Self-sorting in dynamic disulfide assembly: New biphenyl-bridged "nanohoops" and unsymmetrical cyclophanes

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SUPPORTING INFORMATION

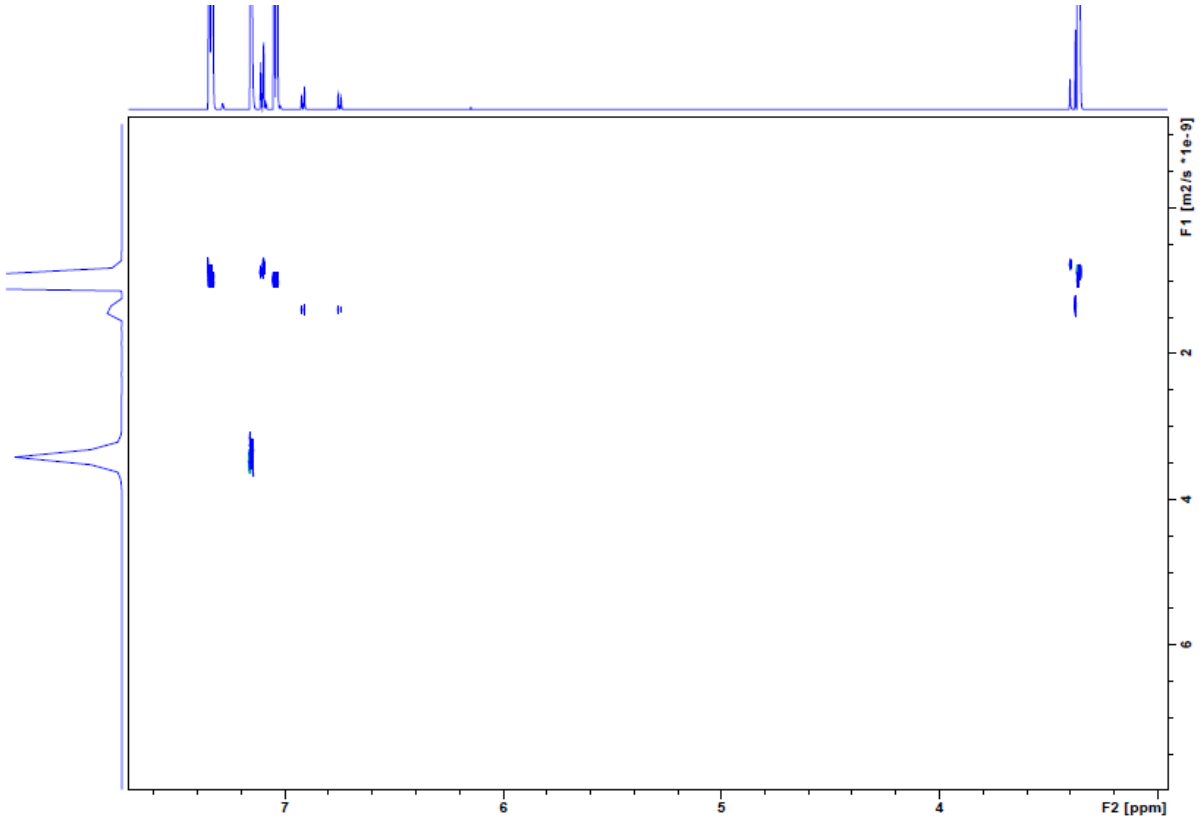

Figure S1: ^{1}H DOSY NMR of structures **1a-4a** ($CDCl_3$ – 7.26 ppm).

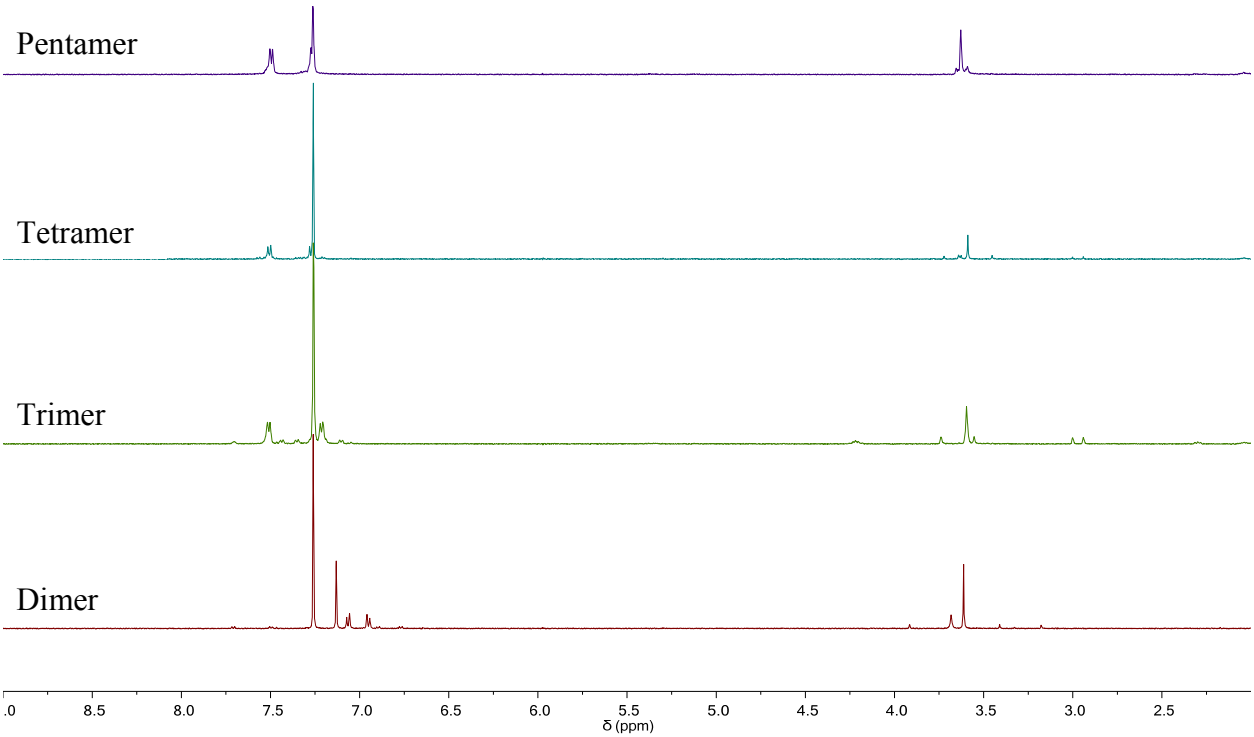

Figure S2: ^{1}H NMR of structures **1a-4a**: pentamer (top), tetramer, trimer and dimer (bottom) ($CDCl_3$ – 7.26 ppm).

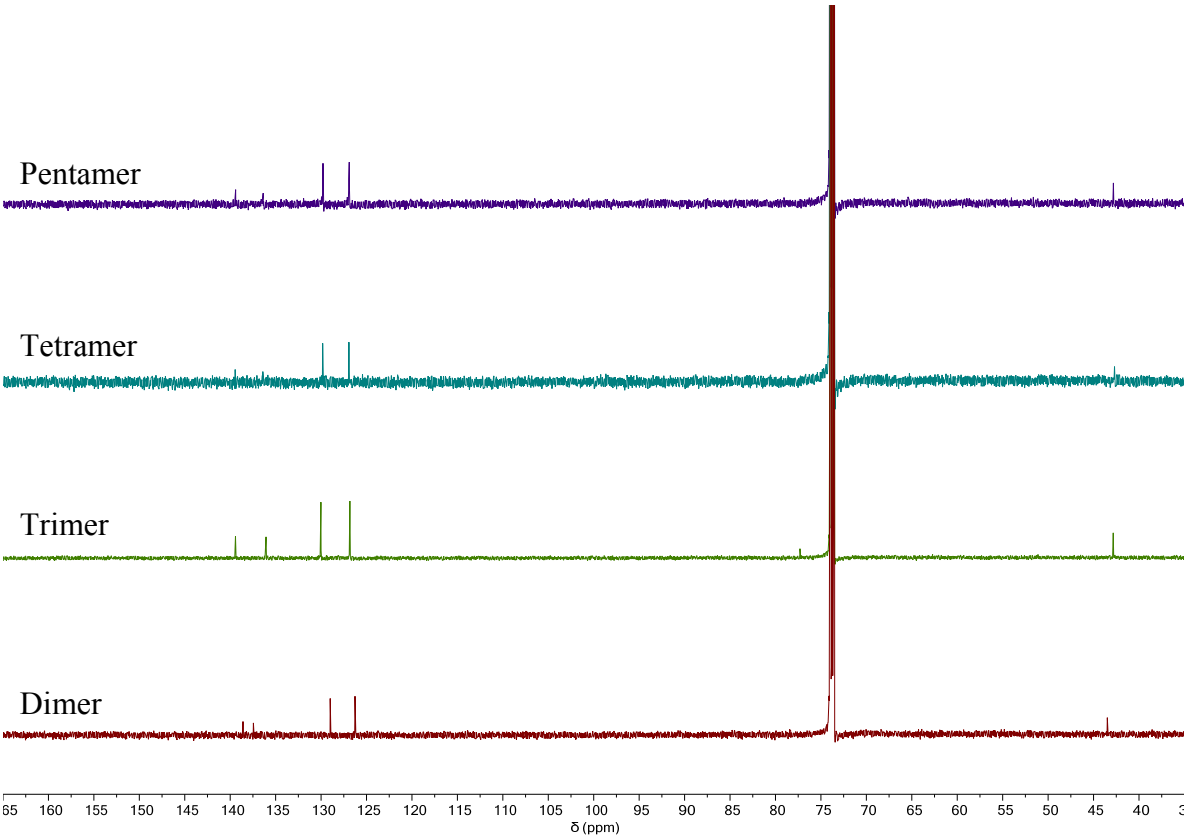

Figure S3: ^{13}C NMR of structures **1a-4a**: pentamer (top), tetramer, trimer and dimer (bottom) (TCE-d_2 – 73.78 ppm).

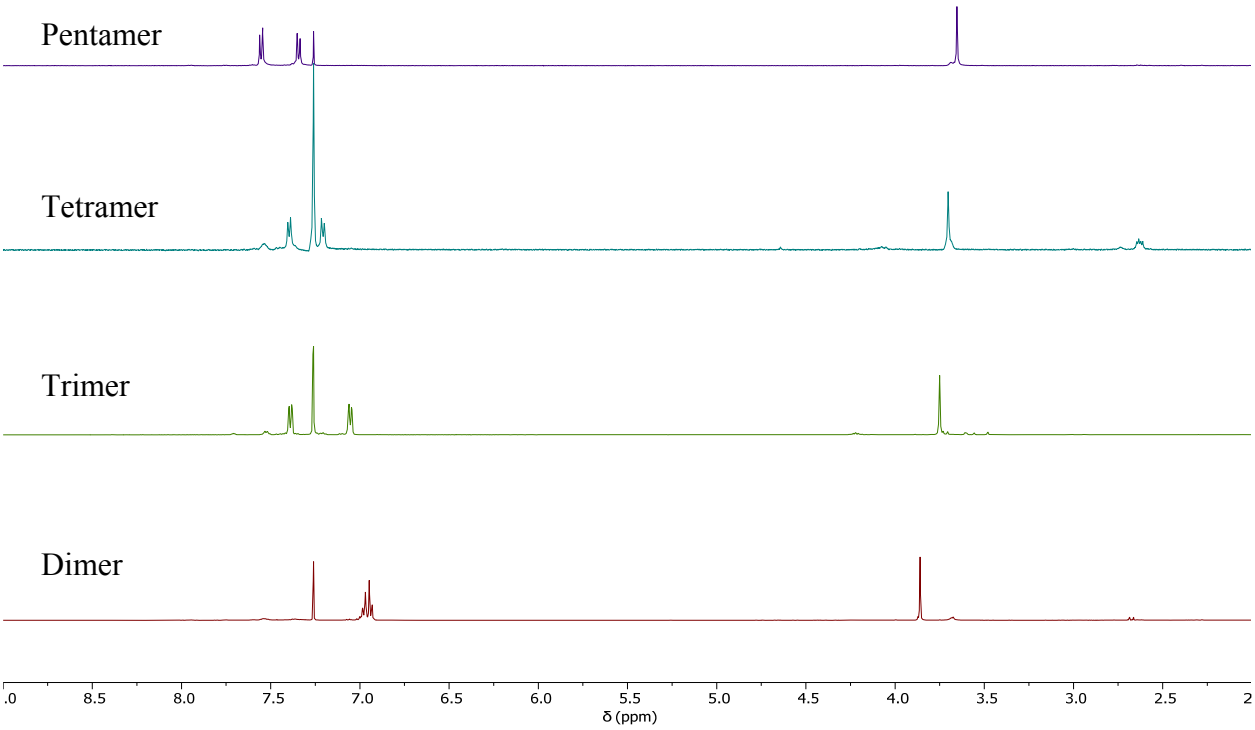

Figure S4: ^{1}H NMR of structures **1b**-**4b**: pentamer (top), tetramer, trimer and dimer (bottom) ($CDCl_3$ – 7.26 ppm).

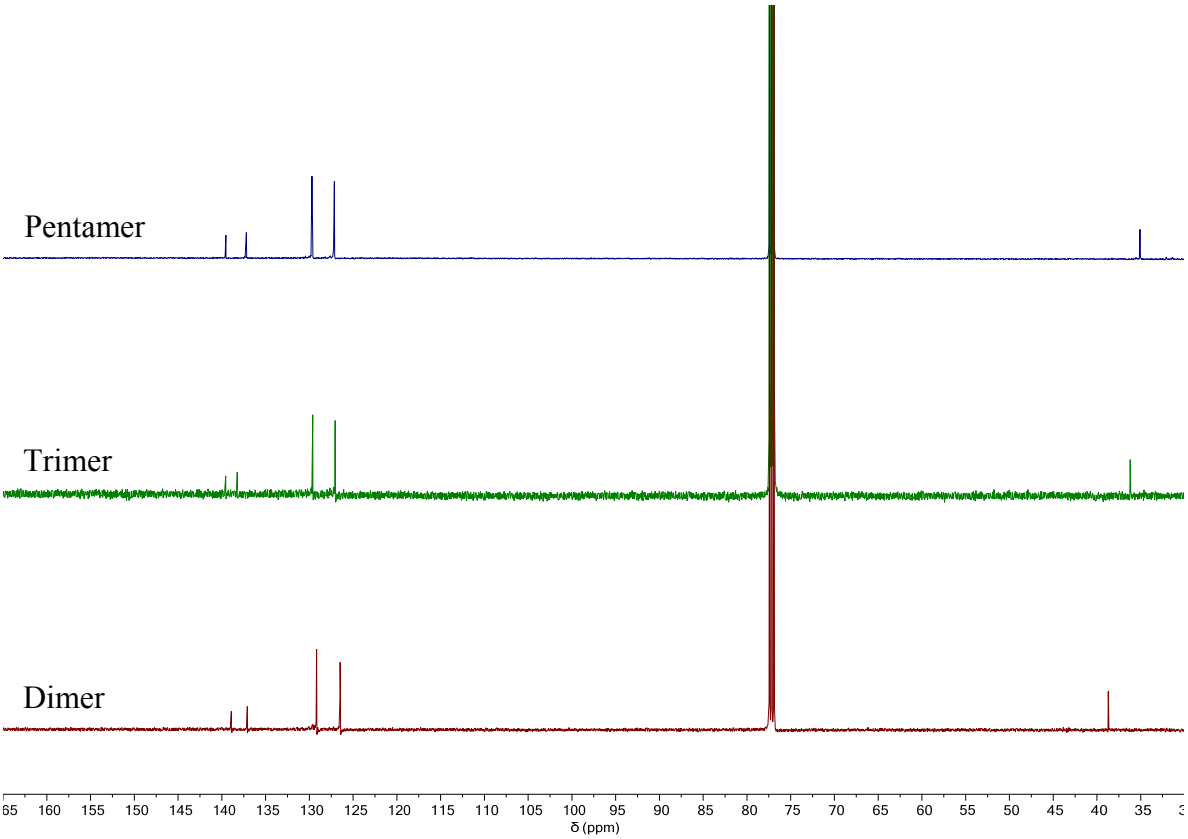

Figure S5: ^{13}C NMR of structures **1b-4b**: pentamer (top), trimer and dimer (bottom) ($CDCl_3$ – 77.16 ppm).

Table S1: Product distribution with excess amount of I_2 (4 eq)

Chloroform	Product Distribution			
Concentration (mM)	Dimer	Trimer	Tetramer	Pentamer
3	38	47	12	3
1	41	43	12	4
0.5	43	41	11	4
0.25	49	40	11	-
0.125	48	44	8	-

Toluene	Product Distribution			
Concentration (mM)	Dimer	Trimer	Tetramer	Pentamer
3	58	42	-	-
1	58	42	-	-
0.5	58	42	-	-
0.25	60	40	-	-
0.125	55	46	-	-

Table S2: Product distribution with different solvents (3 mM)

Solvent	Dimer	Trimer	Tetramer	Pentamer
Chloroform	33	47	15	4
Dichloromethane	11	64	17	6
Benzene	21	56	17	5
Toluene	30	66	3	-
Tetrachloroethane	12	75	13	-

Table S3: Concentration effect in different solvents (2 eq I_2)

Benzene	Product Distribution			
Concentration (mM)	Dimer	Trimer	Tetramer	Pentamer
3	21.5	56	17.5	5
1	30.5	47.5	17.5	4.5
0.5	42	43	15	
0.25	52	36.5	11.5	
0.125	69	31		

DCM	Product Distribution			
Concentration (mM)	Dimer	Trimer	Tetramer	Pentamer
3	17.5	61	16.5	5
1	24	57	14	5
0.5	30	53	12	5
0.25	39	44	11	6
0.125	49	42.5	8.5	-

Toluene	Product Distribution			
Concentration (mM)	Dimer	Trimer	Tetramer	Pentamer
3	36.5	59.5	4	-
1	58	40	2	-
0.5	76	24	-	-
0.25	79	21	-	-
0.125	87.5	12.5	-	-

TCE	Product Distribution			
Concentration (mM)	Dimer	Trimer	Tetramer	Pentamer
3	25	69	6	-
1	33	61.25	5.75	-
0.5	40.25	59.75	-	-
0.25	55.5	44.5	-	-
0.125	66	34	-	-

Steps to calculate statistical distribution:

1. Calculate the contribution of each type of macrocycle within its subset:
   Example calculation shown for dimers: chance of finding A = $\frac{1}{2}$
   chance of finding B = $\frac{1}{2}$

% AA: $\frac{1}{2}$ x $\frac{1}{2} = \frac{1}{4}$

% BB: $\frac{1}{2}$ x $\frac{1}{2} = \frac{1}{4}$

% AB: $\frac{1}{2}$ x $\frac{1}{2} = \frac{1}{4}$

% BA: $\frac{1}{2}$ x $\frac{1}{2} = \frac{1}{4}$

Since AB and BA are the same species, %AB = $\frac{1}{4} + \frac{1}{4} = \frac{1}{2}$

Do the same thing for trimers, tetramers and pentamers.

2. Calculate the total contribution of each subset:

Assume % total dimers = a, then % trimers = $\frac{2}{3}a$

% tetramers = $\frac{2}{4}a$

% pentamers = $\frac{2}{5}a$

Since the sum of all species is 100%, a must be 38.9%
Then % trimers = 26.0%; % tetramers = 19.5%; % pentamers = 15.6%.

3. Calculate the statistical yield of each species (= result from 1 x result from 2).

% AA = $\frac{1}{4}$ x 38.9% = 9.7%
% BB = $\frac{1}{4}$ x 38.9% = 9.7%
% AB = $\frac{1}{2}$ x 38.9% = 19.5%

Do the same thing for all 21 different species.

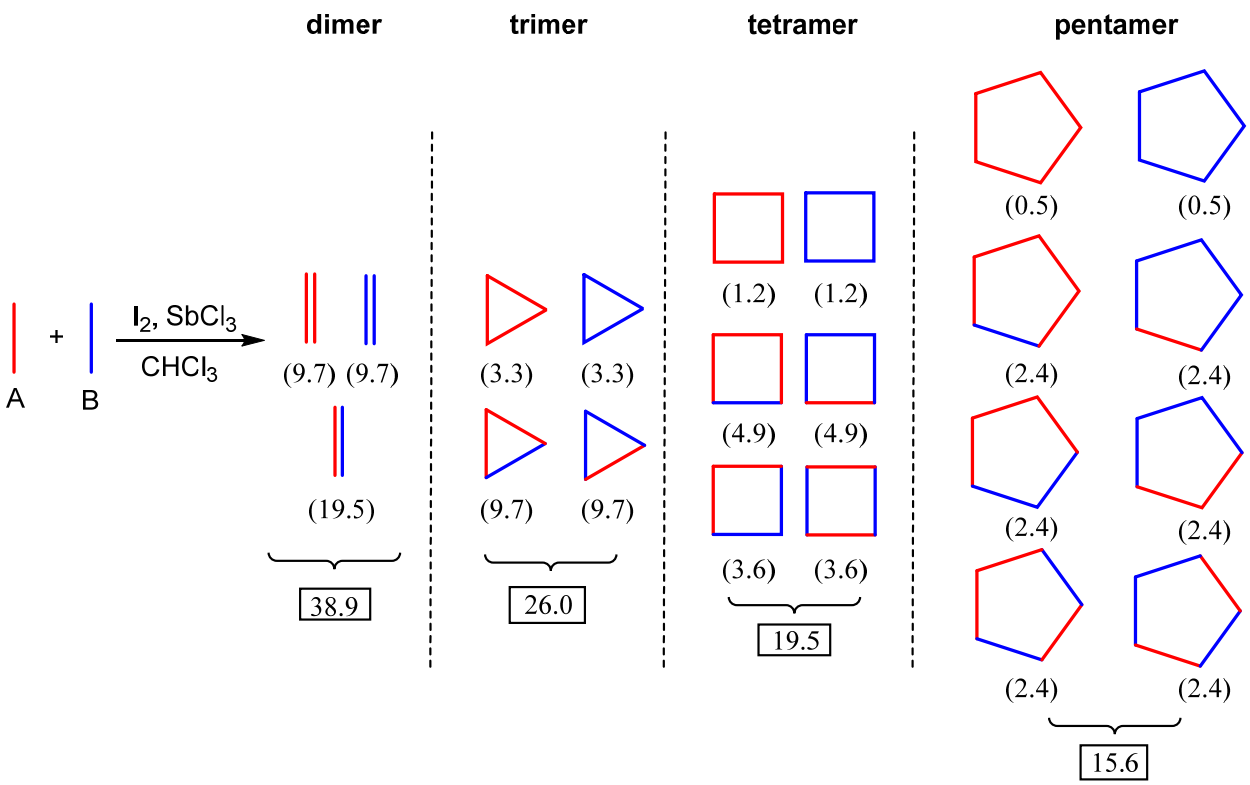

Figure S6: Statistical distribution of symmetric and unsymmetrical species when A:B = 1:1.

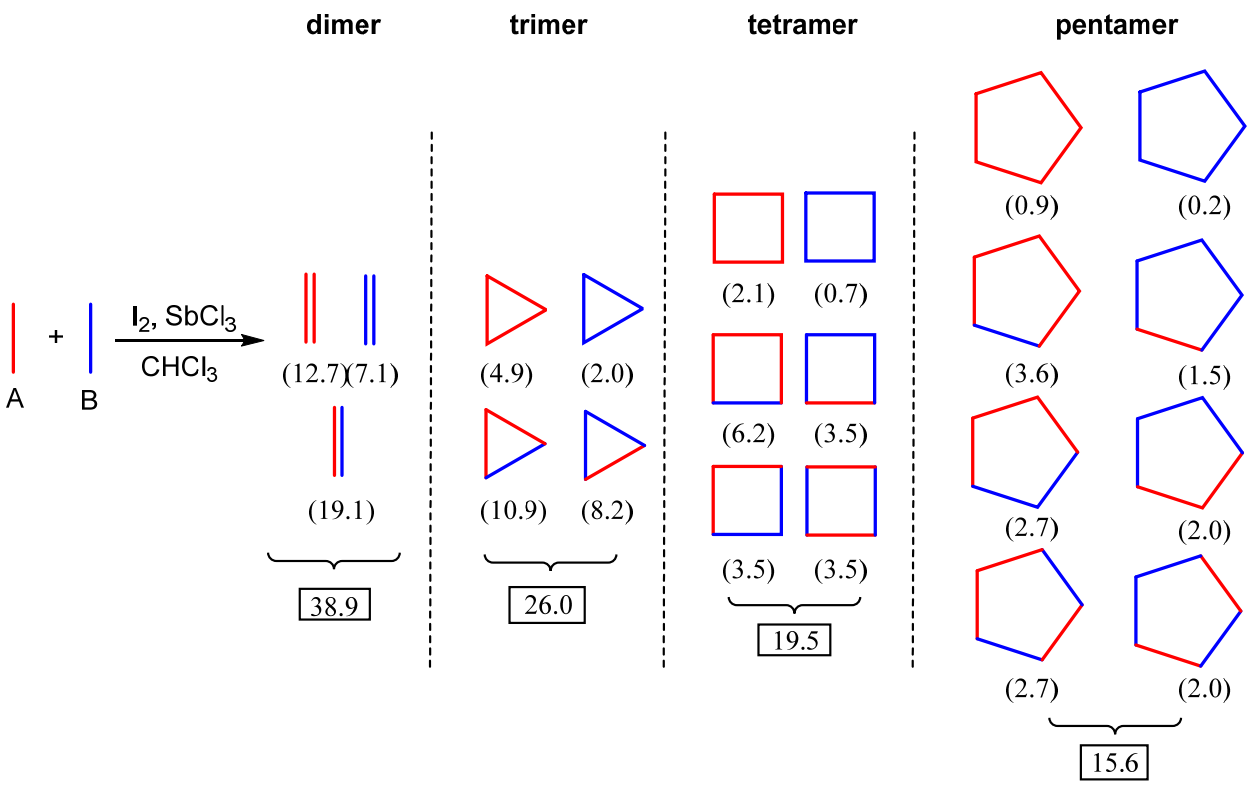

Figure S7: Statistical distribution of symmetric and unsymmetrical species when A:B = 4:3.

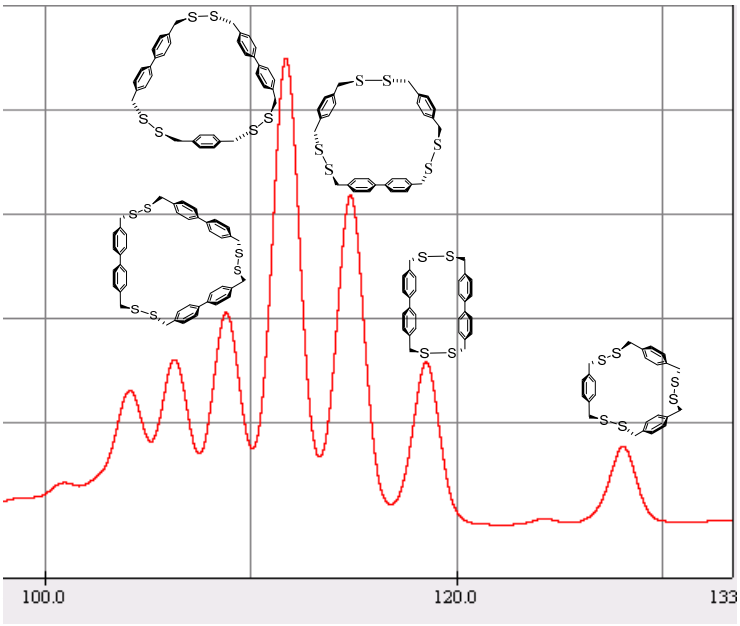

Figure S8: Gel permeation chromatogram (GPC) of different-sized disulfides. The smallest five species contribute to 90% yield of the reaction; the remaining 10% yield comes from oligomers/polymers.

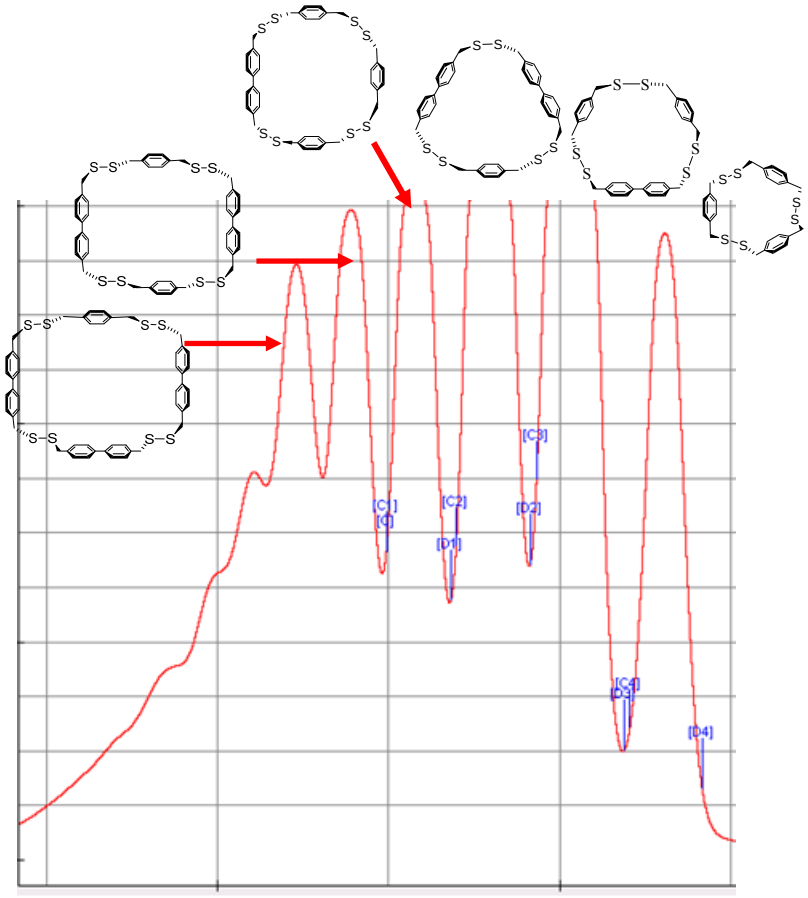

Figure S9: GPC diagram of optimized condition for unsymmetrical trimers **5a** and **6a**. This condition also gives the unsymmetrical tetramers.

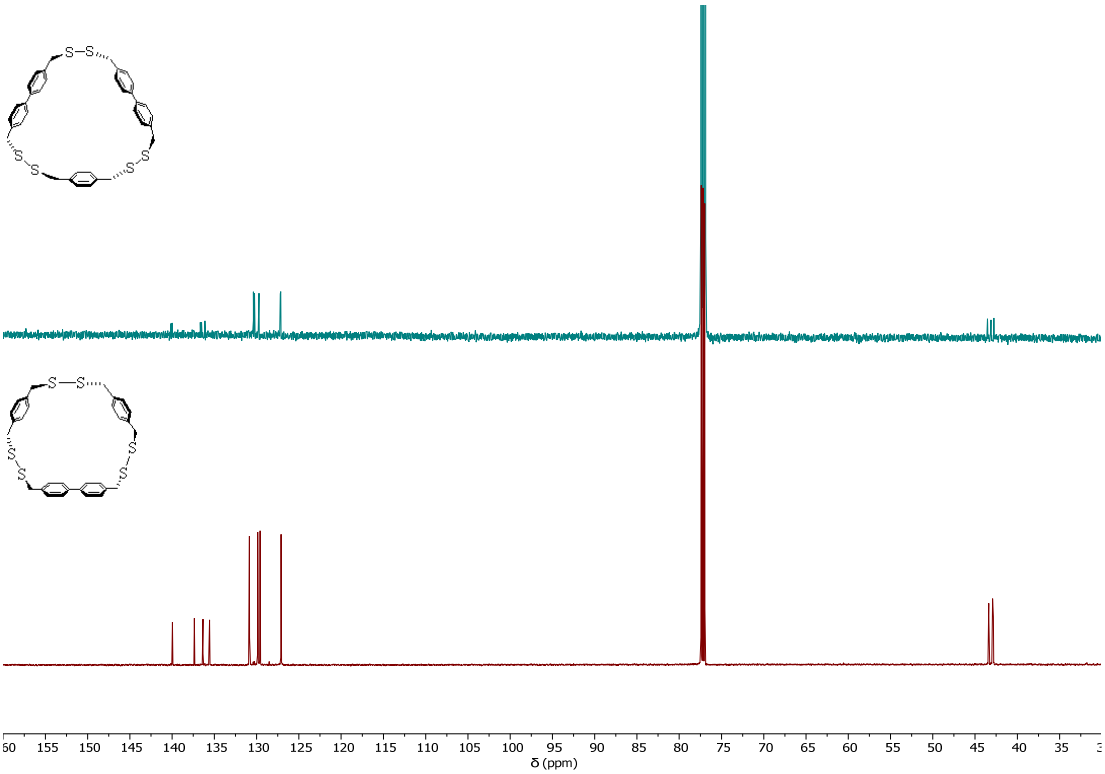

Figure S10: ^{13}C NMR of structures **5a-6a** ($CDCl_3$ – 77.16 ppm).

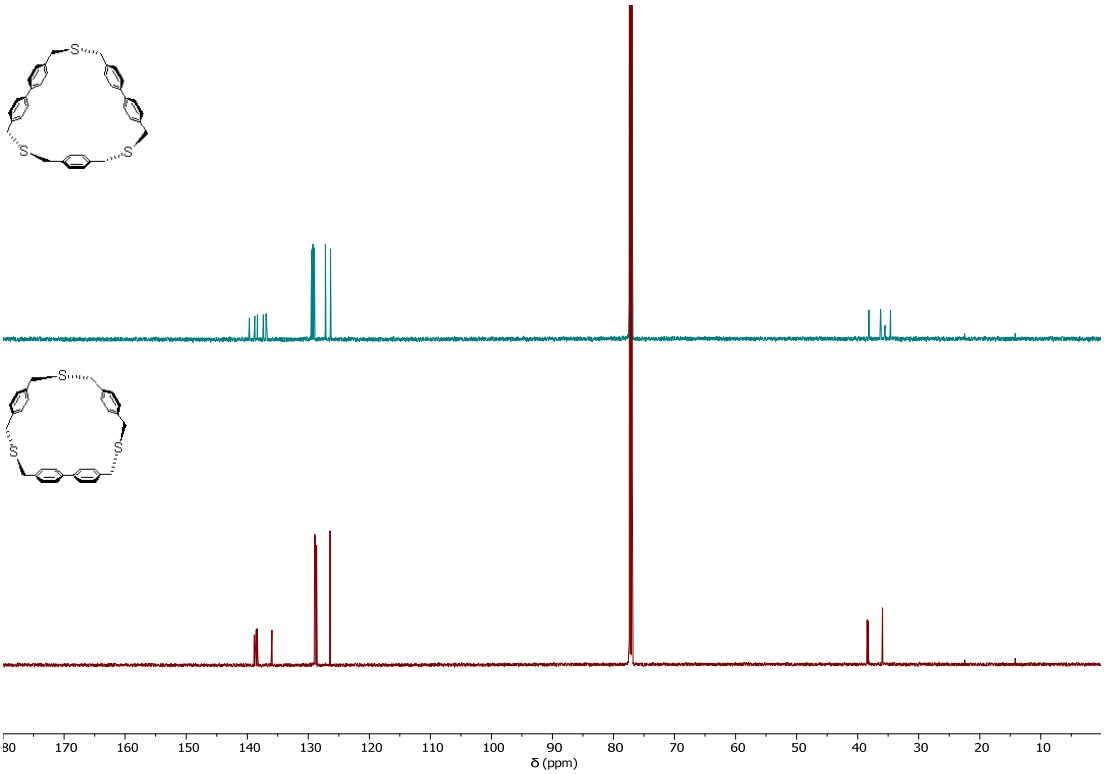

Figure S11: ^{13}C NMR of structures **5b-6b** ($CDCl_3$ – 77.16 ppm).

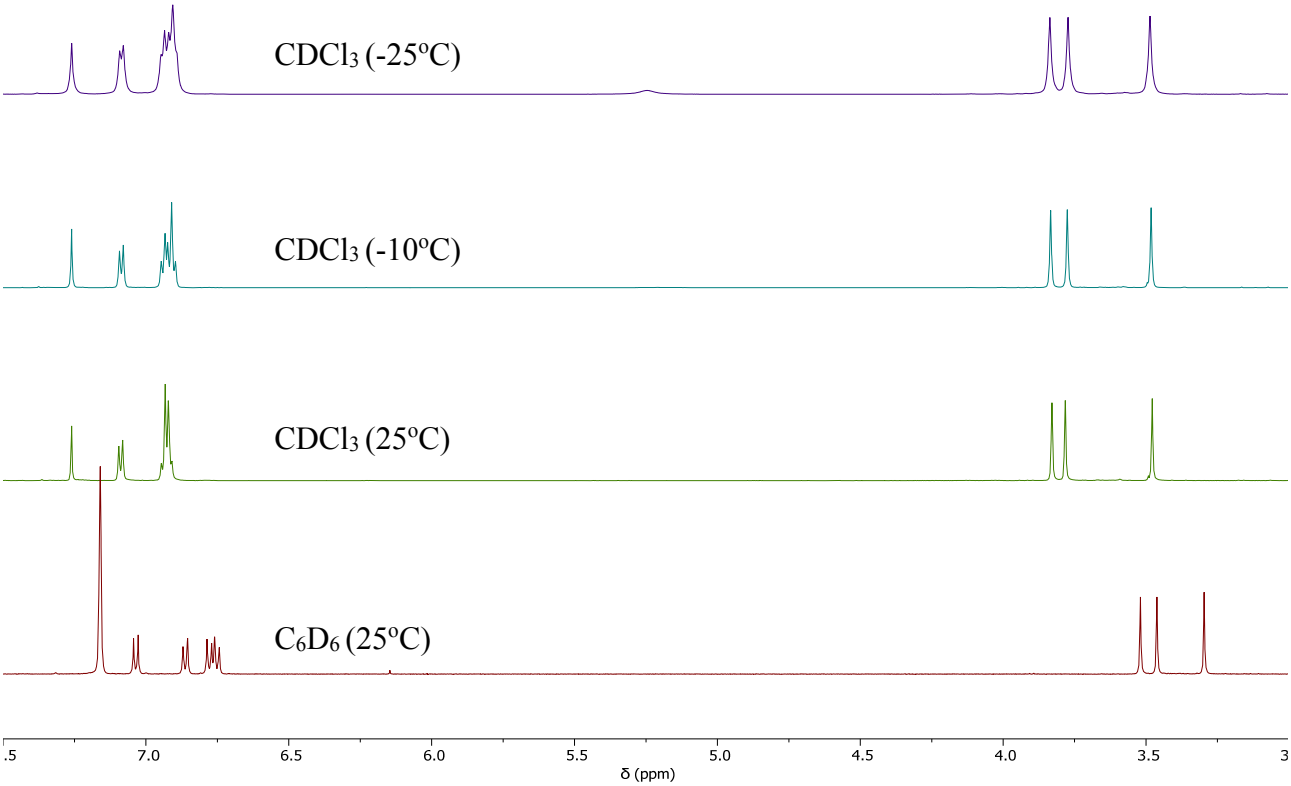

Figure S12: Solvent effect for compound **5b**: aromatic signals coalesce in $CDCl_3$ while they are more spread out in C_6D_6. The spacing between the methylene signals is also closer in C_6D_6.

General procedure

Synthesis of biphenyl-based disulfides structures **1a-4a**

In a 250 mL round bottom flask, ligand B (148 mg, 0.60 mmol) and I_2 (427 mg, 1.68 mmol) were added in 100 mL chloroform. $SbCl_3$ (109 mg, 0.48 mmol) was added to the flask and the dark purple solution was stirred for 16 hours at room temperature. Reaction was quenched with saturated sodium sulfite and the organic layer was washed with deionized water (2X). The solution was dried with $MgSO_4$, filtered and concentrated. The powder was then redissolved in 3 mL of chloroform and purified by GPC (65% combined yield: 20% dimer; 32% trimer, 11% tetramer; 2% pentamer). ^{1}H NMR (500 MHz, $CDCl_3$): dimer: δ = 7.13 (s, 8H, C_6H_2), 7.06 (d, 4H, C_6H_2), 6.96 (d, 4H, C_6H_2) 3.68 (s, CH_2), 3.61(s, CH_2); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ = 138.60, 137.46, 129.00, 126.27, 43.49 ppm; trimer: δ = 7.50 (d, 12H, C_6H_2), 7.22 (d, 12H, C_6H_2), 3.60 (s, 12H, CH_2); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ = 139.42, 136.06, 130.03, 126.83, 42.85 ppm; tetramer: δ = 7.50 (d, 16H, C_6H_2), 7.28 (d, 16H, C_6H_2), 3.59 (s, 16H, CH_2); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ = 139.47, 136.41, 129.83, 126.94, 42.70 ppm; pentamer: δ = 7.49 (d, 20H, C_6H_2), 7.27 (d, 20H, C_6H_2), 3.63 (s, 12H, CH_2); ^{13}C{^{1}H}NMR (125 MHz, $CDCl_3$): δ = 139.41, 136.38, 129.79, 126.91, 42.82 ppm.

Synthesis of biphenyl-based thioethers structures **1b-4b**

An oven-dried 250 mL round bottom flask was charged with the mixture of compound **1a-4a** in dried chloroform (100 mL). The solution was sparged with N_2 for 25 minutes. HMPT (240 µL, 1.30 mmol) was added to the flask and the reaction was allowed to go for 2 days at 60ºC with gentle stirring. The solution was then washed with deionized water and concentrated to give a slightly yellow solid. The solid was sonicated in methanol and filtered through a filter paper. The solid was dissolved in 3 mL of chloroform and purified by GPC (50% combined yield: 10% dimer; 28% trimer, 10% tetramer; 2% pentamer). ^{1}H NMR (500 MHz, $CDCl_3$): dimer: δ = 6.97 (d, 8H, C_6H_2), 6.95 (d, 8H, C_6H_2), 3.86 (s, 8H, CH_2), ^{13}C{^{1}H}NMR (500 MHz, $CDCl_3$): δ = 138.92, 137.08, 129.17, 126.48, 38.71 ppm; trimer: δ = 7.38 (d, 12H, C_6H_2), 7.06 (d, 12H, C_6H_2), 3.75 (s, 12H, CH_2); ^{13}C{^{1}H}NMR (500 MHz, $CDCl_3$): δ = 139.56, 138.25, 129.61, 127.05, 36.20 ppm; tetramer: δ = 7.39 (d, 16H, C_6H_2), 7.22 (d, 16H, C_6H_2), 3.70 (s, 16H, CH_2); pentamer: δ = 7.55 (d, 20H, C_6H_2), 7.35 (d, 20H, C_6H_2), 3.65 (s, 12H, CH_2); ^{13}C{^{1}H}NMR (500 MHz, $CDCl_3$): δ = 139.53, 137.20, 129.71, 127.14, 35.08 ppm.

Product distribution of **1a-4a** in different solvents

In a 20 mL scintillation vial, 6.6 mg of ligand B (0.027 mmol) was added to 13.63 mg of I_2 (0.054 mmol) and 12.18 mg of $SbCl_3$ (0.054 mmol) in 4.47 mL $CDCl_3$ (6 mM solution). Serial dilutions were conducted until a concentration of 0.125 mM was reached. The reactions were allowed to proceed overnight and the solutions in each vial were analyzed through ^{1}H NMR spectroscopy to determine the product distribution. This procedure was repeated using C_6D_6, CD_2Cl_2, $C_2D_2Cl_4$, and $C_6D_6CD_3$.

Synthesis of disulfides in a "mixed" ligands system

In a 250 mL round bottom flask, ligand A (68 mg, 0.40 mmol), ligand B (73.8 mg, 0.30 mmol) and I_2 (1.42 g, 5.60 mmol) were added in 100 mL chloroform. $SbCl_3$ (319 mg, 1.40 mmol) was added to the flask and the black solution was stirred for 4 hours at room temperature. Reaction

was quenched with saturated sodium sulfite and the organic layer was washed with deionized water (2X). The solution was dried with $MgSO_4$, filtered and concentrated. The powder was then redissolved in 3 mL of chloroform (some insoluble solids that were probably polymers), filtered through a 0.45 µm PTFE membrane and purified by GPC (quantitative yield: 28% **6a**, 37% **5a**, 15% trimer AAA, remaining yield is contributed by unsymmetrical tetramers). ^{1}H NMR (500 MHz, $CDCl_3$):

- Compound **5a**: δ = 7.71 (d, 4H, C_6H_2, J = 8.0 Hz), 7.51 (d, 4H, C_6H_2, J = 8.0 Hz), 6.90 (d, 4H, C_6H_2, J = 8.0 Hz), 6.79 (d, 4H, C_6H_2, J = 8.0 Hz), 3.92 (s, 4H, CH_2), 3.42 (s, 4H, CH_2), 3.19 (s, 4H, CH_2); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 139.93, 137.34, 136.32, 135.54, 130.83, 129.84, 129.57, 127.08, 43.36, 42.90, 42.81 ppm.
- Compound **6a**: δ = 7.49 (d, 4H, C_6H_2, J = 8.0 Hz), 7.46 (d, 4H, C_6H_2, J = 8.0 Hz), 7.28 (d, 4H, C_6H_2, J = 8.0 Hz), 7.14 (d, 4H, C_6H_2, J = 8.0 Hz), 7.09 (s, 4H, CH_2), 3.68 (s, 4H, CH_2), 3.63 (s, 4H, CH_2), 3.45 (s, 4H, CH_2); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 140.14, 139.99, 136.66, 136.52, 136.12, 130.38, 130.26, 129.72, 127.20, 127.14, 43.53, 43.12, 42.77 ppm.

Synthesis of compound **5b**

An oven-dried NMR tube was charged with **5a** (28.7 mg, 0.049 mmol) in dried $CDCl_3$ (1 mL). Under a cone of nitrogen, HMPT (120 µL, 0.652 mmol) was added to the NMR tube and the tube was inverted gently several times to mix. The reaction was allowed to sit at ambient temperature for 2 hours. The solution was then washed with deionized water and concentrated to give a white solid. The solid was sonicated in methanol and filtered through a filter paper. The undissolved solid was retrieved from the paper by chloroform giving 10 mg of the product **5b** (42% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.08 (d, 4H, C_6H_2, J = 8.4 Hz), 6.91-6.95 (m, 12H, C_6H_2), 3.83 (s, 4H, CH_2), 3.78 (s, 4H, CH_2), 3.48 (s, 4H, CH_2); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 138.85, 138.52, 138.38, 135.96, 128.95, 128.86, 128.63, 126.45, 38.44, 38.24, 35.94 ppm.

Synthesis of compound **6b**

An oven-dried NMR tube was charged with **6a** (14.6 mg, 0.022 mmol) in dried $CDCl_3$ (800 µL). Under a cone of nitrogen, HMPT (54 µL, 0.294 mmol) was added to the NMR tube and the tube was inverted gently several times to mix. The reaction was allowed to sit at ambient temperature for 2 hours. The solution was then washed with deionized water and concentrated to give a white solid. The solid was sonicated in methanol and filtered through a filter paper. The undissolved solid was retrieved from the paper by chloroform, giving 5.7 mg of the product **6b** (46% yield). Crystals were grown by slow evaporation of chloroform. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.24 (s, 4H, C_6H_4), 7.15 (d, 4H, C_6H_2, J = 8.4 Hz), 7.04 (d, 4H, C_6H_2, J = 8.4 Hz), 6.97 (d, 4H, C_6H_2, J = 7.8 Hz), 6.95 (d, 4H, C_6H_2, J = 7.8 Hz), 3.82 (s, 4H, CH_2), 3.72 (s, 4H, CH_2), 3.59 (s, 4H, CH_2); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 139.66, 138.75, 138.33, 137.37, 136.92, 129.45, 129.25, 129.00, 127.20, 126.37, 38.15, 36.23, 34.61 ppm.

X-ray Crystallography. Diffraction intensities for **CCDC 1884074-1884077 DWJRR205**, **DWJ239**, **DWJR242** and **DWJRR244** were collected at 173 K and at 120 K (**CCDC 1884074**) on a Bruker Apex2 CCD diffractometer using CuKα radiation, λ= 1.54178 Å. Space groups were determined based on systematic absences and intensity statistics (**CCDC 1884076**). Absorption corrections were applied by SADABS[*]. Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms in all structures were refined in calculated positions in a rigid group model. Crystals of the investigated compounds are formed as small thin needles and give weak X-ray diffraction at high angles. Even using a strong *Incoatec* IμS Cu source for **1884074,** it was possible to collected data only up to $2\theta_{max}$ = 89.06° and 99.56°, respectively. Thus resolution for these structures is low, but the found structures clear shown the structure and composition of the compound. One of two solvent molecules $CHCl_3$ in **1884074** is highly disordered in a general position and around an inversion center, respectively. These disordered solvent molecules were treated by SQUEEZE[**]. The corrections of the X-ray data by SQUEEZE are 228 electron/cell; the required values are 232 electron/cell for four $CHCl_3$ molecules in **1884074**. **1884074** structure was refined with using RIGU options in SHELXL. It was found that the needle crystal of **1884075** used for data collection is a twin consisting of two domains with ratio 0.31/0.69. The structure of **1884077** was determined in chiral space group symmetry $P2_12_12_1$ with the Flack parameter is 0.04(2). All calculations were performed by the Bruker SHELXL-2014 package [***].

Crystallographic Data for **1884074**: $C_{44}H_{38}Cl_6S_3$, M = 875.62, 0.12 x 0.02 x 0.015 mm, T = 120(2) K, Monoclinic, space group $P2_1/c$, a = 20.8036(11) Å, b = 5.6365(4) Å, c = 35.382(2) Å, β = 93.946(4)°, V = 4139.0(4) Å^3, Z = 4, D_c = 1.405 Mg/m^3, μ(Cu) = 5.444 mm^{-1}, F(000) = 1808, $2\theta_{max}$ = 89.06°, 11110 reflections, 3149 independent reflections [R_{int} = 0.0651], R1 = 0.1221, wR2 = 0.3368 and GOF = 1.043 for 3149 reflections (450 parameters) with I>2σ(I), R1 = 0.1637, wR2 = 0.3632 and GOF = 1.075 for all reflections, max/min residual electron density +0.416/-0.382 eÅ^{-3}.

Crystallographic Data for **1884075**: $C_{28}H_{24}S_2$, M = 424.59, 0.07 x 0.04 x 0.04 mm, T = 173(2) K, Monoclinic, space group $P2_1/c$, a = 20.9413(14) Å, b = 13.7902(11) Å, c = 14.7593(12) Å, β = 90.050(6)°, V = 4262.3(6) Å^3, Z = 8, Z'=2, D_c = 1.323 Mg/m^3, μ(Cu) = 2.341 mm^{-1}, F(000) = 1792, $2\theta_{max}$ = 133.14°, 35340 reflections, 7416 independent reflections [R_{int} = 0.0761], R1 = 0.0646, wR2 = 0.1558 and GOF = 1.026 for 7416 reflections (542 parameters) with I>2σ(I), R1 = 0.0804, wR2 = 0.1681 and GOF = 1.026 for all reflections, max/min residual electron density +0.853/-0.299 eÅ^{-3}.

Crystallographic Data for **1884076**: $C_{30}H_{28}S_6$, M = 580.88, 0.06 x 0.04 x 0.02 mm, T = 173(2) K, Triclinic, space group P-1, a = 10.1303(4) Å, b = 12.8333(5) Å, c = 22.9283(11) Å, α = 77.847(3)°, β = 83.562(4)°, γ = 78.309(2)°, V = 2846.0(2) Å^3, Z = 4, Z'=2, D_c = 1.356 Mg/m^3, μ(Cu) = 4.573 mm^{-1}, F(000) = 1216, $2\theta_{max}$ = 133.70°, 41027 reflections, 9869 independent reflections [R_{int} =

0.0623], R1 = 0.0561, wR2 = 0.1562 and GOF = 1.033 for 9869 reflections (674 parameters) with I>2σ(I), R1 = 0.0755, wR2 = 0.1698 and GOF = 1.044 for all reflections, max/min residual electron density +0.987/-0.651 eÅ^{-3}.

Crystallographic Data for **1884077**: $C_{36}H_{32}S_3$, M = 560.79, 0.18 x 0.02 x 0.02 mm, T = 173(2) K, Monoclinic, space group $P2_12_12_1$, a = 5.9598(3) Å, b = 12.9349(7) Å, c = 37.287(2) Å, V = 2874.4(3) Å^3, Z = 4, D_c = 1.296 Mg/m^3, μ(Cu) = 2.528 mm^{-1}, F(000) = 1184, $2\theta_{max}$ = 133.14°, 12589 reflections, 4927 independent reflections [R_{int} = 0.0652], R1 = 0.0504, wR2 = 0.1190 and GOF = 0.924 for 4927 reflections (352 parameters) with I>2σ(I), R1 = 0.0722, wR2 = 0.1335 and GOF = 0.924 for all reflections, the Flack = 0.04(2), max/min residual electron density +0.205/-0.212 eÅ^{-3}.

References:

[*] G. M. Sheldrick, *Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, 1998.

[**] Van der Sluis, P. & Spek, A. L. (1990) *Acta Cryst., Sect. A,* **A46**, 194-201.

[***] Sheldrick, G. M. (2015), *Acta Cryst.* A71, 3-8.