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Cycloaddition Reaction of Zirconacyclopentadienes to Quinones: Synthesis of Higher *para*-Quinones

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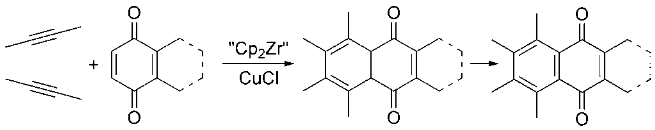
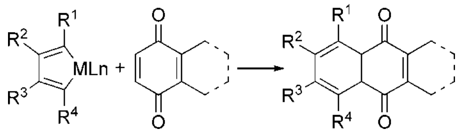
ABSTRACT



Efficient synthetic approaches to higher *para*-dihydroquinones and -quinones have been developed through zirconium/CuCl-mediated cycloaddition reactions of two alkynes and quinone in a one-pot procedure.

Higher *para*-quinone units are ubiquitous components that present a wide variety of substitution patterns in biological systems such as vitamin K_1 or K_3, adriamycin, and daunomycin and in functional materials such as organic photoconductors as well as in dyestuffs.[1−3] Consequently, there is significant interest in the development of new synthetic methodologies to access higher *para*-quinones. Although a number of synthetic methods affording higher *para*-quinones have been reported,[4,5] the most attractive one seems to be the direct cycloaddition reaction of metallacyclopentadienes to quinones. However, there is no precedent for the cycloaddition reaction of metallacyclopentadienes to quinones to form higher *para*-dihydroquinones (Scheme 1), to the best of our knowledge.

Scheme 1



Metallacyclopentadienes are easily prepared by the reaction of low-valent transition metals with alkynes. In this regard, zirconacyclopentadienes, which can be easily prepared by reductive coupling of two alkynes on a zirconocene(II) species[6] and can participate in a number of organic

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(1) (a) Itoh, T. *Chem. Rev.* **1995**, *95*, 2351. (b) Barone, A. D.; Atkinson, R. F.; Wharry, D. L.; Koch, T. H. *J. Am. Chem. Soc.* **1981**, *103*, 1606. (c) Taatjes, D. J.; Gaudiano, G.; Resing, K.; Koch, T. H. *J. Med. Chem.* **1996**, *39*, 4135. (d) Taatjes, D. J.; Gaudiano, G.; Resing, K.; Koch, T. H. *J. Med. Chem.* **1997**, *40*, 1276. (e) Huo, S.; Negishi, E. *Org. Lett.* **2001**, *3*, 3253. (f) Malerich, J. P.; Trauner, D. *J. Am. Chem. Soc.* **2003**, *125*, 9554.

(2) (a) Miki, S.; Yoshida, Z. *Tetrahedron* **1992**, *48*, 1567. (b) Miki, S.; Shimizu, H.; Nakatsuji, H. *Tetrahedron Lett.* **1992**, *33*, 953. (c) Itoh, T.; Katsuolis, D. E.; Mita, I. *J. Mater. Chem.* **1993**, *3*, 1303. (d) Miki, S.; Ito, J.; Noda, R.; Nishijima, N.; Fukunishi, K. *Tetrahedron* **1996**, *52*, 4264. (e) Anthony, J. E.; Eaton, D. L.; Parkin, S. R. *Org. Lett.* **2002**, *4*, 15. (f) Maliakal, A.; Raghavachari, K.; Katz, H.; Chandross, E.; Siegrist, T. *Chem. Mater*. **2004**, *16*, 4980. (g) Payne, M. M.; Odom, S. A.; Parkin, S. R.; Anthony, J. E. *Org. Lett.* **2004**, *6*, 3325. (h) Payne, M. M.; Parkin, S. R.; Anthony, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 8028. (i) Yamaji, M.; Takehira, K.; Itoh, T.; Shizuka, H.; Tobita, S. *Phys. Chem. Chem. Phys.* **2001**, *3*, 5470. (j) Hwang, D. K.; Kim, K.; Kim, J. H.; Im, S.; Jung, D.-Y.; Kim, E. *Appl. Phys. Lett.* **2004**, *85*, 5568.

(3) (a) Morton, R. A. *Biochemistry of Quinones*; Academic Press: New York, 1965. (b) Thomson, R. H. In *Naturally Occurring Quinones*; Academic Press: New York, 1971; p 458. (c) Gadgil, D. D.; Rama Rao, A. V.; Venkataraman, K. *Tetrahedron Lett.* **1968**, *18*, 2223.

(4) (a) Patney, H. K. *J. Org. Chem.* **1988**, *53*, 6106. (b) Bessière, Y.; Vogel, P. *Helv. Chim. Acta* **1980**, *63*, 232. (c) Lepage, L.; Lepage, Y. *Synthesis* **1982**, 882. (d) Christopfel, W. C.; Miller, L. L. *J. Org. Chem.* **1986**, *51*, 4169. (e) Almlof, J. E.; Feyereisen, M. W.; Jozefiak, T. H.; Miller, L. L. *J. Am. Chem. Soc.* **1990**, *112*, 1206. (f) Bingham, S. J.; Tyman, J. H. P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3637. (g) Roberge, G.; Brassard, P. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1041. (h) Cameron, D. W.; Deutscher, D. J.; Feutrill, G. I.; Griffiths, *Aust. J. Chem.* **1981**, *34*, 2401. (i) Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 5, Chapter 4.1.

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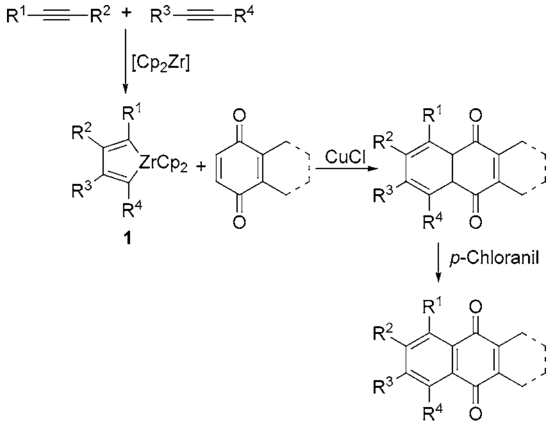
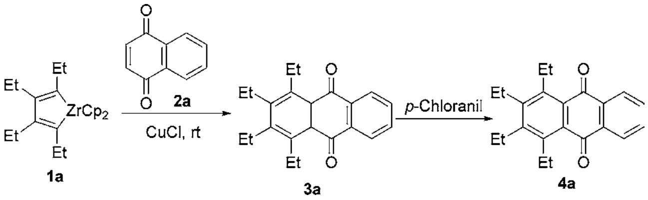
reactions,[7] are especially attractive. Recently, transmetalation of zirconacyclopentadienes onto Cu[8] and Ni[9] has opened new avenues in carbon−carbon bond coupling chemistry. Herein, we would like to report the reaction of zirconacyclopentadienes with quinones in the presence of copper chloride and *p*-chloranil. This reaction provides a novel preparative method for the preparation of higher *para*-dihydroquinones and -quinones (Scheme 2).

Scheme 2



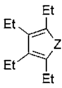
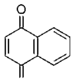
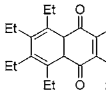
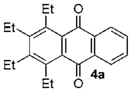
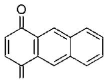
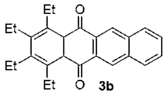
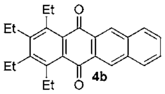
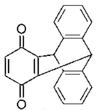
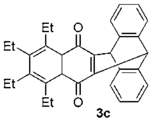
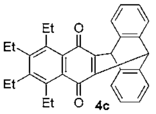
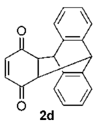
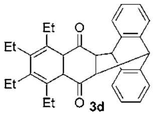
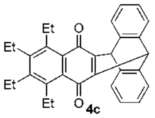
Typically, zirconacyclopentadiene **1a** (1 mmol), prepared from 3-hexyne and zirconcene according to the literature,[6a,b] reacts with 1,4-naphthoquinone **2a** in the presence of 2 equiv of CuCl to afford dihydro-9,10-anthraquinone derivative **3a** in 83% yield (Scheme 3). It is well-known that dihydroquinones could be converted into quinones by treatment with *p*-chloranil or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Therefore, when the reaction mixture was treated with 1 equiv of *p*-chloranil before workup, only the product the 9,10-anthraquinone derivative **4a** was obtained in 79% yield.

Scheme 3



To investigate the scope of the reaction, other quinone derivatives were used. For example, reaction of **1a** with 1,4-anthraquinone **2b**[10] at room temperature in the presence of CuCl gave **3b** or **4b**. Similarly, reaction of **1a** with compound **2c**[11] also gave the desired product in good yield. It is worth noting that in this reaction dihydroquinone **3c** was not obtained and that product **4c** was obtained directly without addition of *p*-chloranil. In this case, 2 equiv of **2c** was necessary to achieve a high yield of the product **4c**. Moreover, reaction of zirconacyclopentadiene **1a** with dihydroquinone **2d**[12] also gave cycloaddition product **3d** in 78% yield or **4d** in 67% yield. The results are summarized in Table 1.

Table 1. Reaction of Zirconacyclopentadiene with Quinone Derivatives

zirconacyclopentadiene	quinones	dihydroquinones	yield(%)[a]	higher quinones	yield(%)[a]
 1a	 2a	 3a	83	 4a	79
1a	 2b	 3b	75	 4b	65
1a	 2c	 3c	0	 4c	69
1a	 2d	 3d	78	 4c	67

[a] Isolated yield.

We recently reported that treatment of zirconacyclopentadienes with 1,4-benzoquinone in the presence of CuCl gave cyclooctatetraene (COT) derivatives.[13a] No incorporation of benzoquinone species was observed in the product. Nevertheless, when compounds **2a**−**2d** were used, higher *para*-

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(5) (a) Wulff, W. D.; Tang, P.-C.; McCallum, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 7677. (b) Müller, E.; Scheller, A.; Winter, W.; Wagner, F.; Meier, H. *Chem.-Ztg.* **1975**, *99*, 155. (c) Hillard, R. L., III; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, *99*, 4058. (d) McDonald, F. E.; Zhu, H. Y. H.; Holmquist, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 6605. (e) Yamamoto, Y.; Hata, K.; Arakawa, T.; Itoh, K. *Chem. Commun.* **2003**, 1290.

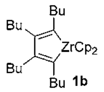
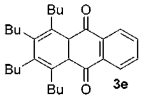
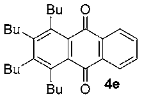
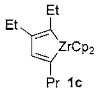
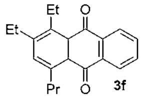
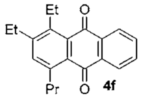
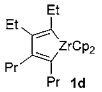
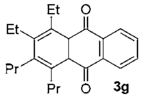
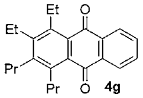
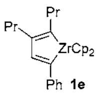
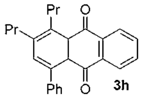
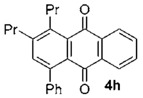
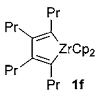
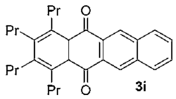
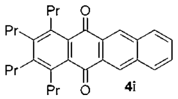
(6) (a) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. (b) Negishi, E.; Holms, S. J.; Your, J.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336. (c) Xi, Z.; Hara, R.; Takahashi, T. *J. Org. Chem.* **1995**, *60*, 4444. (d) Takahashi, T.; Xi, Z.; Rousset, C. J.; Suzuki, N. *Chem. Lett.* **1993**, 1001. (e) Alt, H.; Rausch, M. D. *J. Am. Chem. Soc.* **1974**, *96*, 5936. (f) Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *111*, 2870. (g) Takahashi, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* **1987**, 623. (h) Wagene, B. C. V.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 3495.

(7) Leading references: (a) Takahashi, T.; Li, Y. In *Titanium and Zirconium in Organic Synthesis*, Marek, I. Ed. Wiley-VCH Verlag GmbH & Co. KgaA: 2003; Chapter 2. (b) Negishi, E. In *Organometallics in Synthesis*, 2nd ed.; Schlosser, M., Ed.; Wiley: New York, 2002; Chapter 8. (c) Majoral, J.-P.; Igau, A.; Cadierno, V.; Zablocka, M. *Top. Curr. Chem.* **2002**, *220*, 53. (d) Takahashi, T.; Kotora, M.; Hara, R.; Xi, Z. F. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2591. (e) Negishi, E.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 755. (f) Majoral, J.-P.; Igau, A. *Coord. Chem. Rev.* **1998**, *176*, 1. (g) Majoral, J. P.; Meunier, P.; Igau, A.; Pirio, N.; Zablocka, M.; Skowronska, A.; Bredeau, S. *Coord. Chem. Rev.* **1998**, *178* (part 1), 145. (h) Avarvari, N.; Rosa, P.; Mathey, F.; Le Floch, P. *J. Organomet. Chem.* **1998**, *567*, 151. (i) Whitby, R. J. *Transition Met. Org. Synth.* **1997**, 133. (j) Fillery, S. F.; Gordon, G. J.; Luker, T.; Whitby, R. J. *Pure Appl. Chem.* **1997**, *69*, 633. (k) Ohff, A.; Pulst, S.; Lefeber, C.; Peulecke, N.; Arndt, P.; Burkalov, V. V.; Rosenthal, U. *Synlett* **1996**, 111. (l) Broene, R. D.; Buchwald, S. L. *Science* **1993**, *261*, 1696.

dihydroquinones or -quinones were formed in this work. These results may be attributed to different electrochemical potentials of various quinones ($E° = -0.43$ V vs VCE for 1,4-benzoquinone; $E° = -0.61$ V vs VCE for 1,4-naphthoquinone; $E° = -0.66$ V vs VCE for 1,4-anthraquinone).[14]

Further study involving the use of symmetrically and unsymmetrically substituted zirconacyclopentadienes bearing alkyl and aryl groups resulted in all cases in the formation of higher *para*-dihydroquinones and -quinones in high yields.

Table 2. Reaction of Zirconacyclopentadienes with Quinones

zirconacyclopentadiene	quinones	dihydroquinones	yield(%)[a]	quinones	yield(%)[a]
 **1b**	**2a**	 **3e**	81	 **4e**	-
 **1c**	**2a**	 **3f**	84	 **4f**	66
 **1d**	**2a**	 **3g**	85	 **4g**	-
 **1e**	**2a**	 **3h**	-	 **4h**	72
 **1f**	**2b**	 **3i**	86	 **4i**	85

[a] Isolated yield.

The results are summarized in Table 2. It is worth noting that reactions of zirconaindenes with 1,4-naphthoquinone in the presence of CuCl produced benzocyclobutadienes.[13b] No incorporation of 1,4-naphthoquinone species was observed in the products. This result may be attributed to a proper tuning of the reactivity of zirconaindenes and 1,4-naphthoquinone.

The cycloaddition reaction similarly proceeded under optimal conditions for bicyclic zirconacyclopentadiene **1g** prepared from diynes.[6a,b] It is worth noting that, in this case, **1g** could react with substituted l-1,4-benzoquinone **2e** or **2f** to afford product **4m** or **4n**, whereas monocyclic zirconacyclopentadienes did not react with **2e** to give the desired product. The results are listed in Table 3.

Table 3. Reaction of Bicyclic Zirconacyclopentadiene with Quinone Derivatives

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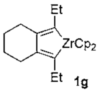
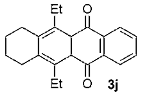
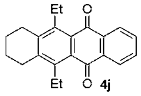
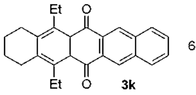
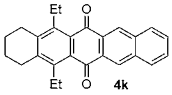
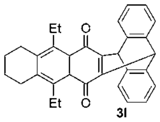
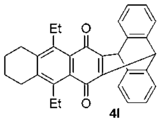
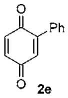
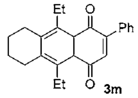
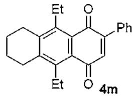
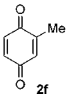
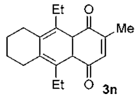
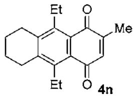
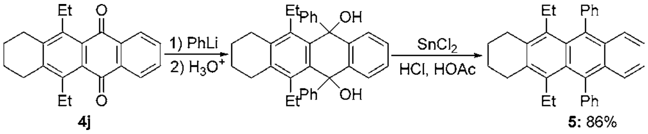
 **1g**	**2a**	 **3j**	67	 **4j**	73
1g	**2b**	 **3k**	63	 **4k**	90
1g	**2c**	 **3l**	-	 **4l**	65
1g	 **2e**	 **3m**	-	 **4m**	63
1g	 **2f**	 **3n**	-	 **4n**	58

[a] Isolated yield.

Recently, polyacenequinones have received much attention for the preparation of functionalized higher acenes.[15] We reacted 9,10-anthraquinone derivative **4j** with phenyllithium, followed by treatment with $SnCl_2$, to afford product **5** with yellow color in high yield (Scheme 4). The preliminary results demonstrated that this reaction presented a novel method for the preparation of polyphenylenes. Further applications of these higher quinones including the study of their optoelectronic material properties are in progress.

Scheme 4



4j **5**: 86%

On the basis of the above-mentioned results, a possible mechanism is shown in Scheme 5. First, the zirconacyclopentadiene **1** undergoes transmetalation with CuCl to form

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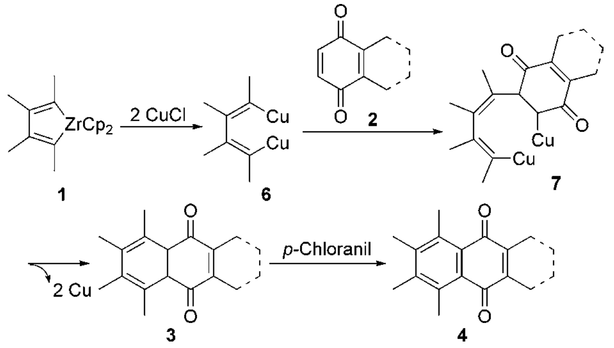
Scheme 5



the diorganocopper intermediate **6**. Michael addition of **6** to quinone forms intermediate **7**.[16] A ring-closure coupling reaction of alkenylcopper and alkylcopper moieties of **7** gives **3**.[8c,i,17] When compound **3** was treated with *p*-chloranil, the higher *para*-quinone was obtained.

In summary, the cycloaddition reaction of zirconacyclopentadienes to various quinones has been achieved. This reaction led to a novel method for the formation of higher *para*-dihydroquinones and -quinones by one-pot intermolecular cyclization of two alkynes and quinones. Further investigation of reactions and applications is now in progress.

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Supporting Information Available: Experimental procedures and full characterization including ^{1}H NMR and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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