

Fully substituted cyclooctatetraenes assembled by the [4 + 4] cross coupling of two different diene units: a shunting strategy of Wilke's metallacyclopentadiene coupling mechanism†

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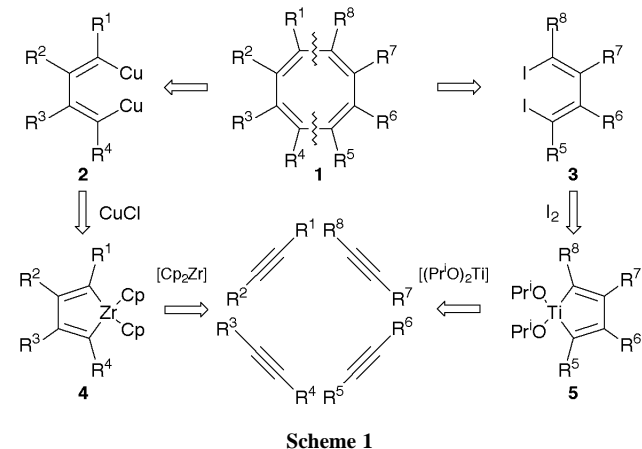
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The first regio- and chemo-selective synthesis of fully substituted cyclooctatetraenes from two or three different alkynes was achieved using the cross-coupling between 1,4-dicuprabuta-1,3-dienes and 1,4-diiodobuta-1,3-dienes.

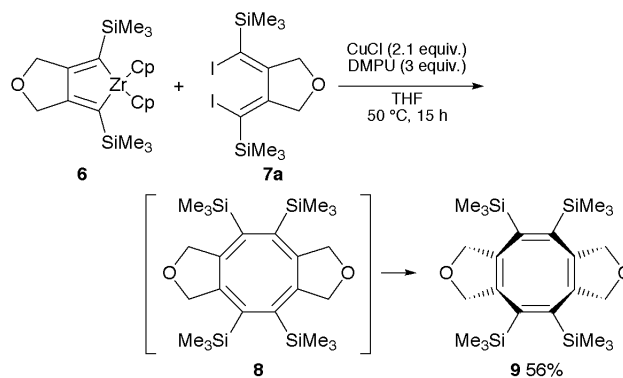
Since Reppe's historical discovery of his cyclooctatetraene (COT) synthesis from acetylene,¹ the nickel-catalyzed cyclo-tetramerization of alkynes leading to COTs has been extensively studied from both synthetic and mechanistic points of view.² The catalytic reactions, however, are generally limited to the parent and terminal acetylenes, and the reaction of monosubstituted alkynes gave the 1,2,4,6-, 1,2,4,7- and 1,3,5,7-substituted isomers depending on the alkyne employed rather than on the nature of the catalyst. Moreover, the concomitant formation of other oligomers and polymers of alkynes is also a problem for the catalytic methods.

Forty years after Reppe's discovery of the Ni-catalyzed COT synthesis,¹ Wilke proposed a fascinating mechanism: two nickelacyclopentadienes generated from four molecules of acetylene couple together to form COT.³ Based on this proposal, we postulated that highly substituted COTs **1** might be chemo- and regio-selectively synthesized if the selective coupling between two different independently prepared metallacyclopentadienes is possible. In order to realize such an idea, the cross-coupling of 1,4-dicuprabuta-1,3-dienes **2** with 1,4-diiodobuta-1,3-dienes **3** was investigated instead of the direct coupling of the parent metallacyclopentadiene counterparts **4** and **5** (Scheme 1).⁴ The vinylcopper reagents **2** can be prepared by the transmetalation of the corresponding zirconacyclopentadienes **4** as reported by Takahashi and coworkers.⁵ The bifunctional electrophile, diiodides **3**, can be readily obtained from the corresponding titanacyclopentadienes **5** and iodine according to the Tamao-Sato procedure.⁶

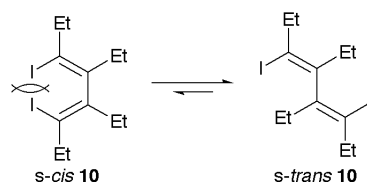
At the outset, we examined the coupling of an isolated bicyclic zirconacyclopentadiene **6** with a cyclic diiodide **7a**.



Interestingly, both diene units **6** and **7a** were prepared from a common precursor, 4-oxa-1,7-bis(trimethylsilyl)hepta-1,6-diyne. In the presence of 3 equiv. of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU), equimolar amounts of **6** and **7a** were treated with 2.1 equiv. of CuCl in THF at 50 °C for 15 h. The usual work-up followed by chromatographic separation gave a symmetrically substituted coupling product **9**⁸ in 56% yield (Scheme 2). Its structure was confirmed based on the following spectral data: in its ¹H NMR spectra, only one singlet of the four trimethylsilyl groups was observed at δ 0.27, indicative of **9** having a highly symmetrical structure. This was also supported by its ¹³C NMR spectra, in which only two sp² signals were observed at δ 116.3 and 143.3 together with a signal of the trimethylsilyl groups and a signal of the methylene carbon α to the ether oxygen at δ -0.6 and 70.1, respectively. Nonaromatic COT is known to exist in a tub shape rather than in a planar structure.⁹ This is also true for **9**; the expected **8** isomerized to the thermodynamically more favorable tub-shaped isomer **9**. This was deduced by the absorption of its methylene protons α to the ether oxygen being observed as a couple of doublets with a geminal coupling constant J = 16.5 Hz.



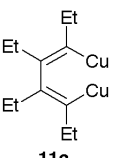
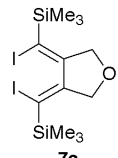
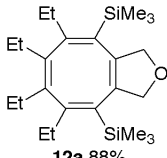
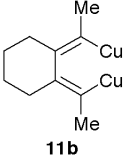
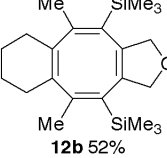
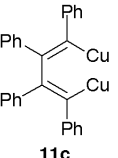
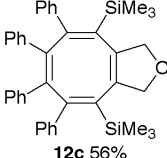
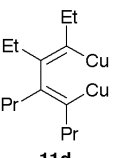
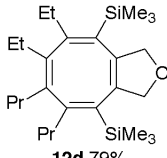
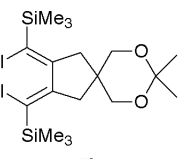
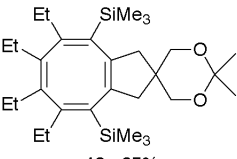
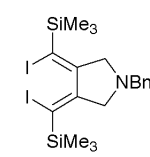
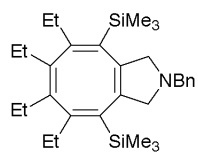
The cyclic structure of **7a** plays a critical role in the present coupling; an acyclic diiodide **10** gave no coupling product under the same reaction conditions. This is attributed to the conformational flexibility of its butadiene moiety. The diiodobutadiene moiety fixed as the *s-cis* form in **7a** is required for the cross coupling, whereas acyclic **10** may mainly exist in the *s-trans* form in order to avoid steric repulsion between the two iodine atoms (Scheme 3).



† Experimental and spectral data for **9** and **12a-f** are available from the RSC web site, see <http://www.rsc.org/suppdata/cc/1999/1543/>

Based on these results, we next examined the generality of this approach (Table 1). According to established methods,⁵ unstable zirconacycles¹⁰ were converted into the corresponding dicopper reagents **11a–d** without isolation. In the presence of DMPU, the diiodide **7a** was reacted with **11a**¹¹ at ambient

Table 1 Cross coupling of dicoppers **11a–d** with diiodides **7a–c**^a

Dicopper	Diiodide	Conditions	Product and yield ^b
		rt 1 h	 12a 88%
	7a	rt 1 h	 12b 52%
	7a	50 °C 1 h	 12c 56%
	7a	rt 1 h	 12d 79%
11a		50 °C 20 h	 12e 65%
11a		rt 20 h	 12f 41%

^a Zirconacyclopentadiene (1 mmol), **7** (0.5 mmol), CuCl (2.1 mmol), DMPU (3 mmol), THF (5 ml). ^b Isolated yields based on **7**.

temperature for 1 h to afford the desired coupling product **12a**⁸ in high yield (88%). In the same manner, a cyclic dicopper **11b** derived from deca-2,8-diyne gave a tricyclic product **12b**⁸ in 52% yield. In contrast, the coupling of a tetraphenyl-substituted dicopper **11c** required higher temperature. The reaction of **11c** with **7a** was carried out at 50 °C for 1 h to afford **12c**⁸ in 56% yield. Similarly, an unsymmetrical dicopper **11d**, prepared from hex-3-yne and oct-4-yne, gave the corresponding unsymmetrical COT **12d**⁸ in 79% yield. In addition to the furan derivative **7a**, a cyclopentane **7b** and a pyrrolidine **7c** can be used as the diiodide units. The reaction with dicopper **11a** gave **12e**⁸ and **12f**⁸ in 65 and 41% yields, respectively.

In conclusion, we successfully developed a novel strategy to assemble fully substituted COTs by imitating Wilke's coupling mechanism of two metallacyclopentadiene moieties for the prototype Ni-catalyzed COT synthesis. This approach allows us to synthesize fully substituted unsymmetrical COTs with complete chemo- and regio-selectivity from 1,4-dicuprabutane-1,3-dienes and 1,4-diiodobutane-1,3-dienes as different diene units.

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Notes and references

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- Although only 1 equiv. is required, 2 equiv. of **11** were used to ensure the complete consumption of **7**.

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