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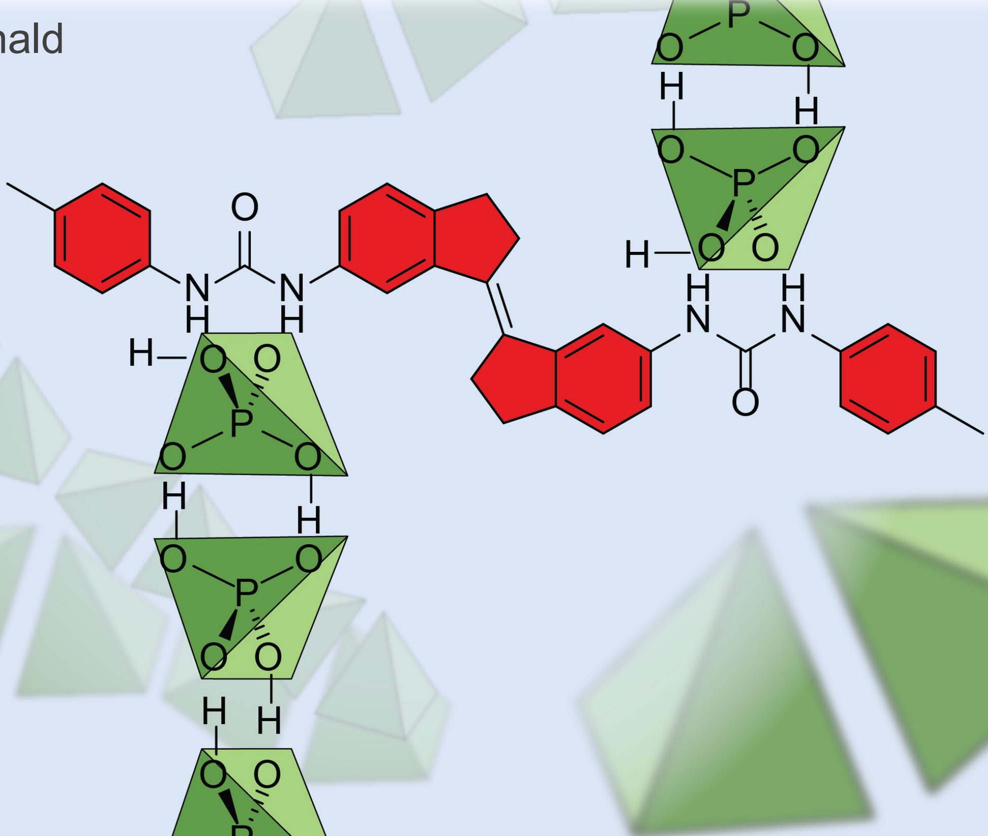
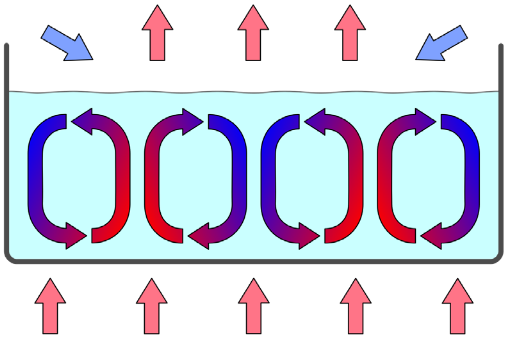
Controlling diffusion with phosphate

Thomas MacDonald

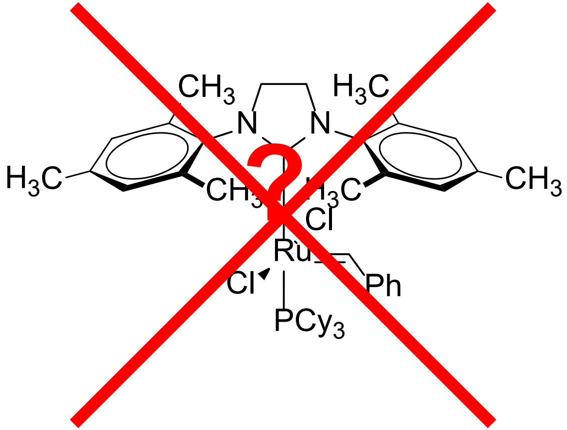


Molecular transport in solution



Convection
(directional flow)

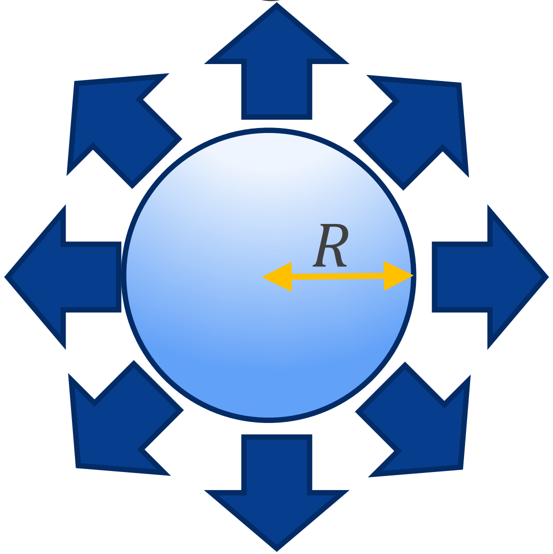
Diffusion
(directionless mixing)

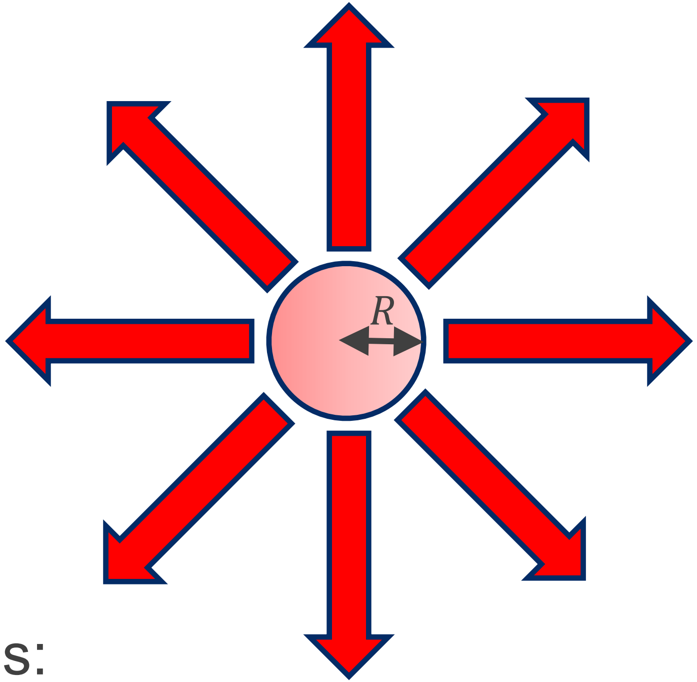


Active propulsion?
Nope, convection again.

Some theories suggests ***directional transport*** can result from ***spatial control*** over diffusion

Controlling diffusion?



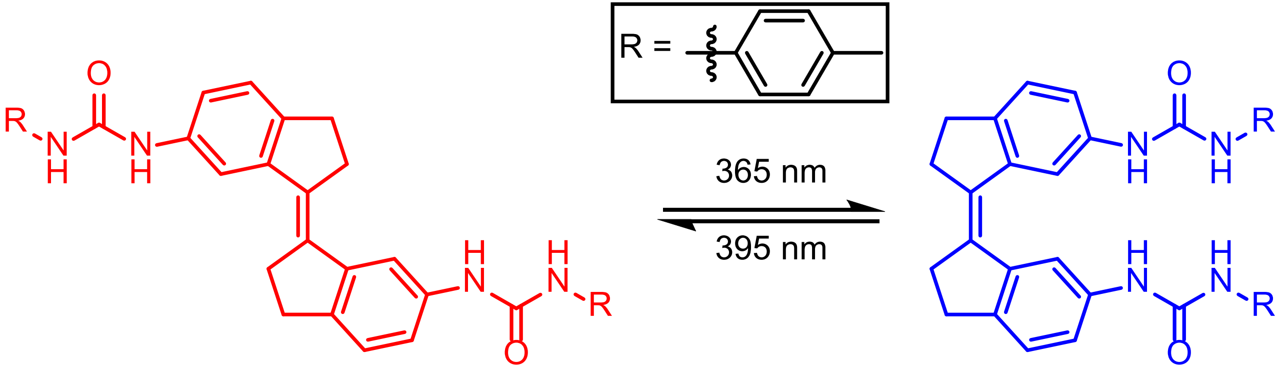


Small things diffuse faster than big things:

$$D \propto \frac{1}{\eta R}$$

Goal: use switchable supramolecular assembly to control *D*.

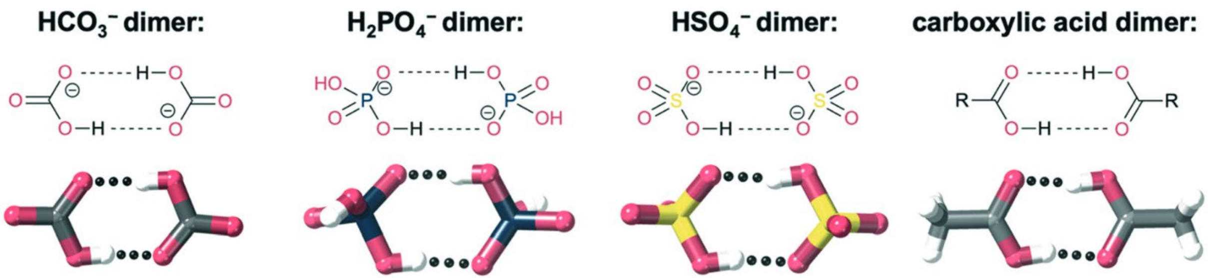
Switchable anion binding



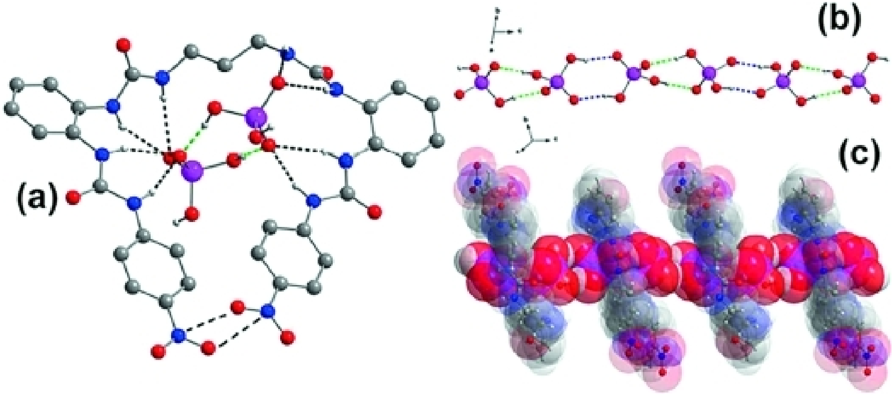
E-**1** *Z*-**1**

- Synthesised a host (with a methyl for easier NMR)
- Best reported *E/Z* selectivity is for $H_2PO_4^-$ ('DHP')
- Turns out DHP is very strange…

Antielectrostatic hydrogen bonding



- Hydrogen bonding can outcompete electrostatic repulsion
- DHP known to form infinite chains in solid state
- Poorly understood in solution
- **Characterisable by diffusion?**



N. G. White, *CrystEngComm* **2019**, *21*, 4855
B. Wu, C. Huo, S. Li, Y. Zhao, X-Y Yang, *Z. Anorg. Allg. Chem.* **2015**, *641*, 1786

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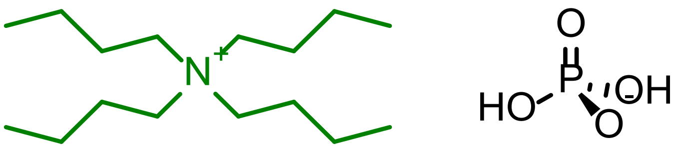
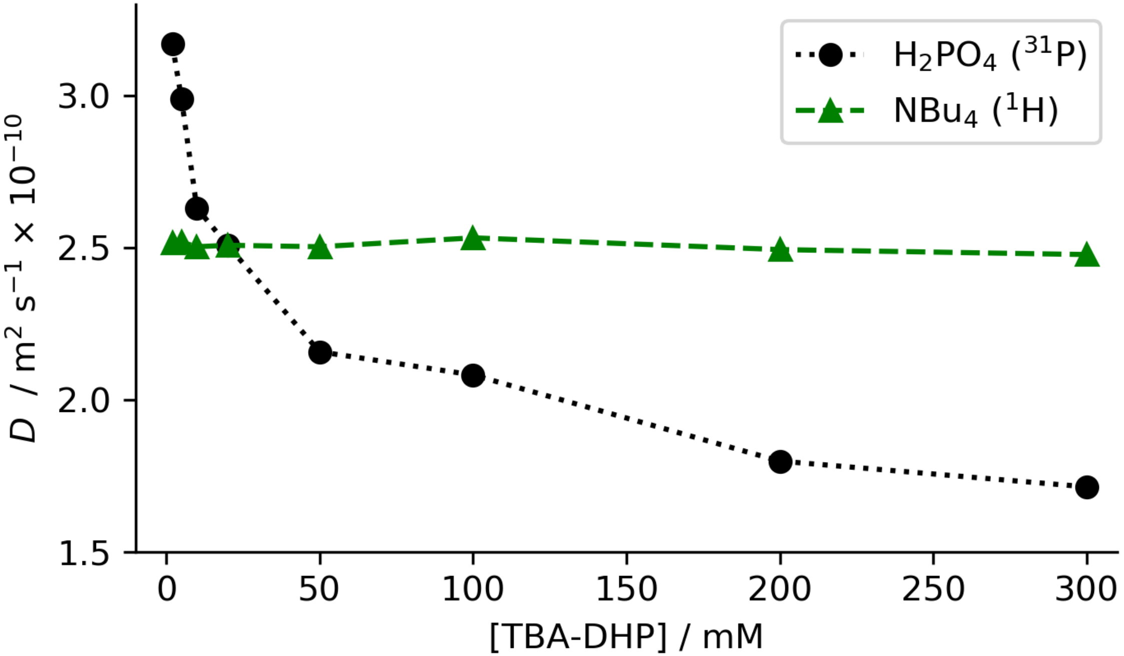
Diffusion studies of pure TBA-DHP

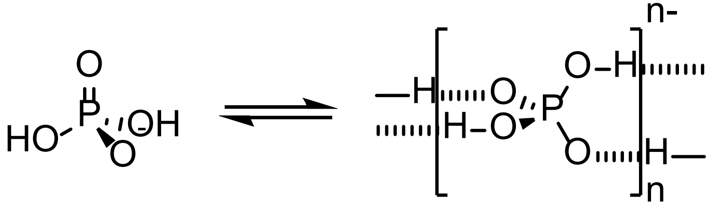


Self-association of DHP?



0 – 300 mM TBA-DHP, DMSO-d_6 with 0.5% added water, ^{1}H PGSTE at 500 MHz, ^{31}P PGSTE at 202 MHz. Values corrected for changes in viscosity.

Diffusion studies of pure TBA-DHP

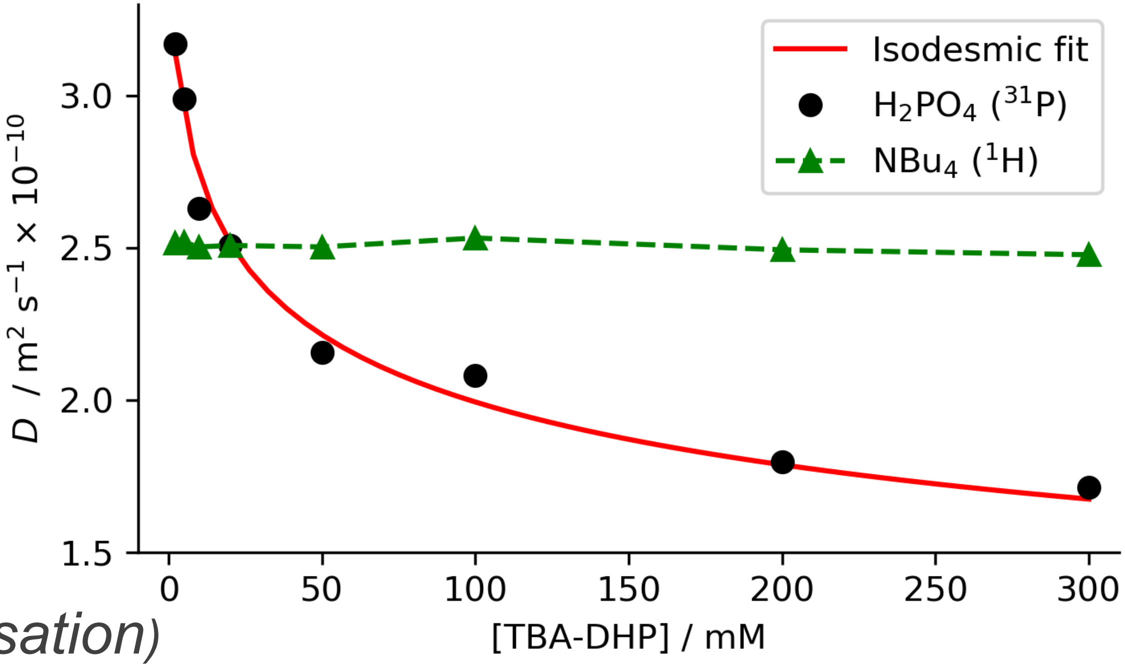


Self-association of DHP?

Isodesmic fit:

K_i = 120 ± 32 M^{-1}

(180 M^{-1} reported for dimerisation)



0 – 300 mM TBA-DHP, DMSO-d_6 with 0.5% added water, ^{1}H PGSTE at 500 MHz, ^{31}P PGSTE at 202 MHz. Values corrected for changes in viscosity.

MacDonald *et al.*, manuscript in preparation; D. Barišić, V. Tomišić, N. Bregović, *Anal. Chim. Acta* **2019**, *1046*, 77 – 92.

Model assumptions

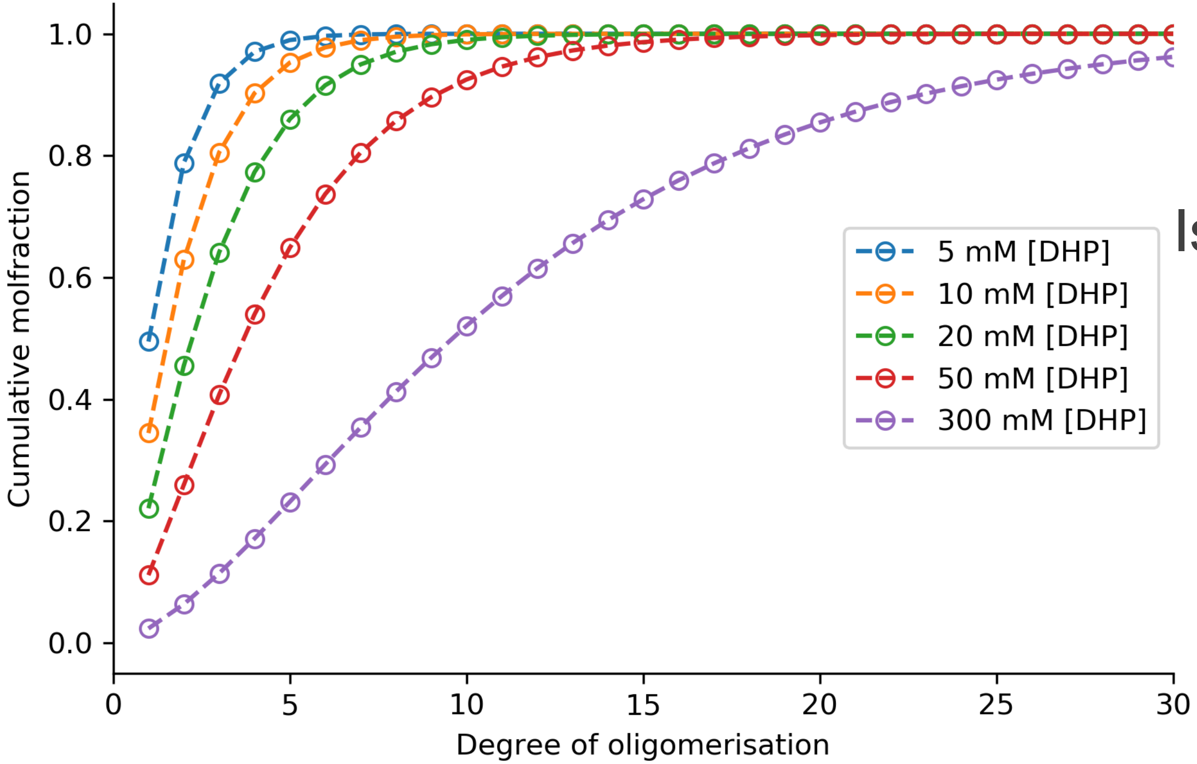
- Self-association is *isodesmic*: each association has same K_i
- Each molecule in solution is a hard sphere

  …but when molecules associate into complexes, those are hard spheres too
- Complexes pack perfectly (volume is additive)

None of these are *true*, but the model seems 'good enough'.

W. S. Price *et al.*, *J. Am. Chem. Soc.* **1999**, *121*, 11503; MacDonald *et al.*, manuscript in preparation

So, how does DHP really behave in solution?

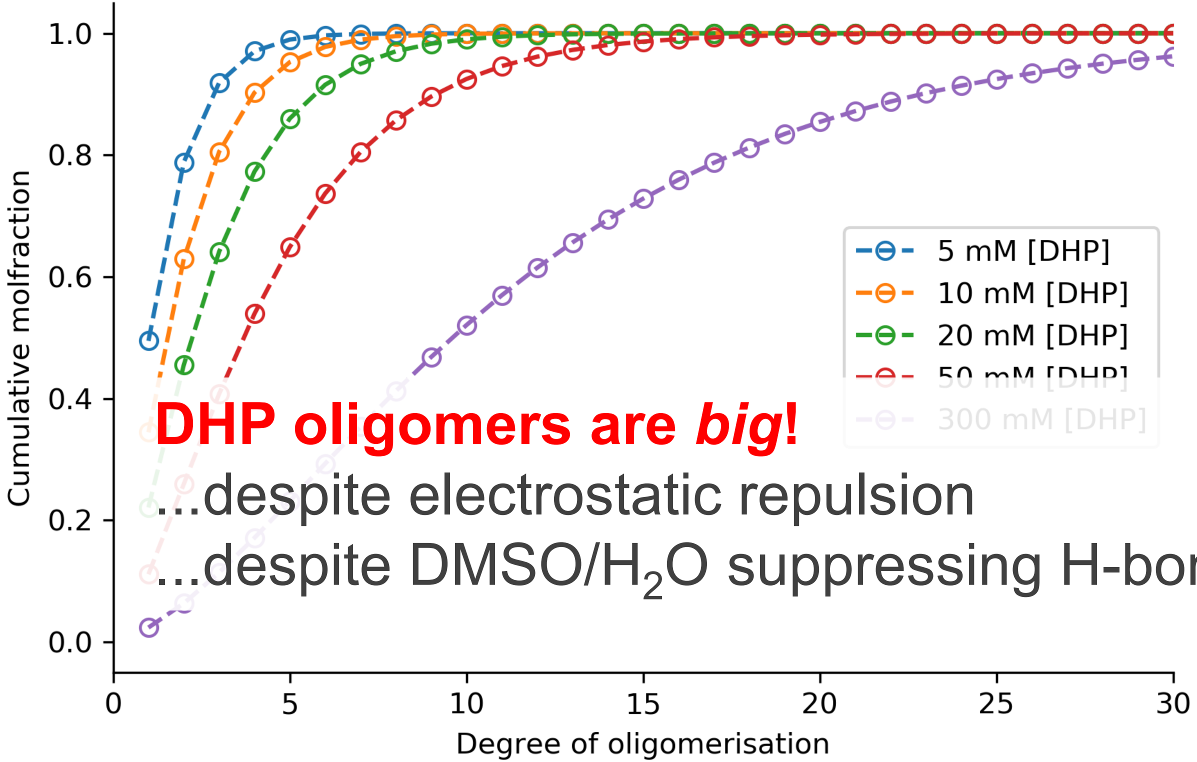


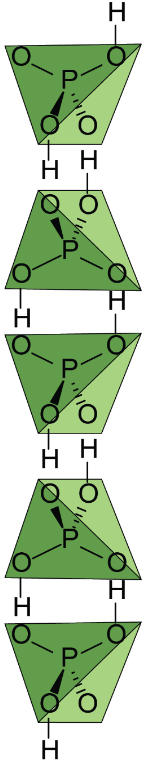
Isodesmic association:

$$K_i = \frac{[A_n]}{[A_{n-1}][A]}$$

K_i = 120 ± 32 M^{-1}

So, how does DHP really behave in solution?



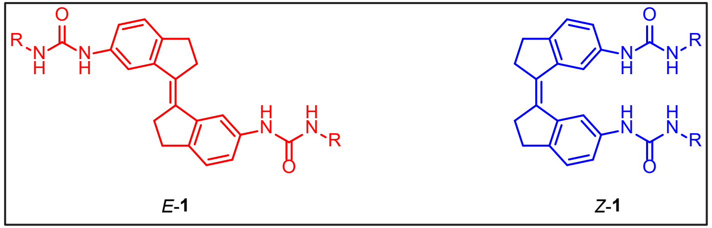


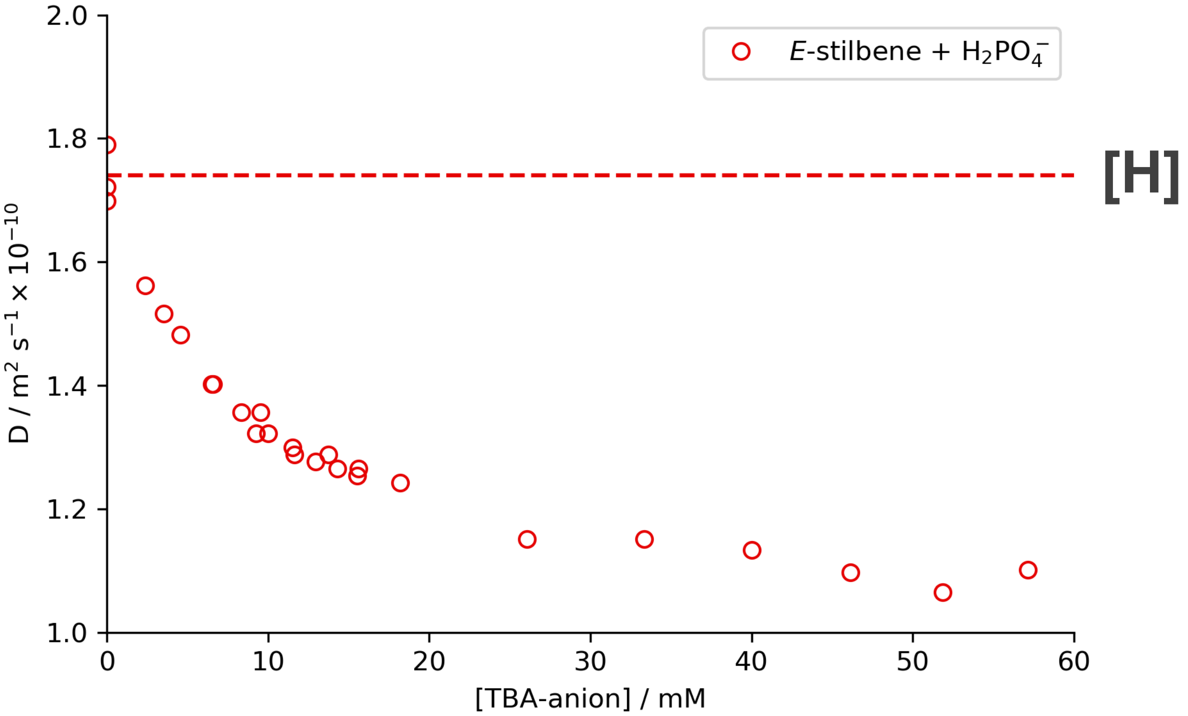
DHP oligomers are *big*!

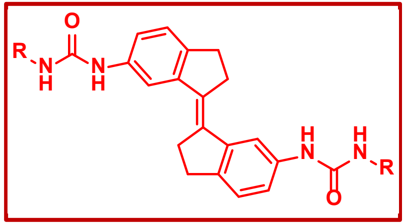
...despite electrostatic repulsion

...despite DMSO/H_2O suppressing H-bonds.

Anion binding with a host







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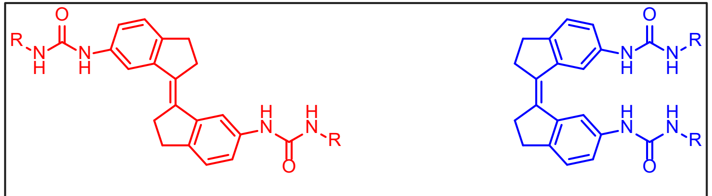

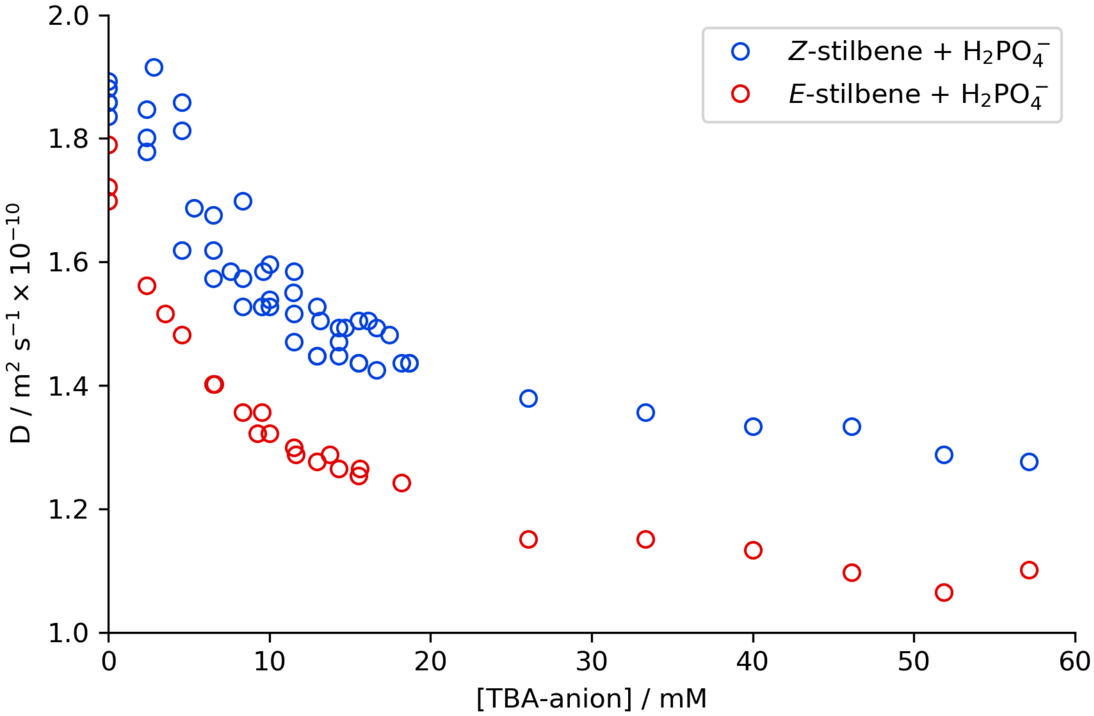

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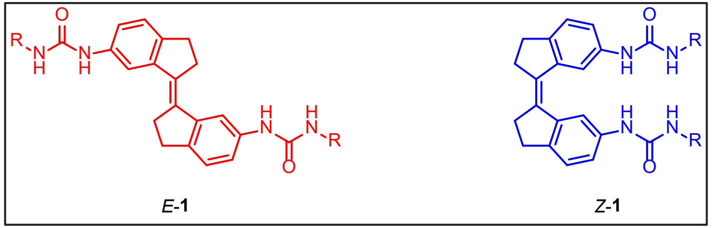

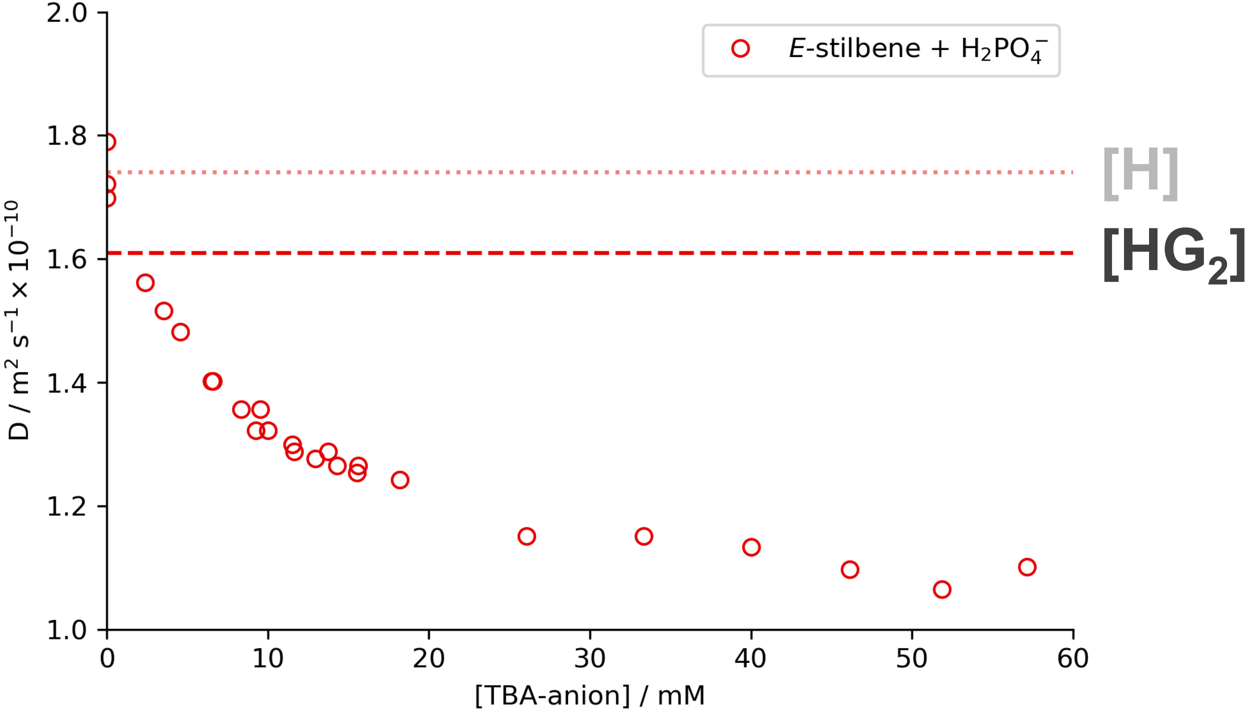

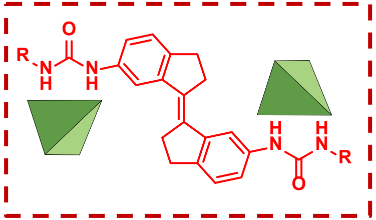

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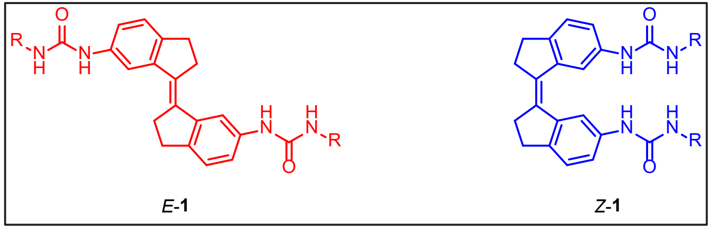
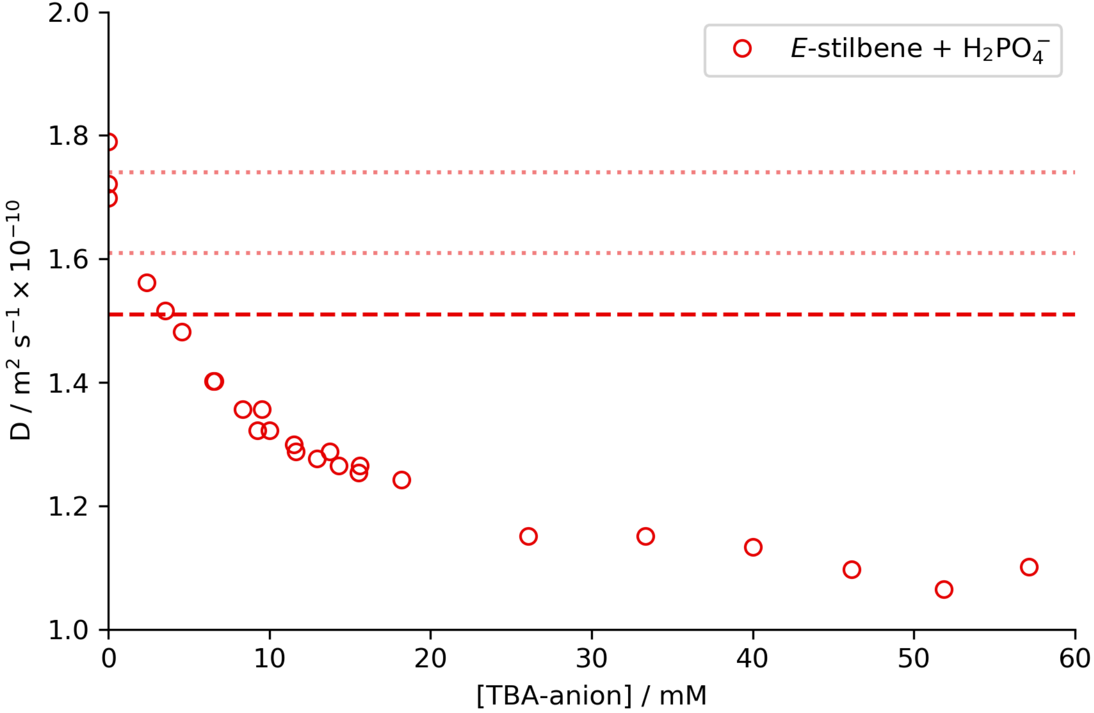
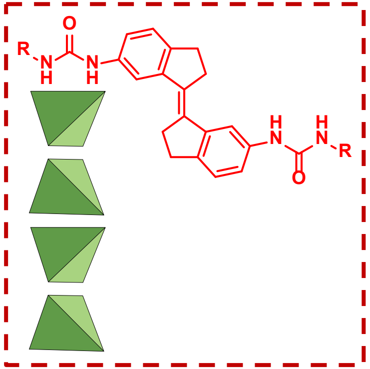




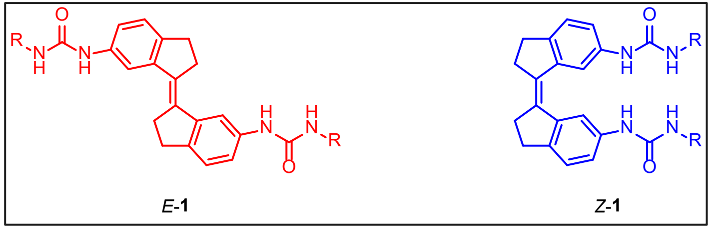
[H]

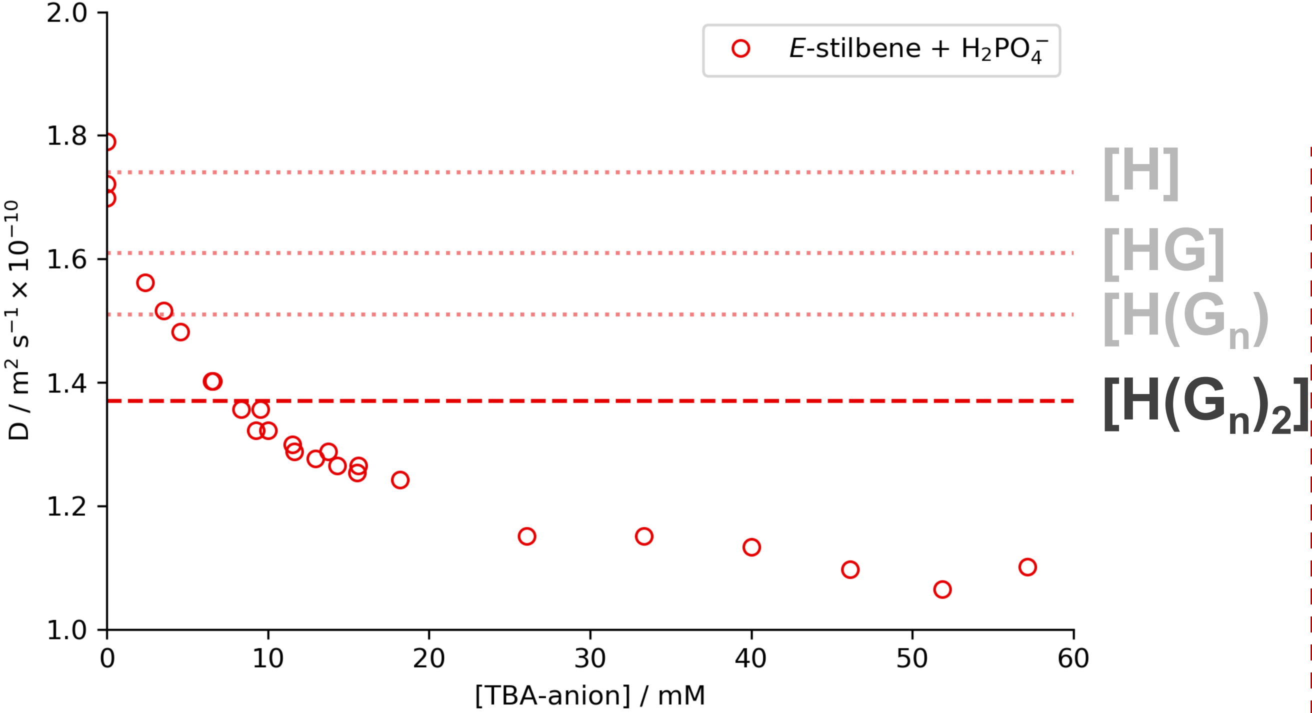
[HG]

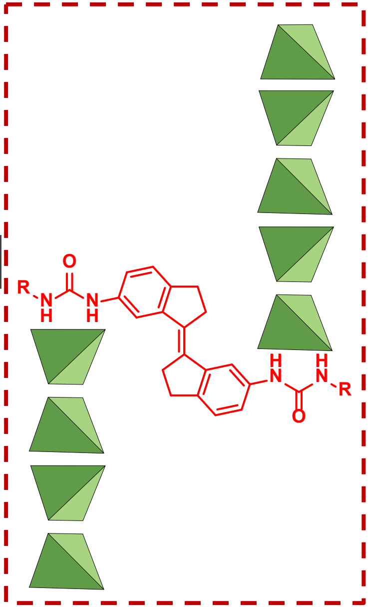
[H(G$_n$)]



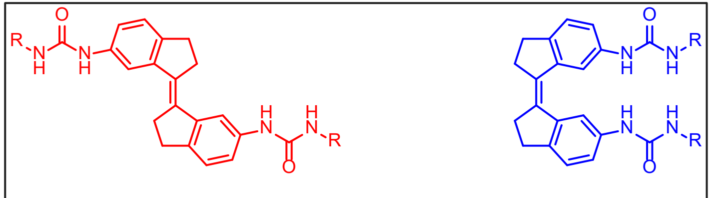
Anion binding with a host

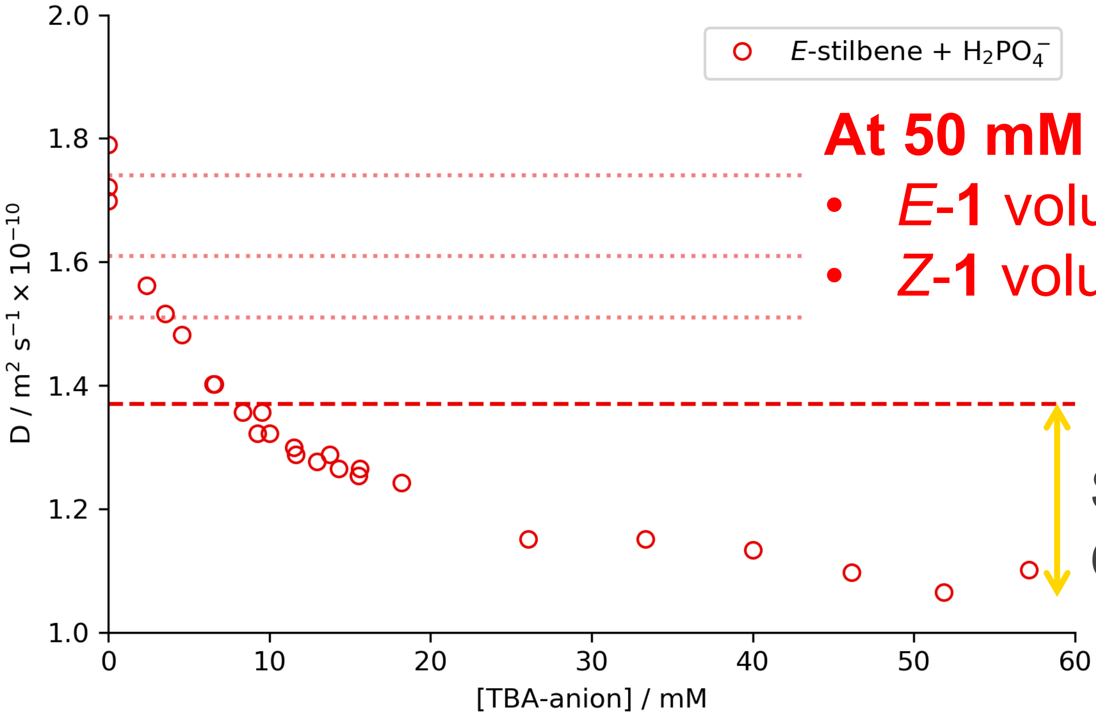






Anion binding with a host





At 50 mM DHP:

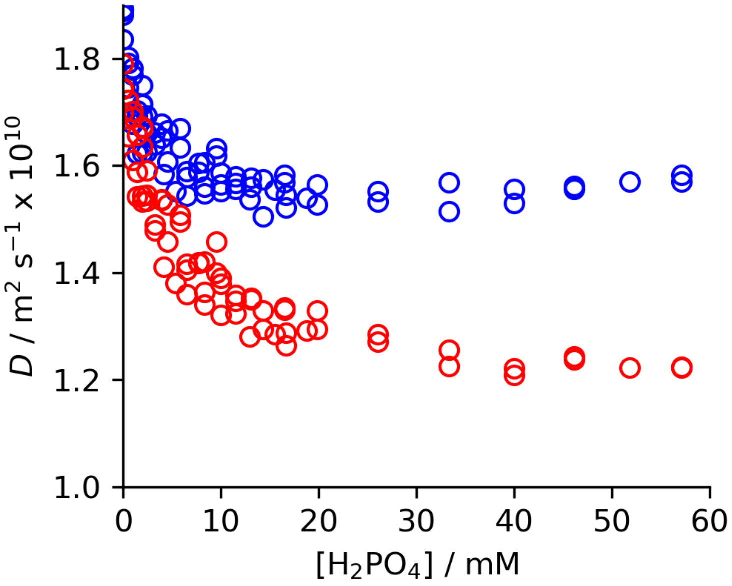
- ***E*-1** volume increases ~3.5-fold
- ***Z*-1** volume increases ~2.5-fold

[H(G$_n$)$_2$]

Still can't explain *D*!

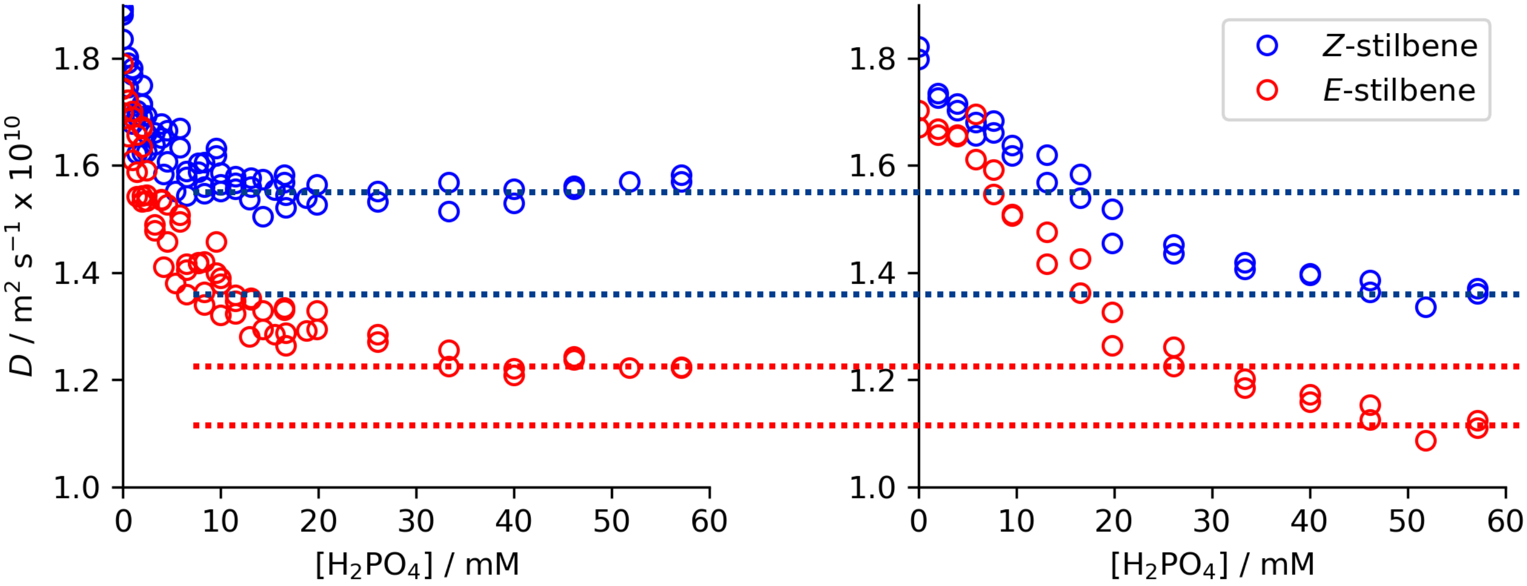
Complexes even larger.

Do complexes incorporate multiple hosts?



1 mM total 1:1 *E*-1:*Z*-1

Do complexes incorporate multiple hosts?



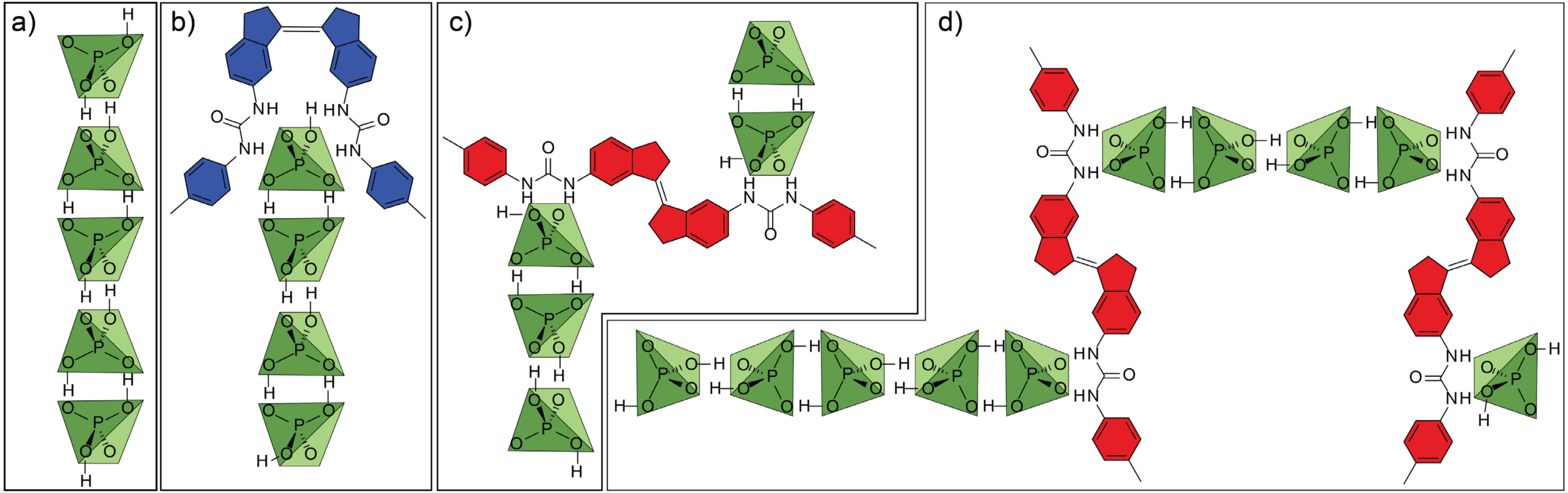
1 mM total 1:1 *E*-1:*Z*-1

10 mM total 1:1 *E*-1:*Z*-1

Increasing host concentration decreases final *D*

Suggests that structures incorporate multiple hosts

What we think is in solution

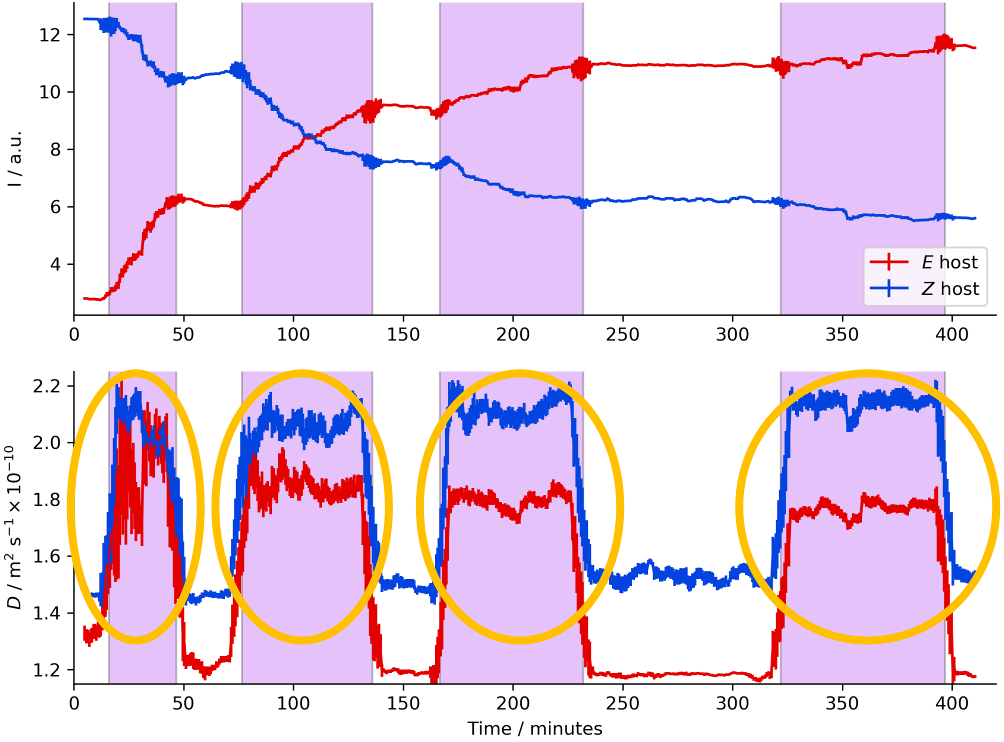


a) DHP chains; **b)** and **c)** $[HG_i]$ complexes; **d)** $[H_n(G_i)_n]$ complexes

Or discrete anion-templated supramolecular structures? Hard to say.

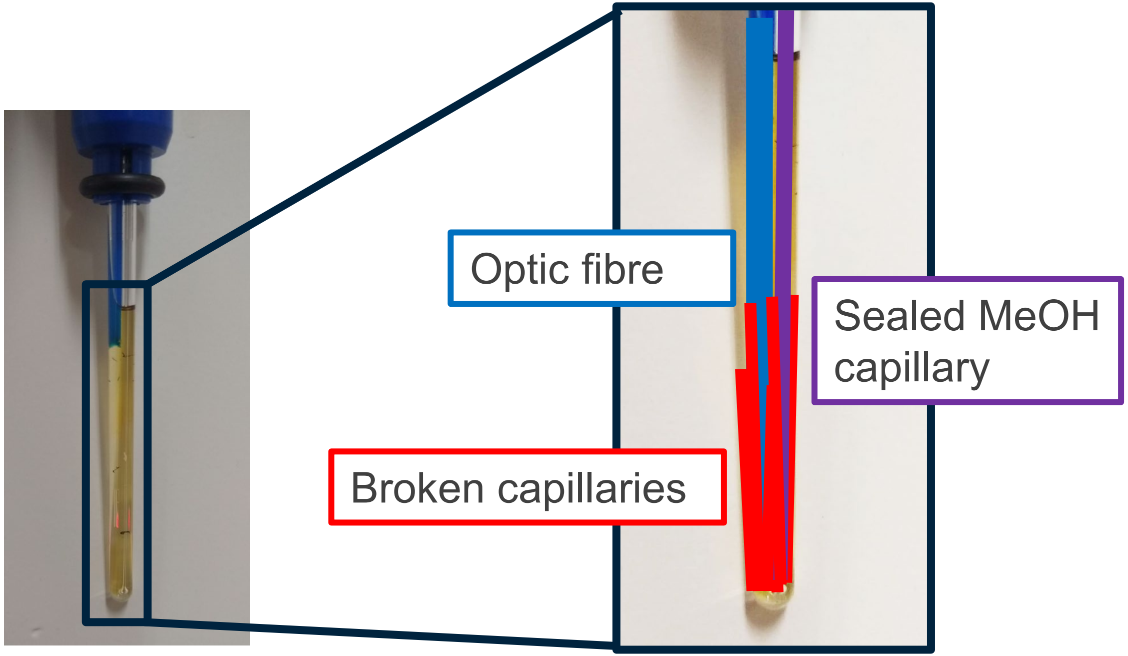
Time-resolved diffusion NMR with *in situ* irradiation

Irradiation causes uneven heating and convection

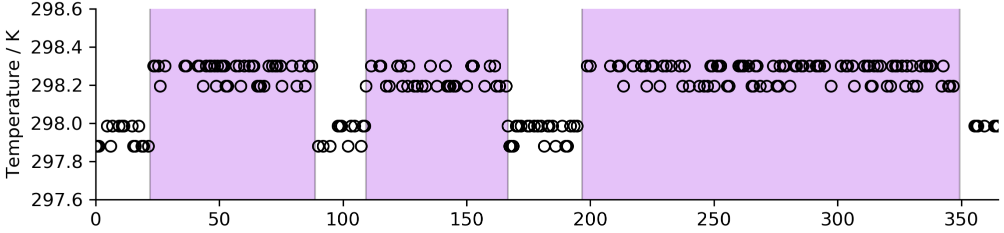


*405 nm LED irradiation. 5 mM Z-**1**, 50 mM TBA-DHP, DMSO-d_6 with 0.5% added water, ^{1}H PGSTE at 500 MHz. Values corrected for changes in viscosity.*

Suppressing convection with NMR crimes



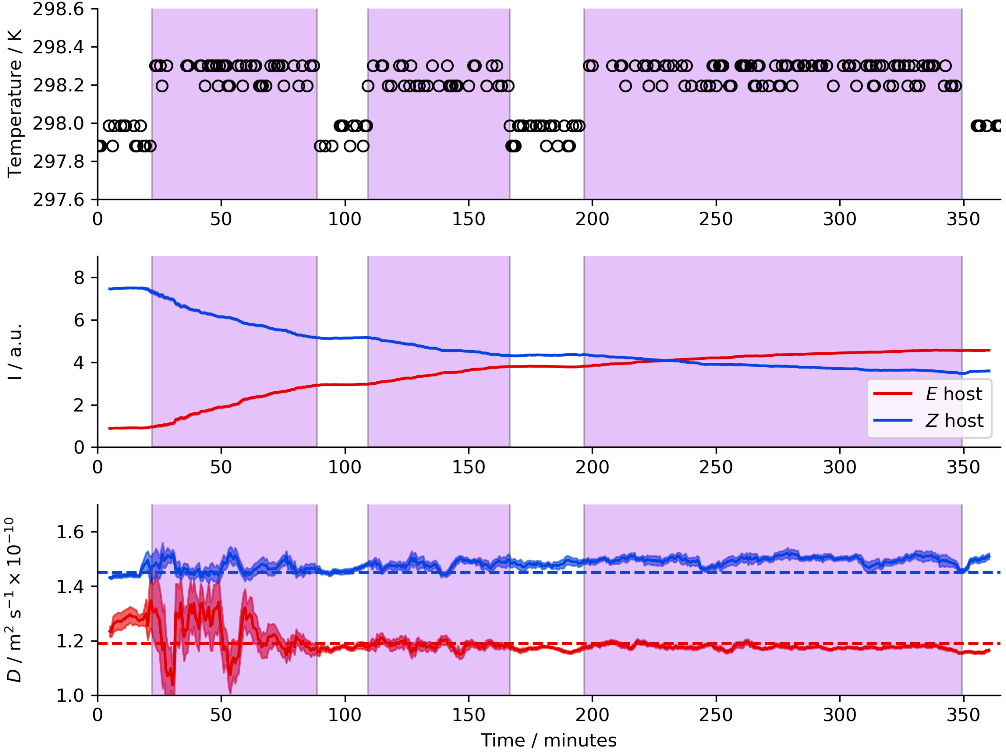
Time-resolved diffusion + *in situ* irradiation



Temperature increases by ~0.3 K under irradiation

*405 nm LED irradiation. 5 mM Z-**1**, 50 mM TBA-DHP, DMSO-d_6 with 0.5% added water, ^{1}H PGSTE at 500 MHz. Values corrected for changes in viscosity.*

Time-resolved diffusion + *in situ* irradiation



Temperature increases by ~0.3 K under irradiation

…but convection is inhibited.

*405 nm LED irradiation. 5 mM Z-**1**, 50 mM TBA-DHP, DMSO-d$_6$ with 0.5% added water, ^{1}H PGSTE at 500 MHz. Values corrected for changes in viscosity.*

Conclusions

- **Dihydrogen phosphate** isn’t what you think: the free anion barely exists in solution (<50% at 5 mM in DMSO + 0.5% water)
- **First solution characterisation** of oligomerisation by antielectrostatic hydrogen bonding (unassisted by other interactions)
  - Diffusion NMR is a good tool for this and other weak associative phenomena
- Can **control diffusion rates** with photoswitchable self-assembly
  - Unresolved: can spatial control over *D* (using light) drive transport?

Acknowledgements

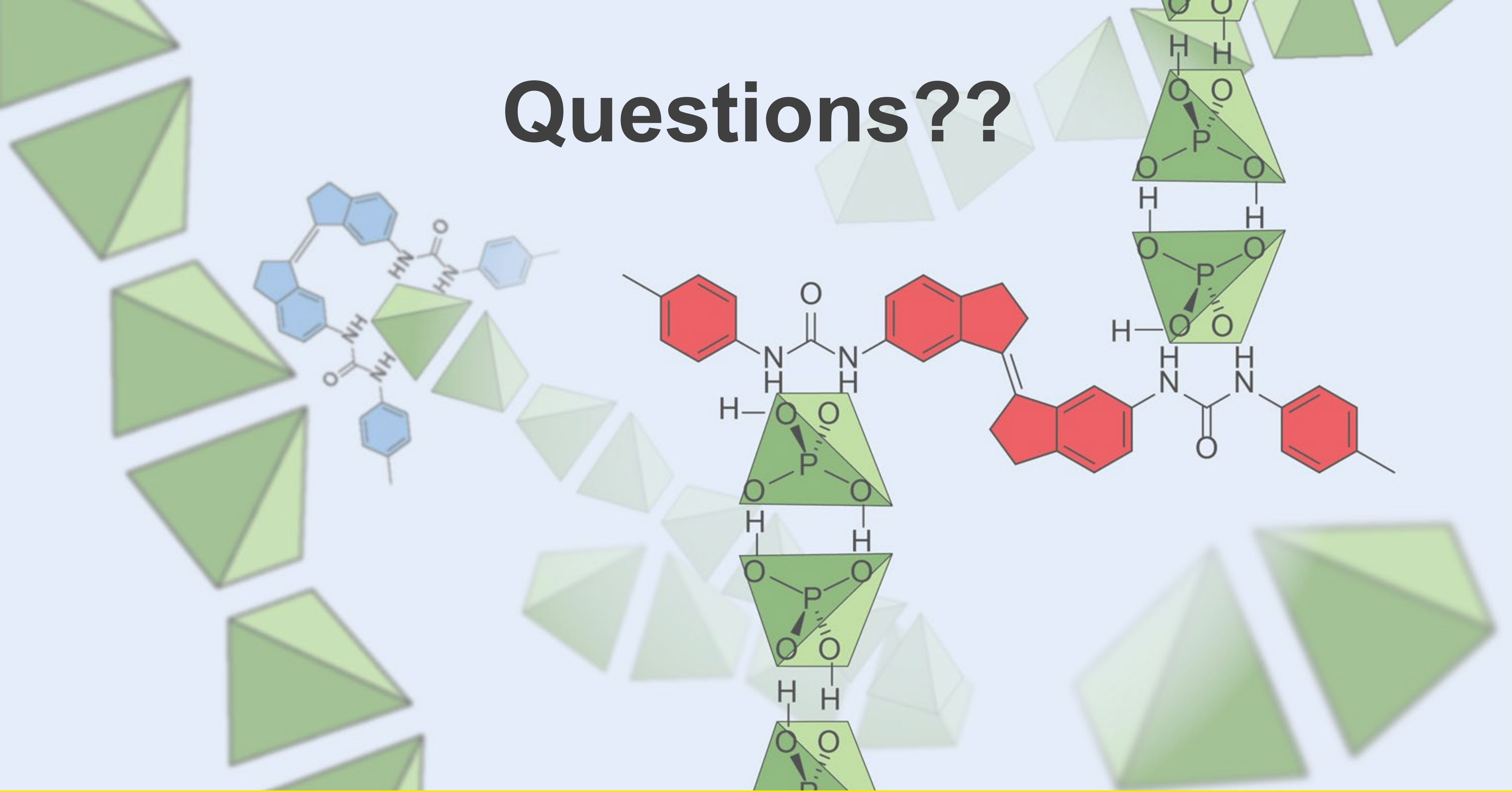
Beves group (UNSW)

Jon and the Bevers

Feringa group (RUG)

Ben, Sander, and the C-wing crew

Questions??



Isodesmic model

Isodesmic association model:

$$K_i = \frac{[\mathrm{A_n}]}{[\mathrm{A}][\mathrm{A_{n-1}}]}$$

Assumption: every stepwise association occurs with same K_i

Diffusion model for an *n*-unit oligomer:

$$D_n = n^{-\frac{1}{3}} D_0$$

Assumption: monomers and oligomers are hard spheres, and monomers pack perfectly

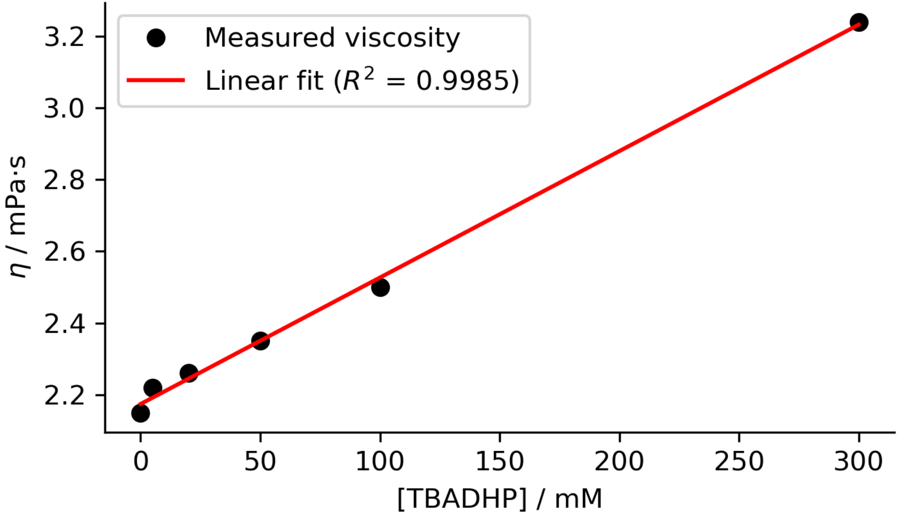
Modelled measured average diffusion:

$$\bar{D} = \frac{D_0}{[\mathrm{A}]_0 K_i} \sum_{n=1}^{\infty} n^{\frac{2}{3}} (K_i[\mathrm{A}])^n = \frac{D_0}{[\mathrm{A}]_0 K_i} \mathrm{Li}_{-\frac{2}{3}}(K_i[\mathrm{A}])$$

Assumption: each species contributes equally to NMR signal, ie no changes in T_1

Viscosity data - TBADHP

[TBADHP] / mM	Density / g·cm^{-3}	Temperature / °C	η / mPa·s	Error / %
0	1.1833	25.04	2.149	0.02
5	1.1833	25.00	2.210	0.08
20	1.1828	25.08	2.259	0.04
50	1.1820	25.04	2.334	0.03
100	1.1805	25.06	2.499	0.01
300	1.1752	25.04	3.251	0.02



Viscosity measurements: TBA + hosts

[TBA-DHP] / mM	[E] / mM	[Z] / mM	Density / g/cm³	Temperature / °C	*η* / mPa·s	Error / %	η/η_0
-	-	-	1.1833	25.04	2.149	0.02	1.000
50	-	-	1.1819	25.06	2.356	0.04	**1.096**
50	5	-	1.1820	25.05	2.390	0.08	**1.112**
50	-	5	1.1818	25.06	2.368	0.03	**1.102**
50	2.5	2.5	1.1820	25.06	2.375	0.02	**1.105**

Tabulated data: 50 mM DHP

Entry	[DHP] / mM	[E-1] / mM	[Z-1] / mM	D_{DHP}[b] / 10^{-10} m^2 s^{-1}	D_E[c] / 10^{-10} m^2 s^{-1}	D_Z[c] / 10^{-10} m^2 s^{-1}	D_{TBA}[c] / 10^{-10} m^2 s^{-1}
1	-	5	-	-	1.74± 0.03	-	-
2	-	-	5	-	-	1.87± 0.01	-
3	50	-	-	2.16 ± 0.03	-	-	2.50 ± 0.02
4	50	5	-	1.93 ± 0.04	1.17 ± 0.03	-	2.39 ± 0.01
5	50	-	5	2.01 ± 0.03	-	1.39 ± 0.01	2.37 ± 0.02
6	50	5	5	1.83 ± 0.08	1.12 ± 0.02	1.36 ± 0.01	2.31 ± 0.01
7	50	2.5	2.5	1.97 ± 0.07	1.19 ± 0.01	1.45 ± 0.03	2.44 ± 0.01
8	50	0.5	0.5	2.05 ± 0.02	1.27 ± 0.03	1.57 ± 0.03	2.52 ± 0.02

[a] DMSO-d_6 with 0.5% added water. [b] 202 MHz ^{31}P PGSTE, δ = 7 ms, Δ = 100 ms, g = 0 – 53.45 G cm^{-1}. [c] 500 MHz ^{1}H PGSTE, δ = 4 ms, Δ = 50 ms, g = 0 – 53.45 G cm^{-1}.

Example spectra: *E*-1 + TBA-DHP