

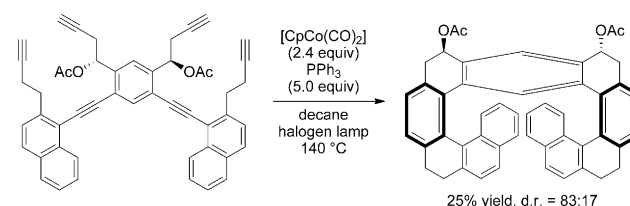
Enantioselective Synthesis of [9]- and [11]Helicene-like Molecules: Double Intramolecular [2+2+2] Cycloaddition**

Yuki Kimura, Naohiro Fukawa, Yuta Miyauchi, Keiichi Noguchi, and Ken Tanaka*

Abstract: The enantioselective synthesis of completely *ortho*-fused [9]- and [11]helicene-like molecules has been achieved through a rhodium-mediated, intramolecular, double [2+2+2] cycloaddition of phenol- or 2-naphthol-linked hexaynes. Crystal structures and photophysical properties of these [9]- and [11]helicene-like molecules have also been disclosed.

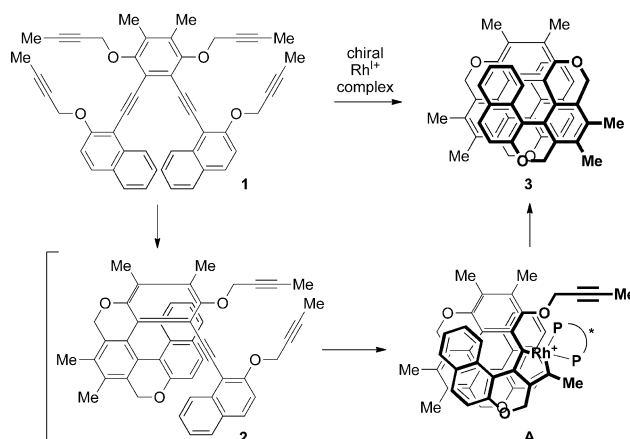
Higher-order helicenes and helicene-like molecules possess fascinating, long helical structures,^[1] however, their enantioselective synthesis is difficult because of steric hindrance.^[2] To date, the enantioselective synthesis of [9]helicenes and helicene-like molecules have been achieved.^[3–6] For example, the transition-metal-mediated enantioselective intramolecular [2+2+2] cycloadditions^[7] of triynes have been applied to the synthesis of [6]- and [7]helicene-like molecules.^[3,4] Stará, Starý, and co-workers pioneered this strategy in the cobalt- or nickel-catalyzed enantioselective intramolecular [2+2+2] cycloaddition, thus leading to [6]helicene-like molecules.^[3] Following this pioneering work, our research group accomplished the enantioselective synthesis of sterically more demanding [7]helicene-like molecules using the cationic rhodium(I)/chiral bis(phosphine) complex to catalyze the intramolecular [2+2+2] cycloaddition of 2-naphthol-linked triynes.^[4] Subsequently, the enantioselective synthesis of [7]- and [9]helicene-like molecules was achieved using the cationic rhodium(I)/chiral bis(phosphine) complex to catalyze a double intermolecular [2+2+2] cycloaddition between 2-

naphthol- or biaryl-linked tetraynes and 1,4-diynes.^[5] In 2009, Stará, Starý, and co-workers reported the cobalt-mediated diastereoselective intramolecular double [2+2+2] cycloaddition of a chiral homopropargyl alcohol-derived hexayne, thus leading to a [11]helicene-like molecule (Scheme 1).^[8] However, the molecule thus obtained is not the completely *ortho*-fused polycyclic compound and contains three sterically less demanding, *para*-fused central rings.



Scheme 1. Diastereoselective intramolecular double [2+2+2] cycloaddition of hexayne to produce a partially *para*-fused [11]helicene-like molecule. Cp = cyclopentadienyl.

To access a sterically more demanding, completely *ortho*-fused [11]helicene-like molecule^[9] starting from commercially available 2-naphthol, we designed an enantioselective rhodium-mediated, double intramolecular [2+2+2] cycloaddition of the 2-naphthol-linked hexayne **1**, thus leading to the [11]helicene-like molecule **3** (Scheme 2). The first cycloaddition of **1** proceeded smoothly to afford the [6]helicene-like molecule **2**. However, the second cycloaddition, leading to **3**, is troublesome because it proceeds through the sterically



Scheme 2. Enantioselective double intramolecular [2+2+2] cycloaddition of the hexayne **1** to produce the completely *ortho*-fused [11]helicene-like molecule (–)-**3**.

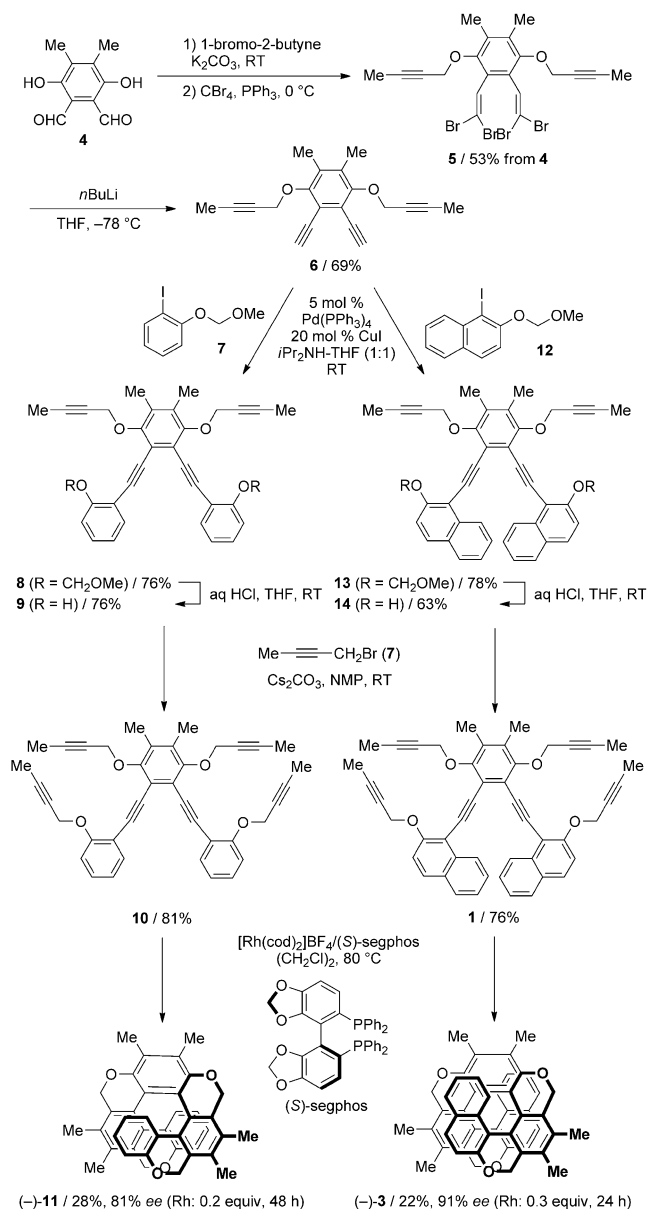
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demanding rhodacycle **A**, the bottom of which is covered completely by the naphthalene ring. Herein we disclose the enantioselective synthesis of completely *ortho*-fused [9]- and [11]helicene-like molecules by the rhodium-mediated, double intramolecular [2+2+2] cycloaddition of hexaynes.^[10]

To verify the feasibility of the above process, we first examined the enantioselective synthesis of the [9]helicene-like molecule **11** by the intramolecular [2+2+2] cycloaddition of the phenol-linked hexayne **10** using a cationic rhodium(I)/chiral bis(phosphine) complex (Scheme 3). The hexayne **10** was prepared starting from the known phthalaldehyde derivative **4**.^[11] Propargylation followed by the Corey–Fuchs reaction of **4** furnished the tetrabromide **5**. Treatment of **5** with *n*-butyllithium furnished the tetrayne **6**. The palladium-catalyzed Sonogashira cross-coupling of **6** with **7** afforded **8**.



Scheme 3. Enantioselective synthesis of [9]- and [11]helicene-like molecules (–)-**11** and (–)-**3**. cod = 1,5-cyclooctadiene, THF = tetrahydrofuran.

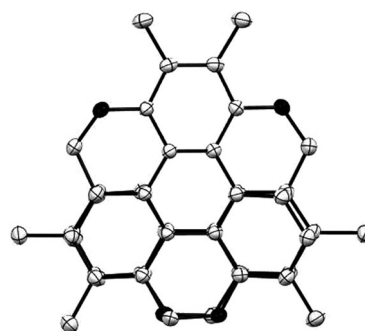


Figure 1. ORTEP diagram of the [9]helicene-like molecule (±)-**11** (top view) with ellipsoids at 30% probability. Hydrogen atoms are omitted for clarity.

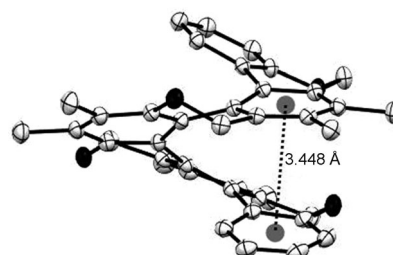


Figure 2. ORTEP diagram of (±)-**11** (side view) with ellipsoids at 30% probability. Hydrogen atoms are omitted for clarity.

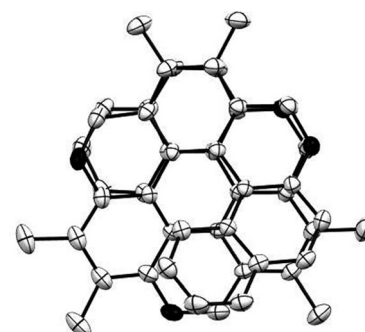


Figure 3. ORTEP diagram of the [11]helicene-like molecule (–)-**3** (top view) with ellipsoids at 30% probability. Hydrogen atoms are omitted for clarity.

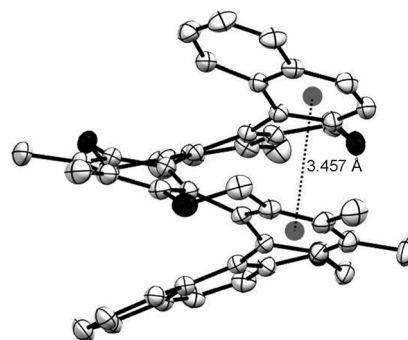


Figure 4. ORTEP diagram of (–)-**3** (side view) with ellipsoids at 30% probability. Hydrogen atoms are omitted for clarity.

Acid hydrolysis of the methoxymethyl (MOM) protecting group furnished the phenol derivative **9**, and propargylation of **9** afforded the hexayne **10**. With the desired **10** in hand, the rhodium-mediated enantioselective intramolecular [2+2+2] cycloaddition of **10** was examined. After screening the reaction conditions, it was found that the desired double cycloaddition proceeded at 80 °C using (*S*)-segphos as a chiral ligand to give the desired [9]helicene-like molecule (–)-**11** with a good *ee* value.

The successful enantioselective synthesis of (–)-**11** prompted our investigation into the enantioselective synthesis of the sterically more demanding **3** (Scheme 3). The Sonogashira cross-coupling of **6** with **12** furnished the tetrayne **13**. Acid hydrolysis of the MOM protecting group furnished naphthol-derivative **14** and propargylation of **14** afforded the hexayne **1**. Pleasingly, the use of the same rhodium complex at 80 °C afforded the desired [11]helicene-like molecule (–)-**3** with a higher *ee* value than that of (–)-**11**, although the product yield was lower than that of (–)-**11**.

The structures of these higher-order helicene-like molecules were unambiguously confirmed by X-ray crystallographic analyses of racemic (±)-**11** and enantiopure (–)-**3** (Figures 1–4).^[12] As shown in the top views (Figures 1 and 3), three and five rings are completely overlapped in (±)-**11** and (–)-**3**, respectively. As shown in the side views (Figures 2 and 4), similar distortions were observed for (±)-**11** and (–)-**3**. The distance between two overlapped benzene rings is 3.448 Å for (±)-**11**, and 3.457 Å for (–)-**3**, which are very close to each other.

Photophysical properties of the [9]- and [11]helicene-like molecules are shown in Table 1. The [11]helicene-like mole-

synthesis of novel higher-order helicenes and helicene-like molecules by the enantioselective aromatic ring construction.^[13]

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Table 1: Photophysical properties of [9]- and [11]helicene-like molecules.^[a]

Compound	Absorption $\lambda_{\max}$ [nm] ^[b]	Fluorescence $\lambda_{\max}$ [nm] ^[b,c]	$\phi_F^{[b,c]}$	$[\alpha]_D^{25[d]}$
(–)- 11	271, 370	470 (370)	0.101 (400)	1118
(–)- 3	300, 352	468 (350)	0.092 (380)	1228

[a] Measured in CHCl₃ at 25 °C. [b] 1.3×10^{-5} M. [c] Excitation wavelength [nm] in brackets. [d] Values are calculated as 100% *ee*.

cule (–)-**3** showed a red-shift of the first absorption maxima compared with that of the [9]helicene-like molecule (±)-**11**. In contrast, almost the same emission maxima were observed for (±)-**11** and (–)-**3**. With respect to fluorescence quantum yields in CHCl₃ solution, (±)-**11** showed slightly higher yield than (–)-**3**. Optical rotation values of these helicene-like molecules were also measured. Unexpectedly, the optical rotation value, which is calculated as 100% *ee*, of (–)-**3** was not significantly larger than that of (–)-**11**.

In conclusion, the enantioselective synthesis of completely *ortho*-fused [9]- and [11]helicene-like molecules has been achieved by the rhodium-mediated intramolecular double [2+2+2] cycloadditions of phenol- or 2-naphthol-linked hexaynes. Crystal structures and photophysical properties of these [9]- and [11]helicene-like molecules have also been studied. Future work will focus on the enantioselective

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