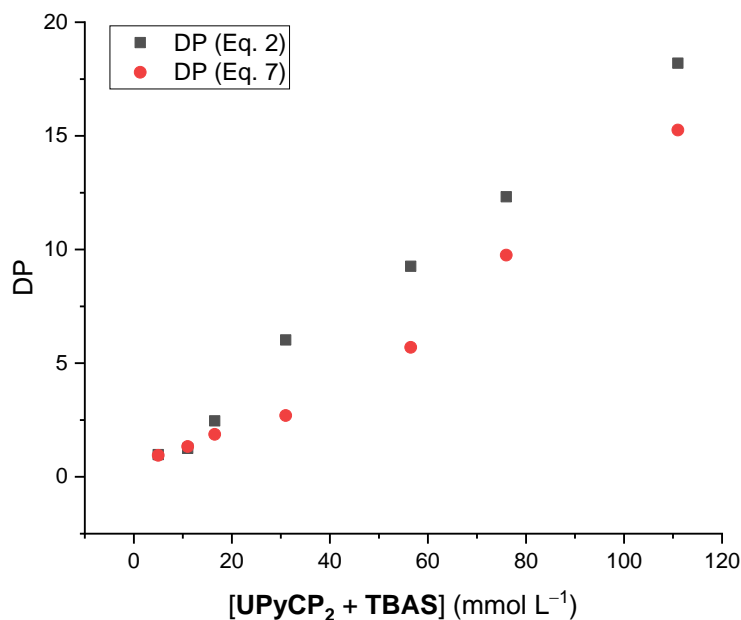

Figure S23. DP values estimated for **UPyCP₂ + TBAS** following the Carothers equation and Garcia de la Torre relationship (L was calculated from Stokes-Einstein equation[7]).

References

1 S. Yuvayapan and A. Aydogan, *Chem. Commun.*, 2019, **55**, 8800-8803.
2 U. Mansfeld, M. D. Hager, R. Hoogenboom, C. Ott, A. Winter and U. S. Schubert, *Chem. Commun.*, 2009, **2009**, 3386-3388.
3 C. Galli and L. Mandolini, *Eur. J. Org. Chem.*, 2000, **2000**, 3117-3125.
4 H. W. Gibson, N. Yamaguchi and J. W. Jones, *J. Am. Chem. Soc.*, 2003, **125**, 3522-3533.
5 J. G. De La Torre, M. C. L. Martinez and M. M. Tirado, *Biopolymers*, 1984, **23**, 611-615.
6 P. A. Gale, J. L. Sessler, V. Kral and V. Lynch, *J. Am. Chem. Soc.*, 1996, **118**, 5140-5141.
7 J. T. Edward, *J. Chem. Educ.*, 1970, **47**, 261.