Electronic Supplementary Material (ESI) for ChemComm.

A Highly Diastereoselective Synthesis of Deep Molecular Baskets

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SUPPORTING INFORMATION

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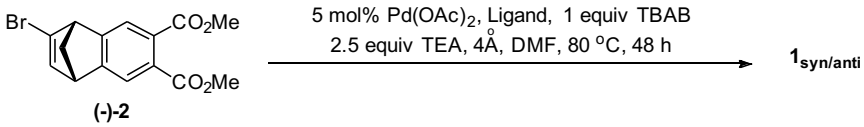
General Information

All solvents were dried before use, following standard procedures. Anhydrous dioxane was purchased from Aldrich and stored inside a glove box before opening. THF, DMF and toluene were collected from a solvent purification system and stored under 4Å MS in a glove box. Unless indicated, all starting materials were obtained from commercial sources and used without additional purification. Analytical thin-layer chromatography (TLC) was performed on silica-gel plates w/UV254. ^{1}H NMR and ^{13}C NMR spectra were recorded with 400 or 600 MHz spectrometers. Chemical shifts are expressed in parts per million (δ, ppm) using residual solvent peaks as internal standard ^{1}H NMR: δ (ppm) for $CDCl_3$ = 7.26; ^{13}C NMR: δ (ppm) for $CDCl_3$ = 77.00.

Synthetic Procedures and Optimizations

Enantioenriched (–)–**2**/(–)–**5** (99% *ee*) and DPPPO were obtained by following procedures from *J. Org. Chem.* **2019**, *84*, 4392 and *Organometallics* **2001**, *20*, 3950, respectively.

Table S1. Cyclotrimerization of 0.24 M (–)–**2** (99% *ee*) was probed following a published procedure (*Tetrahedron Lett.* **2001**, *42*, 3515) with and without PPh_3 ligand. The reported yields of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure below.



(-)-2

entry	Ligand (mol%)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$1_{syn/anti}$ (%)	de (%)
1[a]	PPh_3(10)	16	2	18	78
2	-	30	2	32	88

Note a: 7% of starting material was found by the crude ^{1}H NMR

Experimental Procedure (see Cossu, S.; De Lucchi, O.; Paulon, A.; Peluso, P.; Zonta, C. *Tetrahedron Lett.* **2001**, *42*, 3515): Enantioenriched (–)–**2** (0.1 mmol, 33.7 mg), $Pd(OAc)_2$ (0.005 mmol, 1.12 mg), with (entry 1) or without (entry 2) PPh_3 (0.01 mmol, 2.6 mg), TBAB (0.1 mmol, 32.2 mg), 4 Å molecular sieves (43 mg), were added to 15 ml oven-dried tube, and transferred into glove box. Following, TEA (0.25 mmol, 35 µl), and anhydrous DMF (0.42 mL) were added. The tube was sealed, and the solution stirred at a room temperature for 30 min. The temperature was raised to 80 °C using an aluminum block, and kept constant for 48 h. After cooling the mixture to a room temperature, the solvent was removed under reduced pressure. The crude reaction product was filtered through a pad of silica and washed by 50 ml of CH_3OH:CH_2Cl_2 = 1:15. The solvent was removed under reduced pressure and the residue dissolved in 0.6 ml of $CDCl_3$ (containing 12 µmol of dimethoxyethane as internal standard) for examination with ^{1}H NMR spectroscopy (Figure S1).

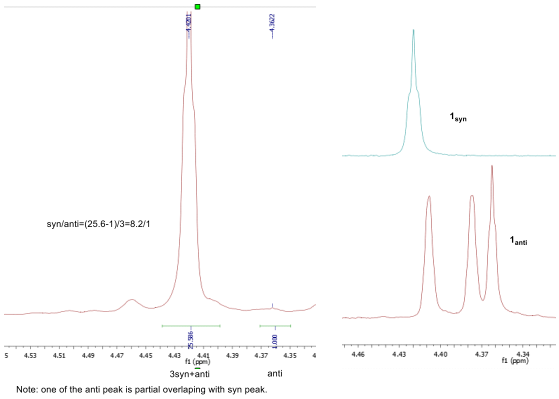
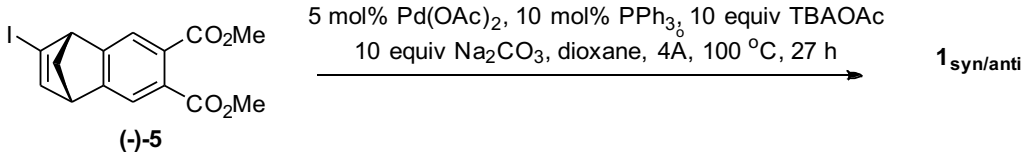


Figure S1. A segment of ^{1}H NMR spectrum (400 ^{1}H NMR, $CDCl_3$) obtained from the reaction mixture (entry 1, Table S1) showing a resonance from $\mathbf{1}_{syn}$ (4.42 ppm) with smaler signals for $\mathbf{1}_{anti}$ (4.36 ppm). On the right, segments from ^{1}H NMR spectra of purified $\mathbf{1}_{syn}$ (top) and $\mathbf{1}_{anti}$ (bottom).

Table S2. Cyclotrimerization of 33 mM (–)–**5** (99% *ee*) was probed following a published procedure (*J. Org. Chem.* **2010***, 75,* 4626). Using thin-layer chromatography, we could not detect any of $\mathbf{1}_{syn/anti}$ forming in the reaction. The experimental procedure for completing the transformation is shown below.

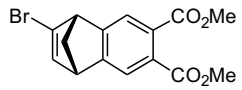


(-)-5

remained sm (%)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$1_{syn/anti}$ (%)	de (%)
0	0	0	0	-

Experimental Procedure (see Higashibayashi, S.; Masud Reza, A. F. G.; Sakurai, H. *J. Org. Chem. 2010*, *75*, 4626): A suspension of $Pd(OAc)_2$ (1.12 mg, 0.005 mmol), PPh_3 (2.62 mg, 0.01 mmol), Bu_4NOAc (0.3 g, 1.0 mmol), Na_2CO_3 (0.11 g, 1.0 mmol) and molecular sieves 4 Å (29 mg) in 1.5 ml of anhydrous dioxane was heated at 100 ºC for a few minutes under nitrogen atmosphere. After the color of the solution turned black, (–)–**5** (38.4 mg, 0.1 mmol) was quickly added to the solution at room temperature in glove box. Sealed the tube and temperature was raised to 80 ºC using an aluminum block and kept constant for 27 h. After the reaction mixture was cooled to ambient temperature, we could not detect any of $\mathbf{1}_{syn/anti}$ forming in the reaction using thin-layer chromatography (SiO_2; $\mathbf{1}_{syn}$, $R_f = 0.3$ and $\mathbf{1}_{anti}$, $R_f = 0.2$ with CH_2Cl_2:acetone = 15:1).

Table S3. Cyclotrimerization of 33 mM (–)–**2** (99% *ee*) was probed following a published procedure (*J. Org. Chem.* **1999***, 64,* 10). In these experiments, we varied the palladium source (second column), ligand (third column), and temperature (third column). The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure below.



(-)-2

catalyst, Ligand, 1.1 equiv Cs_2CO_3
dioxane, 100-140 °C, 42h

→ $\mathbf{1}_{syn/anti}$

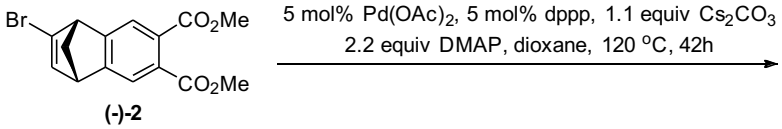
entry	catalyst (mol%)	Ligand (mol%)	T (°C)	$\mathbf{1}_{syn}$ %	$\mathbf{1}_{anti}$ %	$\mathbf{1}_{syn/anti}$ %	de %
1[a]	$Pd_2(ba)_3$ (2.5)	P^tBu_3(5)	105	4	2	6	33
2	$Pd(OAc)_2$ (5)	P^tBu_3(10)	140	3	5	8	25
3	$Pd(OAc)_2$ (5)	PPh_3(10)	120	13	5	18	44
4	$Pd(OAc)_2$ (5)	dppp(5)	120	12	4	16	50
5	$Pd(OAc)_2$ (5)	$PyPPh_2$(10)	120	16	4	20	60
6	$Pd(OAc)_2$ (5)	dppp(5)	140	6	5	11	9
7	$Pd(OAc)_2$ (5)	$PyPPh_2$(10)	100	6	2	8	50

Note a: 16% of starting material was found by ^{1}H NMR, reaction time 24h

Experimental Procedure (see Littke, A. F.; Fu, G. C. *J. Org. Chem.* **1999**, *64*, 10): Enantioenriched (–)–**2** (0.1 mmol, 33.7 mg), Pd catalyst (for quantity, see Tables S3-S13),[a] ligand (for quantity see Tables S3-S13), Cs_2CO_3 (0.11 mmol, 36 mg; see also Table S3-S13) and DMAP (if used, see Table S3-S13) were added to a 15 ml oven-dried tube, and transferred into a glove box. Following, anhydrous dioxane or another solvent (the quantity is adjusted depending on the substrate concentration specified in Tables S3-S13) was added. The tube was sealed and stirred at a room temperature for 30 min. The temperature was raised to a desired value (Tables S3-S13), using an aluminum block, and then kept constant for 42 h. After cooling the reaction mixture to a room temperature, the solvent was removed under a reduced pressure. The residue was dissolved in 0.6 ml of $CDCl_3$, containing 12 μmol of dimethoxyethane (as an internal standard), to be subjected to ^{1}H NMR spectroscopic measurement.

[a]*We noted that adding $Pd(OAc)_2$ as a solid to the reaction mixture (as described above) would give inconsistent results. The inconsistency can be easily overcome by dissolving $Pd(OAc)_2$ in dioxane, prior to the reaction, and keeping it in a glove box for one day. A solution of $Pd(OAc)_2$ in dioxane should be stable for several days.*

Table S4. Cyclotrimerization of enantioenriched (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we varied the concentration of the substrate (second column) by adjusting the volume of dioxane. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.

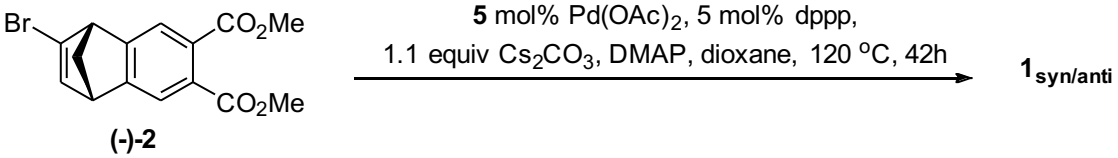


(-)-2

entry	Conc.(mM)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	de (%)
1	33	25	3	28	79
2	56	36	3	39	85
3	79	35	3	38	84
4	100	35	2	37	89
5[a]	150	27	2	29	86

Note a: 15% of starting material was found by ^{1}H NMR

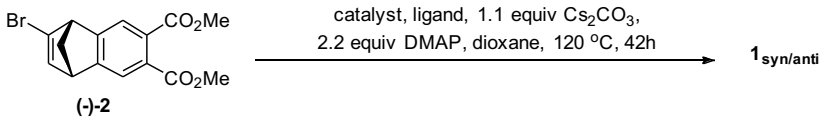
Table S5. Cyclotrimerization of 79 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we varied the quantity of DMAP (second column) while the concentration of the remaining reactants stayed the same (see below). The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



(-)-2

entry	DMAP(equiv)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	de (%)
1	0.5	26	5	31	68
2	1.1	34	4	38	79
3	2.2	35	3	38	84
4	3.3	27	3	30	80

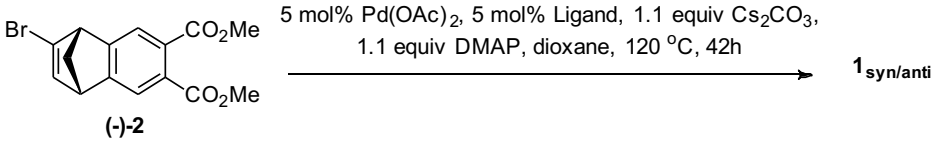
Table S6. Cyclotrimerization of 33 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we varied the quantity of DPPP ligand (fourth column) while the concentration of the remaining reactants stayed the same (see below). The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



(-)-2

entry	Catalyst (mol%)	Ligand	L/Pd	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de** (%)
1	$Pd(OAc)_2$ (5)	DPPP	1/1	25	3	28	79
2	$Pd(OAc)_2$ (5)	DPPP	1.2/1	13	2	15	73
3	$Pd(OAc)_2$ (5)	DPPP	2/1	5	3	8	25
4	$Pd_2(dba)_3$ (2.5)	DPPP	1/1	7	2	9	56
5	$Pd_2(dba)_3$ (2.5)	DPPPO	1/1	26	3	29	79

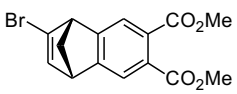
Table S7. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we changed the ligand (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



(-)-2

entry	Ligand	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de** (%)
1	DPPE	22	3	25	76
2	DPPP	34	4	38	79
3	DPPB	25	4	29	72

Table S8. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we changed the palladium source (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



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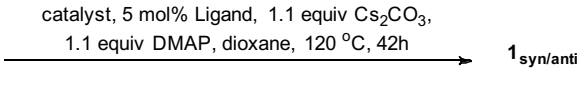
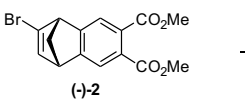


entry	Catalyst (mol%)	Ligand	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de** (%)
1	$Pd(OAc)_2$ (5)	DPPP	34	4	38	79
2[a]	$Pd_2(dba)_3$ (2.5)	DPPPO	42	2	44	91
3	$PdCl_2$ (5)	DPPP	39	1	40	95
4[b]	$PdCl_2(COD)$ (5)	DPPP	11	2	13	69
5	$Pd(CH_3CN)_2Cl_2$ (5)	DPPP	38	2	40	90
6[c]	$Pd(OTFA)_2$ (5)	DPPP	0	0	0	-

Note: a, 2%; b, 17%; c, 60% of the starting material was found by ^{1}H NMR

Table S9. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we varied the ligand (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3. Our assumption is that bidentate ligands (5 mol%) underwent an oxidation of one of their phosphorus atoms to turn into monodentate ligands (for instance, DPPP into DPPPO from entry 1). In this regard, 10 mol % of monodentate ligands were added so that half of this quantity became oxidized.



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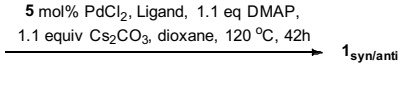
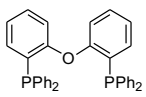
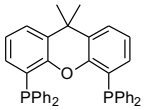


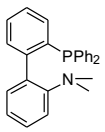
entry	Ligand (mol%)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de** (%)
1	DPPP(5)	39	1	40	95
2	DPEphos(5)	38	2	40	90
3	Xantphos(5)	30	3	33	82
4	Ph-DavePhos(5)	23	2	25	84
5	PPh_3(10)	37	2	39	90
6[a]	P(4-OMe-Ph)$_3$(10)	21	2	23	83
7	Xphos(10)	24	2	26	85
8[b]	TFP(10)	19	5	24	58
9[c]	TPFP(5)	3	1	4	50



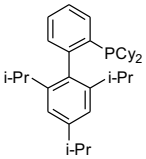
DPEphos



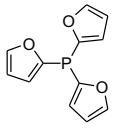
Xanphos



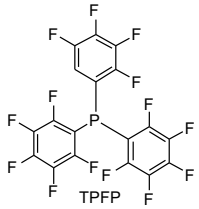
Ph-DavePhos



Xphos



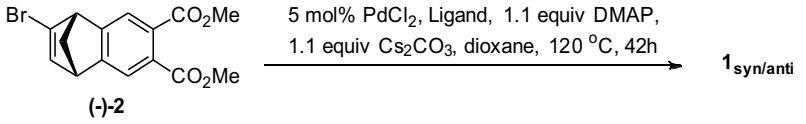
TFP



TPFP

Note: a, 13%; b, 28%; c, 61% of the starting material was found by ^{1}H NMR

Table S10. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we varied the ligand (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



entry	Ligand (mol%)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de** (%)
1	1,10-Phen·H_2O(5)	52	3	55	89
2	DMPHEN(5)	55	2	57	93
3[a]	DTBPY(5)	47	2	49	92
4	DIPHENBPY(5)	49	5	54	81
5[b]	2-(2-pyridyl)-oxazoline(5)	<1	0	<1	-

Note: a, 6%; b, 50% of the starting material was found by ^{1}H NMR

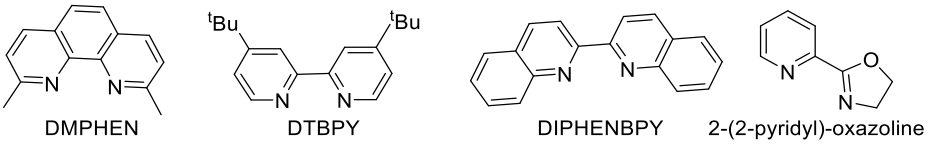
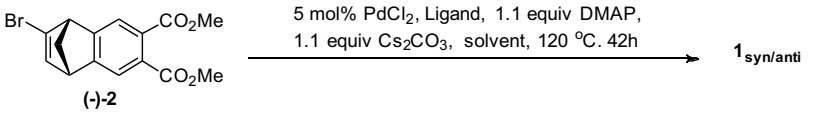


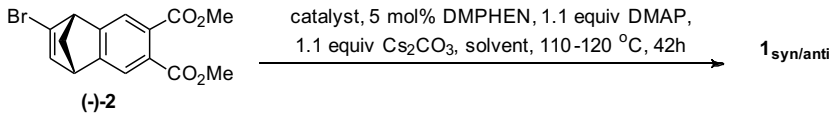
Table S11. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we changed solvent (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



entry	Solvent	Ligand (mol%)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de** (%)
1	dioxane	DPPP(5)	39	1	40	95
2	THF	DPPP(5)	40	5	45	78
3	DMF	DPPP(5)	<1	0	<1	-
4	toluene	DPPP(5)	44	1	45	96
5[a]	toluene	-	36	1	37	95
6[b,c]	dioxane	DPPP(5)	1	2	3	33

Note: a, 22%; b, 19% of the starting material was found by ^{1}H NMR; c, without DMAP

Table S12. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we changed solvent (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.

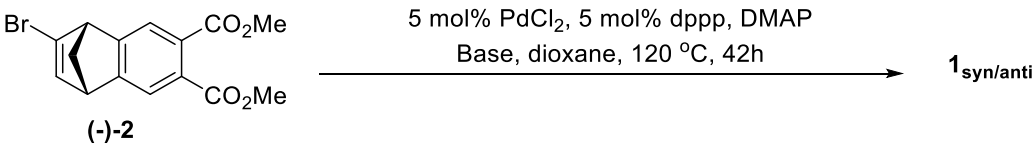


(-)-2

entry	catalyst (mol%)	solvent	Tem. (°C)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$ (%)	**de**(%)
1	$PdCl_2$(5)	dioxane	120	55	2	57	93
2	$PdCl_2$(5)	dioxane	110	53	1	54	96
3[a]	$PdCl_2$(5)	toluene	110	46	1	47	96
4[b]	$PdCl_2$(5)	CH_3CN	120	<1	0	<1	-
5	$PdCl_2$(5)	DME	120	9	3	12	50
6[c]	$Pd_2(dba)_3$(2.5)	dioxane	110	33	2	35	89
7[d,e]	$PdCl_2$(5)	dioxane	120	1	1	2	0

Note: a, 15%; b, 30%; c, 13%; d, 68% of the starting material was found by ^{1}H NMR; e, without DMAP

Table S13. Cyclotrimerization of 100 mM (–)–**2** (99% *ee*) was probed following the experimental procedure described under Table S3. In these experiments, we changed the base (second column) while the remaining reactants stayed the same. The reported yield of $\mathbf{1}_{syn}$ and $\mathbf{1}_{anti}$ diastereomers were obtained with ^{1}H NMR spectroscopy as described in the experimental procedure under Table S3.



(-)-2

entry	Base (equiv)	DMAP (equiv)	$\mathbf{1}_{syn}$ (%)	$\mathbf{1}_{anti}$ (%)	$\mathbf{1}_{syn/anti}$	**de** (%)
1	Cs_2CO_3(1.1)	1.1	39	1	40	95
2[a]	Cs_2CO_3(1.1)	0	1	2	3	33
3[b]	TEA(2.2)	1.1	0	-	0	-
4[c]	-	2.2	0	-	0	-
5	Ag_2CO_3(1.1)	1.1	39	4	43	81
6[d, e]	Ag_2CO_3(1.1)	1.1	11	3	14	57
7	Cs_2CO_3(1.1)+TBAB(1)	1.1	<2	-	<2	-
8	Cs_2CO_3(1.1)+TBAOAc(1)	1.1	25	3	28	79

Note: a, 19%; b, 60%; c, 70%; d, 4% of the starting material was found by ^{1}H NMR; e, DMAc was used as solvent

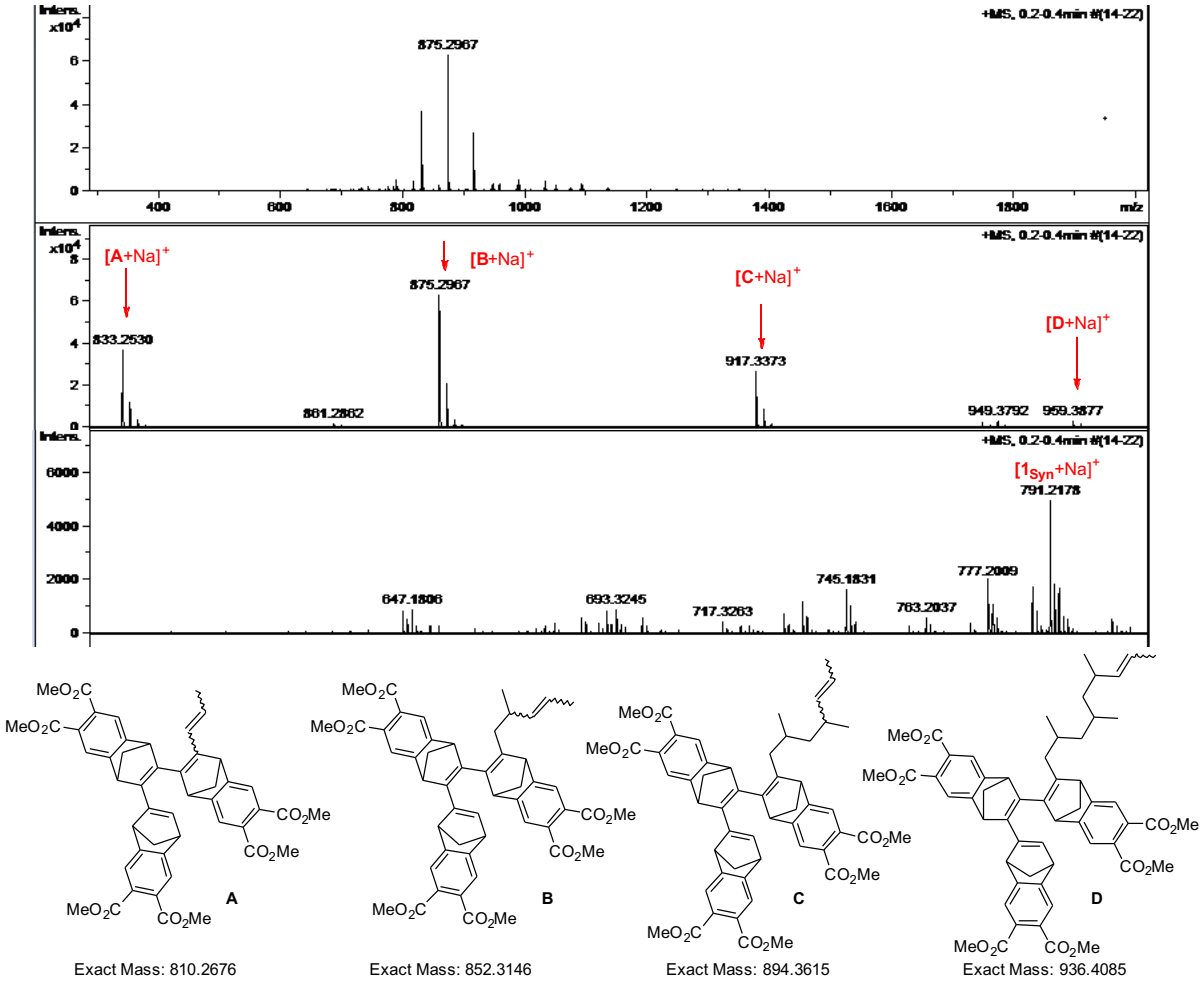


Figure S2. ESI–MS of the reaction mixture in which enantioenriched (–)–**2** was subjected to cyclotrimerization using $PdCl_2$, DPPPO and TBAB as an additive (see Table S13, entry 7); full experimental conditions are given under Table S3.

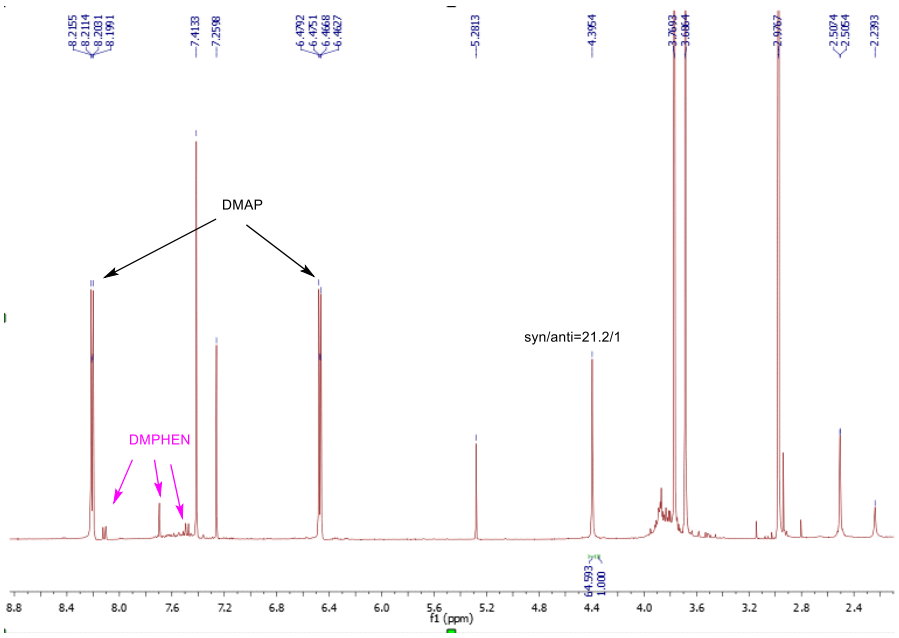


Figure S3. ^{1}H-NMR spectrum (400 MHz, 298 K; $CDCl_3$) of the reaction mixture in which enantioenriched (–)–**2** was subjected to cyclotrimerization using $PdCl_2$ as a catalyst and DMPHEN as a ligand (full experimental conditions are given under Table S3 as well in the scaled-up synthesis of $\mathbf{1}_{syn}$ above).

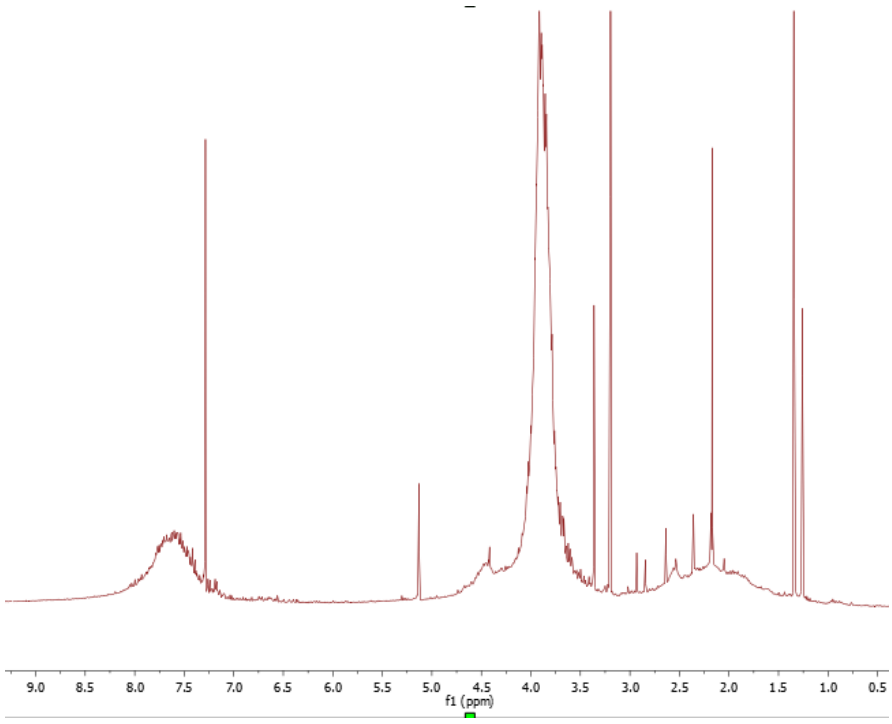


Figure S4. ^{1}H-NMR spectrum (400 MHz, 298 K; $CDCl_3$) of a polar (late) chromatographic fraction obtained in the purification of $\mathbf{1}_{syn}$ prepared on the large scale (see page S15). A set of broaden resonances correspond to norbornene oligomers (Figure S5).

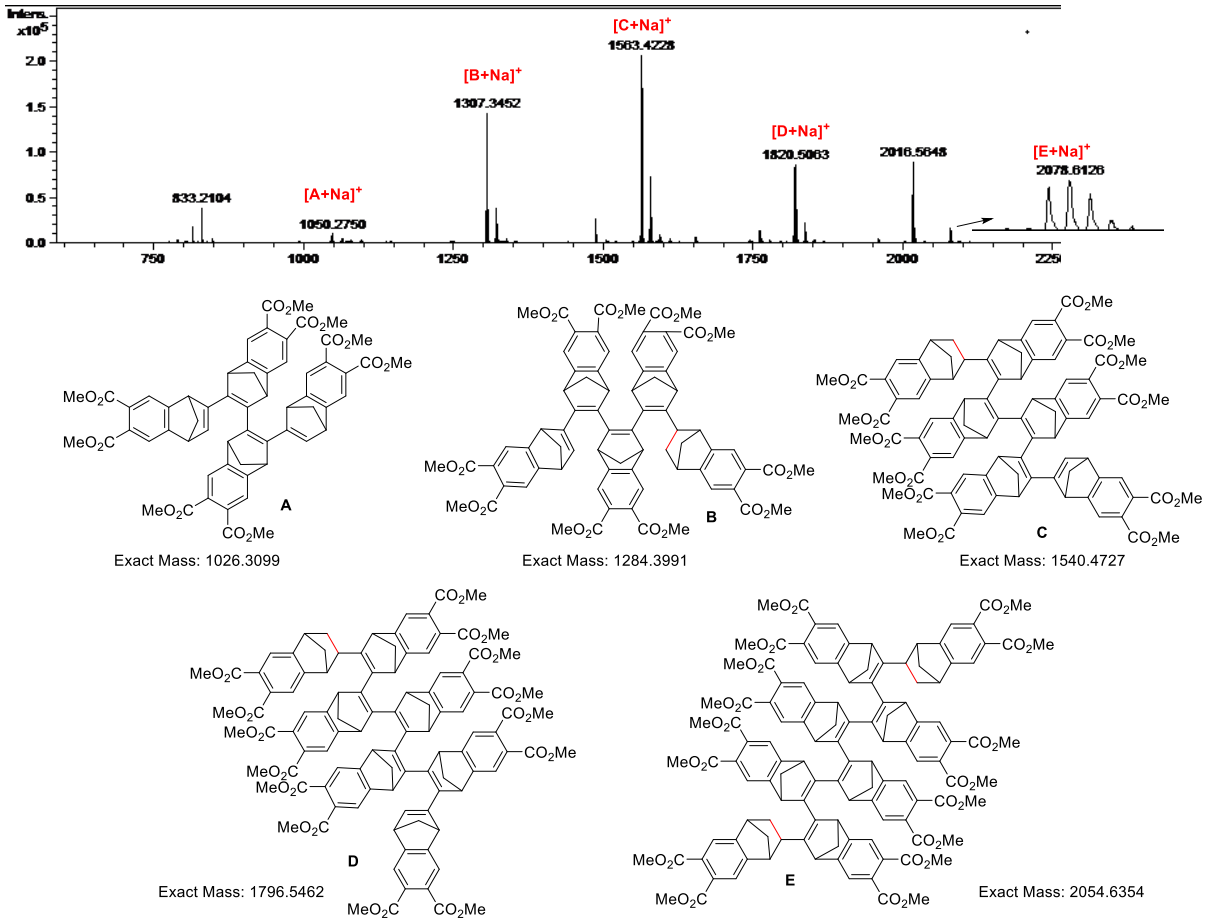
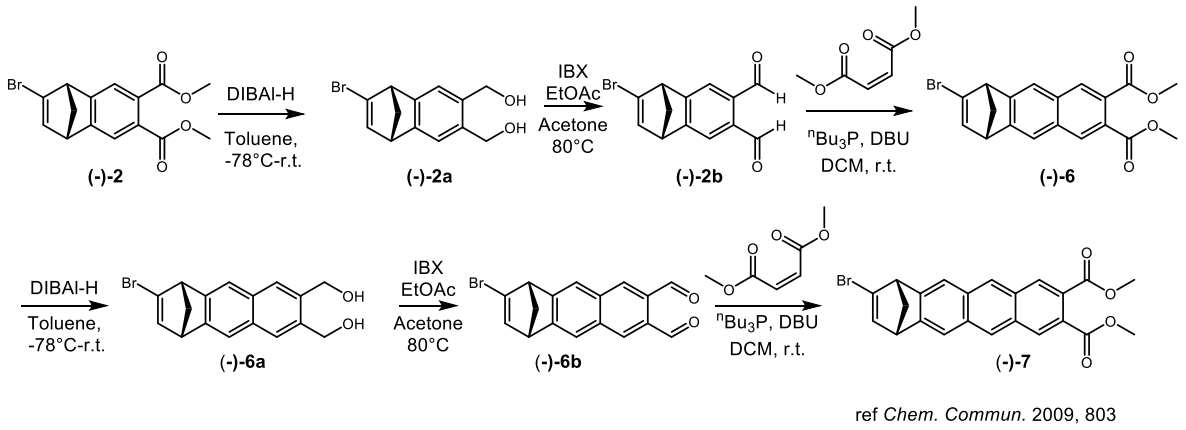


Figure S5. ESI–MS of a polar (late) chromatographic fraction obtained in the purification of $\mathbf{1}_{syn}$ prepared on the large scale. Other more polar fractions, with perhaps longer oligomers, were present but difficult to separate and therefore subject to the analysis. Signals with particular molecular weights correspond to **A**–**E** oligomers.

Scale up and Synthesis of Larger Baskets

Compound 1$_{syn}$: Enantioenriched (–)–**2** (6 mmol, 2.022 g), 5 mol% of $PdCl_2$ (0.3 mmol, 53.2 mg), DMPHEN (0.3 mmol, 62.4 mg), Cs_2CO_3 (6.6 mmol, 2.16 g) and DMAP (6.6 mmol, 806 mg) were added to a 100 ml oven-dried tube, and transferred into a glove box. Following, 60 ml of anhydrous dioxane was added. The tube was sealed and stirred at a room temperature for 60 min. The temperature was raised to 120 ºC using an oil bath, and then kept constant for four days. After cooling the reaction mixture to a room temperature, we decanted the dioxane solution and the remained solid part was filtered through a pad of silica and washed by 500 ml of CH_3OH:CH_2Cl_2 = 1:15. Following, two solutions were combined, and the solvent removed under reduced pressure. The resulting oil was subjected to column chromatography (SiO_2, CH_2Cl_2/acetone from 35:1 to 25:1) until most of **1**$_{syn}$ came out (R_f = 0.2, CH_2Cl_2/acetone = 20/1). Changing the solvent gradient from 20/1 to 15/1 allowed obtaining additional quantity of **1**$_{syn}$ along with oligomers. First fraction: after removing solvent under reduced pressure, the resulting solid was triturated with CH_3OH/Et_2O= 10/1 (2 x 30 ml) to remove trace amounts of impurities, giving 600 mg of **1**$_{syn}$ as a light yellow solid. Second fraction: additional purification by column chromatography (CH_3OH/Et_2O=10/1) and trituration gave 160 mg of **1**$_{syn}$ as a light yellow solid. Overall, we obtained 760 mg of **1**$_{syn}$ (50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.42 (s, 6H), 4.41 (t, J = 1.2 Hz, 6H), 3.78 (s, 18H), 2.54-2.50 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 167.7, 152.6, 137.6, 129.3, 121.2, 65.0, 51.8, 48.5. HRMS(ESI): *m/z* calcd for $C_{45}H_{36}NaO_{12}$: 791.2099 $[M+Na]^+$; found: 791.2098 $[M+Na]^+$.



Scheme S1: Synthesis of enantioenriched **6** and **7** from (–)–**2**.

Compound 6: A solution of diester monomer (–)–**2** (4.5 mmol, 1.516 g) in toluene (50 ml) was cooled to −78 °C. A solution of 1M DIBAL-H in toluene (27 mmol, 27 ml) was dropped in over 30 min. The solution was allowed to warm up to room temperature and then stirred overnight. The mixture was cooled down using an ice bath and was quenched using CH_3OH (20 ml). Ethyl acetate and a saturated solution of Rochelle's salt were added, and the layers were allowed to separate. Aqueous layer was extracted with ethyl acetate (2 x 20 ml). Organic portions were washed with brine, dried with Na_2SO_4, and concentrated in vacuo. Compound **2a** (1.2 g, 95%) was isolated as a white solid and used without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.35 (s, 1H), 7.24 (s, 1H), 6.71 (d, J = 3.3 Hz, 1H), 4.74-4.66 (m, 4H), 3.93 (m, 1H), 3.82 (m, 1H), 2.60 (dt, J = 7.3, 1.6 Hz, 1H), 2.31-2.28 (m,

1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 150.69, 150.23, 140.18, 136.74, 136.15, 135.94, 123.77, 123.37, 69.14, 64.34, 64.29, 58.17, 51.56; note that this intermediate was used in the next reaction without further purification. Compound **2a** (4.0 mmol, 1.124g) was added to a mixture of ethyl acetate (40 ml) and acetone (4ml). Stabilized IBX (7.5 g, 12 mmol, 45%) was added and the suspension was heated to 90 °C for 4 hours. The reaction was cooled and filtered through celite. The filtrate was washed with saturated $NaHCO_3$ (3 x 50 ml). The organic layer was dried with Na_2SO_4 and concentrated in vacuo. The resulting solid was dissolved in CH_2Cl_2 and then filtered through a cotton plug to give **2b** (1.052 g, 95 %) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 10.53 (s, 1H), 10.51 (s, 1H), 7.92 (s, 1H), 7.81 (s, 1H), 6.76 (d, J = 3.3 Hz, 1H), 4.11-4.08 (m, 1H), 3.99-3.97 (m, 1H), 2.69 (dt, J = 7.8, 1.6 Hz, 1H), 2.39-2.36 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 191.73, 191.70, 156.79, 156.40, 139.64, 135.58, 135.34, 134.68, 123.30, 122.67, 68.70, 58.28, 51.76; note that this intermediate was used in the next reaction without further purification. A solution of dimethyl maleate (0.15 ml, 1.2 mmol) in CH_2Cl_2 (2.0 ml) was cooled to 0° C. Tri-*n*-butylphosphine (1.3 mmol, 0.32 ml) was dropped in slowly and the solution stirred for 10 min. The resulting mixture was dropped into a solution of compound **2b** (1.0 mmol, 277 mg) in CH_2Cl_2 (2.0 ml) at 0 °C. A solution of DBU (15 µl, 0.1 mmol) in CH_2Cl_2 (1.0 ml) was added to the reaction. The solution was allowed to warm to room temperature and stir overnight. The reaction mixture was washed with water, dried with Na_2SO_4, and concentrate in vacuo. The resulting oil was subjected to column chromatography (SiO_2, hexanes/ethyl acetate from 12:1 to 4:1) yielding the compound **6** (309.8 mg, 80%) was isolated as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.13 (s, 1H), 8.10 (s, 1H), 7.75 (s, 1H), 7.63 (s, 1H), 6.71 (d, J = 3.3 Hz, 1H), 4.05 (m, 1H), 3.94 (s, 3H), 3.94 (s, 3H), 3.70 (s, 1H), 2.66-2.64 (m, J = 7.9, 1.4 Hz, 1H), 2.33-2.32 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.35, 168.28, 149.72, 149.32, 139.64, 134.96, 132.86, 132.40, 129.72, 129.51, 128.32, 128.18, 120.72, 120.12, 65.49, 57.59, 52.59 (2C), 51.03. HRMS (ESI): *m/z* calcd for $C_{19}H_{15}BrNaO_4$: 409.0046 $[M+Na]^+$; found: 409.0063, $[M+Na]^+$.

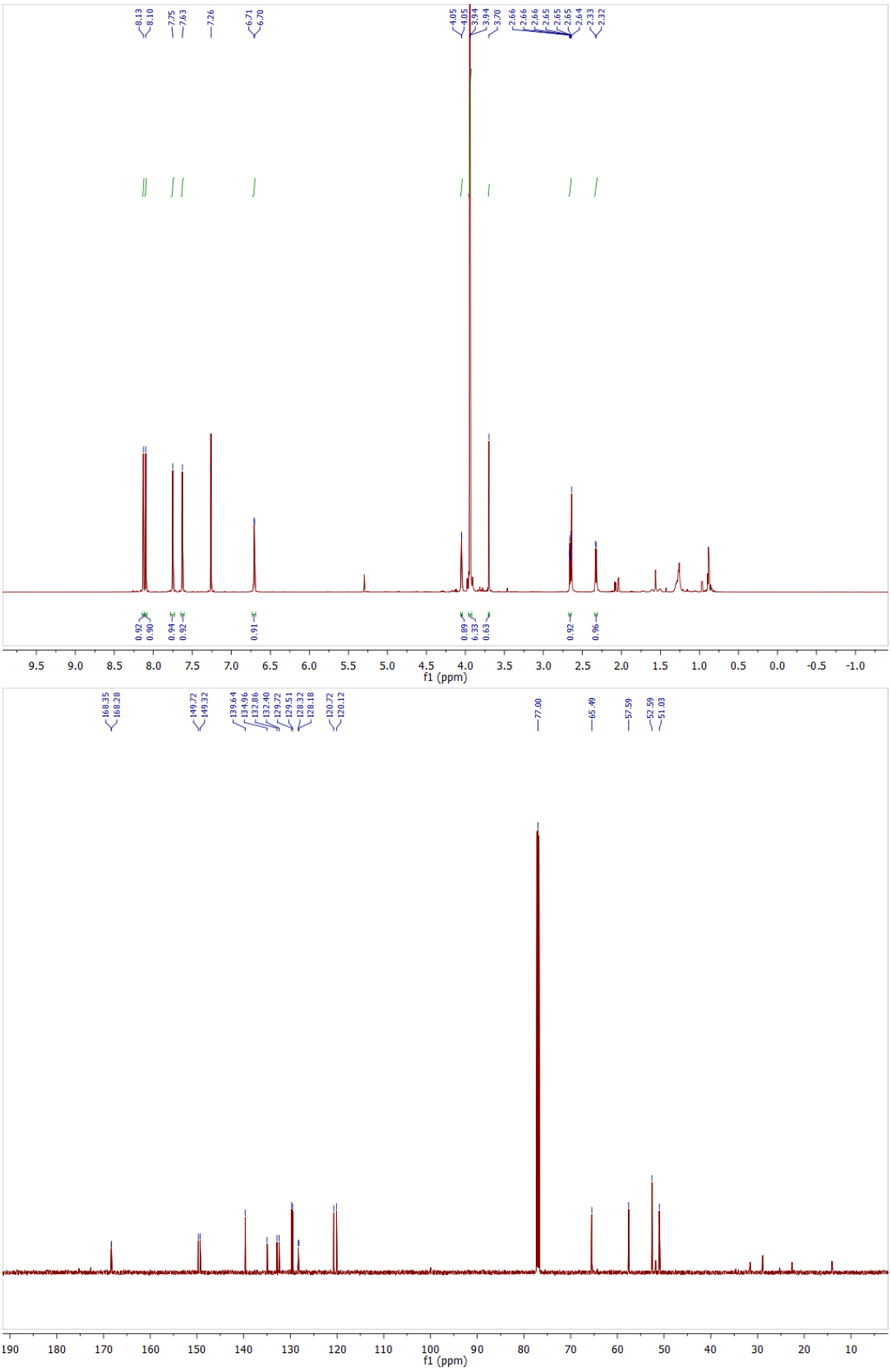


Figure S6. ^{1}H and ^{13}C NMR spectra (600/150 MHz, 298 K) of **6** in $CDCl_3$.

Compound 7: A solution of diester **6** (4.5 mmol, 1.742g) in 50 ml of toluene was cooled to −78 °C. A solution of 1M DIBAL-H in toluene (27 mmol, 27 mL) was dropped in over 30 min. The solution was allowed to warm up to room temperature and stirred overnight. The mixture was cooled down using an ice bath and was quenched using 20 mL of CH_3OH. Ethyl acetate and a saturated solution of Rochelle's salt were added and the layers were allowed to separate. Aqueous layer was extracted with ethyl acetate (2 x 20ml). Organic portions were washed with brine, dried with Na_2SO_4, and concentrated in vacuo. Compound **6a** (1.117g, 75%) was isolated as a white solid and used without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.69 (s, 1H), 7.67 (s, 2H), 7.55 (s, 1H), 6.69 (d, J = 3.3 Hz, 1H), 4.90-4.81 (m, 4H), 4.02-4.01 (m, 1H), 3.91 (m, 1H), 2.64-2.62 (m, 1H), 2.32-2.28 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 147.27, 146.88, 139.72, 136.77, 136.61, 135.05, 132.18, 131.72, 128.91, 128.76, 120.10, 119.46, 65.56, 64.65, 64.63, 57.60, 51.01; note that this intermediate was used in the next reaction without further purification. Compound **6a** (4.0 mmol, 1.325 g) was added to a mixture of ethyl acetate (40 ml) and acetone (4 ml). Stabilized IBX (7.5 g, 12 mmol, 45%) was added and the suspension heated to 90 °C for 4 hours. The reaction mixture was cooled and then filtered through Celite. The filtrated was washed with saturated $NaHCO_3$ (3 x 50 ml). The organic layer was dried with Na_2SO_4 and concentrated in vacuo. The resulting solid was dissolved in CH_2Cl_2 and filtered through a cotton plug to, upon the solvent evaporation, give **6b** as a yellow solid (1.178 g, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 10.67 (s, 1H), 10.63 (s, 1H), 8.37 (s, 1H), 8.35 (s, 1H), 7.92 (s, 1H), 7.80 (s, 1H), 6.76 (d, J = 3.3 Hz, 1H), 4.14-4.12 (m, 1H), 4.02 (br. s, 1H), 2.74-2.72 (m, 1H), 2.41-2.37 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 192.55 (2C), 151.61, 151.21, 139.68, 135.07, 134.18, 133.90, 133.71, 133.36, 132.79, 132.74, 121.55, 121.03, 65.67, 57.71, 51.16; note that this intermediate was used in the next reaction without further purification. A solution of dimethyl maleate (0.15 ml, 1.2 mmol) in CH_2Cl_2 (2.0 ml) was cooled to 0 °C. Tri-*n*-butylphosphine (1.3 mmol, 0.32 ml) was added slowly followed by stirring for 10 min. The resulting mixture was dropped into a solution of compound **6b** (1.0 mmol, 327 mg) in CH_2Cl_2 (2.0 ml) at 0 °C. A solution of DBU (15 µL, 0.1 mmol) in CH_2Cl_2 (1.0 mL) was added to the reaction. The solution was allowed to warm to room temperature to be stirred overnight. The reaction mixture was washed with water, dried with Na_2SO_4, and concentrated in vacuo. The resulting oil was subjected to column chromatography (SiO_2, hexanes/ethyl acetate from 12:1 to 4:1) to give **7** as a yellow oil (262 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.42 (s, 1H), 8.41 (s, 1H), 8.38 (s, 1H), 8.35 (s, 1H), 7.87 (s, 1H), 7.75 (s, 1H), 6.70 (d, J = 3.3 Hz, 1H), 4.08-4.07 (m, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.98 (br. s, 1H), 2.70-2.66 (m, 1H), 2.33-2.32 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 168.23, 168.18, 147.01, 146.59, 139.15, 134.05, 132.77, 132.41, 130.90, 130.80, 130.60, 130.53, 127.41, 127.28, 127.15 (2C), 119.94, 119.26, 63.35, 57.20 (2C), 52.55, 50.64. HRMS (ESI): *m/z* calcd for $C_{23}H_{17}BrNaO_4$: 459.0202, $[M+Na]^+$; found: 459.0981, $[M+Na]^+$.

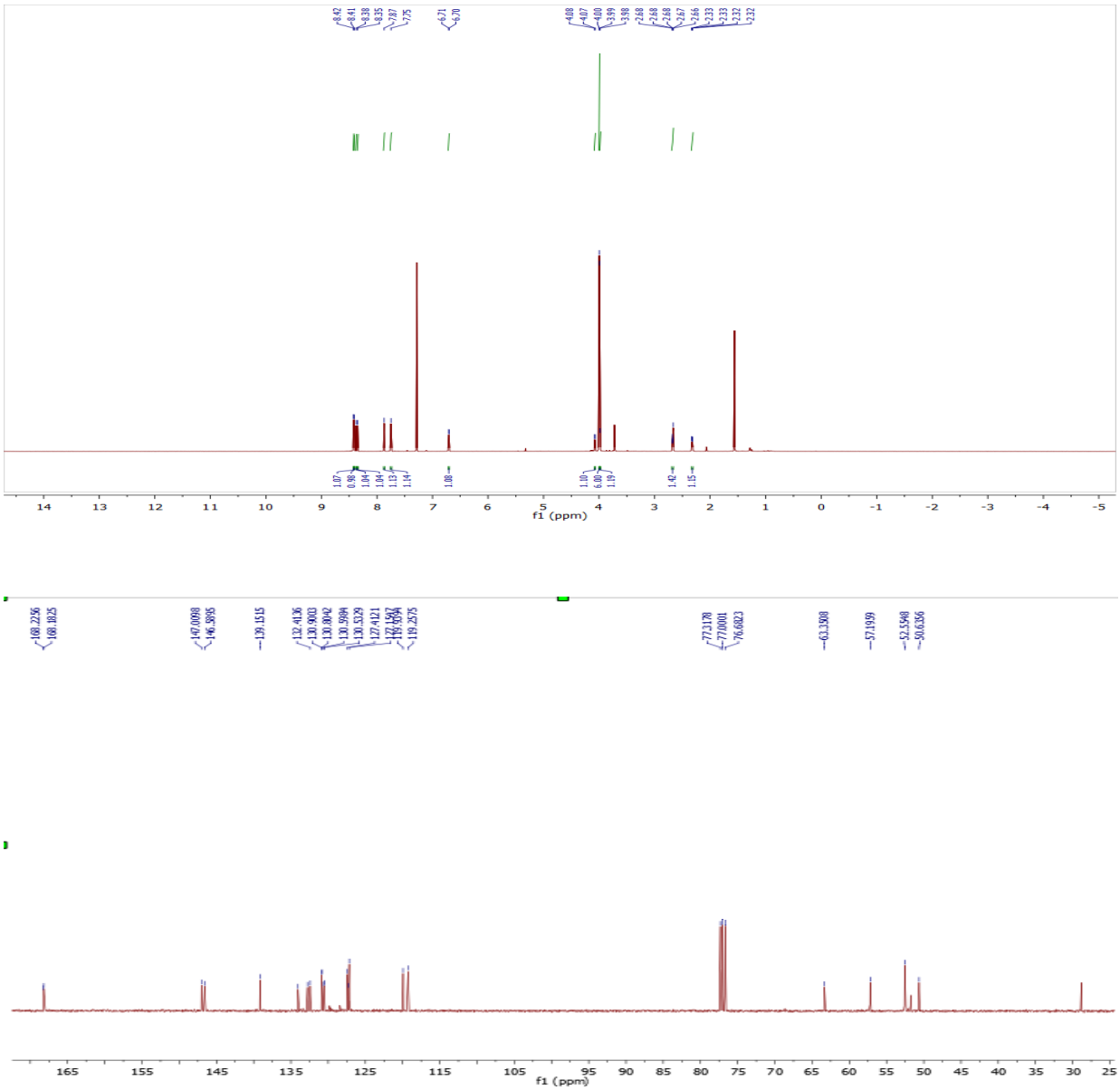


Figure S7. ^{1}H and ^{13}C NMR spectra (600/100 MHz, 298 K) of **7** in $CDCl_3$.

Compound 8$_{syn}$: Compound **6** (0.2 mmol, 77.4 mg), $PdCl_2$ (0.01 mmol, 1.89 mg), DMPHEN (0.01 mmol, 2.08 mg), Cs_2CO_3 (0.22 mmol, 72 mg) and DMAP (0.22 mmol, 26.8 mg) were added to a 15 ml oven-dried tube, which was transferred into a glove box. After adding 2 ml of anhydrous dioxane, the tube was sealed, and the reaction mixture stirred at a room temperature for 60 min. The solvent was removed under reduced pressure and the resulting oil subjected to column chromatography (SiO_2, CH_2Cl_2/acetone from 35:1 to 25:1) until most of **8**$_{syn}$ came out (R_f = 0.2, CH_2Cl_2/acetone = 20/1). Changing the solvent gradient from 20/1 to 15/1 allowed obtaining additional quantity of **8**$_{syn}$ along with oligomers. First fraction: after removing solvent under reduced pressure, the resulting solid was triturated with CH_3OH/Et_2O= 10/1 (1 ml) to remove trace amounts of impurities, giving **8**$_{syn}$ (22.0 mg, 36 %) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.96 (s, 6H), 7.54 (s, 6H), 4.56 (t, J=1.2 Hz, 6H), 3.86 (s, 18H), 2.61 (dt, J = 8.3, 1.5 Hz, 3H), 2.55(dt, J = 8.3, 1.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 168.28, 149.57, 137.64, 132.52, 129.56, 127.78, 119.74, 64.04, 52.47, 48.69. HRMS (ESI): m/z calcd for $C_{57}H_{42}NaO_{12}$: 941.2568 $[M+Na]^+$; found: 941.2604, $[M+Na]^+$.

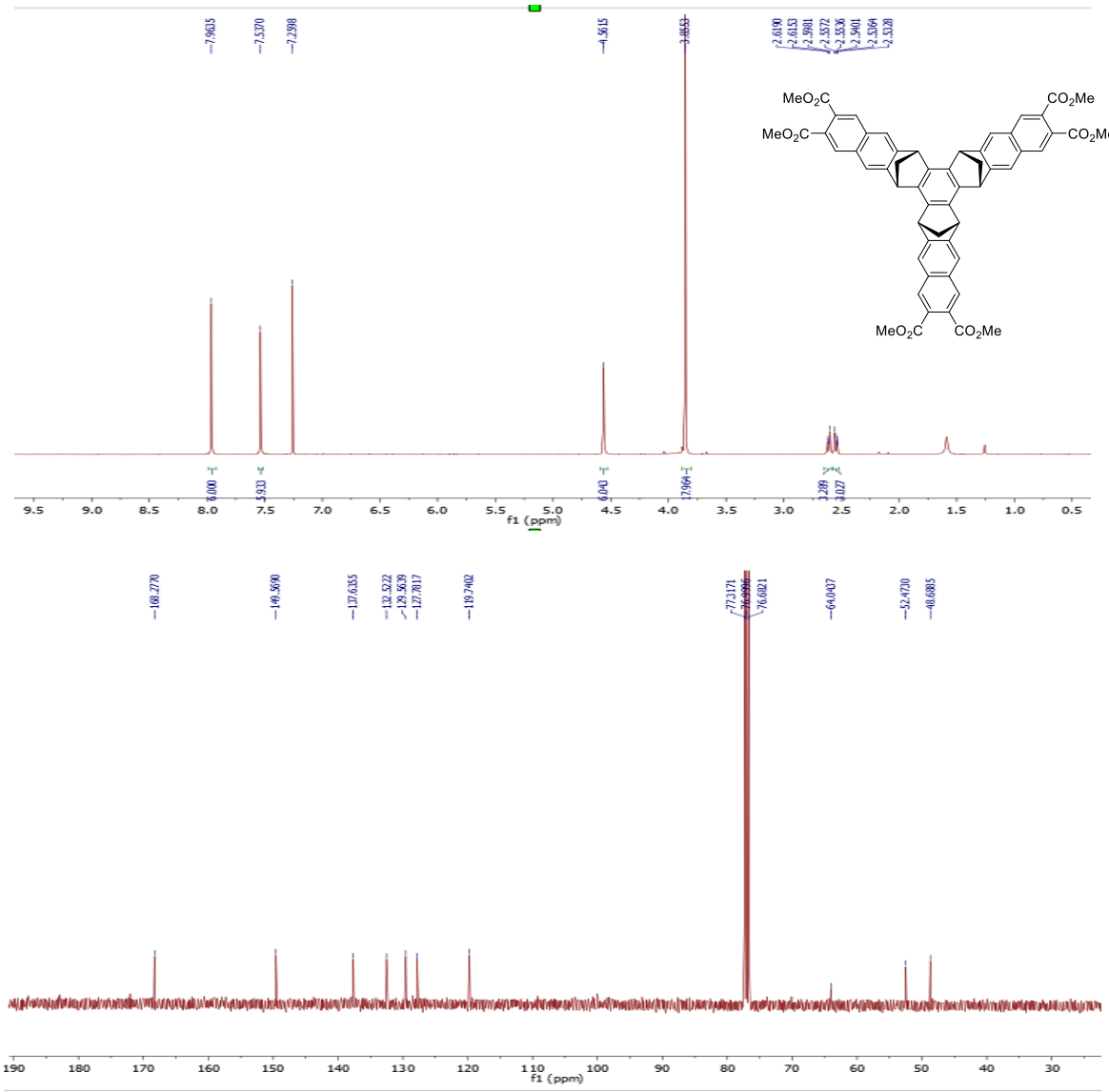


Figure S8. ^{1}H and ^{13}C NMR spectra (400/100 MHz, 298 K) of **8**$_{syn}$ in $CDCl_3$.

Compound 9$_{syn}$: Compound **7** (0.2 mmol, 87.5 mg), $PdCl_2$ (0.01 mmol, 1.89 mg), DMPHEN (0.01 mmol, 2.08 mg), Cs_2CO_3 (0.22 mmol, 72 mg) and DMAP (0.22 mmol, 26.8 mg) were added to a 15 ml oven-dried tube, which was transferred into a glove box. After adding 2 ml of anhydrous dioxane, the tube was sealed and the reaction mixture stirred at a room temperature for 30 min. The solvent was removed under reduced pressure and the resulting oil subjected to column chromatography (SiO_2, CH_2Cl_2/acetone from 35:1 to 25:1) until most of **9**$_{syn}$ came out (R_f = 0.2, CH_2Cl_2/acetone = 20/1). Changing the solvent gradient from 20/1 to 15/1 allowed obtaining additional quantity of **9**$_{syn}$ along with oligomers. <u>First fraction</u>: after removing solvent under reduced pressure, the resulting solid was triturated with CH_3OH/Et_2O= 10/1 (1 ml) to remove trace amounts of impurities, giving **9**$_{syn}$ (21.5 mg, 30%) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.21 (s, 6H), 8.12 (s, 6H), 7.64 (s, 6H), 4.60 (s, 6H), 3.88 (s, 18H), 2.65 (d, J = 8.3 Hz, 3H), 2.55 (d, J = 8.3 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 168.19, 147.27, 137.53, 132.64, 130.81, 130.13, 127.08, 126.93, 118.82, 62.21, 52.46, 48.47. HRMS (ESI): *m/z* calcd for $C_{69}H_{48}NaO_{12}$: 1091.3038, $[M+Na]^+$; found: 1091.3170, $[M+Na]^+$.

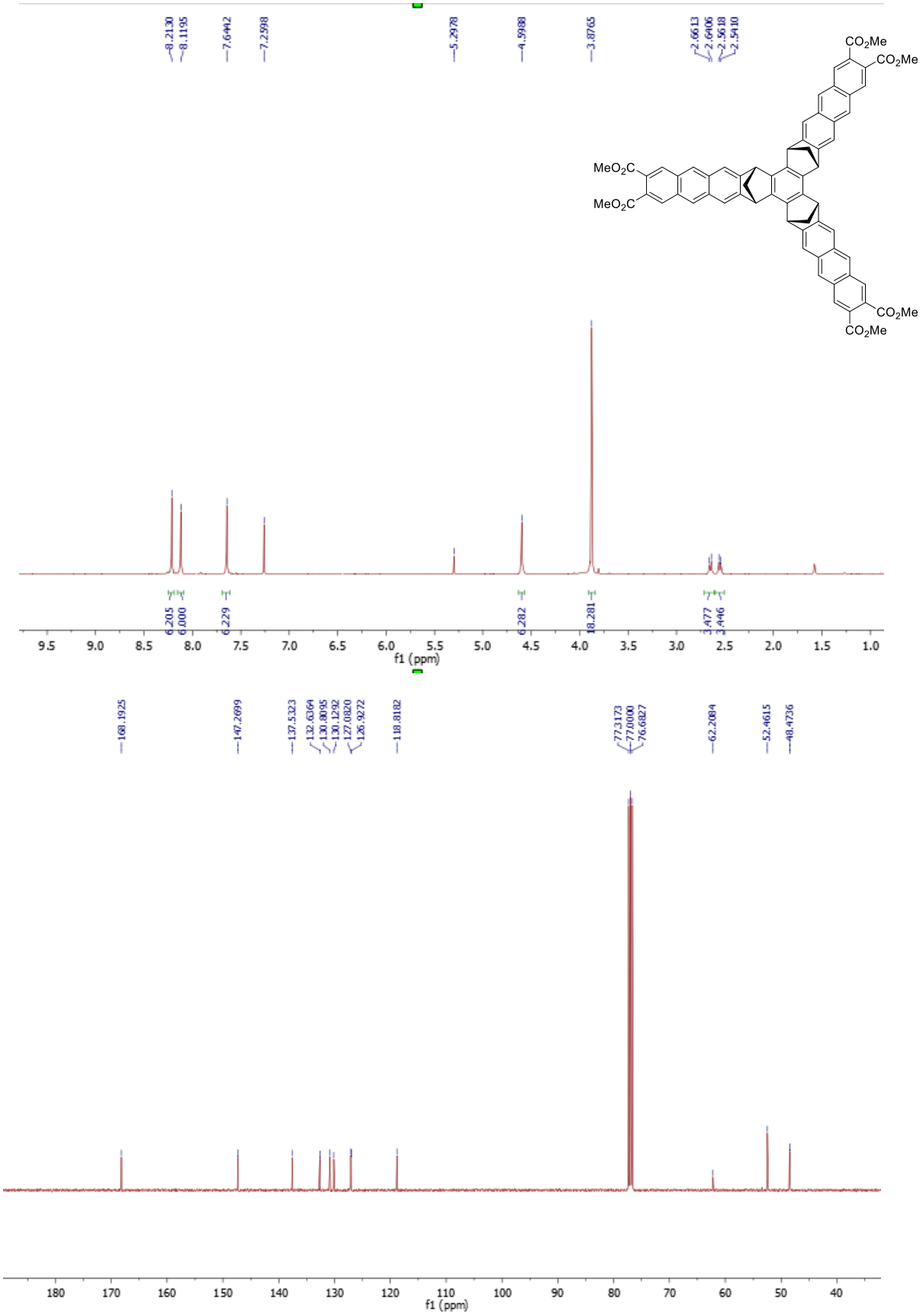


Figure S9. ^{1}H and ^{13}C NMR spectra (400/100 MHz, 298 K) of **9**$_{syn}$ in $CDCl_3$.