Supporting information

Designing new symmetrical facial oligothiophene amphiphiles

Dainius Janeliunas,[a] Rienk Eelkema,[a] Belén Nieto-Ortega,[b] Francisco J. Ramírez Aguilar,[b] Juan T. López Navarrete,[b] Lars van der Mee,[a] Marc C. A. Stuart,[c] Juan Casado,[b] and Jan H. van Esch*[a]

[a] *Department of Chemical Engineering, Faculty of Applied Sciences, Delft University of Technology, Julianalaan 136, 2628BL, Delft, The Netherlands. Fax: +31 (0)15 278 2682; Tel: +31 (0)15 278 4289; E-mail: j.h.vanesch@tudelft.nl*
[b] *Department of Physical Chemistry, University of Malaga, Campus de Teatinos s/n, 29071, Malaga, Spain.*
[c] *Groningen Biomolecular Sciences and Biotechnology Institute, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands.*

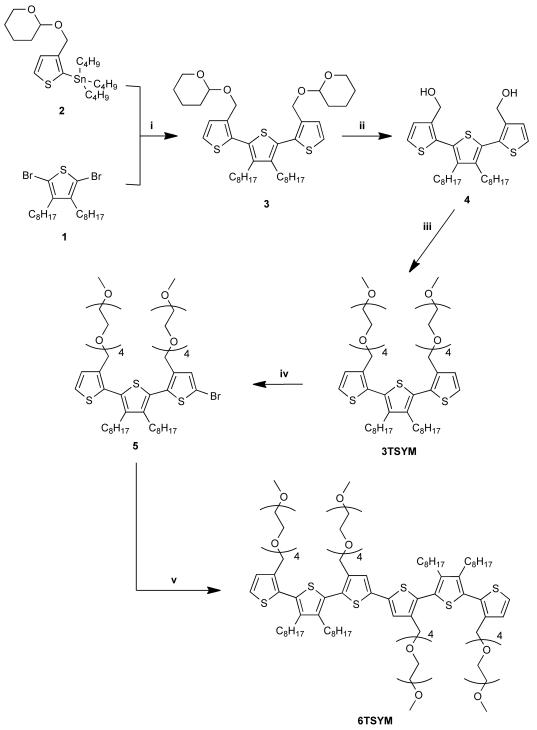
Table of Contents

General Remarks

All reagents and solvents were purchased from commercial sources and were used as provided unless otherwise stated. All reactions, if not otherwise stated, were performed under dry conditions and argon atmosphere. The compounds **2-bromo-3-hydroxymethylthiophene**[i] (a precursor for the derivative **2**), **(2-Bromothiophen-3-yl)methyl tetrahydro-2H-pyran-2-yl ether**[ii], compound **1** (**2,5-dibromo-3,4-dioctylthiophene**)[iii], derivative **2** (tributyl(3-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)thiophen-2-yl)stannane)[iv], **Me(OCH$_2$CH$_2$)OTs**[v] were synthesised according to literature procedures. All reactions were performed under inert argon atmosphere. MilliQ-water and spectroscopic grade solvents were used for measurements. Thin layer chromatography was performed using aluminium-foil backed plates precoated with Kieselgel 60 F_{254}. Flash column chromatography was carried out with Aldrich silica gel Merck grade 9385 (230-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Brucker Avance-400 spectrometer, operating at 399.90 MHz. All NMR spectra were recorded at 298 K, 48 scans each. Chemical shift values are denoted in δ values (ppm) relative to residual solvent peaks ($CDCl_3$, ^{1}H δ = 7.26, ^{13}C δ = 77.00). MS analysis was performed on a Shimadzu Liquid Chromatograph Mass Spectrometer, LCMS-2010, LC-8A pump with a diode array detector SPD-M20, using 0.05% formic acid solution in methanol as a solvent. The MS analysis of compound **4** was performed on a Shimadzu GCMS-QP2010S spectrometer. Dynamic light scattering was performed on a ZetaSizer Nano series Nano-ZS by Malvern Instruments at 20 °C. For UV/Vis measurements an AnalytikJena Specord 250 spectrometer equipped with a deuterium lamp and a halogen lamp was used. Quartz cuvettes with path-length of 0.1 mm were used. For Cryo-TEM, a few microliters of suspension was deposited on a bare 700 mesh copper grid. After blotting away the excess of liquid the grids were plunged quickly in liquid ethane. Frozen-hydrated specimens were mounted in a cryo-holder (Gatan, model 626) and observed in a Philips CM 120 electron microscope, operating at 120 kV. Micrographs were recorded under low-dose conditions on a slow-scan CCD camera (Gatan, model 794). Confocal Laser Scanning Microscopy (CLSM) micrographs were obtained on a Zeiss LSM 700 confocal laser scanning microscope. Excitation was done with 458 nm (NBDPE) laser lines. The laser beam was focused on a 40 X oil immersion objective and the sensitivity of detectors and filters were adjusted accordingly in order to obtain maximum signal to noise ratio. 1064 nm FT–Raman spectra were obtained in an FT–Raman accessory kit (FRA/106–S) of a Bruker Equinox 55 FT–IR interferometer. A continuous–wave Nd–YAG laser working at 1064 nm was employed for excitation. A germanium detector operating at liquid nitrogen temperature was used. Raman scattering radiation was collected in a back–scattering configuration with a standard spectral resolution of 4 cm^{-1}. 2000 scans were averaged for each spectrum. The ground-state molecular geometries, vibrational frequencies, and Raman intensities of the compounds were derived by means of the Density Functional Theory (DFT) approach.

All DFT calculations were performed using the B3LYP functional[vi,vii] and the 6-31G** basis set[viii,ix] as implemented in the GAUSSIAN-09 package.[x]

Synthesis of symmetrical thiophenes 3TSYM and 6TSYM



Scheme S1. Synthesis of **3TSYM** and **6TSYM**.

Terthiophene **4** ((3',4'-dioctyl-[2,2':5',2''-terthiophene]-3,3''-diyl)dimethanol).
A solution of **1** (3.00 g, 6.43 mmol) and palladium(tetrakis)triphenylphosphine (0.37 g, 0.32 mmol) in anhydrous toluene (15 ml) was degassed and stirred for 20 min. A solution of **2** (6.88 g, 14.15 mmol) in toluene (10 ml) was added and the resulting mixture was refluxed 72 hours under nitrogen in a Schlenk tube. The solvent of the reaction mixture was then removed in vacuo and the crude oil was dissolved in petroleum ether. The black solution was passed through a celite column. The solvent was then evaporated and the obtained dark brown oil of crude **3** was suspended in 10% HCl solution in THF/Methanol (10 ml; 50:50). It was stirred at room temperature over night and then quenched with aqueous 10% K_2CO_3 and diluted with water (100ml). The obtained mixture was then extracted with CH_2Cl_2. The organic phase was washed with water until the pH of aqueous washings became neutral. Then it was dried over $MgSO_4$ and the solvent was evaporated in vacuo. The resulting oil was purified by column chromatography (neutral aluminum oxide, eluent methanol/CH_2Cl_2 2%/97%). Compound **4** was obtained as a light yellow oil, which solidified upon standing overnight at room temperature, in 55% yield (1.88 g, 3.53 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): d = 0.87 (t, J = 6.9 Hz, 6H), 1.15 - 1.35 (m, 20H), 1.38 - 1.48 (m, 4H), 1.77 (bs, 2H), 2.46 - 2.53 (m, 4H), 4.58 (s, 2H), 7.18 (d, J = 5.3 Hz, 2H), 7.35 (d, J = 5.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): d = 14.2 ($2CH_3$), 22.9 ($2CH_2$), 28.2 ($2CH_2$), 29.4 ($4CH_2$), 29.9 ($2CH_2$), 30.9 ($2CH_2$), 32.0 ($2CH_2$), 59.1 ($2CH_2$), 125.9 (2CH), 128.3 (2CH), 128.6 (2C), 131.4 (2C), 140.7 (2C), 142.9 (2C) ppm. EI-MS: *m/z* calcd for $C_{30}H_{44}O_2S_3$: 532.25 (monoisotopic); found: 532 [M].

3TSYM (1,1'-(3',4'-dioctyl-[2,2':5',2''-terthiophene]-3,3''-diyl)bis(2,5,8,11,14-pentaoxapentadecane).
To a suspension of NaH (0.19 g (0.31 g of 60% dispersion in oil), 7.872 mmol) in THF (30 ml) at 0 ºC terthiophene **3** (1.75 g, 3.28 mmol, dissolved in 10 ml of THF) was added slowly (over 20 min). The solution was stirred at this temperature until the evolution of gas stopped (for 1 h). Then the reaction was allowed to reach room temperature and mixed additional 2 h. Then the mixture was cooled to 0 ºC again and **Me(OCH_2CH_2)OTs** (2.73 g, 7.54 mmol, dissolved in 15 ml of THF) was added slowly (over 30 min). The reaction vessel was left to reach room temperature over night and then quenched with 30 ml of icy water. The mixture was extracted with ethyl acetate. The organic phase was washed with water until the pH of aqueous washings became neutral. Then it was dried over $MgSO_4$ and the solvent was evaporated in vacuo. The re-

sulting oil was purified by column chromatography (silica gel, eluent ethyl acetate/petroleum ether (gradient 20-50%) with 1% triethylamine added). Compound **3TSYM** was obtained as a light yellow oil, in 70% yield (2.1 g, 2.3 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): d = 0.87 (t, J = 6.9 Hz, 6H), 1.18-1.32 (m, 20H), 1.36-1.45 (m, 4H), 2.44 - 2.52 (m, 4H), 3.69 (s, 6H), 3.51-3.58 (m, 4H), 3.60-3.71 (m, 28H), 4.46 (s, 4H), 7.17 (d, J = 5.3 Hz, 2H,), 7.33 ppm (d, J = 5.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): d = 14.2 ($2CH_3$), 22.7 ($2CH_2$), 28.0 ($2CH_2$), 29.2 ($4CH_2$), 29.8 ($2CH_2$), 30.7 ($2CH_2$), 31.9 ($2CH_2$), 59.1 ($2CH_3$), 67.0 ($2CH_2$), 69.6 ($2CH_2$), 70.6 ($2CH_2$), 70.7 ($2CH_2$), 70.7 ($2CH_2$), 70.7 ($6CH_2$), 72.0 ($2CH_2$), 126.0 (2CH), 128.5 (2CH), 128.8 (2C), 131.8 (2C), 138.3 (2C), 142.5 (2C) ppm; ESI-MS: *m/z* calcd for $C_{48}H_{80}O_{10}S_3$: 912.49 (mono-isotopic); found: 935.8 $[M+Na]^+$.

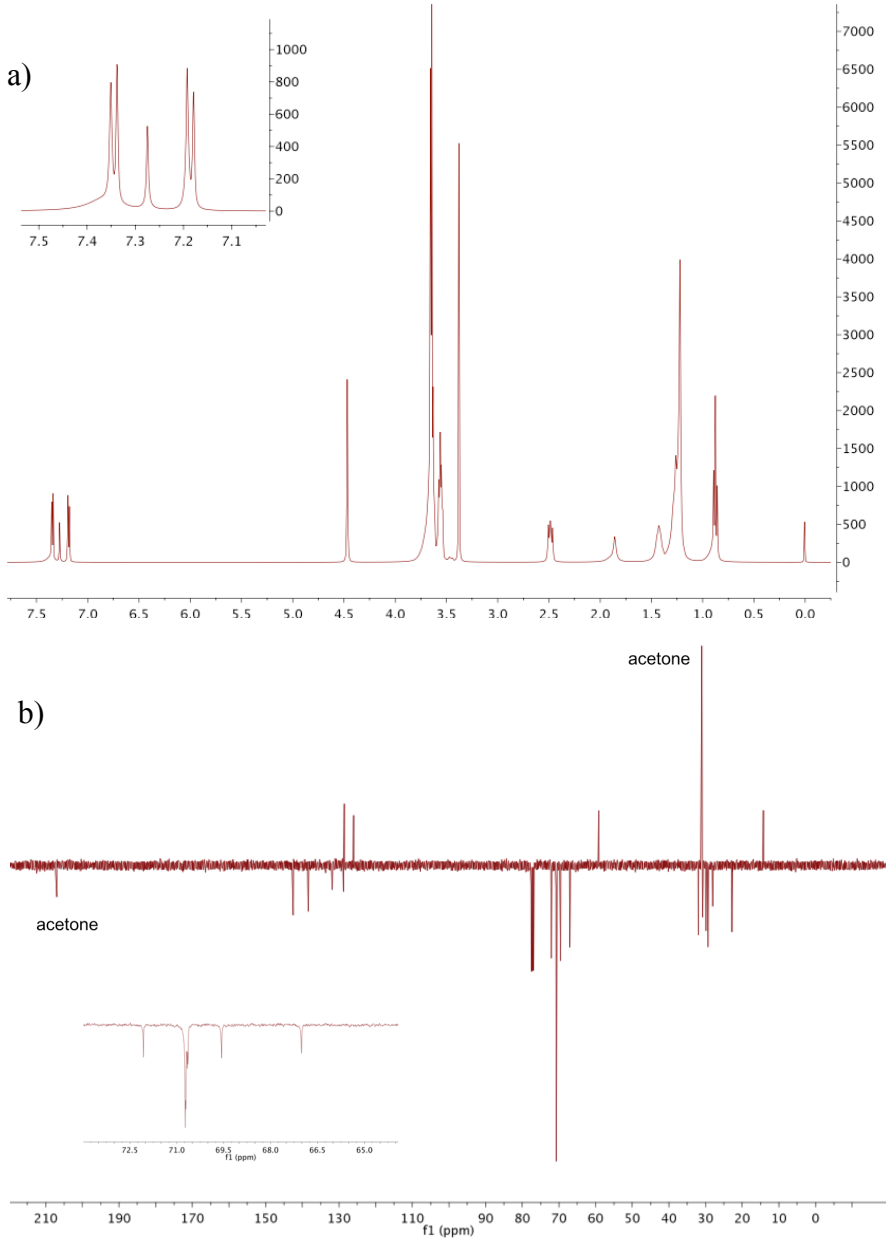


Figure S1. The NMR spectra of **3TSYM** in $CHCl_3$ of: (a) ^{1}H; (b) ^{13}C (APT).

Brominated **3TSYM** derivative **5** (1,1'-(5-bromo-3',4'-dioctyl-[2,2':5',2''-terthiophene]-3,3''-diyl)bis(2,5,8,11,14-pentaoxapentadecane).
N-Bromosuccinimide (0.35 g, 1.97 mmol) was added in 5 portions to a solution of **3TSYM** (1.8 g, 1.97 mmol) in anhydrous DMF (15 ml) over 2 h of time, in the dark. The mixture was stirred overnight and then quenched with 5% aqueous NaOH solution (10 ml). The crude mixture was then diluted with water (20 ml) and extracted with CH_2Cl_2. The organic phase was washed with water until the pH of aqueous washings became neutral. Then it was dried over $MgSO_4$ and the solvent was evaporated in vacuo. Compound **5** was obtained as a yellow oil in 95% yield (1.86 g, 1.90 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): d = 0.88 (t, J = 6.7, 6H), 1.18-1.32

(m, 20H), 1.36 -1.46 (m, 4H), 2.43 - 2.48 (m, 4H), 3.37 (s, 6H), 3.53-3.57 (m, 4H), 3.60-3.70 (m, 28H), 4.38 (s, 2H), 4.44 (s, 2H), 7.14 (s, 1H), 7.34 (d, J = 8.1 Hz, 1H,), 7.80 (d, J = 8.3 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): d = 14.3 ($2CH_3$), 22.9 ($2CH_2$), 27.9 ($2CH_2$), 29.3 ($4CH_2$), 29.9 ($2CH_2$), 30.8 ($2CH_2$), 31.9 ($2CH_2$), 59.1 ($2CH_3$), 66.6 ($2CH_2$), 67.0 ($2CH_2$), 69.6 ($2CH_2$), 69.6 ($2CH_2$), 70.6 ($6CH_2$), 72.0 ($2CH_2$), 126.2 (CH), 127.4 (C), 128.6 (CH), 129.4 (C), 131.3 (CH), 138.6 (C), 139.3 (C), 139.5 (C), 142.7 (C), 143.2 (C) ppm.

6TSYM (1,1',1"-(4"'-(2,5,8,11,14-pentaoxaheptadecyl)-3',3"",4',4""-tetraoctyl-[2,2':5',2":5",2"':5"',2"":5"",2""':5""',2""":sexithiophene]-3,3",3"""-triyl)tris(2,5,8,11,14-pentaoxapentadecane).
A solution of **5** (1.85 g, 1.87 mmol), bis(1,5-cyclooctadiene)nickel(0) (0.62 g, 2.24 mmol), 1,5-cyclooctadiene (0.2 g, 1.87 mmol) and 2,2'-bipyridine (0.35 g, 2.24 mmol) in 20 ml of anhydrous toluene was refluxed for 72h under nitrogen in a Schlenk tube. The reaction mixture was then cooled and the solvent was evaporated. The resulting oil was passed through a celite column. The solvent was then evaporated and the obtained dark brown oil was purified by size exclusion chromatography (Sephadex, THF). Compound **6TSYM** was obtained as a yellow oil in 20% yield (0.34 g, 0.18 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): d = 0.82 - 0.90 (m, 12H), 1.19-1.32 (m, 40H), 1.39 - 1.50 (m, 8H), 2.45 - 2.58 (m, 8H), 3.35 (s, 6H), 3.36 (s, 6H) 3.51 - 3.76 (m, 64H), 4.43 (s, 4H), 4.46 (s, 4H), 7.19 (d, J = 5.24 Hz, 2H), 7.25 (s, 2H), 7.34 (d, J = 5.26, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): d = 14.28 ($8CH_3$), 22.75 ($4CH_2$), 28.01 ($4CH_2$), 29.35 ($4CH_2$), 29.83 ($8CH_2$), 30.83 ($4CH_2$), 32.02 ($4CH_2$), 59.11 ($4CH_3$), 67.05 ($4CH_2$), 69.60 ($4CH_2$), 69.67 ($4CH_2$), 70.65 ($16CH_2$), 71.98 ($8CH_2$), 124.96 (2CH), 128.05 (2CH), 128.25 (2C), 128.97 (2C), 130.80 (2C), 137.06 (2C), 138.21 (2CH), 138.90 (2C) ppm; ESI- MS: *m/z* calcd. for $C_{96}H_{158}O_{20}S_6$: 1822.97 (mono-isotopic); found: 935.1 $[M+2Na]^{2+}$.

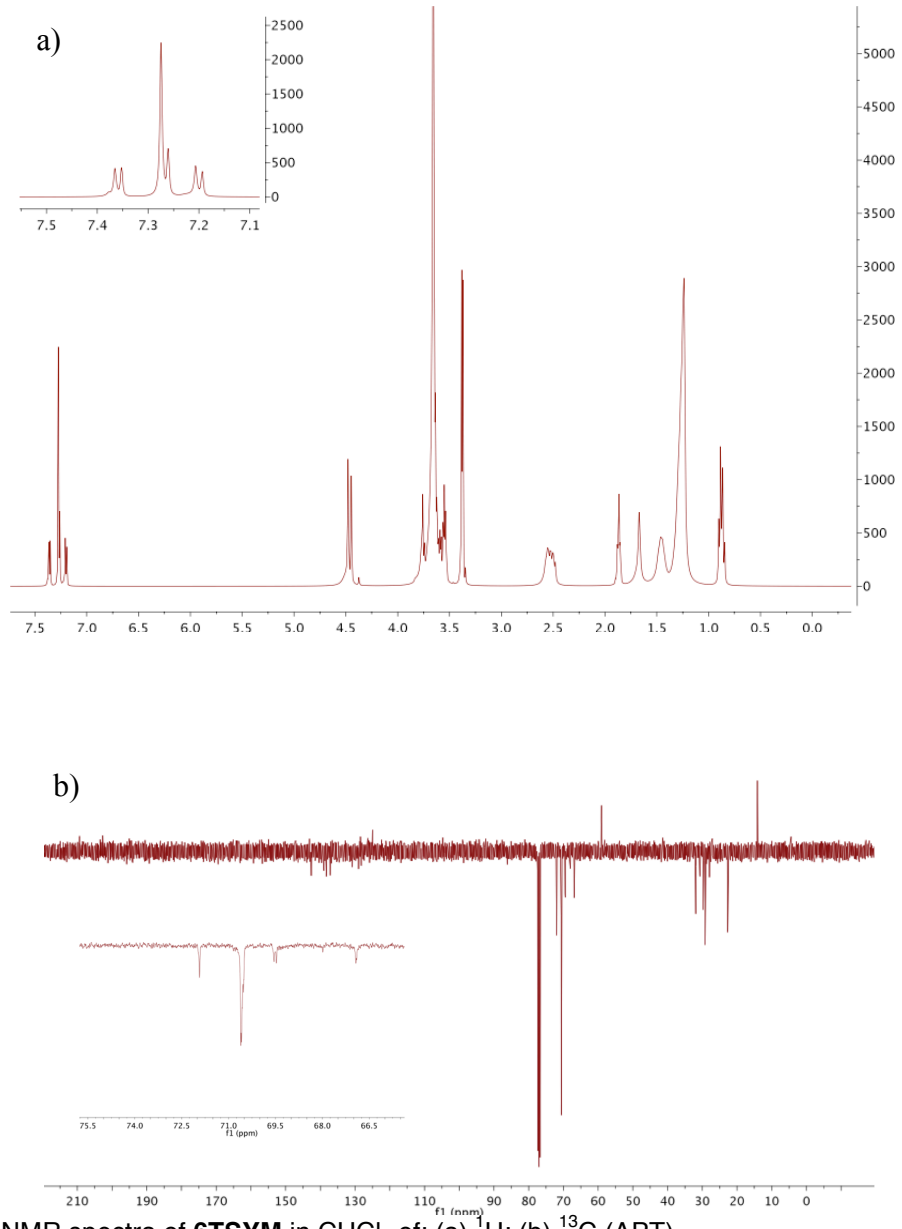


Figure S2. The NMR spectra of **6TSYM** in $CHCl_3$ of: (a) ^{1}H; (b) ^{13}C (APT).

DLS analysis

Critical aggregation concentrations of thiophenes **3TSYM** and **6TSYM** were measured by DLS. Plotting the scattered light intensity versus concentration results a curve with the sharp increase at the CAC, as larger aggregates scatter light much more efficiently than small molecules.

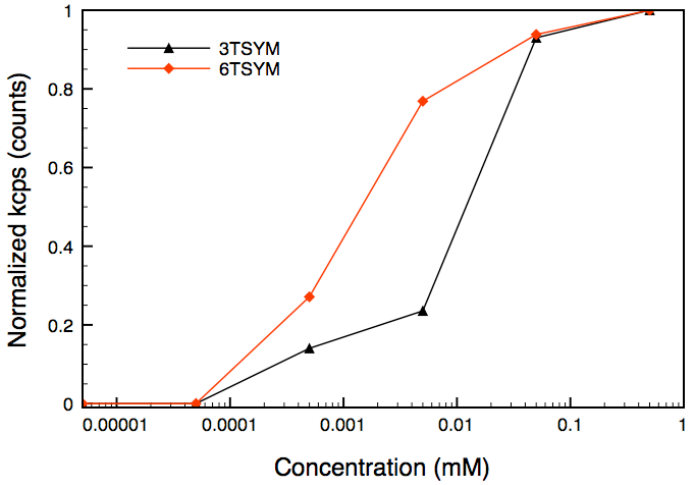


Figure S3. Concentration dependent scattering measurements of **3TSYM** and **6TSYM** in water at 20 ºC.

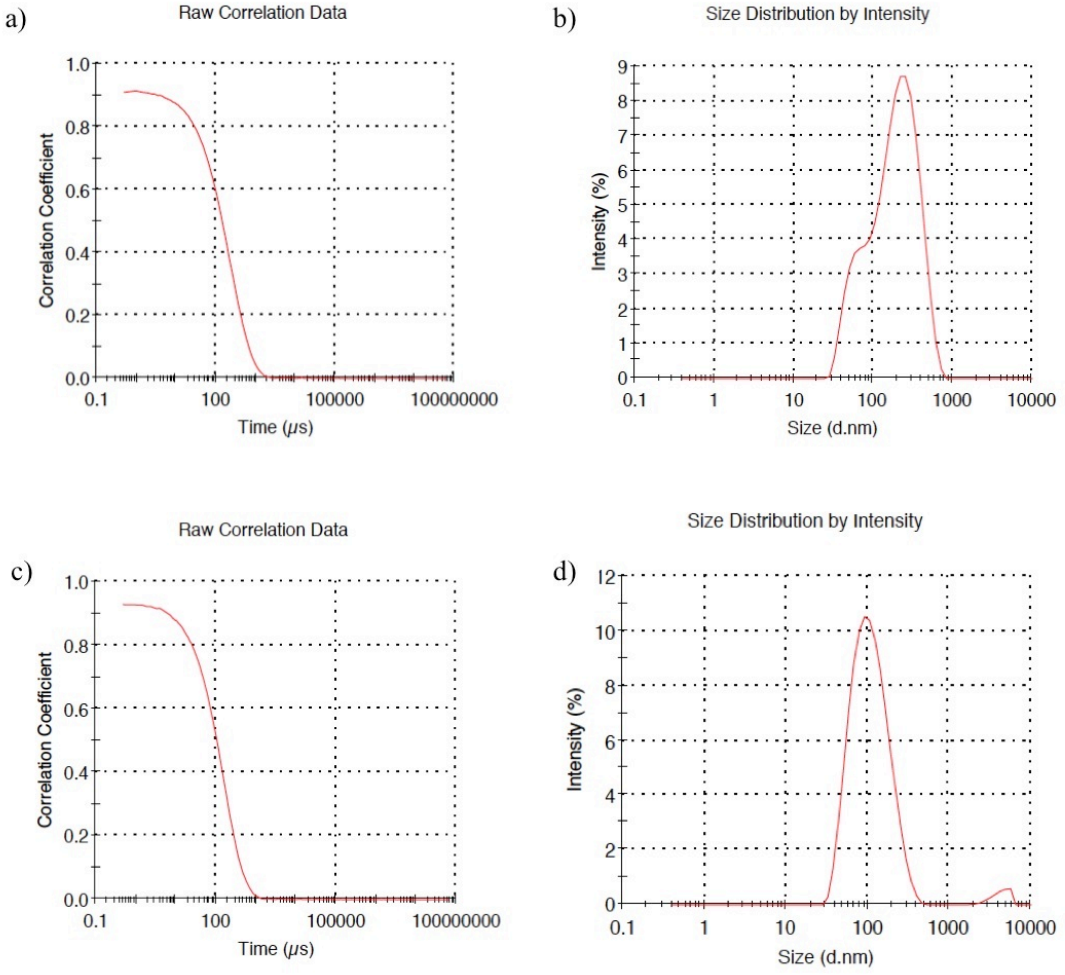


Figure S4. The DLS measurements of 0.5 mM aqueous solutions of: (a) and (b) **3TSYM**; (c) and (d) **6TSYM**. The measurements were performed at 20 ºC.

NR probe studies

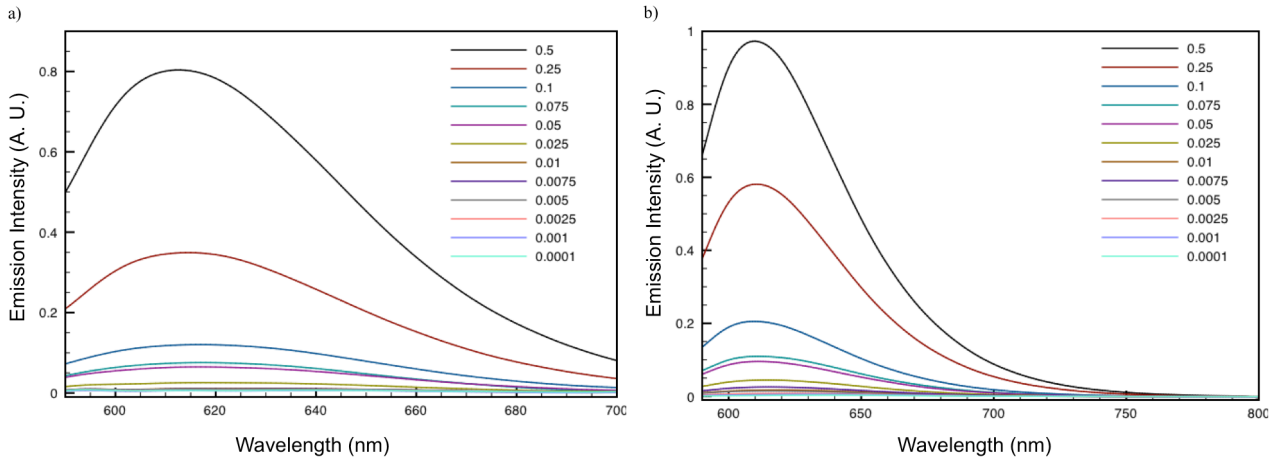


Figure S5. Emission spectra of 0.001 mM Nile Red probe solutions in different concentrations of (a) 3TSYM and (b) 6TSYM. The legends indicate the concentrations of **3** or **6** in mM. The measurements were performed at 20 ºC in water.

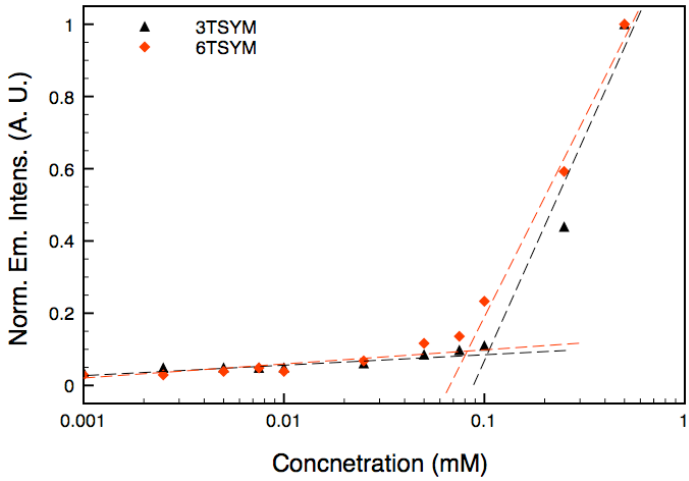


Figure S6. Determination of CAC of **3TSYM** and **6TSYM** with the use of Nile Red probe. The concentration where the intensity drastically increases is taken as a CAC.

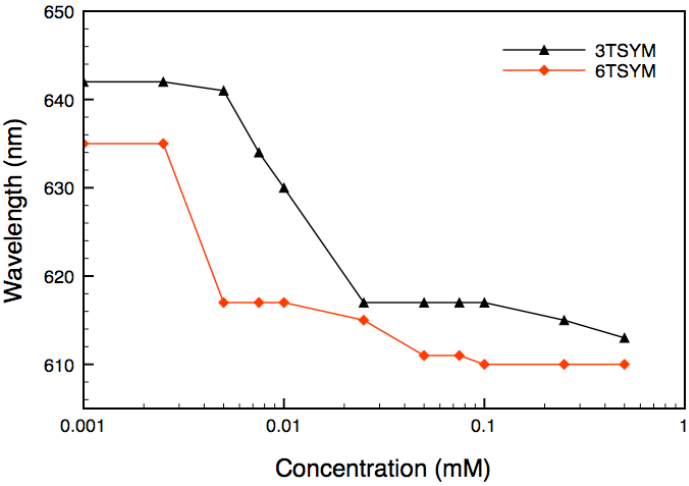


Figure S7. Dependence of the emission wavelength of Nile Red on the concentration of **3TSYM** or **6TSYM** (20 ºC in water).

Cloud point studies

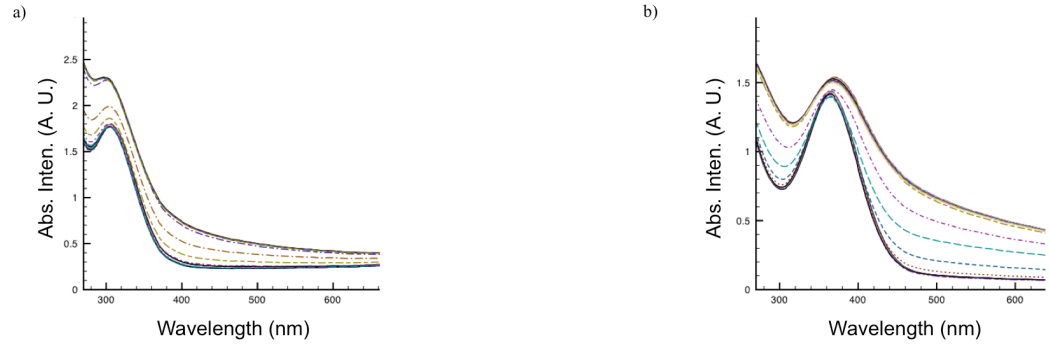


Figure S8. UV-vis absorption of **3TSYM** (a) and **6TSYM** (b) upon changing temperature (3→40 °C, UV-vis absorption plotted for every 1 °C of temperature), at 0.5 mM concentration in water.

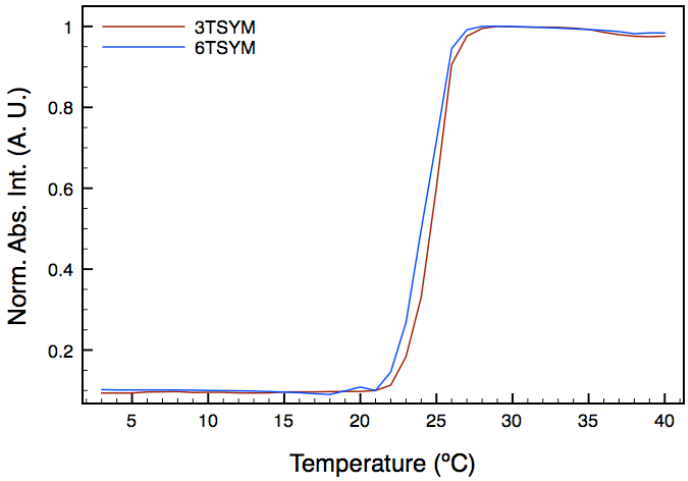


Figure S9. Normalized UV-vis absorption of **3TSYM** and **6TSYM** at 500 nm, upon changing temperature (3→40 °C), at 0.5 mM concentration in water.

DCS studies

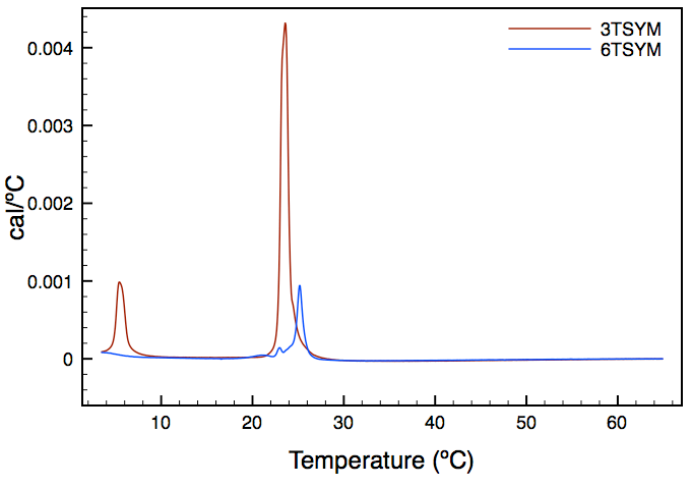


Figure S10. DSC curves of **3TSYM** and **6TSYM** at 1mM in water.

Solvent dependent UV-VIS spectroscopy

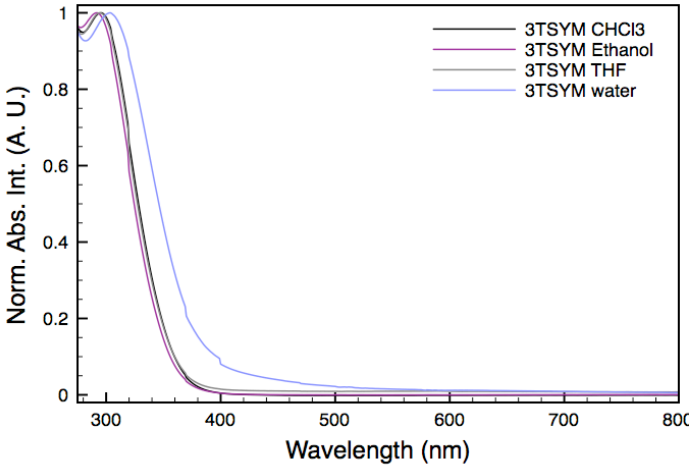


Figure S11. UV-vis absorption of **3TSYM** at 1mM in different solvents at 20 ºC.

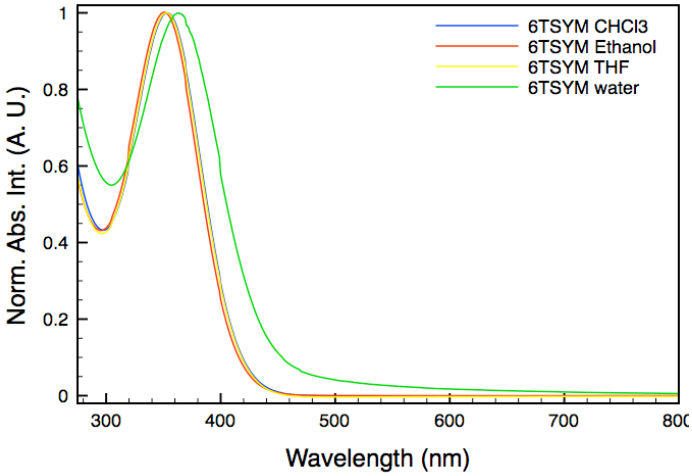


Figure S12. UV-vis absorption of **6TSYM** at 1mM in different solvents at 20 ºC.

PL self-quenching

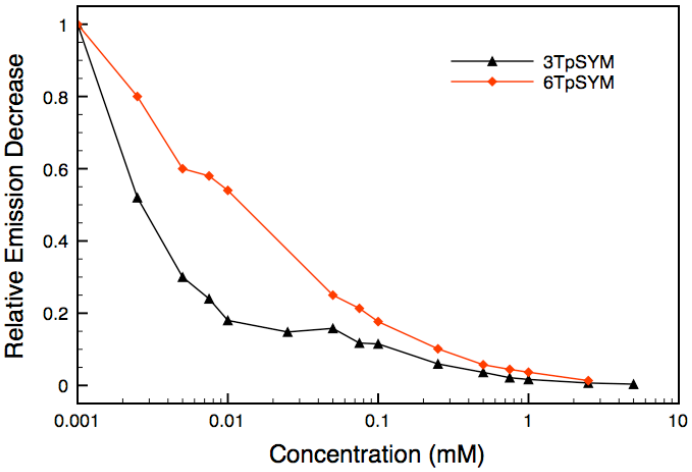


Figure S13. Photoluminescence self-quenching (PL) of **3TSYM** and **6TSYM** with increasing concentration, measured for the intensity at the emission maximum. The measurements were performed in water, at 20 ºC.

References

[i] M. Blouin, Y. Han, J. Burch, J. Farand, C. Mellon, M. Gaudreault, M. Wrona, J.-F. Lévesque, D. Denis, M.-C. Mathieu, R. Stocco, E. Vigneault, A. Therien, P. Clark, S. Rowland, D. Xu, G. O'Neill, Y. Ducharme and R. Friesen, *J. Med. Chem.* **2010**, *53*, 2227.

[ii] M. L. Navacchia, M. Melucci, L. Favaretto, A. Zanelli, M. Gazzano, A. Bongini, G. Barbarella, *Org. Lett.* **2008**, *10*, 3665.

[iii] S. Ko, E. Verploegen, S. Hong, R. Mondal, E. T. Hoke, M. F. Toney, M. D. McGehee, Z. Bao, *J. Am. Chem. Soc. 2011,* 133, 16722.

[iv] WO2009113314 (A1) — 2009-09-17

[v] H. Ajiro, Y. Takahashi, M. Akashi, *Macromolecules* **2012**, *45*, 2668.

[vi] C. T. Lee, W. T. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785-789.

[vii] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648-5652.

[viii] W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257.

[ix] M. M. Francl, W. J. Pietro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. Defrees, J. A. Pople, *J. Chem. Phys.* **1982**, *77*, 3654.

[x] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision A.02; Gaussian, Inc.: Wallingford CT, 2009.