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Synthesis and Chiroptical Properties of Double-Helical (*M*)- and (*P*)-*o*-Oligophenylenes

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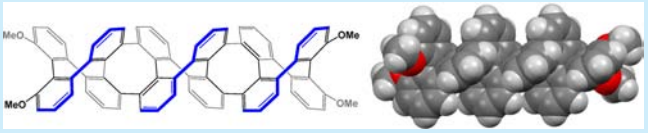
Supporting Information

ABSTRACT: All of the *M* and *P* isomers of optically pure oligophenylenes with 6, 8, 10, and 12 phenyl rings were synthesized and fully characterized. The Suzuki cross-coupling reaction has been revealed to be a viable strategy in the syntheses of tetraphenylene derivatives, which, together with the copper-mediated oxidative cross-coupling reaction, were employed in the quest for the oligophenylenes. X-ray diffraction analysis in combination with specific rotation and circular dichroism spectroscopy unambiguously identified the unique covalent double-helical frameworks of these oligophenylene molecules.



Synthetic endeavors on helical architectures have always been an intensive research area to date because helical structures are important structural motifs of biomacromolecules in nature.[1] For example, double-helical DNA (**1**) efficiently preserves, replicates, and translates genetic information (Figure 1). Inspired by these elegant biological helices, chemists are striving to construct artificial double-stranded helical structures in the form of oligomers (foldamers) and polymers.[2] These helical turns are often stabilized through hydrogen bonds, metal cations, disulfide linkages, and hydrophobic interactions.[2,3] In particular, a sequence of *ortho*-annulations of arylenes via rigid carbon−carbon bonds can provide oligophenylenes **2** with double-helical π systems (Figure 1).[4] Rajca pioneered the synthesis of octaphenylene in 1997 by annulation of two tetraphenylene fragments bearing *tert*-butyl substituents. As a result, a racemic double-helical hydrocarbon was obtained in 4% yield.[5] Subsequently, Marsella constructed racemic conjugated octaaryl double-helical oligomers that utilized achiral cyclooctatetrathiophene as building blocks.[6] Recently, Wang and Negri reported oligoperylenebisimides as nanoribbons via a copper-mediated Ullmann coupling reaction. Their dimers and trimers in enantiomerically pure forms were also obtained by employing a chiral HPLC separation protocol.[7]

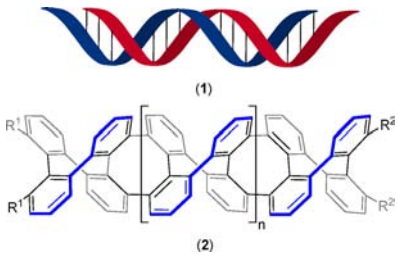


Figure 1. Double-helical DNA (**1**) and the helical structure of oligophenylenes **2**.

Annulated arylenes in short chains, such as tetraphenylene in both achiral and chiral versions, are well-documented.[8,9] However, there are very few preparations of chiral oligomers of tetraphenylene in the form of an extended helical backbone. More importantly, studies on the structures and chiroptical properties of extended helical oligophenylenes are highly desirable. In continuation of our program to develop helical structures utilizing the structural motif of tetraphenylene,[8a] herein we report the synthesis, structures, and chiroptical properties of a series of double-helical oligomers consisting of *ortho*-linked tetraphenylenes bridged by covalent carbon−carbon bonds (note: the synthesis of only one enantiomer is reported in this article, while the synthesis of both enantiomers is described in the Supporting Information (SI)).

Recently, an intermolecular double Suzuki reaction was initially attempted in our laboratory.[10] We therefore considered the synthesis of tetraphenylene derivatives and chiral oligophenylenes by employing double Suzuki cross-coupling reactions.[9a] Diborate (±)-**3** was synthesized from dimethoxy-substituted diiodobiphenyl in 50% yield over two steps (see the SI). 2,2′-Dibromo-6,6′-diiodo-1,1′-biphenyl (**4**) was prepared

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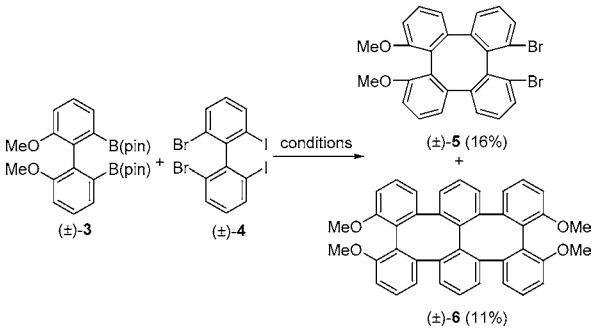
from 2,2′,6,6′-tetrabromo-1,1′-biphenyl according to a reported method.[11] As shown in Scheme 1, the double Suzuki coupling

Scheme 1. Preparation of Tetraphenylene (±)-5 and Oligophenylene (±)-6[a]

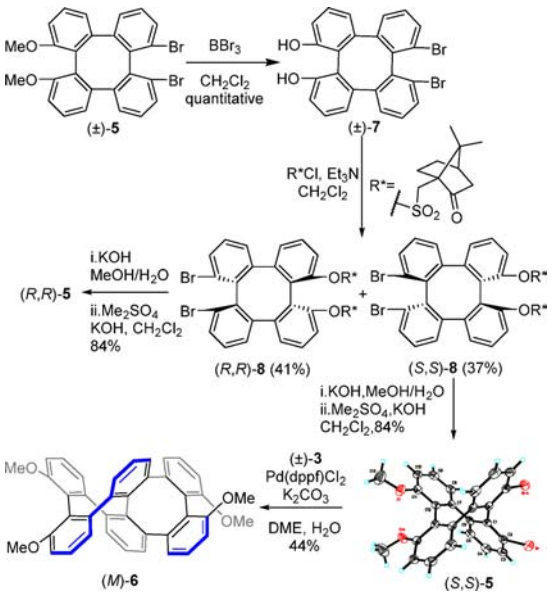


[a]Conditions: $Pd(dppf)Cl_2$ (10 mol %), aq. K_2CO_3 (2.6 M), dimethoxyethane, reflux, 12 h.

reaction of diborate (±)-**3** with (±)-**4** was then performed in the presence of catalytic $Pd(dppf)Cl_2$ in dimethoxyethane (DME) as the solvent, leading to the formation of tetraphenylene (±)-**5** in 16% yield. Interestingly, compound (±)-**6** bearing six phenyl rings, one of our target molecules, was isolated in 11% yield (Scheme 1).

Our next objective was the synthesis of optically pure **6**. As shown in Scheme 2, (*S*,*S*)-**5** and (*R*,*R*)-**5** were obtained from

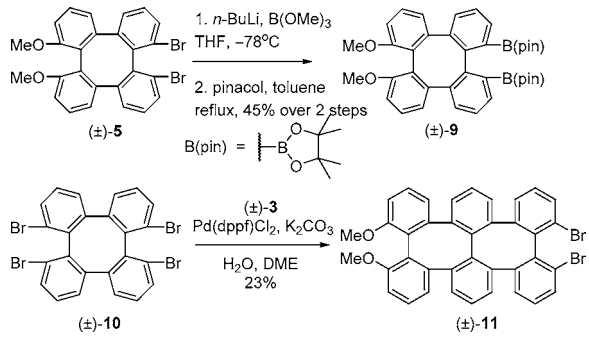
Scheme 2. Preparation of (*S*,*S*)-5, (*R*,*R*)-5, and (*M*)-6



(±)-**5** via a camphorsulfonylation-chromatographic separation-hydrolysis protocol.[12] The absolute configuration of (*S*,*S*)-**5** was established by an X-ray crystallographic analysis. Dibromide (*S*,*S*)-**5** then underwent the double Suzuki coupling with diborate (±)-**3** to form enantiopure (*M*)-**6** in 44% yield. (*P*)-**6** was also synthesized from (*R*,*R*)-**5** in a similar aforementioned transformation. To be utilized the optical rotation studies, the absolute configurations of (*M*)- and (*P*)-**6** were unambiguously confirmed by an X-ray crystallographic analysis of the relevant enantiopure tetrakis(camphosulfonyl)-oligophenylene (see the SI).

Encouraged by the success of the aforementioned double Suzuki coupling reaction, we then expected to apply this protocol to the synthesis of oligophenylenes with more than eight phenyl rings. Tetraphenylene diborate (±)-**9** was obtained from (±)-**5** in 45% yield over two steps as shown in Scheme 3. Unfortunately, Suzuki coupling of (±)-**9** and

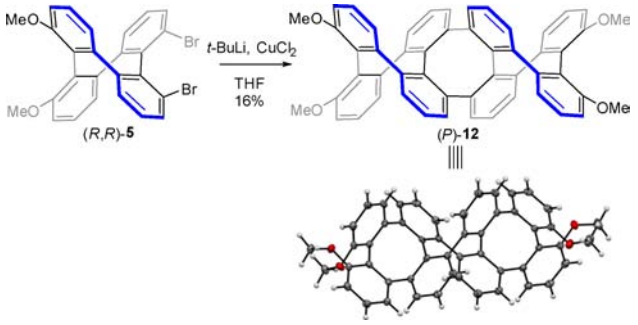
Scheme 3. Preparation of (±)-9 and (±)-11



(±)-**5** failed to provide our desired oligophenylene with eight phenyl rings, presumably because of the steric hindrance of (±)-**9**, which was also supported by the failed Suzuki coupling between (±)-**9** and (±)-**4**. However, Suzuki coupling of less hindered biphenyl diborate (±)-**3** and 1,8,9,16-tetrabromotetraphenylene ((±)-**10**) smoothly afforded the pivotal oligophenylene (±)-**11** in 23% yield (Scheme 3). Therefore, tetraphenylene borate **9** is not an appropriate precursor in the synthesis of longer oligophenylenes via our double Suzuki coupling protocol.

After many attempts to synthesize longer oligophenylenes, the Cu(II)-mediated oxidative coupling reaction was proven to be a better alternative approach. Thus, treatment of (*R*,*R*)-**5** with *t*-BuLi led to a double Li/Br exchange, and then addition of anhydrous $CuCl_2$ at −78 °C provided the corresponding oxidative coupling product (*P*)-**12** in 16% yield (Scheme 4).

Scheme 4. Preparation of (*P*)-12



The enantiomer of (*M*)-**12** was also prepared in a similar manner. Gratifyingly, the structure of (*P*)-**12** was unambiguously confirmed by X-ray crystallographic analysis. As shown in Scheme 4, the eight phenyl rings were cross-linked at the *ortho* positions, forming a rigid helical structure featuring three central eight-membered rings.

Next, we turned to the synthesis of longer double-helical oligophenylenes. Both enantiopure (*P*)- and (*M*)-**11** were eventually obtained via resolution of (±)-**11** using a protocol similar to the aforementioned one (Scheme 2) in 33% and 31% yield, respectively. As shown in Scheme 5, treatment of (*S*,*S*)-**5**

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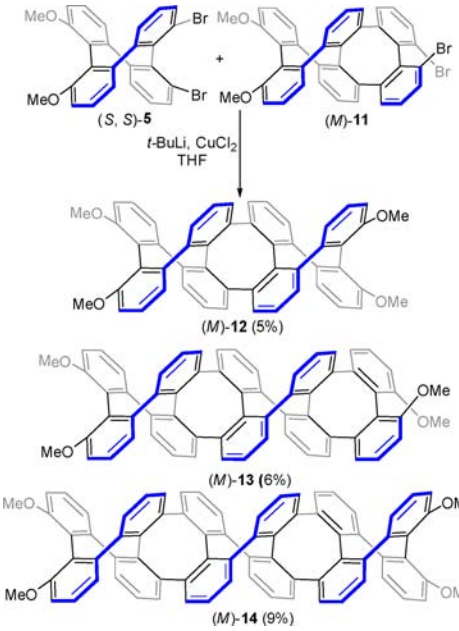
Scheme 5. Preparation of Oligophenylenes (*M*)-12, (*M*)-13, and (*M*)-14



and (*M*)-**11** with *t*-BuLi resulted in copper-mediated oxidative coupling, leading to the formation of (*M*)-**12**, (*M*)-**13**, and (*M*)-**14** in 5%, 6%, and 9% isolated yield, respectively. After many trials, a single crystal of (*M*)-**14** was eventually obtained from a solvent mixture of chloroform and hexane. The molecular structure of (*M*)-**14** was then determined by X-ray crystallographic analysis (Figure 2 top). The space-filling model

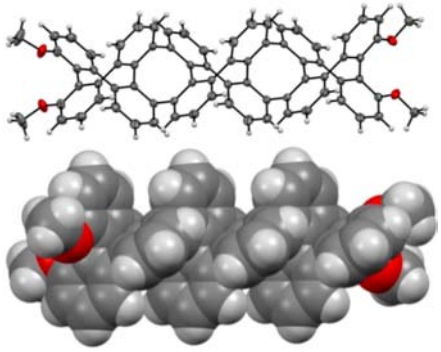


Figure 2. X-ray-derived ORTEP drawing and space-filling model of (*M*)-**14**.

based on the X-ray crystallographic data (Figure 2 bottom) clearly suggests the double-helical structure. In a similar manner, all of the enantiomers, i.e., (*P*)-**12**, (*P*)-**13**, and (*P*)-**14** were also prepared in 12%, 9% and 12% isolated yield, respectively. Thus, all of the enantiomers of oligophenylenes **6**, **12**, **13**, and **14** were prepared. The solution ^{1}H and ^{13}C NMR data are consistent with double-helicene structures. All of the compounds are remarkably stable with melting ranges above 250 °C, and crystalline samples of these compounds are stable at room temperature for months without protection from air and light.

As can be seen in Figure 3, both oligophenylenes (*P*)-**12** and (*M*)-**14** crystallized in the orthorhombic space group $C222_1$. With a twofold screw axis passing through the molecule of (*M*)-

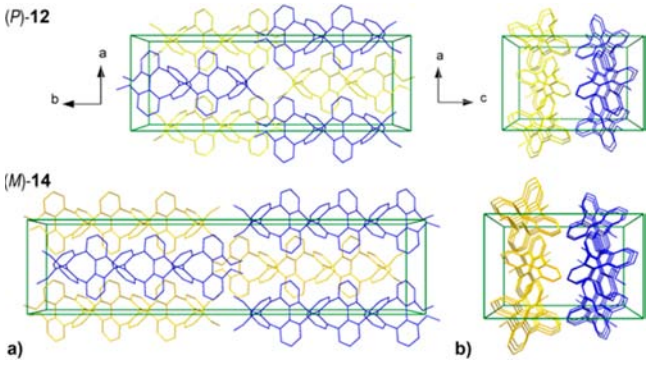


Figure 3. Crystal packing of oligophenylenes (*P*)-**12** and (*M*)-**14**: (a) perspective views of the crystal packing of (*P*)-**12** and (*M*)-**14** along the *c* axis; (b) perspective views of the crystal packing of (*P*)-**12** and (*M*)-**14** along the *b* axis.

14 along the *b* axis, oligophenylenes (*M*)-**14** are packed to form a molecular layer parallel to the *ab* plane. Such layers are interrelated to each other by another twofold axis perpendicular to the *b* axis. Oligophenylene (*P*)-**12** is packed in a similar fashion as (*M*)-**14**.

Studies of this [8−12]helicene family of oligophenylenes (**12**, **13**, and **14**) with eight, 10, and 12 phenyl rings suggested that their chiroptical properties appeared to increase with the helix length.[3,13] Moreover, the large optical rotation values and absolute stereochemistries of these homochiral series of carbohelicenes[13] encouraged us to investigate the structure−property relationships of these helical polyarylenes. Circular dichroism (CD) spectroscopy was performed to give further insight into the stereochemical properties of these molecules. The CD spectra of optically pure **12**, **13**, and **14** showed that their absorption intensities were proportional to the increase in their molecular lengths. The symmetry of the CD spectra demonstrated the chirality of both enantiomers (Figure 4; the

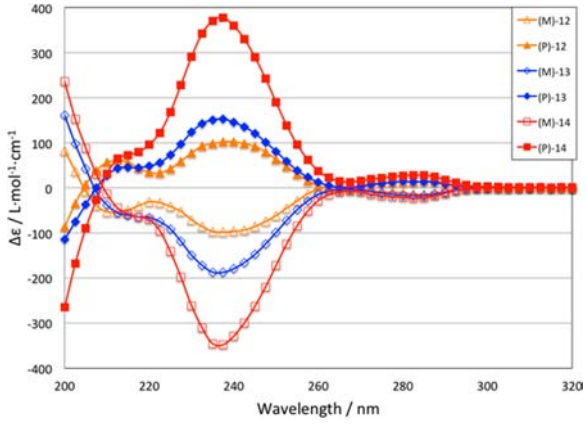


Figure 4. CD spectra of (*M*)- and (*P*)-oligophenylenes **12**, **13**, and **14** in acetonitrile at concentrations of 1.0×10^{-5} M.

relevant UV−vis spectral data of oligophenylenes **12**, **13**, and **14** can be found in Figure S1 in the SI). Next, preliminary studies on the chiroptical properties of oligophenylenes **12**, **13**, and **14** were performed. Interestingly, the average absolute value of the specific rotation ($[\alpha]_D$) was found to increase in a linear manner as the molecular length increased (Figure 5).

In summary, the palladium-catalyzed double Suzuki cross-coupling reaction was discovered to be an efficient method for

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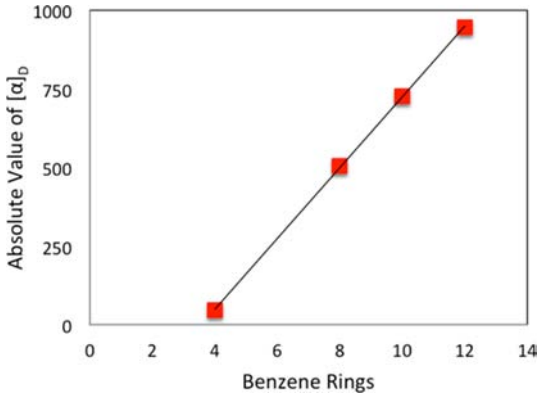

Figure 5. Average absolute values of the specific rotation of 1,8,9,16-tetramethoxytetraphenylene[9b] and oligophenylenes (*M*)- and (*P*)-**12**, **13**, and **14** (CH_2Cl_2, c = 0.10).

the syntheses of tetraphenylenes and trimers of biphenyls. By means of both the oxidative cross-coupling reaction and the Suzuki cross-coupling reaction, optically pure oligophenylenes with 6−12 phenyl rings were successfully synthesized. Three oligophenylenes with six, eight, and 12 phenyl rings were characterized unambiguously by X-ray structural analyses. More importantly, space-filling models based on X-ray crystallographic data suggest the double-helical structures of oligophenylenes. Interestingly, preliminary property studies concerning the oligophenylenes found that the value of the specific rotation is linearly dependent on the molecular length. Further investigations of these molecules are still in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02102.

Experimental procedures and full spectroscopic data for all new compounds (PDF)

Crystallographic data in CIF format for (*S*,*S*)-**5**, (*P*)-**12**, (*M*)-**14**, and (*M*)-**19** (ZIP)

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Notes

The authors declare no competing financial interest.

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