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To Flip or Not To Flip? Assessing the Inversion Barrier of the Tetraphenylene Framework with Enantiopure 2,15-Dideuteriotetraphenylene and 2,7-Dimethyltetraphenylene

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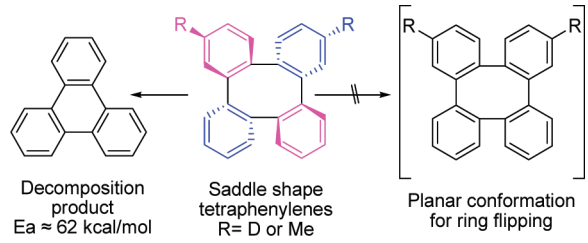

Two chiral tetraphenylenes, 2,15-dideuteriotetraphenylene (**7**) and 2,7-dimethyltetraphenylene (**15**) were synthesized and resolved to address the tetraphenylene inversion barrier problem. Neutron diffraction investigation of enantiopure **7** showed that the molecule retained its chirality integrity during its synthesis from enantiopure precursors and therefore rules out the possibility of the tetraphenylene framework possessing a low-energy barrier to inversion. Thermal study on **15** and tetraphenylene **1** further revealed that their inversion barriers were not overcome up to 600 °C, at which temperature these compounds underwent skeletal contraction into triphenylene with activation energies of 62.8 and 58.2 kcal/mol, respectively. This result is supported by computational studies which yielded an inversion barrier of 135 kcal/mol for tetraphenylene as a consequence of the *peri*-hydrogen repulsions at its planar conformation.

Introduction

Tetraphenylene (**1**)[1] is a unique molecule with a distinct saddle shape in which two opposite pairs of benzene rings are oriented above or below the average plane of the central eight-membered ring (Figure 1).[2,3] This extraordinary geometry facilitates excellent three-dimensional interactions that are crucial for possible realization of double helical conjugated systems,[4] novel molecular clathrates,[5] self-assembly building blocks[6] and asymmetric catalysts.[6d]

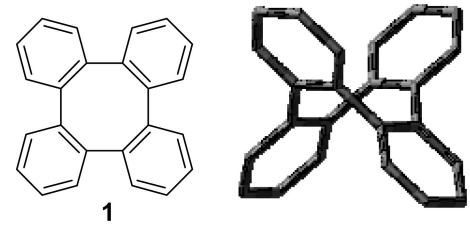

FIGURE 1. Saddle-shape structure of **1**.

Because of the structural stability of this saddle shape geometry, it is likely that there is an energy barrier for inversion

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(1) Rapson, W. S.; Schuttleworth, P. G.; Niekark, J. N. *J. Chem. Soc.* **1943**, 326–327.

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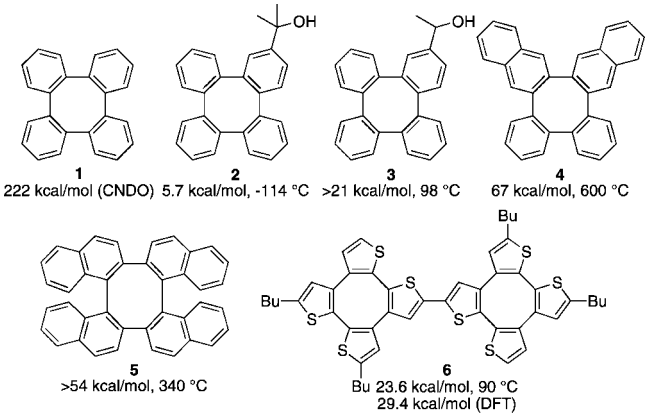


FIGURE 2. Different inversion barrier estimations.

via a planar transition state. However, the magnitude of this inversion barrier remains an unresolved issue with widely varied estimations for more than three decades (Figure 2). The first investigation of this barrier was made by Figeys and Dralants in 1971. On observing the ^{1}H NMR decoalescence of the two diastereotopic methyl groups in **2** at −114 °C, a value of 5.7 kcal/mol was assigned.[7] One year after this preliminary report, a CNDO/2 calculation by Allinger on **1** gave an extremely high barrier of 222 kcal/mol.[8] At the same time, Mislow studied the related molecule **3** at 98 °C and set a lower limit of 21 kcal/mol for its inversion barrier.[9] Later in 1989, our group observed partial racemization of enantiopure **4** at 600 °C, and an energy barrier of 67 kcal/mol was implicated.[10] More recently, Rajca investigated the behavior of chiral tetraphenylene derivative **5** and showed that **5** retained its absolute configuration after being kept at 340 °C for 12 h.[11] Further discordant result was added to the scene when Marsella reported in 2002 that **6**, a dimer of cyclotetrathiophene and a close analog of tetraphenylene, possessed an inversion barrier of 29.4 kcal/mol from a computational study and 23.6 kcal/mol from the ^{1}H NMR spectral analysis at 90 °C.[12]

The determination of the inversion barrier of tetraphenylene derivatives is important because such results are crucial to warrant configurational stability that is vital to the use of these compounds as chiral nonracemic entities in various applications. Moreover, the results obtained would also provide clues for the conditions in achieving planar geometry of tetraphenylenes, which will shed light on their potential use as optoelectronic materials.[13] Motivated by these reasons, we commenced a research project with the aim to answer the inversion barrier question through both experimental and computational techniques. We herein report our findings on two specially designed tetraphenylenes, **7** and **15**.

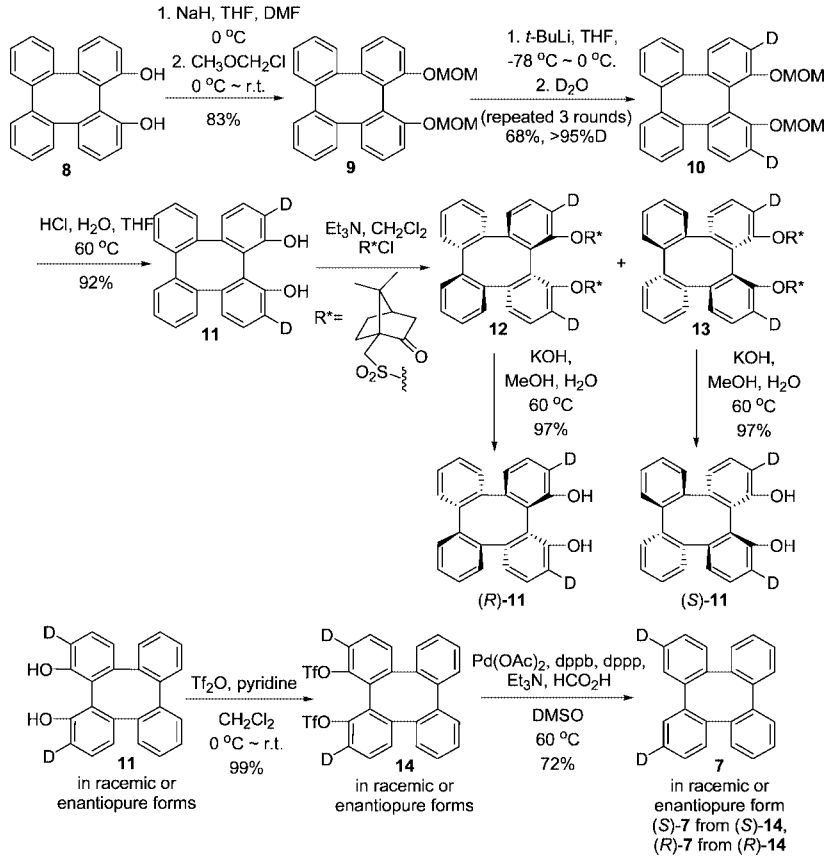
Results and Discussion

Desymmetrization of the tetraphenylene skeleton into a chiral entity can be achieved by mono- or appropriate higher-substitution. When such tetraphenylenes are brought into a planar geometry, they will revert back to the saddle-shape ground-state through two opposite pathways: one leading to the unchanged starting material (not to flip), and the other to the enantiomer with the opposite configuration (to flip). Racemization of an enantiopure tetraphenylene derivative will therefore occur. In the present study, we employed enantiopure 2,15-dideuteriotetraphenylene (**7**) and 2,7-dimethyltetraphenylene (**15**) for the evaluation of their inversion barriers.

Synthesis of Enantiopure 2,15-Dideuteriotetraphenylene (7). The primary goal of our study was to resolve the issue on the inversion barrier of the tetraphenylene core unit using an enantiopure derivative with as little perturbation as possible on its outer periphery as a tool. Since there is no other derivative of tetraphenylene that more closely resembling pristine tetraphenylene itself in structure than a simple deuterated analog, we set forth to undertake the synthesis of 2,15-dideuteriotetraphenylene (**7**) in its enantiopure forms to be used as probes for our investigation on the processes of their racemization. Our quest for **7** in both racemic and enantiopure forms was a scheme starting from 1,16-dihydroxytetraphenylene (**8**) (Scheme 1).[6b] To introduce the two deuterium atoms in a regiospecific manner, an *ortho*-lithiation strategy was employed.[14] The starting dihydroxytetraphenylene **8** was thus first protected as its bisMOM ether **9**, which was then subjected to bis-*ortho*-lithiation with *t*-BuLi at low temperature. Trapping the lithiated species with heavy water led to an inseparable mixture of ∼70% 2,15-bisdeuterated product **10** and ∼30% undeuterated starting material. After carrying out the lithiation-deuteration procedure twice, a sample with >95% deuterio-enrichment was obtained. With this bisdeuterio molecule in hand, the MOM protecting groups were dismantled by acid hydrolysis, and subsequent formation of bis-(*S*)-camphorsulfonates utilizing (*S*)-camphorsulfonyl chloride led to two isolable diastereomers **12** and **13**. The establishment of absolute configurations for these diastereomers was achieved by comparing their ^{1}H NMR spectra with those of the known corresponding 1,16-bis[(*S*)-camphorsulfonyloxy]tetraphenylenes.[6b] Respective desulfonylation of **12** and **13** followed by column chromatographic purification generated the optically pure (*R*)-**11** and (*S*)-**11**, each with >99% *ee*. The quest for **7**, as a racemate or in its enantiopure forms,

(2) Irngartinger, H.; Reibel, W. R. K. *Acta Crystallogr. B* **1981**, *37*, 326–327.
(3) Reviews on tetraphenylene researches.: (a) Mak, T. C. W.; Wong, H. N. C. In *Comprehensive Supramolecular Chemistry*; MacNicol, D. D., Toda, F., Bishop, P., Eds.; Pergamon Press: Oxford, 1996; Vol. 6, pp 351−369. (b) Mac, T. C. W.; Wong, H. N. C. *Top. Curr. Chem.* **1987**, *140*, 141–164. (c) Hou, X.-L.; Huang, H.; Wong, H. N. C. *Synlett* **2005**, 1073–1089. (d) Rajca, A.; Rajca, S.; Pink, M.; Miyasaka, M. *Synlett* **2007**, 1799–1822. (e) Hisaki, I.; Sonoda, M.; Tobe, Y. *Eur. J. Org. Chem.* **2006**, 833–847. (f) Wang, C.; Xi, Z. *Chem. Commun.* **2007**, 5119–5133. (g) Marsella, M. J.; Rahbarnia, S.; Wilmot, N. *Org. Biomol. Chem.* **2007**, *5*, 391–400.
(4) (a) Rajca, A.; Safronov, A.; Rajca, S.; Shoemaker, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 488–491. (b) Marsella, M. J.; Kim, I. T.; Tham, F. *J. Am. Chem. Soc.* **2000**, *122*, 974–975.
(5) Man, Y.-M.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1990**, *55*, 3214–3221.
(6) (a) Lai, C. W.; Lam, C. K.; Lee, H. K.; Mak, T. C. W.; Wong, H. N. C. *Org. Lett.* **2003**, *6*, 823–826. (b) Wen, J.-F.; Hong, W.; Yuan, K.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **2003**, *68*, 8918–8931. (c) Hui, C.; Mak, T. C. W.; Wong, H. N. C. *Tetrahedron* **2004**, *60*, 3523–3532. (d) Peng, H.-Y.; Lam, C.-K.; Mak, T. C. W.; Cai, Z.; Ma, W.-T.; Li, Y.-X.; Wong, H. N. C. *J. Am. Chem. Soc.* **2005**, *127*, 9603–9611. (e) Wu, A.-H.; Hau, C.-K.; Wong, H. N. C. *Adv. Synth. Catal.* **2007**, *349*, 601–608.
(7) Figeys, H. P.; Dralants, A. *Tetrahedron Lett.* **1971**, *42*, 3901–3904.
(8) Finder, C. J.; Chung, D.; Allinger, N. L. *Tetrahedron Lett.* **1972**, *13*, 4677–4679.
(9) Senkler, G. H.; Gust, D.; Riccobono, P. X.; Mislow, K. *J. Am. Chem. Soc.* **1972**, *94*, 8626–8627.
(10) Rashi-Ranjbar, P.; Man, Y.-M.; Sandström, J.; Wong, H. N. C. *J. Org. Chem.* **1989**, *54*, 4888–4892.
(11) Rajca, A.; Safronov, A.; Rajca, S.; Wongsriratanakul, J. *J. Am. Chem. Soc.* **2000**, *122*, 3351–3357.
(12) Marsella, M. J.; Reid, R. J.; Estassi, S.; Wang, L. S. *J. Am. Chem. Soc.* **2002**, *124*, 12507–12510.
(13) For examples see: (a) Rajca, A.; Safronov, A.; Rajca, S.; Ross, C. R.; Stezowsk, J. J. *J. Am. Chem. Soc.* **1996**, *118*, 7272–7279. (b) Rathore, R.; Abdelwahed, S. H. *Tetrahedron* **2004**, *60*, 5267–5270. (c) Rajendra, R.; Magueres, P. L.; Lindeman, S. V.; Kochi, J. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 809–812.
(14) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1–360.

SCHEME 1



was finally accomplished by transforming **11** (correspondingly in both racemic and enantiopure forms) into the bistriflates **14** followed by palladium-catalyzed reductive desulfonyloxygenation.[15]

Single-Crystal Neutron Diffraction Study of 2,15-Dideuteriotetraphenylene (7). In our original plan, the inversion barrier of **7** was to be deduced by checking the chiroptical changes of a single enantiomer of it at different temperatures. However, to our disappointment, compound **7** exhibited very poor optical activities: attempts to resolve racemic **7** on chiral HPLC were unfruitful; samples synthesized from enantiopure precursors **11** of opposite configurations showed near zero specific rotation values and displayed noncharacteristic CD spectra which assumed the shapes of two wiggled lines near the zero line and without any discernible antipodal correlation. Such behavior of **7** raised the question as to whether (a) enantiopure **7** retained its intrinsic chirality which just could not be determined by optical rotation or CD measurements or (b) the inversion barrier was so low that the samples racemized in the course of the formation of **7** from enantiopure **14**.

The inadequacy of the chiroptical methods in solving this problem drove us to resort to neutron diffraction study for an answer, which eventually confirmed that the products obtained from the reactions of enantiopure **14** to **7** were indeed chiral nonracemic substances with their absolute configurations corresponding to those of the starting materials **14**. These results are described below.

Our approach essentially hinges on the different neutron scattering amplitudes of D and H (+6.50 pm for D and −3.78 pm for H).[16] If the barrier to inversion is high [hypothesis (a)], the optically active molecule (**I**) (Figure 3) will not racemize. Nevertheless, because of the similar sizes of D and H, the molecule will still be expected to pack in two different orientations, (**I**) and (**II**), leading to a superimposed model (**III**) in which four of the outer hydrogens are 50% deuterium: 50% hydrogen hybrids (corresponding to an average neutron scattering amplitude equal to +1.36 pm), while the remaining four outer atoms would be pure (100%) H (negative peaks in structure analysis; these are labeled "**H**" in structure **III** in Figure 3).

On the other hand, if the barrier to inversion is low [hypothesis (b)], a racemic molecule would result in which total scrambling of deuterium over all outer positions would occur, and each of these eight positions would consist of 25% D: 75% H hybrids (structure **IV** in Figure 3).

Upon slow evaporation of a saturated dichloromethane solution of (*S*)-**7**, single crystals with suitable size (~10 mm^3) for the neutron diffraction investigation were obtained and the neutron diffraction data were collected at both 30 and 150 K on instrument SXD, the single crystal diffractometer at the ISIS spallation neutron source.[17] For each data collection (at two different temperatures), the crystal orientation was exposed to the neutron beam for 2.5 h per orientation, at positions of $\omega = -90, -150, -40, 0, +90$ (5 orientations). Then the crystal was tilted by 45 degrees in χ and 4 more orientations were collected, $\omega = +90, +150, +130$ and 0, yielding a total of 9 sets of data, with each set consisting of results from 11 detectors. Data reduction, integration and absorption correction were performed

(15) (a) Kurz, L.; Lee, G., Jr.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321–6324. (b) Zhang, A.; Csutoras, C.; Zong, R.; Neumeyer, J. L. *Org. Lett.* **2005**, *7*, 3239–3242.

(16) Bacon, G. E. In *Neutron Diffraction*; Oxford University Press: London, England, 1962.

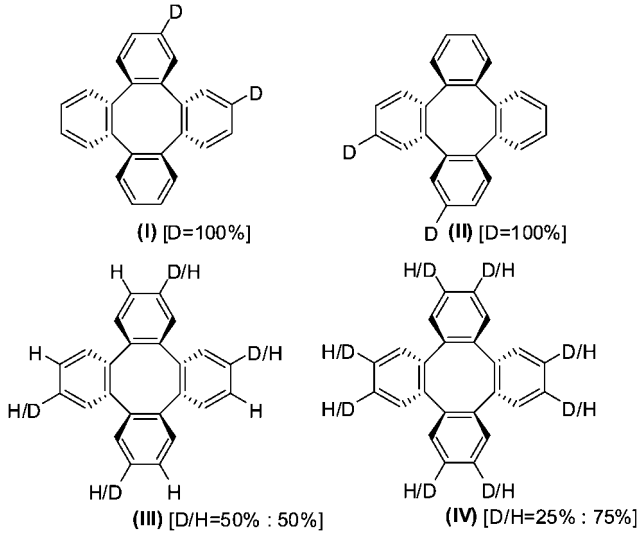


FIGURE 3. Schematic drawing of **7**. Dideuteriotetraphenylene maintaining its chirality consistent with a high barrier of inversion [hypothesis (a)]. The title molecule is shown packed in two orientations (**I** and **II**) and superimposed to yield the disordered structure (**III**), in which four of the outer hydrogens are 50% deuterium: 50% hydrogen hybrids. The remaining four outer hydrogens in (**III**) are 100% pure hydrogen atoms. In contrast, a low barrier to inversion [hypothesis (b)] would cause complete hydrogen/deuterium scrambling throughout all eight outer positions (**IV**), with each position consisting of 25% deuterium: 75% hydrogen hybrids.

using the SXD2001 software. For the absorption correction, the following expression was used: $\mu = 3.1447 + 0.0063 * \lambda$. ($\lambda$ = wavelength in Å, μ in cm^{-1}). The minimum, maximum and average transmission were 1.618, 2.262 and 1.715 respectively. Minimum *d*-spacing is equal to 0.31 Å, and the wavelength ranged from 0.37 to 8.8 Å. The minimum and maximum 2θ values were 12.5 and 165 degrees respectively. As part of the time-sorted Laue procedure, the wavelength range and 2θ range are combined (i.e., at each 2θ value) and the full wavelength range is recorded. The self-consistency index [R(merge)] for the 30 K data was 7.5%. The final refinement of the structural analysis using the best data set, at 30 K, gave agreement factors of 7.5% for 9161 unique reflections, $R_1 = 7.9\%$, $wR_2 = 20.0\%$, with all atoms refined anisotropically (*vide infra*).

As an additional check, a second neutron diffraction data collection of the title compound **7** at room temperature (300 K) was also carried out on instrument BIX-3,[18] a single crystal neutron diffractometer with imaging plate at the reactor JRR-3 in JAEA (Ibaraki, Japan) by using the same crystal measured at the SXD. to investigate the structure of the ambient temperature. The wavelength of incident neutron was 1.41 Å. 159 oscillation images with $\Delta\omega = 3.0°$ were measured. Exposure time for one image was 15 min. The data processing was done by *DENZO*[19] and 3075 unique reflections with $R^{int} = 8.5\%$ were obtained. However, because of the larger number of reflections from the 30 K data collection from ISIS, the discussion of the neutron results in this manuscript will largely focus on the ISIS data.

(17) (a) Keen, D. A.; Gutmann, M. J.; Wilson, C. C. *J. Appl. Crystallogr.* **2006**, *39*, 714–722. (b) Gutmann, M. J. In *SXD2001*; ISIS Facility, Rutherford Appleton Laboratory: Oxfordshire, England, 2005.

(18) Tanaka, I.; Kurihara, K.; Chatake, T.; Niimura, N. *J. Appl. Crystallogr.* **2002**, *35*, 34–40.

(19) Otwinowski, Z.; Minor, W. Processing of X-ray Diffraction Data Collected in Oscillation Mode. *Methods in Enzymology*; Carter, C. W., Jr., Wseet, R. M., Eds.; Academic Press, 1997; Col. 276, Part A, pp 307−326.

At this point, we needed to redo the X-ray analysis of the title compound because of reasons which will be clear in the following discussion. Our crystal was found to be C-centered monoclinic, consistent with the nonsolvated form of tetraphenylene originally reported by Reibel.[2] However, that earlier X-ray crystal structure was solved in the centrosymmetric space group *C*2/*c*, a logical choice since the parent (all-hydrogen) molecule is nonchiral. Recognizing the fact that specific deuteriation was deliberately introduced to yield a chiral molecule (without mirror planes), it was necessary to redo the X-ray analysis in a lower-symmetry (chiral) space group so that the neutron data could be phased correctly.

A small crystal was selected and the X-ray diffraction data were collected and refined in the lower symmetry space group *C*2 (with $a = 15.42$ Å, $b = 13.06$ Å, $c = 16.26$ Å, $\beta = 109.98°$), in which the mirror planes originally present in the original X-ray study[2] (in space group *C*2/*c*) vanished. A similar phenomenon (a change of space group between the X-ray and neutron structure determinations) had been reported before in the analysis of chiral glycolic acid.[20] A minor complication is that, in the lower-symmetry space group *C*2, there are two independent molecules in the crystallographic unit, in contrast to the centric space group *C*2/*c* in which there is only one molecule in the asymmetric unit. The net result of the X-ray analysis is that the asymmetric unit contains the carbon skeletons of two independent molecules (still a centrosymmetric arrangement of atoms in a noncentric space group).

The neutron analysis was then resumed taking the two carbon frameworks from the aforementioned X-ray refinement in space group *C*2. In order to break the symmetry, it was necessary to gradually introduce asymmetry by focusing on one of the two molecules in the asymmetric unit first, and then to tackle the second one later. A difference Fourier map at this point gave numerous negative peaks which corresponded to the many hydrogen positions in the molecule. The 8 "inner" hydrogens of the molecule that had not been deuterated were first refined. Then the outer set of peaks, which could be either D/H hybrids or 100% hydrogens, were gradually identified. Eventually, four atoms which refined acceptably well as pure hydrogens, while the remaining four outer positions refined acceptably well as 50% D/50% H hybrid atoms (Figure 4). Thus, distinguishing the four "pure hydrogens" versus the four 50% D/50% H "hybrid" atoms turned out to be unambiguous, and the model shown in Figure 3, labeled **III**, in the earlier discussion was verified.

The same procedure was applied to the other $C_{24}H_{14}D_2$ molecule ("Molecule Two") in the asymmetric unit. The final refinement of the entire structure gave an agreement factor of 7.5% for 9161 unique reflections, $R_1 = 7.9\%$, $wR_2 = 20.0\%$, with all atoms refined anisotropically. Both molecules were determined to be of the same absolute configuration and are shown side-by-side in Figure 5 (see also Table 1).

The verified structure (**III**) for this neutron experiment effectively supports the maintenance of chirality of our sample and therefore eliminates the possibility of a low-energy barrier to inversion of this regiospecifically substituted eight-membered ring.

Synthesis, Resolution, and Optical Activities of Methyltetraphenylenes. In view of the low optical activity of **7** and the elaborate neutron diffraction procedure required for its inves-

(20) Johnson, C. K.; Gabe, E. J.; Taylor, M. R.; Rose, I. A. *J. Am. Chem. Soc.* **1965**, *87*, 1802–1804.

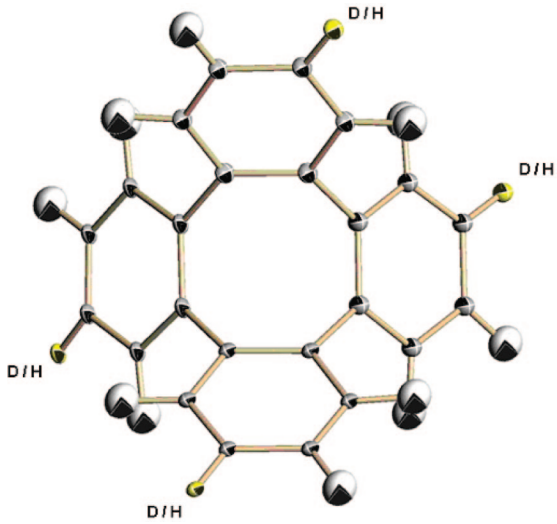


FIGURE 4. ORTEP stereoview of the Molecule One of (*S*)-**7** (neutron results) corresponding to $R_1 = 7.5\%$ with 9161 unique reflections. The C−H and C−(D/H) bond lengths are 1.095 ± 0.006 and 1.095 ± 0.002 Å, respectively. The average C−C−(D/H) angles between neighboring carbons are 120.0 ± 0.9°. The overall result is consistent with structure **III** of Figure 3, with atoms that are labeled D/H being 50% deuterium: 50% hydrogen hybrids. The results are consistent with a molecule whose chirality has been maintained.

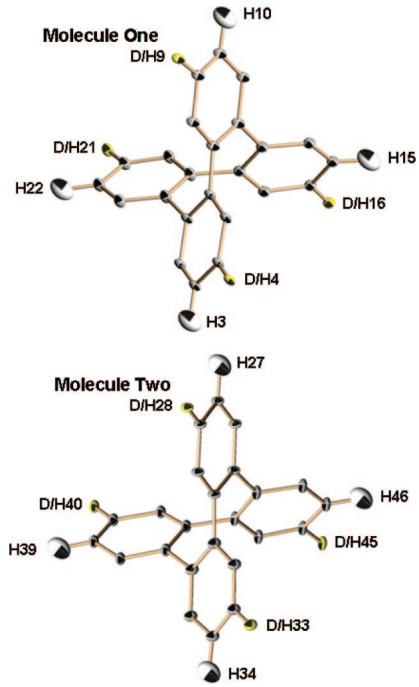


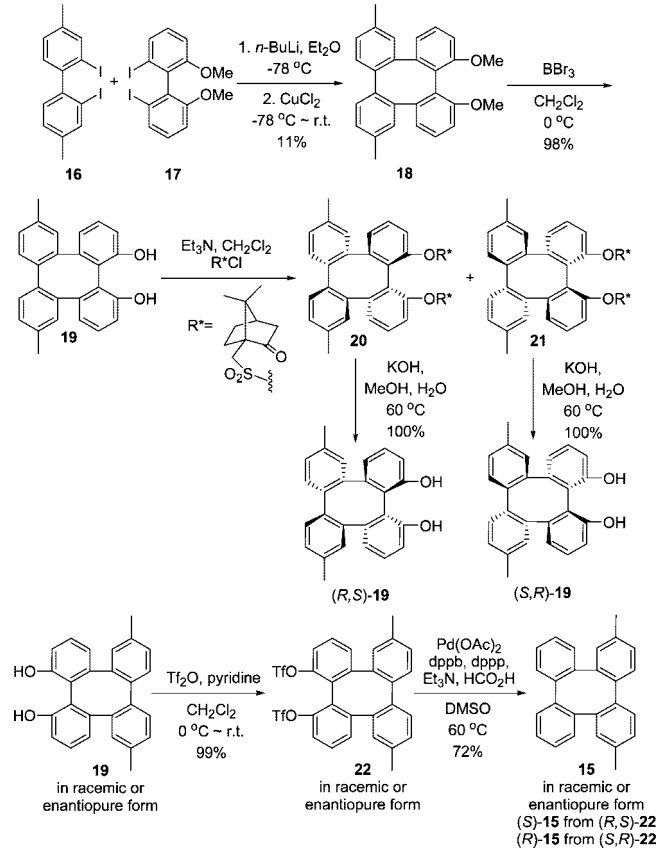
FIGURE 5. Three dimensional rendering of the neutron results from the SXD instrument at ISIS for both Molecule One and Molecule Two in the asymmetric unit of crystals of **7**. Note that the two molecules have retained their intrinsic chirality. The inner hydrogen atoms have been omitted for clarity. The yellow colored atoms represent the 50% D/50% H hybrid atomic positions. Upon close examination, the reader can be convinced that the two molecules have the same chirality and are not mirror images of each other.

tigation; we switched our attention to yet another type of chiral tetraphenylene as a vehicle to examine its inversion barrier. 2,7-Dimethyltetraphenylene (**15**) was chosen as a suitable target for two reasons: the two methyl groups were expected to enhance the chiroptical properties of the system and their non-*peri* locations on the tetraphenylene periphery would not unduly

TABLE 1. Neutron Crystallographic Data for Compound 7

Empirical formula	C24 H14 D2
Formula weight	306.0
Crystal system	Monoclinic
Space group	*C*2
Unit Cell Parameters	$a = 15.423(2)$ Å
	$b = 13.064(3)$ Å
	$c = 16.267(2)$ Å
	$\beta = 100.976(2)°$
Volume	3217.6(8) Å^3
Z	8
Temperature	30(2) K
Crystal size	3.0 × 2.5 × 1.5 mm^3
Wavelength range	0.37−8.80 Å
Min. *d* spacing observed	0.31 Å
No. of refl. collected	32,223
No. of refl. with I > 2σ(1)	9161
No. params. Refined	444
Refinement method	Full-matrix, least -squares on F^2
Final R [I > 2σ(1) data]	$R_1 = 0.075$, $wR_2 = 0.201$

SCHEME 2



impede the attainment of a proposed planar transition state in the ring inversion process. Accordingly, we proceeded to synthesize **15** in the manner as outlined in Scheme 2. A copper(II)-mediated intermolecular cross-coupling approach was adopted in our construction of the central eight-membered ring of this tetraphenylene skeleton.[6a,d,11,21] A mixed solution of diiodides **16**[22] and **17**[23] was treated with *n*-BuLi at −78 °C and 3 equivalents of $CuCl_2$ was subsequently added to furnish a

(21) (a) Rapson, W. S.; Schuttleworth, P. G.; Niekark, J. N. *J. Chem. Soc.* **1943**, 326–327. (b) Rajca, A.; Safronov, A.; Rajca, S.; Schoemaker, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 488–491.

(22) (a) An, B.-K.; Kwon, S.-K.; Jung, S. D.; Park, S.-Y. *J. Am. Chem. Soc.* **2002**, *124*, 14410–14415. (b) Whitesides, G.-M.; Eisenhut, M.; Bunting, W. M. *J. Am. Chem. Soc.* **1974**, *96*, 5398–5407.

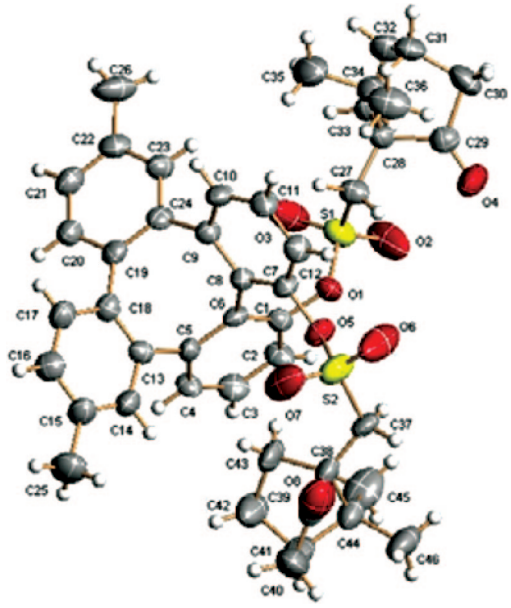


FIGURE 6. ORTEP drawing of **20**.

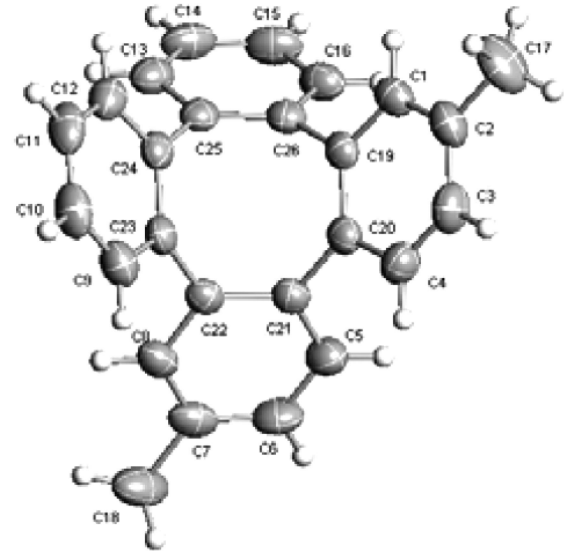


FIGURE 7. ORTEP drawing of **15**.

mixture of inter-, and intramolecular cross-, and self-coupling products from which the desired tetraphenylene **18** was isolated in 11% yield under the optimal lithiation time of 30 min at −78 °C.[24] A molecular ion peak of compound **18** in its ESI mass spectrum was observed at *m*/*z* 415.1656 [M + Na^+], which is in good agreement with the theoretical value of 415.1668 for molecular formula $C_{28}H_{24}O_2Na^+$. The structure of **18** was also supported by comparing its ^{1}H NMR spectrum with that of 1,16-dimethoxytetraphenylene.[6b]

Demethylation of **24** with BBr_3 gave tetraphenylenediol **25** in quantitative yield. Resolution of **25** was effected again by (*S*)-camphorsulfonylation.[6b,d,e] The diastereomeric bis-(*S*)-camphorsulfonates of (±)-**19**, namely, **20** and **21**, were chromatographically separable. With the absolute configuration of the (*S*)-camphorsulfonyl being defined, an X-ray crystallographic analysis of the more polar biscamphorsulfonate **20** therefore led us to confirm the absolute structure of its appended **19** to be of (*R*,*S*)-configuration (Figure 6). In this manner, the absolute stereochemistry of **21** with an appended (*S*,*R*)-**19** was also indirectly deduced. Subsequent desulfonylation of **20** or **21** respectively generated the resolved (*R*,*S*)-**19** or (*S*,*R*)-**19**, each of which having a purity of >99% *ee* as determined by chiral HPLC. Then, following a similar procedure in our synthesis of **7** from **11**, **15** was obtained in both racemic and essentially enantiopure forms.

The structure of **15** was unambiguously confirmed by an X-ray diffraction analysis (Figure 7). The originally highly symmetric D_{2d} point group of tetraphenylene is destroyed by the regiospecifically introduced methyl groups. According to the previous studies on **7**, optical activity of the molecule is expected to be observed on **15** whose central ring inversion barrier should also be high. This was first realized through HPLC on a chiral column (OD column; Hex/*i*-PrOH = 99.3/0.7; 0.7 mL/min; uv, 220 nm) (Figure 8). Compound (*R*)-**15** exhibited a specific rotation of $[\alpha]^{20}_D$: −23 (CH_2Cl_2, *c* = 0.125), which is opposite to that of (*S*)-**15**, $[\alpha]^{20}_D$: +22 (CH_2Cl_2, *c* = 0.125). The CD spectra of (*S*)-**15** and (*R*)-**15** were recorded in methanol (Figure 9). As can be seen, the CD spectrum of (*R*)-**15** showed strong bands at 258(−) nm with a succession of weaker absorption bands at around 286(-) nm. On the other hand, the CD spectrum of (*S*)-**15** showed an antipodal curve, i.e., strong bands at 260(+) nm and weaker bands at 286(+) nm (Figure 9). It is interesting that although the main UV absorption peak of **15** is found at 213 nm, its CD spectrum shows strong signals at regions with longer wavelengths.

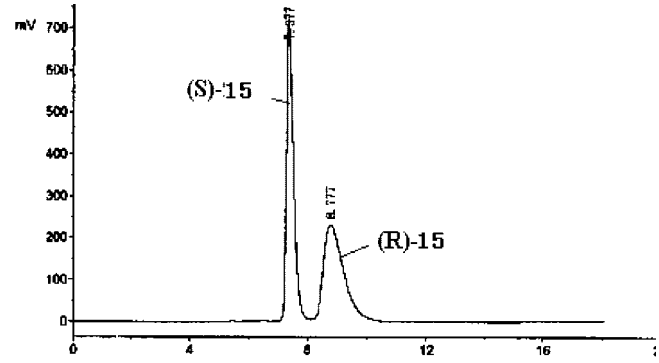


FIGURE 8. Resolution of (±)−**15** through chiral HPLC (OD column; Hex/*i*-PrOH = 99.3/0.7; 0.7 mL/min; UV, 220 nm).

Thermal Study of the Inversion Barrier of the Tetraphenylene Compounds. In light of the strong optical activities as well as its relatively insignificant steric and electronic substituent effects, **15** was taken as a suitable substrate for the inversion barrier investigation. This approach essentially relied on the enantiopurity changes of **15** under different thermokinetic conditions: if the sample is heated to an energy level which is high enough for the flipping to take place, racemization reaction that leads to the loss of *ee*% would be detected. The inversion barrier can therefore be obtained through kinetic deduction of the enantiopurity changes at that temperature.

To our surprise, the (*R*)-**15** sample recovered from heating under argon for 2 h up to 550 °C showed no signs of flipping. Time elongation of the thermal experiment (550 °C, 4 h) or

(23) (a) Baker, W.; Barton, J. W.; McOmie, J. F. W. *J. Chem. Soc.* **1958**, 2658–2663. (b) Cereghetli, M.; Schmid, R.; Schonhner, P.; Rageot, A. *Tetrahedron Lett.* **1996**, *37*, 5343–5346.

(24) (a) Maercker, A.; Theis, M. *Top. Curr. Chem.* **1987**, *138*, 1–61. (b) Bergander, K.; He, R.; Chandrakumar, N.; Eppers, O.; Guenther, H. *Tetrahedron* **1994**, *50*, 5861–5868. (c) Kabir, S. M. H.; Hasegawa, M.; Kuwatani, Y.; Yoshida, M.; Matsuyama, H.; Iyoda, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 159–165. (d) Kabir, S. M. H.; Iyoda, M. *Synthesis* **2000**, 1839–1842.

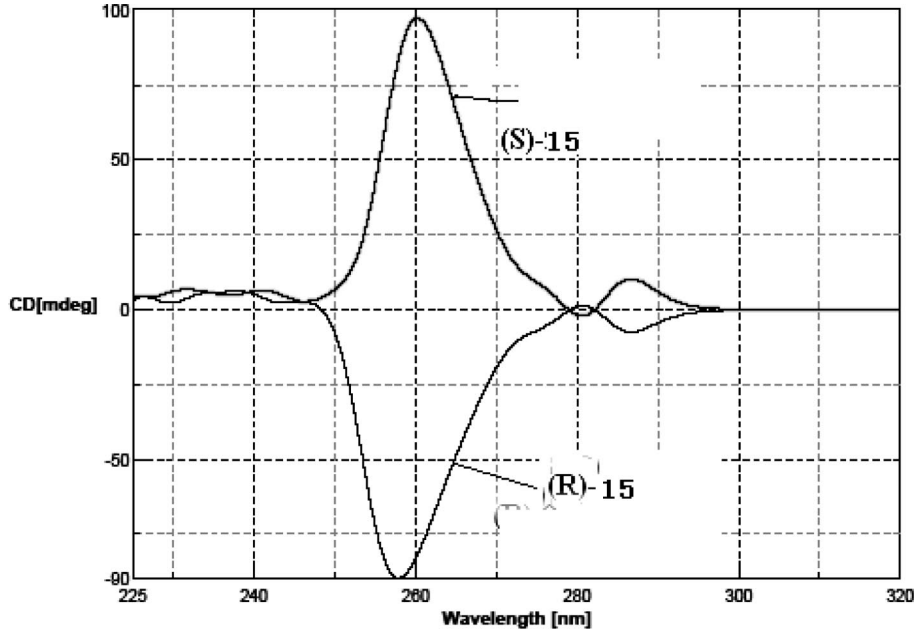


FIGURE 9. CD spectra of (*S*)-**15** and (*R*)-**15** in methanol.

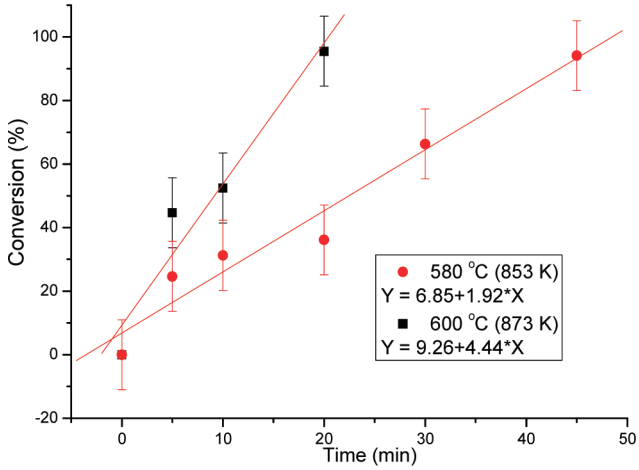


FIGURE 10. Kinetic of decomposition of **15** at 580 and 600 °C.

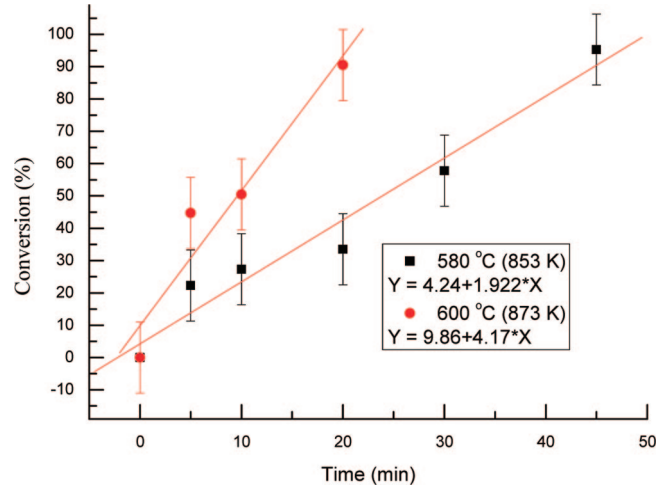


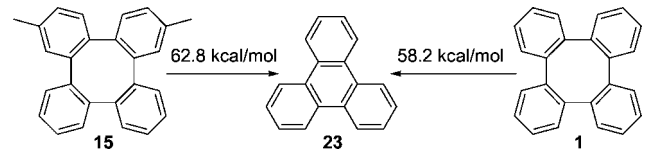
FIGURE 11. Kinetic of decomposition of **1** at 580 and 600 °C.

elevation of the temperature (750 °C, 5 min) also led to no detectable *ee*% change of the recovered starting material even though considerable decomposition of **15** was noted at the latter temperature.

In fact, noticeable decomposition of **15** started to take place at 600 °C giving triphenylene (**23**) as an identifiable product together with some intractable black sheets. To check if this decomposition was caused by the introduction of the methyl groups onto the tetraphenylene skeleton through a relatively weaker sp^2C-sp^3C bond, control experiments were carried out in which deuteriated (*S*)-**7** and substituent-free (all H) tetraphenylene (**1**) were heated to the same temperature. Similar results were observed, and furthermore, upon heating at 600 °C for 30 min, the unscathed (*R*)-**7** exhibited no observable flipping on examination by diffraction method.

It is somewhat astonishing that the inversion barriers of the tetraphenylenes examined are so high that these molecules choose to decompose rather than to flip. Nevertheless, the activation energy (E_a) of their decomposition reactions can be taken as the lower limits of their inversion barriers. Kinetic study of the decompositions of **15** and **1** provided the results shown in Figures 10 and 11. Therefore, the activation energy were finally determined to be E_{a15}= 62.8 kcal/mol and E_{a1}= 58.2 kcal/mol according to the Arrhenius equation[25] (Scheme 3).

SCHEME 3



Computational Study on the Inversion Barriers of the Tetraphenylene and Related Compounds. To have a better understanding of such a prohibitively high inversion barrier, DFT studies have been performed with b3lyp/6−31 g(d,p) basis set on a Gaussian 98 program.[27] After full structural optimization, the energy difference between the saddle shape ground-

(25) Smith, I. W. M. *Chem. Soc. Rev.* **2008**, *37*, 812–826.
(26) (a) Salem, L. *The Molecular Orbital Theory of Conjugated Systems*; Benjamin: New York, 1966; pp 486−491. (b) Englman, R. *The Jahn-Teller Effect in Molecules and Crystals*; Wiley-Interscience: London, 1966; pp 243−245.

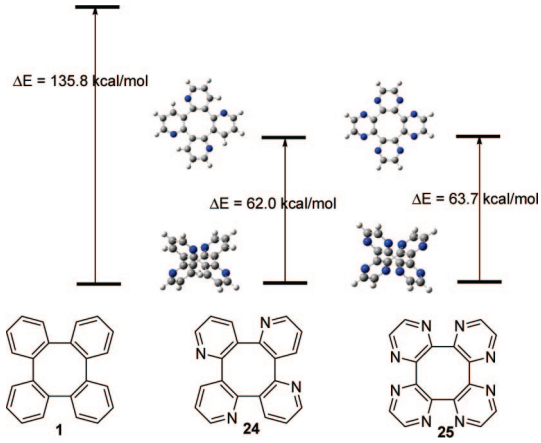


FIGURE 12. Computational energy gaps between the saddle shape ground-state and the planar conformation of **1**, **24**, and **25**.

state of **1** and its planar conformation as the most possible flipping transition state reached to a prohibitively high barrier of 135 kcal/mol. This result is in accordance with the experimental outcome and leads to the conclusion that this planar structure is of extremely high energy.

It is believed that the nonplanarity of **1** was contributed mainly by three factors: a pseudo Jahn−Teller effect originates from unfavorable open-shell triplet arrangement of electrons of the central eight membered ring;[26]increased bond angle strained of the benzene rings in the planar structure and four pairs of H−H nonbonded *peri* effect from the neighboring benzene rings.

The contribution of the pseudo Jahn-Taller effect to the cyclooctatetraene ring has been reported to be at a ∼10 kcal/mol magnitude.[28] However, the latter two factors which are perhaps more important, to the best of our knowledge, have not yet been studied in a quantitative way. Therefore, in order to investigate how severe such H−H interactions are, a *peri* hydrogen free tetra[pyridinzo]cyclooctatetraene (**24**) model was designed and its energy gap was examined in the same manner. This time the energy difference dramatically drops to 63 kcal/mol, less than half of the original tetraphenylene case. A similar result was also obtained on the tetra[pyrazine]cyclooctatetraene (**25**) structure which was designed as a control to eliminate the C−H - nitrogen lone pair nonbonded interaction (Figure 12). These experiments brought a reasonable explanation for the relatively low energy level discovery for cyclooctatetrathiophene (**6**) whose hydrogen repulsions were diminished by smaller thiophene ring size and sulfur substitutions.

Conclusion

In this article, two chiral tetraphenylenes 2,15-bisdeuteriotetraphenylene (**7**) and 2,7-dimethyltetraphenylene (**15**) were synthesized and resolved to address the inversion barrier question. Single crystal neutron diffraction study of **7** essentially eliminates the possibility of a low-energy barrier to inversion of this tetraphenylene molecule.

Thermal studies on **15** and **1** showed that the energy level for the planar transition state structure is too high to be achieved. When the energy supply exceeds a lower limit of 62.8 kcal/mol for **15** or 58.2 kcal/mol for **1**, ring-contraction to triphenylene (**25**) as well as decomposition will take place rather than the flattening of the saddle-shape structure into a planar conformation.

A prohibitively high 135.8 kcal/mol for the planar structure was obtained from computational exercises. This high inversion barrier can be attributed mainly to the *peri*-H repulsions as well as the severe bond angle strain in the planar conformation.

These results also imply that our previously observed racemization of **4** at an energy level of 67 kcal/mol at 600 °C,[10] might be due to some unknown bond cleavage-formation processes instead of flipping through the expected coplanar transition state.

Experimental

1,16-Bis(methoxymethoxy)tetraphenylene (9). To a suspension of NaH (60% in oil, 108 mg, 2.72 mmol) in dry THF (10 mL) and dry DMF (1 mL), 1,16-dihydroxytetraphenylene[6b] (**8**) (100 mg, 0.29 mmol) was added under Ar atmosphere at 0 °C. After stirring for 1 h, chloromethyl methyl ether (1 mL, 8.1 mmol) was added dropwise. The resulting mixture was stirred for additional 8 h and slowly warmed to room temperature. The reaction was quenched with ice water (5 mL), and then THF was removed by evaporation. The residual aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The combined organic phase was washed with brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1: 10) to give 1,16-bis(methoxymethoxy)tetraphenylene (**9**) (105 mg, 83%) as a white solid. mp 104.5−105.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27−7.18 (m, 8H), 7.13−7.10 (m, 2H), 7.01 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.98 (d, J = 6.6 Hz, 2H), 4.87 (d, J = 6.6 Hz, 2H), 3.25 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 143.5, 141.6, 141.5, 128.9, 128.2, 128.0, 127.6, 127.4, 127.2, 123.1, 114.7, 95.4, 55.7; IR (KBr) 2824, 1577, 1458, 1245, 1153, 1003, 754 cm^{-1}; MS(EI) *m*/*z* (relative intensity) 424 (M^+, 11), 348 (70), 320 (77); HRMS: calculated for $C_{28}H_{24}O_4Na^+$ 447.1568; found 447.1566; Anal. calcd for $C_{28}H_{24}O_4$: C, 79.22, H, 5.70; found C, 78.86, H, 6.09.

2,15-Dideuterio-1,16-bis(methoxymethoxy)tetraphenylene (10). To a solution of **9** (81 mg, 0.20 mmol) in anhydrous THF (8 mL), *t*-BuLi (1.6 M solution in hexane, 1.0 mL, 1.6 mmol) was added dropwise under Ar atmosphere at −78 °C. The resulting solution was stirred and slowly warmed to −25 °C over a period of 4.5 h before D_2O (0.5 mL, 25 mmol, 99.8%D) was injected in. The mixture was then allowed to warm to room temperature and stirred overnight. The reaction was quenched with ice water (5 mL), and then THF was evaporated. The residual aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The combined organic phase was washed with brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The crude product was subjected to the above procedure for two additional rounds and was finally purified by column chromatography on silica gel (ethyl acetate/hexane 1:10) to give 2,15-dideuterio-1,16-bis(methoxymethoxy)tetraphenylene (**10**) (56 mg, 68%, >95%D) as a white solid. mp 104−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.10 (m, 10H), 6.84 (d, J = 7.2 Hz, 2H), 4.98 (d, J = 6.6 Hz, 2H), 4.87 (d, J = 6.6 Hz, 2H), 3.25 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.5, 143.4, 141.6, 141.5, 128.9, 128.1, 128.0, 127.5, 127.2, 123.1, 95.3, 55.7; IR (KBr) 3057, 2825, 1565, 1427, 1394, 1379, 1232, 1154, 1000, 756 cm^{-1}; MS(EI) *m*/*z* (relative intensity) 426 (M^+, 9), 322 (65); HRMS calcd for $C_{28}H_{22}D_2O_4Na^+$ 449.1682; found 449.1692.

2,15-Dideuterio-1,16-dihydroxytetraphenylene (11). A mixture of **10** (200 mg, 0.47 mmol) and HCl (3 M, 6 mL, 18mmol) in THF (20 mL) was heated to 60 °C and stirred overnight. THF was

(27) (a) Frisch, M. J.; et al. *Gaussian 98*, revision A.11; Gaussian, Inc.: Pittsburgh, PA, 2001. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284–298. (c) Becke, A. D. *Phys. Rev.* **1988**, *A38*, 3098–3100. (d) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372–1377. (e) Lee, C.; Yang, W.; Parr, R. G. *Phys. ReV.* **1988**, *B37*, 785–789. (d) See the Supporting Information.

removed from the mixture by evaporation and the residual aqueous layer was extracted with ethyl acetate (30 mL × 5). The combined organic phase was washed with brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:3) to give 2,15-dideuterio-1,16-dihydroxytetraphenylene (**11**) (146 mg, 92%) as a white solid. mp >300 °C. ^{1}H NMR (300 MHz, CD_3SOCD_3) δ 7.30−7.22 (m, 8H), 7.12−7.10 (m, 2H), 6.85 (d, J = 7.2 Hz, 2H), 4.90 (s, 2H); ^{13}C NMR (75 MHz, CD_3COCD_3) δ 143.9, 142.1, 141.5, 128.6, 128.2, 128.0, 127.4, 127.2, 127.1, 127.0, 126.5, 120.4; IR (KBr) 3499, 3063, 1566, 1426, 1402, 1323, 1187, 1175, 1094, 757, 749, 676 cm^{-1}; MS (EI) *m/z* (relative intensity) 372 (M^+, 100); HRMS cald for $C_{24}H_{14}D_2O_2H^+$ 339.1360; found 339.1349.

(*R*)-(+)-2,15-Dideuterio-1,16-bis[(*S*)-camphorsulfonyloxy]tetraphenylene (12) and (*S*)-(+)- 2,15-Dideuterio-1,16-bis[(*S*)-camphorsulfonyloxy]tetraphenylene (13). To a solution of (±)-**11** (150 mg, 0.447 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.95 g, 2.30 mmol) in CH_2Cl_2 (15 mL) was added dropwise triethylamine (1.0 mL, 7.15 mmol) at 0 °C. The resulting mixture was stirred for 24 h at room temperature until TLC indicated complete consumption of (±)-**11**. Water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (20 mL × 3). The combined extracts were washed with HCl (1M, 20 mL × 2), brine (30 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:6) to give the diastereomers.

The more polar diastereomer was **12** (124 mg 36%). mp >300 °C. $[\alpha]^{20}_D$: + 13.2 (CH_2Cl_2, c = 0.85); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.12 (m,12H), 3.52 (d, J = 15 Hz, 2H), 2.80 (d, J = 15.1 Hz, 2H), 2.37 (d, J = 18 Hz, 2H), 2.40−1.88 (m, 8H), 1.64−1.55 (m, 2H), 1.45−1.36 (m, 2H), 0.97 (s, 6H), 0.79 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5, 145.9, 145.0, 140.9, 139.8, 129.1, 129.0, 128.2, 127.9, 127.8, 127.7, 127.4, 57.9, 48.9, 47.8, 42.9, 42.4, 26.8, 24.8, 19.7, 19.5; IR (KBr) 3387, 2961, 1748, 1529, 1360, 1168, 909, 761 cm^{-1}; MS (ESI) *m/z* 789 (MNa^+); HRMS calcd for $C_{44}H_{42}D_2O_8S_2Na^+$ 789.2459; found 789.2497.

The less polar diastereomer was **13** (127 mg 37%). mp 236.5−238.0 °C; $[\alpha]^{20}_D$: + 16.3 (CH_2Cl_2, c = 0.55); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38- 7.26 (m, 8H), 7.16−7.11 (m, 4H), 3.18 (d, J = 15.3 Hz, 2H), 2.99 (d, J = 15.0 Hz, 2H), 2.41−2.31 (m, 4H), 2.10−1.90 (m, 4H), 1.61−1.38 (m, 4H), 1.07 (s, 6H), 0.83 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9, 145.0, 140.9, 139.7, 129.3, 129.1, 128.9, 128.3, 128.2, 127.9, 127.4, 57.9, 48.7, 48.0, 42.7, 42.4, 26.9, 24.9, 19.8, 19.6; IR (KBr) 2963, 2927, 1747, 1618, 1373, 1168, 912, 761 cm^{-1}; MS (ESI) *m/z* 789 (MNa^+); HRMS calcd for $C_{44}H_{42}D_2O_8S_2Na^+$ 789.2495, found 789.2493; Anal. calcd for $C_{44}H_{42}D_2O_8S_2$+1/2EtOAc C, 68.12; H, 6.21; found C, 67.66; H, 5.89.

(*R*)-2,15-Dideuterio-1,16-dihydroxytetraphenylene, (*R*)-11, and (*S*)-2,15-Dideuterio-1,16-dihydroxytetraphenylene, (*S*)-11. To a suspension of **12** (112 mg, 0.14 mmol) in methanol (20 mL) was added aqueous solution of KOH (2M, 5 mL, 10 mmol). The resulting mixture was warmed to 60 °C until a clear yellow solution was obtained and TLC indicated the completion of reaction. After the solution was cooled to room temperature, it was acidified with HCl (3M, 10 mL, 30 mmol), and excess methanol was removed from the mixture by evaporation. The residual aqueous layer was extracted with ethyl acetate (30 mL × 4). The combined organic phase was washed with sodium bicarbonate (20 mL × 2) and brine (30 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:2), giving (*R*)-**11** (46.7 mg, 97%) as a white solid, with a purity of 99.1% *ee* as determined by chiral HPLC. The spectroscopic data of (*R*)-**11** were identical to those of (±)-**11**. $[\alpha]^{20}_D$: −58.0 (CH_2Cl_2, c = 0.315).

(*S*)-**11** was prepared according to the same procedure as that for **13** (97%). $[\alpha]^{20}_D$: +62.3 (CH_2Cl_2, c = 0.315).

2,15-Dideuterio-1,16-bis(trifluoromethanesulfonyloxy)tetraphenylene (14). To a suspension of (±)-**11** (28 mg, 0.083 mmol) in dry CH_2Cl_2 (5 mL) was added pyridine (0.1 mL, 1.2 mmol) and then trifluoromethanesulfonic anhydride (0.11 mL, 0.67 mmol) at 0 °C. After the addition, the reaction mixture was stirred for 24 h at ambient temperature. When TLC indicated the reaction was completed, water (5 mL) was added carefully. The mixture was extracted with CH_2Cl_2 (15 mL × 3). The combined organic layer was washed with HCl (1M, 10 mL) and brine (20 mL × 2), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:50) to give (±)-**14** (59 mg, 99%) as a white solid. mp 235 °C (sublimed). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.1 Hz, 2H), 7.36∼7.23 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 145.7, 140.7, 138.8, 130.3, 129.8, 129.6, 129.1, 128.3, 127.8, 127.4, 120.3, 116.0; IR (KBr) 1425, 1217, 1142, 1077, 915, 803, 761, 604 cm^{-1}; MS (ESI) *m/z* 625 (M + Na^+), 641 (M + K^+), 657 (M + MeOH + Na^+); HRMS calcd for $C_{26}H_{12}D_2F_6O_6S_2Na^+$ 625.0156; found 625.0153.

(*R*)-**14** was prepared according to the same procedure as that for (*R*)-**11** (99%). $[\alpha]^{20}_D$: −87.1(CH_2Cl_2, c = 0.92).

(*S*)-**14** was prepared according to the same procedure as that for (*S*)-**11** (99%). $[\alpha]^{20}_D$: +83.3(CH_2Cl_2, c = 0.92).

2,15-Dideuteriotetraphenylene (7). To a mixture of (±)-**14** (30 mg, 0.05 mmol), $Pd(OAc)_2$ (8 mg, 0.035 mmol), and dppb (35 mg, 0.08 mmol), dppp (50 mg, 0.12 mmol) were added dry DMSO (10 mL) and Et_3N (0.2 mL). The mixture was stirred at 0 °C for 0.5 h before anhydrous formic acid was injected in. After being stirred at 100 °C for 24 h, the reaction was quenched with ice water (350 mL), and the residual aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The combined organic phase was washed with brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (hexane) to give 2,15-dideuteriotetraphenylene (**7**) (10.8 mg, 72%) as a white solid. mp 251.5−253 °C. $[\alpha]^{20}_D$: −4 (CH_2Cl_2, c = 0.255); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J = 6.3 Hz, 6H), 7.16 (d, J = 7.2 Hz, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 129.6, 128.0; IR (KBr) 3060, 3014, 1485, 1461, 1436, 1214, 1007, 847, 766, 752, 655, 549, 470 cm^{-1}; MS (EI) *m/z* (relative intensity) 306 (M^+,100); HRMS calculated for $C_{24}H_{14}D_2^+$ 306.1378; found 306.1383.

(*R*)-**7** was prepared according to the same procedure as that for (*R*)-**14** (99%). $[\alpha]^{20}_D$: −4 (CH_2Cl_2, c = 0.255);

(*S*)-**7** was prepared according to the same procedure as that for (*S*)-**14** (99%). $[\alpha]^{20}_D$: −2 (CH_2Cl_2, c = 0.275).

1,16-Dimethoxy-6,11-dimethyltetraphenylene (18). To a suspension of 2,2′-diiodo-4,4′-dimethylbiphenyl (**16**)[22] (174 mg, 0.40 mmol) and 2,2′-dimethoxy-6,6′-diiodobipheny (**17**)[23] (186 mg 0.40 mmol) in Et_2O (30 mL) was added dropwise *n*-BuLi (0.8 mL, 2.5 M in hexane, 2 mmol), at −78 °C. After stirring for 30 min at −78 °C, $CuCl_2$ (376 mg, 2.78 mmol) was added. After stirring for 4 h at −78 °C, the reaction mixture was allowed to warm to ambient temperature overnight. The resulting solution with some precipitate was quenched with NH_3•H_2O (2M, 15 mL), and the residual aqueous layer was extracted with CH_2Cl_2 (30 mL × 4). The combined organic phase was washed with $NaHSO_3$ (2M, 30 mL), brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (CH_2Cl_2/ethyl acetate/hexane 1:1:6) to give 1,16-dimethoxy-6,11-dimethyltetraphenylene (**18**) (17 mg, 11%) as a white solid, mp 176−177 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (t, J = 7.8 Hz, 2H), 7.05−6.97 (m, 6H), 6.79 (ddd, J = 13.5, 8.3, 0.6 Hz, 4H), 3.68 (s, 6H), 2.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 143.4, 141.5, 138.5, 136.4, 128.9, 128.7, 128.0, 127.8, 126.1, 121.8, 109.8, 56.1, 21.0; IR (KBr) 2930, 2833, 1577, 1461, 1431, 1257, 1097, 1039, 819, 789, 738 cm^{-1}; MS (ESI) *m/z* (relative intensity) 392 (M^+, 56); HRMS calcd for $C_{28}H_{24}O_2Na^+$ 415.1668; found 415.1656.

1,16-Dihydroxy-6,11-dimethyltetraphenylene (19). To a suspension of 1,16-dimethoxy-6,11-dimethyltetraphenylene (**18**) (182 mg, 0.5 mmol) in CH_2Cl_2 (20 mL) was added dropwise BBr_3 (4 mL, 1 M solution in CH_2Cl_2, 4 mmol) at 0 °C. The mixture was stirred overnight at room temperature and a clear brownish red solution was obtained. The reaction mixture was quenched with ice water (10 mL), and a white solid precipitated which was dissolved by the addition of ethyl acetate (25 mL). The organic layer was separated and the residual aqueous layer was extracted with ethyl acetate (30 mL × 4). The combined organic phase was washed with $NaHCO_3$ (2M, 30 mL), brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:3) to give 1,16-dihydroxy-6,11-dimethyltetraphenylene (**19**) (164 mg, 97%) as a white solid, mp 222−223 °C. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 7.24 (dd, J = 4.8, 1.2 Hz, 2H), 7.06−6.95 (m, 4H), 6.85 (dd, J = 15.6, 7.5 Hz, 4H), 4.97 (s, 2H), 2.31 (s, 6H); ^{13}C NMR (75 MHz, CD_3COCD_3) δ 154.6, 144.6, 142.6, 139.2, 136.8, 129.3, 129.2, 128.5, 128.2, 124.2, 120.9, 114.6, 20.6; IR (KBr) 3499, 3921, 1573, 1442, 1305, 1279, 1208, 1180, 841, 796 cm^{-1}; MS (EI) *m/z* (relative intensity) 364 (M^+, 100); HRMS calcd for $C_{26}H_{20}O_2Na^+$ 387.1354; found 387.1355; Anal. calcd for $C_{26}H_{20}O_2$+1/2EtOAc C, 82.33; H, 5.92; found C, 82.39; H, 6.08.

(*R*)-(+)-6,11-Dimethyl-1,16-bis[(*S*)-camphorsulfonyloxy]tetraphenylene (20) and (*S*)-(+)- 6,11-Dimethyl-1,16-bis[(*S*)-camphorsulfonyloxy]tetraphenylene (21). To a solution of (±)-1,16-dihydroxy-6,11-dimethyltetraphenylene (**19**) (75 mg 0.225 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.6 g, 2.3 mmol) in THF (8 mL) was added dropwise triethylamine (0.4 mL, 2.86 mmol) at 0 °C. The resulting mixture was stirred for 24 h at room temperature until TLC indicated complete consumption of the starting material. The reaction was quenched with ice water (5 mL), and then THF was evaporated. The residual aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The combined organic phase was washed with brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:8) to give the two diastereomers **20** and **21**. Single crystal of the more polar bissulfonate **20** was grown from ethyl acetate and its absolute configuration was determined on the basis of an X-ray diffraction analysis.

The more polar diasteromer was **20** (124 mg, 36%), mp 235−235.5 °C. $[\alpha]^{20}_D$: + 7.4 (CH_2Cl_2, c = 1.265); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.12 (m, 12H), 3.53 (d, J = 15 Hz, 2H), 2.80 (d, J = 15.1 Hz, 2H), 2.42−2.33 (m, 2H), 2.21−1.89(m, 6H), 1.65−1.55 (m, 8H), 1.45−1.36 (m, 2H), 0.98 (s, 6H), 0.79 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6, 145.9, 145.1, 139.5, 137.9, 136.6, 129.5, 129.0, 128.9, 128.5, 127.7, 127.6, 119.6, 57.7, 48.7, 47.7, 42.7, 42.2, 29.6, 26.7, 24.6, 21.0, 19.6, 19.4; IR (KBr) 2958, 2924, 1747, 1571, 1438, 1365, 1224, 1166, 945, 837, 502 cm^{-1}; MS (ESI) *m/z* (relative intensity) 793 (MH^+); HRMS calcd for $C_{46}H_{48}O_8S_2Na^+$ 815.2682; found 815.2682; Anal. calcd for $C_{46}H_{48}O_8S_2$ C, 61.80; H, 5.52; found C, 61.53; H, 5.88.

The less polar diastereomer was **21** (126.7 mg 37%), mp 109−111 °C. $[\alpha]^{20}_D$: + 35.6 (CH_2Cl_2, c = 0.675); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.26 (m, 4H), 7.16−7.07 (m, 6H), 6.99 (d, J = 8.1 Hz, 2H), 3.22 (d, J = 15.3 Hz, 2H), 2.99 (d, J = 15.0 Hz, 2H), 2.41−2.31 (m, 10H), 2.10−1.90 (m, 6H), 1.61−1.38 (m, 4H), 1.09 (s, 6H), 0.84 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.7, 145.8, 145.1, 142.1, 139.4, 137.8, 136.6, 129.8, 128.9, 128.6, 128.4, 128.0, 127.9, 120.3, 57.8, 48.5, 47.7, 42.6, 42.2, 26.7, 24.8, 20.9, 19.6, 19.4; IR (KBr) 2961, 2924, 1750, 1364, 1176, 1162, 946, 859, 839, 741, 577, 521 cm^{-1}; MS (ESI) *m/z* 793 (MH^+); HRMS calcd for $C_{46}H_{48}O_8S_2Na^+$ 815.2682; found 815.2673; Anal. calcd for $C_{46}H_{48}O_8S_2$+1/2EtOAc C, 68.87; H, 6.26; found C, 68.87; H, 5.86.

(*R*,*S*)-1,16-Dihydroxy-6,11-dimethyltetraphenylene, (*R*,*S*)-19, and (*S*,*R*)-1,16-Dihydroxy-6,11-dimethyltetraphenylene, (*S*,*R*)-19. To a suspension of **20** or **21** (160 mg, 0.2 mmol) in methanol (20 mL) was added aqueous solution of KOH (2M, 5 mL, 10 mmol). The resulting mixture was warmed to 60 °C until a clear yellow solution was obtained and TLC indicated the completion of reaction. After the solution was cooled to room temperature, it was acidified with 3N HCl (10 mL), and excess methanol was removed from the mixture by evaporation. The residual aqueous layer was extracted with ethyl acetate (30 mL × 4). The combined organic phase was washed with sodium bicarbonate (20 mL × 2) and brine (30 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/hexane 1:2), giving (*R*,*S*)−**19** or (*S*,*R*)−**19** (70.6 mg, 97%) as a white solid, with a purity of >99% *ee* as determined by chiral HPLC. The spectroscopic data of (*R*,*S*)−**19** or (*S*,*R*)−**19** were identical to those of (±)-**19**. (*R*,*S*)- **19** $[\alpha]^{20}_D$: −57.4 (CH_2Cl_2, c = 0.50), or (*S*,*R*)−**19** $[\alpha]^{20}_D$: +55.1 (CH_2Cl_2, c = 0.50).

6,11-Dimethyl-1,16-bis(trifluoromethanesulfonyloxy)tetraphenylene (22). To a suspension of (±)-1,16-dihydroxy-6,11-dimethyltetraphenylene (**19**) (36 mg, 0.099 mmol) in dry CH_2Cl_2 (5 mL) was added pyridine (0.1 mL, 1.2 mmol) and then trifluoromethanesulfonic anhydride (0.11 mL, 0.67 mmol) at 0 °C. After the addition, the reaction mixture was stirred for 24 h at ambient temperature until TLC indicated complete consumption of the starting material. The reaction was quenched with ice water (5 mL), and the residual aqueous layer was extracted with CH_2Cl_2 (15 mL × 3). The combined organic layer was washed with HCl (1M, 10 mL) and brine (20 mL × 2), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (CH_2Cl_2/hexane 1:3) to give **22** as a white solid, mp 147−148 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (t, J = 7.8 Hz, 2H), 7.26 (t, J = 7.8 Hz, 4H), 7.12 (d, J = 7.8 Hz, 2H), 7.05−7.01 (m, 4H), 2.34 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0, 138.8, 137.8, 137.0, 130.2, 129.8, 129.0, 127.8, 120.0, 21.0; IR (KBr) 1556, 1459, 1427, 1407, 1212, 1138, 1011, 953, 888, 825, 761, 610, 516 cm^{-1}; MS (ESI) *m/z* 646 ($M + H_2O^+$).

The (*S*,*R*)-**22** or (*R*,*S*)-**22** was synthesized through a similar method as that for (*S*,*R*)-**19** or (*R*,*S*)-**19** respectively, the spectroscopic data of (*S*,*R*)-**22** or (*R*,*S*)-**22** were identical to those of (±)-**22**. (*S*,*R*)-**22** $[\alpha]^{20}_D$: +43.3 (CH_2Cl_2, c = 0.47), (*R*,*S*)-**22** $[\alpha]^{20}_D$: −48.1 (CH_2Cl_2, c = 0.42).

2,7-Dimethyltetraphenylene (15). To a mixture of (±)-**22** (189 mg, 0.3 mmol), $Pd(OAc)_2$ (100 mg, 0.44 mmol), and dppb (70 mg, 0.16 mmol), dppp (100 mg, 0.24 mmol) were added dry DMSO (20 mL) and Et_3N (0.4 mL). The mixture was stirred at 0 °C for 0.5 h before anhydrous formic acid (0.4 mL) was injected in. After being stirred at 60 °C for 24 h, the reaction was quenched with ice water (15 mL), and the residual aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The combined organic phase was washed with brine (20 mL × 4), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (hexane) to give 2,7-dimethyltetraphenylene (**15**) (10.8 mg, 72%) as a white solid. mp 228 °C (sublimed). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29−7.24 (m, 4H), 7.15 (dd, J = 7.2, 2.4 Hz, 4H), 7.04 (t, J = 7.5 Hz, 4H), 6.97 (s, 2H), 2.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 141.6, 141.4, 138.6, 136.6, 129.8, 129.1, 129.0, 128.0, 127.1, 127.0, 21.0; IR (KBr) 3011, 2921, 2851, 1612, 1471, 1435, 1045, 815, 776, 761, 744, 562, 467 cm^{-1}; MS (EI) *m/z* (relative intensity) 332 (M^+,100); Anal. Calcd for $C_{26}H_{20}$ C, 93.94; H, 6.06; found C, 93.81; H, 6.19.

Compounds (*R*)-**15** or (*S*)-**15** were synthesized through a similar method as that for (*S*,*R*)-**22** or (*R*,*S*)-**22** respectively, the spectroscopic data of (*R*)-**15** or (*S*)-**15** were identical to those of (±)-**15**. (*R*)-**15** $[\alpha]^{20}_D$: +22 (CH_2Cl_2, c = 0.125), (*S*)-**15** $[\alpha]^{20}_D$: −23 (CH_2Cl_2, c = 0.125).

General Procedure for the Racemization and Decomposition Experiments on the Tetraphenylenes. Tetraphenylene samples (~50 mg) were placed in short quartz capillaries, which were flame-sealed under argon and then heated for 2 h at 300, 400, 500 or 550

°C in preheated ovens, respectively. The black residue at the bottom of the tube was extracted with CH_2Cl_2 (10 mL × 3). The combined extracts were filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (CH_2Cl_2/hexane 1:40) to give the recovered tetraphenylenes.

HPLC-spectrum indicated (*R*)−**15** with unchanged *ee* within experimental error (±5%, for the near 100% *ee* samples) was recovered under all these circumstances. For all tetraphenylene samples, elongation of the thermal experimental time at 600 °C to 12 h resulted in the complete disappearance of the starting material and the formation of triphenylene (**23**) as a white solid, mp 196 °C.[29] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (dd, J = 6.0, 3.0 Hz, 6H), 7.67 (t, J = 6.0, 3.0 Hz, 6H); MS (EI) m/z 228(M^+).

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Supporting Information Available: Computation results and X-ray and neutron crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) Anet, F. A. L.; Bourn, A. J. R.; Lin, Y. S. *J. Am. Chem. Soc.* **1964**, *86*, 3576–3577.

(29) Zimmerman, H. E.; Hull, V. H. *J. Am. Chem. Soc.* **1970**, *92*, 6515–6520.