Chiral Tetraphenylenes

DOI: 10.1002/anie.200905421

Asymmetric Synthesis of Chiral Tetraphenylenes**

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asymmetric synthesis · chirality · cycloaddition · racemization · tetraphenylenes

Dedicated to Professor Laren M. Tolbert on the occasion of his 60th birthday

Tetraphenylene is a π-conjugated molecule in which four benzene rings are *ortho*-annelated to form an eight-membered ring at the center of the molecule.[1] In this rigid molecule, the four biaryl moieties have aryl–aryl torsional angles fixed at about 60–70°.[2] The twisted biaryl moieties are associated with four chiral axes with the *R*/*S* pairs related by mirror planes.[3] Therefore, tetraphenylene is an achiral molecule (Figure 1).

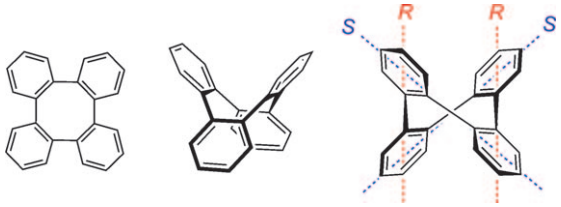

Figure 1. Tetraphenylene. Chiral axes designated with *R* and *S*.

The rigid, annelated tetraphenylene structure adopts a saddle-shaped, three-dimensional (3D) geometry. Substitution or additional annelation may break the D_{2d} symmetry of the parent tetraphenylene to provide chiral π-conjugated systems with D_2, C_2, or C_1 symmetry. In spite of the large aryl–aryl torsional angles, chiral tetraphenylenes possess significant π conjugation, as indicated by their chiroptical properties.[3,4] More importantly, these molecules with chiral π-conjugated systems have extraordinary high barriers for racemization (Figure 2)[3,5,6] compared to those of [*n*]helicenes or typical hindered biaryls such as BINOL (1,1′-binaphthalene-2,2′-diol).[7,8]

Owing to the unique structure and chiral properties of tetraphenylenes, a wide range of potential applications may be expected. Such robust chiral π systems with well-defined 3D geometries are excellent building blocks for chiral materials. Meanwhile the biaryl moieties in tetraphenylenes provide intriguing possibilities for the design of novel ligands

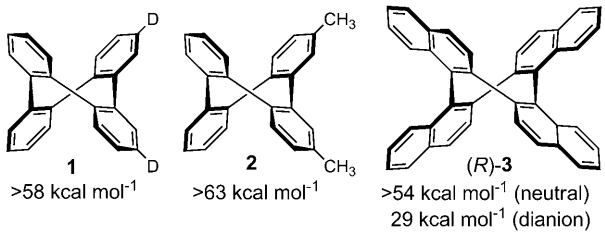

Figure 2. Chiral tetraphenylenes: barriers for racemization.

for asymmetric synthesis. Examples of tetraphenylenes include the chiral rod **4**,[9] planarized tetraphenylene **5** (a fragment of a two-dimensional graphene-like carbon sheet and building block for helical stacks of carbotetranions),[10] the conjugated double helix **6** (a fragment of a Riley's "three-dimensional graphite"),[11,12] and ligand **7** which is used for enantioselective hydrogenation (Figure 3).[9] However, applications of tetraphenylenes are rather limited, primarily because of the difficulty in obtaining the chiral tetraphenylene core, especially by asymmetric synthesis or by resolution.

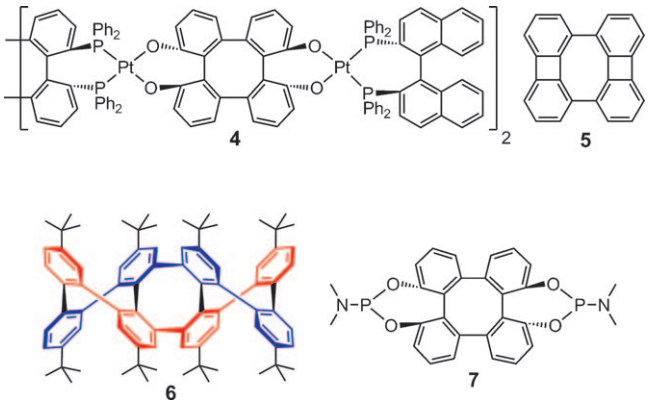

Figure 3. Chiral tetraphenylenes and "planarized" tetraphenylene.

Tetraphenylenes can be prepared by either oxidative coupling of 2,2′-dimetallobiphenyls or by Diels–Alder cycloaddition of furan to the strained alkyne moieties in 1,2,5,6-dibenzocycloocta-3,7-diyne, followed by reductive aromatization.[13,14] Enantiomerically pure tetraphenylenes are effectively obtained by classical resolutions, as implemented for **7** and building blocks of **4**.[6,9] When configurationally stable, enantiomerically enriched biaryls are available, enantiomer-

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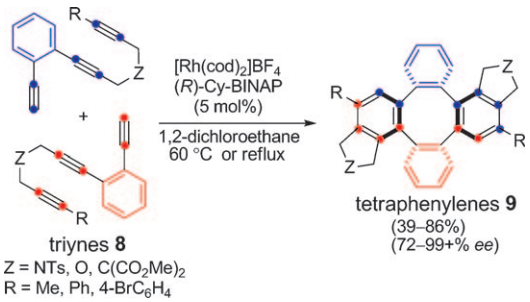
[**] We thank the U.S. National Science Foundation for support of this work through grant CHE-0718117.

ically pure tetraphenylenes can be obtained by oxidative coupling with asymmetric amplification, such as for (*R*)-**3**.[3] In the case of configurationally fluxional biaryls, asymmetric synthesis by oxidative homocoupling of 2,2′-dilithiobiaryls in the presence of (−)-sparteine provides tetraphenylenes in good yields and moderate enantioselectivities.[4,15] Racemic and achiral tetraphenylenes are also efficiently prepared by the metal-mediated and metal-catalyzed C–C bond cleavage of biphenylenes or by pyrolysis of oligophenylenes.[16]

Recently, Shibata and co-workers reported an asymmetric synthesis of tetraphenylenes **9** that relies on the cationic-rhodium-catalyzed [2+2+2] cycloadditions of triyne **8**, forming two benzene rings and the central cyclooctatetraene ring in one procedure (Scheme 1).[17] This approach proceeds in

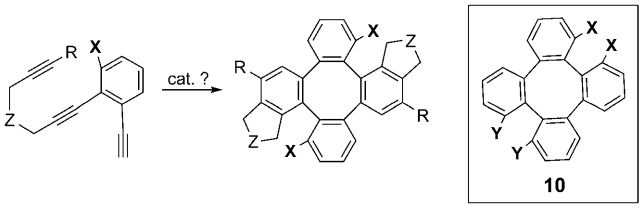


Scheme 1. Asymmetric synthesis of chiral tetraphenylenes. cod = 1,5-cyclooctadiene, Cy-BINAP = 2,2′-bis(dicyclohexylphosphino)-1,1′-binaphthyl.

good yield and high enantioselectivity for triynes with the tethers Z = NTs, O, $C(CO_2Me)_2$, and with R = alkyl (Me) and aryl (Ph and 4-BrC_6H_4). The highest reported enantioselectivity of >99% *ee* is attained for the triyne with Z = O and R = 4-BrC_6H_4. However, the absolute configurations of the product tetraphenylenes **9** are still not firmly established.

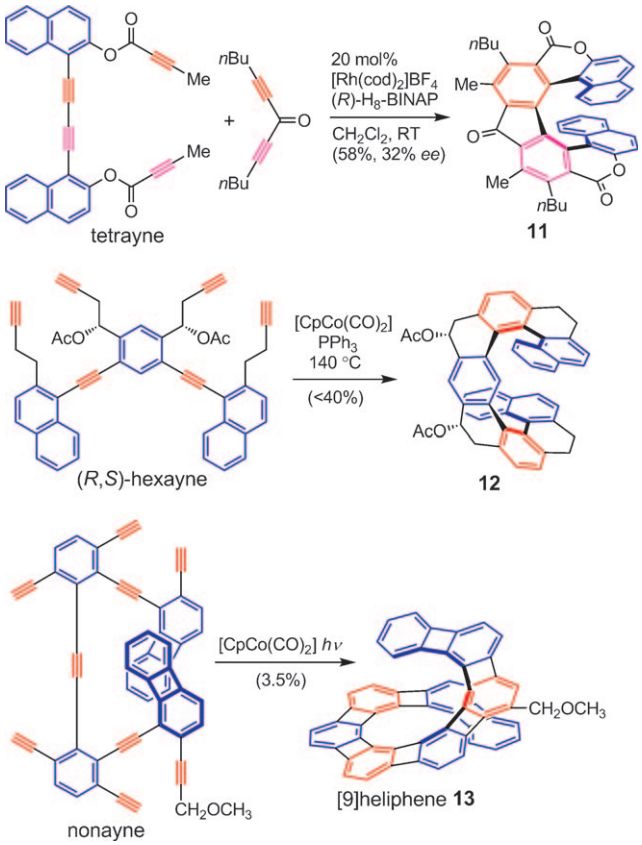
Syntheses of **9** rely on the covalent tethering of two alkynes to provide control of the chemoselectivity during the initial metallacycle formation, similar to the typical [2+2+2] cycloadditions of alkynes that form substituted arenes.[18] The presence of a terminal alkyne in **8** is essential for the intermolecular insertion of the third alkyne into the metallacycle to provide an arene with tethered alkynes. (An intramolecular insertion would give substituted biphenylene.) The subsequent formation of the metallacycle from the other unit of **8** and intramolecular insertion of alkyne provides the second arene and the central cyclooctatetraene ring. The formation of cyclooctatetraene ring is controlled by connectivity of starting triynes **8** and not a result of a [2+2+2+2] cycloaddition.[19] A series of chiral phosphine ligand motifs were screened, and the chiral tetraphenylenes **9** could be obtained in good yields with excellent enantioselectivities. This remarkable asymmetric synthesis could pave the way to a wide range of potential applications of chiral tetraphenylenes.

The use of tetraphenylenes as scaffolds for bidentate ligands in catalysis or as building blocks for chiral materials requires that at least one or preferably two biaryl linkages are *ortho*-disubstituted (Figure 3). Tetraphenylenes **9** are relatively unencumbered; that is, among the four biaryl moieties, only two of them are *ortho*-monosubstituted. (*ortho*-Substitution of the other two biaryl moieties is precluded by the requirement of terminal alkyne in triyne **8**.). As the cationic-rhodium-catalyzed double [2+2+2] cycloaddition was recently applied in the asymmetric synthesis of tetra-*ortho*-substituted biaryls,[20] it would be interesting to see whether analogous cycloadditions are applicable for the more challenging synthesis of *ortho*-substituted tetraphenylenes such as **10** (Scheme 2).



Scheme 2. *ortho*-Disubstituted tetraphenylenes **10**.

Shibata's approach to the synthesis of tetraphenylenes is one of many examples of efficient metal-catalyzed [2+2+2] cycloadditions of oligoalkynes or related compounds to provide chiral polycyclic aromatic compounds. Tanaka and co-workers employed analogous cationic-Rh^I-catalyzed intermolecular double [2+2+2] cycloadditions in the asymmetric synthesis of [9]helicene-like molecules, such as **11** with moderate enantioselectivities (Scheme 3).[21] Stará and co-



Scheme 3. Double and triple [2+2+2] cycloadditions in synthesis of chiral polycyclic aromatic compounds. Cp = cyclopentadienyl.

workers prepared the racemic, [10]helicene-like molecule **12** by the intramolecular $[CpCo(CO)_2]/PPh_3$-catalyzed double [2+2+2] cycloadditions of *meso*-hexayne. Subsequent aromatization of this product gives conjugated molecule with ten *ortho*-annelated aromatic rings.[22]

In this context, perhaps the most remarkable are Vollhardt's syntheses of the fluxional "[*n*]heliphenes", π-conjugated helical molecules with *n* benzene rings and *n*−1 cyclobutadiene rings fused in an alternating fashion ($n \leq 9$).[23] For example, the reaction of $[CpCo(CO)_2]$ with the nonayne precursor results in the formation of nine rings to produce [9]heliphene **13**. Of those nine rings, six are cyclobutadienes, and therefore the estimated ring strain introduced in the triple [2+2+2] cycloaddition step is about 300 kcal mol^{-1}.[23b]

In summary, the proven capability of the metal-catalyzed reactions of oligoalkynes and related compounds to form multiple rings, in particular those in highly strained fused π systems, suggests that similarly efficient asymmetric syntheses may be developed for relatively strained, chiral tetraphenylenes. The search for an effective catalytic system may be rewarded with highly functionalized chiral tetraphenylenes, with robust chiral π systems and rigid biaryl moieties, well suited for applications in chiral materials and as ligands for asymmetric catalysis.

Received: September 28, 2009
Published online: December 22, 2009

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