Supplementary Information

Controlled helical senses of twisting in two-, three- and four-layer cyclophanes with planar chirality

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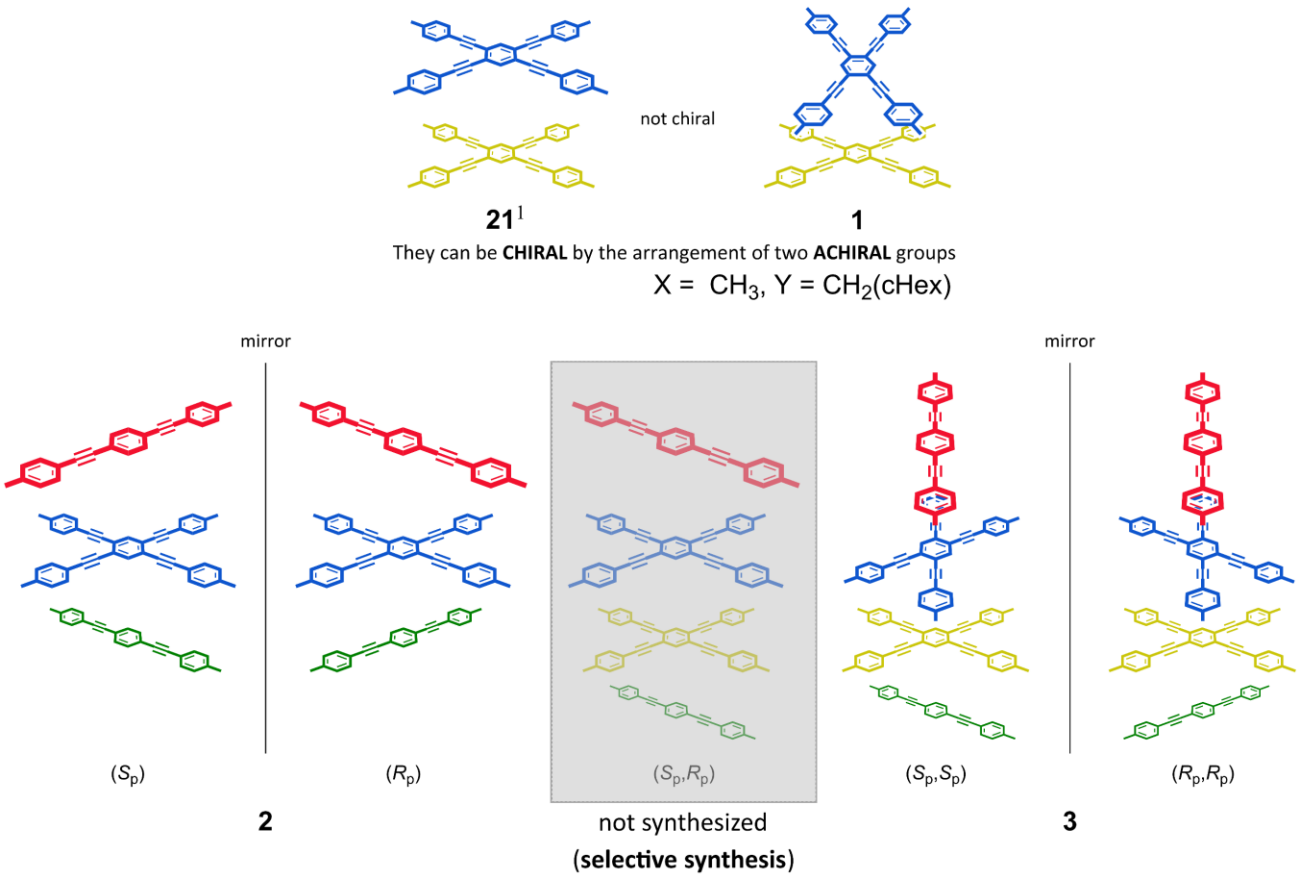

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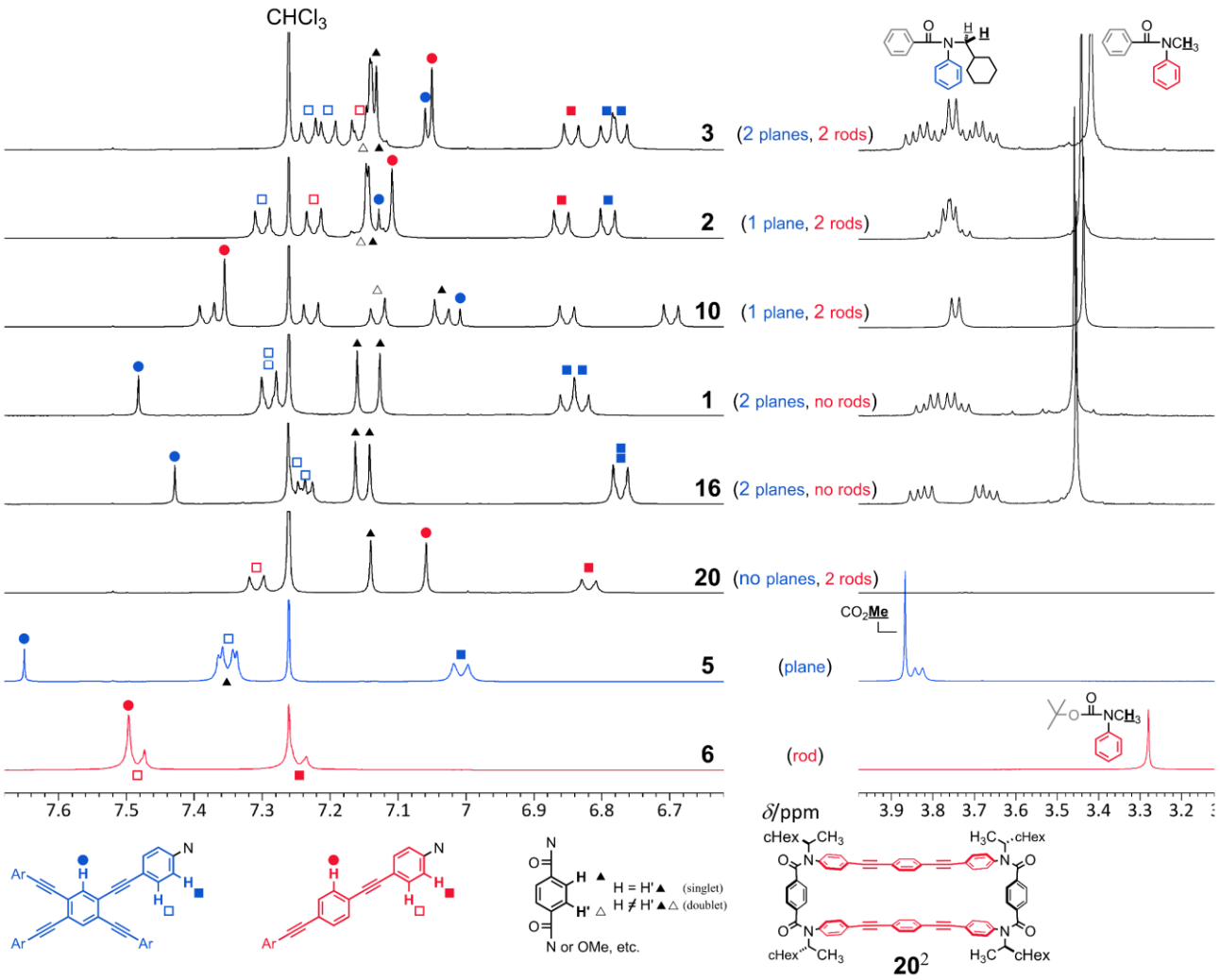


Fig. S1A Partial ^{1}H NMR spectra (400 MHz; left: aromatic protons and right: methylene and methyl protons) of **3**, **2**, **10**, **1**, **16**, **20**^{2}, **5** and **6**, measured in chloroform-*d* at room temperature.

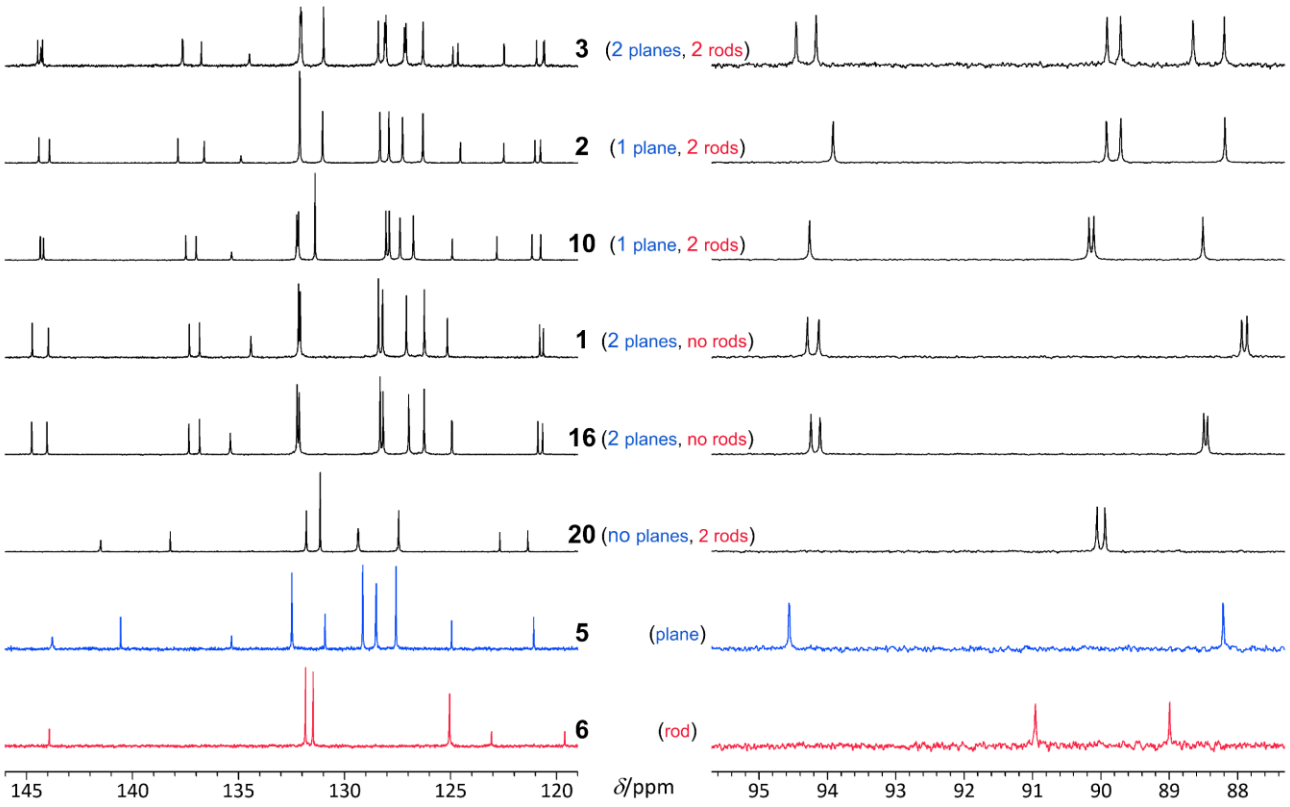


Fig. S1B Partial ^{13}C NMR spectra (100 MHz; left: aromatic carbons and right: acetylenic carbons) of **3**, **2**, **10**, **1**, **16**, **20**[2], **5** and **6**, measured in chloroform-*d* at room temperature.

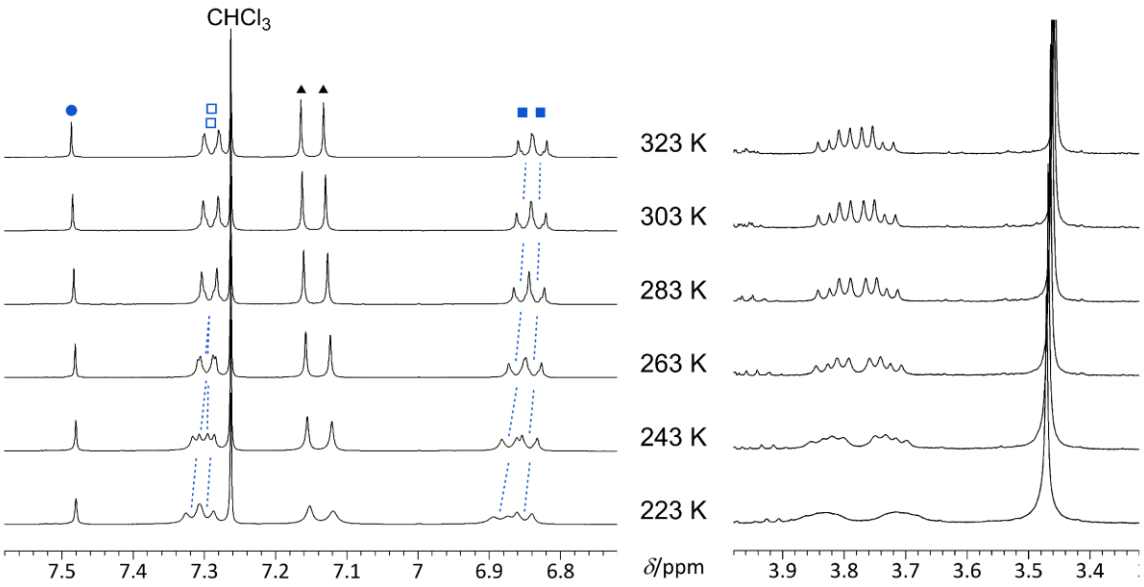


Fig. S2A Partial VT-^{1}H NMR spectra (400 MHz; left: aromatic protons and right: methylene and methyl protons) of **1** (2 planes, no rods), measured in chloroform-*d* at 223-323 K.

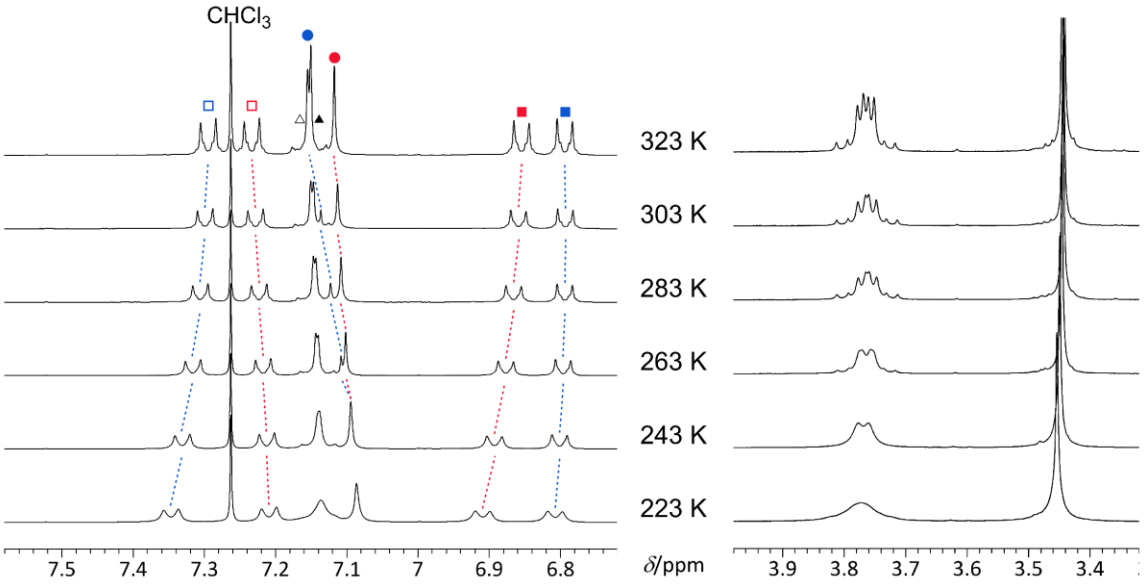


Fig. S2B Partial VT-^{1}H NMR spectra (400 MHz; left: aromatic protons and right: methylene and methyl protons) of **2** (1 plane, 2 rods), measured in chloroform-*d* at 223-323 K.

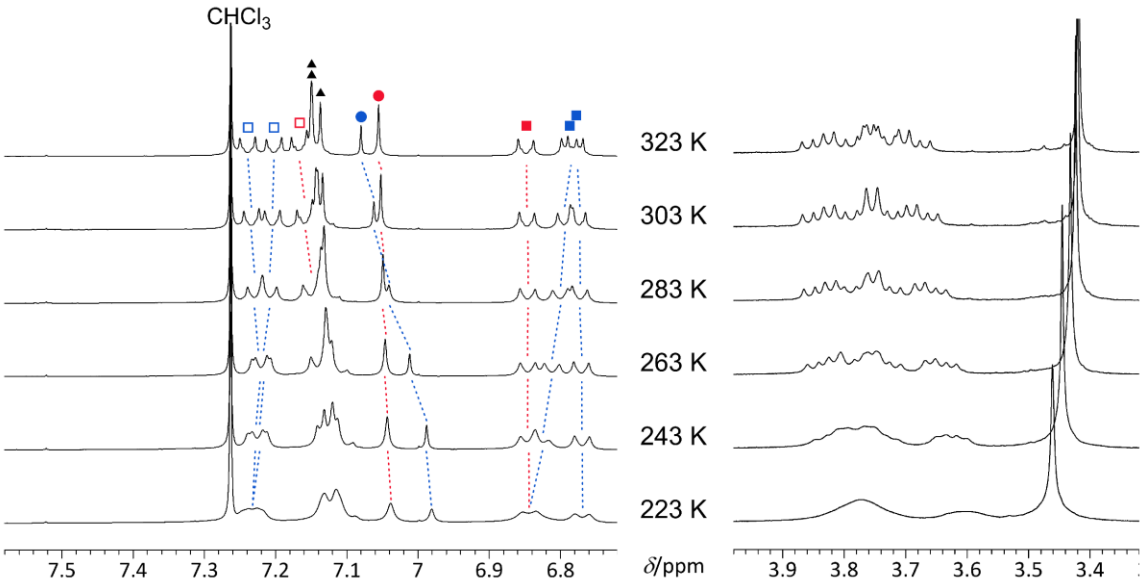


Fig. S2C Partial VT-^{1}H NMR spectra (400 MHz; left: aromatic protons and right: methylene and methyl protons) of **3** (2 planes, 2 rods), measured in chloroform-*d* at 223-323 K.

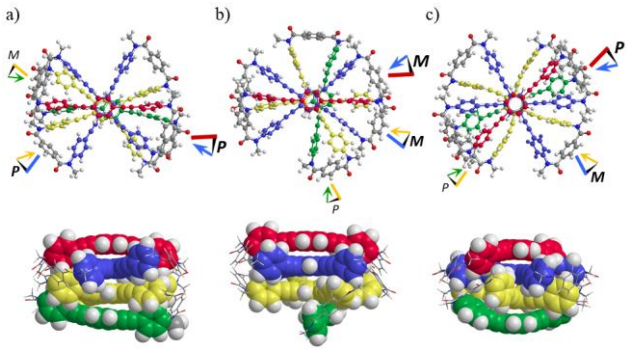


Fig. S3A Energy-minimized structures for (S_p,S_p)-**3'** (X = Y = CH_3): (a) *PPM*-**3'** +41.7 kJ mmol^{-1} (rel. to *MMM*-**3'**); (b) *MMP*-**3'** +41.9 kJ mmol^{-1} (rel. to *MMM*-**3'**); (c) *PMP*-**3'** +61.7 kJ mmol^{-1} (rel. to *MMM*-**3'**), obtained by conformational searches using MacroModel software (v11.8 OPLS3e, Low-frequency-mode search, non-solvated). Top view (ball and stick representation) and side view (space-filling representation for planes and rods, and stick representation for bridges).

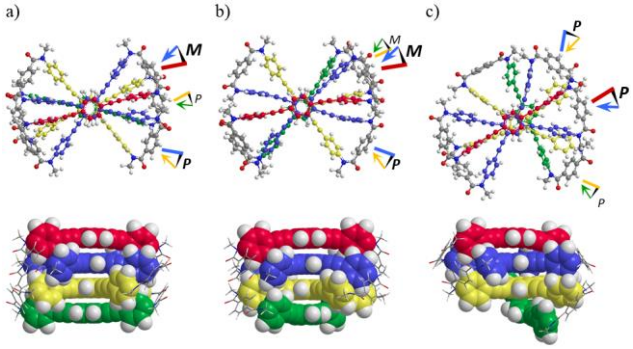
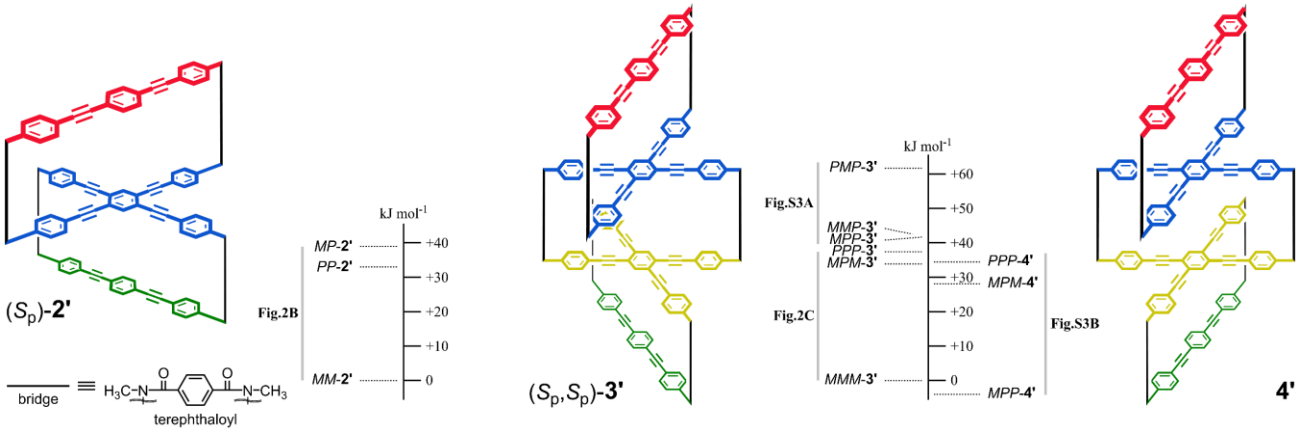


Fig. S3B Energy-minimized structures for **4'** (X = Y = CH_3): (a) *MPP*-**4'** –4.0 kJ mmol^{-1} (rel. to *MMM*-**3'**); (b) *MPM*-**4'** +32.1 kJ mmol^{-1} (rel. to *MPP*-**4'**); (c) *PPP*-**4'** +38.4 kJ mmol^{-1} (rel. to *MPP*-**4'**), obtained by conformational searches using MacroModel software (v11.8 OPLS3e, Low-frequency-mode search, non-solvated). Top view (ball and stick representation) and side view (space-filling representation for planes and rods, and stick representation for bridges). Only one enantiomeric form is depicted for each structure of **4'**.



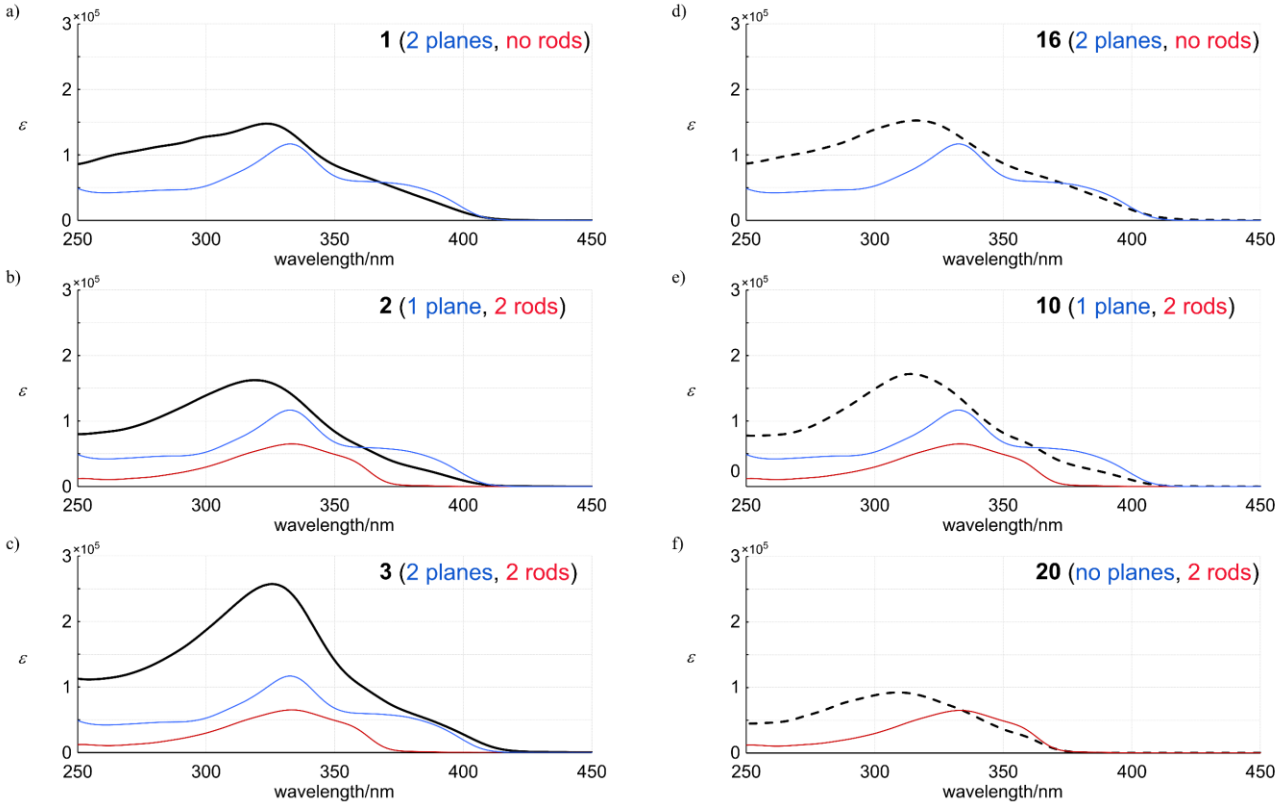


Fig. S4 UV spectra of **1**, **2** and **3** [a), b) and c) black solid line], **16**, **10** and **20**[2] [d), e) and f) black broken line], **5** (blue line) and **6** (red line), measured in dichloromethane at room temperature.

Absorption properties of layered cyclophanes **1** (two planes), **2** (one plane and two rods) and **3** (two planes and two rods) were compared with those of each component **5** (plane) or **6** (rod) (Fig. S4). The UV spectrum of **5** showed two-sectional absorption characteristic of 1,2,4,5-tetrakis(phenylethynyl)benzene. The maximum absorption at 333 nm (ε 1.17×10^5) was related to a planar conjugation with two phenylethynyl groups at a *para*-position, and a shoulder absorption at 363 nm (5.94×10^4) was related to a non-planar conjugation with two phenylethynyl groups at an *ortho*-position. The spectrum of **6** showed absorptions similar to the above (maximum absorption at 333 nm, and a smaller shoulder absorption at 353 nm), which was characteristic of 1,4-bis(phenylethynyl)benzene.

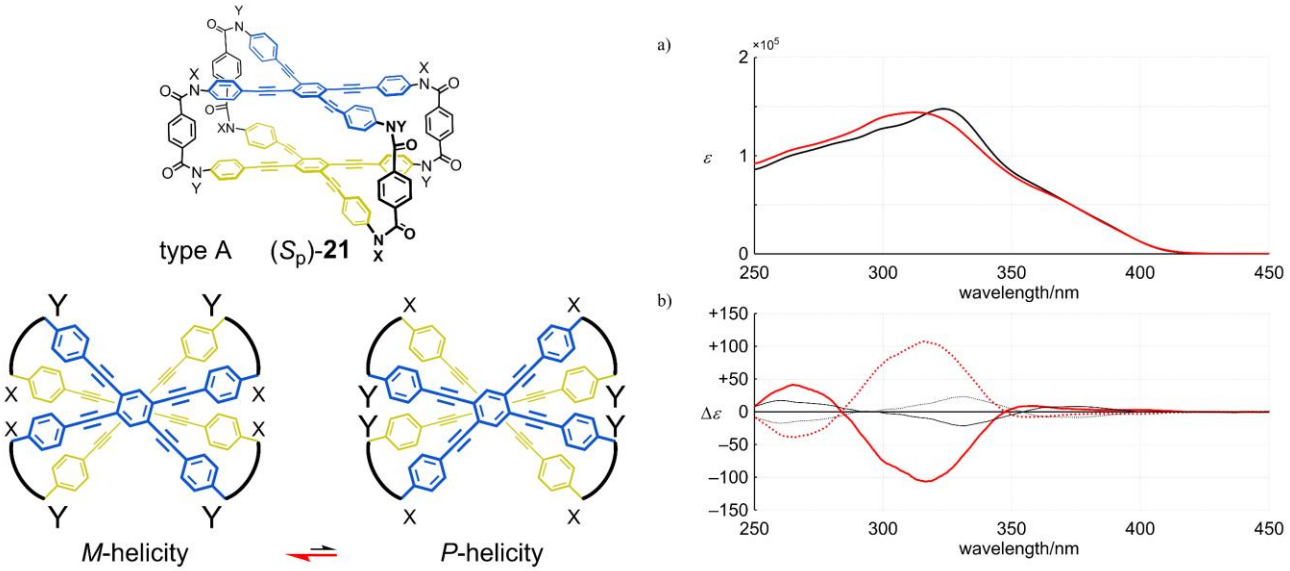
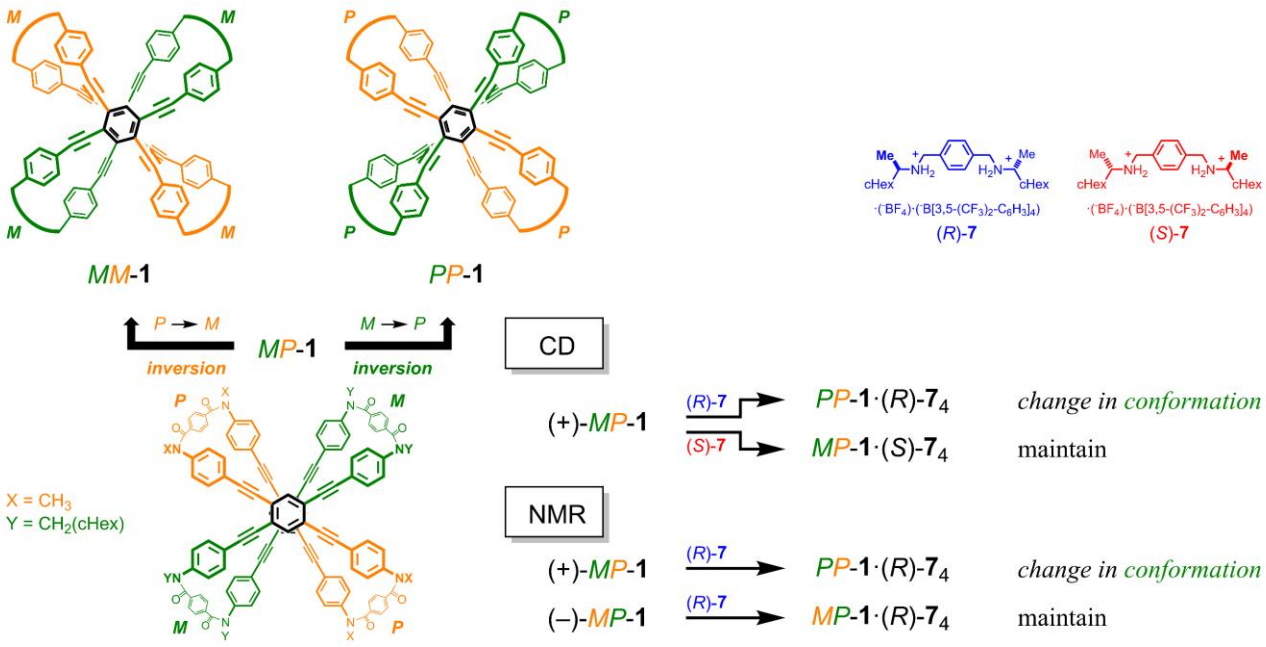


Fig. S5 Chemical structure of an isomeric two-layer cyclophane (S_p)-**21**[1], and (a) UV and (b) CD spectra of (–)-**21** (red solid line), (+)-**21** (red dashed line), (–)-**1** (black solid line) and (+)-**1** (black dashed line), measured in dichloromethane at room temperature. Note that two-layer cyclophanes (type A), **16** and (±)-**21**, are isomers with a difference in the arrangement of X (CH_3) and Y [CH_2(cHex)].

Stereospecific complexation of two-layer **1** and chiral guests (*R*)-**7** or (*S*)-**7**



Racemate of planar chiral **1** was optically resolved by HPLC separation with a chiral stationary column. In the CD spectra of each enantiomer, a mirrored pair of Cotton effects was found (**Fig. 4a**). We designated the diastereomeric conformations of **1** [X = CH_3, Y = CH_2(cHex)] as *MP*, *MM* and *PP*, where *M* and *P* denote the partial helicity that is generated between two bridged phenylethynyl groups. In two-layer **1**, two achiral planes are arranged orthogonally and thus the partial helicity is inherently generated to cancel the neighboring helicity (*MP*). Additional twisting is allowed by the inversion of partial helicity only at a particular two-fold bridge across the central benzene rings of the planes, and would lead to a pair of conformationally interconvertible helical forms *MM* and *PP*. If we consider the origin of the observed Cotton effects, two conclusions can be made. First, a conformation with *MP* is dominant in solution and the Cotton effects are due to the inherent achiral form. Second, the inherently achiral form had little or no effect even with the dominant presence and the Cotton effects were due to a bias of helical-sense preferences between the pseudomirrored pair of *MM* and *PP*, which were expected to be minor conformations in solution. To discuss this issue, we planned stereospecific complexation with enantiomeric guests based on some assumptions:

1. The chiral guest (*R*)-**7** or (*S*)-**7** prefers a particular sense of partial helicity in a complexed state.[2]

2. Every terephthaloyl bridge can capture a guest through the formation of hydrogen bonds. The bridge with X (CH_3) is a dummy site (*M* for S_p isomer, and *P* for R_p isomer) and cannot transfer the chiral information of the guest in a complexed state. A change in conformation (reversal of partial helicity) can be induced only at the bridge with Y [CH_2(cHex)] through transmission of chirality in the guest when the original preference (*M* for R_p isomer and *P* for S_p isomer) in **1** does not match that of the guest.

3. As a result, one enantiomeric guest can stereospecifically induce the host to prefer a particular sense of *MM* (S_p isomer) or *PP* (R_p isomer) in a complexed state. Alternatively, no change in conformation can be induced even in a complex (*MP*) with an antipodal guest.

We monitored the complexation of either isomer (+)-**1** or (–)-**1** with either (*R*)-**7** or (*S*)-**7** by UV, CD (**Fig. S6A**), and NMR (**Fig. S6B**) spectroscopy. Based on the results, we concluded that the original Cotton effects were due to the inherently achiral form (**Fig. 4a**), where cooperative cancellation should be attained by a preference for a particular helical sense of partial helicity that induces the neighboring helicity to prefer the opposite sense.

In the CD spectrum of (+)-**1** in the presence of (*R*)-**7**, the original Cotton effects were remarkably changed to show multiple bisignated Cotton effects. Alternatively, there was a slight change in the original Cotton effects induced by the addition of antipodal (*S*)-**7**. The UV spectra of (+)-**1** in the presence of (*R*)-**7** or (*S*)-**7** showed that absorptions about 1,2,4,5-tetrakis(phenylethynyl)benzene were slightly attenuated, and some conformational change was induced in both complexes.

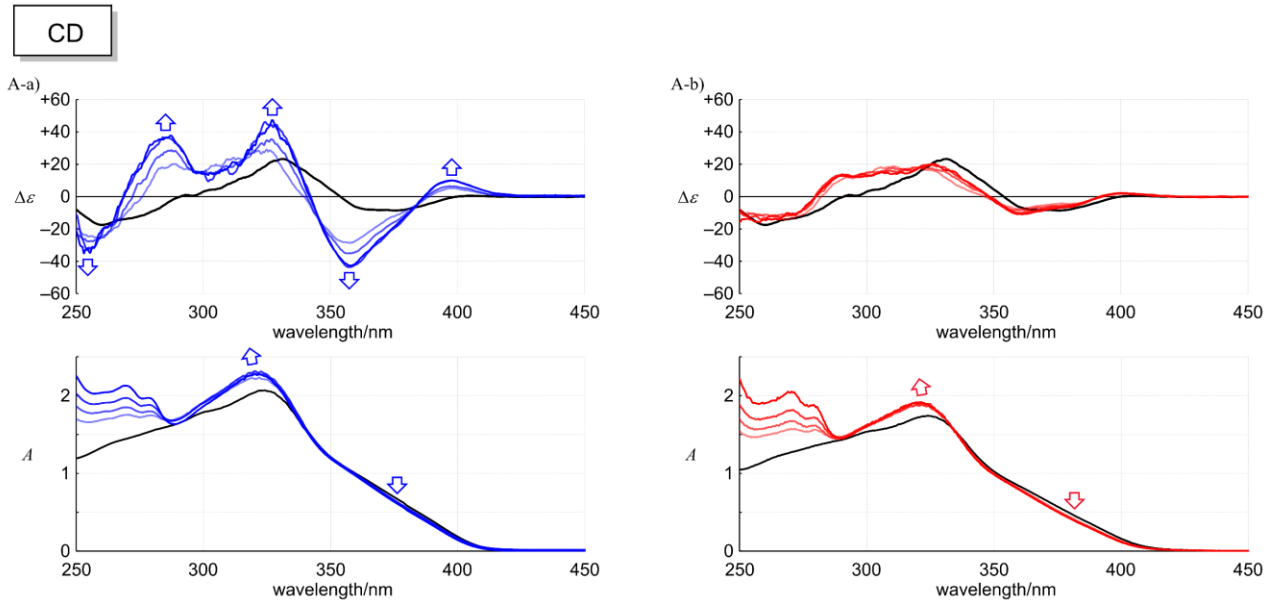


Fig. S6A Complexation of (+)-**1** with a chiral ditopic guest (*R*)-**7** or (*S*)-**7**: UV (lower) and CD (upper) spectra of (a) (+)-**1** (1.4×10^{-4} M) in the presence of (*R*)-**7** [0 equiv. (**1** only, black line), 4, 6, 8 and 12 equiv. (blue lines); (b) (+)-**1** (1.2×10^{-4} M) in the presence of (*S*)-**7** [0 equiv. (**1** only, black line), 4, 6, 8 and 12 equiv. (red lines), measured in dichloromethane at 293 K. Cell length = 0.1 cm.

Similar results were obtained in NMR titration experiments based on changes in the chemical shift on complexation. We found significant upfield shifts for the central phenylene protons (H^D and H^E) in the bridge. This result showed that bridges with X or Y acted as a binding site in each complex. In a complex of (+)-**1** with (*R*)-**7**, we found distinct disparities in the chemical shift between H^B and H^C, and between H^F and H^G, which were assigned to peripheral phenylene protons in the plane. This result showed that, in a complexed state, nonequivalent conformations (*MM* or *PP*) were induced in each partial helicity with X or Y, which was changed from the original equivalent conformation with X or Y (*MP*). Alternatively, in a complex of (–)-**1** with (*R*)-**7**, the corresponding values were close (H^B and H^C, and H^F and H^G). This result showed that the difference in the conformation was not so great between the partial helicity with X or Y even in a complexed state (*MP*), and thus the original conformation was considered to be

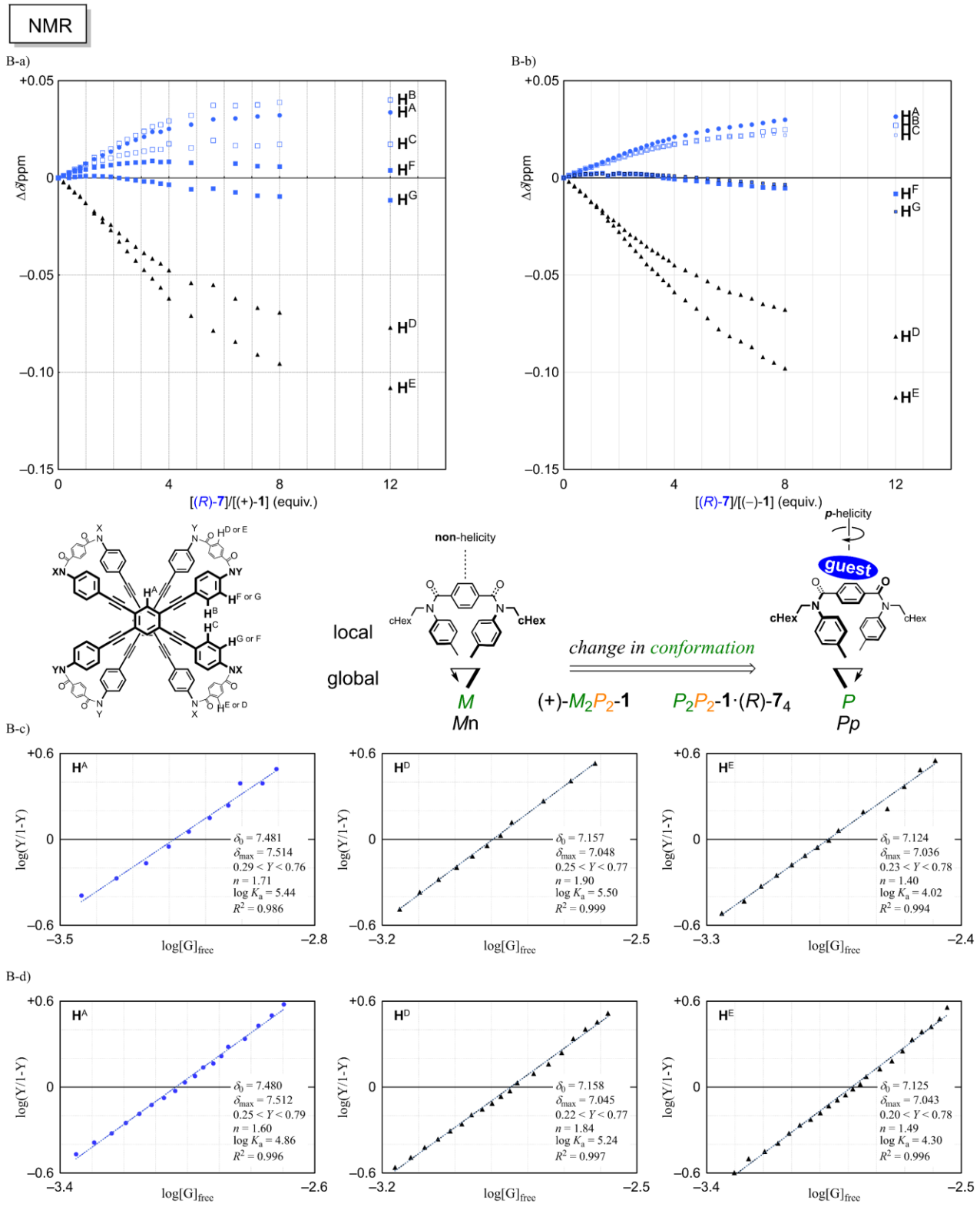


Fig. S6B Complexation of (+)-**1** [(a) and (c)] or (–)-**1** [(b) and (d)] with (*R*)-**7**: (a) and (b) NMR titration curves based on changes in the chemical shift ($\Delta\delta = \delta_{1\cdot7} - \delta_1$) of **1**; (c) and (d) Hill plots, measured in 2vol% acetonitrile-d_3/chloroform-*d* at 303 K. [**1**] = 0.5 mM, [**7**] = 0-6 mM.

maintained. Even in a complex where the original conformation was globally maintained, some local change seemed to be induced from nonhelical to helical (e.g., *M*n to *Mm*, or *P*n to *Pp*) in the partial helicity with Y [CH_2(cHex)], which might be explained by a similarity in the pattern of Hill plots, obtained not only from protons (H^D and H^E) in the binding site, but also from the aromatic protons H^A of the central benzene ring far from the binding site. The sigmoidal feature in the titration curves indicated that cooperative motion was induced in both bridges paired across the central benzene rings of the planes in each complex.

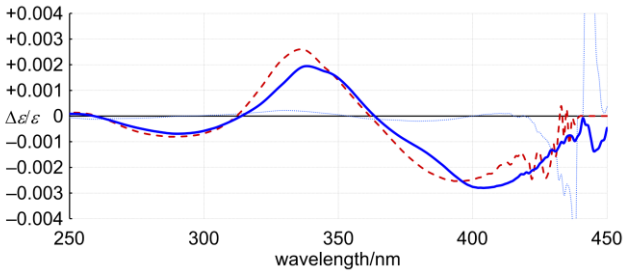


Fig. S7 Plots of $\Delta\varepsilon/\varepsilon$ for (+)-**1** (blue dashed line), (+)-**2** (red dashed line) and (+)-**3** (blue solid line) versus wavelength. All spectra were measured in dichloromethane at 293 K.

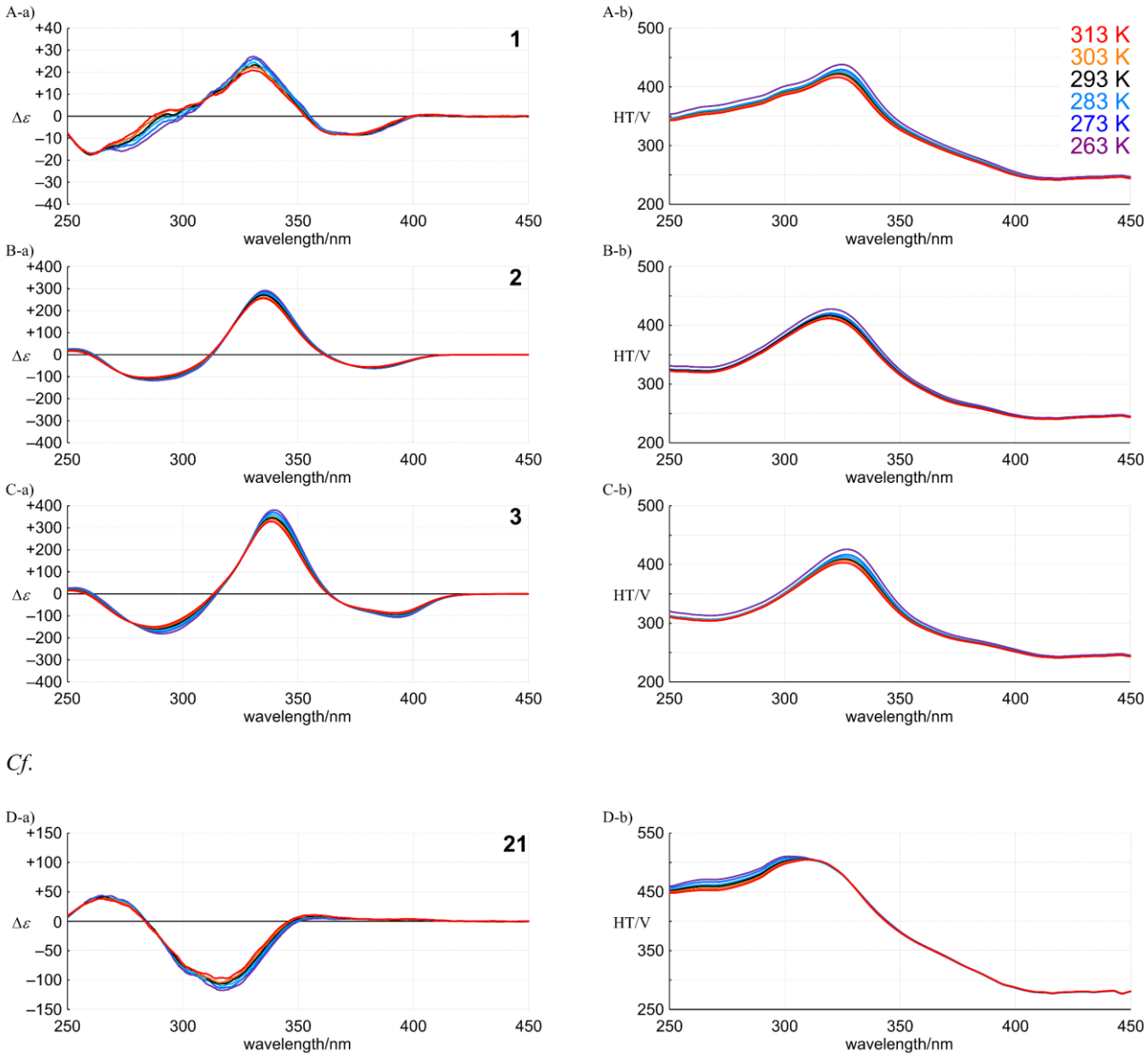


Fig. S8 VT-CD spectra (a) of (A) (+)-**1**, (B) (+)-**2**, (C) (+)-**3** and (D) (–)-**21**, and changes in HT/V (b), measured in dichloromethane at 263-313 K.

Synthesis of two-layer **1**, three-layer **2** and four-layer **3**

In three-layer **2**, two achiral rods of 1,4-bis(phenylethynyl)benzene are arranged above and below a single achiral plane of 1,2,4,5-tetrakis(phenylethynyl)benzene. Each end of the rod is secured at the 1,4- or 2,5-positions of the plane with a two-fold covalent bridge to exert planar chirality (**Scheme S1**). The four-fold bridging was attained in one reaction through the formation of four amide bonds from an acid chloride (**5''**) and an aniline (**6'**). During the reaction, an achiral isomer bridged at the 1,5- and 2,4-positions (**10**) was competitively produced. Since R_f values on SiO_2 for these isomers were close to each other, a mixture was passed through a chiral column to isolate (+)-**2** ($[\alpha]_D$ = +333), (–)-**2** ($[\alpha]_D$ = –314) and **10** in this order (**Chart S1**). The mass spectrum of each isomer confirmed that they had the same molecular weight (*m*/*z* = 2115).

In four-layer **3**, two achiral rods are arranged above and below two achiral planes that are stacked in pairs, and a similar strategy (four-fold bridging) was applied with the corresponding macrocyclic precursor *rac*-**13''** (**Scheme S2**) in place of the single plane of 1,2,4,5-tetrakis(phenylethynyl)benzene **5''** in **Scheme S1**. Since neither plane in each isomer of *rac*-**13** was allowed to rotate, the four-fold bridging led to the desired cyclophane **3** as a racemate, and no isomeric form was found, such as four-layer **4** with a difference in the stacking manner between the two achiral planes.

For the synthesis of two-layer **1**, the above-mentioned four-fold bridging in the final step was modified as a two-fold bridging of macrocyclic precursors *rac*-**14** and **15** with two achiral planes that were stacked in pairs (**Scheme S2**). Neither plane in each form of *rac*-**14** and **15** was allowed to rotate. Since the precursors were obtained as a mixture (**Scheme S3**) and subjected to the final step with no separation, the two-fold bridging with terephthaloyl chloride led to a mixture of two-layer **1** as a racemate and an isomeric form **16**. The mixture was passed through a chiral column to isolate (–)-**1** ($[\alpha]_D$ = –14.9), **16** and (+)-**1** ($[\alpha]_D$ = +11.9) in this order (**Chart S1**). The mass spectrum of each isomer confirmed that they had the same molecular weight (*m*/*z* = 2037).

These macrocyclic precursors *rac*-**13**, *rac*-**14** and **15** were derived from a single common macrocyclic intermediate **18** (**Scheme S3**). Two achiral planes were composed on the intermediate **18** through a four-fold Sonogashira coupling with a corresponding aryl iodide (**9** for *rac*-**13**, or **12** for *rac*-**14** and **15**). These two types of cyclophane are denoted as type A (two planes are arranged *in parallel*) and type B (two planes are arranged *orthogonally*).[1,2]

In the coupling reaction of **18** with **12**, macrocyclic precursors *rac*-**14** and **15** were obtained as a mixture of atropisomers. Based on our understanding of the assignment of an isomeric pair of quadruply-bridged cyclophanes to type A and type B, the chemical shift for the aromatic proton at the 3-position of the central benzene ring of 1,2,4,5-tetrakis(phenylethynyl)benzene in two-layer cyclophanes was observed relatively upfield for type A (**16**) compared to that for type B (**1**) (**Fig. S1**). Thus, we tentatively assigned two species of atropisomers according to the values of the corresponding chemical shift, and estimated the ratio of **15** to *rac*-**14** to be 2.2 based on the ^{1}H NMR spectrum of a purified mixture of *rac*-**14** and **15**.

Unlike the case with **12**, only a single product was obtained as a macrocyclic precursor (*m*/*z* = 2753) by the coupling of **18** with **9**. Since no comparison of the chemical shift was available with only a single product, the

assignment of this isomer (type A or B) was followed by assignment of the final product of the four-fold bridging. Fortunately, we could confirm that the final product was a racemate **3** (m/z = 3298) by the result of passage through a chiral column ($[\alpha]_D$ = +151 for (+)-**3**, **Chart S1**). Thus, we concluded that the single product of the coupling with **9** was *rac*-**13**, not **19**.

The product ratio of these macrocyclic precursors (*rac*-**13** to **19**, or *rac*-**14** to **15**) would depend on an earlier stage where at least one plane is expected to be rotatable until the last part has been introduced. If we consider the bulkiness around the nitrogen in **9** (*N*-cyclohexylmethyl-*N*-arylcarbonyl), the last part would prefer to react in a larger space where each phenylethynyl group already attached to the planes can be located as far as possible from each other.

For imaginary cyclophanes (S_p)-**22** (type B) and **23** (type A), conformational searches predicted that such a larger space could be found in type B (one of the two diastereomeric conformations of type B) rather than type A (**Fig. S9**). There was almost no difference in conformational energy between the two forms when each stereofactor around the nitrogen was minimized (Y = CH_3 and Ar = C_6H_5). We surmised that these two forms could be differentiated in terms of conformational energy with an increase in stereo bulkiness, which could be a reason for the regioselectivity.

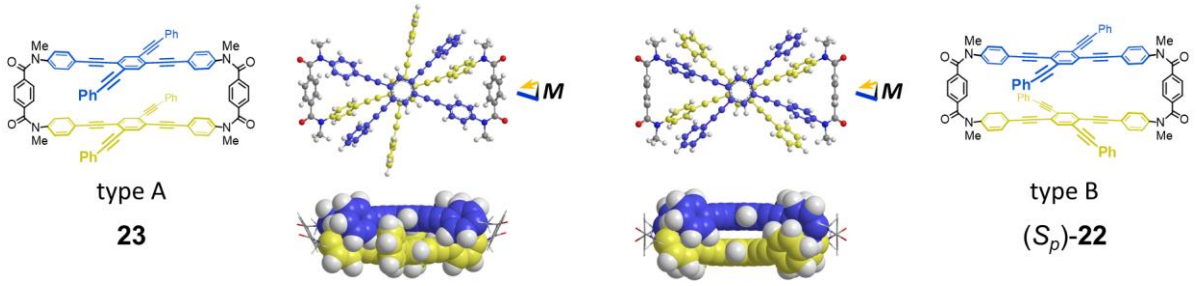


Fig. S9 Energy-minimized structures for (S_p)-**22** and **23**: type B (rel. 0 kJ mol^{-1}) and type A (+0.017 kJ mol^{-1} rel. to type B), obtained by conformational searches, using MacroModel software (v9.9 OPLS_2005, Monte Carlo Multiple Minimum method, non-solvated, 50 000 steps). Only a particular enantiomeric/diastereomeric form with (*M*)-helicity is depicted for **23**/(S_p)-**22**.

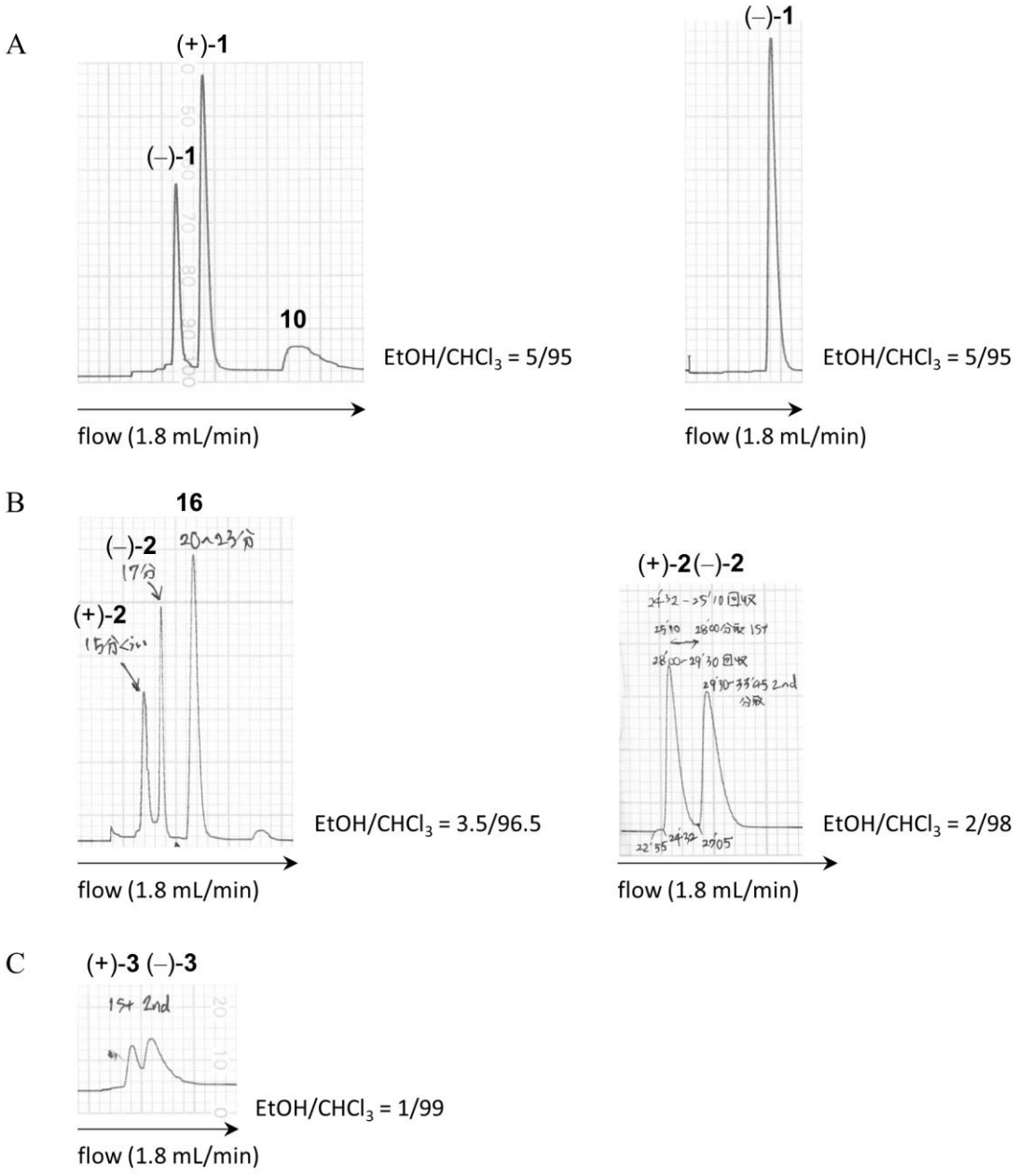
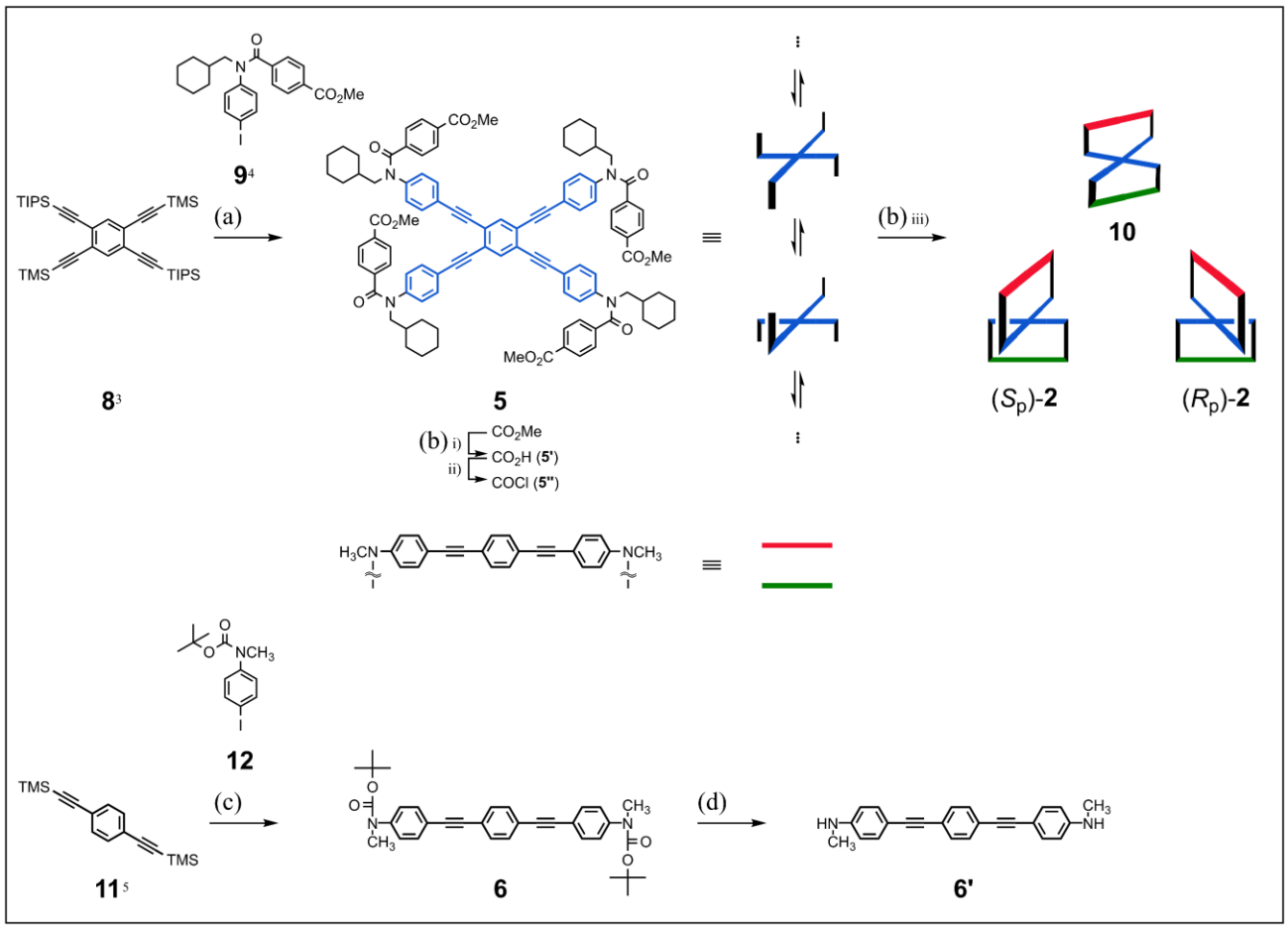


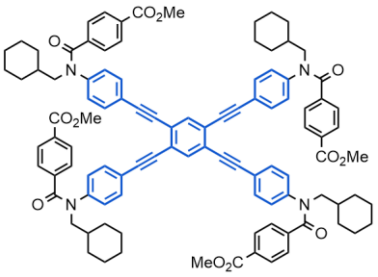
Chart S1 Chromatograms of HPLC with a chiral stationary column (CHIRALPAK IF, DAICEL Co., Japan).

Experimental



Scheme S1. Synthesis of three-layer cyclophanes (+)-**2** and (–)-**2**. Reagents and yields: (a) $Pd(PPh_3)_4$, CuI, tetra-*n*butylammonium fluoride (TBAF), THF, Et_3N (86%); (b) i) LiOH, H_2O, MeOH, THF (91%), ii) $SOCl_2$, benzyltriethylammonium chloride (BTEAC), CH_2Cl_2, iii) **6'**, Et_3N, THF, toluene (49% for *rac*-**2** and **10**); (c) **12**, $Pd(PPh_3)_4$, CuI, TBAF, THF, Et_3N (94%); (d) trifluoroacetic acid (TFA), CH_2Cl_2 (90%).

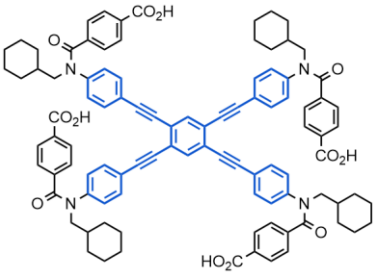
(a) Preparation of **5**



5

To a solution of **8**[3] (106 mg, 0.168 mmol), **9**[4] (641 mg, 1.34 mmol), $Pd(PPh_3)_4$ (52 mg, 0.045 mmol) and CuI (9 mg, 0.05 mmol) in THF (24 mL) and Et_3N (24 mL) was added a diluted solution of TBAF (0.71 mmol) in THF (10.5 mL) at 60 °C via a syringe pump over 12 h under an argon atmosphere, and the mixture was further stirred for 30 min. After removal of the solvents by evaporation, the residue was dissolved in ethyl acetate, which was washed with 1M aq. HCl, dried over magnesium sulfate, and then purified by column chromatography on SiO_2 (ethyl acetate/dichloromethane), followed by GPC (chloroform; JAIGEL-2H & 2.5H, Japan Analytical Industry Co., Ltd., Japan) to give **5** (236 mg) as a white solid in 86% yield. An analytical sample was obtained as a white solid by refluxing in ethanol, followed by collection through filtration. **5**: mp 207-208 °C; IR (neat) ν_{max}/cm^{-1} 2921, 2850, 2198, 1722, 1646, 1598, 1559, 1507, 1270; ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.86 (8H, d, J = 8.4 Hz), 7.65 (2H, s), 7.35 (8H, d, J = 8.4 Hz), 7.35 (8H, d, J = 8.4 Hz), 7.01 (8H, d, J = 8.4 Hz), 3.87 (12H, s), 3.84 (8H, d, J = 7.2 Hz), 1.8-1.6 (24H, br.m), 1.3-1.0 (20H, br.m);

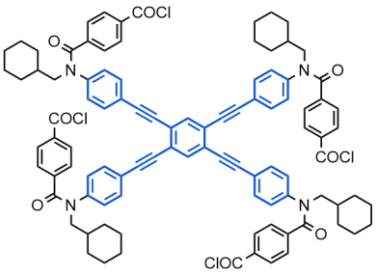
^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.6, 166.2, 143.8, 140.6, 135.3, 132.5, 130.9, 129.1, 128.5, 127.6, 125.0, 121.1, 94.6, 88.2, 56.0, 52.2, 36.4, 30.9, 26.3, 25.8; FD-LRMS *m/z* 1570.72 (M^+, 81%), 1571.73 ($[M+1]^+$, 100), 1572.73 ($[M+2]^+$, 64), 1573.74 ($[M+3]^+$, 30), 1574.74 ($[M+4]^+$, 14); FD-HRMS Found: 1570.71906, Calc. for $C_{102}H_{98}N_4O_{12}$: 1570.71812; UV λ_{max}(CH_2Cl_2)/nm (log ε) 363 (shoulder 4.77), 333 (5.07).



5'

(b) Preparation of (+)-**2** and (–)-**2**

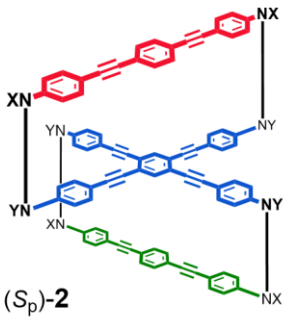
i) To a solution of **5** (925 mg, 0.588 mmol) in THF (24 mL) and MeOH (8 mL) was added a solution of $LiOH·H_2O$ (248 mg, 5.91 mmol) in water (8 mL) at room temperature, and the resulting suspension was stirred at 46 °C for 4 h until it turned transparent. After removal of the organic solvents by evaporation, the residue was acidified with 1M aq. HCl and extracted with ethyl acetate. The organic layer was separated and concentrated. The residue was suspended in refluxed methanol, and then collected through filtration to give carboxylic acid **5'** (810 mg) as a yellow solid in 91% yield.



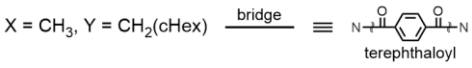
5''

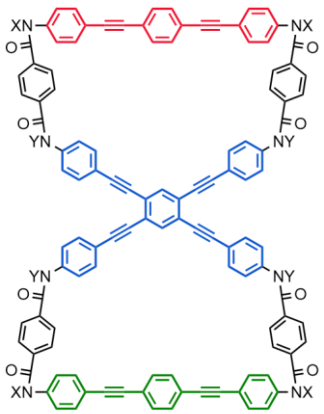
ii) To a refluxed suspension of **5'** (398 mg, 0.263 mmol) in CH_2Cl_2 (33 mL) containing a small amount of BTEAC (6 mg) were added several portions of $SOCl_2$ (0.20+0.25+0.5+0.5 mL, 20 mmol) with an interval of 0.5 h, and concentrated to give acid chloride **5''**, which was dissolved in THF and subjected to the following reaction.

iii) To a refluxed solution of **6'** (162 mg, 0.482 mmol) in THF (200 mL) containing a small amount of Et_3N (0.3 mL) was added the above-prepared solution of **5''** in THF (50 mL), and the mixture was further refluxed for 15 h. The reaction mixture was quenched by 1M aq. NaOH and concentrated by evaporation. The residue was dissolved in dichloromethane, which was washed with satd. aq. $NaHCO_3$, dried over magnesium sulfate, and passed through a Celite/Al_2O_3 pad. The filtrate was concentrated and purified by column chromatography on SiO_2/Al_2O_3 (tetrahydrofuran/dichloromethane), followed by GPC (chloroform) to give a mixture of *rac*-**2** and **10** (250 mg) as a yellow solid in 49% yield. (+)-**2**, (–)-**2** and **10** were roughly separated in this order by HPLC separation with a chiral stationary column (5:95 ethanol/chloroform; CHIRALPAK IF, DAICEL Co., Japan). Finally, each of (+)-**2**, (–)-**2** and **10** was isolated in pure form as a white solid by repeated purification through the same column (eluted with 2:98 ethanol/chloroform for **2** and 3.5:96.5 ethanol/chloroform for **10**).



(S_p)-**2**





10

X = CH_3, Y = CH_2(cHex)

(+)-**2** (first fraction): mp 265-268 °C (dec); $[\alpha]_D^{24}$ = +332.7 (c = 0.252, chloroform); IR (neat) ν_{max}/cm^{-1} 3044, 2922, 2851, 2207, 2199, 1653, 1646, 1636, 1600, 1559, 1516; ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.30 (8H, d, J = 8.8 Hz), 7.23 (8H,

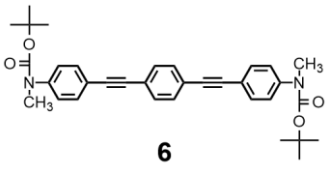
d, J = 8.4 Hz), 7.16 (8H, d, J = 8.8 Hz), 7.13 (8H, d, J = 8.8 Hz), 7.13 (2H, s), 7.11 (8H, s), 6.86 (8H, d, J = 8.8 Hz), 6.79 (8H, d, J = 8.4 Hz), 3.79 (4H, dd, J = 7.2, 13.6 Hz), 3.74 (4H, dd, J = 7.2, 13.6 Hz), 3.44 (12H, s), 1.8-1.0 (44H, m); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.7, 169.4, 144.4, 143.9, 137.9, 136.6, 134.9, 132.1, 131.0, 128.3, 127.9, 127.3, 126.3, 124.5, 122.5, 121.0, 120.8, 93.9, 89.9, 89.7, 88.2, 56.0, 38.0, 36.4, 31.0, 30.9, 26.3, 25.8; FD-LRMS m/z 1057.49 (M^{2+}, 23%), 1057.99 ([M+1]$^{2+}$, 39), 1058.50 ([M+2]$^{2+}$, 39), 1059.00 ([M+3]$^{2+}$, 29), 1059.50 ([M+4]$^{2+}$, 19), 1060.00 ([M+5]$^{2+}$, 10), 2114.99 (M^+, 60), 2115.99 ([M+1]$^+$, 100), 2116.99 ([M+2]$^+$, 88), 2117.99 ([M+3]$^+$, 56), 2118.99 ([M+4]$^+$, 27), 2120.00 ([M+5]$^+$, 14); FD-HRMS Found: 2114.94014, Calc. for $C_{146}H_{122}N_8O_8$: 2114.93856; CD λ(CH_2Cl_2)/nm ($\Delta\varepsilon$) 382 (–58), 335 (+271), 286 (–109), 252 (+21).

(–)-**2** (second fraction): $[\alpha]_D^{24}$ = –314.2 (c = 0.0455, chloroform); FD-LRMS m/z 1057.50 (M^{2+}, 13%), 1058.00 ([M+1]$^{2+}$, 26), 1058.50 ([M+2]$^{2+}$, 26), 1059.00 ([M+3]$^{2+}$, 17), 1059.50 ([M+4]$^{2+}$, 11), 1059.98 ([M+5]$^{2+}$, 11), 2114.99 (M^+, 59), 2115.99 ([M+1]$^+$, 100), 2116.99 ([M+2]$^+$, 89), 2117.99 ([M+3]$^+$, 57), 2118.98 ([M+4]$^+$, 27), 2119.99 ([M+5]$^+$, 13); FD-HRMS Found: 2114.93829, Calc. for $C_{146}H_{122}N_8O_8$: 2114.93856; UV λ_{max}(CH_2Cl_2)/nm (log ε) 380 (sh. 4.48), 360 (sh. 4.79), 318 (5.21); CD λ(CH_2Cl_2)/nm ($\Delta\varepsilon$) 382 (+56), 335 (–256), 286 (+106), 252 (–18).

10 (third fraction): mp >295 °C (dec); IR (neat) ν_{max}/cm^{-1} 3043, 2923, 2850, 2207, 1653, 1648, 1601, 1559, 1516; ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.38 (8H, d, J = 8.8 Hz), 7.36 (8H, s), 7.23 (8H, d, J = 8.8 Hz), 7.13 (8H, d, J = 8.4 Hz), 7.04 (8H, d, J = 8.4 Hz), 7.01 (2H, s), 6.85 (8H, d, J = 8.8 Hz), 6.70 (8H, d, J = 8.8 Hz), 3.75 (8H, d, J = 7.2 Hz), 3.44 (12H, s), 1.8-1.0 (44H, m); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.6, 169.6, 144.4, 144.2, 137.5, 137.0, 135.3, 132.3, 132.2, 131.4, 128.0, 127.9, 127.4, 126.8, 124.9, 122.8, 121.2, 120.8, 94.3, 90.2, 90.1, 88.5, 56.2, 37.5, 36.4, 30.9, 26.3, 25.8; FD-LRMS m/z 1057.49 (M^{2+}, 24%), 1058.00 ([M+1]$^{2+}$, 44), 1058.49 ([M+2]$^{2+}$, 41), 1059.00 ([M+3]$^{2+}$, 30), 1059.49 ([M+4]$^{2+}$, 19), 1060.00 ([M+5]$^{2+}$, 11), 2114.98 (M^+, 59), 2115.99 ([M+1]$^+$, 100), 2116.99 ([M+2]$^+$, 93), 2117.99 ([M+3]$^+$, 60), 2118.99 ([M+4]$^+$, 32), 2119.99 ([M+5]$^+$, 16); FD-HRMS Found: 2114.93983, Calc. for $C_{146}H_{122}N_8O_8$: 2114.93856; UV λ_{max}(CH_2Cl_2)/nm (log ε) 380 (sh. 4.48), 360 (sh. 4.81), 314 (5.24).

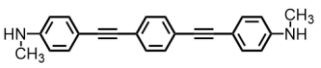
(c) Preparation of **6**

To a solution of **11**[5] (500 mg, 1.85 mmol), **12** (1.48 g, 4.44 mmol), $Pd(PPh_3)_4$ (25 mg, 0.022 mmol) and CuI (22 mg, 0.12 mmol) in THF (7 mL) and Et_3N (25 mL) was added a diluted solution of TBAF (3.7 mmol) in THF (8.3 mL) at 42 °C via a syringe pump over 23 h under an argon atmosphere, and the mixture was further stirred for 30 min. After removal of the solvents by evaporation, the residue was dissolved in ethyl acetate, which was washed with satd. aq. $NaHCO_3$, dried over magnesium sulfate, and then purified by column chromatography on SiO_2 (dichloromethane/hexane) to give **6** (935 mg) as a white solid in 94% yield. An analytical sample was obtained as a white solid by refluxing in methanol, followed by collection through filtration. **6**: mp 186-187 °C; IR (neat) ν_{max}/cm^{-1} 2979, 2929, 2216, 1696, 1604, 1521; ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.50 (4H, s), 7.48 (4H, d, J = 8.4 Hz), 7.25 (4H, d, J = 8.4 Hz), 3.28 (6H, s), 1.47 (18H, s); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 154.4, 143.9, 131.8, 131.5, 125.0, 123.1, 119.6, 91.0, 89.0, 80.7, 37.0, 28.3; FD-LRMS m/z 536.28 (M^+, 100%), 537.29 ([M+1]$^+$, 37), 538.29 ([M+2]$^+$, 8); FD-HRMS Found: 536.26588, Calc. for $C_{34}H_{36}N_2O_4$: 536.26751; UV λ_{max}(CH_2Cl_2)/nm (log ε) 353 (sh. 4.66), 333 (4.81).



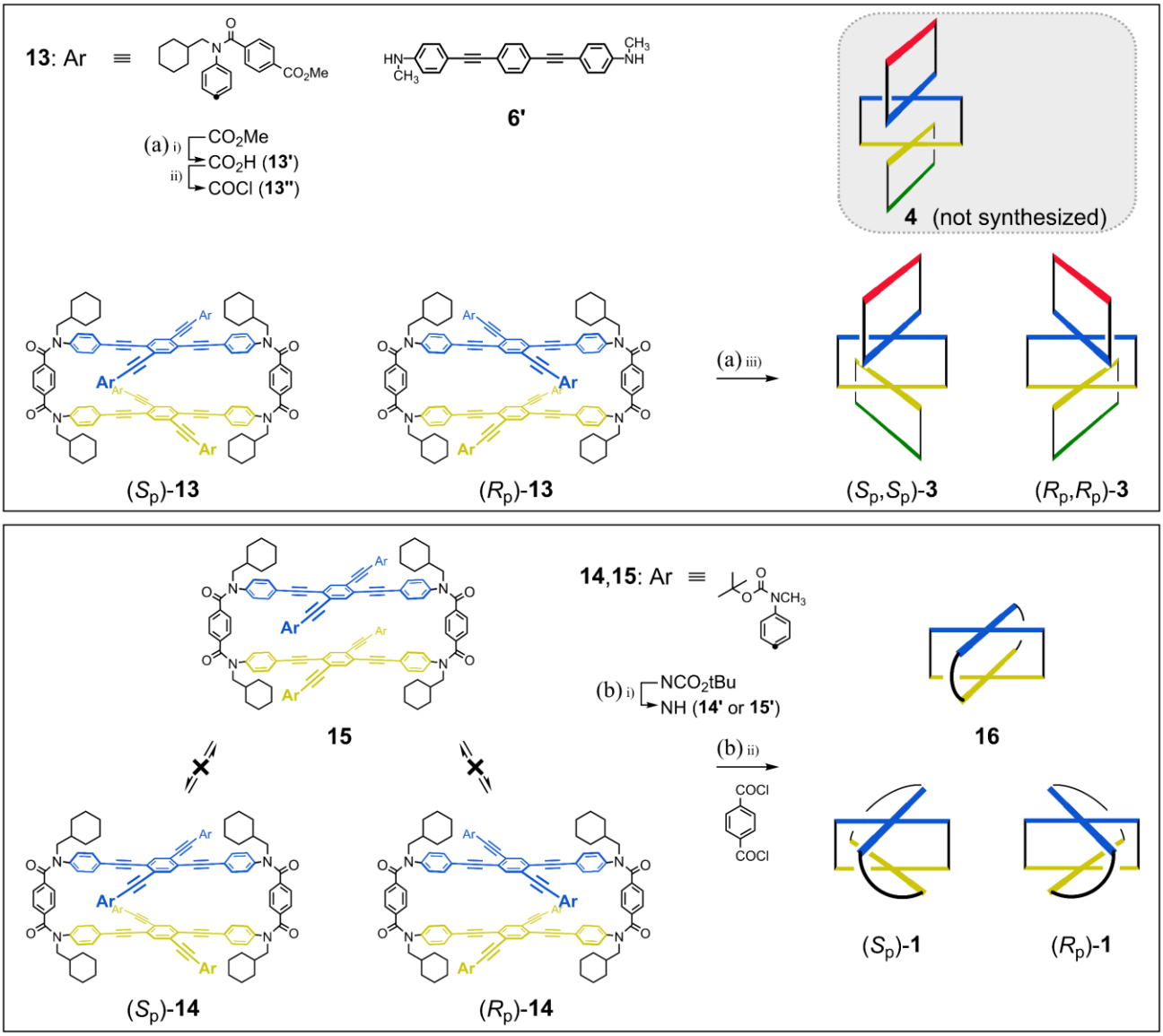
6

(d) Preparation of **6'**



6'

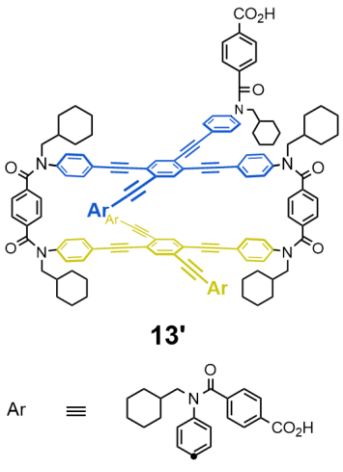
To a solution of **6** (863 mg, 1.61 mmol) in CH_2Cl_2 (100 mL) was added TFA (10 mL) at room temperature, and the mixture was stirred for 1h, diluted with dichloromethane, and then quenched by aq. 1M NaOH. The organic layer was separated, diluted with tetrahydrofuran, dried over magnesium sulfate, and passed through a Celite/SiO_2 pad. The filtrate was concentrated and suspended in methanol. The resulting solid was collected by filtration to give **6'** (485 mg) as a yellow solid in 90% yield. ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.43 (4H, s), 7.36 (4H, d, J = 8.4 Hz), 6.56 (4H, d, J = 8.4 Hz), 3.92 (2H, br.s), 2.86 (6H, s).



Scheme S2. Synthesis of four-layer cyclophanes (+)-**3** and (–)-**3**, and two-layer cyclophanes (+)-**1** and (–)-**1**. Reagents and yields: (a) i) LiOH, H_2O, MeOH, THF, ii) $SOCl_2$, BTEAC, CH_2Cl_2, iii) **6'**, Et_3N, THF (31% for *rac*-**3**); (b) i) TFA, CH_2Cl_2, ii) terephthaloyl chloride, Et_3N, THF, toluene (25% for *rac*-**1** and **16**).

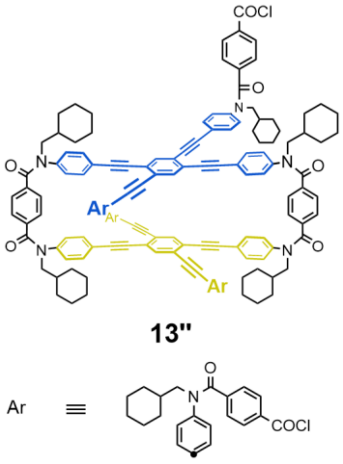
(a) Preparation of (+)-**3** and (–)-**3**

i) To a solution of *rac*-**13** (386 mg, 0.140 mmol) in THF (57 mL) and MeOH (18 mL) was added a solution of $LiOH·H_2O$ (570 mg, 13.6 mmol) in water (18 mL) at room temperature, and the mixture was stirred at room temperature for 1 h and concentrated. The residue was acidified with 1M aq. HCl and extracted with ethyl acetate. The organic layer was separated and concentrated to give a yellow solid (393 mg) containing carboxylic acid *rac*-**13'**.



ii) To a suspension of *rac*-**13'** (393 mg) in CH_2Cl_2 (37 mL) containing a small amount of BTEAC (9 mg) was added $SOCl_2$ (1.6 mL, 22 mmol). The mixture was refluxed for 2 h, and then divided into two portions. Each portion was concentrated to give a solid containing acid chloride *rac*-**13''**, which was dissolved

in THF (200 mg/36 mL and 210 mg/36 mL), and then immediately subjected to the following reaction. The following cyclization reactions were implemented in two batches (*See* Table). The crude products were combined and purified at once.



iii) To a solution of **6'** in toluene and THF containing a small amount of Et_3N was added an above-prepared solution of *rac*-**13''** at room temperature. The mixture was warmed to 80 °C, stirred for 1 h, and then concentrated. The resulting solid was dissolved in dichloromethane, which was washed with 1M aq. NaOH, dried over magnesium sulfate, and then roughly purified by column chromatography on Al_2O_3/SiO_2 (tetrahydrofuran/dichloromethane) to give a solid. The two solids were combined and further purified through GPC (chloroform), followed by HPLC separation with a chiral stationary column (5:95 ethanol/chloroform; CHIRALPAK IF) to give *rac*-**3** (135 mg) as a pale-yellow solid in 31% yield. Finally, only (+)-**3** was isolated in pure form as a white solid through the same column (eluted with 1:99 ethanol/chloroform), while (–)-**3** was obtained as a mixture with low optical/chemical purity.

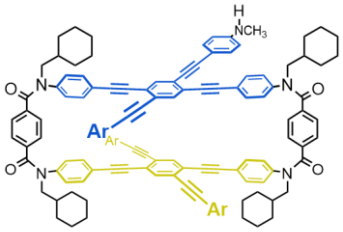
	6'	Toluene	THF	Et_3N	*rac*-**13''**	THF
1	43 mg (0.13 mmol)	66 mL	30 mL	0.1 mL	200 mg	36 mL
2	46 mg (0.14 mmol)	69 mL	33 mL	0.1 mL	210 mg	36 mL

(+)-**3** (first fraction): mp >255 °C (dec); $[\alpha]_D^{24}$ = +151.4 (*c* = 0.346, chloroform); IR (neat) ν_{max}/cm^{-1} 3040, 2922, 2850, 2199, 1653, 1647, 1601, 1559, 1513; ^1H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.23 (8H, d, *J* = 8.4 Hz), 7.20 (8H, d, *J* = 8.8 Hz), 7.15 (8H, d, *J* = 8.8 Hz), 7.15 (8H, d, *J* = 8.8 Hz), 7.13 (8H, s), 7.12 (8H, d, *J* = 8.8 Hz), 7.06 (4H, br.s), 7.05 (8H, br.s), 6.84 (8H, d, *J* = 8.4 Hz), 6.79 (8H, d, *J* = 8.4 Hz), 6.77 (8H, d, *J* = 8.8 Hz), 3.84 (4H, dd, *J* = 7~8, 13.6 Hz), 3.77 (4H, dd, *J* = 7~8, 13.6 Hz), 3.73 (4H, dd, *J* = 7~8, 13.6 Hz), 3.67 (4H, dd, *J* = 7~8, 13.6 Hz), 3.42 (12H, s), 1.8-1.0 (44H×2, br.m); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.6, 169.1, 144.5, 144.3, 144.2, 137.7, 137.6, 136.8, 134.5, 132.1, 132.1, 132.0, 131.0, 128.4, 128.1, 128.0, 127.2, 127.1, 126.3, 124.9, 124.7, 122.5, 120.9, 120.6, 120.6, 94.5, 94.2, 89.9, 89.7, 88.7, 88.2, 56.2, 56.2, 38.0, 36.6, 36.5, 31.1, 31.0, 31.0, 31.0, 26.3, 26.3, 25.9, 25.9, 25.8; FD-LRMS *m/z* 1648.71 (M^{2+}, 17%), 1649.20 ($[M+1]^{2+}$, 50), 1649.70 ($[M+2]^{2+}$, 81), 1650.20 ($[M+3]^{2+}$, 100), 1650.70 ($[M+4]^{2+}$, 84), 1651.20 ($[M+5]^{2+}$, 68), 1651.70 ($[M+6]^{2+}$, 43), 3297.47 (M^+, 18), 3298.43 ($[M+1]^+$, 42), 3299.45 ($[M+2]^+$, 64), 3300.44 ($[M+3]^+$, 59), 3301.45 ($[M+4]^+$, 46), 3302.44 ($[M+5]^+$, 26), 3303.45 ($[M+6]^+$, 14); FD-HRMS Found: 3297.54277, Calc. for $C_{228}H_{200}N_{12}O_{12}$: 3297.54086; UV $\lambda_{max}(CH_2Cl_2)$/nm (log ε) 380 (sh. 4.78), 365 (sh. 4.95), 326 (5.41); CD $\lambda(CH_2Cl_2)$/nm ($\Delta\varepsilon$) 392 (–93), 339 (+347), 289 (–159), 252 (+19).

(–)-**3** (second fraction cont. first fraction): CD $\lambda(CH_2Cl_2)$/nm ($\Delta\varepsilon$) 391 (+34), 337 (–131), 286 (+65).

(b) Preparation of (+)-**1** and (–)-**1**

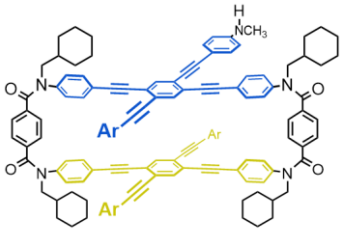
i) To an ice-cooled solution of *rac*-**14** and **15** in CH_2Cl_2 was added TFA, and the mixture was stirred at that temperature for 1.5 h, diluted with dichloromethane, and then quenched by aq. 1M NaOH. The organic layer was separated, dried over magnesium sulfate, and then concentrated. The resulting solid was purified by column chromatography on SiO_2 (tetrahydrofuran/dichloromethane) to give a mixture of *rac*-**14'** and **15'** as a yellow solid.



14'

Ar ≡ 

ii) To a solution of *rac*-**14'** and **15'** in toluene and THF containing a small amount of Et_3N was added terephthaloyl chloride at room temperature. The mixture was warmed to 78-80 °C, stirred for several hours, and then concentrated. The resulting solid was dissolved in dichloromethane, which was washed with 1M aq. NaOH, dried over magnesium sulfate, and then passed through a Celite/Al_2O_3 pad. The filtrates were combined, concentrated, and then purified by column chromatography on Al_2O_3/SiO_2 (tetrahydrofuran/dichloromethane), followed by GPC (chloroform) to give a mixture of *rac*-**1** and **16** (116 mg, **16**/**1** = 1.17) as a pale-yellow solid in 25% yield. Each of (–)-**1**, **16** and (+)-**1** was separated in this order by repeated HPLC separation with a chiral stationary column (5:95 ethanol/chloroform; CHIRALPAK IF) as a white solid in pure form.

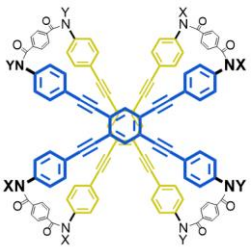


15'

Ar ≡ 

	rac-**14** and **15**	TFA	CH_2Cl_2	*rac*-**14'** and **15'**	Terephthaloyl chloride	Et_3N	Toluene	THF
1	223 mg (0.102 mmol)	6 mL	12 mL	173 mg (0.0973 mmol)	48 mg (0.24 mmol)	0.14 mL	40 mL	22 mL
2	347 mg (0.159 mmol)	9 mL	18 mL	230 mg (0.129 mmol)	63 mg (0.31 mmol)	0.19 mL	54 mL	30 mL

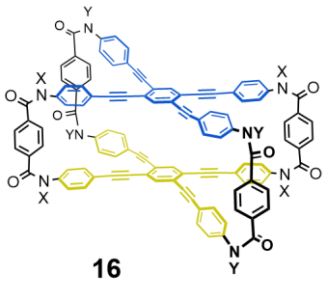
(–)-**1** (first fraction): mp >240 °C (dec); $[\alpha]_D^{23}$ = –7.3 (*c* = 0.241, chloroform); IR (neat) ν_{max}/cm^{-1} 3044, 2922, 2850, 2207, 1653, 1647, 1601, 1559, 1508; FD-LRMS *m*/*z* 1018.46 (M^{2+}, 15%), 1018.98 ($[M+1]^{2+}$, 29), 1019.48 ($[M+2]^{2+}$, 30), 1019.98 ($[M+3]^{2+}$, 17), 1020.49 ($[M+4]^{2+}$, 17), 2036.94 (M^+, 61), 2037.95 ($[M+1]^+$, 100), 2038.95 ($[M+2]^+$, 87), 2039.96 ($[M+3]^+$, 51), 2040.97 ($[M+4]^+$, 23); FD-HRMS Found: 2036.89041, Calc. for $C_{140}H_{116}N_8O_8$: 2036.89161; CD $\lambda(CH_2Cl_2)$/nm ($\Delta\varepsilon$) 405 (–0.6), 376 (+8.1), 332 (–21), 260 (+17).



(S_p)-**1**

X = CH_3, Y = CH_2(cHex)

16 (second fraction): mp >275 °C (dec); IR (neat) ν_{max}/cm^{-1} 3043, 2919, 2850, 2199, 1653, 1647, 1637, 1599, 1559, 1507; ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.43 (4H, s), 7.25 (8H, d, *J* = 8.4 Hz), 7.24 (8H, d, *J* = 8.4 Hz), 7.16 (8H, s), 7.14 (8H, s), 6.77 (8H, d, *J* = 8.4 Hz), 6.77 (8H, d, *J* = 8.4 Hz), 3.83 (4H, dd, *J* = 7.6, 13.6 Hz), 3.67 (4H, dd, *J* = 7.6, 13.6 Hz), 3.45 (12H, s), 1.8-1.0 (44H, m); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.5, 169.2, 144.7, 144.0, 137.3, 136.8, 135.4, 132.2, 132.1, 128.3, 128.2, 127.0, 126.3, 124.9, 124.9, 120.9, 120.7, 94.2, 94.1, 88.5, 88.4, 56.0, 38.0, 36.4, 30.9, 30.9, 26.3, 25.8; FD-LRMS *m*/*z* 1018.47 (M^{2+}, 10%), 1018.97 ($[M+1]^{2+}$, 19), 1019.48 ($[M+2]^{2+}$, 18), 1019.98 ($[M+3]^{2+}$, 14), 1020.48 ($[M+4]^{2+}$, 11), 1020.99

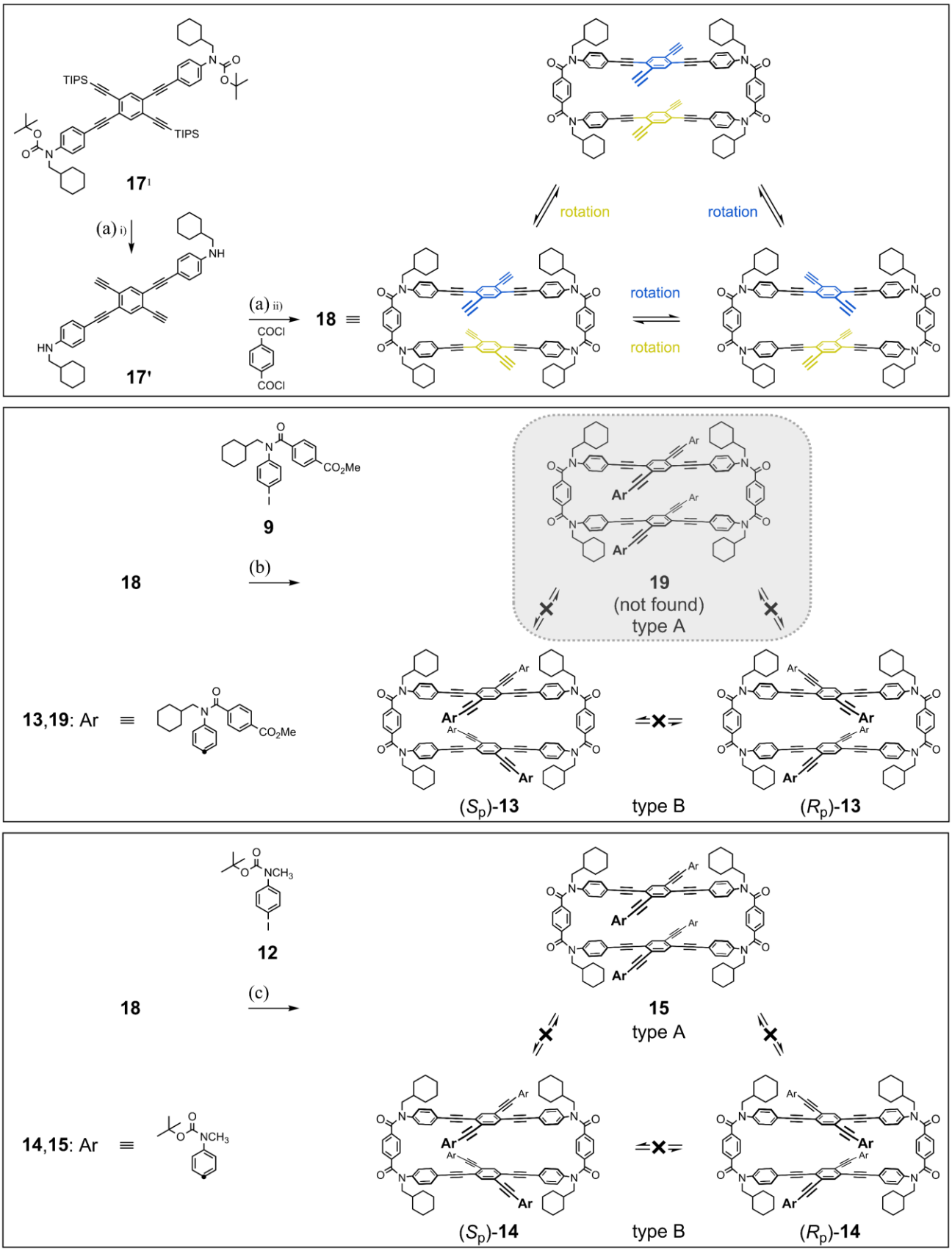


16

X = CH_3, Y = CH_2(cHex)

([M+5]^{2}, 5), 2036.96 (M^{+}, 61), 2037.95 ([M+1]$^{+}$, 100), 2038.97 ([M+2]$^{+}$, 92), 2039.98 ([M+3]$^{+}$, 55), 2040.96 ([M+4]$^{+}$, 27), 2041.99 ([M+5]$^{+}$, 12); FD-HRMS Found: 2036.89185, Calc. for $C_{140}H_{116}N_8O_8$: 2036.89161; UV $\lambda_{max}(CH_2Cl_2)$/nm (log ε) 370 (sh. 4.78), 316 (5.18).

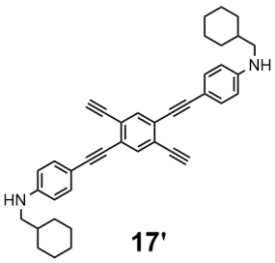
(+)-**1** (third fraction): $[\alpha]_D^{24}$ = +5.9 (c = 0.264, chloroform); ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.48 (4H, s), 7.29 (8H, d, J = 8.4 Hz), 7.29 (8H, d, J = 8.4 Hz), 7.16 (8H, s), 7.13 (8H, s), 6.85 (8H, d, J = 8.4 Hz), 6.83 (8H, d, J = 8.4 Hz), 3.81 (4H, dd, J = 7.6, 13.6 Hz), 3.74 (4H, dd, J = 7.6, 13.6 Hz), 3.46 (12H, s), 1.8-1.0 (44H, m); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.5, 169.2, 144.7, 144.0, 137.3, 136.8, 134.4, 132.2, 132.1, 128.4, 128.2, 127.1, 126.2, 125.2, 125.1, 120.8, 120.6, 94.3, 94.1, 87.9, 87.9, 55.9, 37.9, 36.4, 31.0, 26.3, 25.8; FD-LRMS m/z 1018.47 (M^{2+}, 18%), 1018.97 ([M+1]$^{2+}$, 32), 1019.48 ([M+2]$^{2+}$, 29), 1019.98 ([M+3]$^{2+}$, 20), 1020.49 ([M+4]$^{2+}$, 14), 2036.95 (M^{+}, 61), 2037.95 ([M+1]$^{+}$, 100), 2038.96 ([M+2]$^{+}$, 93), 2039.97 ([M+3]$^{+}$, 59), 2040.96 ([M+4]$^{+}$, 29); FD-HRMS Found: 2036.89114, Calc. for $C_{140}H_{116}N_8O_8$: 2036.89161; UV $\lambda_{max}(CH_2Cl_2)$/nm (log ε) 365 (sh. 4.79), 323 (5.17); CD $\lambda(CH_2Cl_2)$/nm ($\Delta\varepsilon$) 405 (+0.5), 376 (–8.6), 331 (+23), 260 (–17).



Scheme S3. Synthesis of intermediary macrocycles **18**, *rac*-**13,** *rac*-**14** and **15**. Reagents and yields: (a) i) TFA, CH_2Cl_2 (85%), ii) terephthaloyl chloride, Et_3N, THF, toluene (31%); (b) **9**, $Pd(PPh_3)_4$, CuI, Et_3N, THF (44% for *rac*-**13**); (c) **12**, $Pd(PPh_3)_4$, CuI, Et_3N, THF (65% for *rac*-**14** and **15**).

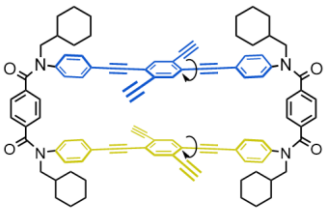
(a) Preparation of **18**

i) To a solution of **17**[1] (2.71 g, 2.55 mmol) in CH_2Cl_2 (120 mL) was added TFA (17 mL) at room temperature. The mixture was stirred at room temperature for 1 h, quenched with 1M aq. NaOH, and then separated. The organic layer was dried over magnesium sulfate, passed through a Celite/SiO_2 pad and concentrated. The residue was dissolved in THF (67 mL) and treated with 1M TBAF solution in THF (5.4 mL). After stirring at room temperature for 20 min, the mixture was concentrated by evaporation. The residue was dissolved in dichloromethane, which was washed with water and separated. The organic layer was dried over magnesium sulfate and passed through a SiO_2 column to give **17'** (1.19 g) as a yellow solid in 85% yield. **17'**: ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.61 (2H, s), 7.36 (4H, d, J = 8.4 Hz), 6.53 (4H, d, J = 8.4 Hz), 3.97 (2H, br.s), 3.40 (2H, s), 2.98 (4H, d, J = 6.4 Hz), 1.9-1.5 (10H, m), 1.3-1.1 (8H, m), 1.1-0.9 (4H, m). The following cyclization reactions were implemented in several batches (*See* Table). The crude products were combined and purified at once.



17'

ii) To a solution of terephthaloyl chloride and Et_3N in toluene was added a solution of **17'** in THF (the first half) at 45 °C via an additional funnel over 0.5 h, and the mixture was warmed to 80 °C. To the warmed solution was added in one stroke a solution of **17'** in THF (the last half), and the whole mixture was stirred at 80 °C for 1 h. All the reaction mixtures were combined, concentrated to some extent by evaporation, and then passed through an Al_2O_3/SiO_2 column, followed by elution with tetrahydrofuran/dichloromethane. The resulting solid was repeatedly purified by column chromatography on Al_2O_3/SiO_2 (tetrahydrofuran/dichloromethane), followed by GPC (chloroform) to give **18** (748 mg) as a white solid in 31% yield. **18**: ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.39 (4H, s), 7.34 (8H, d, J = 8.4 Hz), 7.14 (8H, s), 6.87 (8H, d, J = 8.4 Hz), 3.77 (8H, d, J = 7.2 Hz), 3.37 (4H, s), 1.8-1.0 (44H, m).



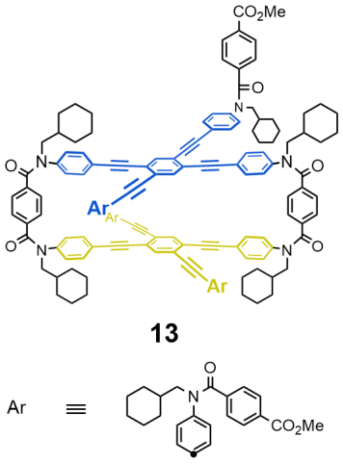
18

	17'	THF (the first, drop time)	THF (the last)	Terephthaloyl chloride	Et_3N	Toluene
1	353 mg (0.643 mmol)	40 mL (36 min)	40 mL	131 mg (0.645 mmol)	0.18 mL	246 mL
2	353 mg (0.643 mmol)	40 mL (31 min)	40 mL	131 mg (0.645 mmol)	0.18 mL	246 mL
3	353 mg (0.643 mmol)	41 mL (30 min)	40 mL	133 mg (0.655 mmol)	0.18 mL	246 mL
4	353 mg (0.643 mmol)	40 mL (42 min)	40 mL	131 mg (0.645 mmol)	0.18 mL	246 mL
5	344 mg (0.627 mmol)	39 mL (40 min)	39 mL	128 mg (0.631 mmol)	0.18 mL	240 mL
6	196 mg (0.357 mmol)	24 mL (36 min)	24 mL	73 mg (0.36 mmol)	0.10 mL	137 mL

(b) Preparation of *rac*-**13**

To a solution of **9** (829 mg, 1.74 mmol), $Pd(PPh_3)_4$ (67 mg, 0.058 mmol) and CuI (13 mg, 0.068 mmol) in THF (20 mL) and Et_3N (41 mL) was added a solution of **18** (293 mg, 0.216 mmol) in THF (22 mL) at 60 °C via a syringe pump over 24 h under an argon atmosphere, and the mixture was further stirred for 2.5 h. After removal of the solvents by evaporation, the residue was dissolved in dichloromethane, which was washed with satd. aq. $NaHCO_3$, dried over magnesium sulfate, and then purified by column chromatography on Al_2O_3/SiO_2

(tetrahydrofuran/dichloromethane), followed by GPC (chloroform) and HPLC with a standard normal-phase column (9:100:900 ethanol/tetrahydrofuran/dichloromethane; YMC-Pack SIL, SIL-06, YMC Co., Ltd., Japan) to give *rac*-**13** (263 mg) as a pale-yellowish-white solid in 44% yield. *rac*-**13**: mp 177-178 °C; IR (neat) ν_{max}/cm^{-1} 3043, 2922, 2850, 2207, 1723, 1645, 1601, 1512, 1273; ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm 7.87 (8H, d, J = 8.4 Hz), 7.36 (8H, d, J = 8.4 Hz), 7.30 (8H, d, J = 8.8 Hz), 7.30 (4H, s), 7.22 (8H, d, J = 8.4 Hz), 7.17 (8H, s), 6.91 (8H, br.d, J = 8 Hz), 6.88 (8H, d, J = 8.4 Hz), 3.87 (4H, dd, J = 7~8, 13.6 Hz), 3.83 (12H, s), 3.80 (8H, d, J = 6.8 Hz), 3.72 (4H, dd, J = 7~8, 13.6 Hz), 1.8-1.0 (44H×2, m); ^{13}C NMR δ_C(100 MHz; $CDCl_3$)/ppm 169.6, 169.4, 166.0, 144.0, 143.6, 140.4, 137.4, 134.4, 132.5, 132.1, 131.1, 129.1, 128.5, 128.1, 127.3, 124.9, 124.9, 121.3, 120.6, 94.5, 94.4, 88.7, 88.2, 56.2, 55.8, 52.2, 36.5, 36.4, 30.9, 30.9, 26.3, 26.2, 25.8, 25.8; FD-LRMS *m*/*z* 1376.69 (M^{2+}, 10%), 1377.19 ($[M+1]^{2+}$, 25), 1377.69 ($[M+2]^{2+}$, 30), 1378.19 ($[M+3]^{2+}$, 23), 1378.70 ($[M+4]^{2+}$, 14), 1379.19 ($[M+5]^{2+}$, 8), 1379.69 ($[M+6]^{2+}$, 7), 2753.36 (M^+, 41), 2754.37 ($[M+1]^+$, 86), 2755.37 ($[M+2]^+$, 100), 2756.37 ($[M+3]^+$, 78), 2757.37 ($[M+4]^+$, 47), 2758.37 ($[M+5]^+$, 25), 2759.37 ($[M+6]^+$, 12); FD-HRMS Found: 2753.32111, Calc. for $C_{184}H_{176}N_8O_{16}$: 2753.32043.

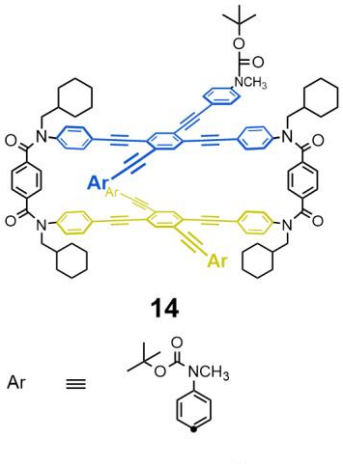


13

Ar ≡

(c) Preparation of *rac*-**14** and **15**

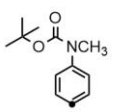
To a solution of **12** (688 mg, 2.06 mmol), $Pd(PPh_3)_4$ (76 mg, 0.066 mmol) and CuI (13 mg, 0.068 mmol) in THF (23 mL) and Et_3N (47 mL) was added a solution of **18** (334 mg, 0.246 mmol) in THF (24 mL) at 60 °C via a syringe pump over 18 h under an argon atmosphere, and the mixture was further stirred for 40 min. After removal of the solvents by evaporation, the residue was dissolved in dichloromethane, which was washed with satd. aq. $NaHCO_3$, dried over magnesium sulfate, and then purified by column chromatography on Al_2O_3/SiO_2 (tetrahydrofuran/dichloromethane), followed by GPC (chloroform) to give a mixture of *rac*-**14** and **15** (347 mg, **15**/**14** = 2.2) as a yellowish-white solid in 65% yield. *rac*-**14** and **15**: ^{1}H NMR δ_H(400 MHz; $CDCl_3$; Me_4Si)/ppm *rac*-**14** (minor) 7.45 (4H, s), 7.29 (8H, d, J = 8.8 Hz), 7.25 (8H, d, J = 8.8 Hz), 7.19 (8H, s), 7.08 (8H, d, J = 8.8 Hz), 6.82 (8H, d, J = 8.8 Hz), 3.9-3.6 (8H, m), 3.23 (12H, s), 1.50 (36H, s), 1.8-1.0 (44H, m); **15** (major) 7.42 (4H, s), 7.40 (8H, d, J = 8.8 Hz), 7.34 (8H, d, J = 8.8 Hz), 7.17 (8H, d, J = 8.4 Hz), 7.17 (8H, s), 6.87 (8H, d, J = 8.4 Hz), 3.9-3.6 (8H, m), 3.27 (12H, s), 1.50 (36H, s), 1.8-1.0 (44H, m).



14

Ar ≡

15

Ar ≡ 

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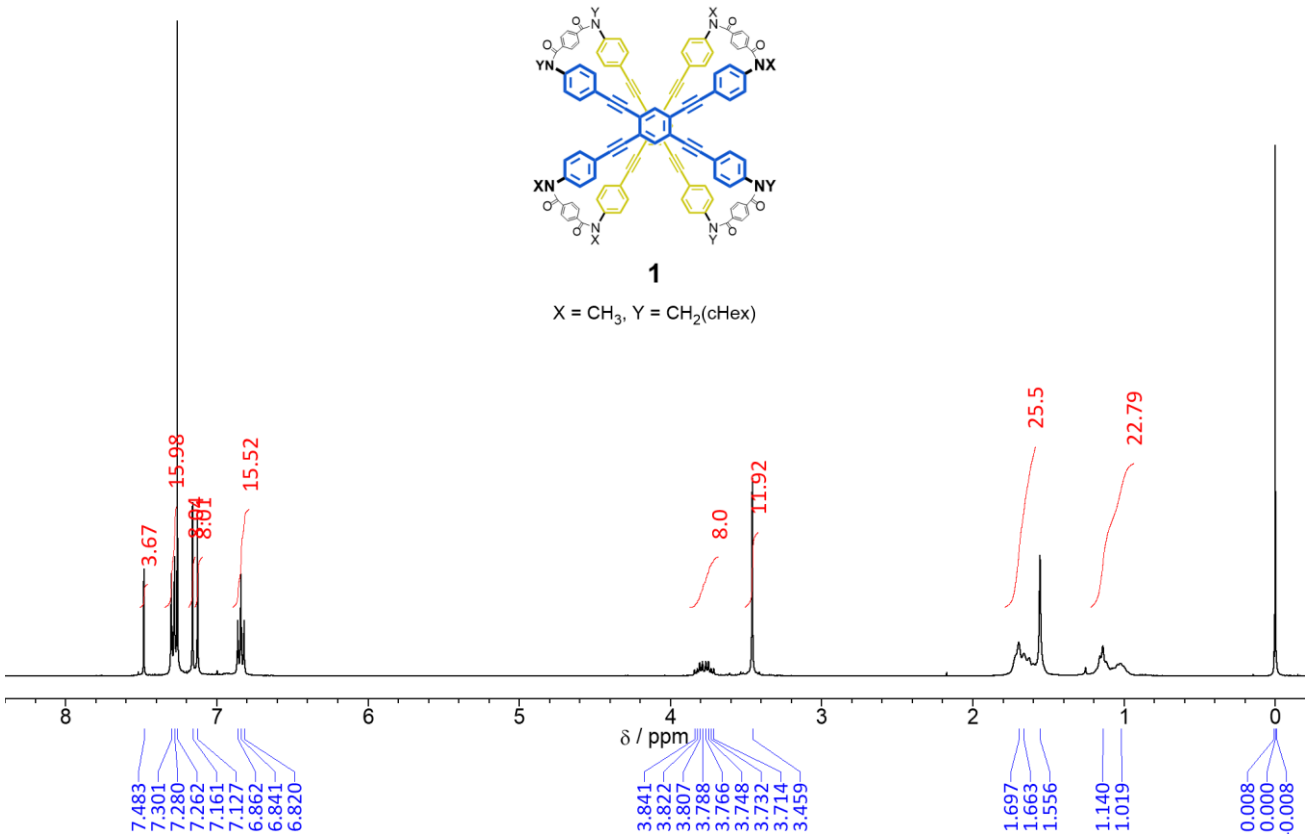
1 R. Katoono and T. Suzuki, *Chem*. *Commun*., 2016, **52**, 1029.

2 R. Katoono, S. Kawai and T. Suzuki, *Chem*. *Sci*., 2016, **7**, 3240.

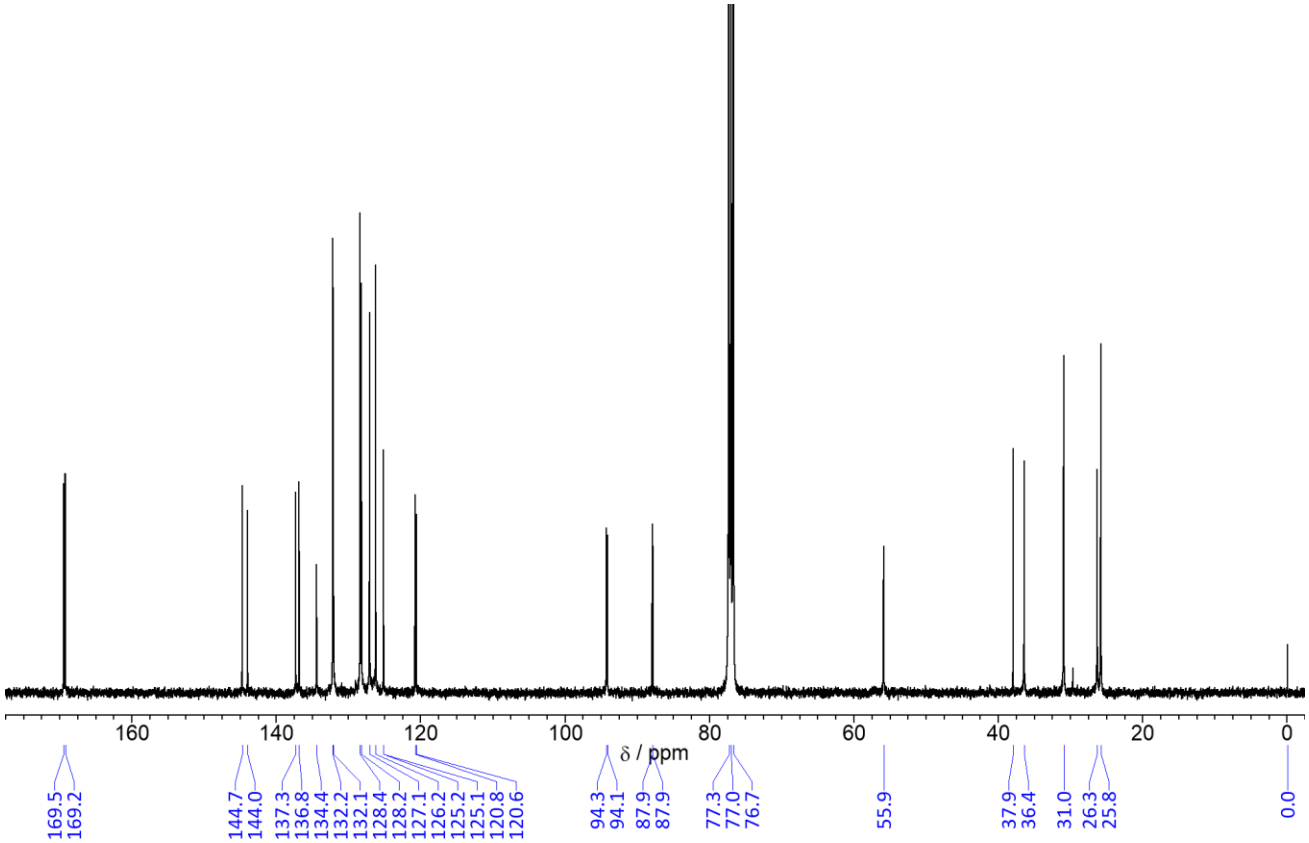
3 J. J. Miller, J. A. Marsden and M. M. Haley, *Synlett*, 2004, 165.

4 R. Katoono, H. Kawai, M. Ohkita, K. Fujiwara and T. Suzuki, *Chem*. *Commun*., 2013, **49**, 10352.

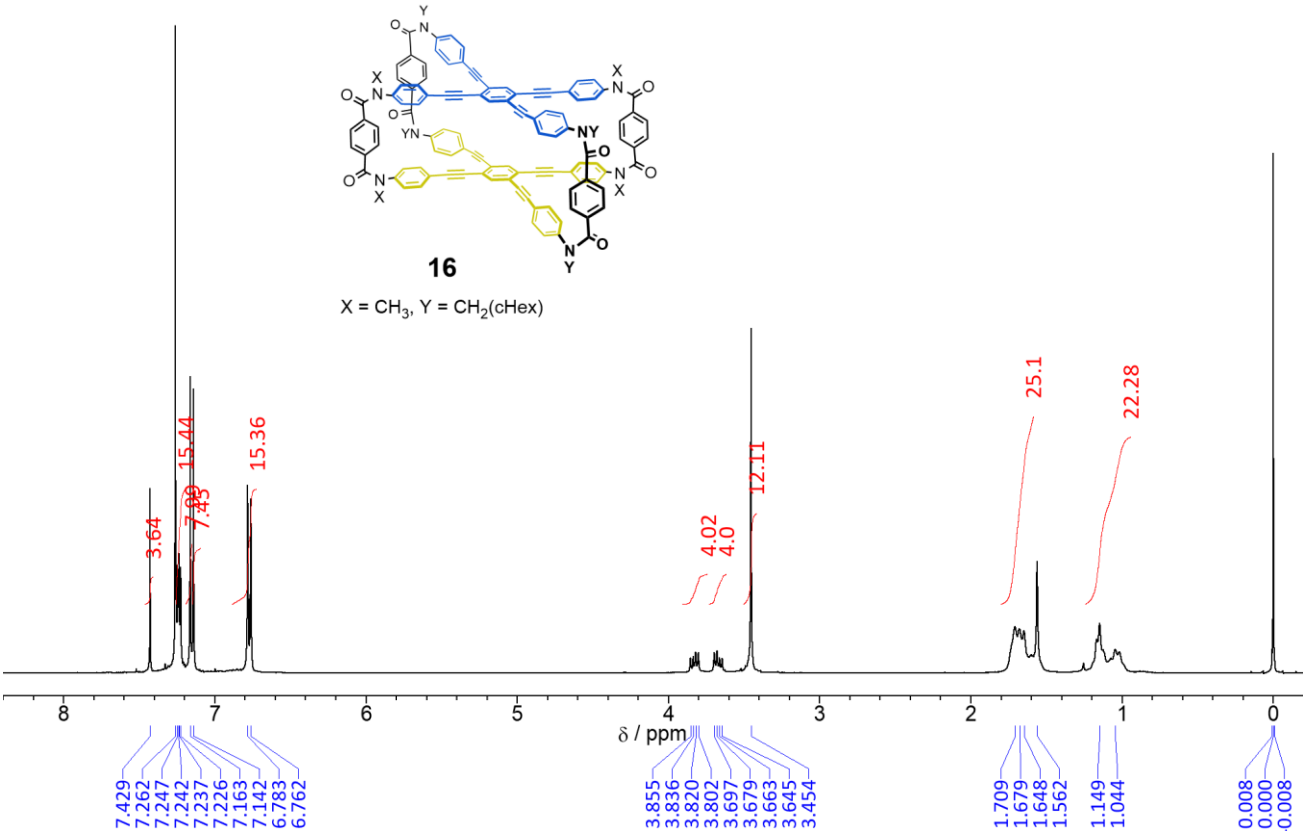
5 S. Takahashi, Y. Kuroyama, K. Sonogashira and N. Hagihara, *Synthesis*, 1980, 627.



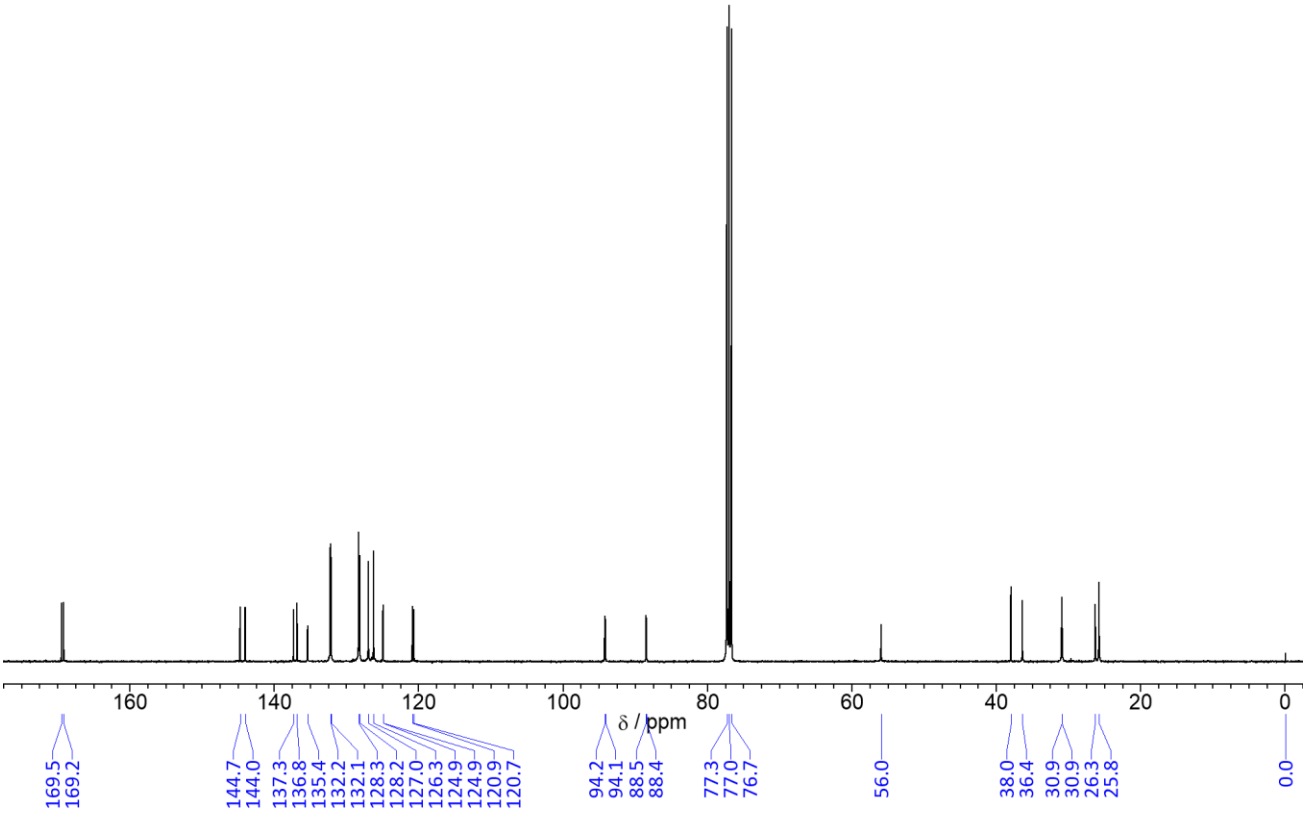
^{1}H NMR spectrum (400 MHz) of (+)-**1**, measured in chloroform-*d* at room temperature.



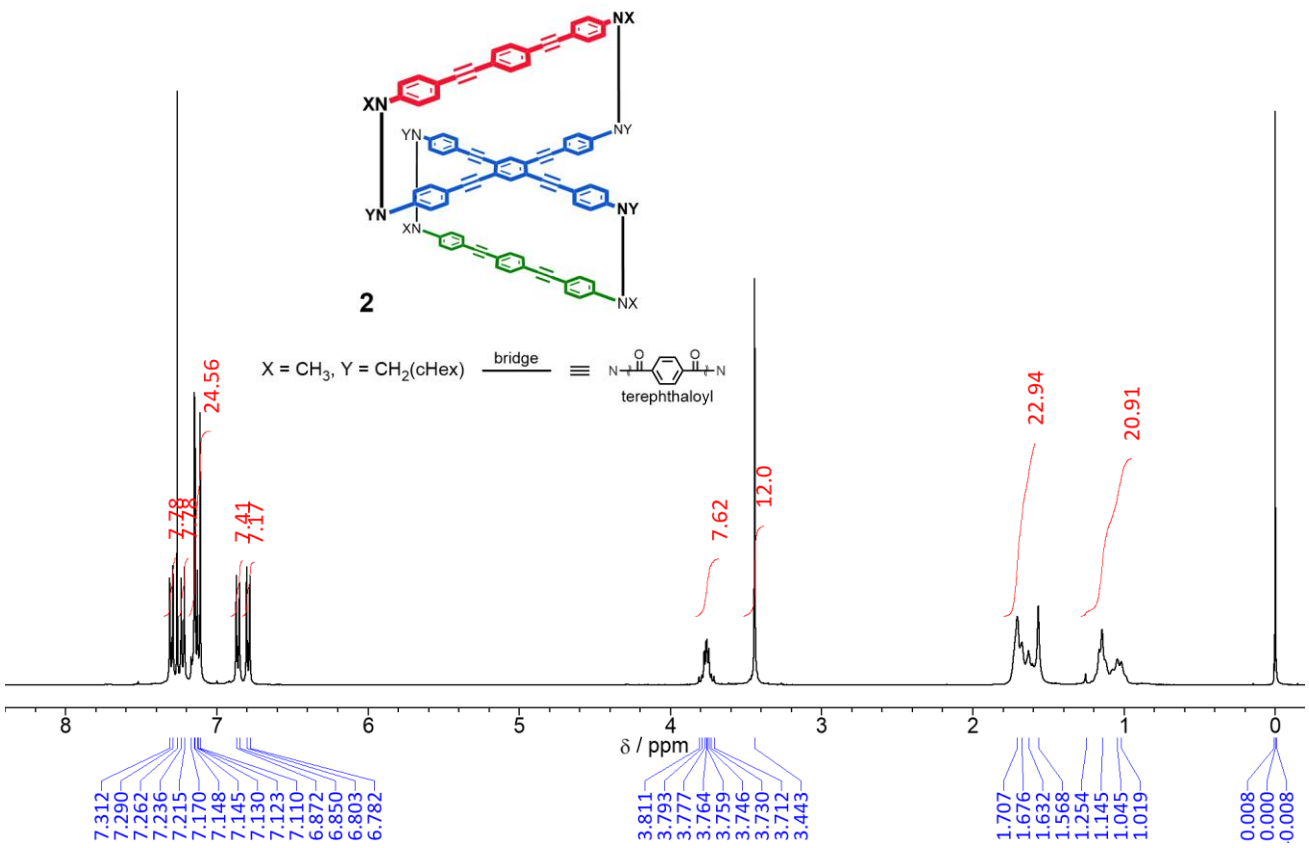
^{13}C NMR spectrum (100 MHz) of (+)-**1**, measured in chloroform-*d* at room temperature.



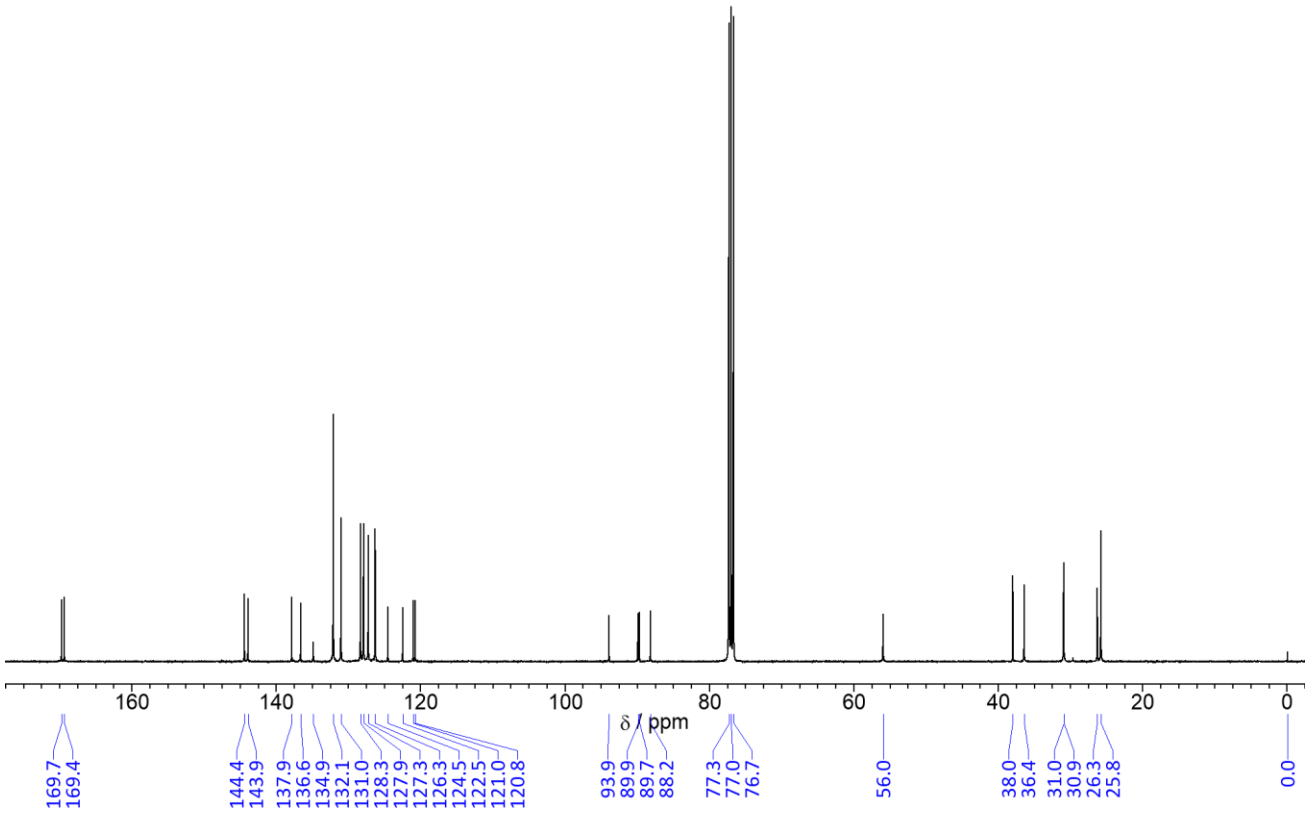
^{1}H NMR spectrum (400 MHz) of **16**, measured in chloroform-*d* at room temperature.



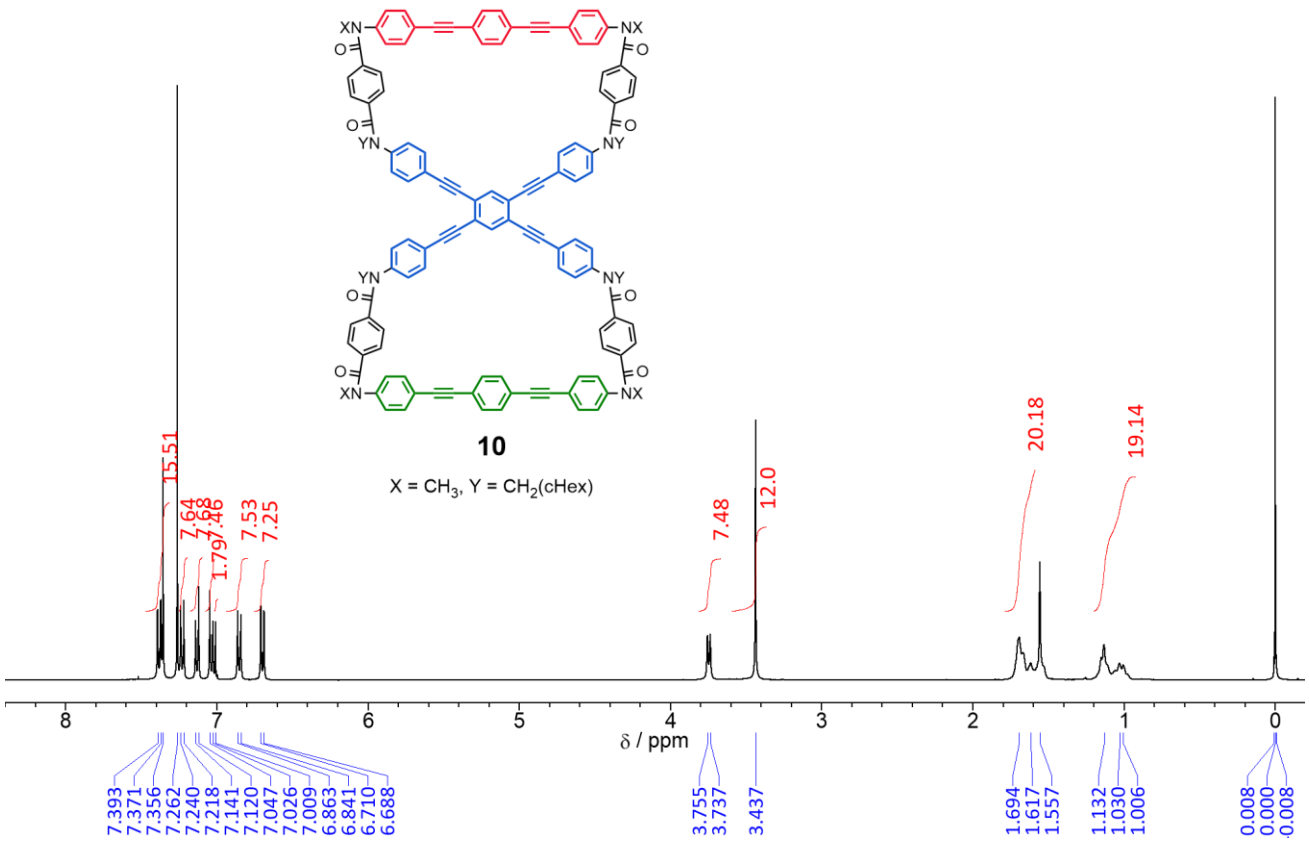
^{13}C NMR spectrum (100 MHz) of **16**, measured in chloroform-*d* at room temperature.



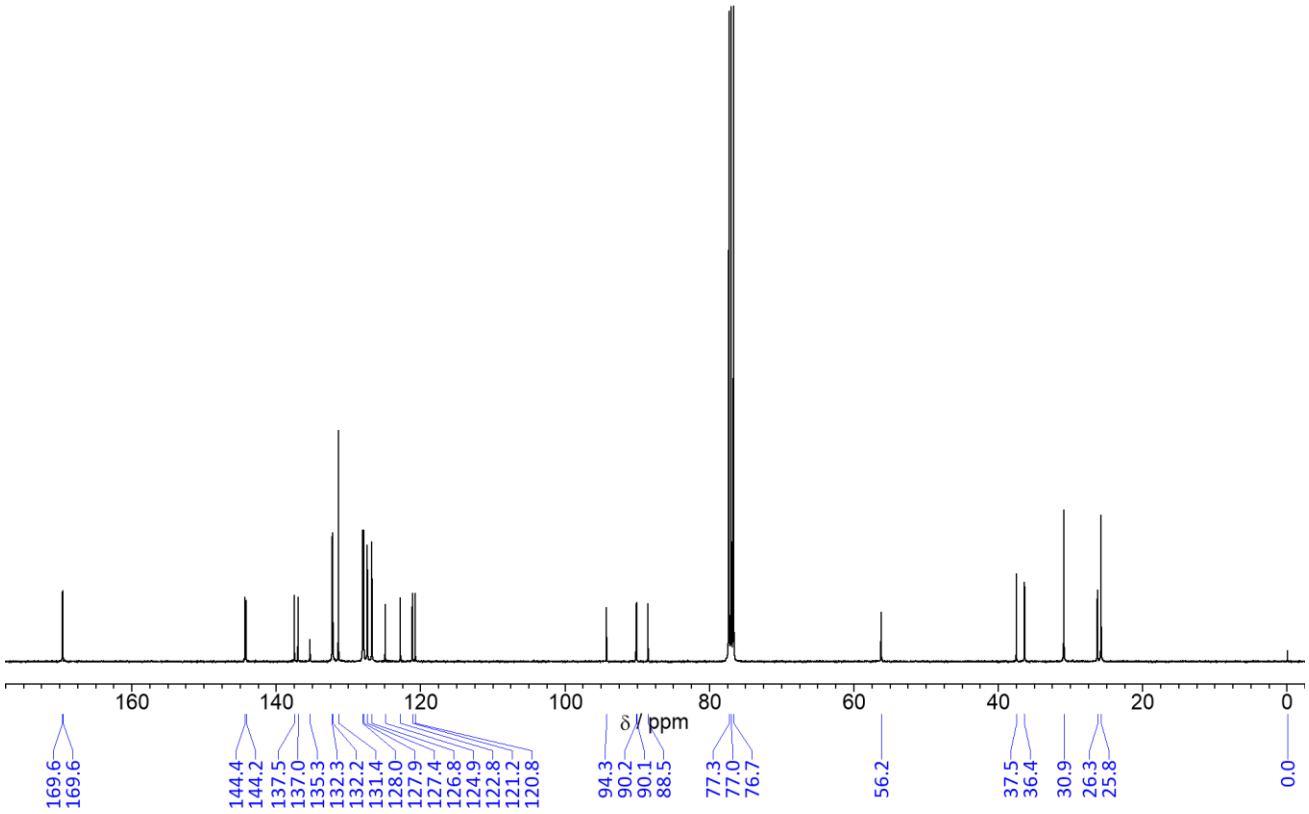
^{1}H NMR spectrum (400 MHz) of (+)-**2**, measured in chloroform-*d* at room temperature.



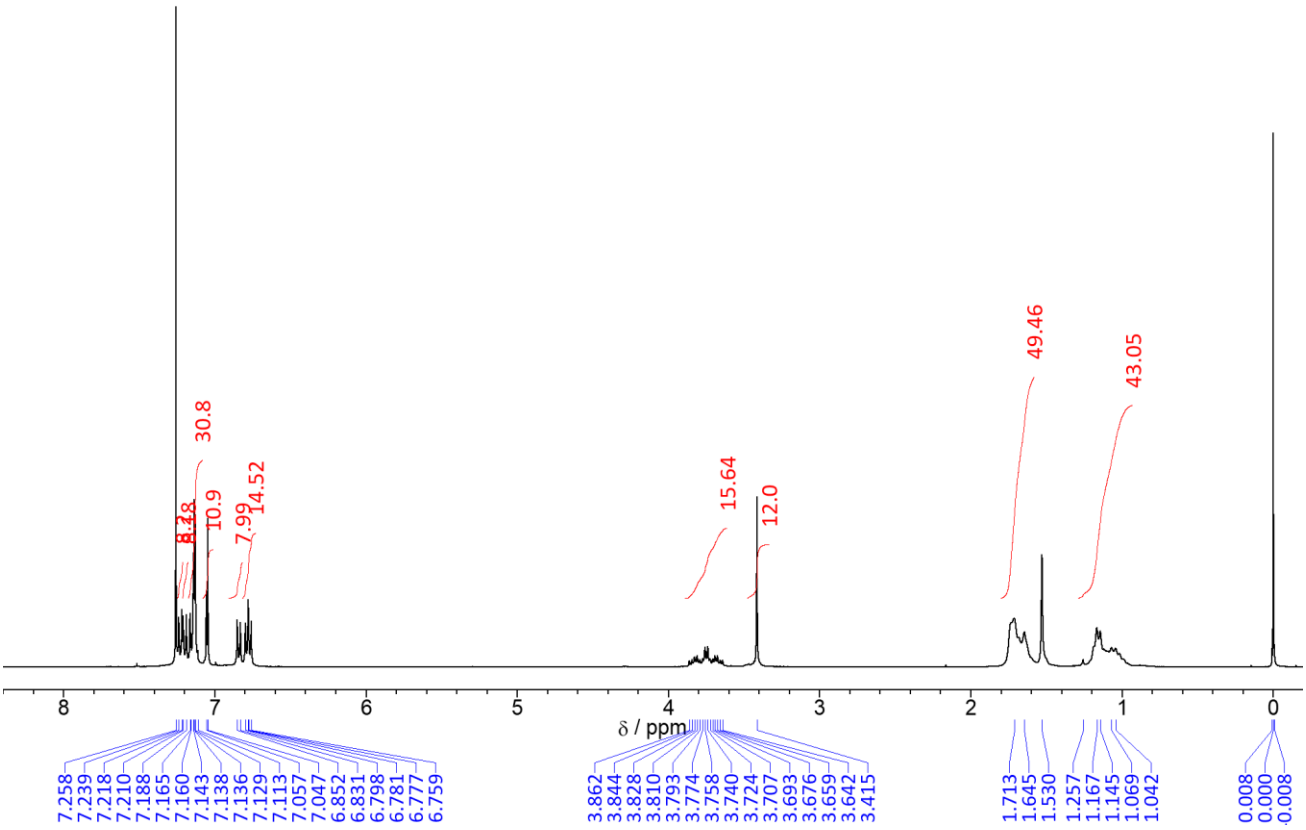
^{13}C NMR spectrum (100 MHz) of (+)-**2**, measured in chloroform-*d* at room temperature.



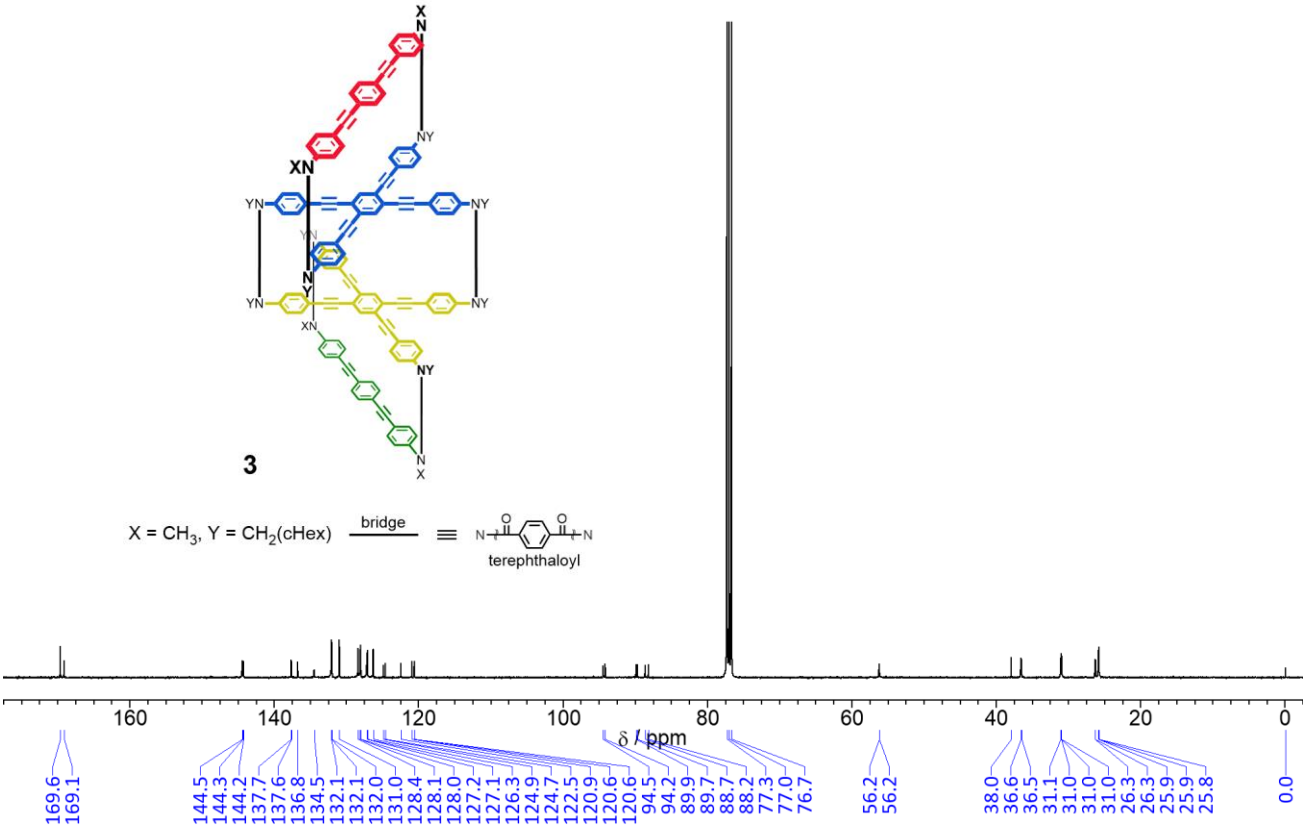
^{1}H NMR spectrum (400 MHz) of **10**, measured in chloroform-*d* at room temperature.



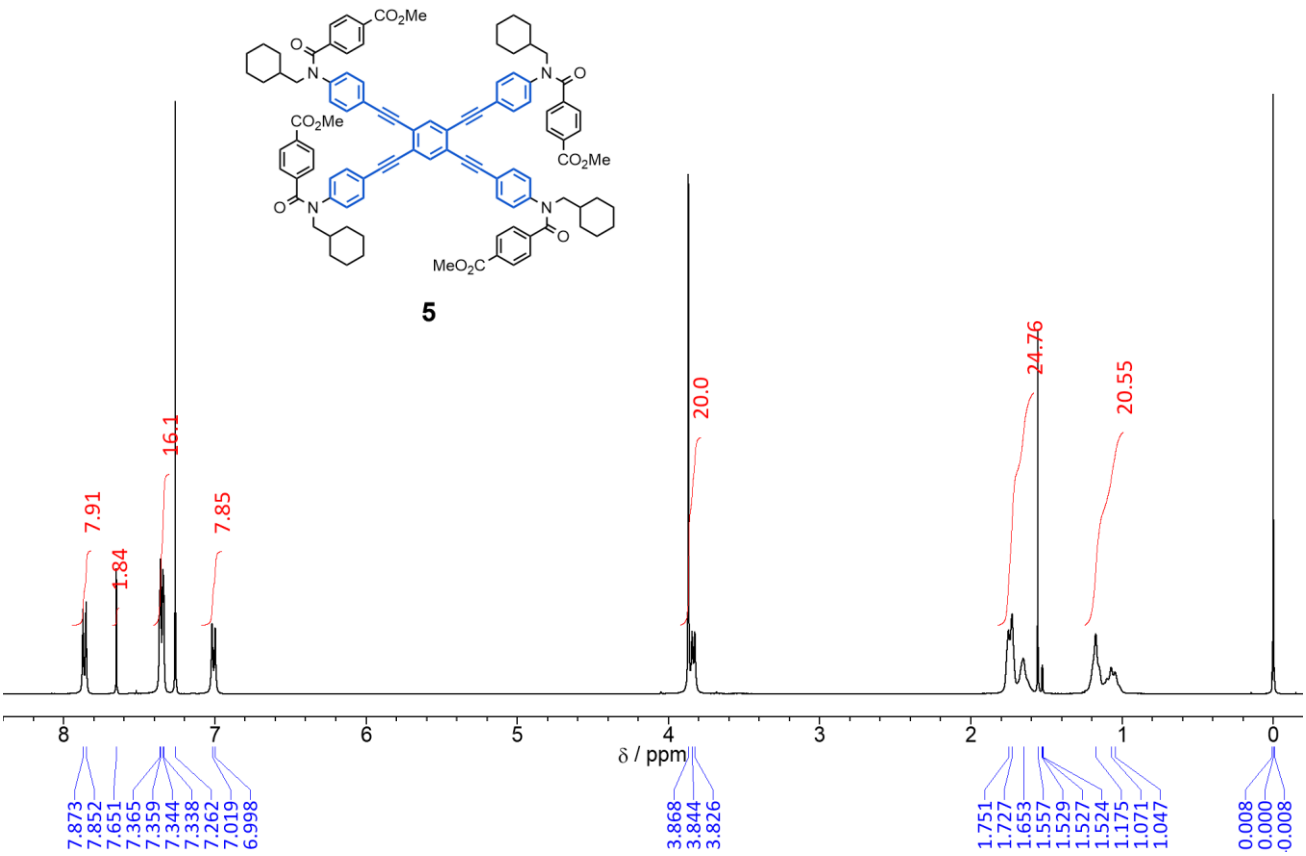
^{13}C NMR spectrum (100 MHz) of **10**, measured in chloroform-*d* at room temperature.



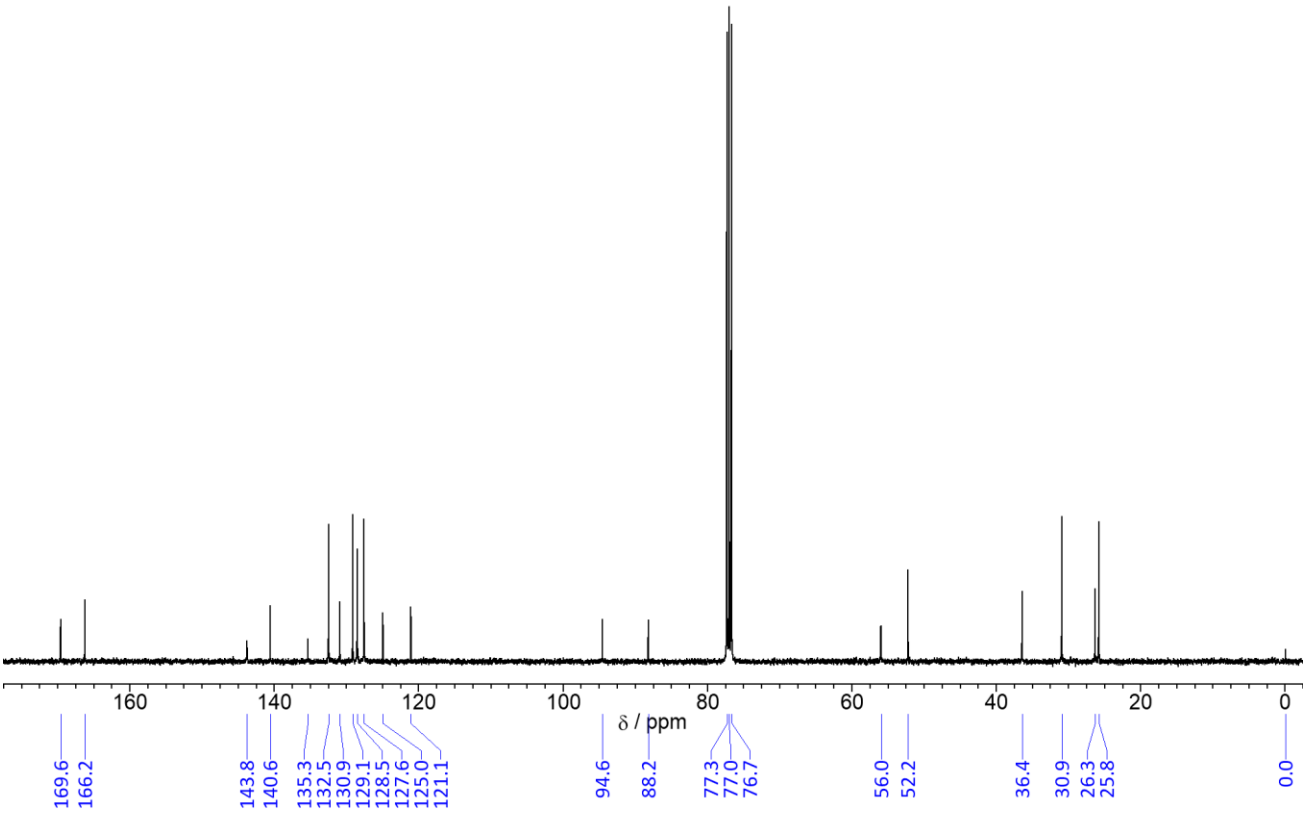
^{1}H NMR spectrum (400 MHz) of (+)-**3**, measured in chloroform-*d* at room temperature.



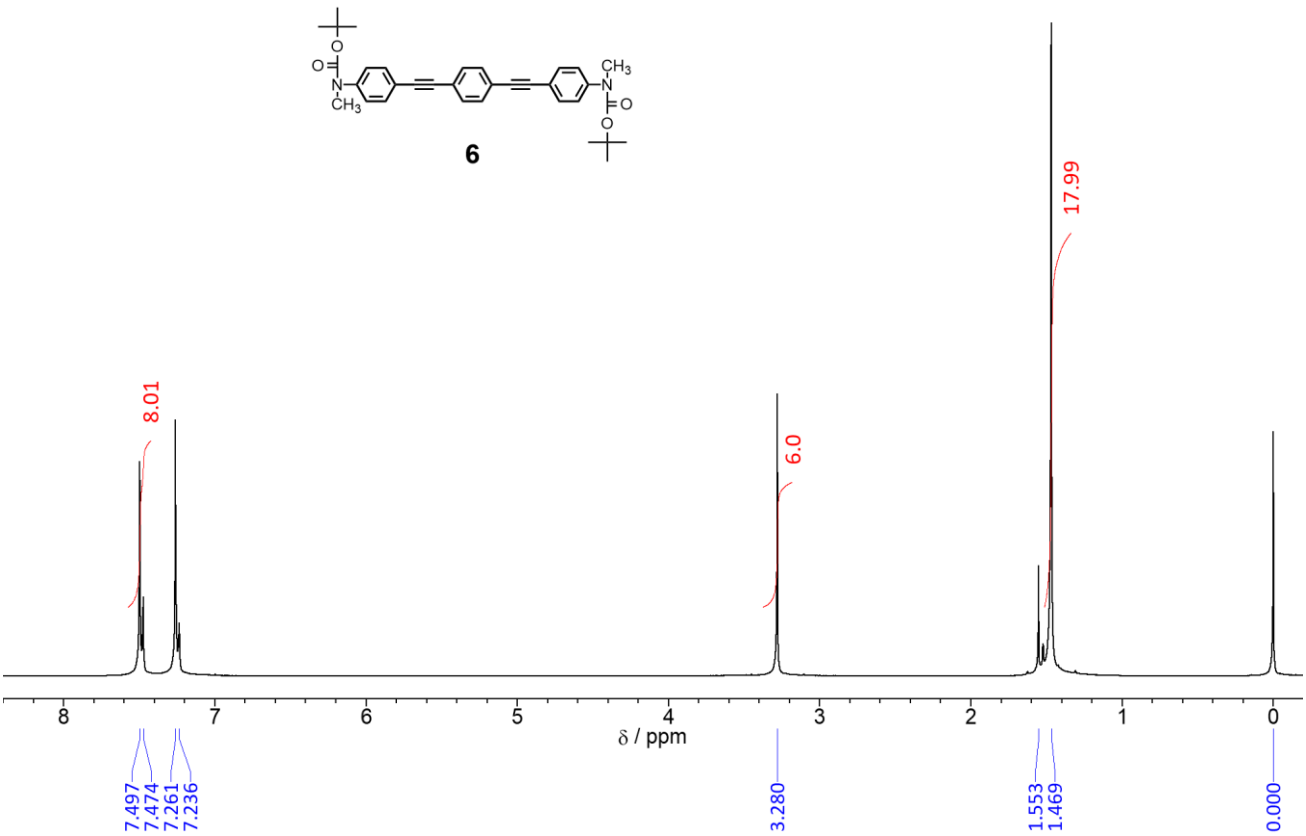
^{13}C NMR spectrum (100 MHz) of (+)-**3**, measured in chloroform-*d* at room temperature.



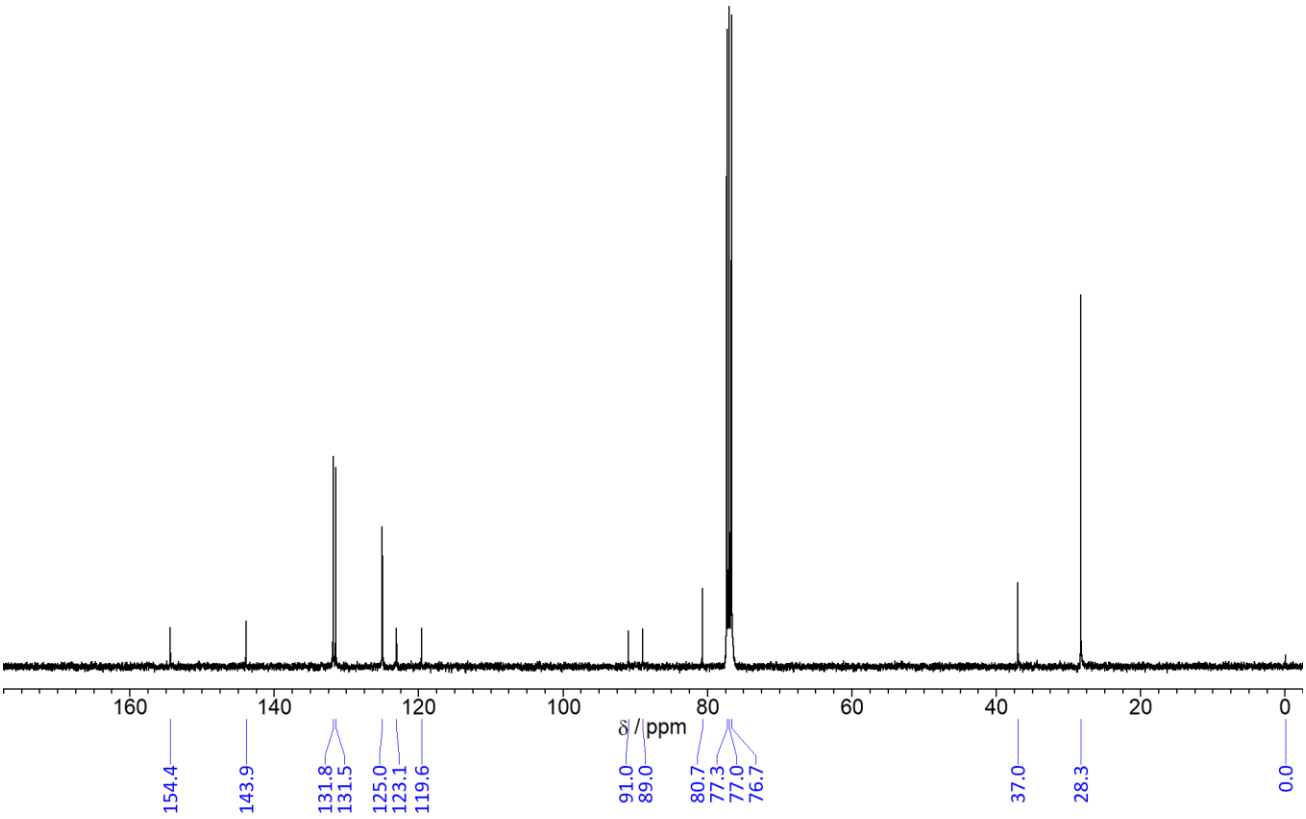
^{1}H NMR spectrum (100 MHz) of **5**, measured in chloroform-*d* at room temperature.



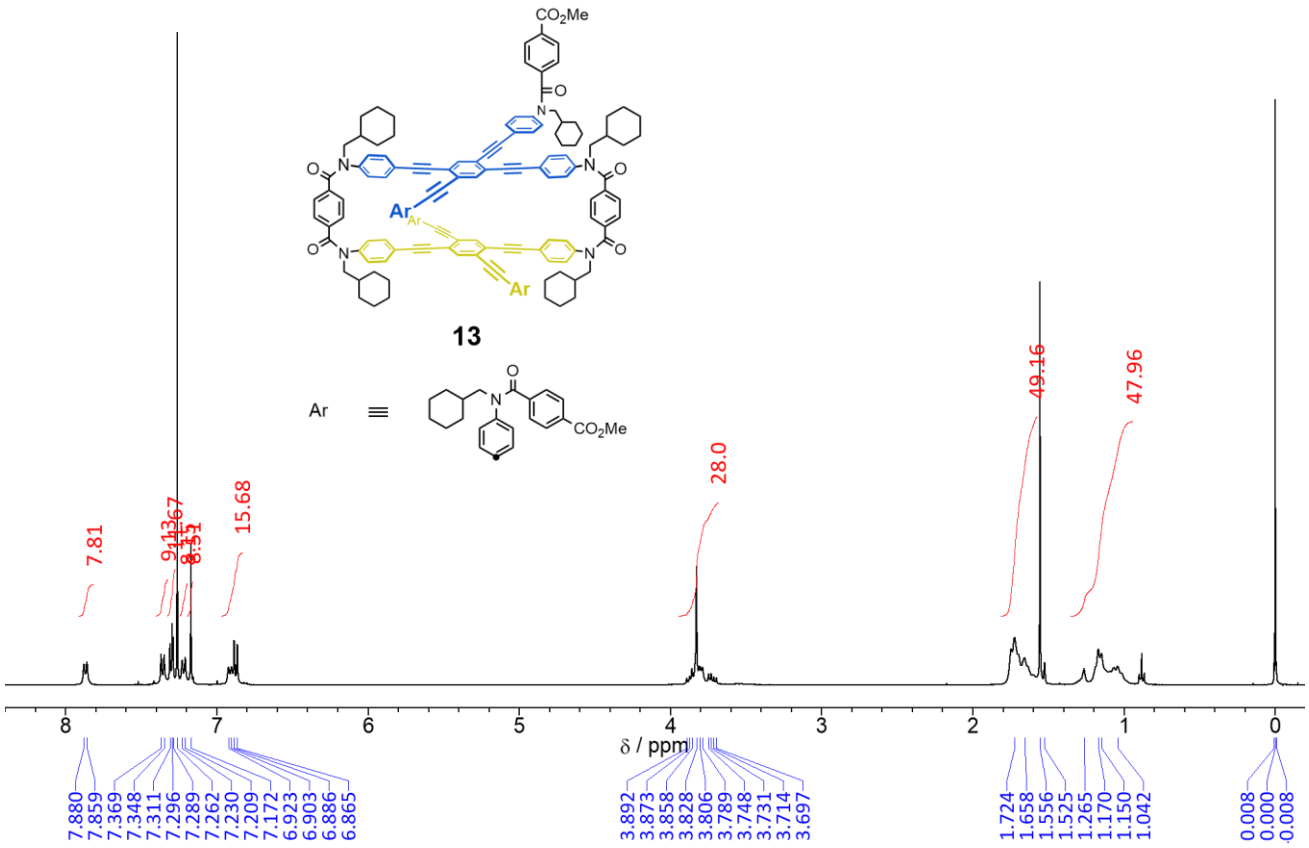
^{13}C NMR spectrum (100 MHz) of **5**, measured in chloroform-*d* at room temperature.



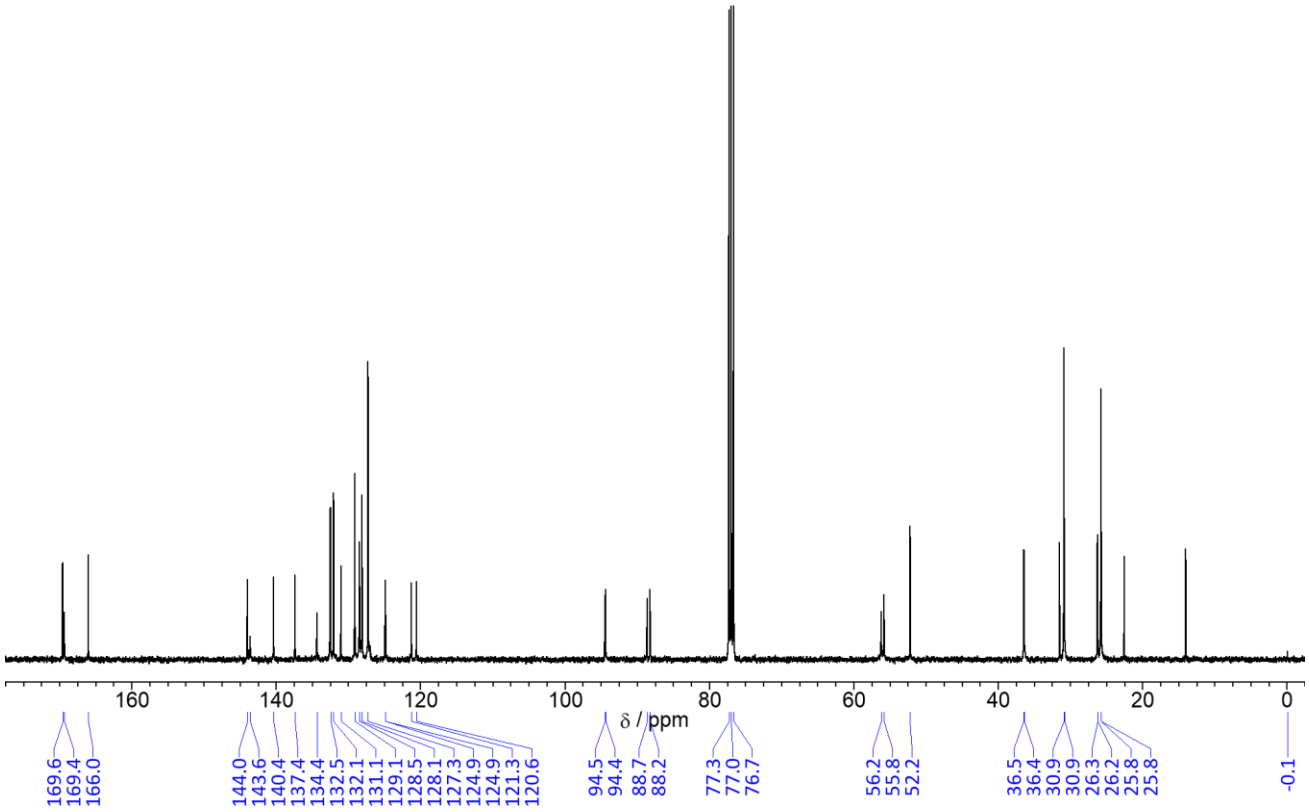
^{1}H NMR spectrum (400 MHz) of **6**, measured in chloroform-*d* at room temperature.



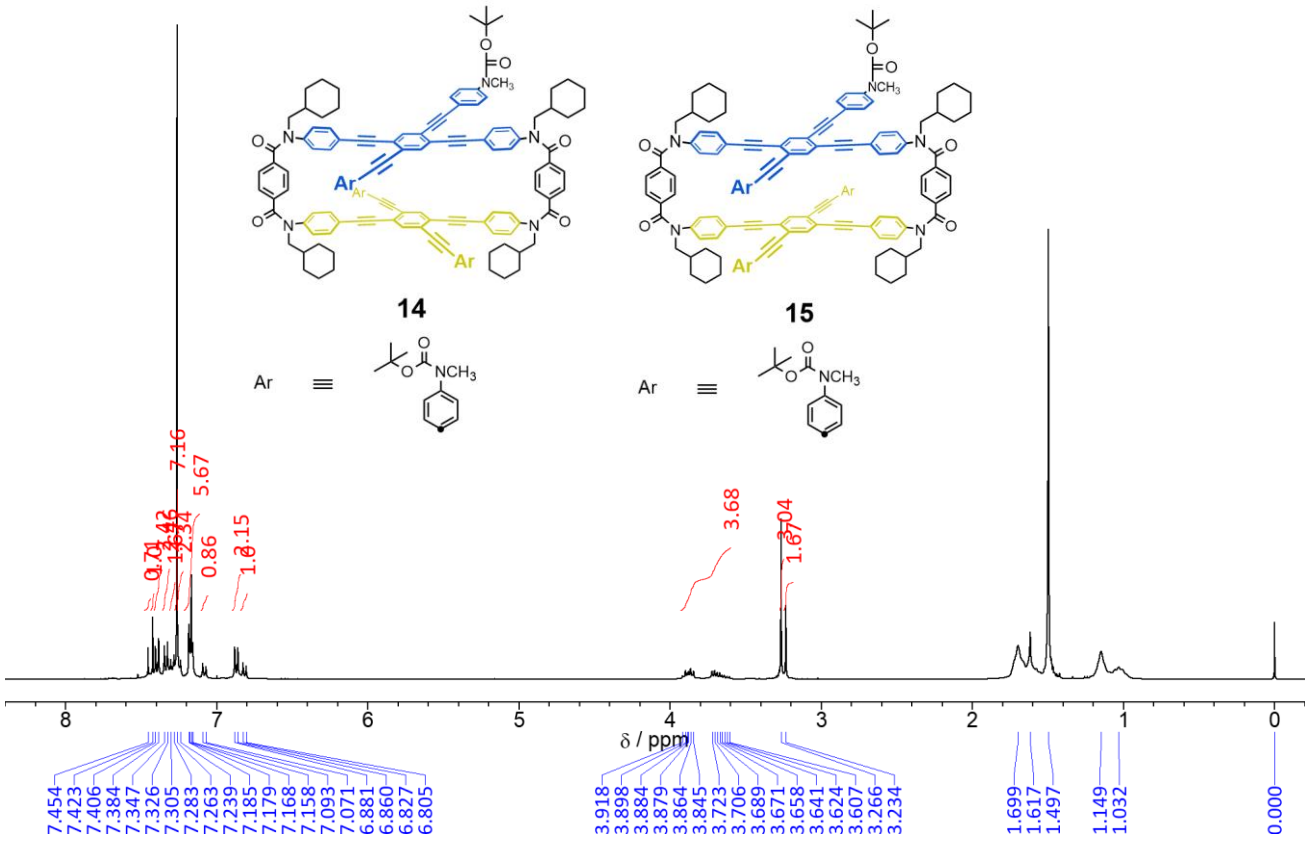
^{13}C NMR spectrum (100 MHz) of **6**, measured in chloroform-*d* at room temperature.



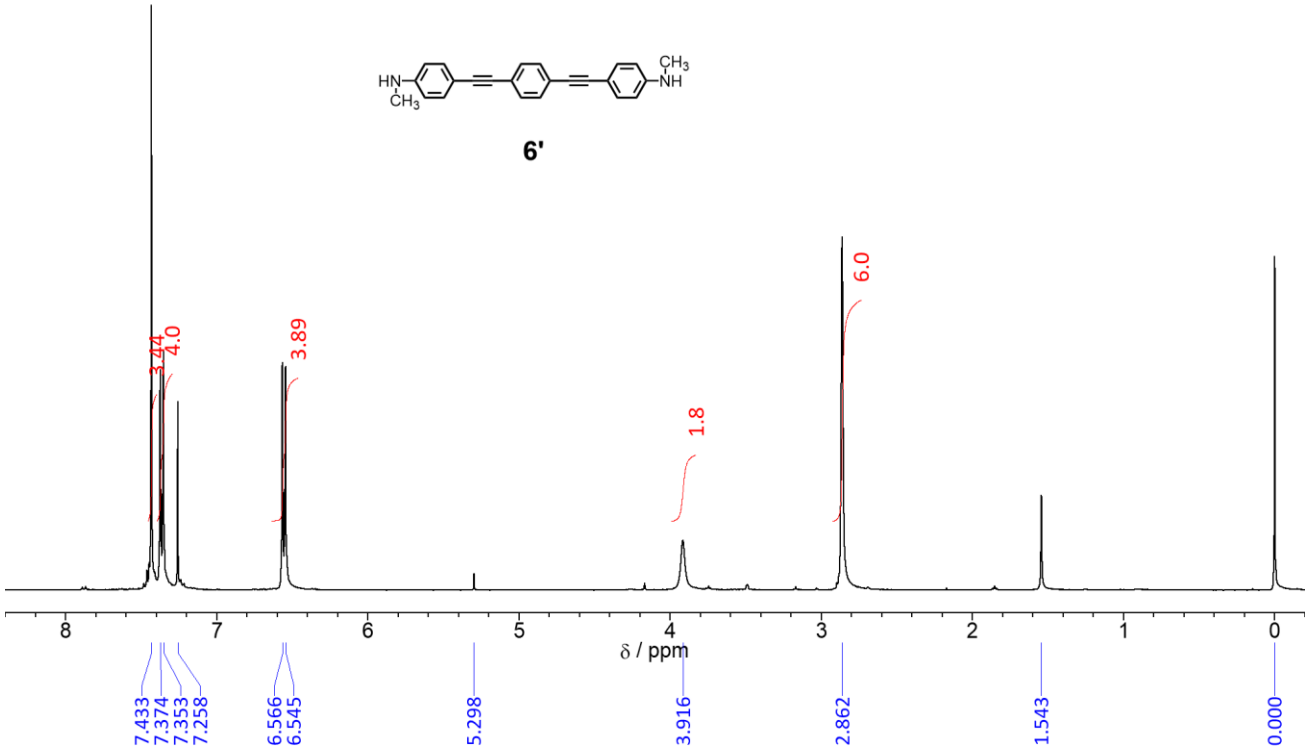
^{1}H NMR spectrum (400 MHz) of *rac*-**13**, cont. residual hexane, measured in chloroform-*d* at room temperature.



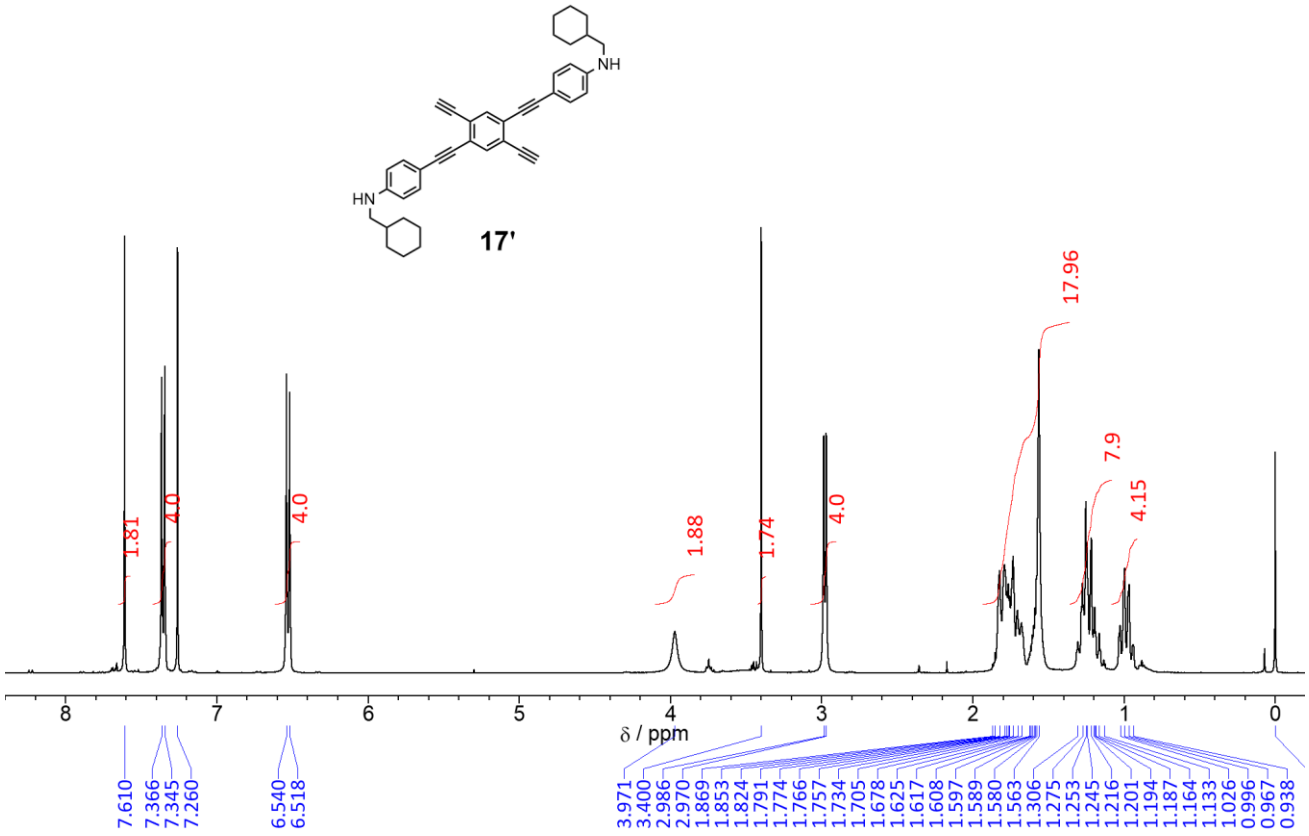
^{13}C NMR spectrum (100 MHz) of (±)-**13**, cont. residual hexane, measured in chloroform-*d* at room temperature.



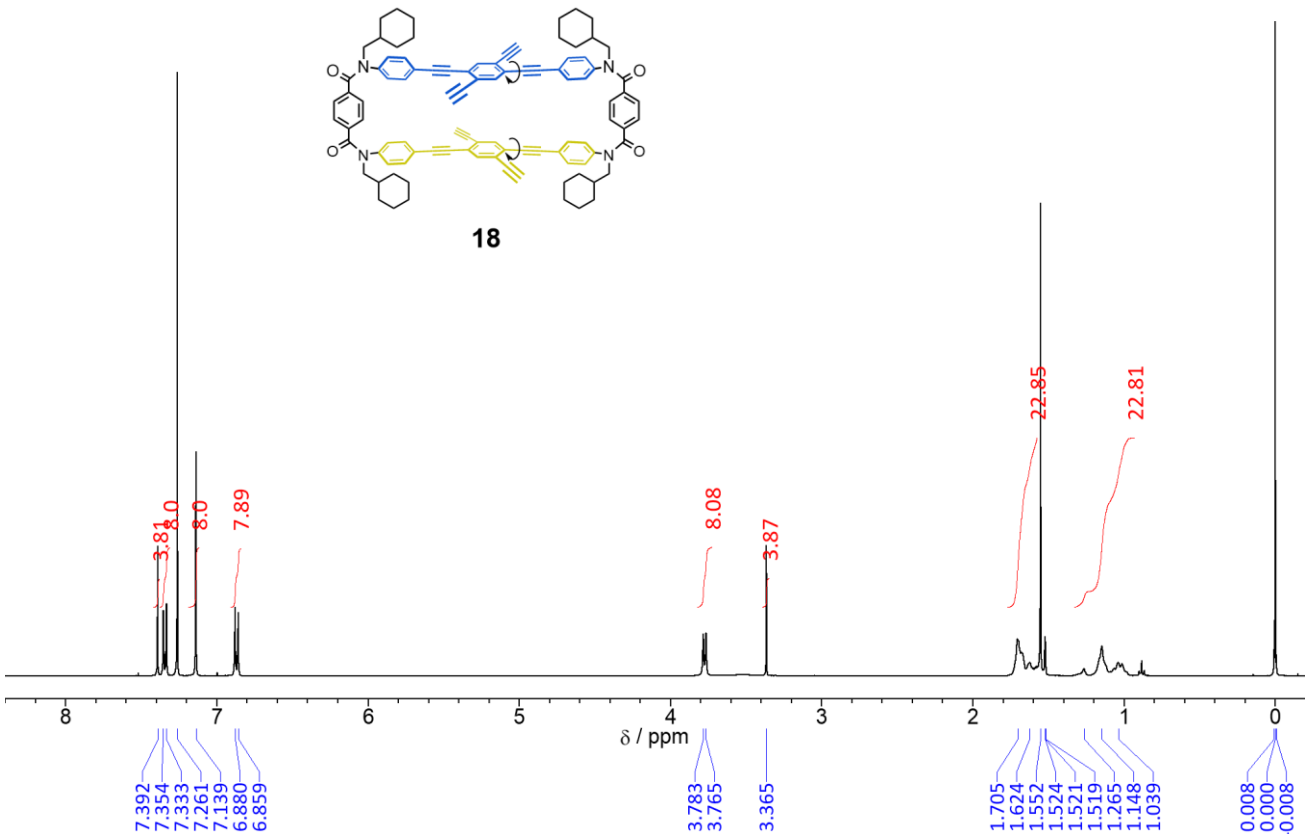
[1]H NMR spectrum (400 MHz) of a mixture of *rac*-**14** and **15** (**15**/**14** = 2.2), measured in chloroform-*d* at room temperature.



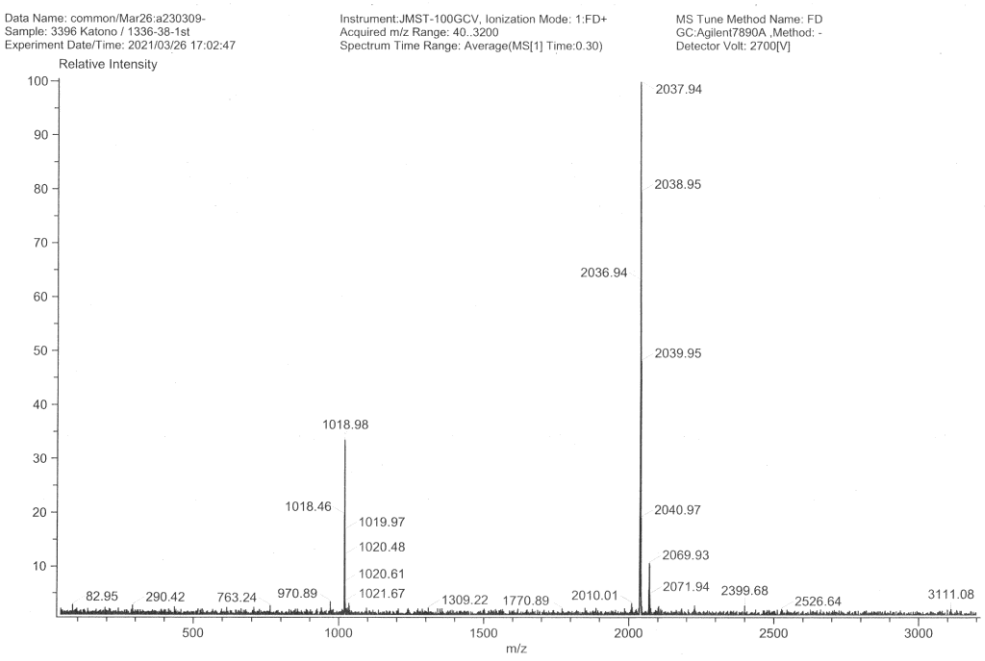
[1]H NMR spectrum (400 MHz) of **6'**, cont. residual dichloromethane, measured in chloroform-*d* at room temperature.



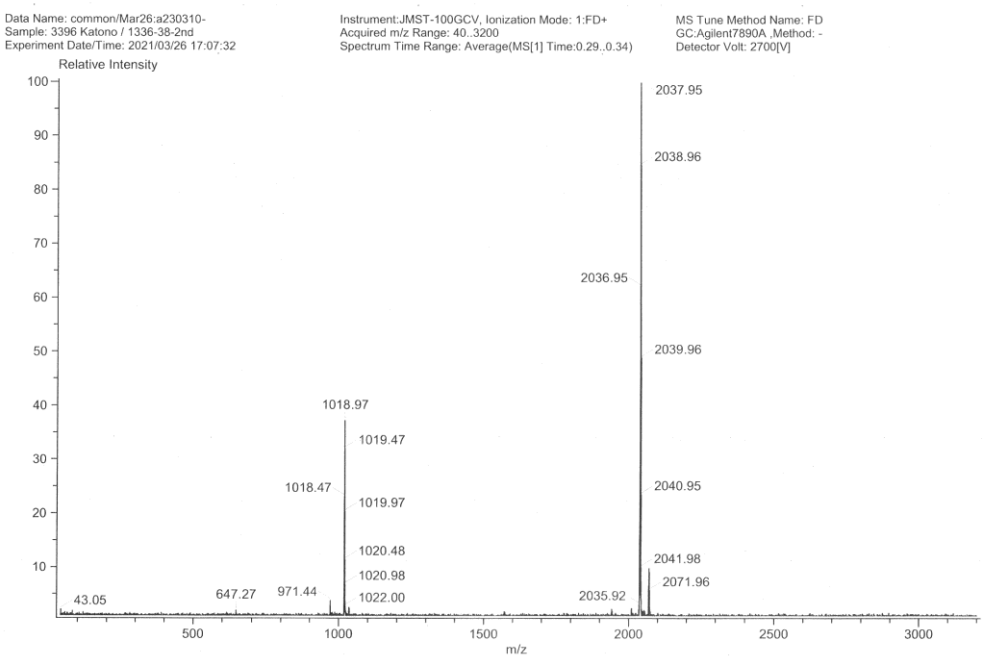
^{1}H NMR spectrum (400 MHz) of **17'**, measured in chloroform-*d* at room temperature.



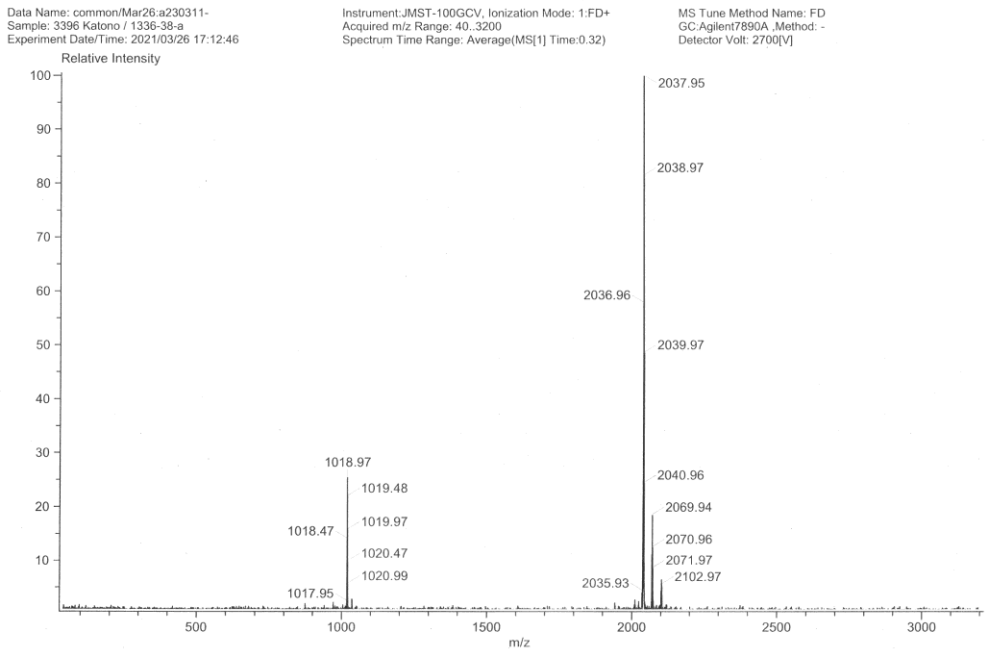
^{1}H NMR spectrum (400 MHz) of **18**, cont. residual hexane, measured in chloroform-*d* at room temperature.



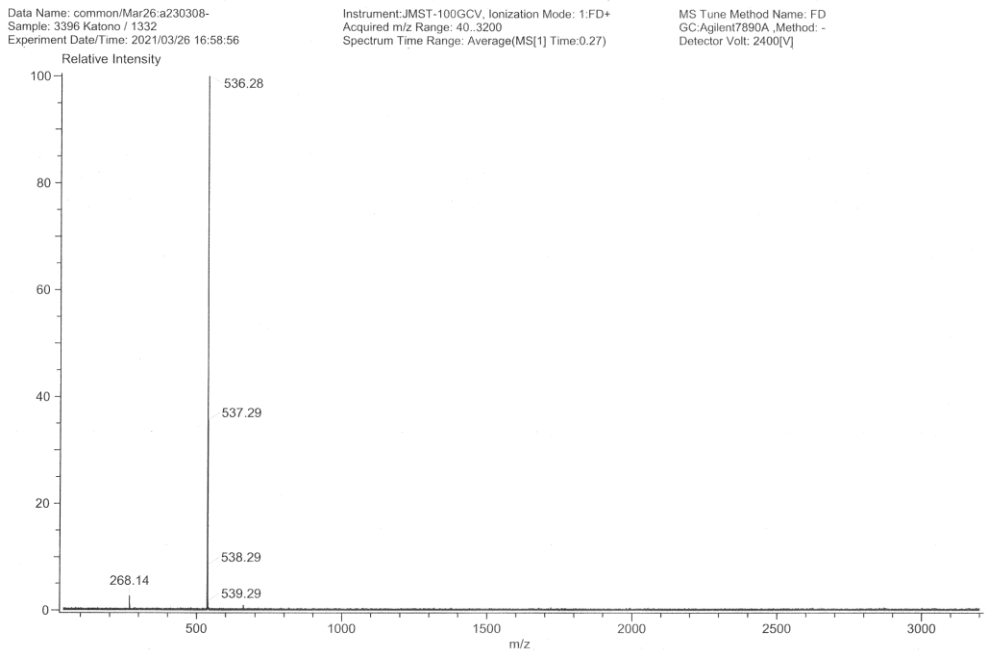
LR MS spectrum (FD) of (–)-**1**.



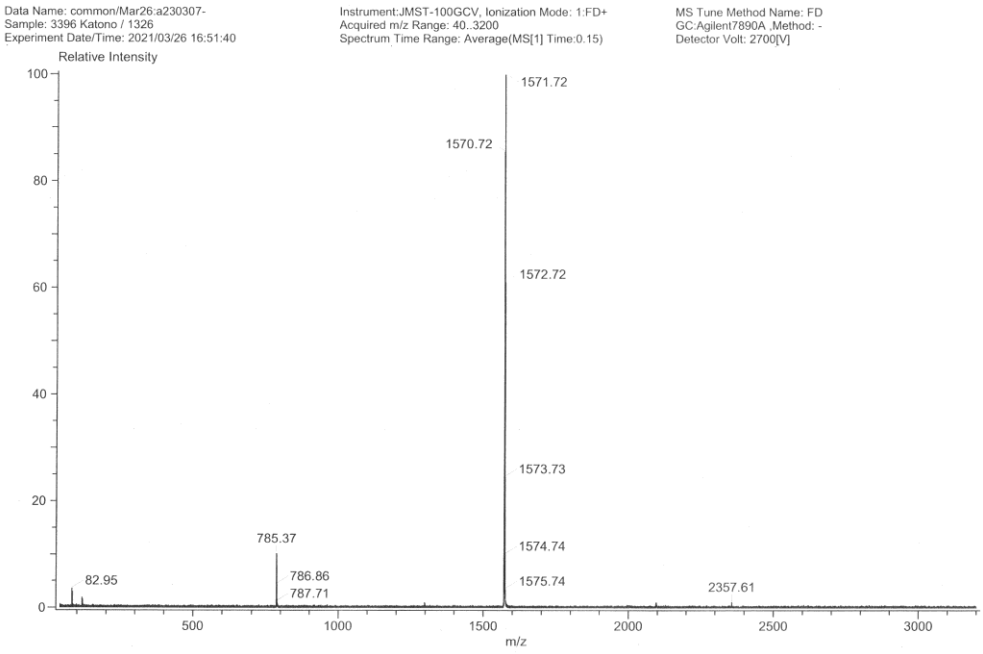
LR MS spectrum (FD) of (+)-**1**.



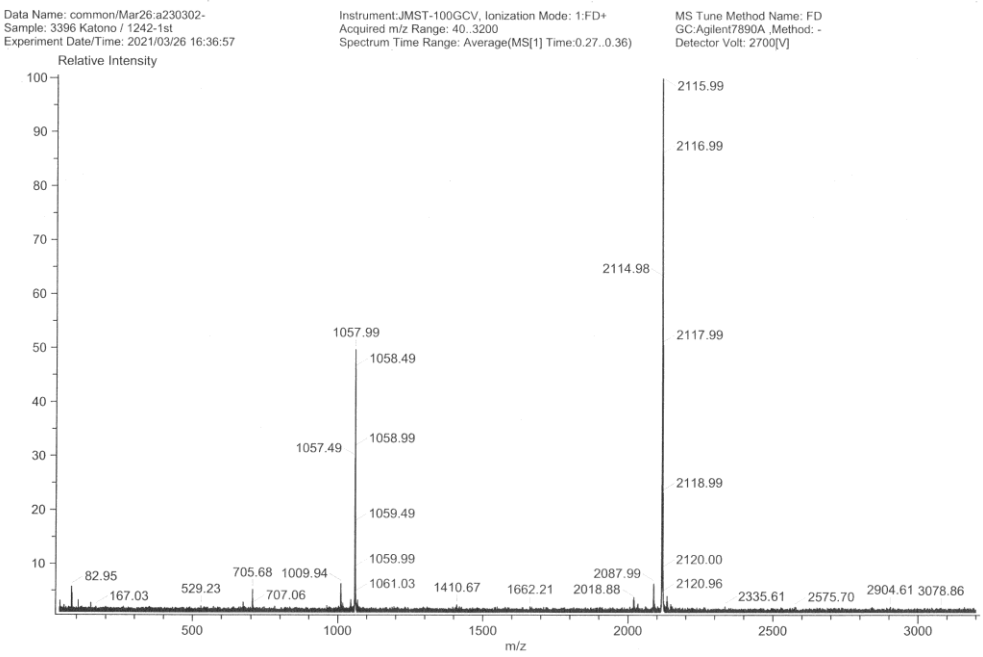
LR MS spectrum (FD) of **16**.



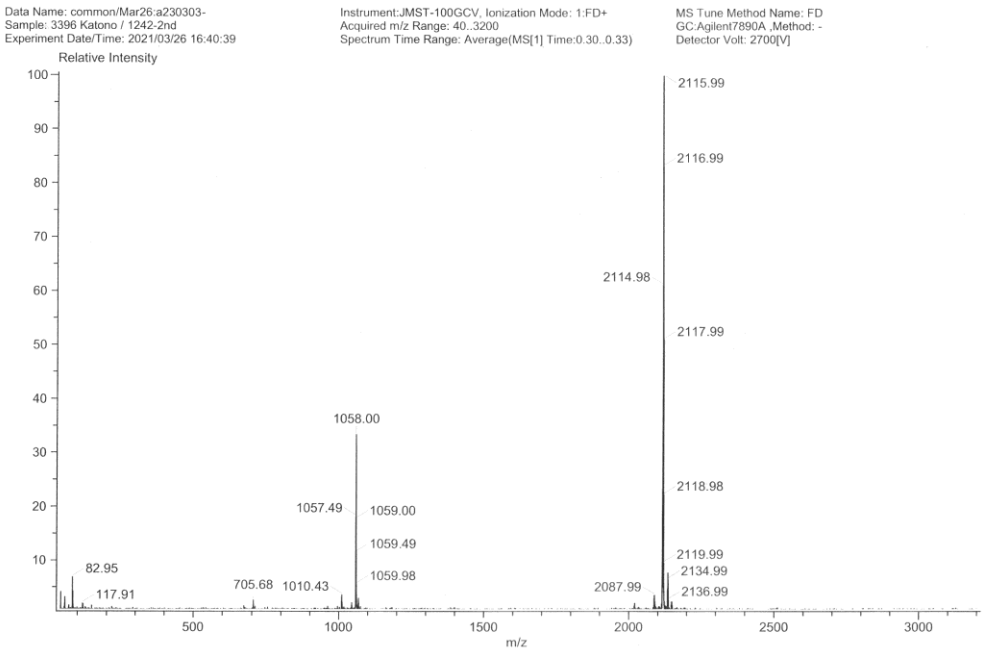
LR MS spectrum (FD) of **6**.



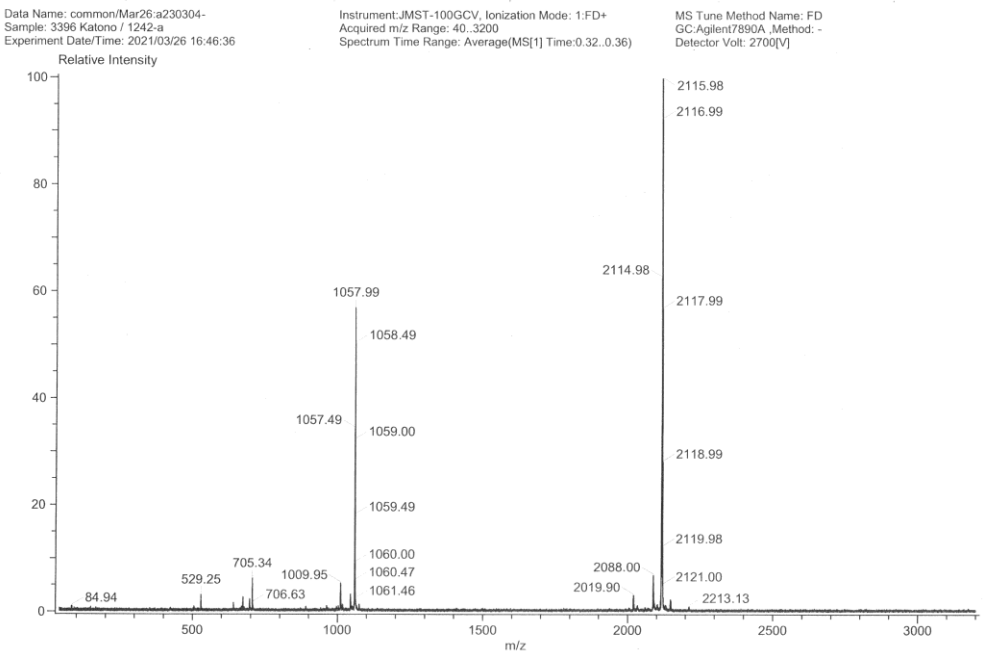
LR MS spectrum (FD) of **5**.



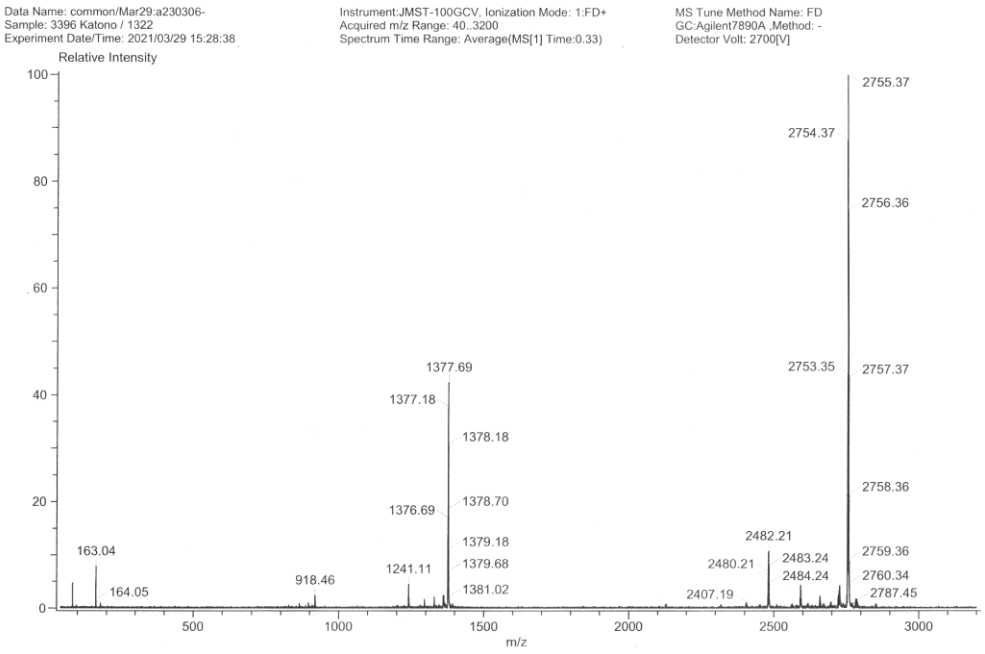
LR MS spectrum (FD) of (+)-**2**.



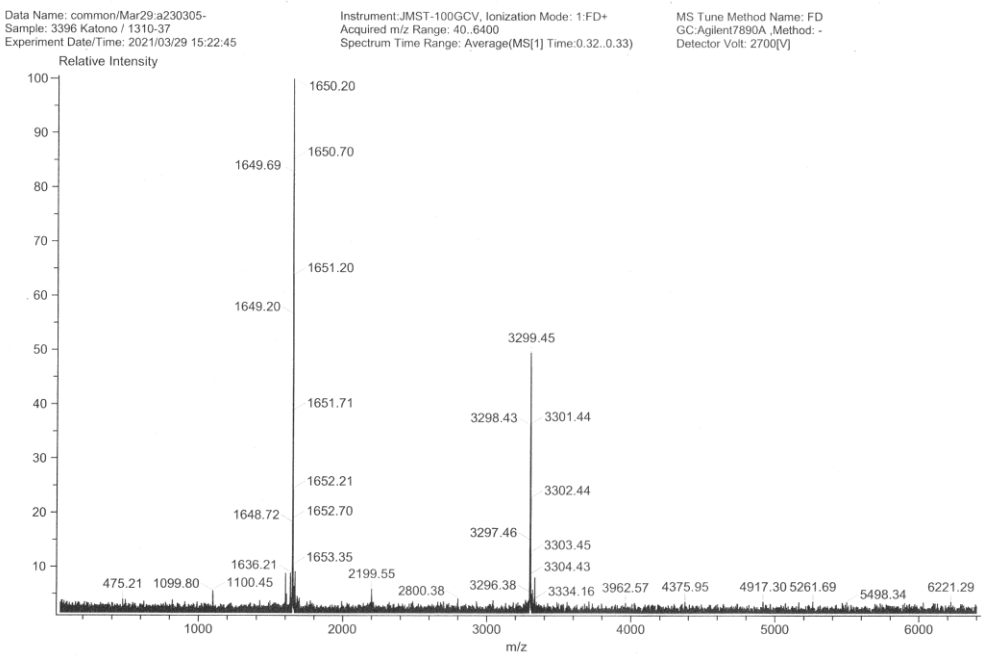
LR MS spectrum (FD) of (–)-**2**.



LR MS spectrum (FD) of **10**.



LR MS spectrum (FD) of **13**.



LR MS spectrum (FD) of (+)-**3**.