Electronic Supplementary Material (ESI) for ChemComm.

Supporting information available for

Diastereoselective Cyclization of Aminobenzoic Acid Derivative and Chiroptical Properties of Triple-Stranded Helical Bis(phenylethynyl)benzene

R. Yamakado, S. Matsuoka, M. Suzuki, D. Takeuchi, H. Masu, I. Azumaya, and K. Takagi*

Table of Contents

S1. Materials and Instruments

All materials were obtained from commercial suppliers and used without purification. 2,5-dibromo-4-hexylaminobenzoate[1] was synthesized following to the previous report. ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR) spectroscopy and H-H correlation spectroscopy (COSY) were investigated on Bruker Avance 200 and 600 FT-NMR spectrometers using tetramethylsilane (^{1}H-NMR, δ 0.00) and solvent residual peaks as the internal standard (^{1}H-NMR and ^{13}C-NMR). Infrared (IR) spectra were recorded on a JASCO FT-IR 460Plus spectrophotometer in the attenuated total reflectance (ATR) method. Melting points (Mp) were determined on a Yanaco micro melting point apparatus MP-J3. Matrix-assisted laser desorption/ionization time-of-fright mass spectra (MALDI-TOF MS) were performed on a JEOL JMS-S3000 in the spiral mode using dithranol as a matrix. Purifications with preparative gel permeation chromatography (GPC) were carried out on a Japan analytical industry LC-9210 system using tandem JAIGEL 1H, 2H, and 2.5H columns ($CHCl_3$ as an eluent, flow rate = 3.5 mL/min) equipped with an ultraviolet (UV) detector monitored at 254 nm. UV-vis and photoluminescence (PL) spectra were recorded on a Shimadzu UV-1650PC spectrophotometer and a Shimadzu RF-5300PC spectrofluorometer, respectively, using a 10 mm quartz cell. Fluorescence quantum yield (QY) in solution was determined relative to quinine sulfate in 0.05 M H_2SO_4 having a QY of 0.55. The circular dichroism (CD) spectra were measured in 10 mm quartz cells on a JASCO J-820 spectropolarimeter. The chiral high performance liquid chromatography (HPLC) analysis was performed on a Shimadzu LC-10AT liquid chromatograph equipped with a UV detector (TOSOH UV-8020) using a CHIRALPAK IA column (Daicel Chemical Industries, Ltd) (0.46 cm (i.d.) × 25 cm). Microwave-assisted reactions were performed in a Biotage microwave reactor (Initiator) using 0.5–2.0 mL microwave reaction vials equipped with a magnetic stirring bar.

S2. Syntheses of materials

2,5-Dibromo-4-hexylaminobenzoic acid (1).

To a solution of methyl 2,5-dibromo-4-hexylaminobenzoate[1] (0.39 g/ 1.0 mmol) in THF (4 mL) and MeOH (4 mL) was added 2M aq. NaOH (4 mL), and the system was stirred for 24 h at 45 ºC. The reaction mixture was acidified using 1M aq. HCl, and the precipitation was collected by the filtration and dried under vacuum. 2,5-Dibromo-4-hexylaminobenzoic acid was obtained as white powder quantitatively.

M.p. 159 – 160 ºC. ^{1}H NMR (δ, 600 MHz, ppm, $CDCl_3$) 8.17 (s, 1H), 6.84 (s, 1H), 4.77 (brs, 1H), 3.21 (m, 2H), 1.69 (m, 2H), 1.5 – 1.3 (6H), 0.92 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (δ, 150 MHz, ppm, $CDCl_3$) 165.6, 148.8, 136.7, 124.4, 117.2, 115.9, 107.1, 43.6, 31.4, 29.0, 26.6, 22.5, 13.9. IR (cm^{-1}) 3947, 3403, 2951, 2931, 2857, 1680, 1583, 1402, 1371, 1331, 1276, 1235, 1136, 1046, 905, 836, 775, 707, 643. Anal. Calcd for $C_{13}H_{17}Br_2NO_2$: C, 41.19; H, 4.52; N, 3.69. Found: C, 41.35; H, 4.47; N, 3.58.

2,5-Bis(phenylethynyl)-4-hexylaminobenzoic acid (2).

To a mixture of 2,5-dibromo-4-hexylaminobenzoic acid (0.38 g, 1.0 mmol), PPh_3 (87 mg, 0.33 mmol), $Cu_2(OAc)_4$ (20 mg, 0.10 mmol) and $Pd(PPh_3)_2Cl_2$ (18 mg, 0.10 mmol) in triethylamine (25 mL) was added dropwise phenylacetylene (0.39 mL, 4.0 mmol), and the system was heated to reflux overnight. After the solvent was removed under vacuum, the residue was dissolved by DCM and washed by saturated aq. NH_4Cl. After drying over $MgSO_4$, solvents were removed by the rotary evaporator. The crude product was purified by column chromatography (DCM/hexane = 3/1) to obtain yellow solid (390 mg/ 93 %).

M.p. 115 – 116 ºC. ^{1}H NMR (δ, 600 MHz, ppm, $CDCl_3$) 7.86 (s, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.51 (m, 2H), 7.40 – 7.34 (4H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.73 (s, 1H), 6.32 (s, 1H), 3.34 (m, 2H), 1.77 (m, 2H), 1.50 (m, 2H), 1.5 – 1.3 (4H), 0.93 (m, 3H). ^{13}C NMR (δ, 150 MHz, ppm, $CDCl_3$) 166.6, 153.2, 145.2, 142.9, 133.5, 131.6, 130.1, 129.5, 128.9, 128.7, 128.1, 122.5, 111.3, 110.6, 106.3, 97.5, 97.3, 43.5, 31.5, 29.0, 26.8, 22.6, 13.9. IR (cm^{-1}) 3444, 3210, 2852, 1756, 1612, 1511, 1333, 1073, 949, 750, 688.

Phenyl 2,5-bis(phenylethynyl)-4-hexylaminobenzoate (3).

To a mixture of 2,5-bisphenyl-4-hexylaminobenzoic acid (0.17 g, 0.4 mmol), phenol (80 mg, 0.86 mmol), triethylamine (36 μL, 0.24 mmol) and pyridine (40 μL, 0.5 mmol) in DCM (25 mL) was added dropwise $SOCl_2$ (56 μL, 0.8 mmol) at 0 ºC, and the system was heated to reflux overnight. The reaction mixture was poured into water and extracted by DCM. After drying over $MgSO_4$, solvents were removed by the rotary evaporator. The resulting solid residue was purified by recrystallization from DCM and hexane to yield yellow powder (0.13 g, 64%).

M.p. 75 – 77 ºC. ^{1}H NMR (δ, 200 MHz, ppm, $CDCl_3$) 7.89 – 7.80 (3H), 7.60 – 7.10 (12H), 7.00 – 6.70 (6H), 6.36 (s, 1H), 3.33 (m, 2H), 1.77 (m, 2H), 1.50 – 1.10 (6H), 0.92 (m, 3H). IR (cm^{-1}) 3405, 2929, 1756, 1610, 1512, 1334, 1073, 949, 750, 685.

Cyclization by LiHMDS (Condition A)

A THF solution of LiHMDS (1.0 M, 1.0 mL) was added dropwise to a THF solution of phenyl 2,5-bisphenylethynyl-4-hexylaminobenzoate (0.1 M, 0.2 mL) and TMEDA (0.15 mL, 1.0 mmol), and the system was stirred for 24 h at 50 ºC. After saturated aq. NH_4Cl was added, an aqueous phase was extracted with DCM. A combined organic phase was dried over $MgSO_4$ and solvents were removed by the rotary evaporator.

Cyclization by Ph_3PCl_2 (Condition B)

To a solution of monomer (0.2 mmol) in 1,1,2,2-tetrachloroethane (5 mL) was added Ph_3PCl_2 (0.19 g, 0.57 mmol), and the mixture was heated reflux for 24 h. The reaction mixture was washed with saturated aq. NH_4Cl. The organic phase was dried over $MgSO_4$ and solvents were removed by rotary evaporator.

Cyclization by $SiCl_4$ (Condition C)

To a solution of monomer (1.0 mmol) in pyridine (7.5 mL) was added dropwise $SiCl_4$ (0.2 mL, 1.5 mmol) at 0 ºC, and the mixture was heated to 120 ºC in the oil bath or microwave reactor. After removal of pyridine, DCM was added and washed with 1M aq. HCl. The organic phase was dried over $MgSO_4$ and solvents were removed by rotary evaporator.

DiBr_C3A

The crude product was purified by the preparative GPC to obtain white powder.

M.p. 170 – 171 °C. ^{1}H NMR (δ, 600 MHz, ppm, $CDCl_3$) 7.70 (s, 3H), 7.69 (s, 3H), 4.25 (m, 3H), 3.15 (m, 3H), 1.67 (m, 3H), 1.55 (m, 3H), 1.48 – 1.20 (18H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (δ, 150 MHz, ppm, $CDCl_3$) 165.2, 140.9, 139.4, 133.9, 130.7, 122.6, 117.7, 47.7, 31.1, 27.0, 26.3, 22.3, 13.8. IR (cm^{-1}) 3073, 2929, 2853, 1659, 1582, 1471, 1392, 1337, 1305, 1067, 724. Anal. Calcd for $C_{39}H_{45}Br_6N_3O_3$: C, 43.24; H, 4.19; N, 3.88. Found: C, 43.36; H, 4.09; N, 3.74. MALDI-TOF MS Calcd for $C_{39}H_{46}Br_6N_3O_3$ $[M+H]^+$: 1083.8578. Found: 1083.8550.

BPEB_C3A

To a mixture of **DiBr_C3A** (0.16 g, 0.15 mmol), PPh_3 (87 mg, 0.33 mmol), $Cu_2(OAc)_4$ (20 mg, 0.10 mmol) and $Pd(PPh_3)_2Cl_2$ (18 mg, 0.10 mmol) in triethylamine (12 mL) was added dropwise phenylacetylene (0.39 mL, 4.0 mmol), and the system was heated to reflux overnight. After the

solvent was removed under vacuum, the residue was dissolved by DCM and washed by saturated aq. NH_4Cl. After drying over $MgSO_4$, solvents were removed by the rotary evaporator. The crude product was purified by the preparative GPC followed by column chromatography (ethylacetate/hexane = 1/3, Rf; 0.33) to obtain pale yellow solid (50 mg/ 28 %).

M.p. 67 – 68 °C. ^{1}H NMR (δ, 600 MHz, ppm, CD_2Cl_2) 7.61 (s, 3H), 7.58 (s, 3H), 7.52 – 7.44 (18H), 7.43 – 7.63 (12H), 4.25 (m, 3H), 3.53 (m, 3H), 1.75 (m, 3H), 1.66 (m, 3H), 1.48 – 1.20 (18H), 0.86 (t, J = 7.5 Hz, 3H. ^{13}C NMR (δ, 150 MHz, ppm, CD_2Cl_2) 168.2, 143.0, 133.6, 132.1, 130.7, 129.7, 129.0, 123.6, 122.5, 120.8, 97.9, 95.9, 86.9, 85.8, 48.7, 32.0, 28.3, 27.1, 22.9, 14.3. IR (cm^{-1}) 3057, 2932, 2856, 2359, 2342, 2211, 1659, 1592, 1503, 1299, 1138, 1024, 904, 753, 687. MALDI-TOF MS Calcd for $C_{87}H_{76}N_3O_3$ $[M+H]^+$: 1210.5887. Found: 1210.5823.

S3. GPC Chart

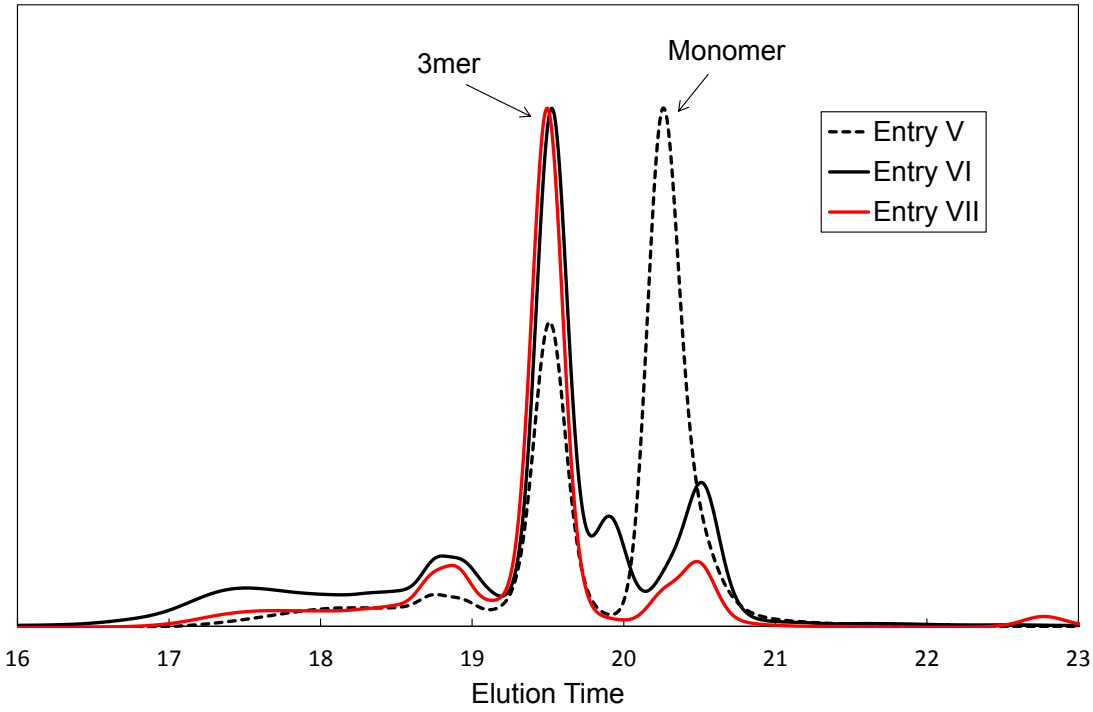

Figure S1. GPC profiles of crude products obtained by cyclic oligomerization of monomer **1** (See Scheme 1 and Table 1 in main text).

S4. MALDI-TOF MS

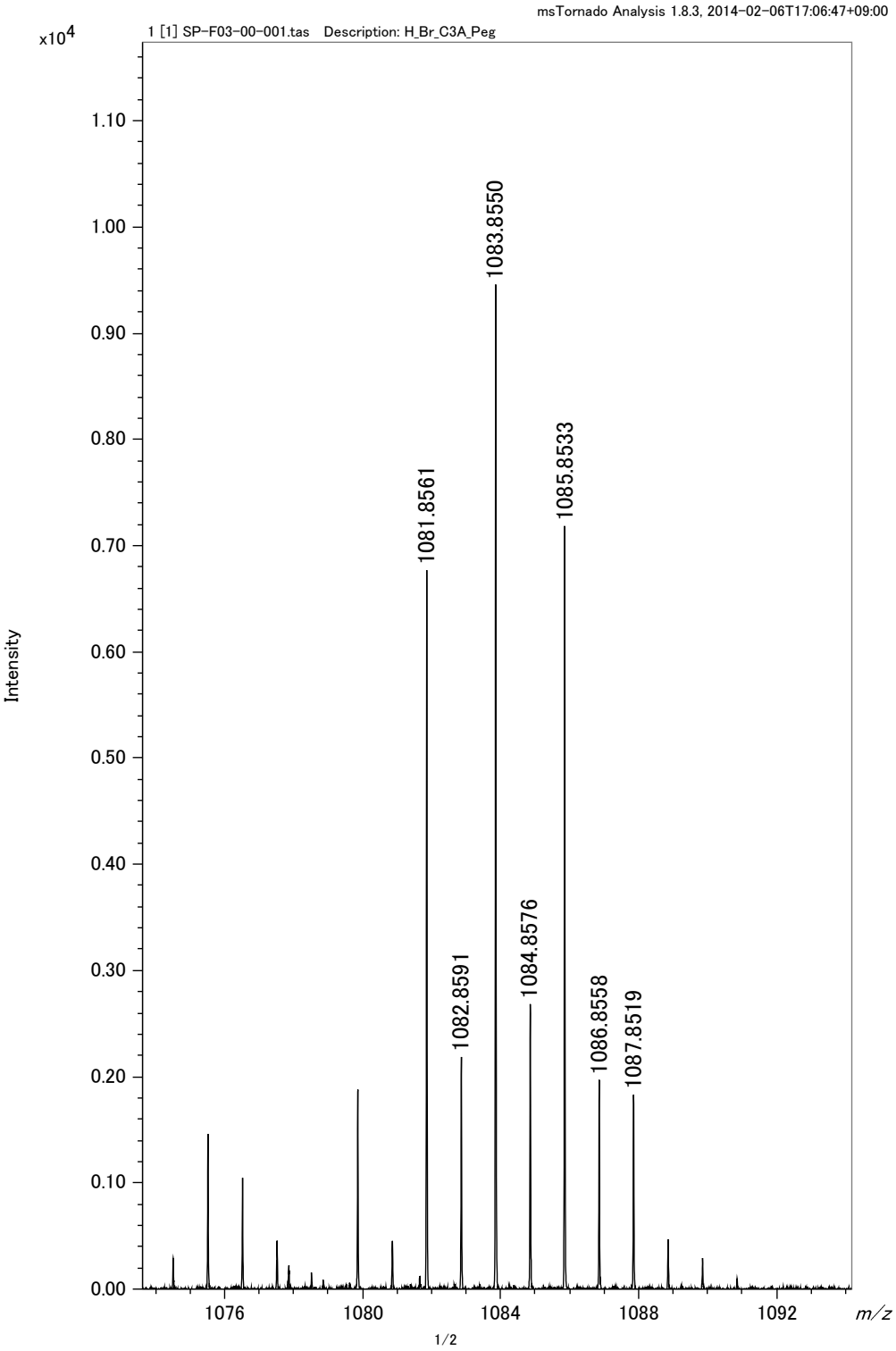

Figure S2. MALDI-TOF MS of **DiBr_C3A**

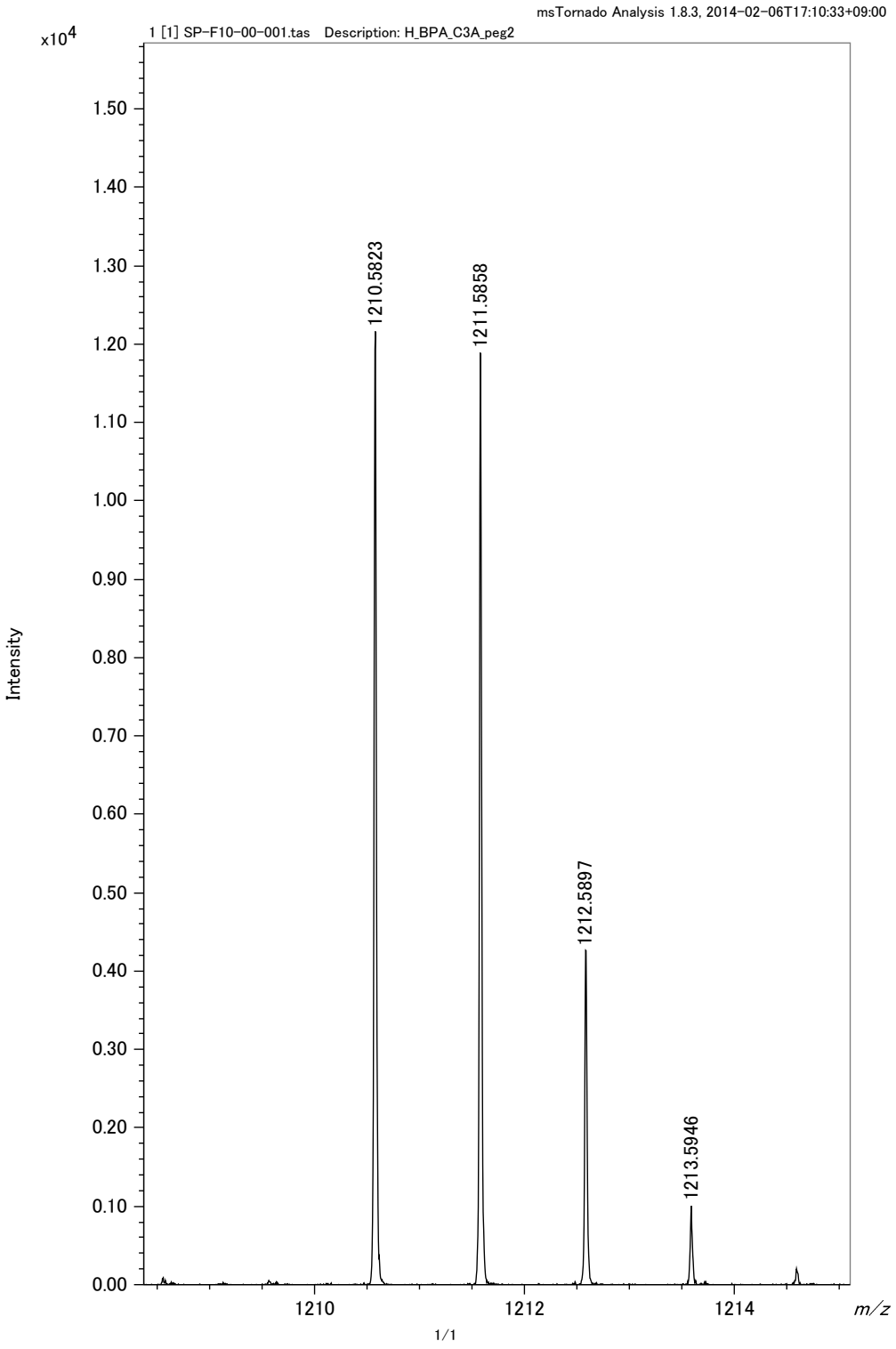

Figure S3. MALDI-TOF MS of **BPEB_C3A**

S5. Chiral HPLC

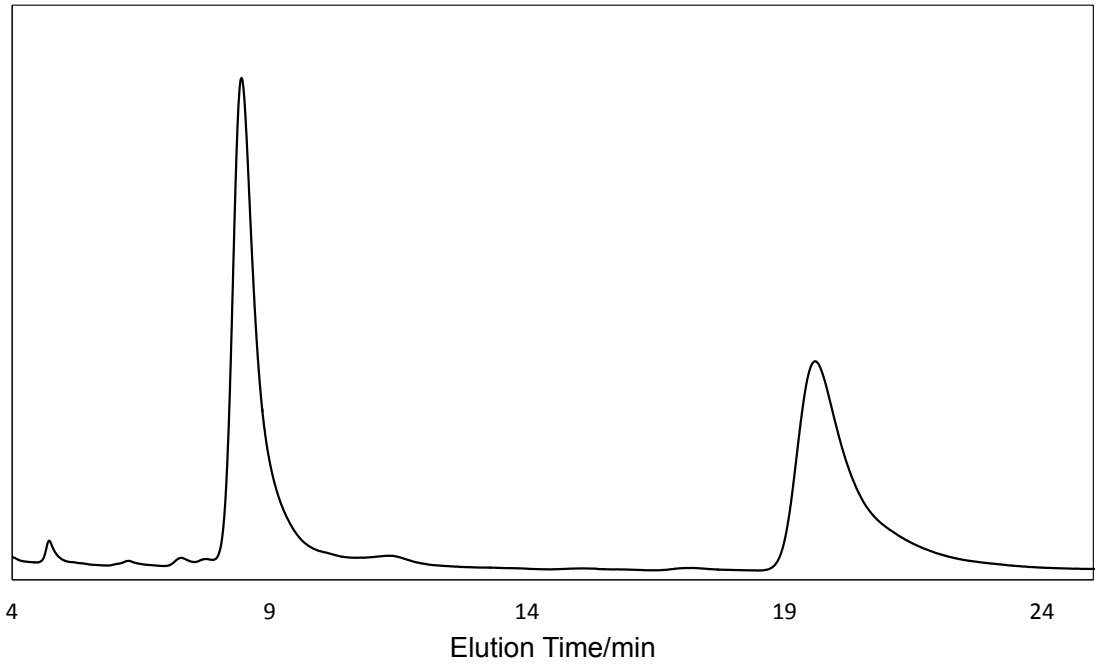

Figure S4. Chiral HPLC chromatogram of racemic mixture of **DiBr_C3A**.

S6. NMR spectra

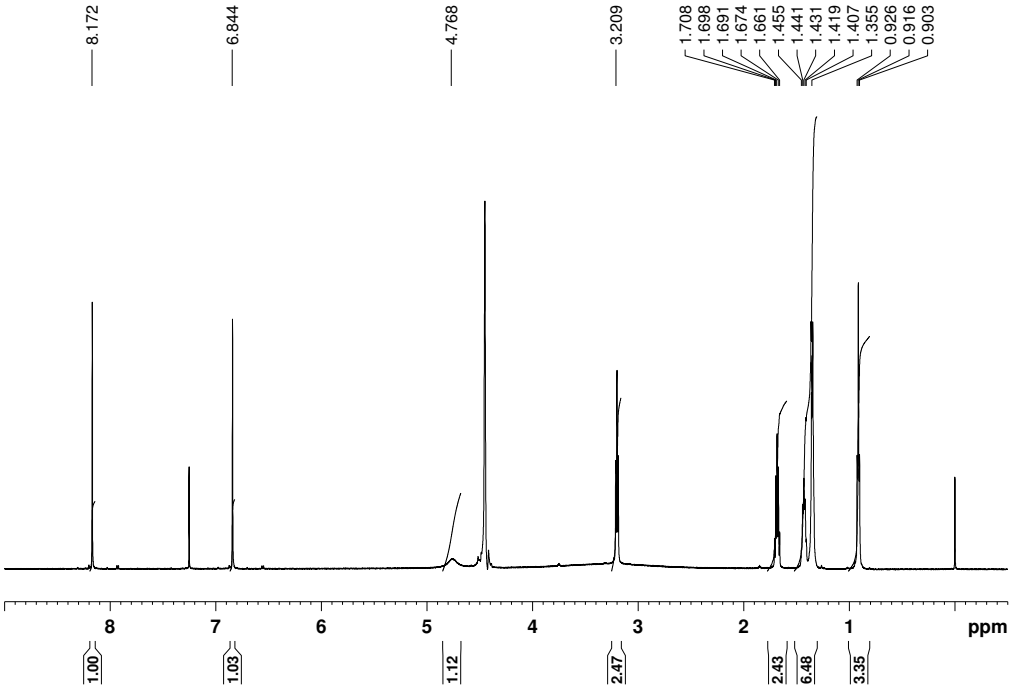

Figure S5. ^{1}H NMR spectrum of **1** in $CDCl_3$ (600 MHz).

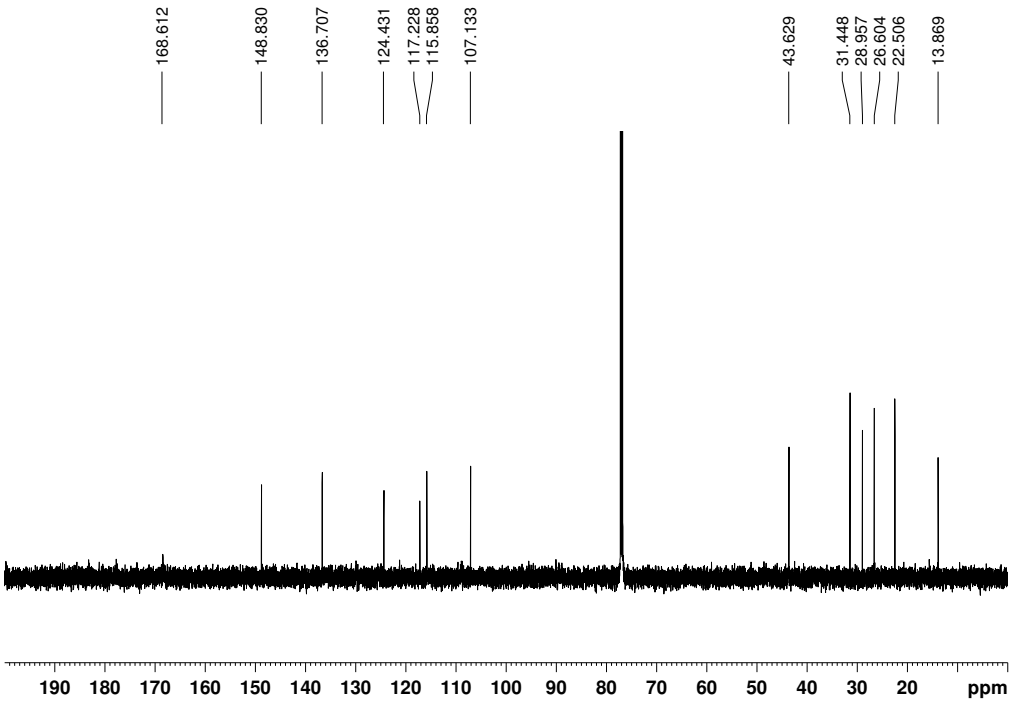

Figure S6. ^{13}C NMR spectrum of **1** in $CDCl_3$ (150 MHz).

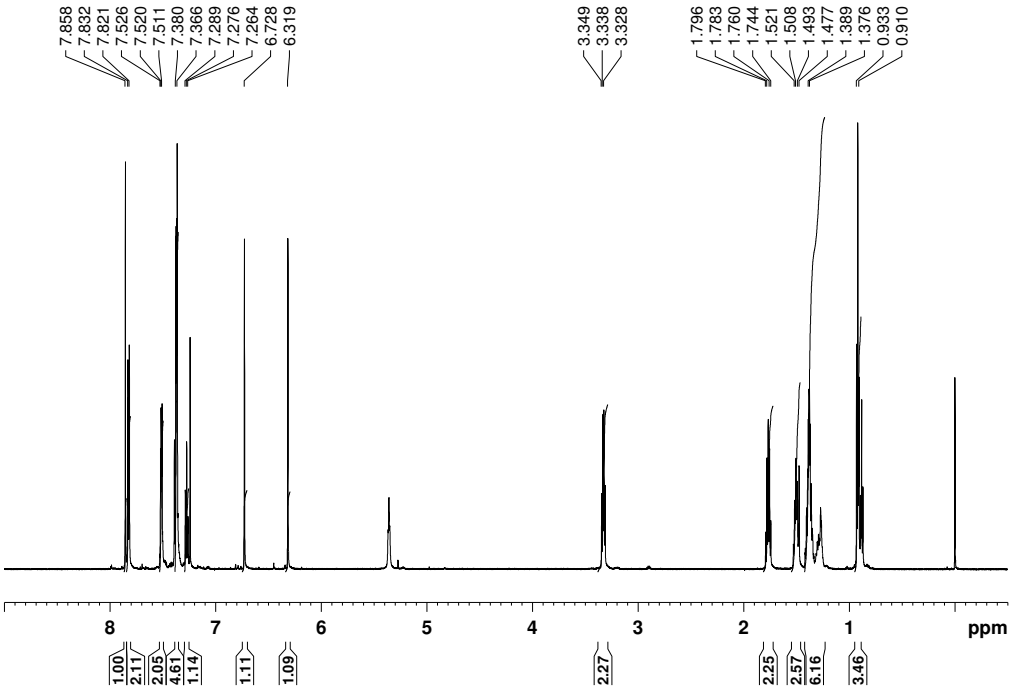

Figure S7. ^{1}H NMR spectrum of **2** in $CDCl_3$ (600 MHz).

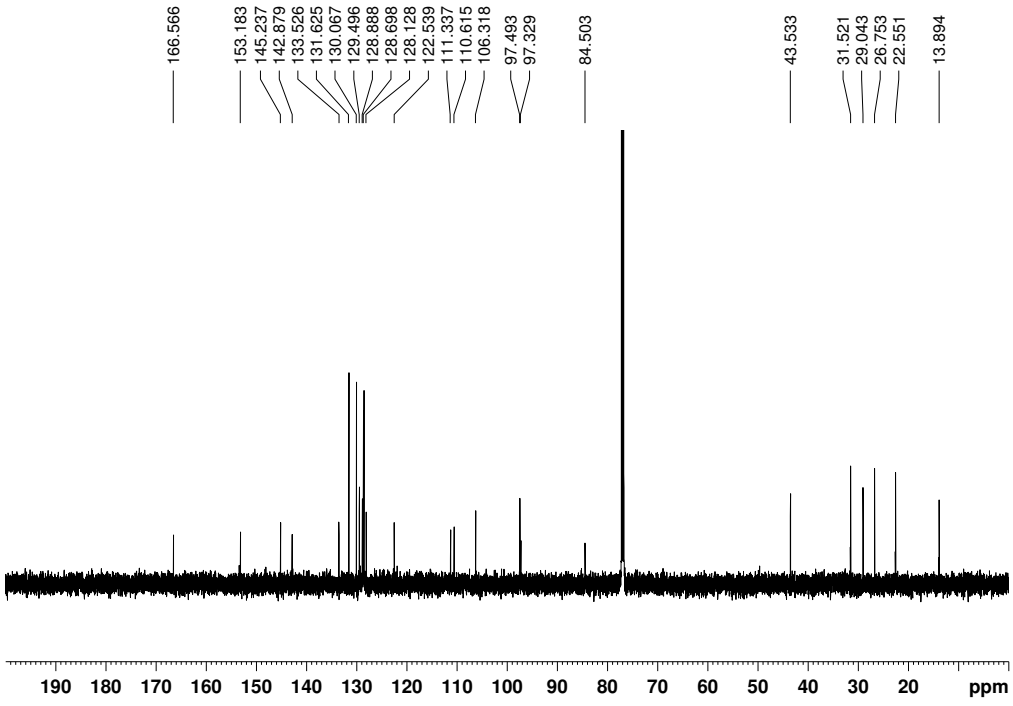

Figure S8. ^{13}C NMR spectrum of **2** in $CDCl_3$ (150 MHz).

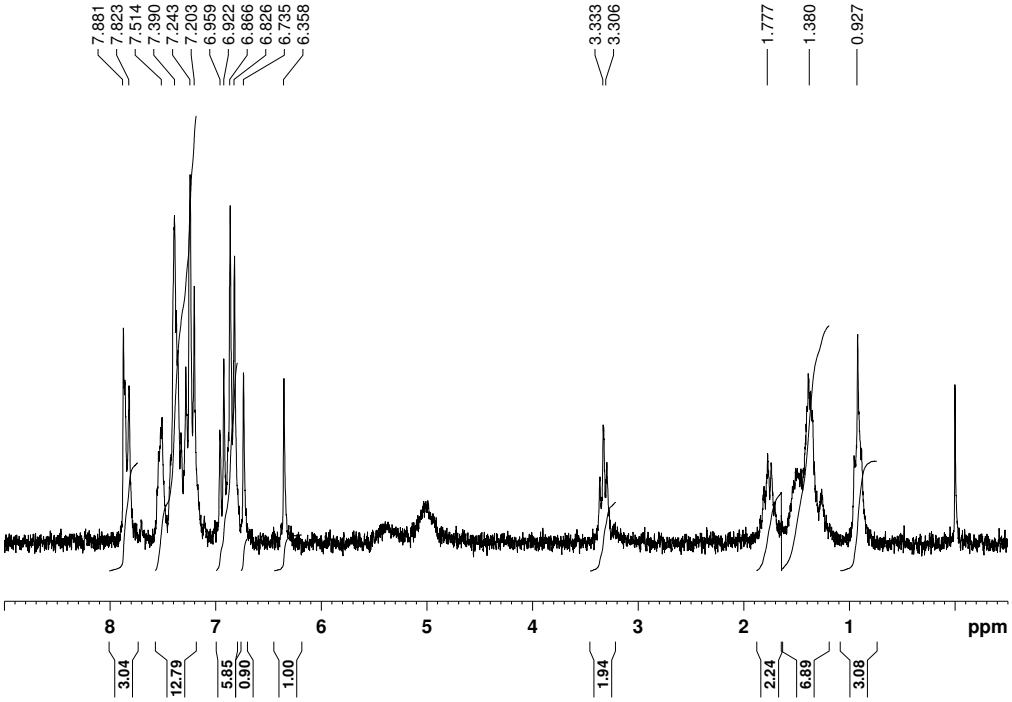

Figure S9. ^{1}H NMR spectrum of **3** in $CDCl_3$ (200 MHz).

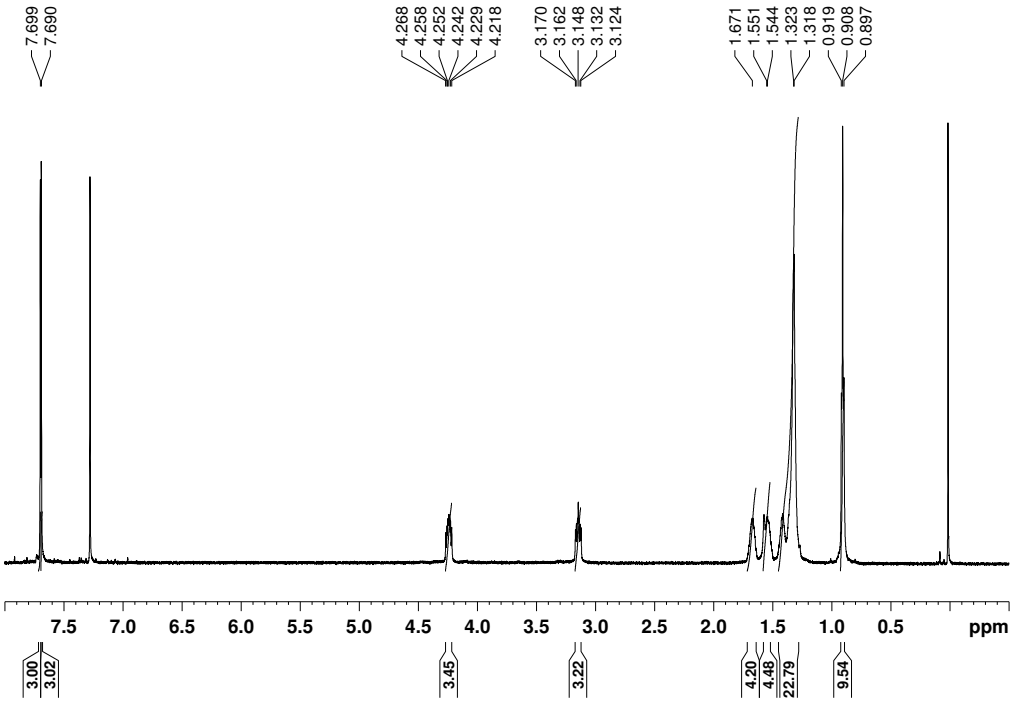

Figure S10. ^{1}H NMR spectrum of **DiBr_C3A** in $CDCl_3$ (600 MHz).

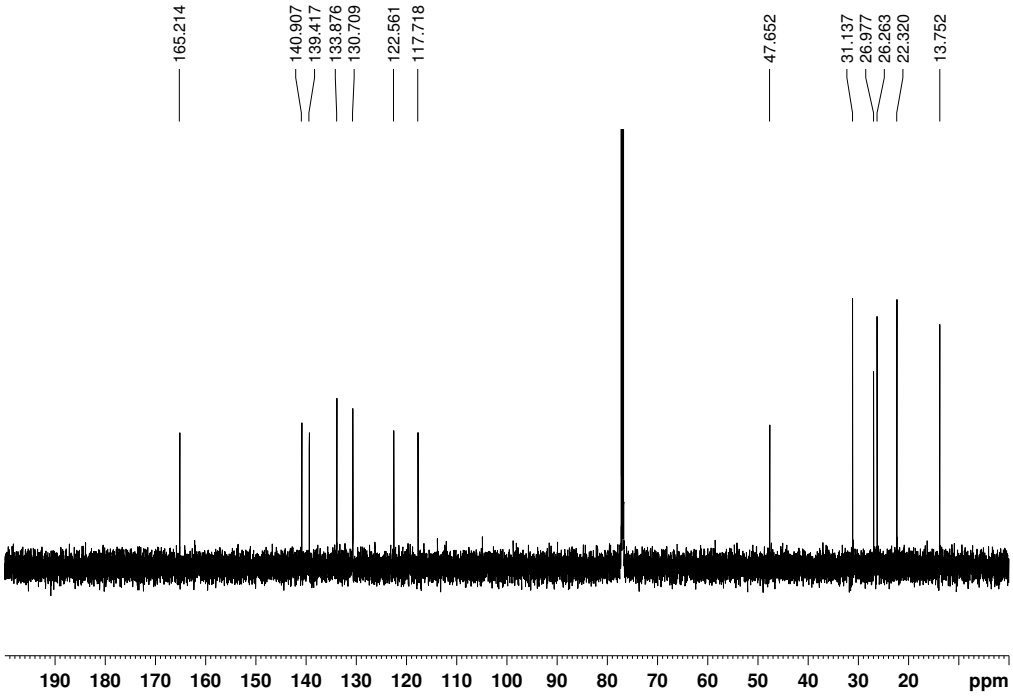

Figure S11. ^{13}C NMR spectrum of **DiBr_C3A** in $CDCl_3$ (150 MHz).

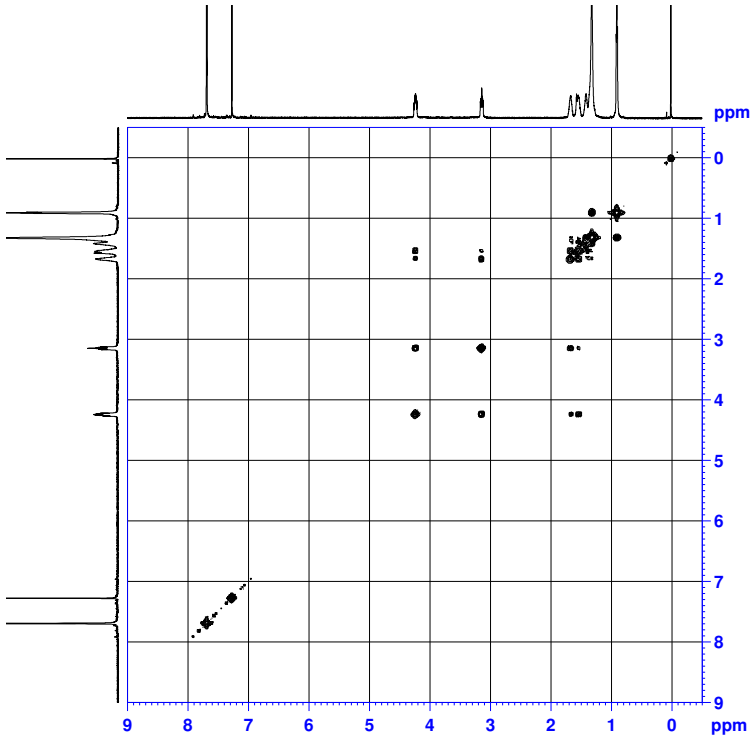

Figure S12. H-H COSY of **DiBr_C3A** in $CDCl_3$ (600 MHz).

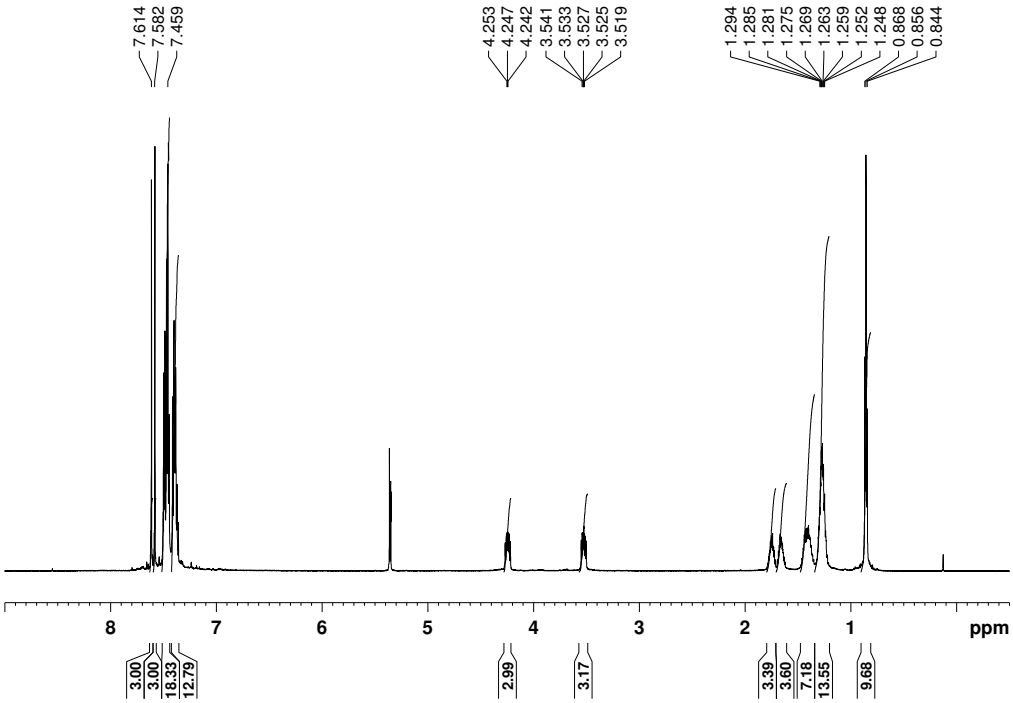

Figure S13. ^{1}H NMR spectrum of **BPEB_C3A** in CD_2Cl_2 (600 MHz).

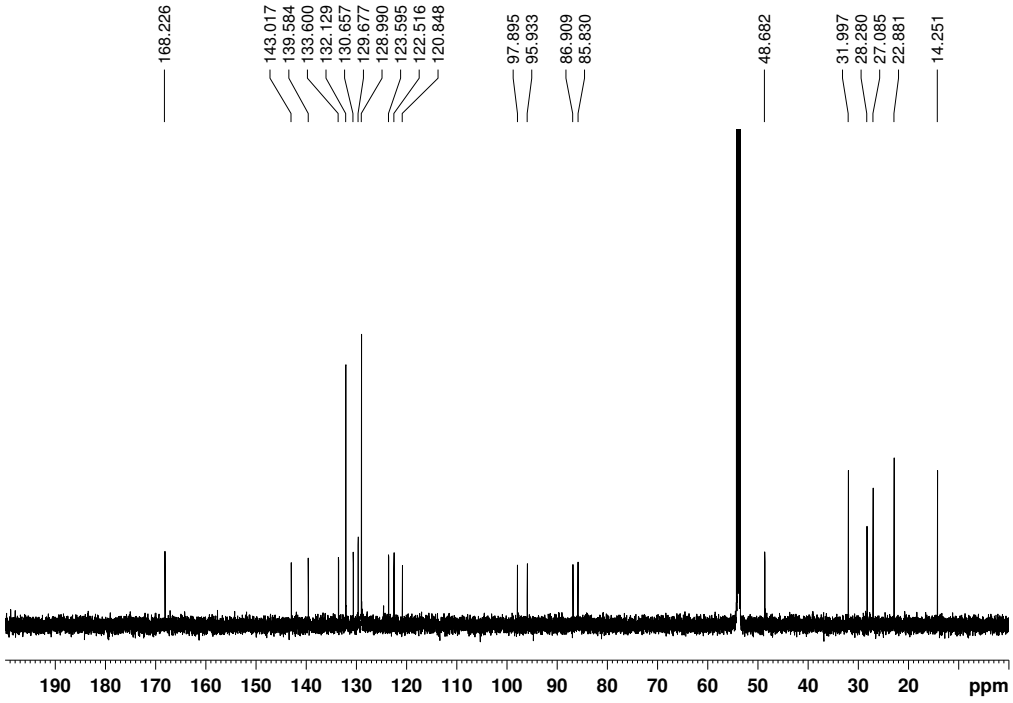

Figure S14. ^{13}C NMR spectrum of **BPEB_C3A** in $CDCl_3$ (150 MHz).

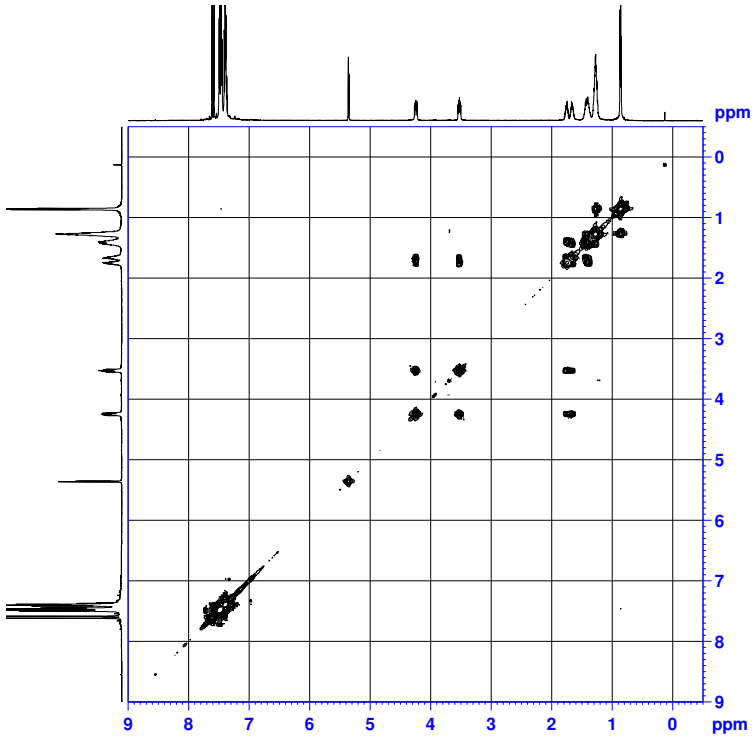

Figure S15. H-H COSY of **BPEB_C3A** in CD_2Cl_2 (600 MHz).

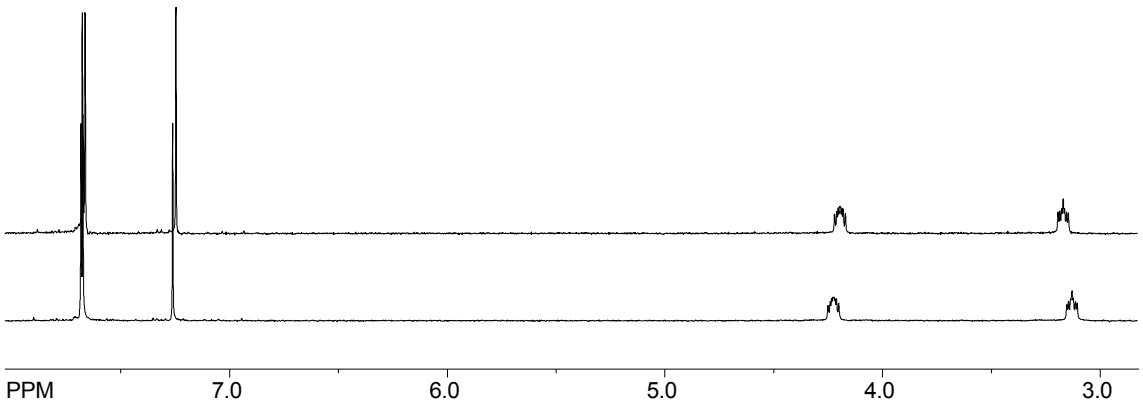

Figure S16. Expanded ^{1}H NMR spectra of **DiBr_C3A** in $CDCl_3$ at 50 ^{o}C (top) and 25 ^{o}C (bottom) (600 MHz).

S7. CD spectra

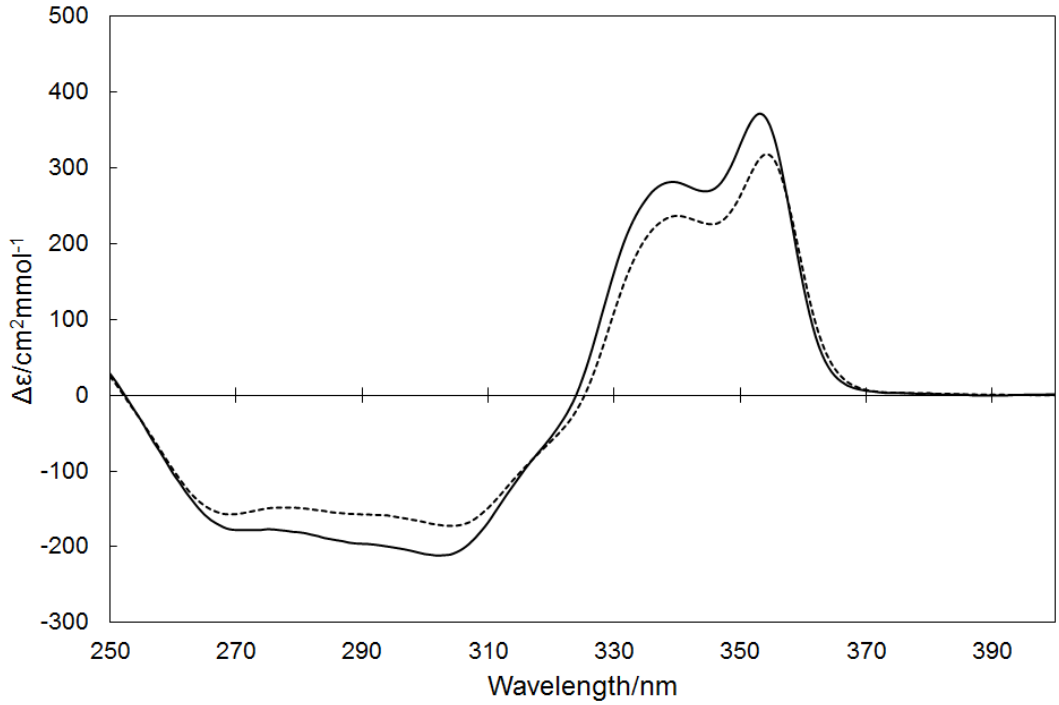

Figure S17. CD spectra of 1st fraction in THF (solid line) and DCM (dotted line)

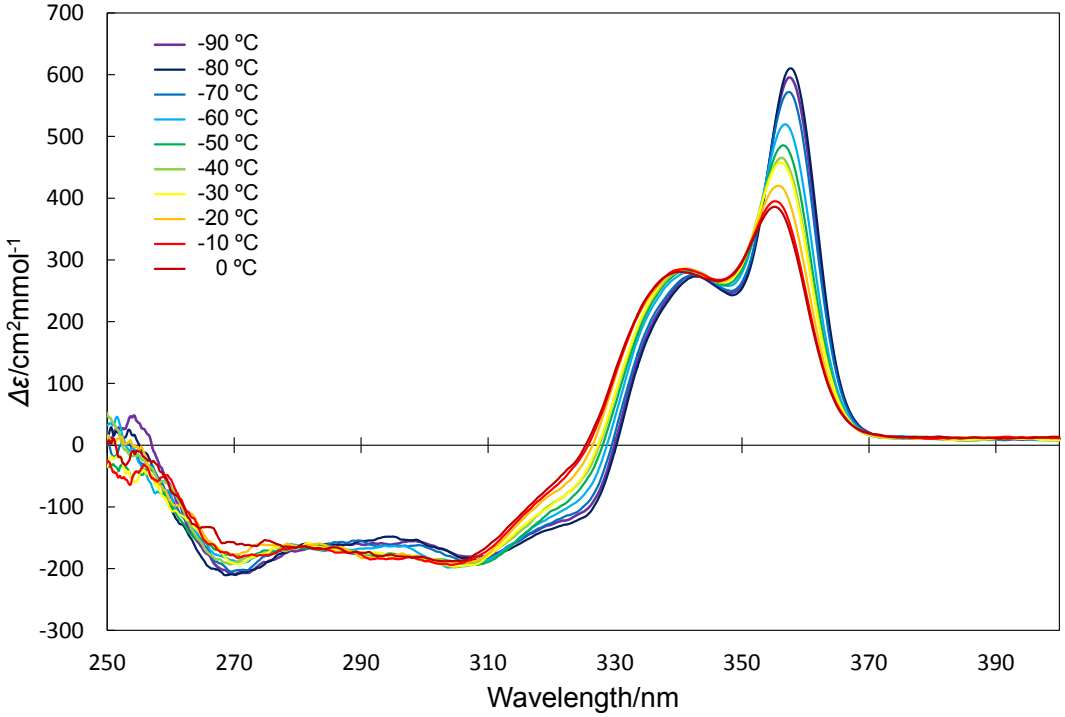

Figure S18. Temperature dependent CD spectra of 1st fraction in THF.

S8. UV-vis and fluorescence spectra

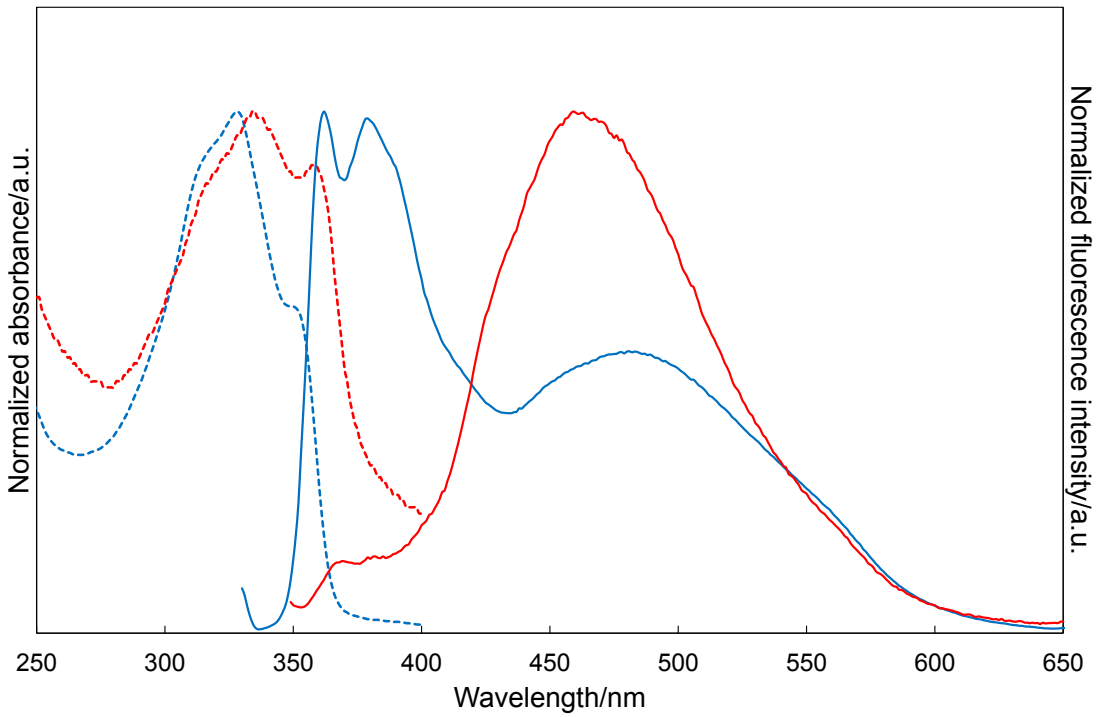

Figure S19. Normalized absorption and emission spectra of **BPEB_C3A** in THF (blue, 5×10^{-6} M) and solid state (red) ($\lambda_{ex} = \lambda_{abs}$, room temperature)

S9. Crystal structure

Measurement. Crystallographic data of **DiBr_C3A** was collected on a CCD diffractometer with Cu Kα (λ = 1.54178 Å) radiation. Data collections were carried out at low temperature (173 K) using liquid nitrogen. All of the crystal structures were solved by direct methods with SHELXS-97 and refined with full-matrix least-squares SHELXL-2013.[2] All non-hydrogen atoms were refined anisotropically and hydrogen atoms were included at their calculated positions.

Crystal data for DiBr_C3A: $C_{39}H_{45}Br_6N_3O_3$, M_r = 1083.22, Monoclinic, *C*2/*c*, a = 34.3269(6), b = 16.0953(3), c = 17.3532(3) Å, β = 115.9592(6), γ = 93.660(2)°, V = 8620.3(3) Å^3, Z = 8, D_c = 1.669 Mg m^{-3}, $2\theta_{max}$ = 136.688°, T = 173 K, 30833 reflections measured, 7887 unique (R_{int} = 0.0169), μ = 7.031 mm^{-1}. The final R_1 and wR_2 were 0.0256 and 0.0709 ($I > 2\sigma(I)$), 0.0272 and 0.0724 (all data). CCDC 1045865 Some atoms of terminal alkyl groups are disordered to two positions (C26A (C26B)–C27A (C27B) and C33A (C33B) in Figure S20). The occupancies of the disordered atoms were refined.

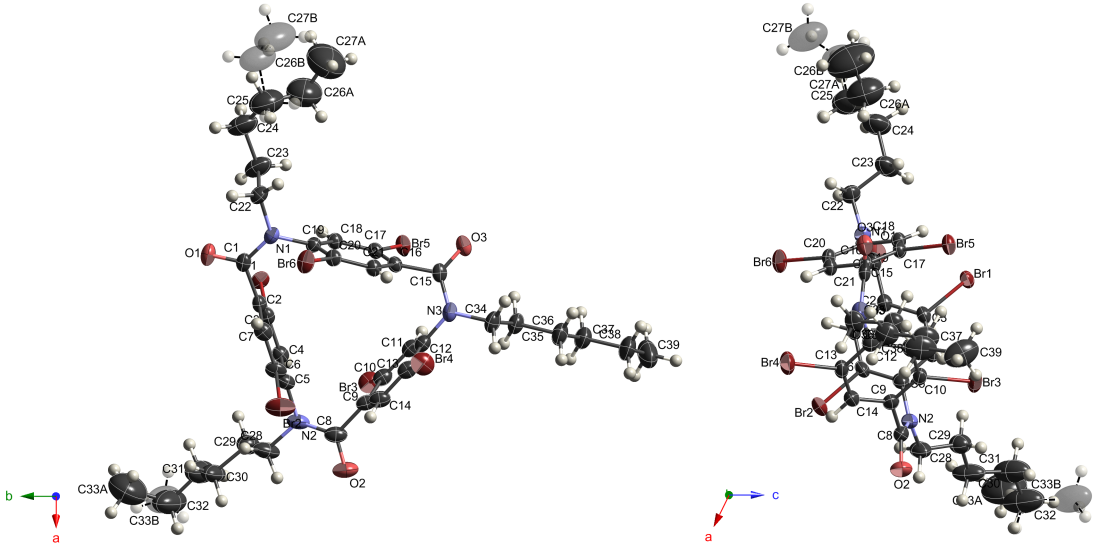

Figure 20. Thermal ellipsoid model of crystal of **DiBr_C3A**. Front view (left) and side view (right). The ellipsoids are drawn at 50% probability level while isotropic hydrogen atoms are represented by spheres of arbitrary size. Disordered atoms which have minor occupancy are colored transparently. The labels of hydrogen atoms are omitted for clarity.

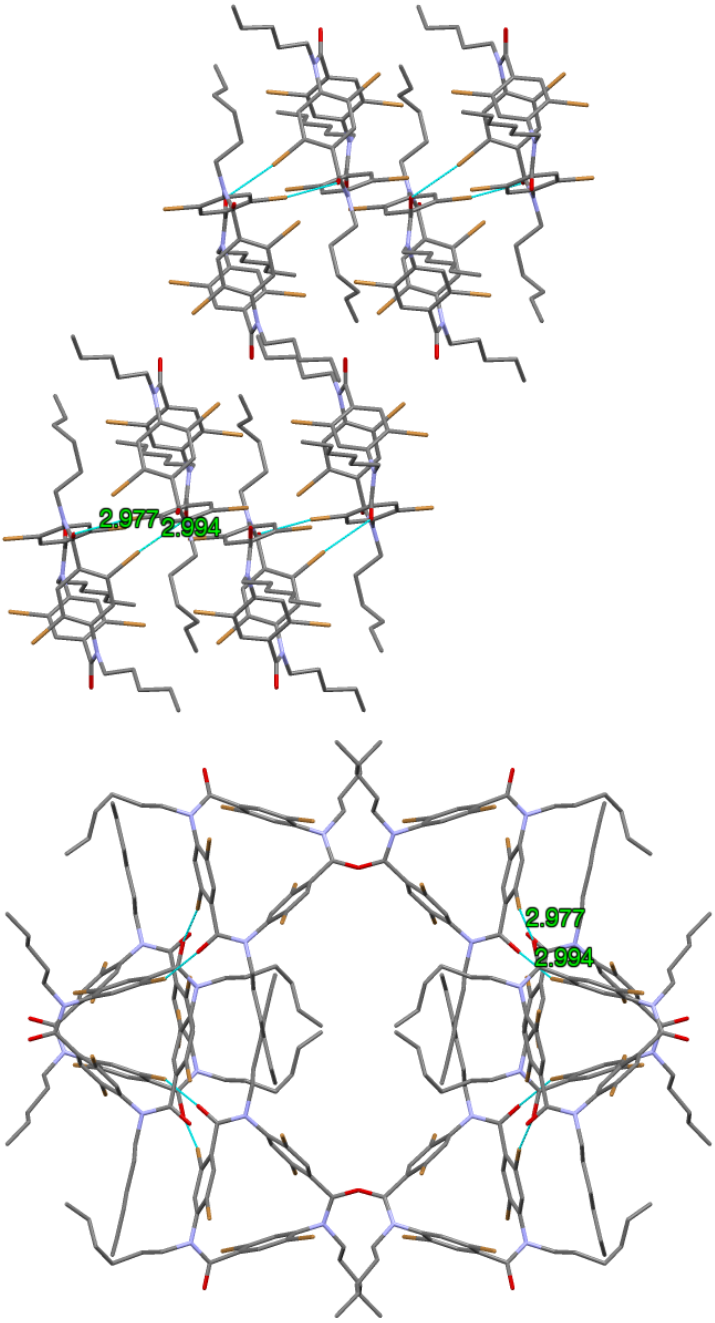

Figure S21. Packing structure of **DiBr_C3A** along the *b* axis (top) and *c* axis (bottom). Hydrogen atoms are omitted for clarify.

S10. Reference

1) M. Moroni, J. L. Moigne, T. A. Pham, and J.-Y. Bigot, *Macromolecules*, 1997, **30**, 1964.
2) A short history of SHELX. G. M. Sheldrick, *Acta Cryst*. 2008, **A64**, 112–122.