Aqueous Interfacial Gels Assembled from Small Molecule Supramolecular Polymers

Alexander S. Groombridge, Aniello Palma, Richard M. Parker, Chris Abell and Oren A. Scherman*

Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK.
**Corresponding author; Fax: +44 (0)1223 334866; Tel: +44 (0)1223 331508; E-mail: oas23@cam.ac.uk*

Contents

1 Supplementary Information

1.1 Materials and Methods

All chemicals were purchased at the highest purity available from Sigma-Aldrich unless otherwise specified. Perfluorocarbon solvents FC-72, Novec7100, Novec7500 and Fluorinert FC-40 were obtained from 3M.

1.1.1 Instrumentation

^{1}H NMR (400 MHz) spectra were recorded using a Bruker Avance QNP 400. Chemical Shifts are recorded in ppm in $CDCl_3$, D_2O and d_6-DMSO with internal references set to δ 7.26 ppm, 4.79 ppm, and 2.50 ppm respectively. COSY 2D NMR experiments were carried out where appropriate to aid in assigning peaks. ATR FT-IR spectroscopy was performed using a PerkinElmer Spectrum 100 series FT-IR spectrometer equipped with a universal ATR sampling accessory. UV-Vis spectra were recorded on a Varian Cary 4000 UV-Vis spectrophotometer in aqueous solutions with 1 nm resolution at 25 °C. Photoirradiation was carried out using a LZC-ORG photoreactor from Luzchem Research Inc. equipped with UVA lamps centered at 360 nm.

Microdroplets were imaged using a Vision research Phantom Miro ex4-M fast camera, attached to an Olympus IX71 inverted microscope (10x - 64x objectives). Microfluidic devices were fabricated from PDMS by soft lithography, where the network was designed in silico (AutoCAD), printed as a negative photo-mask, and transferred onto a silicon wafer spin-coated with SU-8 photoresist via UV photolithography to form a mould. PDMS and the cross-linker (Sylgard 184 elastomer kit, Dow Corning) in a 10:1 ratio were poured into the mould and allowed to stand overnight at 70 °C. The PDMS layer was removed and inlets and outlets were imprinted with a biopsy punch (1 mm). The imprinted PDMS and a glass substrate were exposed to an oxygen plasma for 8 s, then pressed together to seal the channels. To render the channels fluorophilic they were immediately flushed with a 0.5 *v/v*% solution of trichloro(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane (Alfa Aesar) in FC-40 and subsequently cured at 120 °C overnight.

Monodisperse water-in-oil microdroplets were generated with a fluorophilic flow-focussing microfluidic channel. The diameter of the junction was 60 or 80 μm with a channel depth of 50 or 75 μm respectively. To generate microdroplets, the continuous oil phase and the discrete aqueous phase were injected with 1 mL syringes (NORM-JECT) into the microfluidic device via two syringe pumps (PHD 2000, Harvard Apparatus) and tubing (PORTEX, polyethene 1.09 OD, 0.38 ID) with flow rates typically of 150 and 100 μL h^{-1}, respectively. At the intersection, shear forces and surfactant self-assembly caused the formation of aqueous droplets in oil. The continuous phase comprised of the perfluorinated oil FC-40, with 2 *wt.*% neutral triblock fluorosurfactant (XL171, Sphere Fluidics). To this was added 1 *wt.*% of Krytox 157-FSL (a carboxylic acid-terminated perfluoropolyether, Dupont, K^-) or K^+. The dispersed phase consisted of an aqueous solution of monomers and CB[8], and dissolved 500 kDa dextran at 2 mg mL^{-1} in some cases. For a typical experiment, a concentration of 0.55 mM A_2, 0.37 mM B_3, and 1.1 mM CB[8] was used. Once formed, droplets were output onto the surface of a glass slide.

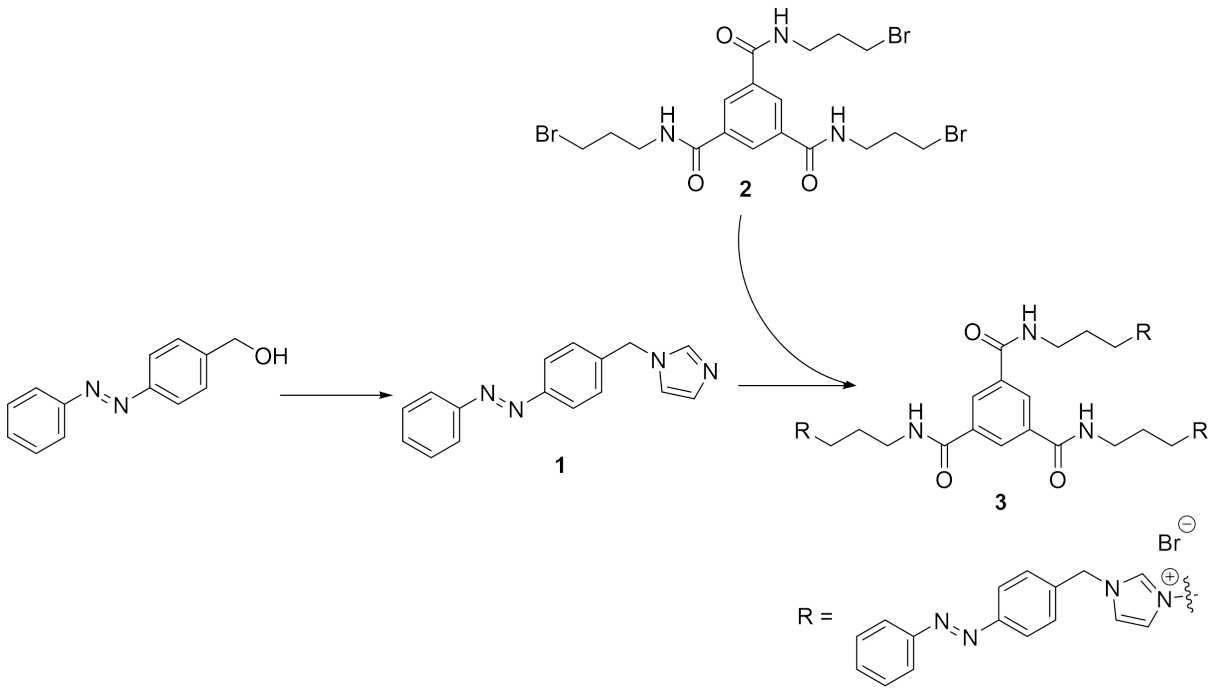
Pendant droplet measurements were performed using a commercial instrument (First Ten Angstroms, FTA1000). The higher density oil-phase (FC-40, 0.001 *wt.*% K^- or 0.01 *wt.*% K^+) was hung from a 22 gauge needle (0.7176 mm OD, 0.4143 mm ID) and allowed to equilibrate with the continuous lighter aqueous phase for 45 mins. For interfacial compression the droplet volumes were reduced from 5 μL until buckling was observed at 0.1 μL s^{-1}. Adamantylamine hydrochloride was then added until in excess and the hanging drop was then allowed to equilibrate for a further 45 mins before measurement. UV exposure of the aqueous solution was carried out similarly to the NMR measurements for 1 h before equilibrating again. Each measurement was subject to 3 repetitions.

1.1.2 A_2 Synthesis

A_2 was synthesised according to literature procedures.[1]

1.1.3 B_3 Synthesis

(4-(phenyldiazenyl)phenyl)methanol was prepared according to previously reported literature procedures.[2]



1-(4-(phenyldiazenyl)benzyl)-1*H*-imidazole (**1**) was synthesised as follows. (4-(phenyldiazenyl)phenyl)methanol (3.04 g, 14.3 mmol) was dissolved in anhydrous NMP (36 mL) under a flow of N_2, to which was added CDI (3.02 g, 18.6 mmol). The reaction mixture was heated and stirred at 150 °C for 3 h. After cooling, DCM was added (50 mL) and extraction with water (25 mL x2) was carried out, followed by brine (25 mL). The organic phases were combined and DCM was added until a final volume of 150 mL. Water (100 mL) was added, followed by dropwise addition of aqueous HCl (5 M) until phase transfer to the aqueous phase occurred. The phases were separated, and the organic phase was extracted with further aqueous HCl (2 M, 10 mL x2). After combining the aqueous phases, saturated $NaHCO_3$ was added until reaching pH 7. The product precipitate was filtered and dried to purity as an orange amorphous solid (0.98 g, 26%). δH ($CDCl_3$, 400 MHz) 7.89-7.93 (4H, m), 7.46-7.55 (3H, m), 7.29 (2H, d, 8.6 Hz), 7.60 (1H, s), 7.13 (1H, t), 6.94 (1H, t), 5.21 (2H, s) ppm. δC ($CDCl_3$, 100 MHz) 152.5 (ArC), 152.4 (ArC), 138.9 (ArC), 137.5 (ImCH), 131.3 (ArCH), 130.1 (ArCH, 2C), 129.1 (ArCH, 2C), 127.9 (ImCH), 123.4 (ArCH, 2C), 122.9 (ArCH, 2C), 119.3 (ImCH), 68.0 (CH_2) ppm. HRMS calculated for $[M + H]^+$: $C_{16}H_{15}N_4$ 263.1297, found 263.1262. FT-IR ν_{max}/cm^{-1} 3114brd, 3064brd, 2942brd, 1605, 1582, 1505, 1442. TLC (SiO_2 on glass) DCM:Acetone 1:1, R_f = 0.10.

3,3',3"-(((benzene-1,3,5-tricarbonyl)tris(azanediyl))tris(propane-3,1-diyl))tris(1-(4-(phenyldiazenyl)benzyl)-1*H*-imidazol-3-ium) bromide (**3**):

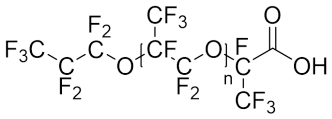
N^1,N^3,N^5-tris(3-bromopropyl)benzene-1,3,5-tricarboxamide[3] (**2**, 0.30 g, 0.53 mmol) was dissolved in ACN (10 mL) and treated with **1** (0.83 g, 3.2 mmol) which was previously dissolved in ACN (2 mL). The reaction mixture was heated under reflux for 7 days until a viscous precipitate was

formed. The reaction mixture was cooled at room temperature and decanted. The precipitate was suspended in deionized water (500 mL) and stirred overnight. The suspension obtained was filtered, and the liquid phase was freeze dried to yield the desired compound **3** as an orange amorphous solid (85 mg, 12%). δH (d_6-DMSO, 400 MHz, *E*-isomer) 9.60 (3H, s), 9.15 (3H, m), 8.68 (3H, s), 7.92-7.80 (21H, m), 7.60-7.28 (12H, m), 5.50 (6H, s), 4.32 (6H, m), 3.36 (6H, m, under H_2O solvent peak detected by COSY), 2.15 (6H, m). δC (d_6-DMSO, 400 MHz, *E*-isomer) 165.5 (CO), 151.8, 137.9 (ArC), 136.8, 134.5 (ArCH), 131.9 (ArCH, 2C), 129.5 (ArCH, 2C), 129.4, 123.0 (ArCH, 2C), 122.6 (ArCH, 2C), 51.5 (CH_2), 47.0 (CH_2), 36.1 (CH_2), 29.4 (CH_2). HRMS calculated for $[M\text{-HBr}]^{2+}$: $C_{66}H_{65}O_3N_{15}$ 557.7692, found 557.7695. FT-IR ν_{max}/cm^{-1} 3403brd, 2922brd, 2852brd, 1729, 1654, 1542, 1448. UV λ_{max}(H_2O with 0.7 *v/v*% of DMSO)/nm 324 nm, 426 nm.

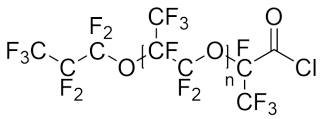
1.1.4 CB[8] Synthesis

CB[8] was prepared according to previously reported literature procedures.[4]

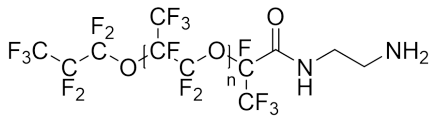
1.1.5 K^+ Synthesis



Krytox 157-FSL



Krytox-Cl



K^+

The synthesis of K^+ was adapted from literature procedures from microwave chemistry to simple conventional synthetic techniques.[5] Krytox 157-FSL was purified before use by dissolution in FC-72 and solvent extraction with THF (x3) followed by removal of solvent *in vacuo*. FT-IR ν_{max}/cm^{-1} 1779 (CO).

Krytox-Cl:

Krytox 157-FSL (6.78 g, 3.4 mmol) was dissolved in Novec7100 (8 mL) under N_2. Oxalyl chloride (0.92 mL, 10.9 mmol) was added by syringe followed by 1 drop of catalytic DMF. The reaction was stirred vigorously at room temperature for 16 h. The reaction was quenched by removal of solvent and starting material *in vacuo*. The residue was dissolved in FC-72 (10 mL) and extracted from THF (5 mL x3) followed by removal of solvent *in vacuo* to give a colourless oil **Krytox-Cl** (5.95 g, 88%). ν_{max}/cm^{-1} 1809 (CO).

K^+:

Ethylene diamine (9.0 mL, 134.6 mmol) was heated to 60 °C under N_2. Krytox-Cl (5.05 g, 2.5 mmol) in Novec7500 (7 mL) was added by syringe over 30 mins. The reaction was heated to 80 °C and stirred vigorously for 24 h. After cooling, MeOH (10 mL) was added and the mixture stirred for 1 h. The solvents were removed *in vacuo*, and the residue was dissolved in FC-72 (15 mL). The dispersion was filtered, and then extracted with THF (10 mL x3). The perfluorocarbon phases were

combined and dried *in vacuo* to give K^+ as a slightly yellow oil (4.85 g, 96%). δH (5 *v/v*% $CDCl_3$ in perfluoroctane, 400 MHz) 7.38 (1H, br), 3.67-3.83 (2H, br), 3.51 (1H, br), 3.01 (1H, t), 1.13 (2H, br). FT-IR $\nu_{max}/\mathrm{cm}^{-1}$ 3344brd (NH), 1705 (CO), 1539 (NH).

1.2 Supplementary Figures

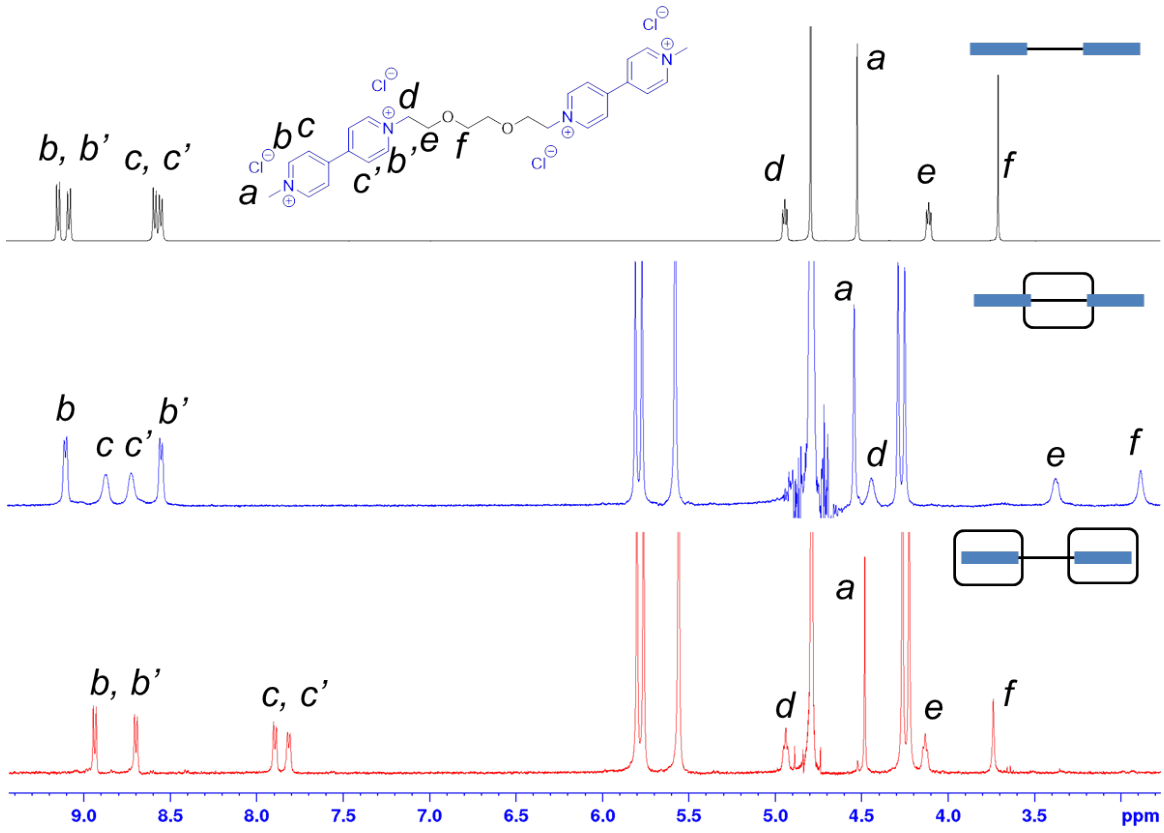


Fig. S 1 Stacked ^{1}H NMR spectra in D_2O of ditopic A_2 monomer. The top spectrum is first the A_2 molecule alone, then A_2 with 1 *equiv.* CB[8], and then 2 *equiv.* CB[8]. The peaks shift as previously observed.[1]

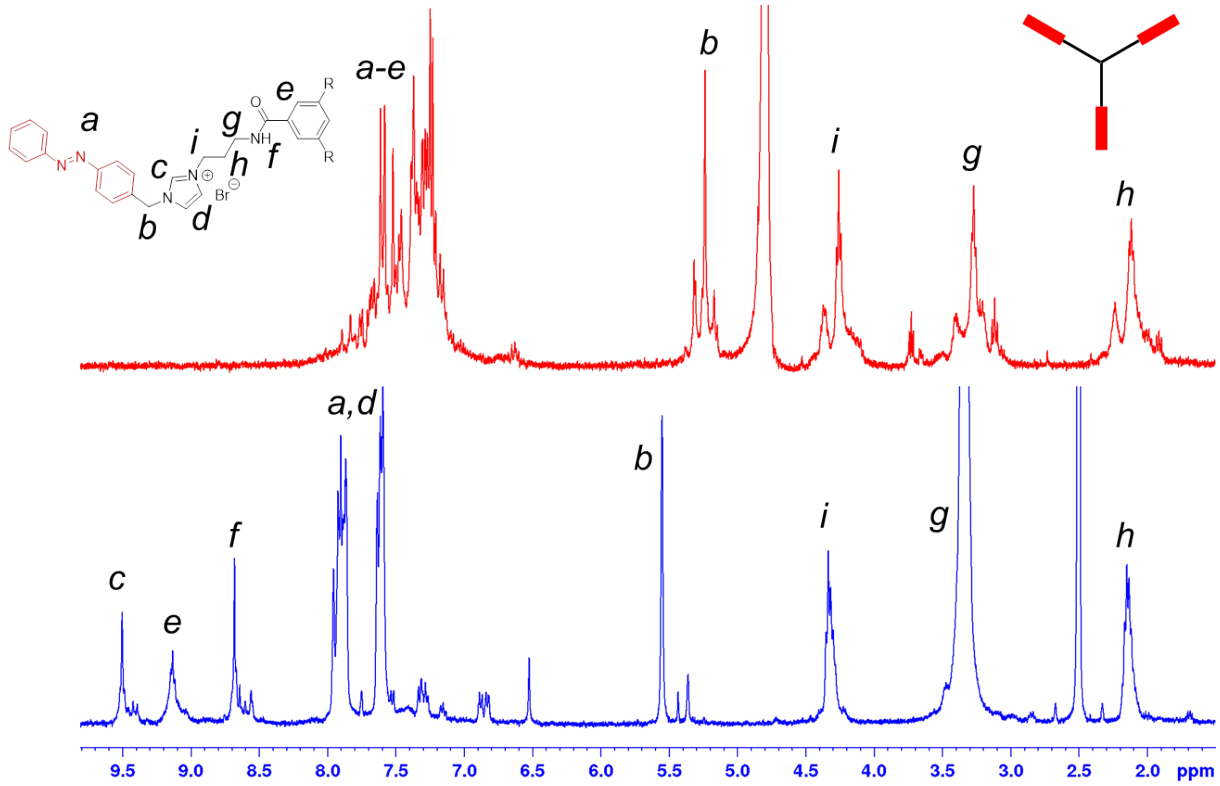


Fig. S 2 Stacked ^{1}H NMR spectra in D_2O (top) and d_6-DMSO (bottom) of tritopic B_3 monomer. The aromatic region in D_2O is characteristic of that when π-π stacking interactions are occurring, this is not the case when in d_6-DMSO as this deaggregates the molecule.

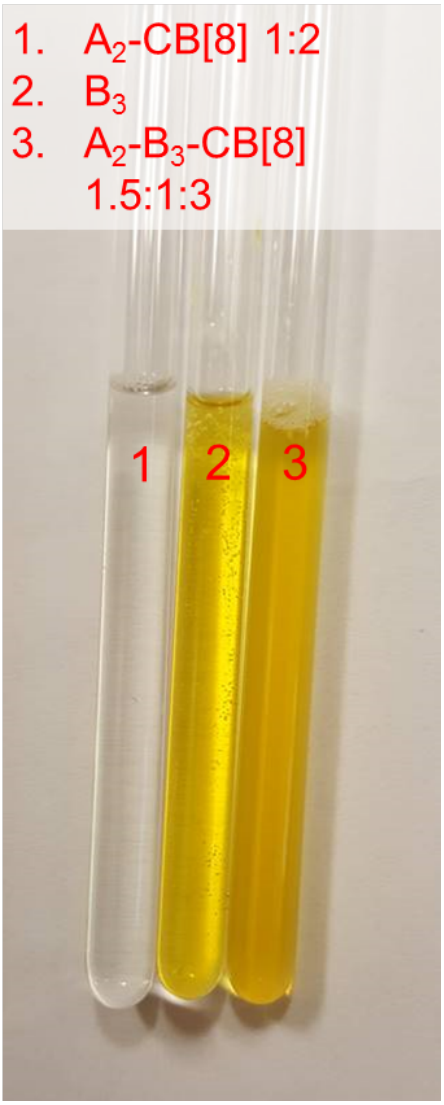


Fig. S 3 A photo to illustrate the precipitation occurring upon assembly of the supramolecular polymer at higher concentrations. Concentrations are as follows: A_2 1.1 mM, B_3 0.73 mM, CB[8] 2.2 mM. Concentrations used in ^{1}H NMR measurements were half of this, at the limit before significant precipitation occurs.

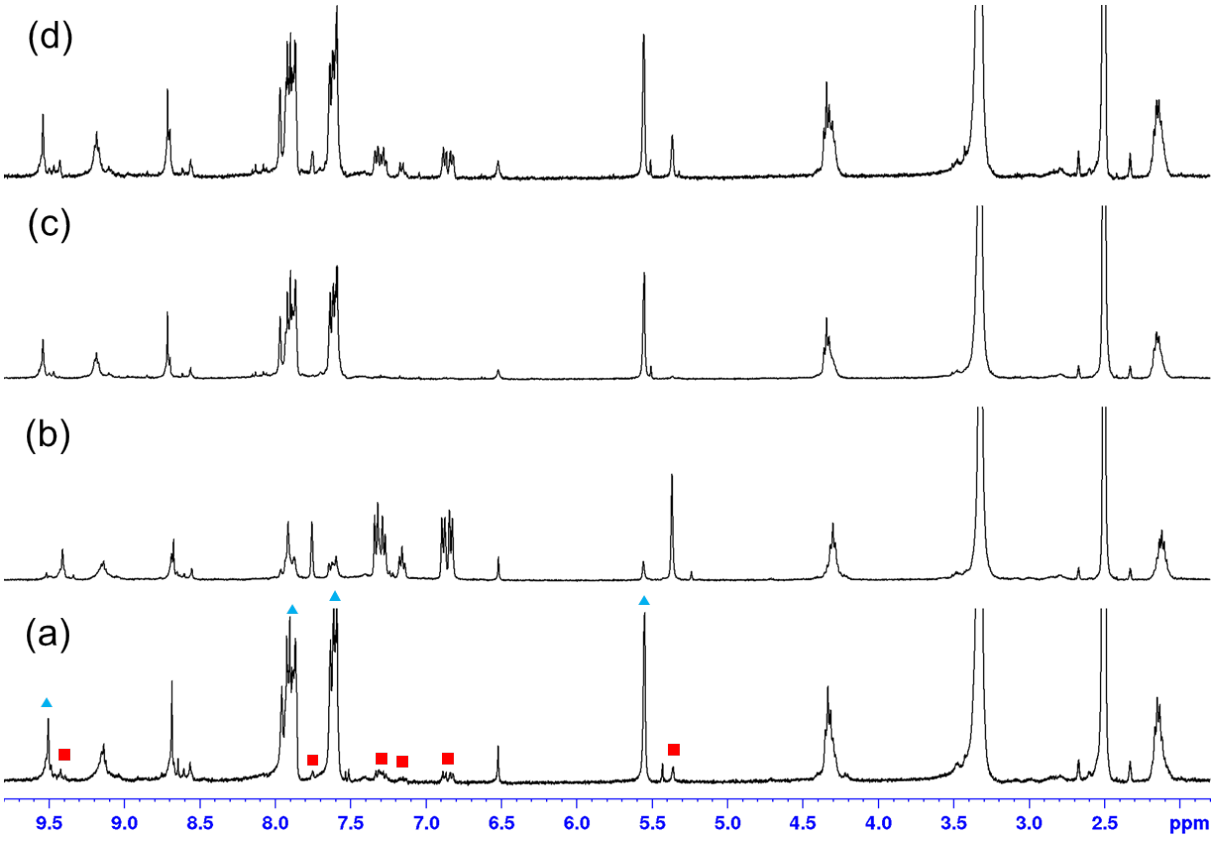


Fig. S 4 Stacked ^{1}H NMR spectra in d_6-DMSO of tritopic B_3 monomer in response to UVA light treatment. (a) Original photostationary state immediately after dissolution; (b) after exposure to UVA light for 1 h; (c) after heating at 80 °C for 6 h; (d) after leaving to reach equilibrium state in ambient conditions for 12 h. The proportion of the *E* and *Z* isomers were calculated from comparing integration of the aromatic peaks corresponding to each isomer, and that of the CH_2 at *ca.* 5.5 ppm. Blue triangles represent peaks for the *E* isomer, and red squares for the *Z* isomer.

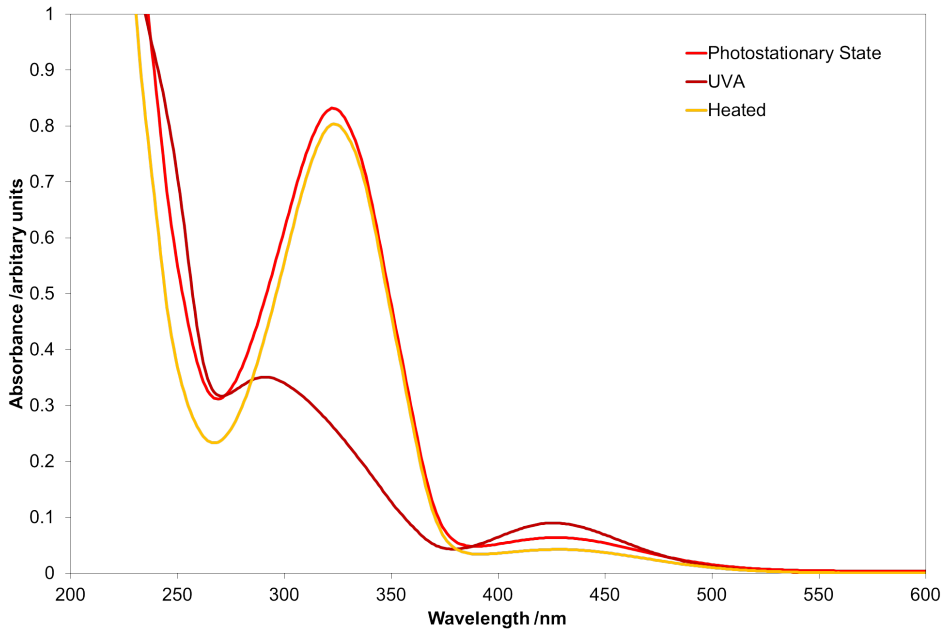


Fig. S 5 UV-vis measurements taken of the B_3 monomer in water (0.7 *v/v*% DMSO). As is characteristic for azobenzene photoisomerisations, the n to $\pi*$ transition at 324 nm is altered dramatically upon UV-triggered isomerisation, while the π to $\pi*$ transition absorbance at 426 nm increases. After heating, the photoisomerisation can be completely reversed.

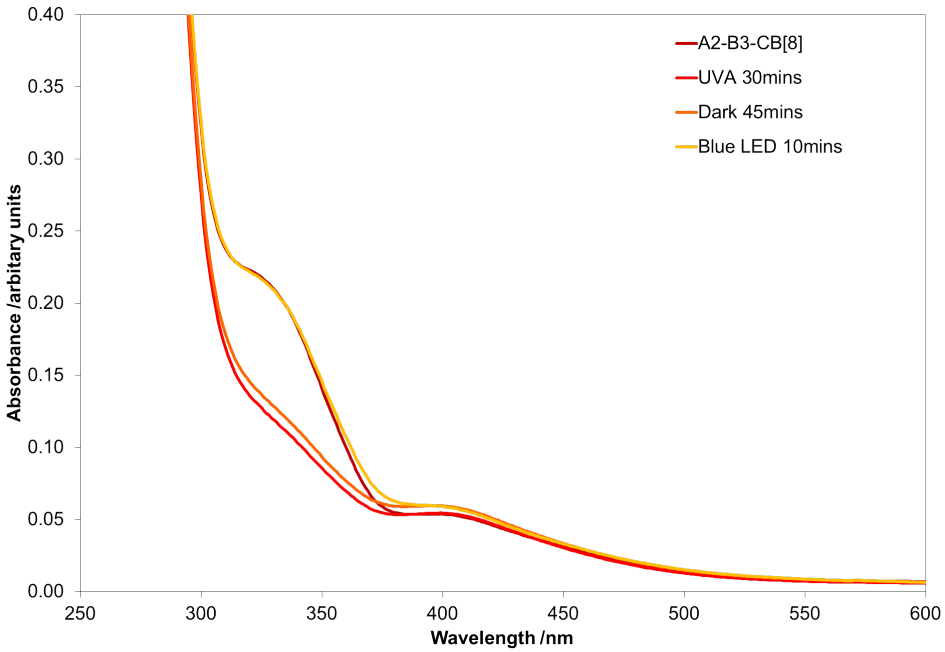


Fig. S 6 UV-vis measurements taken of the assembled A_2-B_3-CB[8] diluted 20x from the microfluidic stock solution. A similar trend in photoisomerisation is observed as for the B_3 monomer alone. At room temperature in the dark, a small amount of recovery of the equilibrium is observed. Here a blue LED light exposure is sufficient to drive the recovery of the *E* isomer due to the low concentration used.

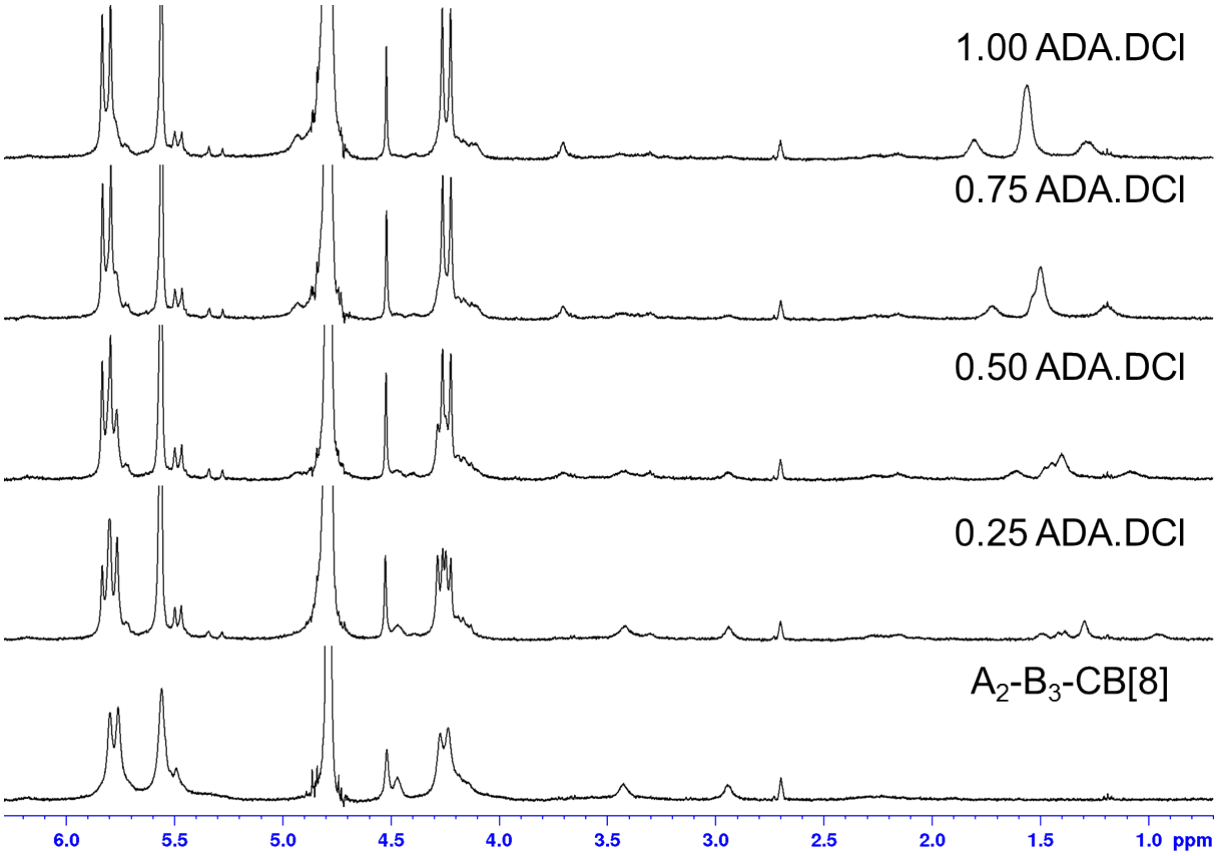


Fig. S 7 ^{1}H NMR stack in D_2O of A_2-B_3-CB[8] SHP with up to 1 molar equivalent of ADA·DCl. Concentrations in all cases were A_2 0.55 mM, B_3 0.37 mM, CB[8] 1.11 mM.

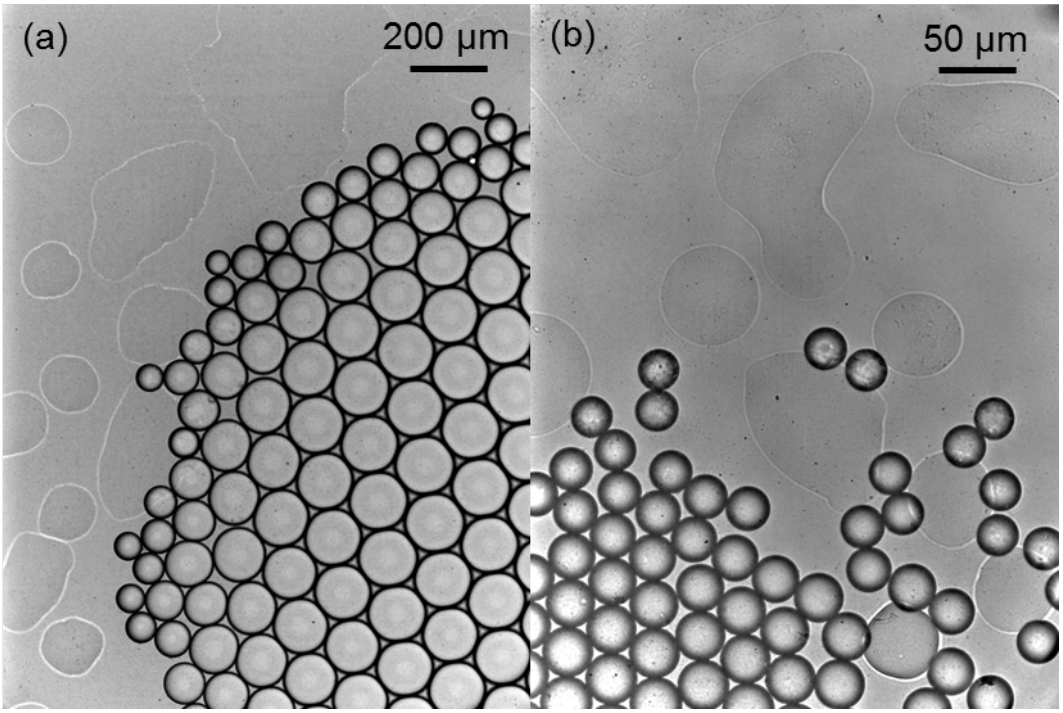


Fig. S 8 Transmission optical micrographs of microfluidic microemulsions output onto glass slides. (a) Aqueous microdroplets containing A_2-B_3 and no CB[8]; (b) aqueous microdroplets containing A_2-B_3-CB[7]. Continuous phase was 2 *wt.*% XL171, 1 *wt.*% K^- in FC-40. Upon evaporative concentration, the droplets without CB[8] destabilise and burst whilst still relatively large, thought to be due to the high charge density preferentially wetting the hydrophilic glass surface. When CB[7] is present no buckling transition is observed, but droplets decrease in size until nearly all water has evaporated before destabilising; this is likely due to the charged moieties binding to the CB[7].

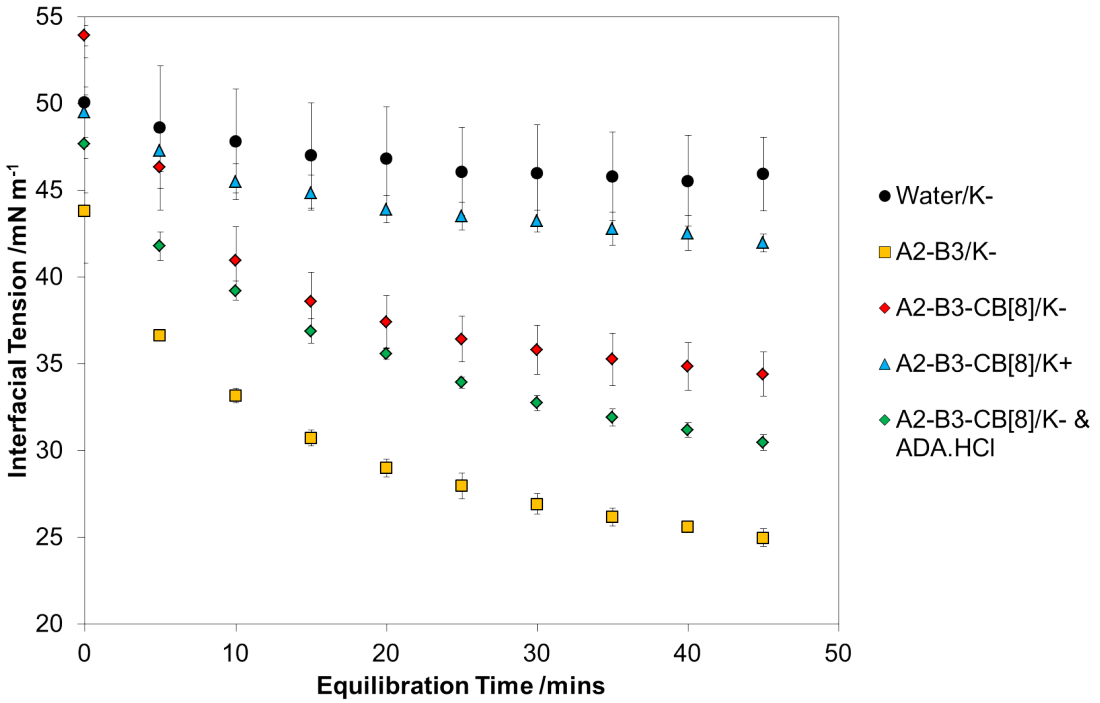


Fig. S 9 Plots showing how the IFT changes with equilibration time for different experiments. K^- was in FC-40 at 0.001 *wt.*%, K^+ was in FC-40 at 0.01 *wt.*%, A_2-B_3-CB[8] was diluted 20x from the microfluidic stock solution. ADA·HCl was added in excess to facilitate rapid complexation to CB[8].

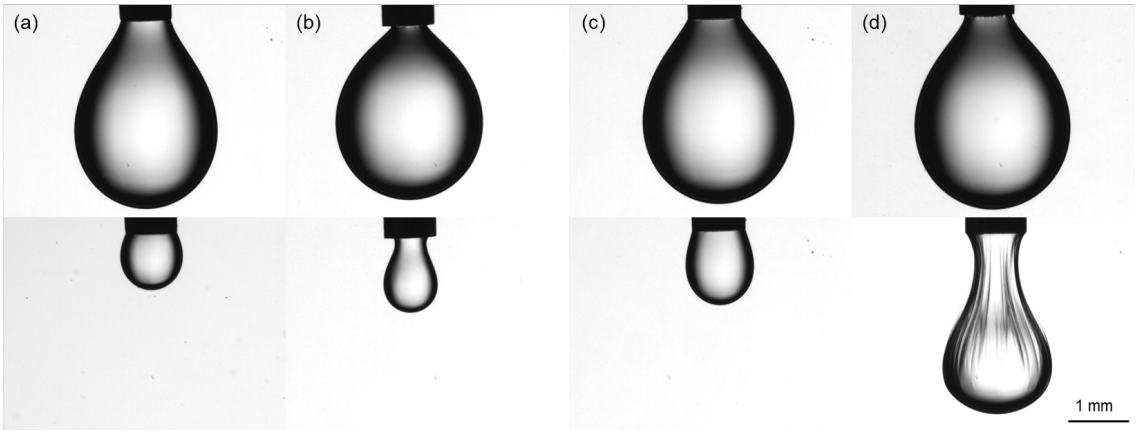


Fig. S 10 Transmission micrographs of the pendant droplet during IFT measurements at equilibrium and then after subsequent pumping in. (a) Aqueous A_2-B_3 and droplet of K^- in FC-40; (b) aqueous A_2-B_3-CB[8] and droplet of K^+ in FC-40; (c) aqueous A_2-B_3-CB[8] and excess ADA·HCl and droplet of K^- in FC-40; (d) aqueous A_2-B_3-CB[8] after 1 h UVA irradiation and droplet of K^- in FC-40. After exposure to UVA light, buckling is still observed. This was a result of incomplete conversion of the B_3 azobenzene moieties to their *Z* isomers, even with CB[8] present. Some recovery of the equilibrium was also observed, as evidenced by UV-vis measurements in Fig. S11. It was theorised that the low concentration of remaining B_3 in the *E* isomer was still sufficient to accumulate at the hanging drop interface and form a cross-linked film due to the massive concentration factor at the interface when compared to bulk. This is also supported by buckling still being observed after an order of magnitude dilution in Fig. S12.[6]

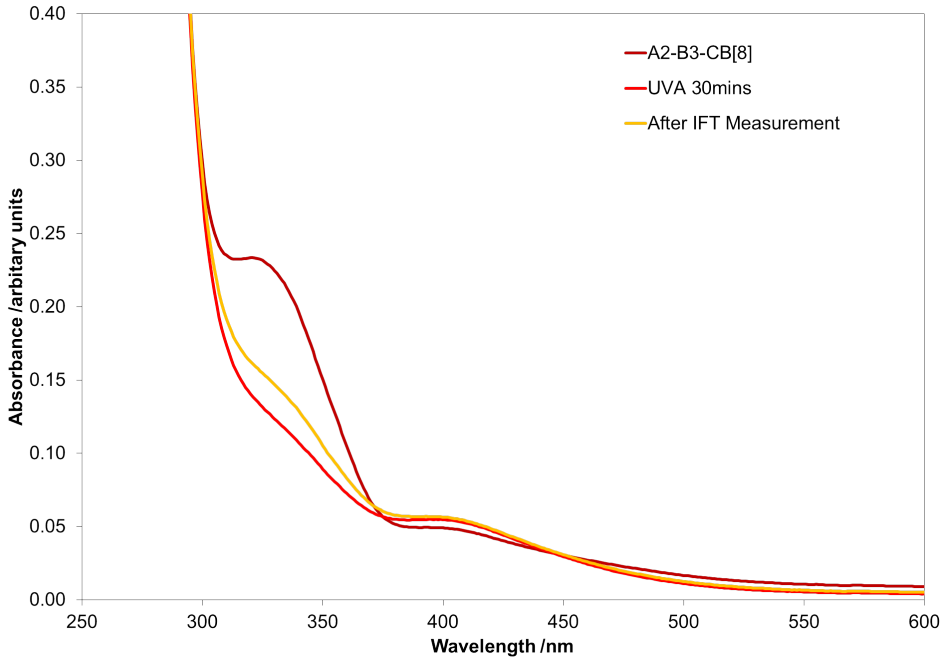


Fig. S 11 UV-vis measurements as above, showing the extent of equilibrium recovery after pendant droplet IFT measurement. Assuming a linear correlation between absorbance at 324 nm, and similar extents of photoisomeration as that observed in NMR, after the IFT measurement *ca.* 34% of B_3 is the *Z* isomer. This partial recovery is due to the limited light exposure necessary in running these experiments, and contributed to the observed interfacial gel still present after UVA exposure as shown in Fig. S10.

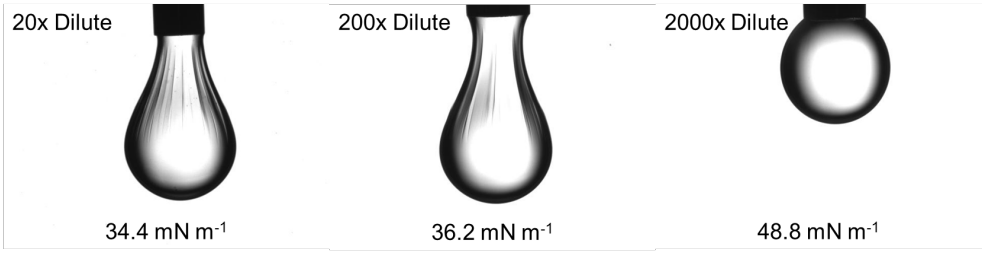


Fig. S 12 Transmission micrographs of the pendant droplet during IFT measurements after 45 min equilibration and subsequent pumping in at different concentrations of aqueous A_2-B_3-CB[8]. Here buckling can be observed at a 20x and 200x dilution, but not at a 2000x dilution relative to the microfluidic stock solution. The quoted IFT values are those at equilibrium before pumping in. It can be clearly observed that there is a lower density of wrinkling at a 200x dilution, implying a thinner crosslinked network had been formed, thus a 20x dilution was used throughout this work.

References

[1] S. Deroo, U. Rauwald, C. V. Robinson and O. A. Scherman, *Chem. Commun.*, 2009, 644–646.

[2] P. Fatás, E. Longo, F. Rastrelli, M. Crisma, C. Toniolo, A. I. Jiménez, C. Cativiela and A. Moretto, *Chem. - A Eur. J.*, 2011, **17**, 12606–12611.

[3] S. Y. Kim, Y. H. Ko, J. W. Lee, S. Sakamoto, K. Yamaguchi and K. Kim, *Chem. - An Asian J.*, 2007, **2**, 747–754.

[4] J. Kim, I. Jung, S. Kim, E. Lee, J. Kang, S. Sakamoto, K. Yamaguchi and K. Kim, *J. Am. Chem. Soc.*, 2000, **122**, 540–541.

[5] R. M. Parker, J. Zhang, Y. Zheng, R. J. Coulston, C. A. Smith, A. R. Salmon, Z. Yu, O. A. Scherman and C. Abell, *Adv. Funct. Mater.*, 2015, **25**, 4091–4100.

[6] A. R. Salmon, R. M. Parker, A. S. Groombridge, A. Maestro, R. J. Coulston, J. Hegemann, J. Kierfield, P. Cicuta, O. A. Scherman and C. Abell, *Langmuir*, 2016, under review.